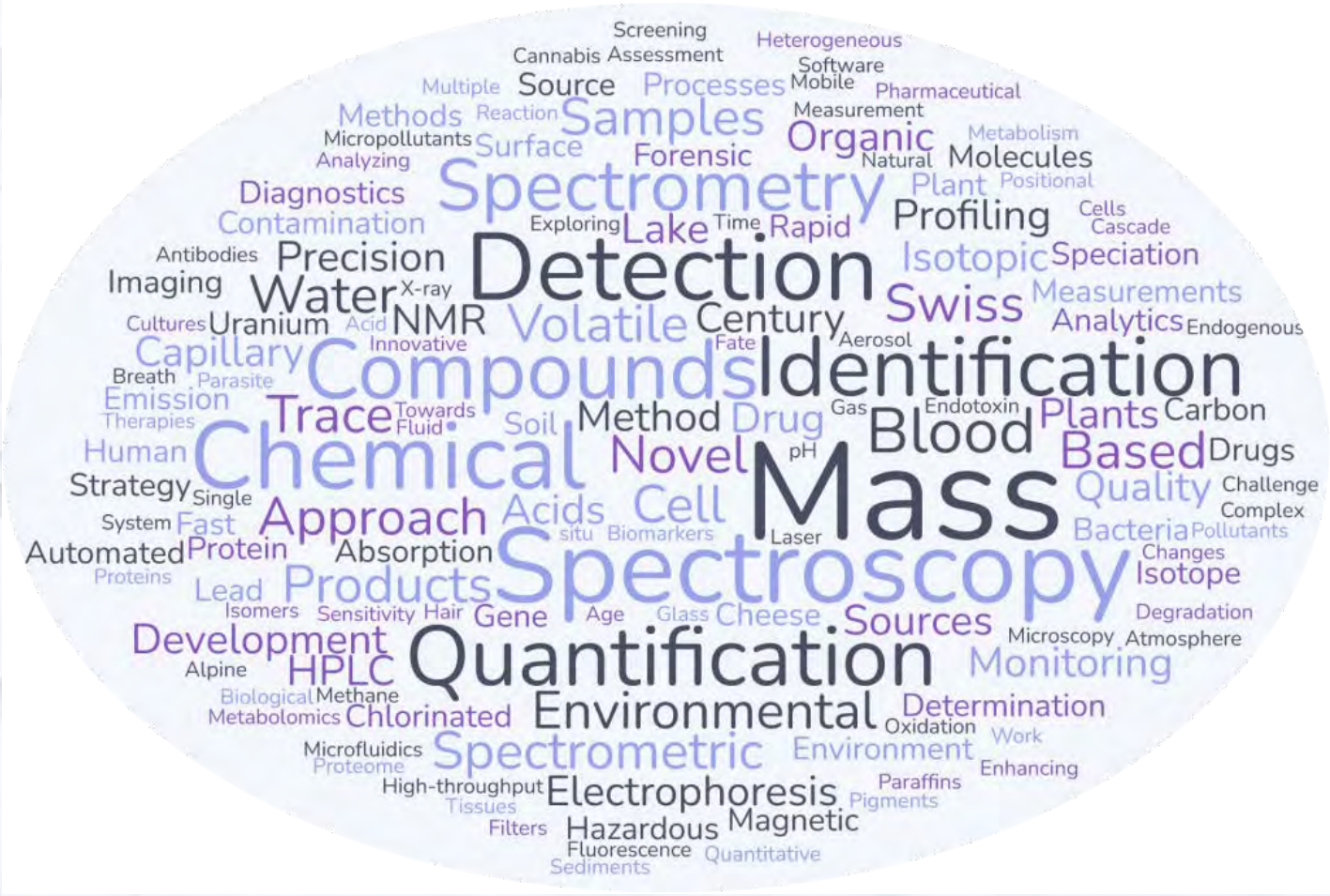
CHIMIA.ch CHIMIA.ch/e-version

CHIMIA

Highlights of Analytical Sciences in Switzerland

Columns edited by Veronika Meyer 2005 - 2025



SCS
Swiss Chemical Society

A Tribute to Veronika Meyer

The CHIMIA column ‘Highlights of Analytical Sciences in Switzerland’ is one of the oldest and most consistently published columns to appear in CHIMIA. The columns are an undeniable success story, showcasing the excellent research that has been and is carried out in Switzerland in the field of analytical sciences.
This is all entirely thanks to Veronika Meyer, who initiated the column (then called Highlights of Analytical Chemistry in Switzerland) in 2005 and who served as its editor for the past 20 years. As a passionate, recognized analytical chemist (honoured as IUPACs Distinguished Woman in Chemistry in 2017), author of a highly successful book ‘Practical High-Performance Liquid Chromatography’, and mountaineer (climbing Qomolangma), she has always sought new heights. She was able to identify and select important reports on cutting-edge research in the analytical sciences in Switzerland.
She convinced authors to prepare a strict one-page roundup for readers of CHIMIA. These reports not only had an impact in dissemination of the research, but also on the initiation of collaborations across different research groups and disciplines, which is perfectly illustrated by more than 200 citations they received. In total the columns she edited were authored by almost 700 scientists from Swiss institutions and international teams.
The columns span a broad range including fundamental research and the use of analytical methods applied in the laboratory and in the field, illustrated by the word map on the title page of this virtual issue. Almost every technique used in the routine analytical chemical lab and specialized research centres has been covered at least once. This topical breadth in particular highlights her openness to the field and advanced analytical view and interests.
Their overall quality also set the standard for the other Division-led columns in CHIMIA enabling the readers a view of current research across the chemistry disciplines in Switzerland.
As the editor of the Highlights, she has now met her target number of 200 contributions, the last of which was published in the issue 10/2025 of CHIMIA. This virtual edition collects all 200 columns published to date and also provides a snapshot of the many developments made in the analytical sciences in Switzerland over the past two decades.

The members of the CHIMIA Editorial Board past and present, the Swiss Chemical Society, and the members of the Board of the Division of Analytical Sciences of the Swiss Chemical Society express their deepest gratitude and acknowledge the enormous effort Veronika has put into this editorial work.

CHIMIA Editorial Board | Swiss Chemical Society | Board of the Division of Analytical Sciences

CHIMIA **2005**, *59*, No. 1/2

Highlights of Analytical Chemistry in Switzerland

Characterization of Polymers in Nanometer Sized Atmospheric Aerosol Particles

Markus Kalberer*, Mirjam Sax, and Vera Samburova
Department of Chemistry and Applied Biosciences, ETH Zürich, Zürich

**Correspondence:* Dr. Markus Kalberer, Laboratorium für Organische Chemie Wolfgang-Pauli-Str. 10, ETH Hönggerberg, HCI E 330, CH–8093 Zürich
Tel. +41 1 633 48 34, Fax +41 1 632 12 92, E-Mail: kalberer@org.chem.ethz.ch

Keywords: Aerosol particles · Aerosol precursors · Atmospheric chemistry · Smog chamber

Atmospheric aerosol particles of about 3 nm–10 μm diameter play a crucial role in many aspects of the earth's climate system. In recent years it also became evident that aerosol particles pose a public health problem, since studies showed that increased aerosol concentrations cause higher morbidity and mortality rates. The chemical composition of the particles is important in both climatological and health-related issues; however, it is only poorly understood. Atmospheric aerosols contain up to 50% organic material, but despite a large effort in the past decades not more than about 10–20% of the organic mass could be resolved on a molecular basis.

To identify and investigate their chemical composition organic aerosols were generated in a newly built smog chamber at the Paul Scherrer Institute (PSI) in Villigen, where organic particles can be generated under conditions similar to the ambient atmosphere. Due to the complex chemical mixture of compounds present in the aerosols a large variety of analytical techniques was used such as different mass spectrometric methods coupled with gas and liquid chromatography and infrared spectroscopy. The determination of the molecular weight distribution with Laser Desorption/Ionization Mass Spectrometry (LDI-MS) showed for the first time that up to 50% of the aerosol mass generated from anthropogenic and biogenic volatile organic precursors is composed of polymers with molecular masses up to about 900 Da. This result was a significant step towards a comprehensive knowledge of organic aerosol composition. Mass spectra of synthetic co-polymers formed from known oxidation products of important aerosol precursor compounds were compared with the smog chamber results and showed that a major fraction of the aerosol polymer can be explained by acetal polymerization of small carbonyls, which are abundant oxidation products of volatile organic compounds (VOCs).

A comparison with ambient aerosol samples collected at the ETH Zürich showed that the mass distribution of the polymeric fraction of the ambient samples closely matches the mass distribution of aerosols from biogenic VOC precursors. This result suggests that biogenic sources are a major contributor to the ambient organic aerosol mass even in urban areas.

The chemical characterization of these polymers is still at the very beginning and a large effort will be necessary to understand the influence of these compounds on health related issues and the climate.

Received: January 3, 2005

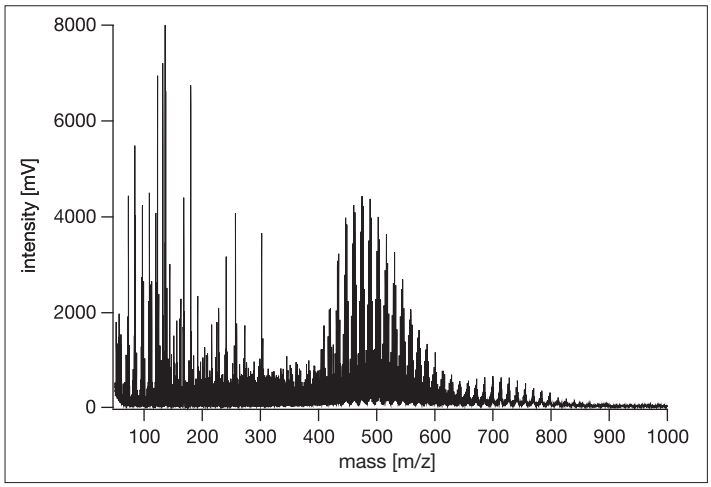
Acknowledgements

We thank R. Zenobi and U. Baltensperger together with the smog chamber crew for their support. This project was supported by the Swiss National Science Foundation.

Reference

M. Kalberer, D. Paulsen, M. Sax, M. Steinbacher, J. Dommen, A.S.H. Prevot, R. Fisseha, E. Weingartner, V. Frankevich, R. Zenobi, U. Baltensperger, *Science* **2004**, *303*, 1659.

27 m^3 large smog chamber at PSI



LDI-MS spectrum from a smog chamber aerosol sample (Kalberer *et al.*, **2004**)

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Tel.: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

CHIMIA **2005**, *59*, No. 4

Highlights of Analytical Chemistry in Switzerland

Investigations of Ancient Lead White Pigments Using Lead Isotope Abundance Ratios

Giuseppino Fortunato[a]*, Axel Ritter[a], and Daniel Fabian[b]
[a]EMPA St. Gallen; [b]Fabian & Samuels, Stäfa

*Correspondence: Dr. G. Fortunato, Functional Fibers and Textiles, EMPA St. Gallen, Lerchenfeldstr. 5, CH-9014 St. Gallen
Tel.: +41 71 274 76 77, Fax: +41 71 274 78 62, E-Mail: giuseppino.fortunato@empa.ch

Keywords: Arts · Lead isotope ratio · Lead white · Provenance

Lead white ($2\ PbCO_3 \cdot Pb(OH)_2$), a common component in 17th century artists' painting materials, was singled out to study the potential and limits of lead isotope abundance ratios in the field of origin assignment. Paintings by P.P. Rubens, A. van Dyck and other old masters were chosen for this study.

Natural lead consists of four isotopes, ^{204}Pb, ^{206}Pb, ^{207}Pb, and ^{208}Pb. The last three isotopes derive partly from the radioactive decay of the nuclides of uranium (^{238}U and ^{235}U) and thorium (^{232}Th). The isotopic compositions depend primarily on the age as well as on the U/Pb and Th/Pb amount content ratios of the rocks forming the ore deposits from which the lead was extracted. Historically, lead was among the first metals extracted from ores by man, and because it is abundant in nature and relatively inexpensive, lead is found on a great many archaeological sites. The principle of object provenancing is to make comparative isotopic analyses of the lead present in artifacts and in a sufficient number of ore deposits.

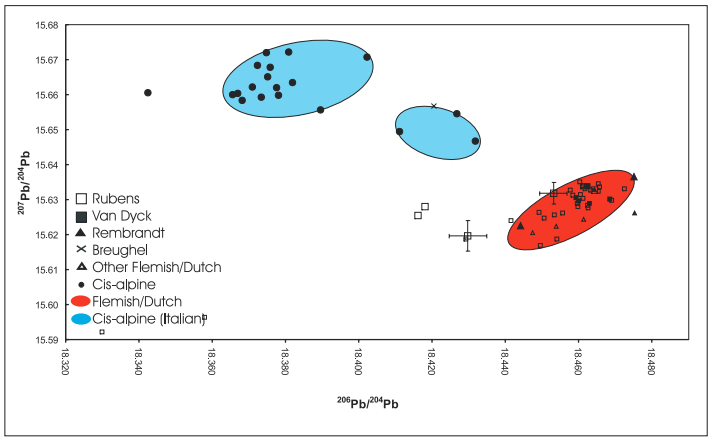
Minute samples (50–200 μg) taken from paintings from art collections worldwide were investigated using multi-collector inductively coupled mass spectrometry (MC-ICP-MS), scanning electron microscopy (SEM) and energy-dispersive X-ray spectroscopy (EDX).

The scatter plots of the measured isotope abundance ratios of the painting pigments from P.P. Rubens, A. van Dyck and other Flemish painters show a very narrow distribution forming a cluster with relative widths of 0.55% and 0.2%. The comparison of these data with cis-alpine (Italian) sample pigments from paintings of the same time period reveals a clear distinction between the isotopic arrays. With respect to European ore lead isotope data we assume that the pigment isotope ratio distribution is a direct representation of the very distinct origin of raw materials. Presumably, no mixing of different lead ores from Europe took place. The comparison of the measured white lead isotope ratio values (Flemish paintings) and the data from ore samples lead to the unexpected conclusion that British or German products and not local ores were used for the pigment production.

The results to date show great promise as a further tool in the identification and authentication of works of art. It is now important to build up a white lead data base and to examine the lead ore isotope ratio values in a more detailed way.

Received: March 1, 2005

One of the investigated paintings: Peter Paul Rubens, Clara Serena Rubens, 1616, Oil on Canvas, Collections of the Prince of Liechtenstein, Vaduz-Vienna



Lead isotope abundance ratio values for cis- and trans-alpine pigment samples. Bars denote typical combined measurement uncertainties (coverage factor k = 2)

Acknowledgements

We thank the following persons and institutions for their help and support: HSH Prince Hans-Adam II of Liechtenstein, Vaduz and the Swiss National Science Foundation.

Reference

G. Fortunato, A. Ritter, D. Fabian, *Analyst* **2005**, in press.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

CHIMIA **2005**, *59*, No. 6

Highlights of Analytical Chemistry in Switzerland

Screening of Samples for the Presence of Chemical Warfare Agents by Nuclear Magnetic Resonance

Urs C. Meier

Correspondence: Dr. Urs. C. Meier, Swiss NBC Defence Establishment, Spiez Laboratory, CH-3700 Spiez
Tel. +41 33 228 16 92, Fax +41 33 228 14 02, E-Mail: urs.meier@babs.admin.ch

Keywords: Chemical warfare agents · Chemical Weapons Convention · Nuclear magnetic resonance spectroscopy · Organophosphorus nerve agents · Sarin

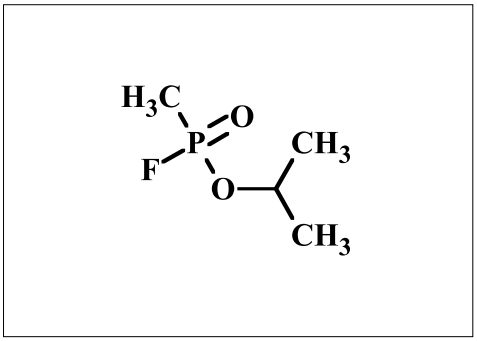
Chemical weapons were first used on a large scale in World War I. At this time the main chemical warfare agents (CWA) were blistering agents (mustard gas) and asphyxiating agents (phosgene). Since the 1930s organophosphorus nerve agents (*e.g.* sarin, VX) have been synthesized. Public interest in this topic was stressed in the Iran-Iraq conflict (1980–1988) and through a terrorist attack in the Tokyo subway system. In 1995 sarin was released by the Aum sect resulting in 12 deaths and 5000 poisoned or injured people.

On 29 April 1997, the Chemical Weapons Convention (CWC) entered into force. The convention prohibits the development, production, stockpiling and deployment of these weapons. The Organisation for the Prohibition of Chemical Weapons (OPCW) is responsible for the implementations of the CWCs provisions, including verification of its compliance. Ever since, the OPCW has organized interlaboratory proficiency tests to designate laboratories for the verification of the CWC. Spiez Laboratory is one of several designated laboratories worldwide.

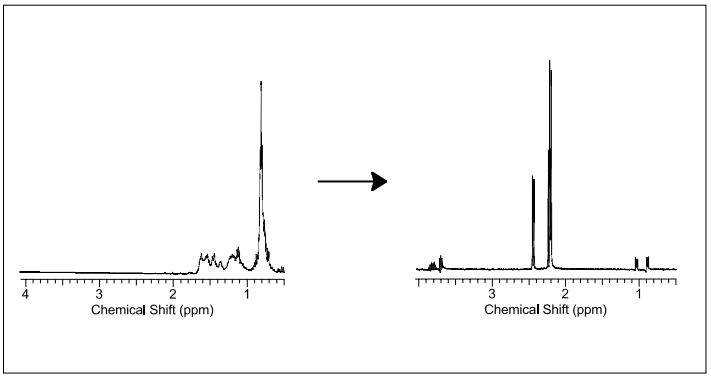
Modern analytical methods for the detection and unambiguous identification of CWAs are needed for the verification of the CWC, the protection of the population and the proper medical treatment of victims. The samples to be analysed may be a liquid, soil or shell fragments. After a sample preparation step, they are subjected to instrumental analysis.

Among other techniques, nuclear magnetic resonance (NMR) spectroscopy is suitable for the analysis of CWAs. Traditionally, the screening is done by ^{1}H and $^{31}P\{^{1}H\}$ NMR. ^{1}H NMR is limited by the high level of background present in environmental samples, $^{31}P\{^{1}H\}$ by its low sensitivity and poor information content. Recently, nonselective 1D ^{1}H–^{31}P inverse NMR experiments were shown to be the most sensitive NMR methods to selectively screen samples for the presence of nerve agents. Only signals stemming from the nerve agents are detected and the background is completely eliminated. Samples spiked at the 5 ppm level can be screened within an hour, whereas for $^{31}P\{^{1}H\}$ an overnight acquisition is necessary.

Various types of samples suspect of contamination with chemical warfare agents



Sarin



The spectrum on the left shows a standard ^{1}H spectrum, whereas the ^{1}H-^{31}P HSQCTOCSY spectrum of the same solution is shown on the right. The background present in the ^{1}H spectrum is completely eliminated in the ^{1}H-^{31}P HSQTOCSY experiment and the previously hidden signals belonging to organophosphorus compounds are exclusively detected.

Reference

U.C. Meier, *Anal. Chem.* **2004**, *76*, 392.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

CHIMIA **2005**, *59*, No. 9

Highlights of Analytical Chemistry in Switzerland

High-Speed Identification of Designer Drugs by Multiple Mass Spectrometry

Stephan Kölliker and Michael Oehme*

*Correspondence: Prof. Dr. M. Oehme, Organic Analytical Chemistry, University of Basel, Neuhausstr. 31, CH-4057 Basel

Tel.: +41 61 639 23 01, Fax: +41 61 639 23 00, E-Mail: michael.oehme@unibas.ch

Keywords: Amphetamines · Designer drugs · Multiple mass spectrometry · Structure elucidation

Amphetamines and related drugs are rather frequently used at techno parties. Many different derivatives are on the market. The residues R1, R2 and R3 (also di-substituents) can vary greatly. New modifications show up frequently. The relation between structure and the desired psychedelic effect is largely unknown. The range between any effect and toxic properties can be rather small. Experimenting with dose and intake of different products can be fatal. A quick identification of the active component in pills is therefore important. The questions are: Is the compound already known? If not, what is its structure?

Multiple mass spectrometry (MSn) is a rather new technique introduced in 1995. Our group received the first instrument worldwide and has studied its possibilities for structure elucidation since then. Collision-induced dissociation with defined energies allows the cleavage of specific bonds in an ion trap mass spectrometer. In the case of amphetamines *etc.* the following information is obtained:

Mass spectrum (MS): Mass of compound and hetero atoms present

1st fragmentation (MS2): Loss of -N-R1

2nd fragmentation (MS3): Loss of -R2

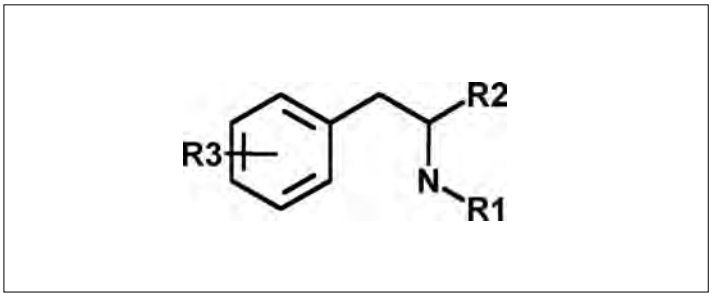
3rd fragmentation (MS4): Number, position and kind of R3 (based on reference spectra unique for ring positions)

This information allows the structure elucidation of a drug in a pill after only dissolution, filtration and a 15 min experiment. By-products can be identified after a pre-separation by high-performance liquid chromatography.

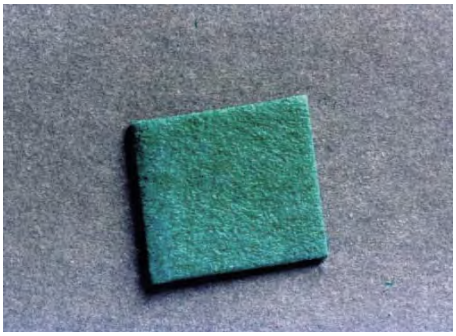
Received: July 6, 2005

Reference

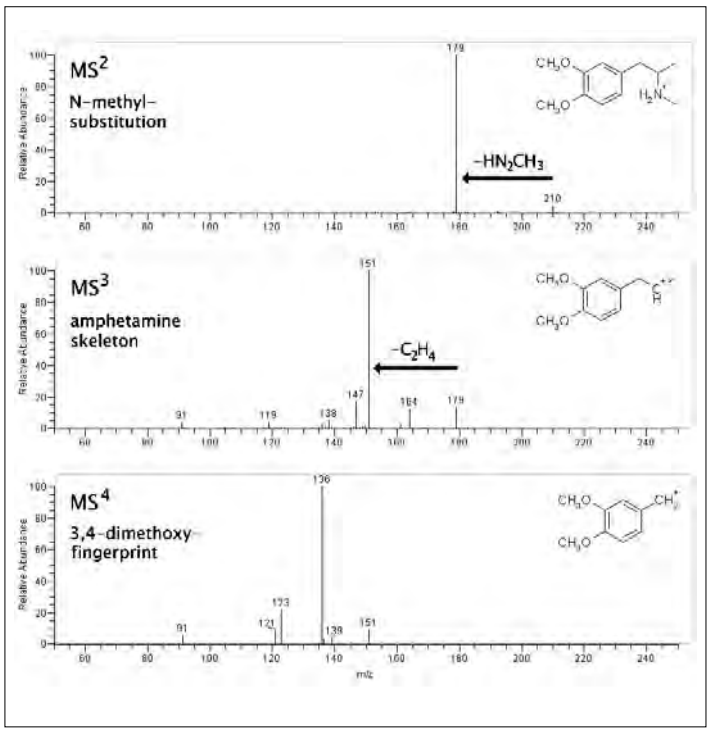
S. Kölliker, M. Oehme, *Anal. Bioanal. Chem.* **2004**, *61*, 215.



Structure of designer drugs with functional groups in various combinations: R1: -NH_2, -$NHCH_3$, -$NHCH_2CH_3$; R2: -H, -CH_3, -CH_2CH_3; R3: -OCH_3, methylenedioxy-, -CH_3, -SCH_3, -Cl, -Br, -I



A designer drug pill



Identification of N-methyl-3,4-dimethoxy-amphetamine as impurity in the pill

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen

Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

CHIMIA **2005**, *59*, No. 11

Highlights of Analytical Chemistry in Switzerland

Elucidating the Secrets of the Maillard Reaction Cascade – The Role of Amadori Compounds

Tomas Davídek and Imre Blank*

*Correspondence: Dr. I. Blank, Nestlé Research Center, Vers-chez-les-Blanc, CH-1000 Lausanne 26

Tel.: +41 21 785 86 07, Fax: +41 21 785 85 54, E-Mail: imre.blank@rdls.nestle.com

Keywords: Amadori compounds · Flavor chemistry · Maillard reaction · Umami taste

The reaction of reducing sugars with amino acids and proteins, referred to as the Maillard reaction or non-enzymatic browning, is the major source of color, taste and aroma that is characteristic for many heated foods, such as meat, bakery, and cocoa. For example the almost odorless green coffee beans are transformed into dark brown roasted coffee with delicious taste and aroma. Amadori compounds, 1-amino-1-deoxyketoses, play a pivotal role in the Maillard reaction cascade. It is also assumed that they participate in the formation of advanced glycated end products (AGEs) under physiological conditions. Pentose-based Amadori compounds are very unstable compared to their hexose-based analogues and have rarely been reported in the literature.

It is rather challenging to obtain reliable data on the nature, amounts, and fate of Amadori compounds due to (i) the high complexity of Maillard systems and (ii) the high diversity in polarity of Amadori compounds. Modern analytical methods combine chromatographic separation efficiency and mass discrimination by tandem mass spectrometry (MS/MS). Separation by high-performance cation-exchange chromatography (HPCEC) followed by electrochemical detection (ECD) or tandem MS in the positive electrospray ionization (ECI^+) mode turned out to be the most suitable approach. Alternatively, capillary electrophoresis coupled to MS/MS can be used.

We have succeeded for the first time to monitor pentose-based Amadori compounds, such as N-(1-deoxy-D-xylulos-1-yl)glycine (Xyl-Gly). Reaction of D-xylose and glycine at 90 °C (pH 6) for 2 h showed rapid formation of Xyl-Gly (~12 mol %, 15 min) followed by slow decrease over time. Analysis of pentose-derived Amadori compounds represents a major breakthrough in studying occurrence, formation, and decomposition of these labile Maillard intermediates.

Several hexose-based Amadori compounds could be identified and quantified in an aqueous extract of dried vegetables and fruits. Sample preparation consisted of maceration of dried tomatoes in water, homogenization, and filtration. N-(1-deoxy-D-fructos-1-yl)-L-glutamic acid (Fru-Glu) was found as the major Amadori compound in dried tomatoes. About 1.5 g/100 g of Fru-Glu was determined, known for its umami taste properties that are also characteristic for dried tomatoes. Such data are now readily accessible to reveal taste-active constituents of natural products. Several other Amadori compounds could also be detected, *i.e.* Fru-Ala, Fru-Leu and Fru-Phe, indicating that no further clean-up was required.

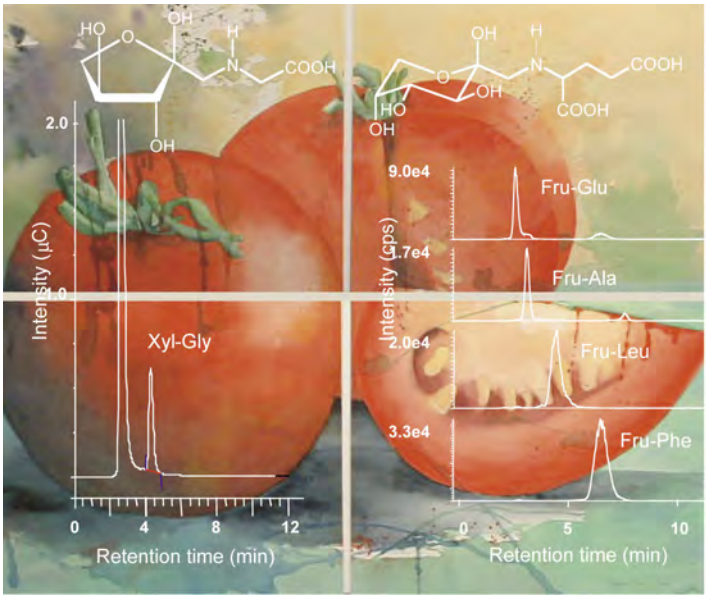
Simultaneous analysis of non-volatile Maillard reaction products such as Amadori compounds combined with a minimum of sample clean-up opens new avenues to study reaction mechanisms of the Maillard reaction cascade and elucidate new constituents in thermally processed foods and natural products with interesting sensory and other bio-active properties.

References

T. Davidek, K. Kraehenbuehl, S. Devaud, F. Robert, I. Blank, *Anal. Chem.* **2005**, *77*, 140.

J. Hau, S. Devaud, I. Blank, *Electrophoresis* **2004**, *25*, 2077.

E. Beksan, P. Schieberle, F. Robert, I. Blank, L.B. Fay, H. Schlichtherle-Cerny, T. Hofmann. *J. Agric. Food Chem.* **2003**, *51*, 5428.



Rapid HPCEC-ECD analysis of the pentose-based Amadori compound N-(1-deoxy-D-xylulos-1-yl)glycine (Xyl-Gly), shown in the major β-anomeric form. HPCEC-MS/MS analysis of hexose-based Amadori compounds found in dry tomato, *e.g.* N-(1-deoxy-D-fructos-1-yl)-L-glutamic acid (Fru-Glu) shown in the major β-pyranoid form ($^2C_5$ conformation). The picture is taken from *http://www.arton5th.com/hennig/tomaten.html* and was painted in watercolors by Claudia Hennig.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

CHIMIA **2005**, *59*, No. 1

Highlights of Analytical Chemistry in Switzerland

Monitoring of Water Chemistry in Forest Soils: An Indicator for Acidification

Elisabeth Graf Pannatier*, Jörg Luster, Stephan Zimmermann, and Peter Blaser

*Correspondence: Dr. E. Graf Pannatier, Swiss Federal Institute for Forest, Snow and Landscape Research, CH-8903 Birmensdorf

Tel.: +41 44 739 23 30, Fax: + 41 44 739 22 15, E-Mail: elisabeth.pannatier@wsl.ch

Keywords: Acid deposition · Acidification · Lysimetry · Recovery · Soil solution

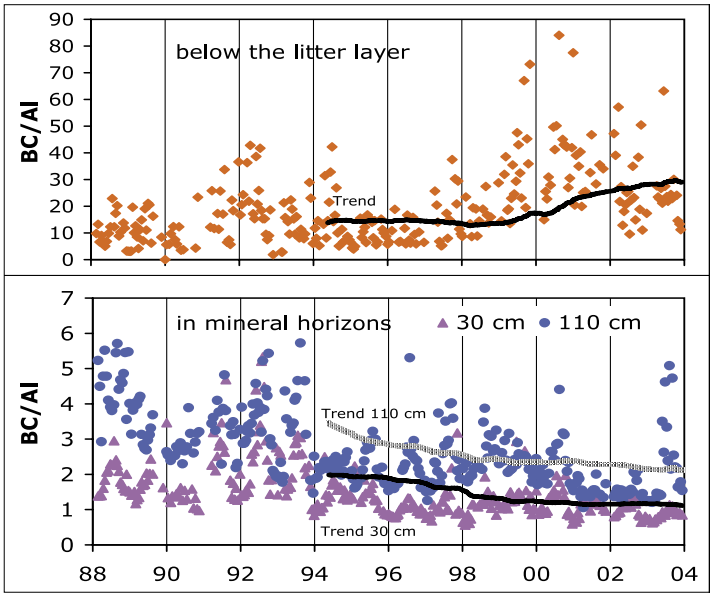
Acid atmospheric deposition can affect the chemistry of soils and drainage waters in forest ecosystems and accelerate the acidification of soils. In acidic soils, the input of acidifying compounds increases the mobility of aluminum that can reach toxic levels for sensitive plant species. In addition, leaching losses of nutrients such as Ca, Mg and K may increase as a result of acidic deposition. These cations are important for tree nutrition and a depletion can affect both biomass production and, by an imbalanced nutrition, tree health and sensitivity to pests.

The soil water chemistry in a chestnut forest at Copera near Monte Ceneri in Ticino has been monitored since 1987 to measure the soil response to atmospheric acid deposition. This area, with its mainly acidic bedrock, is very sensitive because the soil is poorly buffered. It has received high loads of acidifying compounds due to local and long-range emissions from the industrial Po Valley in Italy. Acid deposition declined through the 1980s and 1990s, mainly because of the reduction of SO_2 emissions following air pollution abatements. This raised the question whether the forest soil has recovered since then. The ratio of base nutrient cations (BC = Ca^{2+} + Mg^{2+} + K^+) to dissolved aluminum (BC/Al) in the soil solution was used to assess soil acidification and the associated ecological risks.

Water samples were collected fortnightly with tension lysimeters. The main chemical characteristics of the soil solutions were measured routinely: pH, electric conductivity, dissolved organic carbon, concentrations of major cations and anions. A significant decrease in BC/Al ratios has been observed since 1987, indicating a rapid soil acidification. However, initial signs of recovery were detected recently below the litter layer. In the mineral horizons, the ratios have stabilized since the late 1990s, suggesting that acidification has slowed down.

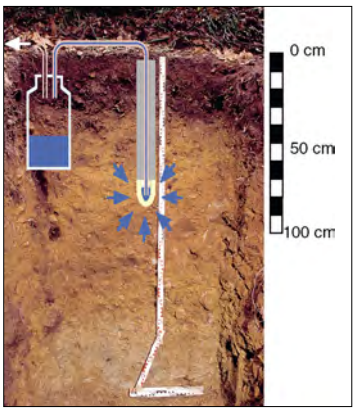
Reference

E. Graf Pannatier, J. Luster, S. Zimmermann, P. Blaser, *Environ. Sci. Technol.* **2005**, *39*, 7761.



BC/Al ratios in the soil solution below the litter layer, in the (AE) eluvial horizon (30 cm) and in the $B_{(s)}C$ transition horizon to bedrock (110 cm). Thick lines are moving averages with a time window of six years

Chestnut forest stand at Copera



Tension lysimeter in soil profile

Installation of a lysimeter

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

CHIMIA **2006**, *60*, No. 1/2

Highlights of Analytical Chemistry in Switzerland

Entry Pathways of UV Filters from Sunscreens to Swiss Lakes

Marianne E. Balmer*, Hans-Rudolf Buser, and Thomas Poiger

*Correspondence: Dr. M.E. Balmer, Agroscope FAW Wädenswil, Swiss Federal Research Station for Horticulture, P.O. Box 185, CH-8820 Wädenswil
Tel.: +41 44 783 62 66, Fax: +41 44 783 64 39, E-Mail: marianne.balmer@faw.admin.ch

Keywords: Chemical marker for domestic wastewater · 4-Methylbenzylidene camphor · Methyl triclosan · Surface waters

Organic UV filters, compounds which absorb ultraviolet light, are used in various personal care products such as shampoos, body lotions or lipsticks and, of course, in considerable amounts in sunscreen products. Some years ago, studies indicating that UV filters may be endocrine disruptors raised public concern. Particularly 4-methylbenzylidene camphor (4-MBC), a frequently used UV filter, was discussed in newspapers and consumer magazines.

The rather lipophilic 4-MBC was found in small concentrations in various lakes. Its presence in treated wastewater clearly indicated that this 'indirect' input pathway does contribute to some extent to the load of this compound in surface waters. Nevertheless, 'direct inputs' from recreational activities such as swimming and bathing in lakes and rivers may also occur. Another lipophilic compound, methyl triclosan, was used to investigate the relative importance of such direct inputs.

Methyl triclosan, a transformation product of the widely used bactericide triclosan, is formed in small amounts in wastewater treatment plants and emitted to surface waters with the effluent. Its concentration is expected to be directly linked to the population living in the catchment area of a lake and the compound is considered as a suitable chemical marker for the burden of domestic wastewater to a lake. In fact, the concentration of methyl triclosan was highest in Greifensee, the lake with the largest population relative to its water throughflow, whereas concentrations were lower in Zürichsee. In Hüttnersee, a small lake that receives no wastewater inputs, methyl triclosan was not detected. In contrast, the concentrations of the UV filter 4-MBC, measured in summer 2002, were highest in Hüttnersee and higher in Zürichsee than in Greifensee.

Organic UV filters from sunscreen products may enter surface waters as 'indirect inputs' *via* wastewater treatment plants or as 'direct inputs' from swimming and bathing in lakes and rivers. Photo: Keystone/Philip Mark.

Thus, concentrations of 4-MBC appear to be linked to the use of these lakes as recreational and swimming areas. The fact that the concentrations of 4-MBC and the chemical marker methyl triclosan do not correlate at all indicates that wastewater is not the main source of the UV filter, but direct inputs from recreational activities to surface waters are important, at least during summer.

Acknowledgements

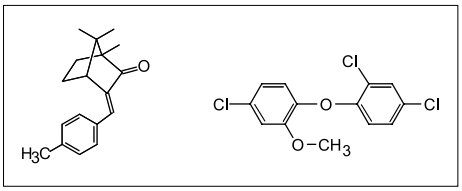
This project was supported by the Swiss Federal Agency for the Environment, Forests and Landscape (BUWAL).

Received: December 16, 2005

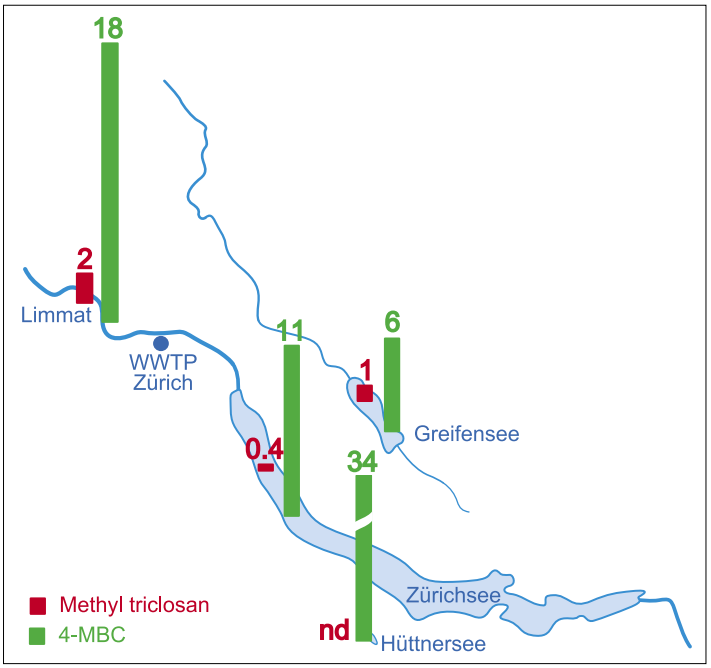
References

M.E. Balmer, H.R. Buser, M.D. Müller, T. Poiger, *Environ. Sci. Technol.* **2005**, *39*, 953.

M.E. Balmer, T. Poiger, C. Droz, K. Romanin, P.A. Bergqvist, M.D. Müller, H.R. Buser, *Environ. Sci. Technol.* **2004**, *38*, 390.



Chemical structures of the UV filter 4-methylbenzylidene camphor (left) and the chemical marker methyl triclosan (right)



Concentrations of 4-MBC and methyl triclosan in three lakes and the river Limmat in summer 2002, suggesting significant direct inputs of the UV filter from recreational activities to Hüttnersee and Zürichsee. The numbers indicate the concentrations in ng l^{-1} as estimated from the analysis of SPMDs (semipermeable membrane devices) which were used for passive sampling of surface waters (nd: not detected, <0.02 ng l^{-1}).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

CHIMIA **2006**, *60*, No. 3

Highlights of Analytical Chemistry in Switzerland

Micro-scale Chemical Speciation of Highly Heterogeneous Cementitious Materials Using Synchrotron-based X-Ray Absorption Spectroscopy

André M. Scheidegger*, Marika Vespa, Erich Wieland, Messaoud Harfouche, Daniel Grolimund, Rainer Dähn, Andreas Jenni, and Karen Scrivener

**Correspondence*: PD Dr. A.M. Scheidegger, Laboratory for Waste Management, Paul Scherrer Institute, CH-5232 Villigen PSI
Tel.: +41 56 310 2184, Fax: +41 56 310 4554, E-Mail: Andre.Scheidegger@psi.ch

Keywords: Cement · Micro-scale chemical speciation · Micro-X-ray absorption spectroscopy · Micro-X-ray fluorescence · Radioactive waste · Swiss Light Source

Mixing 'fugitive' hazardous waste products into a cementitious binder system improves the stabilization and the solidification of radioactive and industrial waste materials. Consequently, the migration of radionuclides and other heavy metals from cement-based landfills and nuclear underground waste repositories into the environment can be significantly retarded and possible impacts on the environmental quality can be minimized. From a chemical standpoint cement minerals are typically present as discrete particles in the size range of a few nanometers to a few hundred micrometers (Fig. 1). The complexity of the hydrated assemblage and the reactivity of the minerals make it very difficult to investigate cementitious systems.

Molecular-level investigations on Co(II) doped hardened cement paste were carried out at the Advanced Light Source (ALS) using synchrotron-based micro-X-ray fluorescence (XRF) and micro-X-ray absorption spectroscopy (XAS). XAS is exclusive to synchrotron light sources and can yield spatially-resolved information (*e.g.* type of neighboring atoms, bond length and coordination numbers) on the variability of chemical speciation in complex and highly heterogeneous samples. A hard X-ray micro-probe facility optimized for micro-XRF and micro-XAS with a spatial resolution of a few μm^2 has now also become available at the Swiss Light Source (SLS).

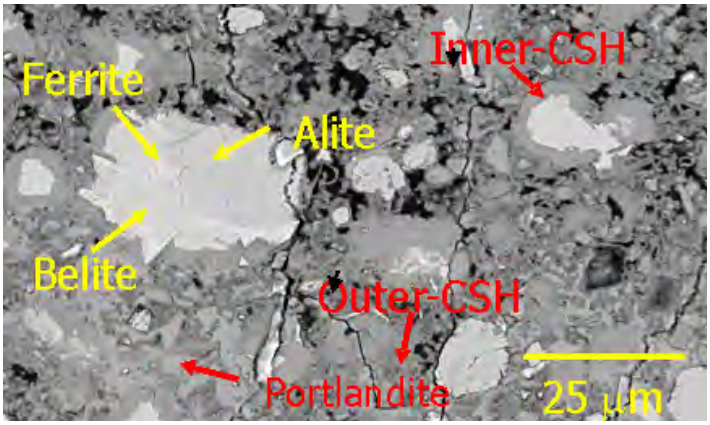


Fig. 1. SEM image illustrating the micro-scale heterogeneity of hardened cement paste. Examples of clinker minerals (ferrite, belite and alite; yellow) and hydrated phases (calcium silicate hydrates (CSH) and portlandite; red) are outlined.

The micro-XRF maps show that Co is heterogeneously distributed in the Co-doped cement matrix (Fig. 2). Typically Co-rich spots up to ~50 μm^2 in size (*e.g.* spot 1) as well as characteristic Co-rich ring-like structures with diameters up to ~200 µm (*e.g.* spot 2) were observed. XAS data analysis revealed the presence of a Co(II)-hydroxide-like phase ($Co(OH)_2$ and/or Co-Al layered double hydroxide) at spot 1 and a Co(III)OOH-like phase at spot 2. This finding is illustrated by the shorter Co–O and Co–Co distances at spot 2 (Fig. 3).

Co oxidation is environmentally relevant since it results in a reduction of the Co mobility in cement. A surprising result of the micro-spectroscopic study is that oxidation of Co(II) is a locally occurring process. ***This finding demonstrates that the inherent micro-scale heterogeneity of cement may well control the overall chemical reactivity of Co in cement.***

Received: January 26, 2006

References

Website of the microXAS at SLS: *http://sls.web.psi.ch/view.php/beamlines/mxas/index.html*.

M. Vespa, R. Dähn, D. Grolimund, M. Harfouche, E. Wieland, A.M. Scheidegger, *J. Geochem. Exploration* **2006**, in press.

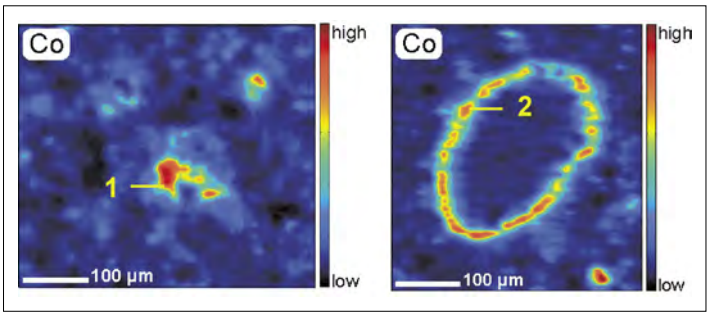


Fig. 2. Micro-XRF maps showing the elemental Co distribution in a hydrated Co-doped hardened cement paste at different locations (beam size ~ 5x5 μm^2)

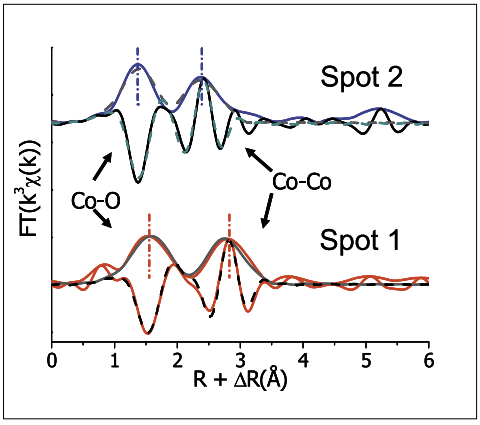


Fig. 3. Experimental (solid line) and theoretical (dashed line) Fourier transforms (modulus and imaginary parts) of k^3-weighted micro-EXAFS spectra collected at spot 1 and 2. The spectra are uncorrected for phase shift (R + ΔR).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

CHIMIA **2006**, *60*, No. 4

Highlights of Analytical Chemistry in Switzerland

Detection of Carbon Monoxide-Treated Tuna by Headspace-Gas Chromatography/Mass Spectrometry

Thomas Frey*, Bernard Roux, and Werner Eymann

*Correspondence: T. Frey, Kantonales Laboratorium Basel-Stadt, Kannenfeldstr. 2, CH-4056 Basel

Tel.: +41 61 385 25 18, Fax: +41 61 385 25 09, E-Mail: thomas.frey@kl.bs.ch

Keywords: Carbon monoxide · Fraud · GC/MS · Headspace · Tasteless smoke · Tuna

In recent years sushi has become more and more popular in Switzerland, resulting in an increased demand for high quality raw fish such as tuna. A main criterion for freshness and quality of tuna flesh is its red colour. Under natural conditions, as a result of oxidation of myoglobin ($MbFe^{2+}$) to metmyoglobin ($MetMbFe^{3+}$) the colour rapidly turns an unattractive brown, particularly during frozen storage. For some years in Asian countries, *e.g.* Philippines and Indonesia, tuna fillets and loins have been treated with carbon monoxide (CO) or tasteless smoke, which contains CO. This treatment results in the stabilization of a bright red colour due to the higher affinity of CO for the Fe(ii) binding site of myoglobin. Thus, the muscle tissue is prevented from discolouration and its red colour lasts for an extended period of time. Even if the bright red of treated tuna looks rather artificial, consumers are attracted and product sales are increased.

CO is not approved as a food additive in Switzerland. Consequently, trading of foodstuffs treated with CO or tasteless smoke is prohibited by the Swiss food law. As CO-treated tuna retains its red colour even during spoilage, consumers may not only be deceived about product freshness but also are subject to a possible food poisoning due to the potential generation of biogenic amines.

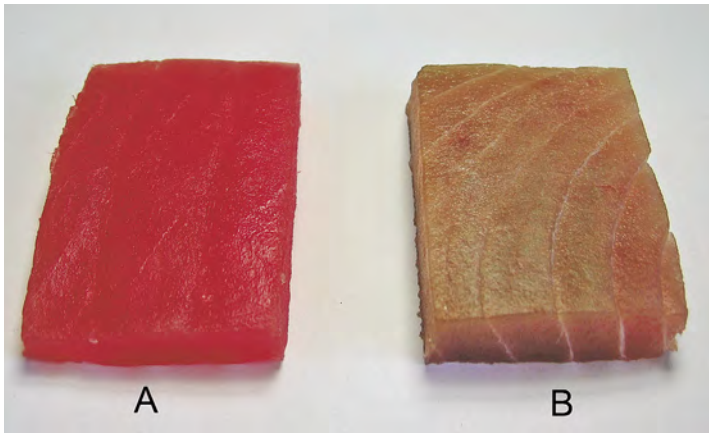
We have implemented a fast and simple analytical method to test raw tuna for treatment with CO or tasteless smoke. First, myoglobin is extracted with ice water from the sample. Bound CO is then released from the extract by acidification and quantified using automated headspace gas chromatography/mass spectrometry.

To monitor the Swiss market, samples of raw tuna were collected from distributors and importers as well as by the border veterinarians and analysed for CO. In 21 of the samples collected in 2005, CO contents ranged from 29 to 177 μg/kg. These values are in agreement with indigenous CO contents in tuna as reported by other researchers. Furthermore, they are below the limit of 200 μg/kg which is proposed by Japan and EU member states for distinction of untreated from CO-treated tuna. However, six samples reached CO concentrations between 680 and 2430 μg/kg. These values are significantly above naturally occurring concentrations and indicated a treatment with CO or tasteless smoke. Consequently, these samples, all originating from the Philippines, were objected to by the responsible food control authorities.

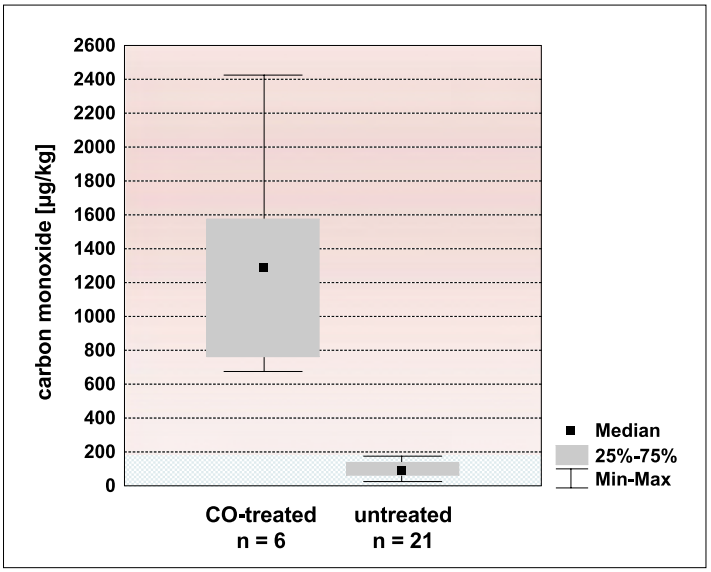
Received: February 17, 2006

References:

http://www.kantonslabor-bs.ch/files/18/Jahresbericht.pdf



Different colours of carbon monoxide-treated (A) and untreated (B) tuna fillets after frozen storage



Clear distinction of untreated from CO-treated tuna samples by analysis of carbon monoxide content

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

CHIMIA **2006,** *60,* No. 5

Highlights of Analytical Chemistry in Switzerland

Cannabis Profiling: Which Analytical Strategy to Apply?

Yara Ilias, Serge Rudaz, Philippe Christen, and Jean-Luc Veuthey*

**Correspondence*: Prof. J.-L. Veuthey, Laboratory of Pharmaceutical Analytical Chemistry, School of Pharmaceutical Sciences, University of Geneva & University of Lausanne, Boulevard d'Yvoy 20, CH-1211 Geneva 4

Tel.: +41 22 379 63 36, Fax: +41 22 379 68 08, E-Mail: jean-luc.veuthey@pharm.unige.ch

Keywords: Cannabis · Cannabinoid profile · Headspace solid-phase microextraction · Hierarchical cluster analysis · Principal component analysis

Cannabis sativa L. with its long history is an interesting example of the complexity of plants. In numerous domains, this plant occupies an important place in society. Indeed, besides its recognised pharmacological and toxicological properties, cannabis and derivatives are also implicated in social and economical aspects. For many years they have been subject to discussion and controversy in Switzerland, where political and legal institutions are currently debating legalization. In case of acceptance, a strict control would be performed to determine the plant origin as well as its quality. Only plants cultivated in Switzerland would be allowed and their content in Δ^9-tetrahydrocannabinol (Δ^9-THC), the psychoactive component, would have to be indicated.

The chemistry of cannabis is complex. Among the natural components, cannabinoids are abundant characteristic C_{21} compounds belonging to the class of terpenophenols. It is now largely accepted that the cannabinoid content varies with the geographical origin. Therefore, tracing a cannabinoid profile can be of prime importance not only to determine the Δ^9-THC content but also for localization if plants are cultivated outdoors.

Cannabis chromatographic profiles can easily be performed by combining a solvent-free sample preparation technique, such as headspace solid-phase microextraction, with gas chromatography/mass spectrometry. In addition, chemometric tools such as principal component analysis and hierarchical cluster analysis allow the treatment and interpretation of the phytochemical fingerprinting determined on the basis of the cannabinoid content. ***Thanks to these tools, discrimination of cannabis samples originating from different locations can be achieved.***

Received: March 27, 2006

Fig 1. Where was this cannabis plant grown? Cannabinoid profiling gives the answer.

References

Y. Ilias, S. Rudaz, P. Mathieu, P. Christen, J.-L. Veuthey, *J. Sep. Sci.* **2005,** *28,* 2293.

Y. Ilias, S. Rudaz, P. Mathieu, J.-L. Veuthey, P. Christen, *Chimia* **2004**, *58*, 219.

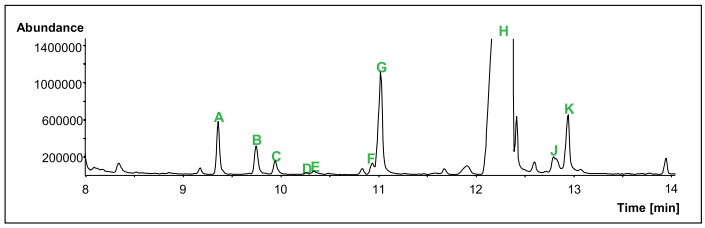


Fig 2. Cannabis GC/MS profile showing ten cannabinoids (A to K)

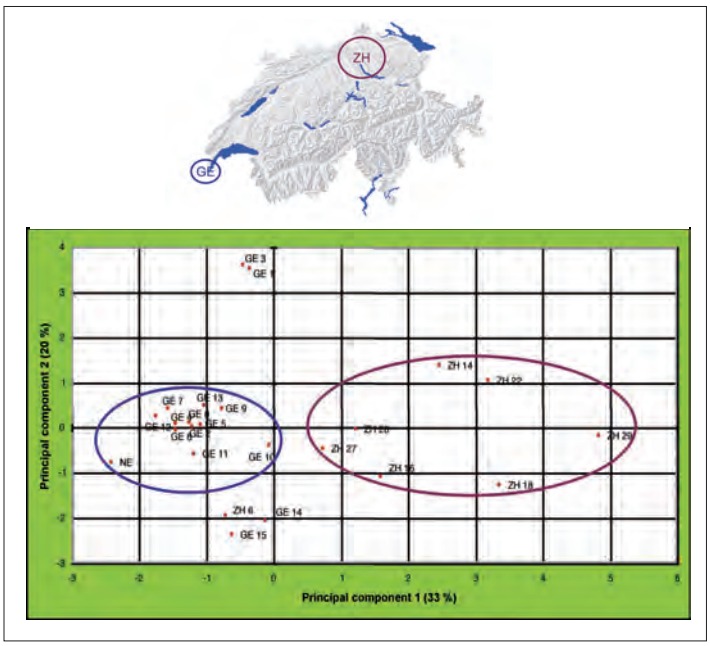


Fig 3. Discrimination of cannabis samples from different locations in Switzerland

CHIMIA **2006**, *60*, No. 6

Highlights of Analytical Chemistry in Switzerland

An Environmental Case History of Platinum

Urs Krähenbühl*[a], Céline Fragnière[a,b], and Max Haldimann[b]

Correspondence: Prof. Dr. U. Krähenbühl[a], [a]Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern, Tel.: +41 31 631 42 65, Fax: +41 31 631 42 20, E-Mail: urs.kraehenbuehl@iac.unibe.ch
[b]Swiss Federal Office of Public Health, CH-3003 Bern

Keywords: Car emissions · Catalytic converter · Peat bog · Platinum Group Elements · Platinum in the environment

In recent years, the air quality in the vicinity of motorways has improved due to the distinct reduction of hazardous car emissions such as VOC, CO, and NO_x thanks to the introduction of exhaust catalytic converters. They effect combined oxidation and reduction reactions in the presence of platinum group elements (PGE).

The first generation of catalytic converters contained Pt and Rh as active compounds. In the latest generations a large fraction of Pt has been replaced by the more abundant Pd. A combination of several PGEs is needed for the optimum decrease of noxious car emissions. The operation of any car equipped with a catalytic converter results in nano-gram quantities of PGEs being lost to the environment for each kilometer driven. So, PGEs may accumulate near streets and highways. Our research is focused on Pt emissions.

Peat cores were collected from Guin/Düdingen near the national highway A12 and from St Moritz, a remote area secluded from the Swiss midlands. Individual layers of the peat material were dated, digested, and analyzed for Pt using a Finnigan sector field ICP-MS. For the interference-free measurement of Pt a very dry aerosol is needed. Otherwise HfO^+ is formed, which overlaps the platinum isotopes of analytical interest. An APEX drying system reduced the Hf oxide interference by three orders of magnitude.

From the presented results it is quite evident that the emissions are proportional to the amount of traffic on the nearby road.

There is no clear understanding of PGE behaviour in the environment. Further work will focus around the speciation of the PGE emissions, since their toxicity is strongly influenced by the chemical form. In the meantime, PGE concentrations in the environment will continue to increase as long as PGE-based catalysts will be in use.

Received: March 27, 2006

Reference

C. Fragnière, M. Haldimann, A. Eastgate, U. Krähenbühl, *J. Anal. At. Spectrom.* **2005**, *20*, 626.

Cars are now equipped with exhaust catalytic converters – but not all environmental problems are solved

Reduction Catalyst

$NO + CO \rightarrow CO_2 + 1/2\ N_2$

Coating = Pt & Pd

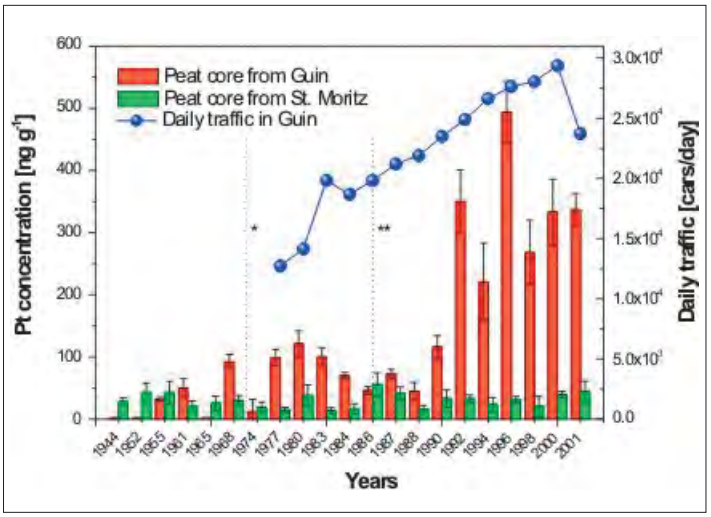
Oxidation Catalyst

$H_xC_y + z\ O_2 \rightarrow m\ CO_2 + n\ H_2O$

$2\ CO + O_2 \rightarrow 2\ CO_2$

Coating = Pt & Rh

Reaction schemes in catalytic converters



Peat bogs are ideal archives for unravelling the time dependent anthropogenic deposition of heavy metals. * Start of construction of highway A12. ** Introduction of catalytic converters for cars.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2006.499 CHIMIA **2006**, *60*, No. 7/8

Highlights of Analytical Chemistry in Switzerland

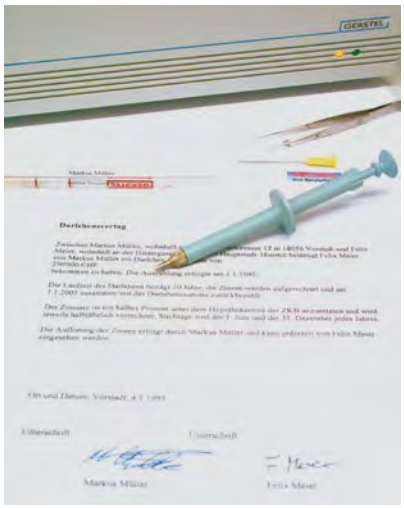
New Analytical Methods for the Forensic Document Experts

Andreas Rippert*

*Correspondence: PD Dr. A. Rippert, Kantonspolizei Zürich, Kriminaltechnische Abteilung, Urkundenlabor, Postfach, CH-8021 Zürich
Tel.: +41 44 247 24 15, Fax: +41 44 247 24 39, E-Mail: ripp@kapo.zh.ch

Keywords: Cryofocusing · Document forgery · GC/MS · Ink analysis · Paper analysis · Thermal desorption

The aim of forensic science is to find the right facts for unexplainable or unclear circumstances. For the document expert this means: he has to explain if the impression marks (handwritten or printed) on a document are genuine or falsified, *e.g.* are there any alterations since the creation of the document or is the document as a whole a forgery?



Sample cutting from a document under investigation

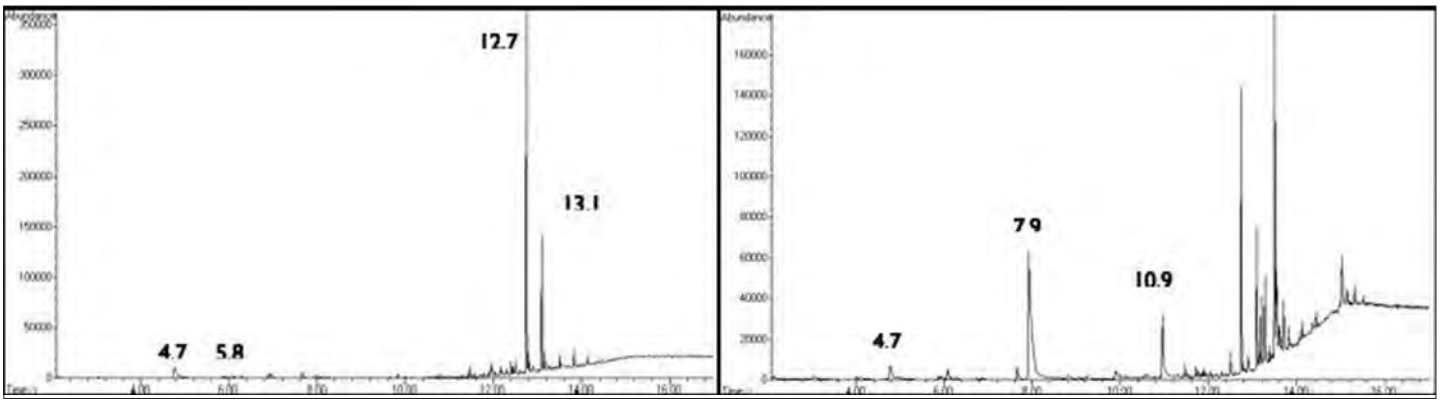
Documents are altered or forged for the advantage of a person or a group of persons, *e.g.* to increase the amount of money in a loan is to the advantage of the lender. But forgery is a criminal offense and is punishable by law.

In forensic science the presence of documents can also shed new light on unsolved cases. Therefore, it is important to find scientific methods to clarify whether forgery took place and to find answers about the timeframe in which alteration could have taken place.

A well-suited analytical technique is GC/MS because of its great sensitivity. However, to obtain information about printing or writing systems on a molecular basis it is necessary to transfer the relevant molecules to the gas phase. Aggravating circumstances are on the one hand that the paper matrix retains the molecules of interest, and on the other hand that chemical substances from the paper itself evaporate that interfere with the important compounds of the writing devices. Therefore attempts to use pyrolysis GC on document samples led to numerous peaks, coming from the writing device under investigation and from the paper; in addition, cross products at high pyrolysis temperature between writing device and paper make the interpretation of the results even more difficult. What is needed is a GC injection method where the temperature can be lowered and the evaporated gases of the sample can be measured at different temperature steps. Thermal desorption at controlled temperature for a certain period of time (several minutes) and a continuous gas flow over the paper with the writing ink are necessary. The compounds of interest will continuously desorb in low amounts. To obtain a measurable signal, the desorption products are first collected before they enter the GC; this is best done by cryofocusing with liquid nitrogen.

In our laboratory we are using a thermodesorption system combined with a cryofocus from Gerstel connected to a GC/MS from Agilent. With this system we can detect and differentiate writing devices of the same type (*e.g.* two ballpoint pens from different producers) or detect the age of the paste of ballpoint pens. For such an analysis document cuttings as small as 5 mm are sufficient to elucidate complicated and unclear cases.

Received: June 28, 2006



GC/MS results using a thermodesorption/cryofocus unit from two 5 mm ballpoint pen strings from different producers on normal office paper

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2006.631 CHIMIA **2006**, *60*, No. 9

Highlights of Analytical Chemistry in Switzerland

Using Bacteria to Quantify Arsenic Contamination in Potable Water

Jan Roelof van der Meer*[a], Michael Berg[b], and Pham Thi Kim Trang[c]

*Correspondence: Prof. Dr. J.R. van der Meer[a]
[a]University of Lausanne, Department of Fundamental Microbiology, Bâtiment de Biologie, CH-1015 Lausanne, Tel. +41 21 692 56 30, Fax: +41 21 692 56 05, E-Mail: JanRoelof.VanDerMeer@unil.ch
[b]Eawag, Swiss Federal Institute of Aquatic Science and Technology, CH-8600 Dübendorf
[c]Centre for Environmental Technology and Sustainable Development (CETASD), Hanoi University of Science, Vietnam

Keywords: Arsenic analysis · Arsenite · Biosensor · Drinking water

Everyday quality measurements of drinking water usually rely on advanced chemical methods. However, for arsenic, which contaminates potable water in millions of family-based groundwater wells in Asia, this is no trivial business. To measure arsenic accurately, expensive machines such as AAS or ICP-MS are necessary. Such equipment is mostly absent in developing countries. Field test kits can be used as alternatives, but they are often unreliable at low arsenic concentrations. Accurate quantification of arsenic even at low concentrations is important to avoid chronic and toxic exposure, and the current WHO guideline for arsenic in drinking water is 10 µg/l. Trang *et al.* recently reported the successful validation of a completely different analytical method that is based on light emission from engineered bacterial cells.

From the laboratory …

How can bacterial cells detect arsenic and emit light? In order to do so, Stocker *et al.* equipped *Escherichia coli* bacteria with the ArsR protein, which is a naturally occurring arsenite-sensing protein in the bacterial arsenic-detoxification system. By genetic engineering techniques they then created a circuit in which ArsR controls the expression of a reporter protein, such as the enzyme luciferase. When the cells encounter arsenite, luciferase is synthesized and the cells start to emit light, which can be easily measured. Within a certain range the light emission is proportional to the arsenite exposure.

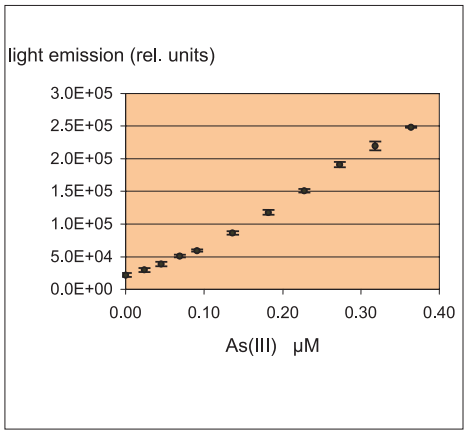
… to the field

A set of simple bioassays was designed on this principle enabling the accurate detection of arsenic in aqueous samples with widely different chemical composition and within 30 min to 2 h. To validate the bioassay performance in analyzing arsenic in real groundwaters, we recently used the light-emitting biosensors in a region in Vietnam where Berg *et al.* had reported serious arsenic contamination. A total of 194 groundwater samples were collected in the Red River and Mekong River Delta and analyzed both by AAS and by the arsenic bioassay. ***Compared to AAS the bacterial assay falsely predicted samples to have less than 10 µg arsenic per liter in 8% and more in 2.4% of all cases, which is far better than the performance of chemical field test kits and thus holds great promise for their use in drinking water analysis in developing countries.***

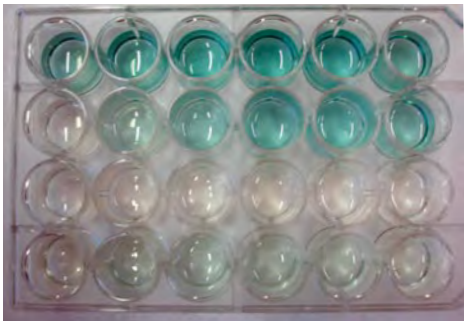
Received: July 11, 2006

References

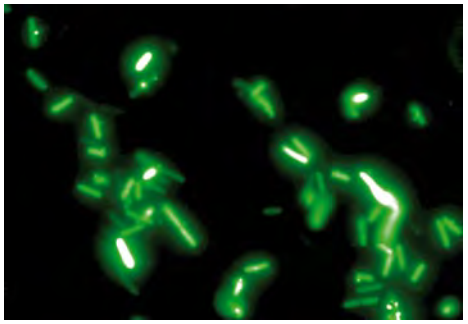
P.T.K. Trang, M. Berg, P.H. Viet, N.V. Mui, J.R. van der Meer, *Environ. Sci. Technol.* **2005**, *39*, 7625.
J. Stocker, D. Balluch, M. Gsell, H. Harms, J.S. Feliciano, S. Daunert, K.A. Malik, J.R. van der Meer, *Environ. Sci. Technol.* **2003**, *37*, 4743.
M. Berg, H.C. Tran, T.C. Nguyen, H.V. Pham, R. Schertenleib, W. Giger, *Environ. Sci. Technol.* **2001**, *35*, 2621.



Calibration curve with the bioluminescent arsenic biosensor. Incubation time: 1.5 h at 30 °C. Measurement: Luminometer plate reader.



Colorimetric arsenic bioassay. Cells produce beta-galactosidase in response to the presence of arsenite in the medium. Image shows different cell lines (in rows) with varying response kinetics. Arsenite concentrations (left to right): 0, 0.1, 0.2, 0.5, 1.0 and 2.0 µM. Incubation time 3 h at 35 °C. Image courtesy: Jan R. van der Meer.



Escherichia coli bacteria producing Green Fluorescent Protein in response to the presence of arsenite in the medium. The GFP signal can be quantified by epifluorescence microscopy, but more easily in steady state fluorimetry. Incubation time: 2.5 h at 30 °C with 0.5 µM As(III). Image courtesy: Jan R. van der Meer.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

CHIMIA 2006, 60, No. 10

Highlights of Analytical Chemistry in Switzerland

Monitoring a Catalyst at Work

Jan-Dierk Grunwaldt*[a], Stefan Hannemann[a], Pit Boye[b], Christian G. Schroer[b], and Alfons Baiker[a]

*Correspondence: PD Dr. J.-D. Grunwaldt[a], Tel.: +41 44 632 30 93, Fax: +41 44 632 11 63, E-Mail: grunwaldt@chem.ethz.ch, [a]Department of Chemistry and Applied Biosciences, ETH Zurich, CH-8093 Zurich, [b]Technische Universität Dresden, Institut für Strukturphysik, D-01062 Dresden, Germany

Keywords: Catalysts · Catalytic partial oxidation · EXAFS · Methane · Micro-scale chemical speciation · Structure–activity relationships

Structure–performance relationships gained by studying catalysts at work are considered the key to further development of catalysts. This requires the structural identification of catalysts preferentially under process conditions while measuring the catalytic activity at the same time. *In situ* X-ray absorption spectroscopy is a well-suited technique for this purpose since it can identify the chemical states of both crystalline and amorphous structures. Up to now studies were performed in an 'integral' way, *i.e.* averaged over the whole reactor.

Here, we studied the partial oxidation of methane over a 2.5wt% Rh/Al_2O_3 catalyst, which is a promising reaction for the production of hydrogen from natural gas. The experimental arrangement and a transmission X-ray image of the catalyst bed are shown in Fig. 1. When the catalyst was heated up in a CH_4/O_2 mixture (ratio 2:1), the reaction to hydrogen and CO ignited at about 320 °C, and at the same time the Rh particles were reduced. However, a closer look revealed that the Rh particles at the inlet of the catalyst bed (*ca.* 12 mm in length) were oxidized whereas towards the outlet they were in metallic state. This can be extracted from the characteristic spectra for oxidized and reduced Rh (Fig. 1). In a next step we aimed at 2-D mapping of the oxidation state of Rh on a micrometer scale. An X-ray camera was installed behind the reactor to record the transmitted intensity with and without the reactor as function of the energy. In this way 160 X-ray absorption images were taken around the Rh K-edge, four of them being shown in Fig. 2 (top). These X-ray absorption images contain the full absorption spectroscopic information in the XANES region at each point of the reactor. Therefore reconstruction of the spectra and a linear combination fit with spectra for Rh^0, Rh^{3+} and an uncharacteristic background allows extracting the 2-D distribution of these components (Fig. 2, bottom). Alternatively, also microXAS studies using a beam of a few micrometers in size would provide similar insight into the reactor. A parallelization using dispersive EXAFS or the use of a quick scanning monochromator would, however, be needed for the latter approach. Parallelization in the present study was achieved using the X-ray camera.

The results demonstrate that the structure of a catalyst may vary inside a catalytic reactor. For the first time 2-D mapping of a catalyst bed under catalytic reaction conditions was achieved.

Acknowledgement

HASYLAB (DESY, Hamburg) is gratefully acknowledged for providing beamtime for this study.

Received: July 20, 2006

References

J.-D. Grunwaldt, A. Baiker, *Catal. Lett.* **2005**, *5*, 99.

J.-D. Grunwaldt, S. Hannemann, C.G. Schroer, A. Baiker, *J. Phys. Chem. B* **2006**, *110*, 8674.

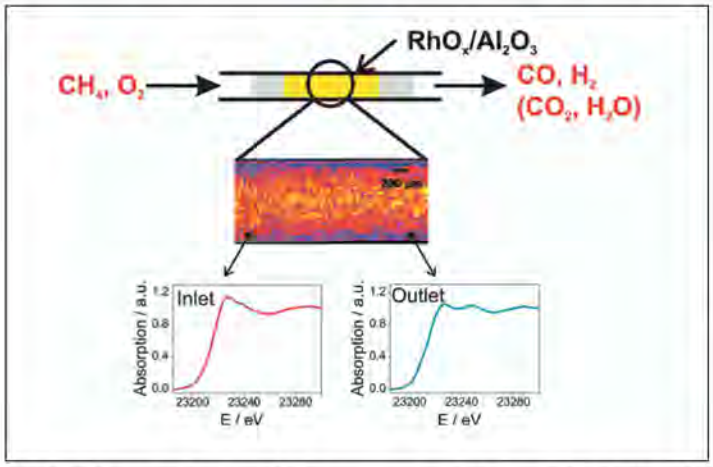


Fig. 1: Schematic drawing of the microreactor during partial oxidation of methane with a 2.5wt% Rh/Al_2O_3 catalyst (top), an image of the catalyst bed (100-200 µm particles, middle), and characteristic X-ray absorption spectra recorded at 362 °C at the inlet (red, oxidized Rh) and the outlet of the reactor (blue, metallic Rh).

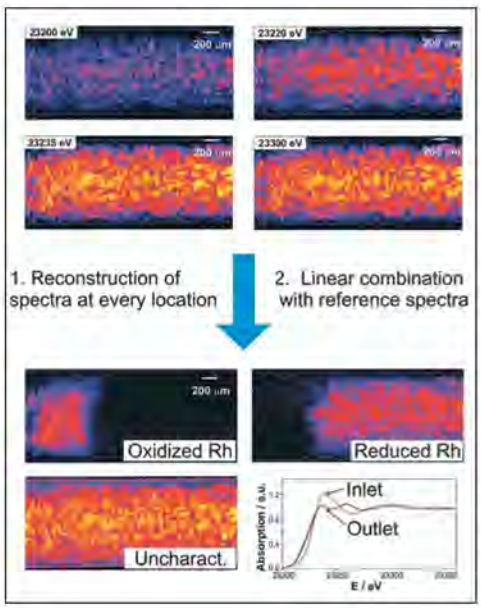


Fig. 2: Selected X-ray transmission images at different energies and the distribution of oxidized and reduced Rh in the catalyst bed. Uncharacteristic X-ray absorption stems from the absorption of the further elements. (The 160 images used for the reconstruction of the XANES-spectra at each location of the reactor can be downloaded as movie from: *http://www.baiker.ethz.ch/people/Scistaff/Grunwaldt/ESI.*)

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2006.817 CHIMIA **2006**, *60*, No. 11

Highlights of Analytical Chemistry in Switzerland

High Precision Carbon Dioxide and Oxygen Measurements Onboard of a Passenger Airplane

Markus Leuenberger*[a], Luca Valentino[a], Peter Nyfeler[a], Hans-peter Moret[a], and the CARIBIC Team[b]

*Correspondence: PD Dr. M. Leuenberger[a], Tel.: +41 31 631 44 70, Fax: +41 31 631 87 42, E-Mail: leuenberger@climate.unibe.ch
[a]Division of Climate and Environmental Physics, Physics Institute, University of Bern, Sidlerstrasse 5, CH-3012 Bern; [b]Max Planck Institute for Chemistry, Atmospheric Chemistry Division, Joh.-Joachim-Becher-Weg 27, D-55128 Mainz, Germany, Tel.: +49 6131 305 0, Fax: +49 6131 305 388

Keywords: Carbon cycle · Climate change · Fuel cell · Troposphere-stratosphere exchange

It is well known that emissions of fossil fuels lead to an enhancement of the Earth's greenhouse effect. Therefore, it is important to improve our knowledge about the carbon cycle, in particular the distribution of carbon dioxide in the atmosphere. Until recent years, mainly ground-based measurements were performed. Hence information about vertical distribution was lacking. In order to learn more about tropospheric CO_2 at high altitudes, we took advantage of the logistics of the already running CARIBIC project (*http://www.caribic-atmospheric.com*). Oxygen concentration – an additional constraint for the carbon cycle – is linked to variations in CO_2 due to photosynthesis/respiration processes as well as fossil fuel emissions. There are different principles for continuous oxygen determination, but most are vibration dependent and not suitable for moving platforms. We decided to use the fuel cell technology for our precise oxygen measurements and a conventional infrared absorption instrument for CO_2.

The principle of the electro-chemical cell or fuel cell is based on the oxidation of a light acidic fluid within the cell producing a small electron current, which is transformed into a small voltage in the mV range over a resistance. The output of the fuel cell varies linearly with the oxygen content of the sample.

Annual changes in CO_2 are in the order of 1–2 ppm, therefore variations in oxygen are of similar absolute magnitude. This corresponds to changes in the order of 0.0001 percent oxygen at a mean concentration of 20.95 percent. In order to achieve this precision temperature, pressure and gas flow have to be controlled to the highest level possible. The graph documents a comparison of two oxygen technologies, the fuel cell and the paramagnetic principle for a laboratory experiment. Despite an offset, which is calibration dependent, a good consistency was observed.

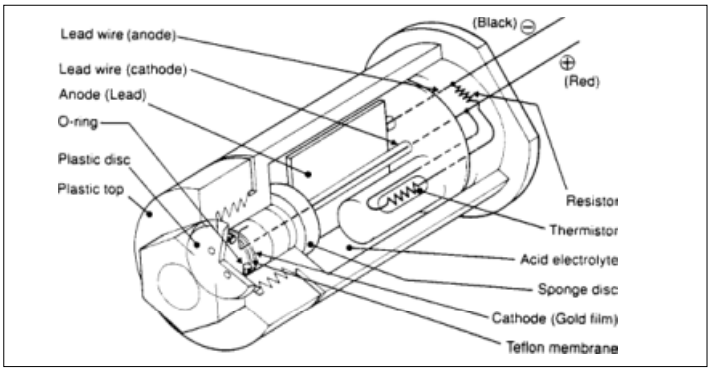
Our instrument is mounted on a cargo-container of a Lufthansa Airbus passenger airplane. Up to now about 60 flights have been performed. Results have shown that the precision for oxygen is not yet reached in comparison to CO_2, mainly because of the high temperature sensitivity of the fuel cells. A long-term temperature stability of 0.01 °C is required.

Received: September 26, 2006

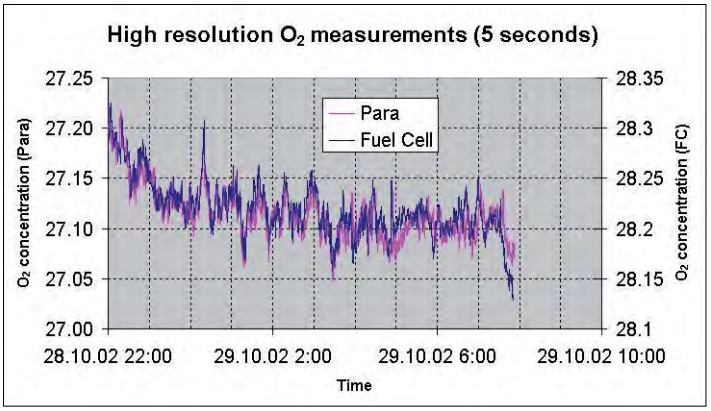
Reference

C.A.M. Brenninkmeijer, F. Slemr, C. Koeppel, D.S. Scharffe, M. Pupek, J. Lelieveld, P. Crutzen, A. Zahn, D. Sprung, H. Fischer, M. Hermann, M. Reichelt, J. Heintzenberg, H. Schlager, H. Ziereis, U. Schumann, B. Dix, U. Platt, R. Ebinghaus, B. Martinsson, P. Ciais, D. Filippi, M. Leuenberger, D. Oram, S. Penkett, P. van Velthoven, A. Waibel, *Eos Trans. AGU* **2005,** *86*(8), 77, 10.1029/2005EO080001.

Acknowlegements:
We would like to thank the financial support from the Gebert Ruf Stiftung.



Design of the fuel cell for oxygen monitoring (Figaro, USA, Inc.)



Comparison between the paramagnetic and fuel cell method

View of the fuel cell setup in an Airbus passenger airplane

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2006.854 CHIMIA **2006**, *60*, No. 12

Highlights of Analytical Chemistry in Switzerland

Label-Free Detection of Single Native Proteins: Ultimate Sensitivity and Convenience

Stefan Seeger*

*Correspondence: Prof. Dr. Stefan Seeger, University of Zurich, Institute of Physical Chemistry, CH-8057 Zürich
Tel.: +41 44 635 44 51, Fax: +41 44 635 68 13, E-Mail: sseeger@pci.unizh.ch

Keywords: Autofluorescence · β-Galactosidase · Protein · Single molecule spectroscopy

Proteins are the workhorses in nature. Cellular physiology, intercellular communication, and regulation depend on the diversity and the reliable activity of proteins.

Hence, the analysis of these processes has a strong impact in many areas, such as drug discovery, medical diagnosis, food processing, *etc.* Analytical chemistry methods, *e.g.* immunodiagnostics, proteomics, DNA diagnosis and many other fields are based on powerful and sensitive observation techniques. In order to achieve appropriate sensitivity, different labeling methods have been developed, *e.g.* labeling with enzymes, radio nuclides, and fluorescent dyes. However, the labeling procedure is usually time consuming, expensive and due to purification steps substance can be lost.

Direct and sensitive detection of proteins without any labeling, use of surfaces or other additives is therefore a challenging goal for analytical technology development. Recently, we could show for the first time the detection of a single native protein molecule without any labeling. For detection, a pulsed picosecond laser system is used to excite the native autofluorescence of β-galactosidase from *Escherichia coli* (*Ecβ Gal*) in a tiny volume of a few femtoliter (10^{-15} l) with a wavelength of only 266 nm. A time gate filters scattered light from delayed fluorescence emission of the protein to enhance the signal-to-noise ratio.

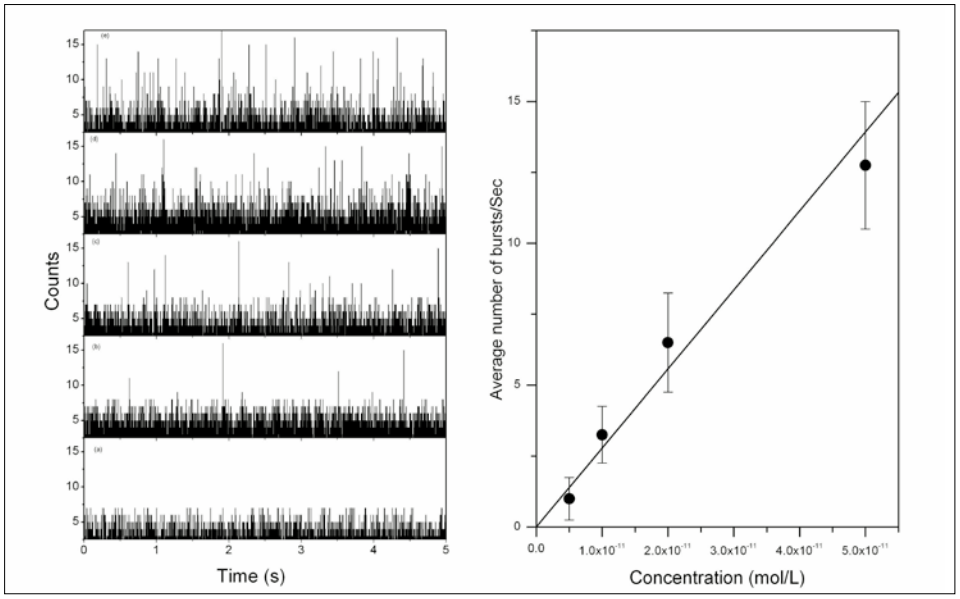
Although single molecule detection is not essential in many analytical tasks, the method offers high sensitivity in general. Low background signal, small sample volume, fast response time *etc.* are obvious advantages for the user.

Received: October 26, 2006

References

Q. Li, S. Seeger, *Anal. Chem.* **2006**, *78*, 2732.
Q. Li, T. Ruckstuhl, S. Seeger, *J. Phys. Chem. B* **2004**, *108*, 8324.

Experimental setup for the deep UV laser-based fluorescence lifetime microscopy system. In order to see the UV laser beam path, quartz tubes filled with fluorescence dye POPOP (1,4-bis(5-phenyl-2-oxazolyl)benzene) were placed into the beam path for visualization.



Left: The fluorescence photon bursts observed from (a) sodium phosphate buffer solution, (b) 5×10^{-12} mol/l, (c) 1×10^{-11} mol/l, (d) 2×10^{-11} mol/l, and (e) 5×10^{-11} mol/l Ecβ Gal solution, respectively. Data acquisition was performed at a speed of 1000 data points per second (1 ms integration time). Right: The dependence of number of fluorescence bursts on lower concentrations of Ecβ Gal solutions.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2007.48 CHIMIA **2007**, *61*, No. 1/2

Highlights of Analytical Chemistry in Switzerland

The Influence of Vine Harvesting Dates on the Quality of Pinot Noir Wines

Philippe Cuénat*

*Correspondence: Dr. P. Cuénat, Station de recherche, Agroscope Changins-Wädenswil ACW, Route de Duillier, case postale 1012, CH-1260 Nyon 1
Tel.: +41 22 363 43 37, Fax: +41 22 362 13 25, E-Mail: philippe.cuenat@acw.admin.ch

Keywords: Anthocyanins · Grape ripening · Tannins · Vine harvesting · Wine bouquet

The date of the vine harvest has a notable influence on the quality and style of wine produced. The wine-making process in red wines is more complex than that of white wines. The level of tannin maturity plays a vital role in determining the sensorial quality of the wine. For a given grape variety and vineyard, vine harvesting at an early date will give a dry wine, with green tannins and a more or less herbal aromatic character. On the other hand, although a later harvesting date produces a more full-bodied, smoother wine, the unique grape fruit quality is masked and the resulting aroma penalised. The choice of date of vine harvesting is therefore the result of a compromise between these various properties and will depend, in particular, on the style of wine that the wine-maker wishes to produce.

Overall grape maturity is difficult to capture since it depends on several criteria whose discriminating factors differ accordingly to the desired type of wine. Sugar content (reflected by density or 'Oechsle'), together with acidity, is the most widely used parameter. As far as red wines are concerned, phenol compounds and especially the quality of tannin in grape skins and seeds should be equally taken into consideration. The study of their development during the ripening period is therefore of considerable interest. During the time of ripening, the content of anthocyanins increases, reaches a peak and then falls off again. Tannins behave differently as their content decreases in grape skins and seeds. The decrease in fruit skins is small. The tannin decrease in seeds, however, is much greater and non-linear.

The determination of anthocyanins involved total reaction of free anthocyanins in the presence of SO_2 to form colourless bislufite compounds. The determination of tannins (proanthocyanidins) is based on hot oxidative depolymerisation in a mineral acid environment of proanthocyanidins to form anthocyanidins with a red absorbance reading at 550 nm.

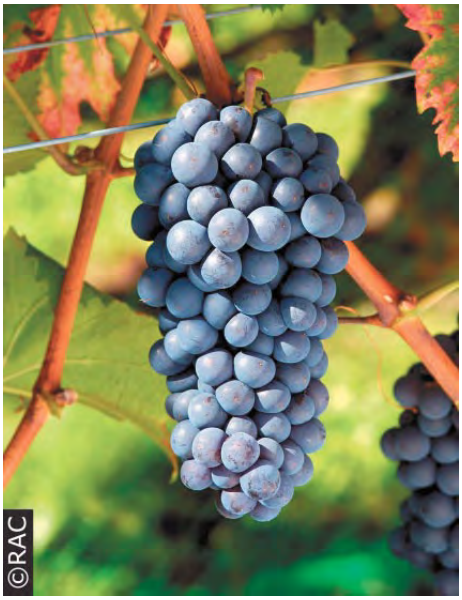
The best wines are obtained from grapes harvested about ten days after the peak of anthocyanin content has been reached. In spite of occasionally higher alcohol content and a less pronounced bouquet, the ample and smooth tannin content confers silkiness and harmony to these wines. These findings enable wine-producers to integrate all the influencing parameters and serve as a guideline in choosing an optimum vine harvesting date, according to the stage of grape growth and the type of wine required.

Received: December 18, 2006

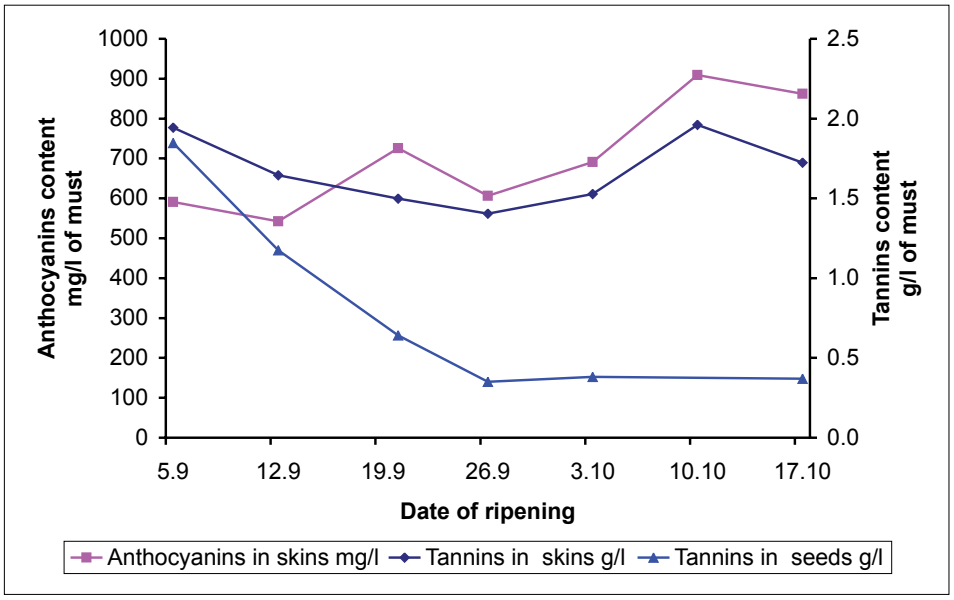
References

P. Cuénat, C.-A. Brégy, E. Zuffery, *Revue Suisse Vitic. Arboric. Hortic.*, in press.

A.M. Jordao , J.M. Ricardo-Da-Sila, O. Laureano, *Am. J. Enol. Vitic.* **2001**, *52*, 230.



A ripe Pinot Noir grape (copyright: *acw.admin.ch*)



Evolution of the content of anthocyanins and tannins in grape skins and seeds during maturation (Pinot noir, Valais 2005)

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, CH-9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2007.111 CHIMIA **2007**, *61*, No. 3

Highlights of Analytical Chemistry in Switzerland

Spatially Resolved Plant Physiological Analysis Using LA-HR-ICP-MS

Andrea Ulrich*[a], Timothée Barrelet[b], and Urs Krähenbühl[c]

*Correspondence: Dr. A. Ulrich[a], Tel.: +41 44 823 46 61, Fax: +41 44 823 46 14, E-Mail: andrea.ulrich@empa.ch
[a]EMPA – Swiss Federal Laboratories for Material Testing and Research, Überlandstrasse 129, CH-8600 Dübendorf; [b]Federal Office of Public Health (FOPH), CH-3003 Bern; [c]University of Bern, Department for Chemistry and Biochemistry, Freiestrasse 3, CH-3012 Bern

Keywords: Elemental distribution in trees · Laser ablation · Norway spruce · Plasma mass spectrometry · Seasonal profiles · Tree rings

Investigations of elemental distribution in trees are interesting in plant physiological and environmental research. Seasonal element variations within single tree rings would provide important information on metabolism studies but they have not been accessible so far. Thus, a direct micro-analytical method involving laser ablation (LA) coupled to high-resolution double-focusing magnetic sector field inductively coupled plasma mass spectrometry (HR-ICP-MS) was developed. Particularly challenging aspects in method development were the high background levels of certain elements and the lack of appropriate calibration standards.[1,2]

Seasonal element profiles of macronutrients in Norway spruce trees from different sampling sites, altitudes and environmental conditions could be established for the first time. The method allows the measurement of low concentrations even in narrow year rings. Table 1 shows typical element concentrations. Table 2 presents wood density and seasonal profiles of sulphur, phosphorus and potassium in a tree in Düdingen (CH). Depending on the tree ring width, the number of laser spots per ring varied between four and eight. For discussion purposes, each ring was divided in four distinct zones commonly used in dendrology: early earlywood (EEW), late earlywood (LEW), early latewood (ELW) and late latewood (LLW).

Elements	Literature Values [mg/kg]				Frieswil 46° 58' 60" N, 7° 16' 0" O	Düdingen 46° 51' 0" N, 7° 12' 0" O	St. Moritz 46° 29' 40" N, 9° 50' 45" O
	Average	Median	Min	Max			
S	344	79	56	896	24–80	34–72	50–93
P	31	38	9.2	47			
K	810	390	15	2570	269–566	169–430	266–884
Ca	855	809	100	1800	458–1406	433–1085	622–957
Mg	113	113	95	131	253–357	98–356	237–578
Mn	159	65	32	566	88–386	47–248	
Zn	18	12	6.4	48	5–17	2–18	6–12

Table 1. Typical element content in Norway spruce stem-wood [mg/kg]. Background picture: Norway spruce.

The sulphur profile displayed seasonal variations with decreasing contents in LEW and ELW, which leads to the assumption that stem sulphur is used for seasonal growth. When accrescence stops in autumn, sulphur reserves are stored in preparation for next year's growth. Nabais *et al.* support this seasonal hypothesis, since methionine in tree sap was found to increase in March until July and decrease in August.[3]

A seasonal pattern was also found for phosphorus. This contradicts the hypothesis of a constant supply by mycorrhizal fungi and implies that reserves are stored towards the end of growing season for use the following spring. The linear relationship between P and S underlines a strong biochemical coupling of both elements.

Other macronutrients like potassium show different profiles. K is of particular importance in needles and probably mostly needed during the growing season, which explains the decrease from EEW to LEW and a higher accumulation in LLW. These seasonal profiles reveal new aspects of Norway spruce metabolism.

Received: January 25, 2007

References

[1] T. Barrelet, A. Ulrich, H. Rennenberg, U. Krähenbühl, *Plant Biology* **2006**, *8*, 462.
[2] T. Barrelet, 'Norway Spruce as an Environmental Archive for Sulphur Dioxide', Inauguraldissertation der phil.-nat. Fakultät der Universität Bern, 26.1.**2006**.
[3] C. Nabais *et al.*, in 'Plant Nutrition for Sustainable Food Production and Environment', Eds. T. Ando *et al.*, Kluwer, Dordrecht **1997**, p. 33–35.

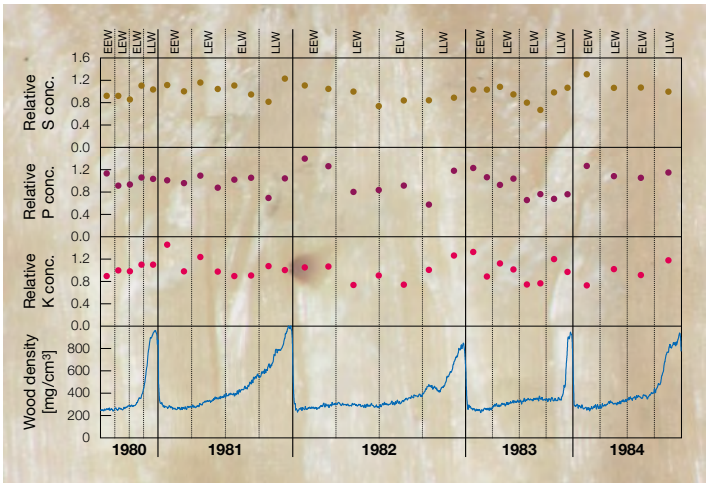


Table 2. Seasonal sulphur, phosphorus and potassium profiles and wood density in single tree rings of a Norway spruce tree in Düdingen. Background picture: Laser spot in wood with a typical spot size of about 100 µm.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2007.199 CHIMIA **2007**, *61*, No. 4

Highlights of Analytical Chemistry in Switzerland

Highlights of Analytical Chemistry in Switzerland

Does A.M. Have a Tumour in the Pancreas?

Ursula Gutteck-Amsler and Katharina M. Rentsch*

*Correspondence: PD Dr. K.M. Rentsch, Institute for Clinical Chemistry, University Hospital Zurich, CH-8091 Zürich
Tel.: +41 44 255 22 90, Fax: +41 44 255 45 90, E-Mail: rentsch@ikc.uzh.ch

Keywords: APCI · Blood analysis · HPLC-MS ·Hypoglycaemia · Sulfonylurea drugs

The aim of the clinical toxicological laboratory is to identify substances which might harm the patient. This may be the elucidation of an acute intoxication due to the intake of an overdose, the clarification of a chronic toxic process or the verification of an intake of substances which should not be taken by a patient.

Patients with recurring hypoglycaemia either have a deregulation in glucose metabolism, a tumour in the pancreas or take antidiabetic drugs without having diabetes.

A.M. was admitted to the hospital with recurring hypoglycaemic events in order to clarify the symptoms. One of the first tests performed is the fasting test, which does not allow the patient to eat during max. 72 h in order to evaluate the regulation of glucose metabolism. Regularly blood samples are taken to measure glucose concentration, different hormone levels, and in order to exclude the intake of antidiabetic drugs, a screening for these drugs should be offered. Thus A.M. had to fast and at the beginning and the end of the fasting test a blood sample was taken for the quantification of the antidiabetic drugs.

The laboratory therefore needs a fast, specific and sensitive analytical method for the quantitative determination of sulfonylurea drugs.

Due to their chemical structure the commonly used GC-MS methods used in clinical toxicological laboratories cannot be applied for the quantification of sulfonylurea drugs. Consequently, an HPLC-MS method has been developed using atmospheric pressure chemical ionisation and a chromatographic separation on a C18 column with ammonium carbonate buffer and acetonitrile as mobile phase. The plasma samples are extracted using solid-phase extraction. The subsequent HPLC-MS separation can identify and quantify the drugs in question due to their retention times and molecular masses.

In the serum of A.M. the antidiabetic drug glibenclamide was detected, which was intended for use by her husband only. She has no pancreatic tumour.

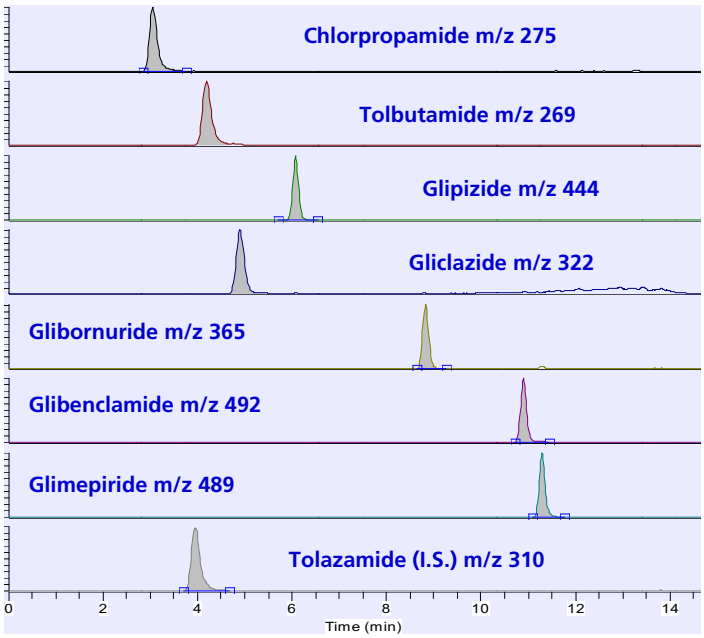
Applying this method on samples from patients with recurring hypoglycaemia helps to reduce costs for invasive diagnostic tools, which are necessary to look for tumours in the pancreas.

Received: February 16, 2007

Reference

K. M. Rentsch, U. Gutteck, A. von Eckardstein, *Ther. Drug Monit.* **2003**, *25*, 501.

Blood samples being transferred to the centrifuge



HPLC-MS chromatograms showing the separation of the seven sulfonylurea drugs available in Switzerland

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2007.283 CHIMIA **2007**, *61*, No. 1/2

Highlights of Analytical Chemistry in Switzerland

Increase of ^{129}I in the European Environment

Herbert Reithmeier[a], Margit Schwikowski*[b], Vitali Lazarev[a], Werner Rühm[c], Heinz W. Gäggeler[bd], Eckehart Nolte[a†]

*Correspondence: Dr. M. Schwikowski[b], Tel. +41 56 310 41 10, Fax: +41 56 310 44 35, E-Mail: margit.schwikowski@psi.ch

[a]Physics Departments E15, TU München, D-85748 Garching, Germany; [b]Laboratory for Radiochemistry and Environmental Chemistry, Paul Scherrer Institute, CH-5232 Villigen; [c]Institute of Radiobiology, LMU München, D-80336 Munich, Germany; [d]Departement for Chemistry and Biochemistry, University of Bern, CH-3012 Bern

[†]Deceased

Keywords: Accelerator mass spectrometry · Ice core · ^{129}Iodine · Nuclear fuel processing

^{129}I is a long-lived (half-life = 15.7 Ma) radionuclide with a natural abundance of ^{129}I/^{127}I of about 6.5×10^{-13}. Its main sources are the spontaneous fission of uranium in the lithosphere and the interaction of cosmic ray particles with xenon in the upper atmosphere. The prenuclear abundance has been drastically enhanced due to anthropogenic emissions from atmospheric nuclear weapon tests and nuclear fuel reprocessing. In Europe nuclear fuel processing plants have been operated in Sellafield (Great Britain), Marcoule, and La Hague (both France). While reliable data on ^{129}I releases from La Hague exist for the whole period of operation, less is known about contributions from Sellafield and Marcoule. Emissions of the latter two were estimated based on the amount of fuel reprocessed, indicating that Marcoule was the major European source of airborne ^{129}I, contributing about 45% to the total gaseous releases.

The estimated total emissions were compared with the ^{129}I deposition fluxes for the time period 1970–2002, obtained from the analysis of an ice core from the Fiescherhorn glacier, Swiss Alps (46°33'N, 8°04'E, 3900 m asl). The temporal evolution of the ^{129}I deposition agrees well with the total ^{129}I releases into the atmosphere from the European reprocessing facilities and from atmospheric nuclear weapons tests, supporting our estimated release rates. ^{129}I was analyzed in the ice samples by means of accelerator mass spectrometry at the Maier-Leibnitz laboratory in Garching, after extraction and purification of total iodine using a carbon tetrachloride method and precipitation as silver iodide.

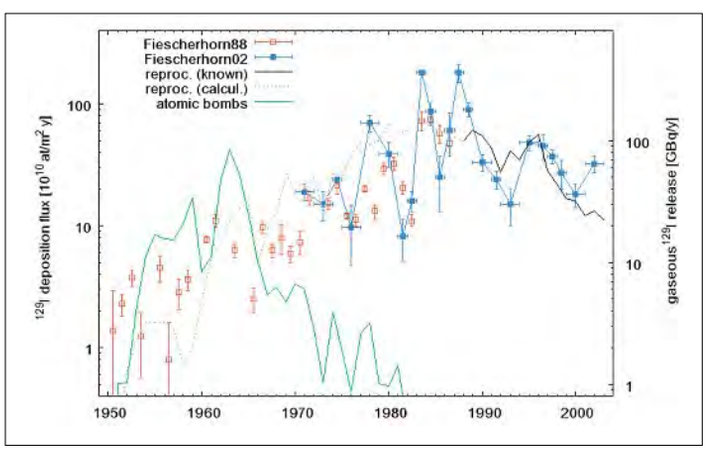
Received: March 9, 2007

References

H. Reithmeier, V. Lazarev, W. Rühm, M. Schwikowski, H. W. Gäggeler, E. Nolte, *Environ. Sci. Technol*. **2006**, *40*, 5891.

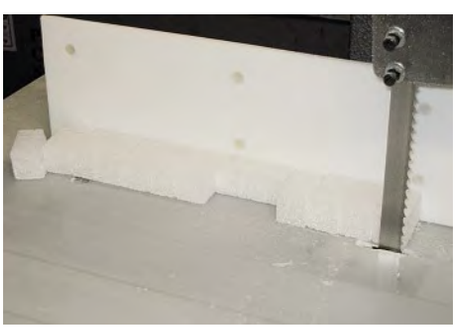
M. J. M. Wagner, B. Dittrich-Hannen, H.-A. Synal, M. Suter, U. Schotterer, *Nucl. Instrum. Methods. Phys. Res. Sect. B* **1996**, *113*, 490.

H. Reithmeier, V. Lazarev, F. Kubo, W. Rühm, E. Nolte, *Nucl. Instrum. Methods. Phys. Res. Sect. B* **2005**, *239*, 273.



^{129}I deposition fluxes determined at the Fiescherhorn glacier (■), and those based on data published by Wagner *et al.* 1996 (□). For this comparison, the latter data were scaled with the ratio of the mean net accumulation rates of the period 1950–1974. In addition, airborne emissions of ^{129}I from the European reprocessing facilities (black lines) and the total ^{129}I which was deposited in the northern hemisphere as a result of the atmospheric atomic bomb explosions (green line) are shown. ^{129}I releases before 1988, which had to be estimated, are dashed.

View of the Fiescherhorn glacier from the Northeast with ice core drilling site (photo: A. Schwerzmann)



Ice core sample cutting with a band saw (photo: A. Ciric).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2007.387 CHIMIA **2007**, *61*, No. 6

Highlights of Analytical Chemistry in Switzerland

Automated Target Preparation for Gene Expression: Oligonucleotide Microarrays

Frédéric Raymond*, Sylviane Metairon, and Martin Kussmann

*Correspondence: F. Raymond, Nestlé Research Center, Vers-chez-les-Blanc, CH-1000 Lausanne 26

Tel.: +41 21 785 86 11, Fax: +41 21 785 94 86, E-Mail: frederic.raymond@rdls.nestle.com

Keywords: Automation · Gene expression analysis · Microarray target preparation · Standardization

DNA microarray technology allows for massively paralleled monitoring of gene expression, as well as the study of gene regulation and gene interactions at a global scale. Despite a ten-year history of DNA microarray analysis, the technology still suffers from limitations such as inter-experiment variability. While technical differences may influence gene expression results, standardized procedures, high-quality microarrays, and appropriate data collection and transformation are able to generate reproducible and comparable results across experimental replicates and even laboratories. This is especially the case if a common platform and a joint set of procedures are used.

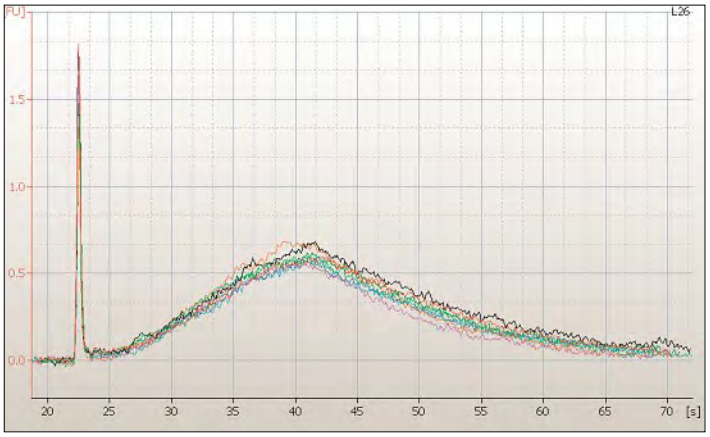
Therefore, standardization of sample preparation and inter-study consistency has to be improved. We have equipped our laboratory with a Hamilton Microlab Star robot programmed to fulfill all requirements of the microarray target preparation. The automated method follows in principle the manual procedure regarding enzymatic reactions, but with substantial technical adaptations for the robot and the external devices. Thus, we implemented a complete method, from the total RNA starting material to the final hybridization mix ready for chip application.

We have examined the reproducibility and quality of the automated RNA target preparation. Our data illustrate good RNA quality and high reproducibility of the automatic RNA target preparation. The variations observed for cRNA yields, cRNA quality, and hybridization intensities across automated target preparations are so low that we suggest the implementation of our robotic method and equipment for microarray analyses in general and on a routine basis. Most importantly, we show that the technical inter-experiment variation is less pronounced than with manually prepared samples. **The low variability and the high reproducibility result in a standardized and fully integrated protocol for microarray experiments.**

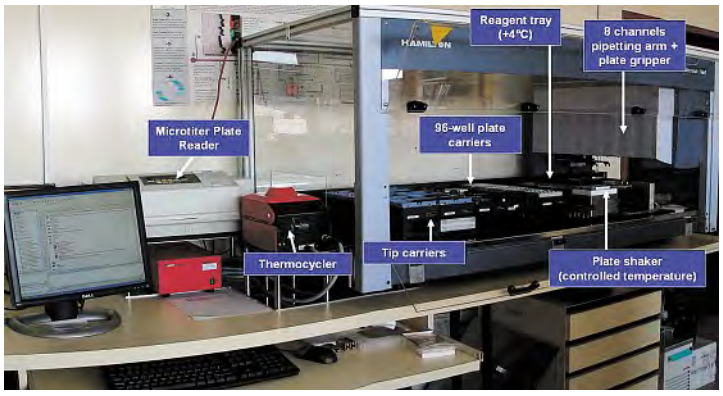
Received: March 22, 2007

Reference

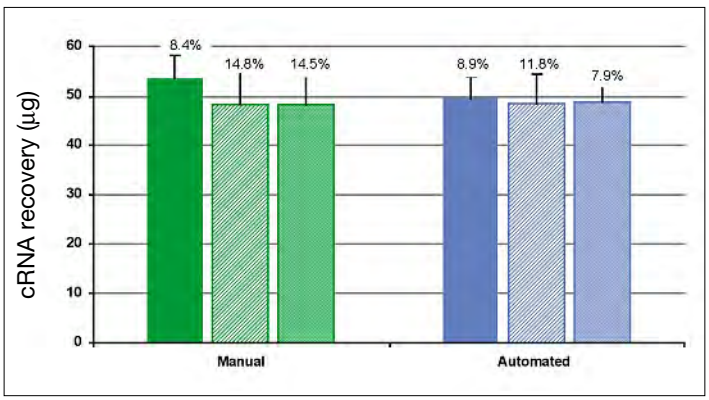
F. Raymond, S. Metairon, R. Borner, M. Hofmann, M. Kussmann, *Anal. Chem.* **2006**, *78*, 6299.



Synthesis of eight cRNA from the same mouse liver total RNA. Electropherogram view of Bioanalyser results. The automated target preparation produces cRNA with good quality (peak > 34 sec. cRNA fragment size ≈ 1800 bp).



The automation system includes the robotic platform for sample, enzyme, and reaction management, the thermocycler for incubations, and the microtiter plate reader for RNA quantification. The whole set-up is integrated and controlled by the Vector software.



Target preparation. Three series of eight identical mouse RNA samples (5 µg) were processed both manually and automatically. While both methods show comparable yields, the automated procedure induces a reduced variability across target preparations.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2007.532 CHIMIA **2007**, *61*, No. 7/8

Highlights of Analytical Chemistry in Switzerland

Are Lake Thun and Lake Brienz Contaminated with Explosive Residues?

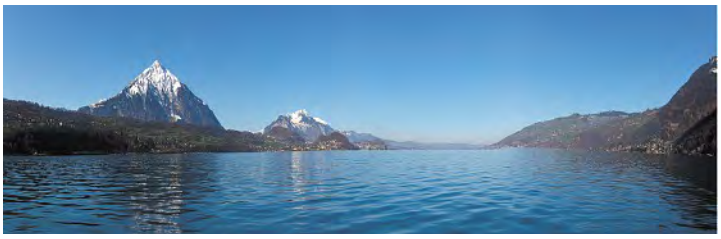
Jean-Daniel Berset*, Ueli Ochsenbein, and Markus Zeh

*Correspondence: J. D. Berset, Water and Soil Protection Laboratory of the Canton of Bern (GBL), Schermenweg 11, CH-3014 Bern
Tel.: +41 31 634 23 83, Fax: +41 31 634 23 96, E-Mail: jean-daniel.berset@bve.be.ch

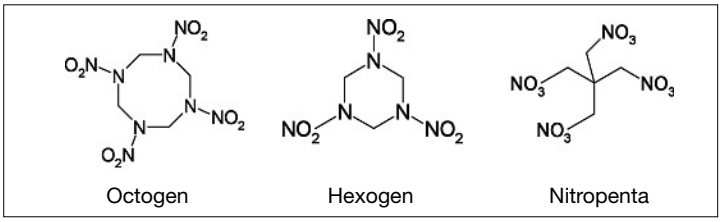
Keywords: Ammunition · External sources · Gonad alterations · HMX · LC/MS/MS · PETN · RDX · Surface waters · White fish

Between 1920 and 1963 roughly 4600 tonnes of ammunition, containing mainly TNT as explosive, were disposed in Lake Thun. Smaller amounts (280 tonnes) were dumped in Lake Brienz just after World War II. In 2000, fishermen reported the occurrence of a large number of white fish with morphologically altered gonads in Lake Thun. Could this ammunition be the cause of these phenomena? In a preliminary study carried out by a research group of Agroscope Wädenswil, no explosive residues above the limit of quantification were found in either the lake water or the sediments. In 2006, the GBL acquired a highly sensitive LC-tandem mass spectrometer (API 5000) allowing detection at the lowest ng/l levels. Thus a monitoring program was performed. Grab samples were taken at different time periods and depths of Lakes Thun and Brienz as well as of several tributaries. Additionally, several hot spots and environmental blank samples were analyzed. Samples were enriched using solid phase extraction (SPE), injected into the LC-MS/MS, and identified and quantified using the MRM mode.

Much to our surprise, traces of three explosives could be clearly identified in both lakes: Octogen (HMX), Hexogen (RDX) and Nitropenta (PETN) at concentrations of 0.1–0.4 ng/l. No concentration gradients of these explosive residues could be observed in the different lake profiles indicating a homogeneous distribution. Of the tributaries analyzed, only the Kander and Aare rivers contained minute amounts of at least one of the explosives found in the lake. The analysis of environmental blanks (*e.g.* the Oeschinensee) revealed no traces of explosives. Hot spot samples, *e.g.* from the ammunition dump site Steingletscher-Susten, showed concentrations of several explosives such as TNT and its mono- and diamino metabolites, HMX, RDX and PETN at µg/l levels. These results indicate that external sources such as military activities and ammunition dump sites close to water might play an important role in the contamination of the lakes. It must be emphasized, however, that the concentrations of explosives found in Lake Thun and Brienz are far below health-based drinking water guide values as suggested by German authorities and therefore are not expected to have a negative impact on lake water quality. **Such low concentrations of explosives do not seem to be responsible for the gonad alterations in white fish. This statement is supported by the fact that the specific gonad changes observed exclusively in Lake Thun are not found in Lake Brienz which also contains traces of explosives.**



Lake Thun: a major tourist attraction in the Bernese Oberland (picture: GBL, M. Zeh)



Acknowledgements

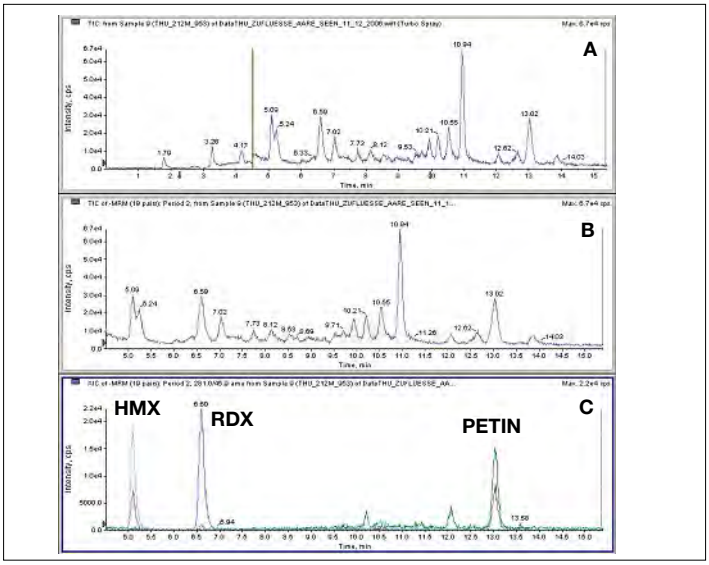
This project is supported by Armasuisse and the GSA (Amt für Gewässerschutz und Abfallwirtschaft) Bern. We thank Kim Hays for reviewing the manuscript.

Received: March 28, 2007

References

Chimia **2004**, *60*, issue 6 on Explosives, 351–413.

J. van Stuijvenberg, Geologische Beratungen Schenker–Korner GmbH, 'Gefährdungsabschätzung zu militärischen Munitionsversenkungen in Schweizer Seen', Ostermundigen & Meggen, **2005**.



LC/MS/MS run of a water sample taken at a depth of 212 m (Lake Thun): A) TIC, B) TIC 2nd period (ESI), C) EIC: 2nd period showing the presence of HMX, RDX and PETN

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2007.588 CHIMIA **2007**, *61*, No. 9

Highlights of Analytical Chemistry in Switzerland

Spider Venom: A Rich Source of Highly Active Molecules

Lucia Kuhn-Nentwig*[a], Helmut Kubista[b], and Wolfgang Nentwig[a]

*Correspondence: Dr. L. Kuhn-Nentwig[a], Tel: +41 31 631 45 32, Fax: +41 31 631 48 88, E-Mail: lucia.kuhn@zos.unibe.ch
[a]Zoological Institute, University of Bern, CH-3012 Bern; [b]Center for Biomolecular Medicine & Pharmacology, Institute of Pharmacology, Medical University of Vienna, A-1090 Vienna, Austria

Keywords: Antimicrobial peptides · Spider venoms · Toxic polypeptides · Voltage-gated calcium channel blocker

Venoms of toxic animals contain a plethora of pharmacologically active molecules. Although only few of these molecules have been identified, several of the already well-characterised toxins are meanwhile being used in wide areas of cell biology as 'chemical scalpels' to dissect molecular mechanisms.

The Central American spider *Cupiennius salei* rapidly anaesthetises its prey by injecting venom which acts through complex and synergistic interactions of its components. Besides several proteins and low molecular mass compounds, more than fifty different polypeptides have been identified. These polypeptides are the main focus of our research, which to date has revealed interesting structural and functional information as well as indications for potential applications: Cupiennins (2–4 kDa) are cationic linear peptides adopting an amphipathic α-helical structure in membrane environments. In submicromolar concentrations they act bactericidally as well as cytolytically by permeating membranes in a non receptor-mediated manner. In the light of the rapid increase of multidrug resistant bacteria, the cupiennins may help as tools to analyse the general cytolytic membrane action as well as the molecular prerequisites for high antimicrobial selectivity.

CSTX-1 (the ***C**upiennius **s**alei* **t**oxin-1, 8 kDa), the main toxic acting peptide in the venom of *C. salei*, contains the cystine-knot motif, a structural characteristic of several ion channel blockers. Indeed, functional studies have revealed that CSTX-1 inhibits insect calcium channels. Thus the paralysis of prey animals by *C. salei* venom appears to be largely due to an inhibition of Ca^{2+} influx into nerve and/or muscle cells. Interestingly, due to its special structure, this peptide enables a high affinity interaction with a subtype of L-type calcium channels expressed in mammalian neurons. Up to now, subtypes of L-type calcium channels have been clearly identified by molecular biology techniques but it has not yet been possible to isolate them by pharmacological means. **With CSTX-1, a new pharmacological tool is now available that may aid in dissecting the structure and function of L-type calcium channel subtypes.**

Acknowledgements

We thank the Swiss National Science Foundation for their longstanding financial support, the Austrian Science Fund, and especially U. Kämpfer, J. Schaller and S. Schürch (Analytical Research and Services, Department of Chemistry and Biochemistry, University of Bern) for their long-term collaboration.

June 30, 2007

References

L. Kuhn-Nentwig, J. Schaller, W. Nentwig, *Toxicon* **2004**, *43*, 543.
H. Kubista, R. Mafra, Y. Chong, G. Nicholson, P. Beirão, J. Cruz, S. Boehm, W. Nentwig, L. Kuhn-Nentwig, *Neuropharmacol.* **2007**, *52*, 1650.

An adult female *Cupiennius salei* sits in the axilla of a plant, holding its cocoon, which can contain up to 1500 eggs. In the upper part of the illustration the amino acid sequence of cupiennin 1a is given and structurally important lysines are highlighted with a coloured box. The amino acid sequence as well as the disulfide bridge arrangement (cysteines are highlighted with a coloured box) of CSTX-1 is presented at the bottom of the illustration.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2007.671 CHIMIA **2007**, *61*, No. 10

Highlights of Analytical Chemistry in Switzerland

Metabolic Profiling in Pharmaceutical Drug Discovery – Robust and Automated Analysis of Metabonomic Data Sets

Götz Schlotterbeck*[a], Frank Dieterle[b], Alfred Ross[a], and Hans Senn[a]

*Correspondence: Dr. G. Schlotterbeck[a], Tel.: +41 61 688 07 52, Fax: +41 61 688 74 08, E-Mail: goetz.schlotterbeck@roche.com
[a]F. Hoffmann-La Roche, Pharmaceutical Division, PRBD-E, CH-4070 Basel
[b]Novartis Pharma AG, Exploratory Development, CH-4002 Basel

Keywords: Biofluid · Mass spectrometry · Metabolic profiling · Metabolite projection analysis · Metabolomics · Metabonomics · NMR spectroscopy

Metabolic profiling of biofluids or tissues, also known as metabonomics or metabolomics is a platform to investigate the metabolic state of a biological system. Metabonomics is applied in nutrition, agricultural research and more widely in pharmaceutical preclinical and clinical settings for safety assessment of drug candidates, *e.g.* relating to nephrotoxicity, hepatotoxicity, phospholipidosis or peroxisome proliferation.

Metabonomics involves the determination of changes in the concentration levels of low molecular weight endogenous metabolites in biological samples resulting from physiological stimuli or genetic modification. The aim of metabolic profiling is to extract latent biochemical information that is of diagnostic and prognostic value and which reflects 'actual' biological events in the network of metabolic pathways, as opposed to the potential for such events reflected by DNA or mRNA. Thus metabolomics provides a complementary aspect and useful connection between other '-omics' platforms (transcriptomics/proteomics) and the actual metabolic state and tissue histology.

The analytical technologies typically include nuclear magnetic resonance (NMR) and mass spectroscopy (MS) in combination with a separation method such as gas or liquid chromatography (GC, LC). NMR and MS complement each other in capturing metabolic data, both in terms of sensitivity, ability for quantification, and potential for structure elucidation of unknowns. Due to the complexity of spectra of biofluids or tissues, statistical and multivariate data analysis tools are used to identify and quantify significant changes of metabolites.

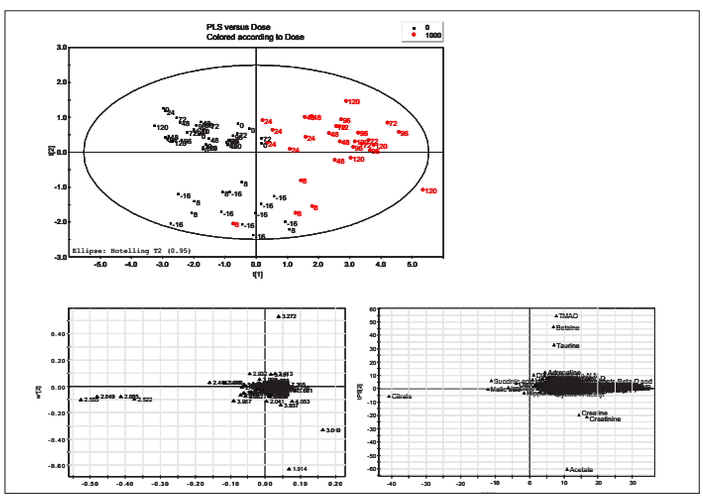
Recently, we introduced metabolite projection analysis (MPA), a fast and automated way supporting identification of significantly changed metabolites in a set of NMR spectra taken on body fluids of treated and control group individuals.

Fast and robust preprocessing of complex metabolic profiling data for multivariate data analysis can now be achieved. Significantly changed metabolites in metabonomics data sets can be easily identified and assigned to metabolites without the need to inspect a high number of NMR spectra. Thus metabonomics data sets can now be analyzed easier, faster, more reliable and more accurate.

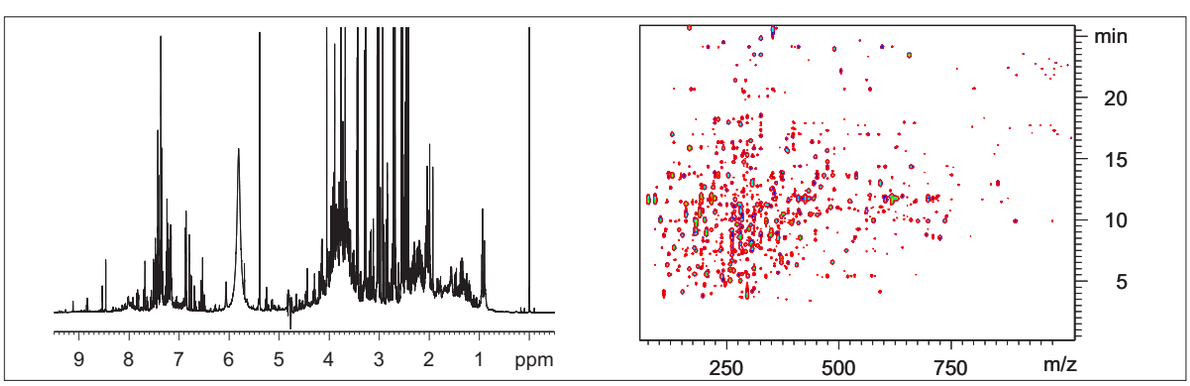
Received: July 31, 2007

References

F. Dieterle, A. Ross, G. Schlotterbeck, H. Senn, *Anal. Chem.* **2006**, *78*, 3551.
G. Schlotterbeck, A. Ross, F. Dieterle, H. Senn, *Pharmacogenomics* **2006**, *7*, 1055.



Score plot of a Projection to Latent Structures (PLS) model of rat urine samples colored by dose level (top). In the standard weights plot (bottom left), the class-separating variables are labeled with chemical shifts. The corresponding score plot of MPA is shown at the bottom right. Here, the read out are significantly changed metabolites rather than only chemical shifts.



^{1}H NMR spectrum of rat urine recorded at 600 MHz (left) and LC-MS profile (positive mode) of rat urine (right)

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2007.743 CHIMIA **2007**, *61*, No. 11

Highlights of Analytical Chemistry in Switzerland

Pigment Analysis on the 16th Century St. Gallen Globe

Kilian Anheuser[a], Beat Gnädinger[b], Vera Hubert*[c], Katja Hunger[c], Daniel Minder[d], Gaby Petrak[c], Martina Rohrbach[b], Geneviève Teoh[c], Robert Tobler[c], and Marie Wörle[c]

*Correspondence: Dr. Vera Hubert[c], Tel.: +41 44 762 13 92, Fax: +41 44 762 13 61, E-Mail: vera.hubert@slm.admin.ch
[a]Musée d'art et d'histoire, rue Charles-Galland 2, 1211 Genève 3
[b]Staatsarchiv des Kantons Zürich, Winterthurerstrasse 170, 8057 Zürich
[c]Collections Centre, Swiss National Museums, Lindenmoosstrasse 1, 8910 Affoltern am Albis
[d]Zeltweg 42, 8032 Zürich

Keywords: Cultural heritage · Non-destructive analysis · Pigments · St. Gallen globe · X-ray fluorescence

In 1712, the Zurich authorities removed a collection of precious manuscripts from the St. Gallen monastery, including a terrestrial and celestial globe of c. 1570, to keep them in their own city. As part of a settlement of the ensuing centuries-old dispute between the cantons of Zurich and St. Gallen, the parties agreed in 2006 that an identical copy of the richly painted globe should be created for future display in St. Gallen whilst the original should remain in Zurich.

This decision presented a welcome opportunity to investigate the materials and techniques used for the creation of this rare object. Analysis of the pigments on the painted surfaces of the globe formed an essential part of the research. In the analysis of valuable cultural heritage, the choice of techniques is usually restricted to those with minimal interference with the integrity of the object. In this particular case, taking samples for analysis had been ruled out.

Many traditional mineral pigments contain characteristic chemical elements, permitting their completely non-destructive identification *in situ* by qualitative X-ray fluorescence spectrometry. A portable Bruker AXS Artax spectrometer was used because conservation and security concerns did not allow the large, heavy and partially disassembled globe to be moved from the Collections Centre of the Swiss National Museums to an external laboratory. A 0.65 mm diameter collimator permitted the analysis of small painted details. Unlike most other XRF spectrometers, this particular instrument, designed specifically for use in museums, can be set up directly in front of an object, without using a vacuum chamber. A red laser points through the collimator towards the object and indicates precisely the spot to be analysed.

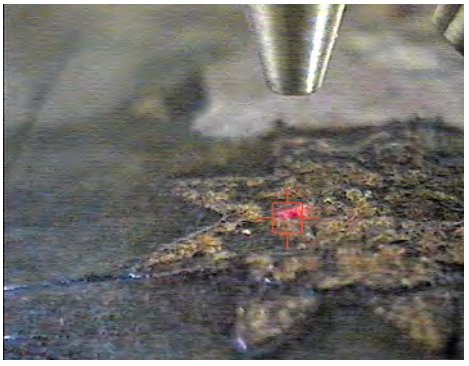
A series of analyses of the different colours, painted ornaments and letters led to the identification of the historic pigments used.

With the help of the results of this investigation, a true-to-the-original replica will be created, displaying the 'old' colours in a fresh appearance – as the globe most probably looked in 1570.

Received: September 20, 2007

Setting up the XRF spectrometer for analysis

The St. Gallen globe at the Swiss National Museum, Zurich



Focussing the X-ray beam on one of the gilded stars

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2007.843 CHIMIA **2007**, *61*, No. 12

Highlights of Analytical Chemistry in Switzerland

Direct Analysis of Living Objects by Extractive Electrospray Ionization Mass Spectrometry

Huanwen Chen and Renato Zenobi*

**Correspondence:* Prof. Dr. R. Zenobi, Department of Chemistry and Applied Biosciences, ETH Zürich, HCI E 329, CH-8093 Zürich
Tel.: +41 44 632 43 76, Fax: +41 44 632 12 92, E-Mail: zenobi@org.chem.ethz.ch

Keywords: Breath analysis · EESI · Extractive electrospray ionization mass spectrometry · Food analysis · Non-invasive analytical techniques · Screening

50 tons of spoiled meat discovered in Bavaria – authorities need to screen hundreds of warehouses! Spinach contaminated with *E. coli* leaves 200 people sick in the USA – rapid screening needed for suspected food! Epidemic – thousands of patients need to be rapidly screened in emergencies… What do these and similar headlines have in common? They all challenge modern analytical science in terms of sensitivity, specificity, speed, and especially throughput.

It appears that extractive electrospray ionization mass spectrometry (EESI) provides a viable solution to these and other challenges. EESI is a variant of electrospray ionization (ESI). In ESI, the sample is present in solution and is nebulized and ionized under the influence of high voltage and with the aid of a desolvation gas. Mass analysis is performed with a mass spectrometer having an atmospheric pressure ionization inlet; many different instruments for this purpose are available commercially. In EESI, the ion formation is turned 'upside down': a pure solution – usually water, which is sometimes acidified – is sprayed, and the sample, in the form of a gas, an aerosol, a volatilized liquid, or material desorbed from a solid, enters the charged mist through the desolvation gas line. The sample molecules get efficiently ionized by charge transfer processes and can be analyzed in a standard fashion.

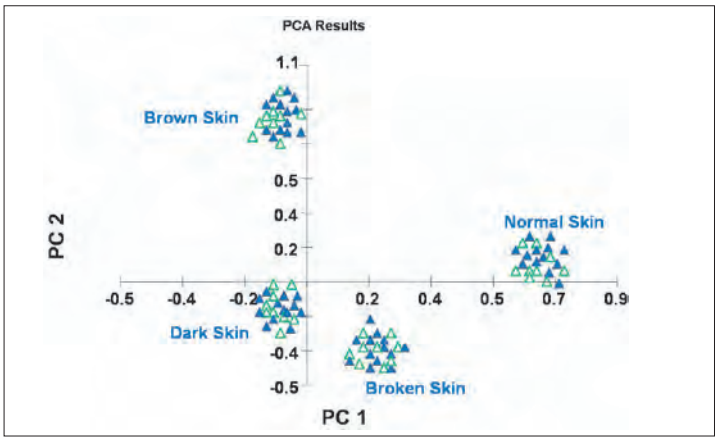
The power of EESI has been demonstrated in a number of practical applications: i) The rapid *in vivo* fingerprinting of breath without sample pre-treatment. Metabolic dynamics was promptly reflected in the EESI data.[1] ii) Non-invasive investigation of the maturity of fruit with high sensitivity, specificity, and high throughput. EESI fingerprinting of compounds released from various fruits yielded information on their ripening stages; the data were successfully differentiated by principal component analysis.[2] iii) Direct, on-line analysis of biological matter such as skin, meat (even in the frozen state), and vegetables by directing a jet of N_2 gas onto the sample followed by EESI-MS of the compounds liberated.[3]

Currently, unsolved questions concern the nature of the charging mechanism, whether nonvolatile compounds can indeed be sampled and analyzed, and the identity of many of the signals showing up in the mass spectra (to be investigated by tandem-MS). **This novel analytical strategy represents a 'green' procedure for fast chemical characterization of virtually any biological object. It will have many applications in areas such as metabolic fingerprinting, homeland security, food safety, and medical diagnostics.**

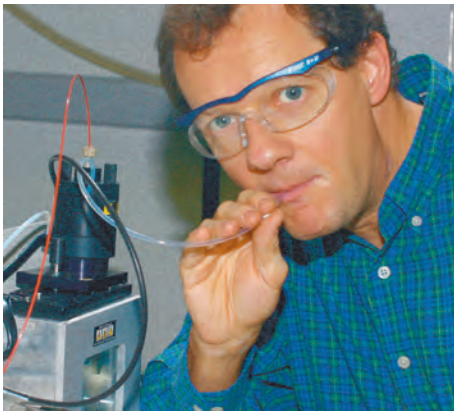
Received: October 10, 2007

References

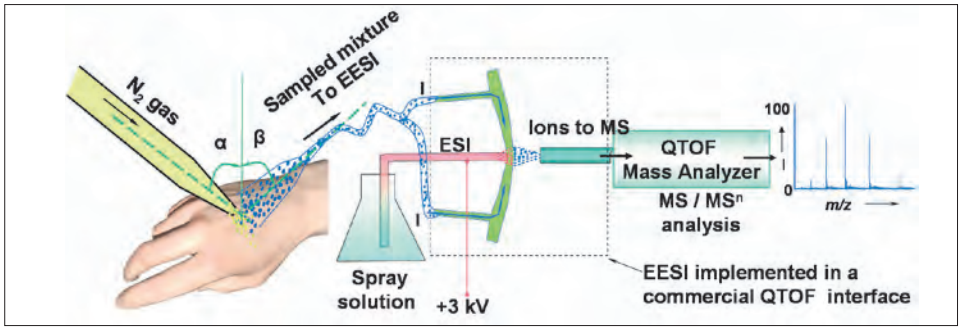
[1] H. Chen, A. Wortmann, W. Zhang, R. Zenobi, *Angew. Chem., Int. Ed.* **2007**, *46*, 580.
[2] H. Chen, Y. Sun, A. Wortmann, H. Gu, R. Zenobi, *Anal. Chem.* **2007**, *79*, 1447.
[3] H. Chen, S. Yang, A. Wortmann, R. Zenobi, *Angew. Chem., Int. Ed.* **2007**, *46*, 7591.



Principal component analysis of fruit skin (banana samples)



Fingerprinting of breath



On-line analysis of skin

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2008.43 CHIMIA **2008**, *62*, No. 1/2

Highlights of Analytical Chemistry in Switzerland

Impact of the Altitude of Pasture on Fatty Acid Composition of Milk

Marius Collomb and Karin Wehrmüller*

*Correspondence: K. Wehrmüller, Agroscope Liebefeld-Posieux Research Station ALP, Schwarzenburgstrasse 161, CH-3003 Bern, Tel.: +41 31 325 30 31, Fax: +41 31 323 82 27, E-mail: karin.wehrmueller@alp.admin.ch

Keywords: CLA isomers · Fatty acids · Highlands · Milk · MUFA · Omega-3 fatty acids · PUFA

Several publications have shown that milk from the lowlands, mountains and highlands have different fatty acid compositions. Milk production and processing is an important economic sector in the mountain areas of Switzerland. Better knowledge of the quality of milk fat and its influencing factors can lead to the development of products in these areas with a higher added value which could also be communicated to consumers.

The classical ISO method for the determination of the composition of fatty acids (*i.e.* gas-liquid chromatography of methylester derivatives) allows only the determination of 18 fatty acids. With a high-resolution gas chromatographic method it is possible to quantify about 70 fatty acids. Conjugated linoleic acid isomers (CLAs) are analyzed by silver-ion (Ag^+)-HPLC.

Milk fat from the highlands (1275–2120 m) and mountains (900–1210 m) contained a smaller amount of saturated- and more monounsaturated fatty acids (MUFA). A nearly constant increase with increasing altitude is seen for polyunsaturated fatty acids (PUFA), linoleic acid (C18:2) and the sum of CLA isomers. The essential omega-3 fatty acids are high in milk fat from the highlands. Investigation on the influence of the seasons (summer and winter) in mountain regions show that summer milk had a significantly lower concentration of saturated fatty acids and significantly higher contents of MUFA, PUFA and CLA.

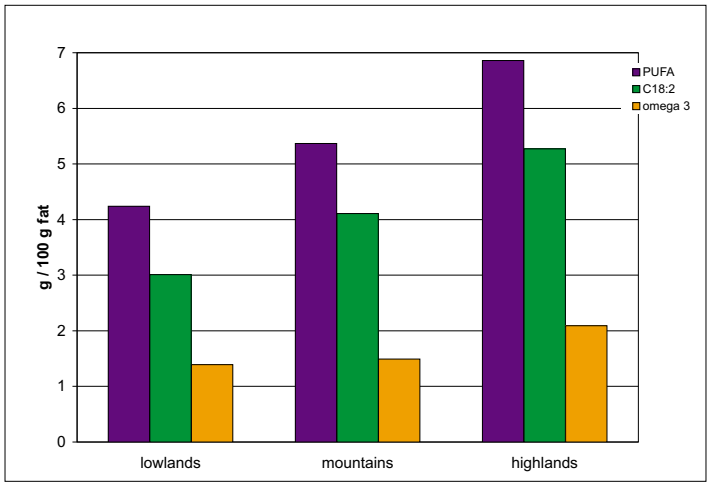
The differences in the composition of fatty acids of milk fats depending on the altitude are likely to be due to botanical differences. It was, however, shown that the increasing CLA content is not due to the altitude, but rather coincidentally correlates with it. It is also hypothesized that the increase *e.g.* in the CLA content of alpine summer milk is mainly due to pasture feeding and the absence or low amounts of concentrates. These effects could be also amplified by specific body fat mobilization in cows with alpine-specific hypoxia as well as reduced ruminal biohydrogenation due to energy shortage or secondary plant ingredients that inhibit the hydrogenating microorganisms in the rumen.

Milk fat from highlands appears interesting from the nutritional point of view because of the great reduction of saturated and the increase of polyunsaturated fatty acids. This could provide a positive opportunity for the promotion of alpine milk as healthy products.

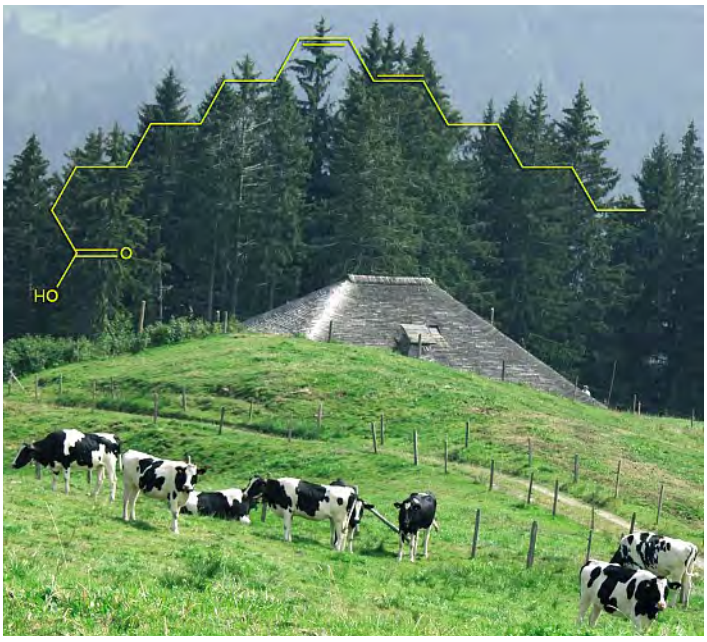
Received: December 4, 2007

References

M. Collomb, U. Bütikofer, R. Sieber, B. Jeangros, J.O. Bosset, *Int. Dairy J.* **2002**, *12*, 649.
M. Collomb, R. Sieber, U. Bütikofer, *Lipids* **2004**, *39*, 355.
W. Bisig, P. Eberhard, M. Collomb, B. Rehberger, *Lait* **2007**, *87*, 1.
M. Collomb, W. Bisig, U. Bütikofer, R. Sieber, M. Bregy, L. Etter, *J. Dairy Res.* **2007**, submitted.



Fatty acid composition of milk from different altitudes



Happy cows in the Swiss highlands. The molecule shown is *cis*-9,*trans*-11 octadecadienoic acid, the most important CLA isomer in cow milk.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2008.170 CHIMIA **2008**, *62*, No. 3

Highlights of Analytical Chemistry in Switzerland

Analytical Concepts and Tools for Speciation Studies

Stéphane Bayen*, Mary-Lou Tercier-Waeber, Nalini Parthasarathy, and Jacques Buffle

*Correspondence: Dr. S. Bayen, CABE, Université de Genève, Sciences II, 30 Quai Ernest Ansermet, CH-1211 Genève 4

Tel.: +41 22 379 60 46, Fax: +41 22 379 60 69, E-mail: stephane.bayen@cabe.unige.ch

Keywords: Bioanalogical sensor · Chemical speciation · Gel integrated microelectrode · *In situ* measurement · Microextraction · Permeation liquid membrane · Voltammetry

Speciation studies, *i.e.* the determination of the proportions and physico-chemical properties of the various species of a chemical substance, receive increasing attention as they set the basis for environmental management (*e.g.* pollution monitoring, water treatment), process control (food industry), and biomedical analysis. Historically, speciation has dominantly dealt with trace elements, but these concepts are now applied to organic substances, such as hydrophobic contaminants (*e.g.* PAHs, pesticides).

At the CABE (Analytical and Biophysical Environmental Chemistry) group, one of the research interests is to study the role of speciation of chemical substances on the transport of these substances through (bio)interfaces (Fig. 1). For this purpose, we develop and apply analytical tools for dynamic speciation.[1,2] We focus on bioanalogical sensors[1] based on permeation liquid membrane,[3,4] voltammetry,[1,3,5] and liquid-phase microextraction (Fig. 2). These sensors are based on the measurement of the fluxes of given chemical species through their interface[1–3] (Fig. 2b and d). These fluxes can be used in models to predict the bioavailability of chemical species.

These techniques have been applied in the laboratory, *e.g.* to investigate the association of trace elements with aquatic colloids,[5,6] biological exudates,[5] and antibiotics.[7] In addition, they were used to study trace element biouptake of biological systems such as algae[6] and plant roots.[5] These analytical tools have also been deployed to perform *in situ* measurements of trace metal speciation in fresh and seawaters[3,4,5,8] and to study biogeochemical cycles.[8]

Received: January 30, 2008

References

[1] J. Buffle, M. L. Tercier-Waeber, *Trends Anal. Chem.* **2005**, *24*, 172.
[2] H.P. van Leeuwen *et al.*, *Environmental Science & Technology* **2005**, *39*, 8545.
[3] *'In Situ* Monitoring of Aquatic Systems', Eds. J. Buffle, G. Horvai, IUPAC Series on Analytical and Physical Chemistry of Environmental Systems, vol. 6, **2000**, Chaps. 9–10.
[4] N. Parthasarathy, M. Pelletier, J. Buffle, *J. Chromatogr. A* **2004**, *1025*, 33.
[5] M. L. Tercier-Waeber *et al., Electroanalysis* **2007**, DOI :10.1002/elan.200704067.
[6] S. Bayen, I. Worms, N. Parthasarathy, K. Wilkinson, J. Buffle, *Anal. Chim. Acta* **2006**, *575*, 267.
[7] S. Bayen, K. J. Wilkinson, J. Buffle, *Analyst* **2007**, *132*, 262.
[8] M. L. Tercier-Waeber, M. Taillefert, *J. Environ. Monit.* **2008**, *10*, 30.

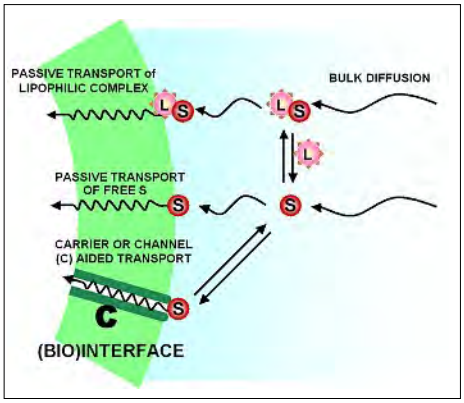


Fig. 1. Examples of mechanisms for the transport through a biointerface of a chemical substance **S** (*e.g.* an inorganic or organic pollutant) in the presence of a complexant **L**.

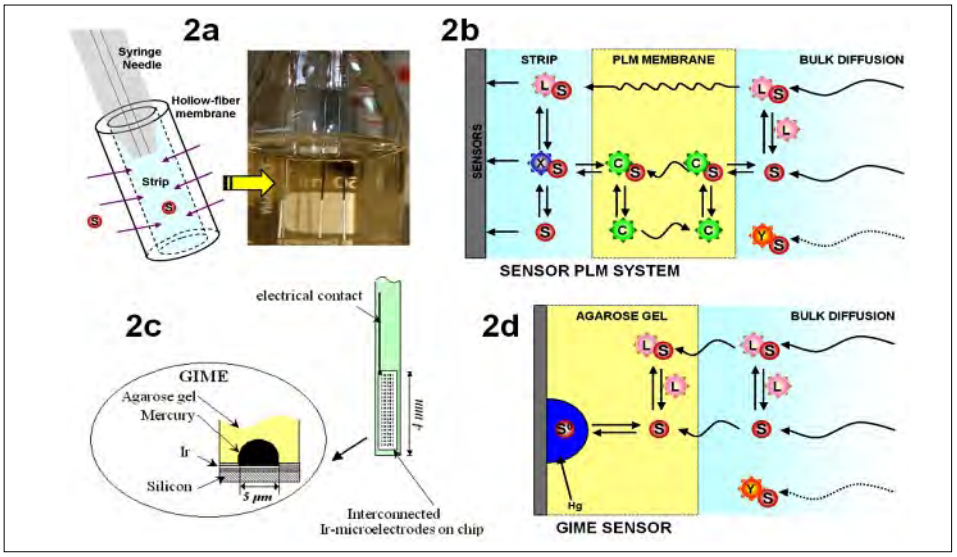


Fig. 2. Analytical tools for dynamic speciation studies, based on permeation liquid membrane (PLM) (a, b) and gel integrated microelectrodes (GIME) coupled with voltammetric detection (c,d). Schematic representation of chemical processes occurring at the sensor/solution interface for PLM (b) and GIME (d) devices. S: chemical substance of interest (metal or organics), L: complexant, C: carrier, X: strip complexant, YS: non reactive complex.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2008.301 CHIMIA **2008**, *62*, No. 1/2

Highlights of Analytical Chemistry in Switzerland

Does Ski Tourism Affect Alpine Bird Fauna?

Susanne Jenni-Eiermann*[a] and Raphael Arlettaz[ab]

*Correspondence: Dr. S. Jenni-Eiermann[a], Tel.: +41 41 462 97 00, Fax: +41 41 462 97 10, E-mail: susi.jenni@vogelwarte.ch

[a]Swiss Ornithological Institute, CH-6204 Sempach; [b]Zoological Institute, University of Bern, CH-3012 Bern

Keywords: Capercaillie · Faecal corticosterone metabolites · Grouse · Human disturbance · Stress ecology · Winter snow sports

Human-generated stress of wildlife, through continually developing outdoor recreational activities, is of increasing conservation concern as it often adds to other factors already adversely affecting the dynamics of vulnerable populations. It remains unclear, however, to what extent rapidly spreading free-riding snow sports, as a result of the intensifying winter tourism industry, actually elicit detrimental stress upon wildlife, with associated fitness and survival costs. Using a non-invasive method, we evaluated the levels of physiological stress induced by free-riding snow sports onto free-ranging black grouse and capercaillie, both declining species of alpine ecosystems. The concentration of stress hormone metabolites were measured in droppings collected in the snow.

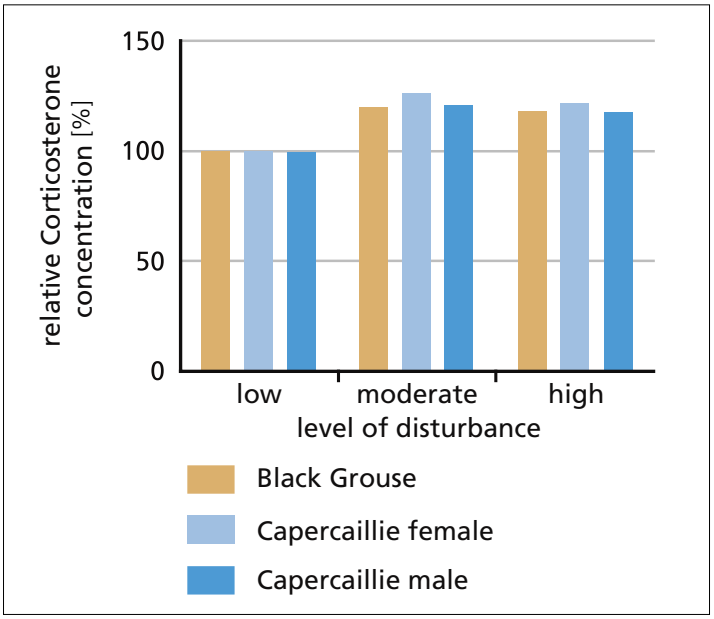
In black grouse the effect of human encounter on the concentration of the faecal corticosterone metabolites (FCM) was investigated experimentally. During wintertime black grouse rest most of the time in igloos, which they burrow after each feeding session – twice a day – anew. Hence, faeces are deposited twice daily and every time in a new igloo. In an undisturbed habitat radiomonitored birds were actively flushed from their snow burrows once a day, during four consecutive days. The concentration of the faecal corticosterone metabolites (FCM), determined with enzyme immunoassay, increased continuously from control day throughout the end of the experiment. Since flushing of black grouse and faecal sample collection took place in the early afternoon, birds apparently remained in a stressed state up to a minimum of 16 h after a flushing event.

In a comparative analysis, FCM of black grouse and capercaillies were analysed in droppings collected in habitats of various levels of human impact in the Alps as well as in the Black Forest. In both species the FCM concentration was significantly increased in birds living in areas with moderate to high recreation intensity compared to those with low recreation intensity.

The analysis of the metabolites of the stress hormone corticosterone in droppings proved to be a valuable method to monitor the effect of human recreation activities on the metabolism of free-ranging grouse. The studies showed that repeated disturbances may clearly induce stress and, therefore, potential long-lasting physiological effects which affect the birds' fitness and survival.

Received: February 23, 2008

Male capercaillie (Photo: © Gilbert Hayoz)



Faecal corticosterone metabolites of black grouse and capercaillie living in sites with various levels of disturbance by skiers and snowboarders. The level of 'low disturbance' was set at 100%.

References

D. Thiel, S. Jenni-Eiermann, V. Braunisch, R. Palme, L. Jenni, *J. Appl. Ecology*, in press.

R. Arlettaz, P. Patthey, M. Baltic, T. Leu, M. Schaub, R. Palme, S. Jenni-Eiermann, *Proc. Royal Soc. London* **2007**, *274*, 1219.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2008.440 CHIMIA **2008**, *62*, No. 5

Highlights of Analytical Chemistry in Switzerland

The Mechanism of Chlorophyll Degradation in Plants

Stefan Hörtensteiner*[a], Thomas Müller[b], and Bernhard Kräutler[b]

*Correspondence: Dr. S. Hörtensteiner[a], Tel: +41 44 634 82 82, Fax: +41 44 634 82 04, E-Mail: shorten@botinst.uzh.ch

[a]Institute of Plant Biology, University of Zurich, CH-8008 Zurich; [b]Institute of Organic Chemistry & Centre of Molecular Biosciences, University of Innsbruck, A-6020 Innsbruck, Austria

Keywords: Antioxidants · Chlorophyll catabolites · Chlorophyll degradation · Leaf senescence · NCC

The autumnal coloration of deciduous trees is a most spectacular natural phenomenon and coincides with the disappearance of chlorophyll (Chl). The fate of Chl was unknown until 1991 when the first structure of a relevant Chl catabolite was elucidated by preparative HPLC, UV, MS, and NMR.[1] Nowadays the path of Chl breakdown is largely resolved, including the structure elucidation of catabolites and the cloning of genes from catabolic enzymes.[2,3]

The structures of colorless Chl catabolites (NCCs) from leaves and fruits of various plant species exhibit a common backbone with an oxygenolytically opened chlorin ring. All remaining *meso*-carbons are saturated and as a consequence NCCs do not absorb visible light. These features indicate a largely conserved pathway of Chl breakdown within higher plants. However, different plant species also perform various peripheral modifications (R1-R3 in the Fig.), which increase polarity and allow deposition of NCCs inside the vacuole.

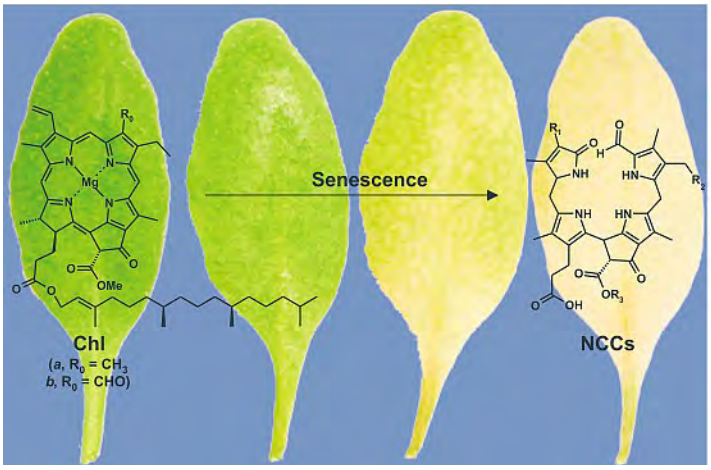
For a long time, Chl degradation during leaf senescence and fruit ripening was rationalized by the plant's aim to remobilize Chl-derived nitrogen. Obviously this is not the case. Yet Chl metabolism is a prerequisite for nitrogen reuse from Chl binding proteins, accounting for about 20% of total cellular nitrogen. Mutants defective in several of the enzymatic steps show cell death phenotypes and accumulation of photo-reactive intermediates of Chl degradation. Thus, Chl breakdown is a detoxification process. **NCCs seemed to be waste products without function, but recently they were shown to be potent antioxidants, which might contribute to the viability of ripe fruits, such as apples or pears.**[4]

Received: April 14, 2008

References

[1] B. Kräutler, B. Jaun, K. Bortlik, M. Schellenberg, P. Matile, *Angew. Chem., Int. Ed.* **1991**, *30*, 1315.
[2] W. Mühlecker, K. H. Ongania, B. Kräutler, P. Matile, S. Hörtensteiner, *Angew. Chem., Int. Ed.* **1997**, *36*, 401.
[3] S. Hörtensteiner, *Annu. Rev. Plant Biol.* **2006**, *57*, 55.
[4] T. Müller, M. Ulrich, K. H. Ongania, B. Kräutler, *Angew. Chem.* **2007**, *119*, 8854.

Autumn leaves – a symphony in green, red, and yellow



Major stages of leaf senescence in *Arabidopsis thaliana* (thale cress). The structures of chlorophyll (Chl) and final degradation products (NCCs) are shown. R1–R3 are sites of modifications found in NCCs from different plant species.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2008.530 CHIMIA **2008**, *62*, No. 6

Highlights of Analytical Chemistry in Switzerland

In situ Element-Specific and Time-Resolved Investigation of Micro-Corrosion Processes

Nadzeya Homazava*[ab], Andrea Ulrich[a], and Urs Krähenbühl[b]

*Correspondence: N. Homazava[a], Tel.: + 41 44 823 43 54, Fax: +41 44 823 40 41, E-mail: nadzeya.homazava@empa.ch

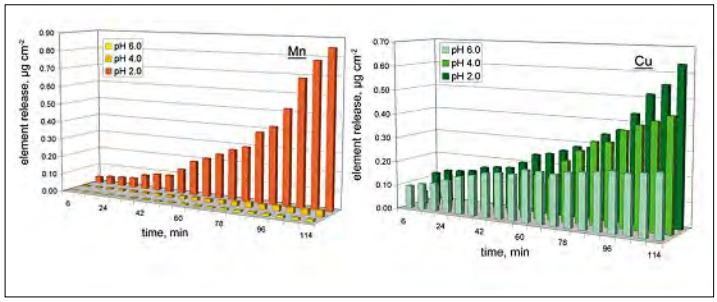
[a]EMPA, Swiss Federal Laboratories for Materials Testing and Research, Ueberlandstrasse 129, CH-8600 Dübendorf

[b]University of Bern, Department of Chemistry and Biochemistry, Freiestrasse 3, CH-3012 Bern

Keywords: Corrosion · Element-specific, time-resolved analysis · Flow injection analysis · Inductively coupled plasma mass spectrometry · Localized corrosion

Detailed information on corrosion processes provides the key to effective prediction and minimization of corrosion damages. The initiation stage of material decomposition plays a special role, since the corrosion often starts at the weakest locations such as surface defects, grain boundaries, segregations or inclusions. However, surface analysis or electrochemical methods commonly used in corrosion research (*e.g.* electrochemical methods, SEM-EDX, *etc.*) cannot present local element-specific and online *in situ* information at the same time.

Corrosion is an economic issue since it destroys material goods



Time-resolved dissolution behavior of Mn and Cu in AA 6111 using 0.1 M NaCl corrosive media at different pHs

As a solution a technique for localized element-specific investigations of corrosion processes has been developed. The technique is based on an adjustable online microflow-capillary set-up especially designed for local *in situ* experiments at trace and ultratrace concentration levels. The capillary is online connected *via* flow injection (FI) analysis system to an inductively coupled plasma mass spectrometry ICP-MS. FI allows a transient sample introduction, whereas ICP-MS is designed for highly sensitive multi-element quantification.

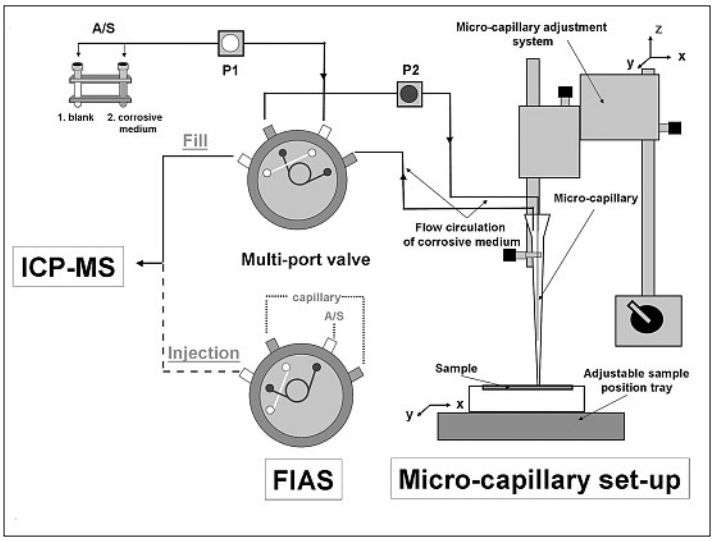
The efficiency of the developed technique could be proved by corrosion susceptibility analysis of a commercial aluminum alloy. The influence of various factors such as exposure time or pH value of corrosive media on the element-specific dissolution rates was studied in alloy AA 6111. This information is especially valuable for alloying elements present in the alloy in sub-percent quantities, which could also be detected in very low concentrations in the solution as *e.g.* Cu and Mn. The element-specific investigation of corrosion behavior of AA 6111 revealed a relatively high release of the secondary alloying element Cu in the studied pH range. **New insights into the behavior of copper during the corrosion process, not fully understood so far, can be obtained with the newly developed *in situ* experiments.**

Received: April 24, 2008

References

N. Homazava, A. Ulrich, M. Trottmann, U. Krähenbühl, *J. Anal. Atom. Spectrom.* **2007**, *9*, 1122.

N. Homazava, A. Ulrich, U. Krähenbühl, *Spectrochim. Acta, Part B,* submitted.



Principle of the novel microcapillary FI-ICP-MS set-up

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2008.685 CHIMIA **2008**, *62*, No. 7/8

Highlights of Analytical Chemistry in Switzerland

Plant Metabolomics – Strategies for Biomarker Detection, Isolation, and Identification

Elia Grata[ab], Julien Boccard[bc], Gaëtan Glauser[ab], Davy Guillarme[a], Pierre-Alain Carrupt[c], Jean-Luc Wolfender[b], and Serge Rudaz*[a]

*Correspondence: Dr. S. Rudaz[a], Tel.: +41 22 379 65 72, Fax: +41 22 379 68 08, E-Mail: serge.rudaz@pharm.unige.ch
[a]LCAP, [b]LPP, [c]LCT, Ecole de Pharmacie Genève-Lausanne, Section des Sciences Pharmaceutiques, Université de Genève, Université de Lausanne, CH-1211 Genève

Keywords: *Arabidopsis thaliana* · Capillary NMR · Data mining · Metabolomics · Plant metabolism · Stress-induced metabolites · UPLC-TOF-MS

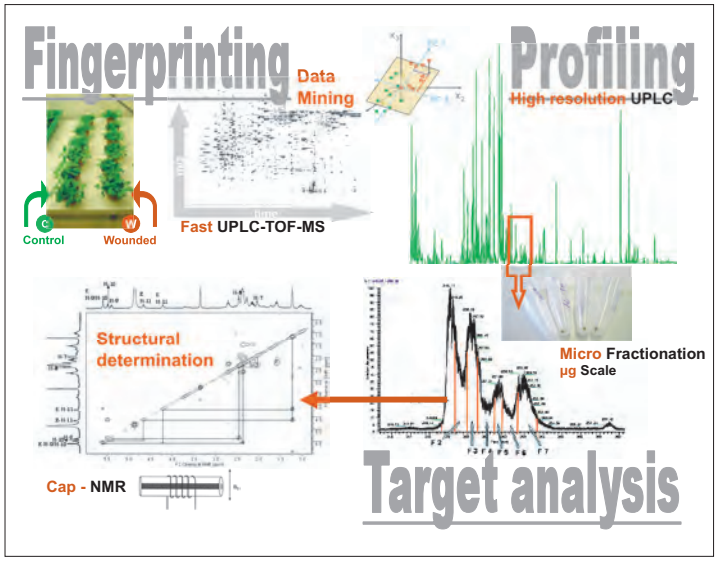
Recent developments in analytical methods and data mining have permitted metabolomics to evolve from an ambitious concept to a valuable technology which provides a global picture of molecular organisation at the metabolite level.

A strategy was developed for the detection, isolation, and identification of stress-induced metabolites produced in *Arabidopsis thaliana* after wounding the leaves, which mimics the herbivore attack. Although several defence signalling compounds are identified, the expression of some of the defence genes is probably dependent on original compounds, which still need to be characterized. Therefore, the structure determination of these biomarkers represents an important analytical challenge since they are only found in minute amounts in plants, occur as closely related isomers and are convoluted with major constitutive plant secondary metabolites.

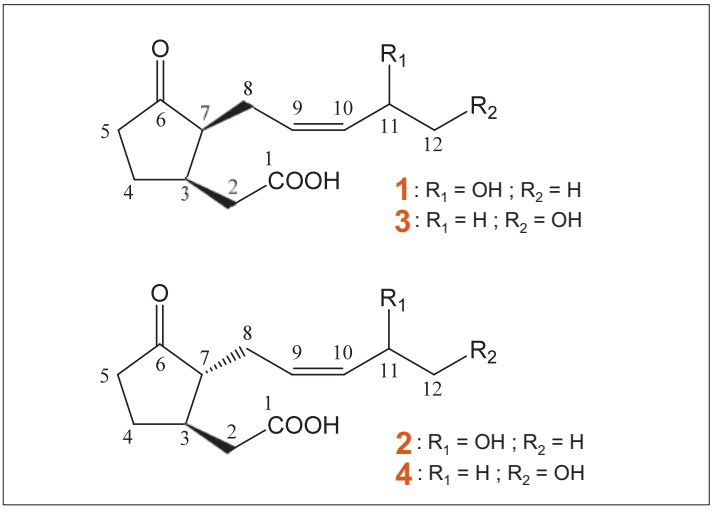
The developed metabolomic approach was based on a sequential strategy:

1) High-throughput metabolite *fingerprinting* involving rapid UPLC-TOF-MS gradients on numerous wounded and unwounded leaf samples.
2) *Data mining* for group discrimination and determination of peaks responsible for the main metabolome variations.
3) High-resolution metabolite *profiling* of selected pool samples on high peak capacity UPLC columns after efficient gradient transfer for the localisation and deconvolution of the selected ions.
4) Targeted LC-MS triggered *microfractionation* of the biomarkers at the semi-preparative level based on computed LC conditions from UPLC gradients.
5) Complete *structural determination* of the unknown compounds based on at-line capillary-NMR experiments at the microgram level.

Thank to this strategy a broad survey of wound-biomarkers with various physicochemical properties was obtained and, besides known signalling molecules, original oxylipins and related products (jasmonates) were identified. **This approach provides a rapid estimation of the significant wound metabolome variations, the identification of biomarkers involved in these changes and detailed information on their temporal and spatial dynamics.**



Analytical steps for the identification of stress biomarkers in plants



Jasmonic acid derivatives identified as wound biomarkers

Acknowledgements

The Swiss National Science Foundation (grant n° 205320-116274/1 to J.L Wolfender and S. Rudaz) is thanked for supporting this work.

Received: May 10, 2008

References

J. Boccard, E. Grata, A. Thiocone, J. Y. Gauvrit, P. Lanteri, P.-A. Carrupt, J. L. Wolfender, S. Rudaz, *Chemometr. Intell. Lab. Syst.* **2007**, *86*, 189.
G. Glauser, D. Guillarme, E. Grata, J. Boccard, A. Thiocone, P.-A. Carrupt, J. L. Veuthey, S. Rudaz, J. L. Wolfender, *J. Chromatogr. A* **2007**, *1180*, 90.
E. Grata, J. Boccard, G. Glauser, P.-A. Carrupt, E. E. Farmer, J. L. Wolfender, S. Rudaz, *J. Sep. Sci.* **2007**, *30*, 2268.
G. Glauser, E. Grata, L. Dubugnon, S. Rudaz, E. Farmer, J. L. Wolfender, *J. Biol. Chem.* **2008**, *283*, 16400.
E. Grata, J. Boccard, D. Guillarme, G. Glauser, P.-A. Carrupt, E. E. Farmer, J. L. Wolfender, S. Rudaz, *J. Chromatogr. B* **2008**, *871*, 261.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2008.751 CHIMIA **2008**, *62*, No. 9

Highlights of Analytical Chemistry in Switzerland

Calibrating Sensitive Analytical Instruments – or How Much is 'Zero'?

Hans-Peter Haerri*

**Correspondence:* Dr. H.-P. Haerri, Federal Office of Metrology METAS, Lindenweg 50, CH-3003 Bern-Wabern
Tel.: +41 31 323 35 34, Fax: +41 31 323 32 10, E-Mail: hans-peter.haerri@metas.ch

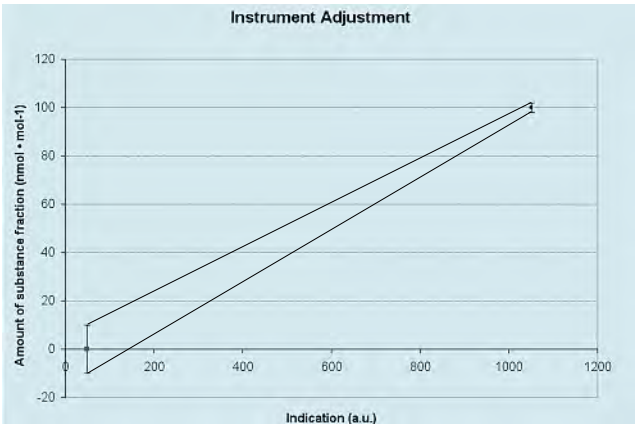
Keywords: Instrument adjustment · Measurement uncertainty · Sensitivity · Standard gas mixture · Trace gas analysis · Zero air generator

Monitoring the ground-level air quality requires sensitive gas analysers capable of detecting air pollutants at the nmol • mol^{-1} or mm^3 • m^{-3} level. Quality systems require *e.g.* that gas analysers be periodically adjusted with certified reference gas mixtures for the span points and with so-called zero gas for the zero point. At low concentration values however already trace amounts of analytes in the zero gas at the time of instrument adjustment contribute considerably to the measurement uncertainty.

Under field conditions it is not guaranteed that zero air generators are working permanently as specified, specially *e.g.* at periods of high ambient air pollutant concentrations or extreme weather conditions. Residual amounts of analytes may therefore accidentally be present in zero air and cause adjustment and thus measurement errors.

METAS has therefore established the infrastructure to measure traces of numerous pollutants in zero air from zero air generators under simulated operating conditions allowing specifying residual amounts of analytes under close application conditions.

To measure the performance of zero air generators, they are fed with a series of standard gas mixtures with known 'worst case' ground-level concentrations. Ambient air concentrations vary with time and can not be used for this purpose. For the detection of the remaining analyte traces the best suited, *i.e.* most sensitive and specific available analytical methods are used. For *e.g.* NO and NO_2 it is the chemiluminescence method with O_3, for CO non-dispersive infrared absorption. The sample with the unknown amount is the outlet gas mixture of the generator.



The trend of the measurement uncertainty contribution for the instrument adjustment at the zero point with an assumed uncertainty of 10 % and at the span point at 100 (nmol • mol^{-1}) of 2 % for the standard gas mixture, respectively, is shown.

Summary of test results for three analytes for a modern zero air generator, the specifications and regulatory requirements. *U:* expanded uncertainty with a confidence interval of ≈ 95 % for values above the detection limit. [a]Detection limit. [b]Sum of x NO_2 and x *NO*. n.s.: not specified.

Sample	Amount of substance fraction (x) of analyte (nmol • mol^{-1})					
	x NO_2	U	x NO	U	x CO	U
Standard gas mixture at inlet	76.7	1.0	65.0	0.8	2025	22
Outlet gas	<0.7[a]		0.7	0.2	<6[a]	
Specifications of generator	<1[b]		<1[b]		<10	
Swiss regulatory requirements for zero air	<0.56		n.s.		urban: <88.5 rural: <8.8	

The results show, that this zero air generator meets the specifications and regulatory requirements under the test conditions. The chemiluminescence method for NO_2 and NO is just fit for purpose to reach the necessary detection limits.

Measurement capabilities are presented for testing the performance of zero air generators under close operating conditions. The analytical methods meet the required sensitivities for critical analytes, but need further developments for other analytes, *e.g.* CH_4, to approach 'zero' closer

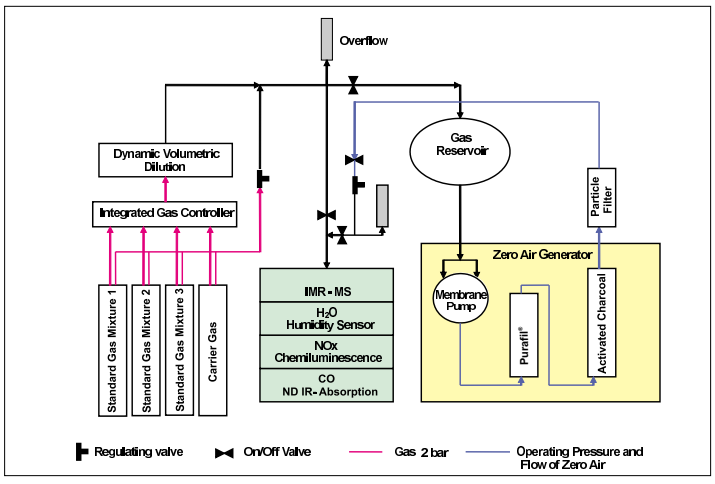
Received: July 3, 2008

References

Luftreinhaltevorschriften: Rechtsgrundlagen *http://www.bafu.admin.ch/luft/00632/00634/index.html*

H.-P. Haerri, M. Quintilii, *Chimia* **2007**, *61*, 420.

M. Quintilii, J. Brunner, METinfo, 15, 1/**2008**, 14, *www.metas.ch/metasweb/Dokumentation/Publikationen.*



Schematic of measurement set-up for zero air generators with the gas supply and the analytical methods. IMR-MS: ion molecule reaction mass spectrometer. The zero air generator is shown only with the compressor and the final filter elements.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2008.860 CHIMIA **2008**, *62*, No. 10

Highlights of Analytical Chemistry in Switzerland

Deep-UV Detector for HPLC with Light-Emitting Diode

Stefan Schmid[a], Mirek Macka[b], and Peter C. Hauser*[a]

*Correspondence: Prof. Dr. P. C. Hauser, Tel.: +41 61 267 1003, Fax: +41 61 267 1013, E-mail: peter.hauser@unibas.ch

[a]Department of Chemistry, University of Basel, Spitalstrasse 51, CH-4056 Basel

[b]Department of Chemical Sciences, Dublin City University, Glasnevin, Dublin 9, Ireland

Keywords: Detector · HPLC · LED · UV

Light-emitting diodes (LEDs) give off relatively narrow spectral bands whose wavelengths are directly related to the bandgap energy between the p- and n-doped semiconducting materials employed. They were commercialised in the early 1970s and were first made available for the infrared and then the red region of the visible spectrum. Subsequently LEDs with ever shorter wavelengths, which are more difficult to produce due to the higher energies involved, have become available. At the same time it was also possible to increase the intensities to the point that they now become attractive as more efficient replacements for conventional light sources. Standard LEDs have emission bandwidths of about 30 nm, matching well the absorption bandwidths of molecules. Thus the use of LEDs as radiation sources for spectrophotometric instrumentation, eliminating the need for monochromators, was suggested in 1973. LEDs now have found application in analytical instruments where compactness and low power consumption are required and low cost is desired, but where flexibility in wavelength setting is not needed.

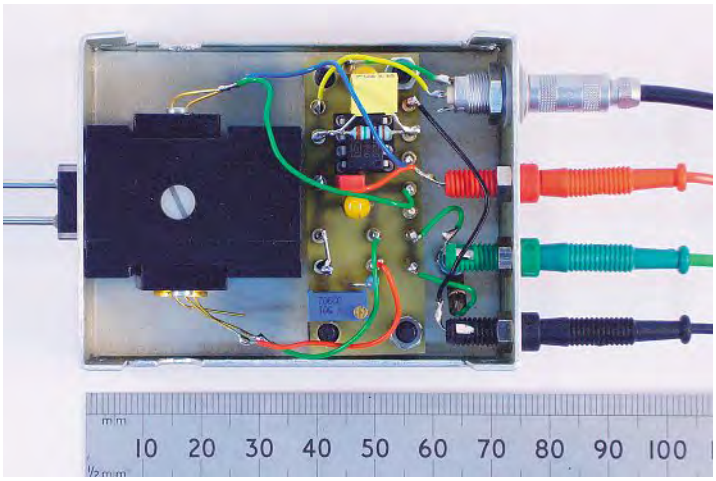
Recently the wavelengths attained with LEDs have reached the deep UV-range below 300 nm, and this opens up new possibilities. While the intensities are presently not adequate for excitation in fluorescence, absorbance measurements are feasible. This has allowed the construction of an unprecedented simple and compact detector for HPLC. For measuring the intensity of the UV-light, a special photodiode, which had been designed for UV-radiometry, was employed. The photocurrent was converted to an output voltage by using a simple operational amplifier in an integrated circuit package. The wavelength of 255 nm is useful for many aromatic compounds.

Test mixtures of benzoic acid, nitrobenzene, benzyl acetate and methyl benzoate were separated using an acetonitrile/water gradient elution program. Limits of detection of 750 ng·ml^{-1}, 5.8 µg·ml^{-1} and 12 µg·ml^{-1} were obtained for nitrobenzene, benzoic acid, and methyl benzoate, respectively. These values correspond to the relative absorptivities of the compounds at 255 nm and are close to the detection limits obtained with conventional commercial detectors. The detection limit for benzyl acetate was not determined as the sensitivity for this compound is low, due to a poor spectral match. **Further improvements in deep-UV LED technology in terms of intensity and shorter wavelengths can be expected. They will lead to lower limits of detection, which match or surpass those of conventional detectors, and to an even wider range of applications in absorbance measurements.**

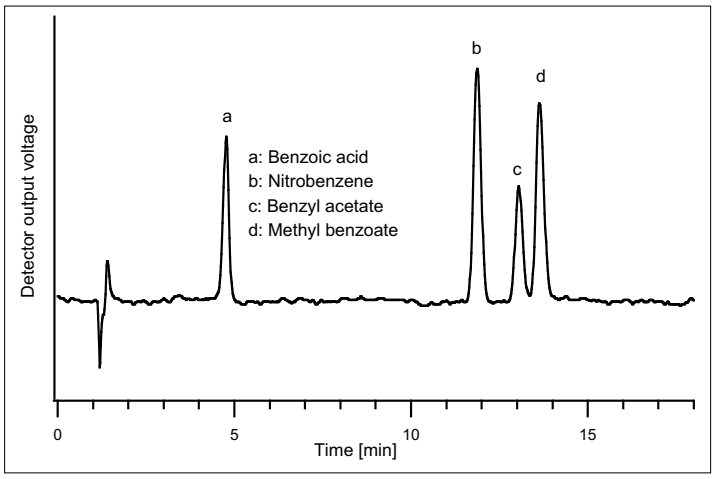
Received: September 5, 2008

References

H. Flaschka, C. McKeithan, R. Barnes, *Anal. Lett.* **1973**, *6*, 585.
S. Schmid, M. Macka, P. C. Hauser, *Analyst* **2008**, *133*, 465.



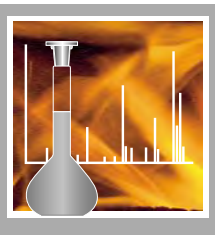
The flow-through cuvette is fixed in the black holder; the UV-LED and the photodiode are attached on its sides



HPLC chromatogram of a test mixture

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2008.936 CHIMIA **2008**, *62*, No. 11



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Hexabromocyclododecanes: From Smart Molecules to Persistent Pollutants

Norbert Heeb*[a], W. Bernd Schweizer[b], Regula Haag[a], Andreas Gerecke[a], Peter Schmid[a], Martin Kohler[ac], Markus Zennegg[a], and Heinz Vonmont[a]

*Correspondence: Dr. N. Heeb[a], Tel.: +41 44 823 42 57, Fax: +41 44 823 46 14, E-Mail: norbert.heeb@empa.ch

[a]EMPA, Swiss Federal Laboratories for Materials Testing and Research, Ueberlandstrasse 129, CH-8600 Dübendorf; [b]ETH Zurich, Laboratory of Organic Chemistry, CH-8093 Zürich; [c]present address: Kantonale Lebensmittelkontrolle, CH-4509 Solothurn

Keywords: Absolute configuration · Brominated flame retardants · Hexabromocyclododecanes · Regio- and stereoselective bromine migration · Structure–activity relations · Structure elucidation

In the seventies, about 70% of the world's bromine production of 400 000 t/y was used for 1,2-dibromoethane synthesis, a fuel additive for leaded gasolines. The implementation of three-way catalysts stopped these activities. Nowadays, brominated flame retardants (BFRs) such as polybrominated diphenyl ethers (PBDEs), tetrabromobisphenol A, and hexabromocyclododecanes (HBCDs) are the major bromine products. BFRs are added to polymers used in electronic devices, textiles, and insulation materials to lower their flammability. The EU has banned the use of penta- and octa-BDEs, but HBCDs, currently produced at >20 000 t/y, are still allowed.

Persistence, bioaccumulation potential, and toxicity are important aspects to decide which BFRs have to be regulated as persistent organic pollutants under the Stockholm convention. It is our interest to elucidate the fate of such chemicals, to study their transformation processes and to develop safer alternatives.

When the EU started a risk assessment on HBCDs, we realized that neither HBCD stereochemistry nor selective analytical methods were known. We isolated eight of the 16 HBCD stereoisomers and assigned the absolute configurations of three pairs of enantiomers (**6a/b**, **7a/b**, **8a/b**). Lately, the two *meso* forms could be assigned to structures **9** and **10**. In parallel, we developed LC-MS methods to distinguish different stereoisomers.

A conformational analysis revealed that HBCDs are remarkably similar. We identified a structural motive consisting of three pairs of equally oriented synclinal and two antiperiplanar torsion angles. We found increased reactivity in the flexible part, whereas the conserved motive was less reactive. The understanding of such structure–activity relations is a key element to model environmental transport and transformation.

Some HBCDs accumulate in the environment. Most striking is the fact that γ-HBCDs (8a/b) are abundant in technical products, but α-HBCDs (6a/b) dominate in biological samples. The left-handed form of both α-HBCD enantiomers (6a) is enriched in human breast milk.

A comprehensive risk assessment for chemicals of such high-production volume requires detailed structural information and selective analytical methods to study the fate and toxicity of the individual isomers. In this respect our odyssey on HBCDs might be considered as an analytical highlight but further challenges are ahead of us to assess benefits and risks of HBCDs.

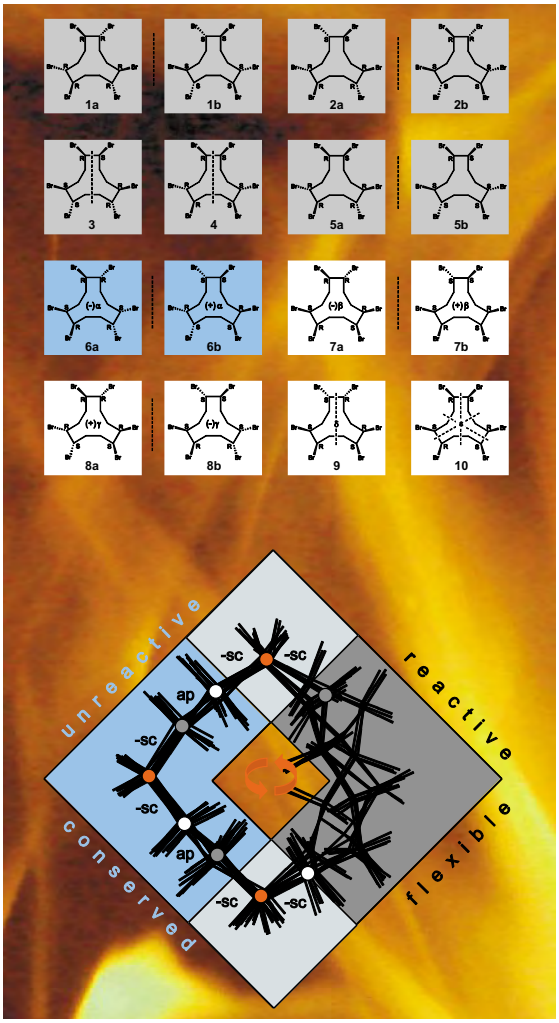
Received: October 6, 2008

References

N. V. Heeb, W. B. Schweizer, P. Mattrel, R. Haag, M. Kohler, P. Schmid, M. Zennegg, M. Wolfensberger, *Chemosphere* **2008**, *71*, 1547.

N. V. Heeb, W. B. Schweizer, P. Mattrel, R. Haag, A. C. Gerecke, M. Kohler, P. Schmid, M. Zennegg, M. Wolfensberger, *Chemosphere* **2007**, *68*, 940.

N. V. Heeb, W. B. Schweizer, M. Kohler, A. C. Gerecke, *Chemosphere* **2005**, *61*, 65.



Structure elucidation of eight of the 16 possible 1,2,5,6,9,10-HBCDs was achieved by XRD and NMR analyses. Compounds **6a/b** are more persistent and bioaccumulative than the others. A structural motive consisting of three pairs of synclinal and two antiperiplanar torsion angles was found to be conserved and less reactive.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2008.981 CHIMIA **2008**, *62*, No. 12

Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Mass Extinction and Mass Spectrometry: Pursuing the Fate of the Earliest Multicellulars

Thomas F. Nägler

**Correspondence:* Prof. Dr. T. Nägler, Institute of Geological Sciences, University of Bern, Baltzerstrasse 1-3, CH-3012 Bern
Tel.: +41 31 631 87 52, Fax: +41 631 48 43, E-Mail: naegler@geo.unibe.ch

Keywords: Ediacara · Isotope fractionation · Mass extinction · MC-ICP-MS · Molybdenum isotopes · Precambrian/Cambrian boundary

Since the middle of the last century, stable isotope analyses have been successfully applied to earth science problems. Up to ten years ago only the lighter elements (mainly H, O, C, N, and S) were analysed, as isotope fractionations of heavier elements were analytically not resolvable. The invention of multicollector plasma source mass spectrometers (MC-ICP-MS) largely overcame these problems. In 1998, the Institute of Geological Sciences in Bern acquired a NuInstruments™ MC-ICP-MS. One of the developments of our group has been the protocol for measuring the Mo isotope fractionation to study the evolution of free oxygen through Earth history. The principle is that Mo is very soluble as oxyanion (molybdate), but immobile in reducing environments. The variations of the $^{98}Mo/^{95}Mo$ ratio in present-day oceans are as large as 3 permil, which is well-resolved given our analytical uncertainty of 0.1 permil.

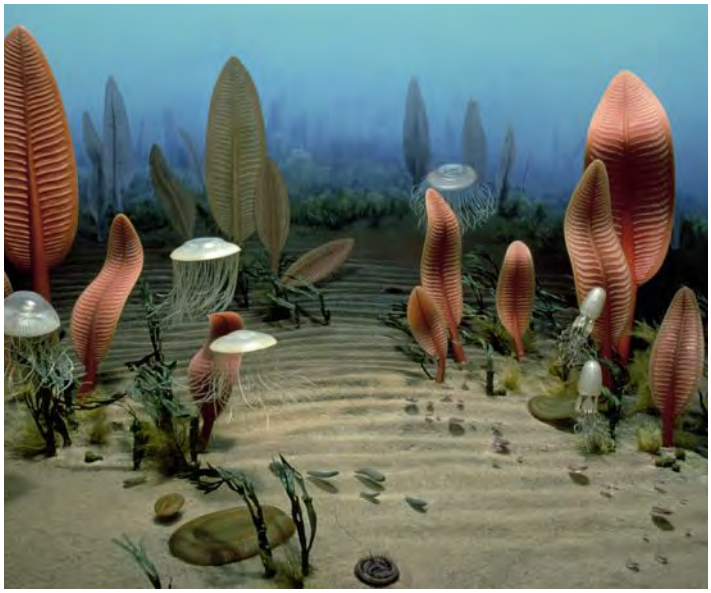
About 600 million years (Ma) ago, at the end of the Precambrian era, the dominant life forms were a group of the earliest multicellular, soft-bodied animals, the so-called *Ediacara* fauna. About 540 Ma ago, at the Precambrian/Cambrian boundary, this biota was wiped out. This mass extinction provided room for new lifeforms, notably species with skeletons.

Late Precambrian oceans were stratified, with a deep layer where the decomposition of settling organic matter led to H_2S production by sulfate reducing bacteria. Dissolved molybdate (deriving from weathering of continents) accumulated in the upper layer. According to our hypothesis, a major change in ocean circulation produced an upwelling of the deeper waters and thus the mixing of H_2S-rich deep waters with Mo-rich upper waters. **H_2S is the only scavenging agent that could have been present in large enough amounts to produce the quasi complete Mo removal from ocean water, and this dramatic removal is necessary to explain the observed fast fluctuation of the Mo isotope signal, which is archived in coeval black shales. This sudden burst of toxic H_2S erased the shelf-dwelling *Ediacara* fauna.** Subsequent oxidation of H_2S by atmospheric oxygen allowed the shallower oceans to become habitable again.

Received: October 23, 2008

Reference

M. Wille, T. F. Nägler, B. Lehmann, S. Schröder, J. D. Kramers, *Nature* **2008**, *453*, 767.

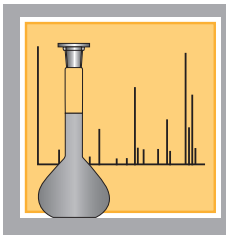


Ediacaran fauna, painting by Mary Parrish (Courtesy of Smithsonian Institution, Washington, DC)

Earliest Cambrian black shales (Yangtze Platform, China), rocks which carry the Mo isotope signal following the extinction event

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2009.77



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Bile Acids as Potential New Biomarkers for Metabolic Syndrome

Carine Steiner*, Tanja Keller, Arnold von Eckardstein, and Katharina M. Rentsch

*Correspondence: C. Steiner, Institute for Clinical Chemistry, University Hospital Zürich, Rämistrasse 100, CH-8091 Zürich
Tel.: +41 44 255 67 86, Fax: +41 44 255 45 90, E-mail: Carine.Steiner@usz.ch

Keywords: Atmospheric pressure chemical ionization · Bile acids · Electrospray ionization · Enterohepatic circulation · Reversed phase liquid chromatography · Selective reaction monitoring

Bile acids are the major degradation products of cholesterol and important mediators of dietary lipid absorption. They undergo considerable structural modification through hepatic and intestinal metabolism, which leads to a pool of over 20 similar compounds being reuptaken to a great extent by an efficient enterohepatic circulation. Thus, bile acids can be detected in the systemic circulation of healthy volunteers at concentrations in the micromolar range.

Moreover, bile acids are biologically important as ligands of the nuclear receptor farnesoid X receptor (FXR) and hence regulators of lipid and carbohydrate metabolism. In particular the primary bile acid chenodeoxycholic acid (CDCA) is known as the most potent natural activator of human FXR, whereas more hydrophilic species such as ursodeoxycholic acid (UDCA) are poor activators. Our interest lies in determining whether changes in bile acid pattern are linked with an imbalance in glucose or lipid metabolism and thus the occurrence of metabolic diseases.

Currently, quantification of bile acids based on an enzymatic assay is performed routinely as a diagnostic tool in several diseases. Unfortunately, this method is only applicable for the determination of total bile acids. We therefore developed a method based on liquid chromatography/mass spectrometry for the differentiated and sensitive analysis of these compounds.

A second method was developed for the bile acid precursor 7α-hydroxy-4-cholesten-3-one (C4) in order to provide information about the input of *de novo* biosynthesis out of cholesterol in contrast to the input coming from intestinal reabsorption of bile acids.

Both developed methods are based on solid-phase extraction, reverse phase chromatography and selective reaction monitoring (SRM). Ionization is performed either by electrospray ionization for the 15 major human bile acids or by atmospheric pressure chemical ionization for C4.

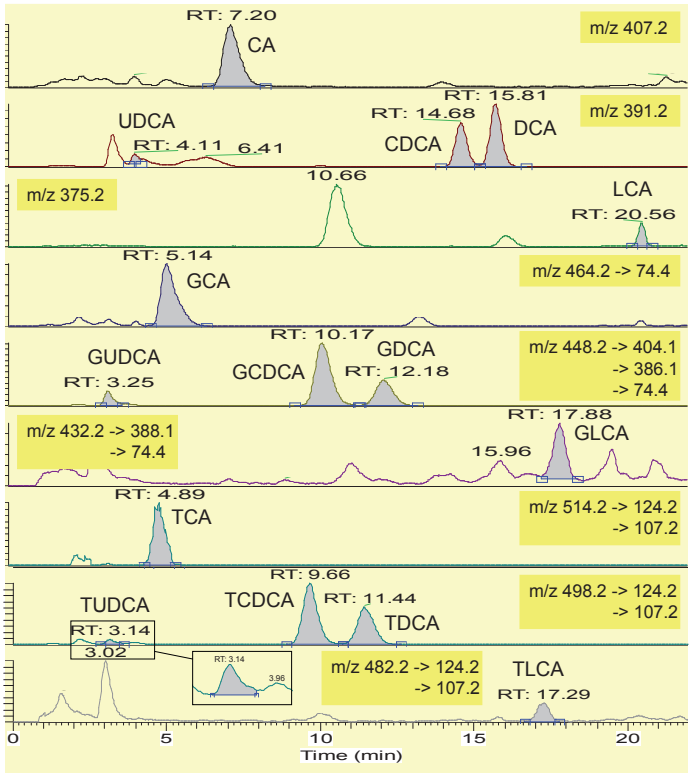
The main benefits of these methods are the rapid separation of 15 similar compounds including isomers, little sample preparation and low sample volume (100 µl serum for the bile acids and 250 µl for C4, respectively).

The described methods will allow us to determine the significance of bile acid quantification in patients suffering from various diseases including metabolic syndrome.

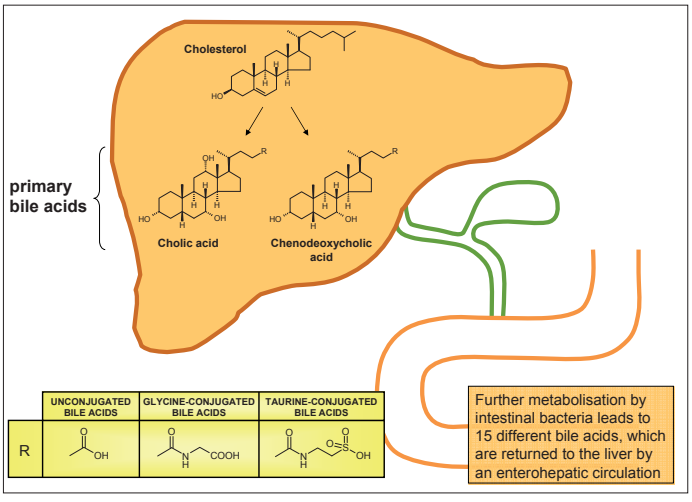
Received: December 9, 2008

Reference

I. Burkard, A. von Eckardstein, K. M. Rentsch, *J. Chromatogr. B* **2005**, *826*, 147.



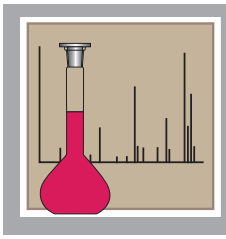
Chromatogram showing the 15 major bile acids in an extracted serum from a healthy volunteer (sample volume = 100 µl)



Biosynthesis of bile acids

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2009.169



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Identification of a Red Wine Marker in Residues from a 13th Century Cellar

David Drissner*[a], Peter Gehrig[b], Reto Marti[c], Erwin Hildbrand[d], and Frank Hesford[a]

*Correspondence: Dr. D. Drissner[a], Tel.: +41 44 783 64 29, Fax: +41 44 783 62 24, E-Mail: david.drissner@acw.admin.ch

[a]Agroscope Changins-Wädenswil Research Station ACW, Food Microbiology & Special Analytics, Schloss, CH-8820 Wädenswil; [b]Functional Genomics Center Zurich, University of Zurich and ETH Zurich, Winterthurerstrasse 190, CH-8057 Zurich; [c]Archäologie Baselland, Amtshausgasse 7, CH-4410 Liestal; [d]The Swiss National Museums, Collections Centre, Lindenmoosstrasse 1, CH-8910 Affoltern a. Albis

Keywords: MALDI-TOF/TOF · Matrix-Assisted Laser Desorption/Ionisation-Time Of Flight/Time Of Flight mass spectrometry · Oenological history · Red wine marker · Syringic acid

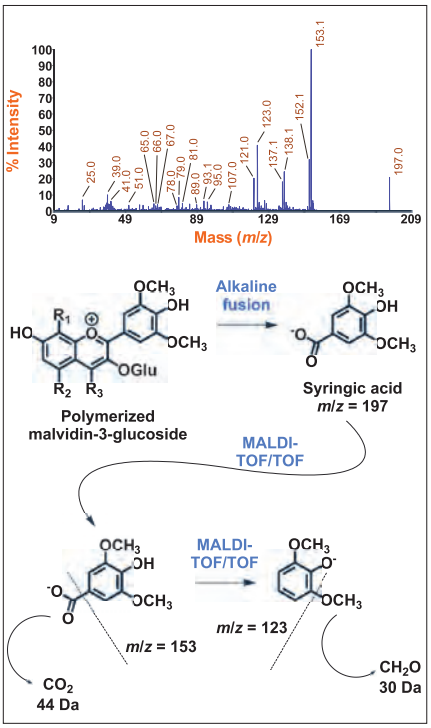
In 2007, archaeologists of the canton Baselland discovered the remains of a building from the late 13th century in Pratteln. These buildings were part of the medieval Meier yard (Latin: *maior*, local bailiff) belonging to the monastery St. Alban in Basel founded in 1083. Castings of timber beams in the floor of one cellar have been interpreted as supports for wine barrels. Puzzling red-brownish colorations in the floor of the neighboring cellar were postulated to be caused by red wine and to indicate the location of the wine press, respectively. To test this, we applied the highly specific and sensitive technique of MALDI-TOF/TOF mass spectrometry for the first time to screen for the red wine marker syringic acid in the colored floor samples.

Upon ageing, malvidin-3-glucoside, a major natural pigment in red wine, polymerizes to complex, stable, red-brownish pigments. Alkaline fusion releases syringic acid from the malvidin-3-glucoside present in these complex pigments. Analyses of prepared samples were performed with an Applied Biosystems 4800 MALDI-TOF/TOF Analyzer in the negative-ion mode using 3-aminoquinoline as the matrix.

We detected a specific signal with m/z = 197 (corresponding to deprotonated syringic acid) in the colored floor sample. This signal was absent in controls from non-colored sites of the floor. Collision-induced dissociation of that precursor ion resulted in prominent fragment ions with m/z = 153 and 123, which could be explained by the loss of CO_2 (44 Da) and of CH_2O (30 Da) molecules from the molecular ion. Comparison of the fragmentation pattern with that of a syringic acid reference finally proved the presence of syringic acid in the colored samples. The identification of syringic acid thus revealed the red wine origin of the preserved, colored residues in the medieval cellar.

In support of historical records, these results provide the first proof by analytical chemistry that red wine was produced already in the 13th century in Pratteln. In this study, MALDI-TOF/TOF mass spectrometry helped to identify the ancient Meier yard as a wine farmhouse and is proof of one of the oldest medieval wine farmhouses in Switzerland. This application of a MALDI-TOF/TOF instrument has helped to unravel oenological history in Switzerland, and it is also a promising tool for future applications in food sciences.

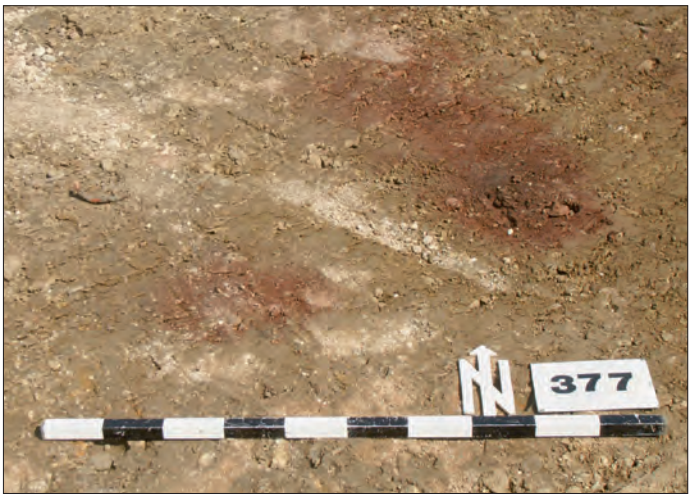
Received: January 8, 2009



MALDI-TOF/TOF spectrum of syringic acid in the colored sample (top). Release of syringic acid from malvidin-3-glucoside through alkaline fusion and subsequent analysis by MALDI-TOF/TOF MS. The structures of malvidin-3-glucoside in the polymerized pigment, syringic acid, and the two fragment ions with m/z = 153 and 123, respectively, are shown (bottom).

Reference

D. Drissner, P. Gehrig, E. Hildbrand, R. Marti, F. Hesford, *Schweiz. Zeitschr. Obst- und Weinbau* 2008, *24*, 4.



Red-brownish colorations in the floor of the medieval cellar (Picture: Archäologie Baselland)

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2009.229

Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Hair Testing: A New Area in Forensic Toxicology

Christian Staub*

*Correspondence: PD Dr C. Staub, University Center of Legal Medicine, West Switzerland; 1 rue Michel Servet, CH-1211 Geneva 4
Tel.: +41 22 379 56 08, Fax: +41 22 789 24 17, E-Mail: christian.staub@hcuge.ch

Keywords: Doping analysis · Drugs · Forensic toxicology · Hair analysis · Pharmaceuticals

Interesting methodological developments in the last twenty years have increased the role of hair in forensic toxicology. The first period (1989–1998) was devoted to the analysis of classical drugs of abuse, such as opiates, cocaine, cannabinoids, amphetamines and benzodiazepines (the most abused pharmaceuticals in Europe and Switzerland). Most of the developed methods for these compounds were the work of active researchers regrouped under the auspice of the international Society of Hair Testing (SoHT) founded in December 1995. The second period (1999–2008) was characterized by the detection in hair of a single exposure and the related applications in doping control or in drug-facilitated crimes. Hair analysis can essentially contribute to doping analysis in special cases, in addition to urine. Some methods were also published for the determination of biomarkers (*e.g.* ethylglucuronide, a marker of alcohol abuse), since ethanol is not directly detectable in hair. Still more recently, hair analysis was also presented as a powerful tool for documenting a clinical case of dioxine over-exposure.

The first step in hair testing is the sampling: the hair is collected from the vertex posterior as close as possible to the scalp. Generally a lock of 20 to 30 hairs is collected. When a segmental analysis is required, the laboratory has to cut the hair in sections of 1 to 3 cm. Then the hair is pulverized, incubated in a solution of acid or organic solvent in order to extract the compound(s) of interest from the hair matrix. After a purification step, the extract is analyzed by gas or liquid chromatography coupled to mass spectrometry (*e.g.* GC/MS, GC/MS/MS, LC/MS or LC/MS/MS). All these techniques are recognized as the 'gold standard' in hair analysis.

Hair analysis has opened a new area in forensic toxicology because hair is the unique sample which allows having toxicological history over a time window of weeks to months.

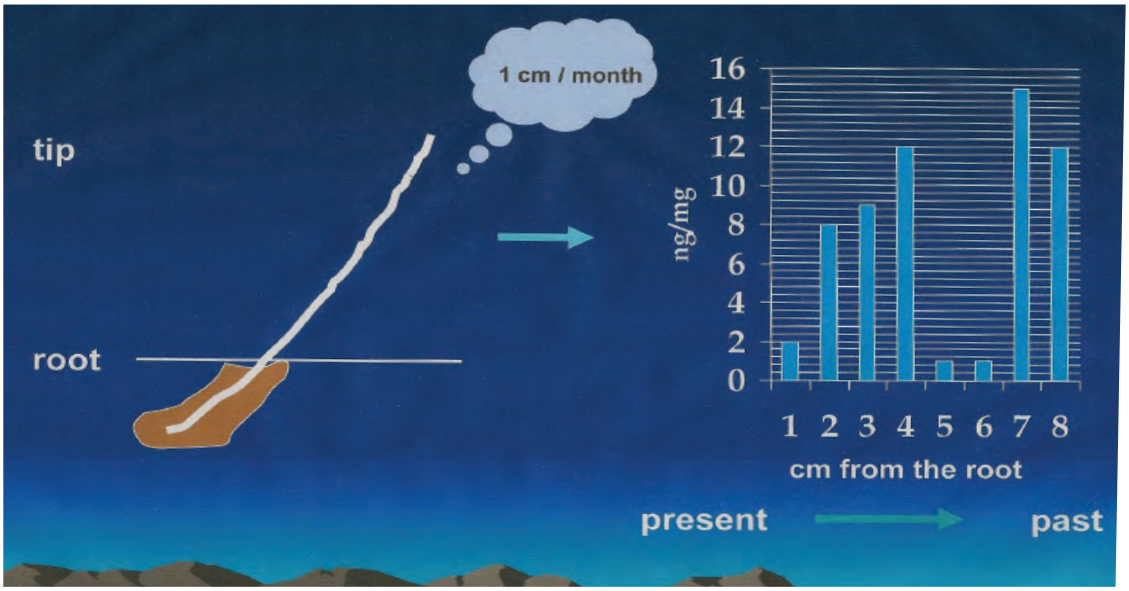
Received: 21. Feb. 2009

References

'Analytical and Practical Aspects of Drug Testing in Hair', Ed. P. Kintz, CRC Press, Boca Raton, **2006**.

V. Cirimele, M. Villain, G. Salquèbre, C. Staub, P. Kintz, *Forensic Sci. Int.* **2008**, *176*, 51.

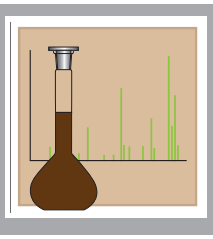
Hair sampling: the first important step in hair testing



Principle of hair analysis: decrease of consumption with two month of abstinence (concentration of cocaine in hair)

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2009.292



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

When Machine Tastes Coffee: Successful Prediction of Coffee Sensory Profiles by Instrumental Methods Based on On-line PTR-MS

Christian Lindinger*[a], Chahan Yeretzian[b], and Imre Blank[c]

*Correspondence: Dr. C. Lindinger[a], Tel.: +41 21 785 93 84, Fax: +41 21 785 85 54, E-mail: christian.lindinger@rdls.nestle.com
[a]Nestlé Research Center, Vers-chez-les-Blanc, CH-1000 Lausanne 26
[b]Zurich University for Applied Sciences, Department Life Sciences and Facility Management, Institute for Chemistry & Biological Chemistry, CH-8820 Wädenswil
[c]Nestlé Product Technology Center, CH-1350 Orbe

Keywords: Chemometrics · Coffee flavour · Predictive modelling · PTR-MS · Sensory profiling

Flavour scientists have long been exploring what makes coffee smells so good. Analytical chemists have discovered a range of impact compounds contributing to coffee flavour, while sensory scientists have developed hedonic methods for accurate coffee flavour profiling. Although both approaches look at the same phenomenon, albeit from different perspectives, correlating instrumental data with sensory profiles has proven to be a difficult task. This is due to two fundamental challenges.

First, intensity scales in sensory and analytical measurements are of fundamentally different nature. Sensory attributes are evaluated within an arbitrary range (*e.g.* 0 to 10). In contrast, instrumental measurements result in signals that are not restricted in intensity, thus leading to very different relationships between the intensities of sensory versus analytical signals. Second, sensory scores are not proportional to concentration and each odorant follows a specific non-linear sigmoid dose–response curve. In contrast, instrumental signals are in general linear with concentration. Hence, diluting coffee by a defined factor will result in instrumental intensities reduced by the given factor leaving the signal intensity ratios unaltered. However, diluting coffee makes its sensory profile not just less intense, but may result in a flavour profile of its own.

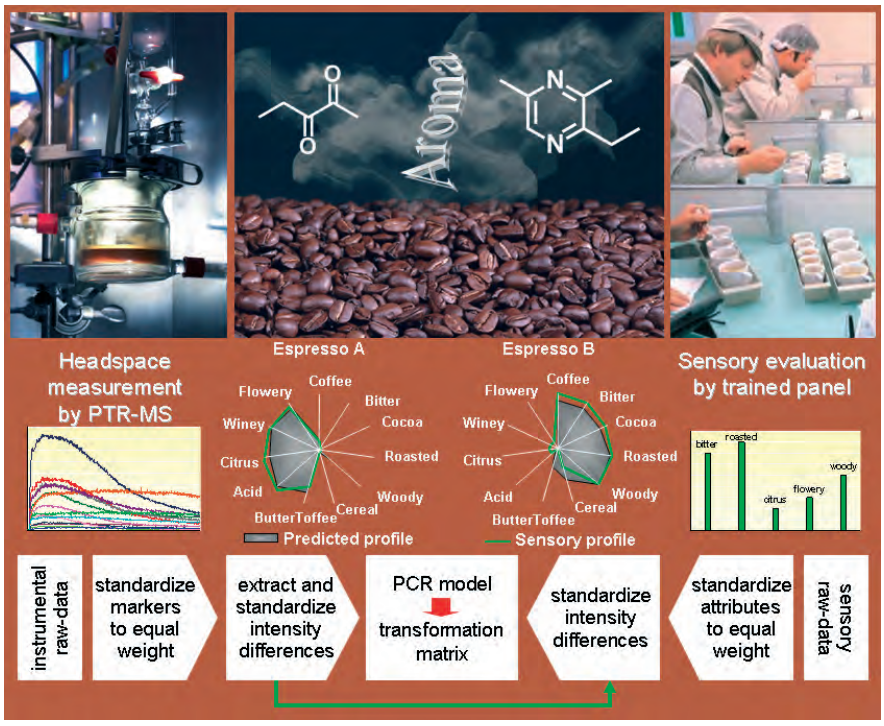
We have succeeded to accurately predict sensory profiles of espresso coffees of different cup sizes and flavour profiles based on instrumental Proton Transfer Reaction-Mass Spectrometry (PTR-MS) data, by applying a novel chemometric strategy. Correlation was conducted according to a knowledge-based standardization of sensory and instrumental data. The key to success was a procedure removing the information of absolute intensities leading to data sets essentially containing only quality information (sensory profiles and instrumental data; green arrow in the Fig.). From here on, the correlation could be completed according to well known procedures of principle component regression (PCR).

The result is a powerful predictive tool for coffee sensory profiles (Fig. centre), applicable to short cups as well as Lungo coffees. The predictive model was validated on a set of eight additional coffees. Furthermore, the prediction of sensory profiles can be accomplished by on-line PTR-MS within two minutes.

Received: March 6, 2009

Reference

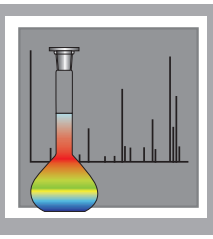
C. Lindinger, D. Labbe, P. Pollien, A. Rytz, M.-A. Juillerat, C. Yeretzian, I. Blank, *Anal. Chem.* **2008**, *80*, 1574.



Sensory predictive model: Once the sensory attributes and analytical signals are selected for maximum differentiating potential, PTR-MS data and sensory profiles are standardized to equal weight. In the case of sensory data, only a few corrections are needed since all attributes are already evaluated within an arbitrary range (0 to 10). PTR-MS data were standardized to the mean value for each individual chemical marker considering all samples. This data treatment, which is different from that of the sensory data, does not entail any limitation to a minimum or maximum value, thus allowing subsequently adding even more extreme coffee samples to the model. A knowledge-based standardization and normalization procedure of both datasets (green arrow) permits removing the information of absolute intensities and focusing on data that essentially contain only quality information. The correlation of both datasets by using PCR resulted in a robust and reproducible predictive model. Centre: Two examples of distinctively different coffees showing the sensory profiles and model results.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2009.350



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

21st Century HPLC Method Development

Barbara Channer*[a], Claudia Retz[a], Melvin R. Euerby[b], and Frank Moffatt[a]

*Correspondence: Dr. B. Channer[a], Tel.: +41 61 686 60 83, Fax: +41 61 686 65 65, E-mail: barbara.channer@solvias.com
[a]Solvias AG, P.O. Box, CH-4002 Basel; [b]Hichrom Ltd., 1 The Markham Centre, Station Road, Theale, Reading, Berks., RG7 4PE, UK

Keywords: Fast chromatography · HPLC · Impurities · Method development · Related substances

Developing chromatographic methods to separate impurities in drug substance and product can require indefinite amounts of time and effort and result in methods that may still not be robust. The Solvias approach considers all of the operating parameters in such a way that methods are developed in the shortest time whilst also delivering the highest assurance of robustness. How is this achieved?

Method Development Strategy

1. Assess the physico/chemical properties of the analytes.
2. Use short sub-3 micron LC columns for fast chromatography.
3. Select up to six stationary phases, based upon selectivity differences and security of supply of columns.
4. Select up to two organic and twelve aqueous mobile phases, *e.g.* different pH values based upon pKa, log P, and theoretical stability of the analytes.
5. Select the gradient times.
6. Select as many temperatures as desired.
7. Model the results using retention modelling software. Decide upon the best conditions considering speed, resolution, and robustness (areas of the design space in which changes would still produce an adequate performance).
8. Verify the optimum conditions predicted by the software.
9. Up-scale to a longer LC column (if required).
10. Optimise the reporting.
11. Proceed to method validation.

Established methods for quality control have a well-defined design space making it an easy task to incorporate new data from stability studies to expand the model reliably for stability indicating purposes. For example, the resolution map shows the optimum separation of 11 components (the red part of the diagram). The predicted separation was verified and showed a good fit.

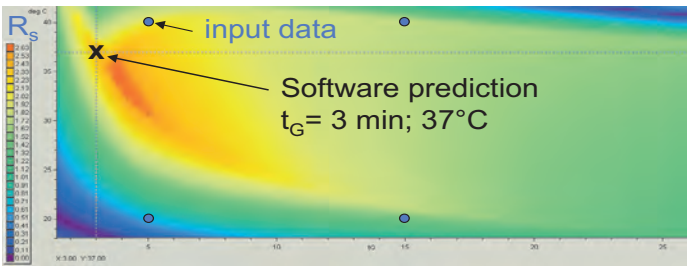
Chromatographic separations are often developed in an unsystematic *ad hoc* manner leading to problems later on. State of the art practices and experience can be used to accelerate method development and to provide robust methods that are supported by scientifically sound design space.

Received: April 22, 2009

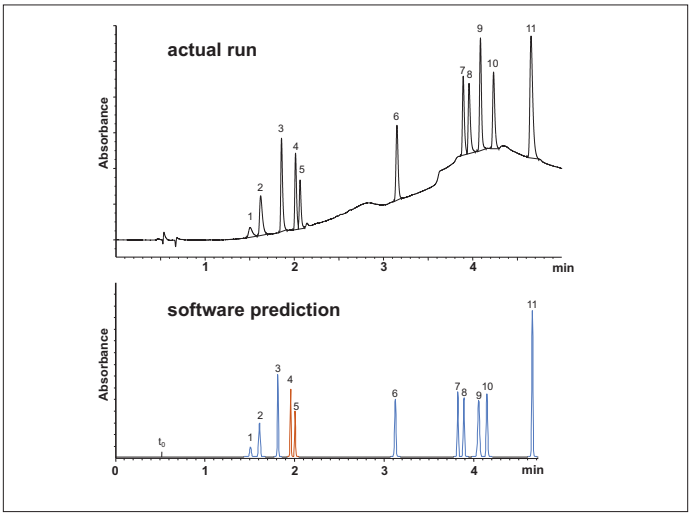
References

M. R. Euerby, P. Petersson, *J. Chromatogr. A* **2003**, *994*, 13.
P. Petersson, M. R. Euerby, *J. Sep. Sci.* **2007**, *30*, 2012.

HPLC method development platform with high pressure option up to 600 bar.



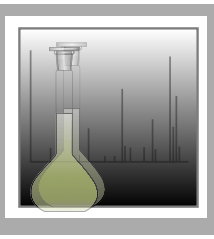
Resolution map for the gradient time/temperature model for eleven compounds.



Comparison between predicted and experimental separation of eleven compounds.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2009.522



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Alcohol Markers Reveal Relapse Drinking Episode

Christian Lanz[a], Balthasar Jung[a], Jitka Caslavska[a], Veronika Deiss[b], and Wolfgang Thormann*[a]

*Correspondence: Prof. Dr. W. Thormann[a], Tel.: + 41 31 632 32 88, Fax: + 41 31 632 49 97 ; E-mail: wolfgang.thormann@ikp.unibe.ch

[a]Department of Clinical Pharmacology, University of Bern, Murtenstrasse 35, CH-3010 Bern

[b]Meditest Bulle SA, rue de la Promenade 42, CH-1630 Bulle

Keywords: Alcohol marker · Capillary electrophoresis · CDT · Ethyl sulfate

Alcohol abuse and alcohol dependence are major public health problems. Because of the known ability of alcohol abusers to hide their addiction and the importance of an early diagnosis of alcohol abuse, assays for the verification of alcohol intake are required. Direct ethanol metabolites (ethyl glucuronide and ethyl sulfate) and changes in the isoform pattern of transferrin (Tf) present in serum are biomarkers for recent and chronic excessive alcohol intake, respectively. The two ethanol metabolites are non-volatile, water soluble and stable. They can be detected in serum and urine hours after complete elimination of the ingested alcohol. The microheterogeneity of Tf isoforms changes upon chronic consumption of large amounts of ethanol: the relative amount of desialylated isoforms becomes higher compared to the pattern of healthy teetotalers and social drinkers. Carbohydrate-deficient transferrin (CDT) encompasses Tf isoforms with zero (asialo-Tf) and two (disialo-Tf) sialic acid residues in the carbohydrate side chains of the molecule.

Longitudinal monitoring of individuals with a history of alcohol abuse is important for the early detection of relapse drinking after abstinence and in legal cases. Alcohol, alcohol metabolites, and CDT levels should therefore be determined on a regular basis over an extended period of time. In sera of a patient collected over a period of more than four months, alcohol could not be detected. The same was true for ethyl sulfate in the first sample collected after a three-week break. Analysis of CDT, however, revealed about a twelve-fold increase of CDT after the three-week interval without sample collection. CDT levels before the break and again in the samples collected later than five weeks after the break were normal. Sera were analyzed by a capillary electrophoresis assay for which the upper reference value was determined to be 1.70%. Asialo-Tf could be unambiguously detected in the first four samples after the break. The presence of asialo-Tf and the high amounts of disialo-Tf and thus CDT monitored and the characteristic decay of these levels thereafter unambiguously revealed an episode of relapse drinking of this patient. **This example demonstrates that the capillary electrophoresis assay applied to samples from patients with suspected chronic excessive alcohol consumption provides a solid basis to identify alcohol abusers.**

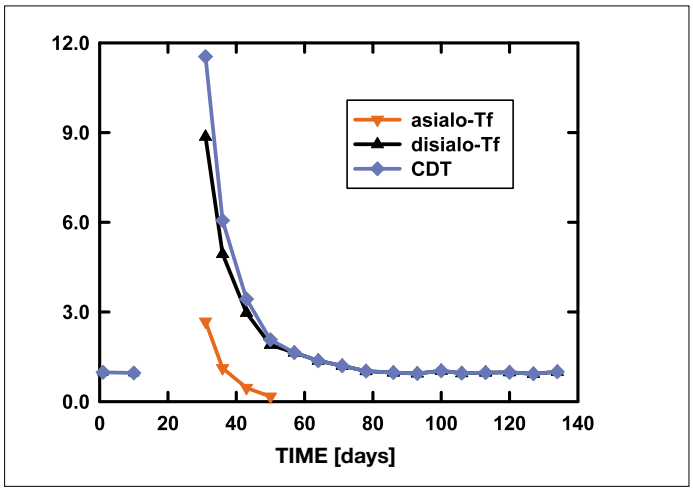
Received: May 15, 2009

References

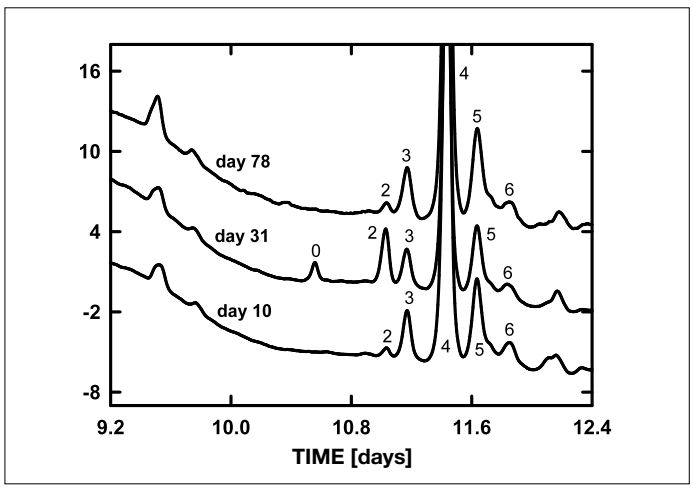
C. Lanz, M. Kuhn, V. Deiss, W. Thormann, *Electrophoresis* **2004**, *25*, 2309.

B. Jung, J. Caslavska, W. Thormann, *J. Chromatogr. A* **2008**, *1206*, 26.

How much is too much?



CDT, disialo-Tf and asialo-Tf serum levels determined by capillary electrophoresis in samples of a patient collected over a 132-day period.



Electropherograms showing the transferrin patterns of three sera. 0, asialo-Tf; 2, disialo-Tf; 3, trisialo-Tf; 4, tetrasialo-Tf; 5, pentasialo-Tf; 6, hexasialo-Tf. Data at days 10 and 78 show normal transferrin patterns whereas that at day 31 is typical for an alcohol abuser.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen

Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2009.580

Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Human Fingerprint Imaging by Scanning Electro-Chemical Microscopy (SECM)

Fernando Cortes-Salazar[a], Meiqin Zhang[a], Andy Becue[b], Jean-Marc Busnel[a], Michel Prudent[a], Christophe Champod[b], and Hubert H. Girault*[a]

*Correspondence: Dr. H. H. Girault, Tel.: +41 21 693 31 45, Fax: +41 21 693 36 67, E-mail: hubert.girault@epfl.ch
[a]Laboratoire d'Electrochimie Physique et Analytique, Ecole Polytechnique Fédérale de Lausanne, Station 6, CH-1015 Lausanne
[b]Institut de Police Scientifique, Ecole des sciences criminelles, Université de Lausanne, Batochime, CH-1015 Lausanne

Keywords: Fingerprint imaging · Forensic science · Latent fingermarks · Scanning ElectroChemical Microscopy

Fingerprints constitute a valuable tool for human identification because of their permanence and extreme discriminating power. The latter is thanks to the fact that fingerprints are characterized by a unique combination of specific features like the flow of the ridges (*i.e.* overall pattern), the ridge path deviations (*e.g.* ridge endings, bifurcations), and finally the intrinsic ridge characteristics (*e.g.* ridge shape, pores). As a consequence, forensic scientists have used fingerprint analysis for identification purposes for more than a hundred years. Human identity verification is obtained by the comparison of a fingermark found at a crime scene with the fingerprints collected on a suspect, or stored in a database. Therefore, the quality of the obtained image when imaging fingermarks is a major issue. Indeed, most of the time, marks left on touched objects and surfaces are not visible to the naked eye (*i.e.* latent fingermarks). This is due to the fact that they are composed of a mix of organic and inorganic compounds in small quantities which are deposited on the surfaces when touched by bare hands. During the last decades, the development of new techniques for fingerprint detection has been extensively pursued, since traditional methods of fingerprint detection may be unable to provide high quality images when dealing with not ordinary surfaces (*e.g.* multicoloured backgrounds, contamination with body fluids or other components, and porous surfaces).

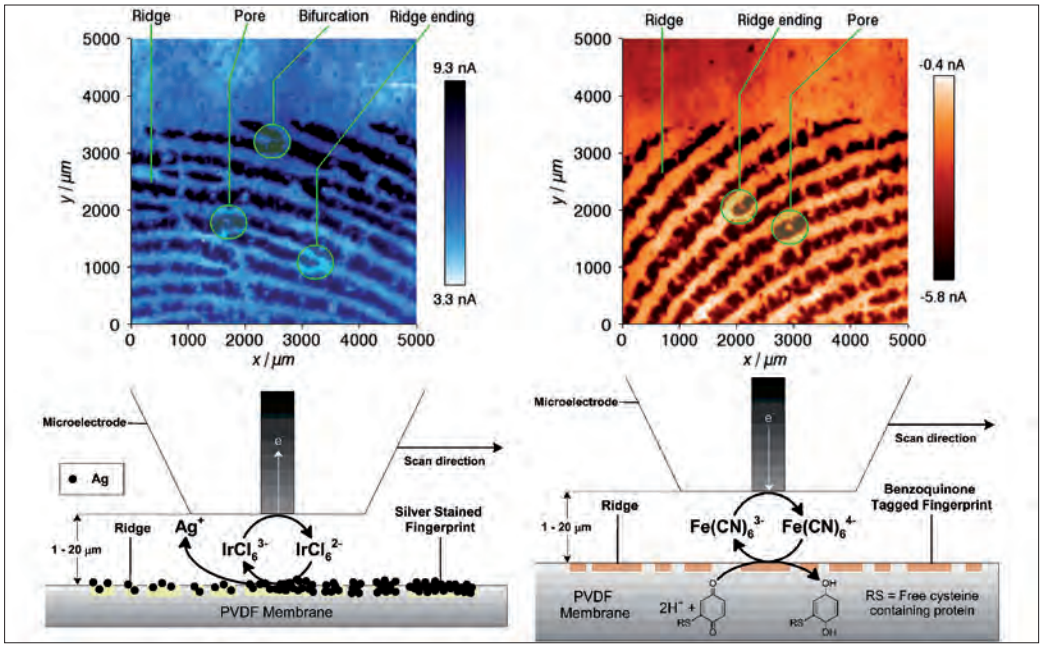
Recently, it has been shown that visualization of latent fingermarks can be enhanced by using Scanning ElectroChemical Microscopy (SECM) combined with silver-staining (left side of the Fig.), benzoquinone tagging (right side of the Fig.) or multi-metal-deposition technology. In the first two cases the protocol is based on the staining of latent fingerprints by silver salts or benzoquinone, whereas in the latter case the latent fingerprint is coated first with gold nanoparticles that are then coated with silver by electroless deposition, allowing the fingerprint detection by the same principle showed on the left side of the Fig.

SECM provides the forensic scientist a new tool for the visualization of human fingerprints on unusual surfaces. In addition, fingerprint images are obtained with such a high resolution and sensitivity that information on pore shape and position can be easily obtained to be used for the identification process.

Received: June 25, 2009

References

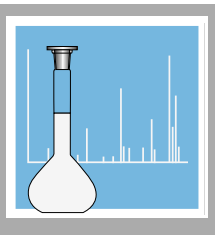
M. Zhang, H. H. Girault, *Electrochem. Comm.* **2007**, *9*, 1778.
M. Zhang, A. Becue, M. Prudent, C. Champod, H. H. Girault, *Chem. Comm.* **2007**, *38*, 3948.
M. Zhang, H. H. Girault, *Analyst.* **2009**, *134*, 25.
F. Cortes-Salazar, J. M. Busnel, F. Li, H. H. Girault, *J. Electroanal. Chem.*, **2009**, accepted.



Top: Constant height SECM images of a fingerprint developed by silver staining (left) or benzoquinone tagging (right). Bottom: Schematic representation of the detection principle of silver nanoparticles containing fingerprints (left) and benzoquinone-tagged fingerprints (right).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2009.694



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

How Should the Release of Bisphenol A from Baby Bottles be Determined?

Sandra Biedermann-Brem and Koni Grob*

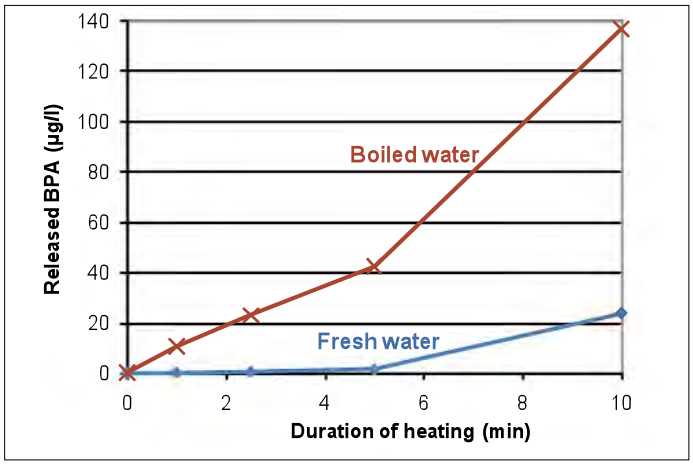
*Correspondence: Dr. K. Grob, Kantonales Labor Zürich, Fehrenstrasse 15, CH-8032 Zürich
Tel.: +41 43 244 71 31, Fax: +41 43 244 71 01; E-mail: koni@grob.org

Keywords: Baby bottles · Bisphenol A · Estrogenic effect · Polycarbonate

Bisphenol A (BPA) is probably the most famous synthetic chemical known to have an estrogenic effect. The Agence Française de Sécurité Sanitaire des Aliments (AFSSA) dealt with the question of whether microwave heating could result in higher concentrations of BPA from the polycarbonate of the bottle wall than considered so far, starting out from the bench mark of 50 µg/kg supported by the European Food Safety Authority (EFSA). Initially it seemed to be simple: polycarbonate absorbs little energy. Ehlert *et al.* supported this view: concentrations were clearly below 1 µg/l, as many tests reported with conventional heating. There was a single contrasting report from 2003, and it was from the German consumer journal *Oeko-Test*: BPA concentrations reached 157 µg/l with microwave heating, almost 1000 times more than all the scientific papers gave.

It turned out that the data reported by Oeko-Test was obtained with tap water. This opened the eyes to a more fundamental problem: In the past, milk was simulated by distilled water, focusing on migration, *i.e.* on diffusion to the surface of the plastic and transfer into the food. However, we have shown that BPA migration is negligible compared to release by hydrolysis of the polymer, primarily in alkali media. Upon heating of tap water, CO_2 evaporates which shifts the hardness equilibrium towards the carbonate and increases the pH to about 9. It is this high pH which caused the high levels of BPA reported by *Oeko-Test* – and since baby milk is made with tap water, the use of distilled water did not adequately simulate reality.

The graph shows the release of BPA into tap water during microwaving in a baby bottle. Using fresh water, the pH gradually increases and in the first 5 min, only 1.5 µg/l BPA was released, whereas 23 µg/l was measured during the second 5 min. Using water previously boiled in a pan, with a pH of 9.5, BPA was released at far higher rate: after 5 min (recommended for sterilization), the BPA concentration was 36 µg/l and it reached 137 µg/l after 10 min.



Increase of BPA concentration into tap water boiled by microwaving in a baby bottle.

Conclusions

- **Microwave heating does not increase the PBA release *per se*, but since it is the only practical way of boiling water in a baby bottle, it is indirectly responsible for the highest concentrations.**
- **Simulation designed for migration testing is not adequate for predicting release by chemical attack. With tap water, the release can be at least 100 times higher than with distilled water.**
- **Under reasonable worst case conditions, BPA release from baby bottles still did not exceed the 50 µg/l, but this value was approached.**
- **If tap water of no more than 60 °C is filled into baby bottles, BPA concentrations remain below 1 µg/l, which is lower than that in human milk.**

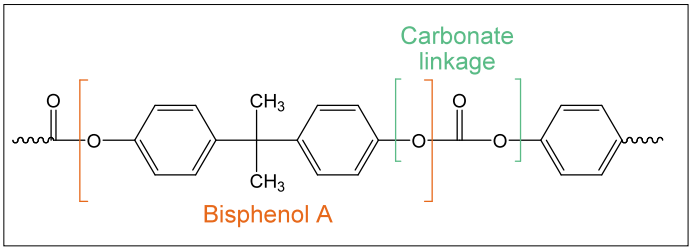
Received: August 6, 2009

References

S. Biedermann-Brem, K. Grob, P. Fjeldal, *Eur. Food Res. Technol.* **2008**, *227*, 1053.
S. Biedermann-Brem, K. Grob, *Eur. Food Res. Technol.* **2009**, *228*, 679.

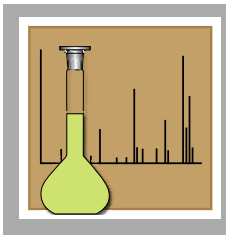
Bottles waiting for hungry babies.

Polycarbonate with the building block BPA and the chemically labile carbonate link.



Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2009.777



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Transcriptomics: A New Strategy to Screen for Hazardous Contaminants in Food

Katerina Lancova*[a], Hans Gmuender[b], Thomas Ellinger[c], and Hanspeter Naegeli[a]

*Correspondence: Dr. K. Lancova[a], Tel.: + 41 44 635 87 64, Fax: + 41 44 635 89 10, E-mail: katerina.lancova@vetpharm.uzh.ch

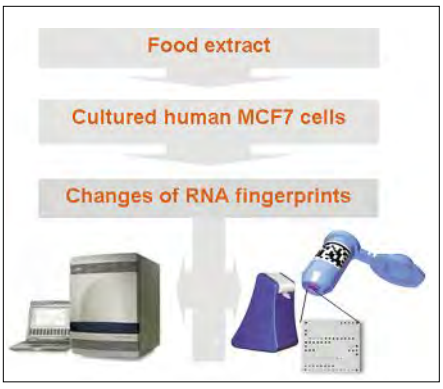
[a]Institute of Pharmacology and Toxicology, University of Zurich-Vetsuisse, CH-8057 Zurich; [b]Genedata AG, Maulbeerstr. 46, CH-4016 Basel; [c]Clondiag GmbH, Löbstedter Str. 103–105, D-07749 Jena

Keywords: DNA microarray · Food safety · Microchip · Real-time PCR · Trichothecenes

Type A trichothecenes (primarily T-2 and HT-2) are naturally occurring food contaminants originating from fungal infection of crop plants or mould infestation after harvest. These *Fusarium* mycotoxins display potent cytotoxic as well as immunosuppressive effects and are considered potential warfare agents. Based on animal studies, a temporary tolerable daily intake (t-TDI) of 0.06 µg/kg body weight/day for the sum of T-2 and HT-2 has been issued in the European Union. However, exposure assessments suggest that the combined intake of these mycotoxins exceeds in many countries the adopted t-TDI threshold. Therefore, to guarantee consumer protection, sensitive methods are necessary to detect T-2 and HT-2 toxins at parts per billion levels.

Towards that goal, we have recently established a new screening assay where cultured human cells are used as 'cytosensors' of hazardous contaminants in food. This assay is based on the observation that even traces of T-2 or HT-2 are able to induce massive and fast changes of gene expression in breast cancer cells. Two different platforms have been used to monitor these genomic effects at the transcriptional level: i) quantitative real time polymerase chain reaction (qPCR) with the fluorescent TaqMan® technology, and ii) miniaturised DNA microarrays (microchips) with colorimetric detection of biotin-labelled targets. In brief, the assay is carried out by exposing cultured human cells for 8–24 h to food extracts processed through MycoSep® clean-up columns. Next, selected RNA transcripts are converted to complementary DNA by reverse transcription and quantified either by qPCR or hybridisation on microchips. After normalization of expression changes against endogenous housekeeping controls, the resulting data are finally translated to T-2 toxin equivalents.

This novel bioassay strategy offers many important benefits for risk assessment and risk management, including its high sensitivity and its ability to detect multiple endpoints in a toxicologically relevant target system. In the future, this transcriptomic strategy will be extended to other food contaminants and it will also be used for mechanistic studies to analyse additive or antagonistic interactions between the individual components of complex contaminant mixtures.



Simplified scheme of transcriptomic-based methods for the detection of type A trichothecenes by qPCR (Applied Biosystems) and DNA microchips (Clondiag Chip Technologies).

Acknowledgements

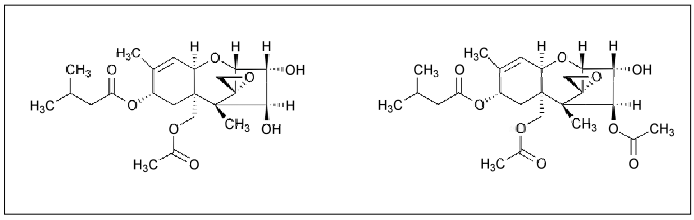
This research was supported by the European Commission (FOOD-CT-2005-006988).

Received: August 22, 2009

References

P. Bowens, K. Lancova, R. Dip, V. Povilaityte, J. Stroka, H. Naegeli, *Analyst* **2009**, *134*, 939.

K. Lancova, P. Bowens, J. Stroka, H. Gmünder, T. Ellinger, H. Naegeli, *World Mycotoxin J.* **2009**, *2*, 247.



Chemical structures of two major representatives of type A trichothecenes, HT-2 (left) and T-2 toxins (right).

Barley ear and grain infected with *Fusarium* fungi that are the major producers of trichothecene mycotoxins.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2009.889

Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Temperature Changes in the Altai Are Driven by Solar and Anthropogenic Forcing

Anja Eichler*[ab], Susanne Olivier[c], Keith Henderson[a], Andreas Laube[a], Jürg Beer[d], Heinz W. Gäggeler[ae], Tatyana Papina[f], and Margit Schwikowski[ab]

*Correspondence: Dr. A. Eichler[a], Tel.: +41 56 310 20 77, Fax: +41 56 310 44 35, E-Mail: anja.eichler@psi.ch

[a]Laboratory for Radiochemistry and Environmental Chemistry, Paul Scherrer Institute, CH-5232 Villigen

[b]Oeschger Centre for Climate Change Research, University of Bern, CH-3012 Bern

[c]Kantonales Laboratorium, Muesmattstrasse 19, CH-3012 Bern

[d]Department of Surface Waters, EAWAG, CH-8600 Dübendorf

[e]Department of Chemistry and Biochemistry, University of Bern, CH-3012 Bern

[f]Institute for Water and Environmental Problems, 656038 Barnaul, Russia

Keywords: Altai · Ice core · Isotope mass spectrometry · $\delta^{18}O$ · Temperature

In order to place recent climate change in a longer term context and to answer the important question whether the magnitude and rate of the 20th century climate change exceed the natural variability, highly resolved, millennial scale temperature reconstructions are required. Whereas there is already a high data coverage for certain areas in the world (as *e.g.* Europe), only very few long-term temperature reconstructions are available for West-Siberia. The Altai region is of particular interest, since it is within a highly continental area, revealing a stronger warming than other regions in the world during the last 50 years.

In 2001, a 139 m long ice core was drilled at the Belukha glacier, near the highest mountain of the Altai. The ice core was cut into 3600 samples at –20 °C in the cold room. The deepest sample was dated to the year 1250. Thus, the ice core contains climate information covering the past 750 years.

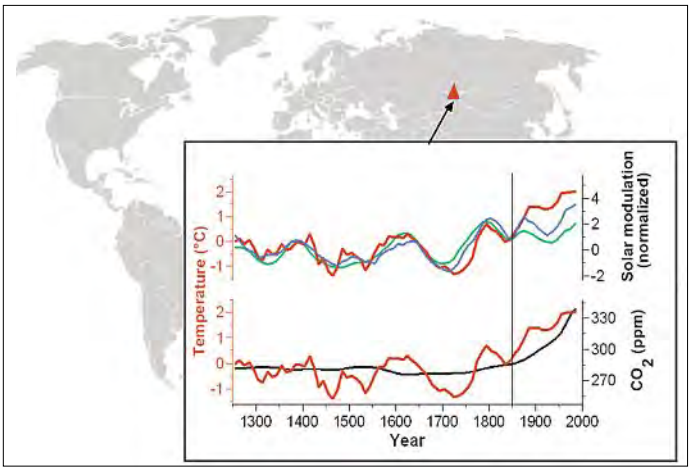
Temperatures in the Altai were reconstructed using the ice core oxygen isotope ($\delta^{18}O$) record, measured with an isotope mass spectrometer. It was demonstrated that the $\delta^{18}O$ record followed closely the atmospheric temperatures at a nearby weather station over the past 130 years and can therefore be used as a temperature proxy. The established temperature record was compared with proxy records of solar activity (solar modulation derived from ^{10}Be measurements in polar ice cores and ^{14}C records from tree rings). The Altai temperature record is significantly correlated with the solar activity proxies in the period 1250–1850, suggesting that the sun was one of the main driving forces for the temperature variation during the pre-industrial period. The temperatures followed the solar forcing with a time lag of 20 years, underlining the importance of indirect sun-climate mechanisms involving ocean-induced changes in atmospheric circulation. During the past 150 years, however, the temperatures in the Altai have shown a much higher rate of increase than that of solar activity. The strong increase in the industrial period correlates with the increase in the concentration of the greenhouse gas CO_2 over this time.

Our results clearly demonstrate that at this continental site in the Altai region the 20th century temperatures are beyond the natural range of variability of the preceding 700 years.

Received: September 11, 2009

Reference

A. Eichler, S. Olivier, K. Henderson, A. Laube, J. Beer, T. Papina, H. W. Gäggeler, M. Schwikowski, *Geophys. Res. Lett.* **2009**, *36*, L01808, doi:10.1029/2008GL035930.



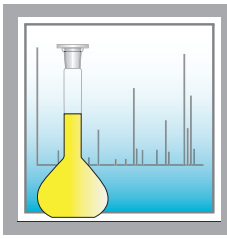
Location of the drilling site (triangle) and the Altai temperature reconstruction (red) compared with solar activity inferred from ^{10}Be (blue) and ^{14}C (green) and CO_2 concentration (black). The solar modulation curves were shifted by 20 years (average value of the lag between solar forcing and temperature response). The vertical line divides the pre-industrial era (1250–1850) from the last 150 years.

Belukha massif in the Siberian Altai and the Ak-kem lake (photo: Patrick Ginot). The 139 m long ice core was drilled in 2001 in the saddle between west and east summit (49°48'N, 86°34'E, 4062 m asl).

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2010.95



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Identification of Dioxin Metabolites in the Poisoning Case of Victor Yushchenko

Markus Zennegg*[a], Olivier Sorg[b], Peter Schmid[a], and Jean-Hilaire Saurat[b]

*Correspondence: M. Zennegg[a], Tel.: + 41 44 823 46 15, Fax: + 41 44 823 40 41, E-Mail: markus.zennegg@empa.ch

[a]Swiss Federal Laboratories for Materials Testing and Research (Empa), Laboratory for Analytical Chemistry, Ueberlandstrasse 129, CH-8600 Dübendorf

[b]Dermato-Toxicology, Swiss Center for Human Applied Toxicology and Department of Dermatology, University Hospital, CH-1205 Geneva

Keywords: Dioxin elimination pathways · Dioxin metabolites · Dioxin poisoning · TCDD metabolites · Victor Yushchenko

In autumn 2004, the current Ukrainian president, Victor Yushchenko, suffered a severe dioxin poisoning. First blood serum levels of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), measured in December 2004, were 110'000 pg/g lipid weight. These blood serum levels were more than 50'000 times higher than those in the general population and represent the second highest ever measured concentrations of TCDD in a human. We monitored the levels of TCDD and its metabolites for more than three years in various samples of blood serum, adipose tissue, skin, urine, faeces, and sweat of Victor Yushchenko. The work was only possible thanks to the cooperation and expressed consent of Victor Yushchenko.

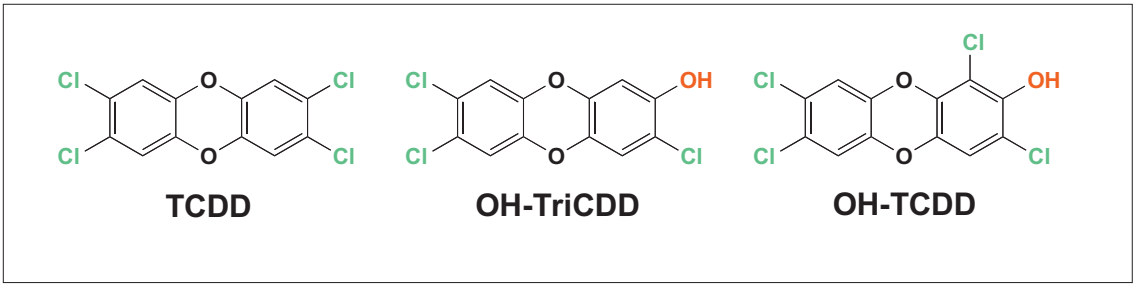
For the first time in a human, two polar metabolites of TCDD, 2,3,7-trichloro-8-hydroxydibenzo-*p*-dioxin and 1,3,7,8-tetrachloro-2-hydroxy-dibenzo-*p*-dioxin were identified in serum, faeces, and urine using gas chromatography–high resolution mass spectrometry. Highest amounts of these metabolites were detected in faeces whereas serum and urine contained only traces. The relative amount of TCDD metabolites excreted *via* faeces accounts to approximately 40% of the totally eliminated TCDD *via* this route. As only small amounts of TCDD metabolites were detected in urine, renal excretion of these transformation products can be considered as a minor elimination pathway. In serum, the relative amount of metabolites was 50 times lower than in faeces, probably due to the rapid elimination of the metabolites after formation in the liver by phase I and II enzymes and transferred *via* the bile to the intestine. In our analyses, 98% of the total loss of the toxin and its metabolites could be recovered by the above-mentioned different elimination routes. **The elimination half-life of TCDD determined in Victor Yushchenko was 15.4 months, being much shorter than the half-life of 5–10 years reported for humans in the literature. Obviously, the strongly elevated TCDD blood serum levels caused the induction of detoxifying enzymes responsible for the transformation and elimination of the toxin.**

Received: December 9, 2009

Reference

O. Sorg, M. Zennegg, P. Schmid, R. Fedosyuk, R. Valikhnovskyi, O. Gaide, V. Kniazevych, J.-H. Saurat, *The Lancet* **2009**, *374*, 1179.

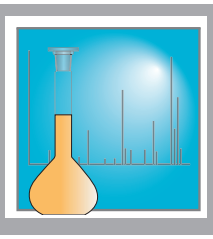
Victor Yushchenko before the dioxin poisoning (A), 3.5 months (B), and 3.5 years (C) after the poisoning incident



Structures of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) and the two metabolites 2,3,7-trichloro-8-hydroxydibenzo-*p*-dioxin (OH-TriCDD) and 1,3,7,8-tetrachloro-2-hydroxydibenzo-*p*-dioxin (OH-TCDD)

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2010.196



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

What Damage Can Biodiesel Cause in Jet Fuel?

Vladimir Purghart* and Hans Jäckle

*Correspondence: Dr. V. Purghart, Intertek Caleb Brett (Schweiz) AG, Wagistrasse 2, CH-8952 Schlieren, Tel.: +41 43 433 78 10, Fax: +41 43 433 78 19, E-mail: schlieren@intertek.com

Keywords: Biodiesel · FAME · Fatty acid composition analysis · Fatty acid methyl ester · Jet fuel

The term 'bio' has became very popular in the past years. It is often associated with ecological and environmental benefits. There is not only 'bio'-food but also 'bio'-fuel. A lot of car drivers think they are doing something good for the environment by using 'bio'-diesel fuel. Biodiesel in Europe is mostly prepared from rape, palm or soy oil. In the process of biodiesel production, the glyceride bonds are broken and methyl esters of the long chain fatty acids are formed (known as FAME = fatty acid methyl ester). Of course, FAME can be used instead of conventional diesel in diesel engines, but it has some different physical properties. The major differences are storage stability and cloudiness at lower temperatures. The latter phenomenon causes problems if jet fuel (Jet A-1) is contaminated by FAME. Even minor contamination at ppm levels could cause a jet turbine to fail. Therefore, the FAME content in jet fuel must not exceed 5 ppm. Such contaminations can be caused *e.g.* by transportation.

Air plane taking off (Copyright Roland Graf, cloning.ch)

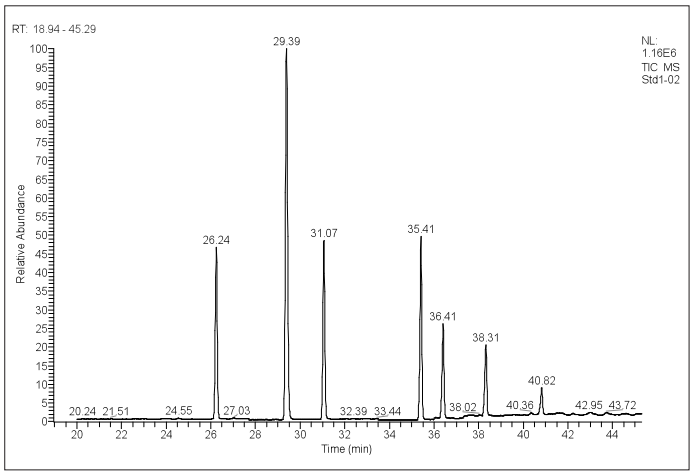
Table 1. Selected fatty acid methyl esters for the quantification in Jet A-1

Species to be detected	Significant SIM masses [Da]	Expected retention time [min]
Methyl-palmitate C16:0	227, 239, 270, 271	24.9–26.4
Methyl-margarate C17:0	241, 253, 284	30.1–31.4
Methyl-stearate C18:0	255, 267, 298	34.7–35.5
Methyl-oleate C18:1	264, 265, 296	35.5–36.5
Methyl-linoleate C18:2	262, 263, 264, 294, 295	37.7–38.6
Methyl-linolenate C18:3	236, 263, 292, 293	40.3–41.1

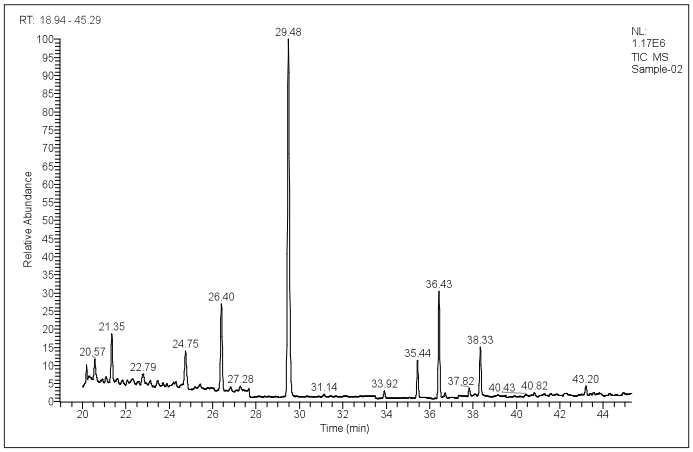
A GC-MS test method was developed by the Institute of Petroleum (IP PM-DY/09) to monitor methyl esters of the most representative fatty acids present in biodiesel derived from the above-mentioned oils (a summary is given in Table 1). To obtain a sensitive GC-MS method, the SIM-mode (selected ion monitoring) was used (see 'Significant SIM masses' in the Table). The advantage of measurement in SIM mode is that the signals of any other non-relevant compounds in the chromatogram are suppressed or even eliminated. The Figures show a chromatogram of a standard solution containing 2 ppm of each fatty acid as well as a chromatogram of a real jet fuel. This sample contains a total amount of 5 ppm FAME.

This quality control process of jet fuel is important for air traffic security.

Received: January 7, 2010



Standard solution containing 2 ppm of each fatty acid methyl ester (compare with the data given in the Table). The signal at 29.39 minutes is the internal standard (d33 - methyl-margarate)



Real Jet A-1 sample showing a total amount of 5 ppm FAME. The signal at 29.48 minutes is the internal standard (d33 - methyl-margarate)

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2010.267

Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Metabolite Profiling Reveals that Dark Chocolate May Beneficially Modulate the Stress-related Metabolism in Humans

François-Pierre J. Martin, Serge Rezzi, Sebastiano Collino, and Sunil Kochhar*

*Correspondence: Dr. S. Kochhar, Nestlé Research Center, Vers-chez-les-Blanc, CH-1000 Lausanne 26
Tel.: +41 21 785 93 36, Fax: +41 21 785 94 86, E-mail: sunil.kochhar@rdls.nestle.com

Keywords: Chronic stress · Dark chocolate · Metabonomics · Mass spectrometry · Nuclear magnetic resonance spectroscopy

Many studies have demonstrated the potential health implications of dark chocolate constituents, but rarely as a whole product. For instance, cocoa is rich in flavonoids, mainly flavan-3-ols, which are associated with benefits for cardiovascular health by maintaining low blood pressure, improving endothelial function, and by reducing thrombotic, oxidative and inflammatory states. Other cocoa-containing bioactive molecules include theobromine and amines (phenylethylamine, N-oleoyl- and N-linoleoyl-ethanolamine), which are reported to reduce blood pressure and act on the central nervous system metabolism, respectively. There is thus growing evidence on the health benefits associated with chocolate.

We have sought to capture a global view of the metabolic changes associated with chocolate consumption in healthy men and women using metabonomics. Nutrimetabonomics provides a system approach to assess the systemic metabolic status of an individual, which encapsulates information on genetic and environmental factors, gut microbiota activity, lifestyle and food habits. We have used proton nuclear magnetic resonance (^{1}H NMR) spectroscopy and mass spectrometry (MS) as complementary analytical platforms to monitor metabolic changes associated with a daily intake of 40 g of dark chocolate over a period of two weeks in the urine and blood plasma of 30 individuals classified according to their self-reported anxiety trait.

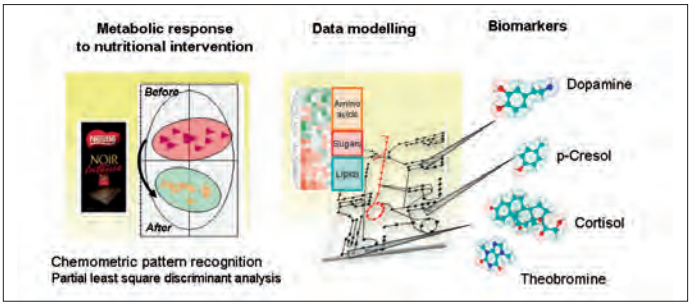
Human subjects with higher anxiety trait showed a distinct metabolic profile indicative of a different energy homeostasis (lactate, citrate, succinate, trans-aconitate, urea, proline), hormonal metabolism (adrenaline, DOPA, 3-methoxy-tyrosine) and gut microbial activity (methylamines, *p*-cresol sulfate, hippurate). Dark chocolate reduced the urinary excretion of the stress hormone cortisol and catecholamines and partially normalized stress-related differences in energy metabolism (glycine, citrate, *trans*-aconitate, proline, β-alanine) and gut microbial activities (hippurate and *p*-cresol sulfate). **The study provides evidence that a daily consumption of 40 g of dark chocolate over a period of two weeks is sufficient to modify the metabolism of healthy human subjects.** Therefore, subtle changes in dietary habits are likely to modulate the metabolic status that might be associated with long-term health consequences, in particular *via* the activity of the symbiotic bacterial partners.

Received: January 29, 2010

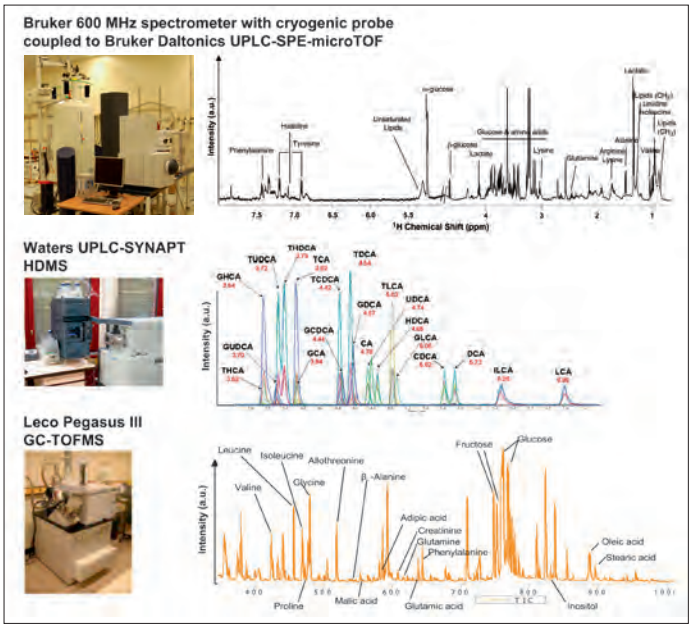
Reference

F. P. Martin, S. Rezzi, E. Pere-Trepat, B. Kamlage, S. Collino, E. Leibold, J. Kastler, D. Rein, L.B. Fay, S. Kochhar, *J Proteome Res.* **2009**, *8*, 5568.

The world of chocolate.



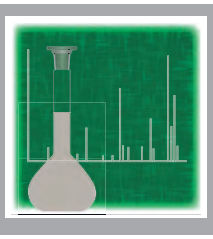
Flowchart of nutritional metabonomics. Chemometric and bioinformatic analyses allow modelling of nutrition-induced metabolic changes and identification of biomarkers associated with food habits and health benefits.



Typical NMR- and MS-based metabonomic analytical platforms. NMR offers a holistic profile of hundreds of metabolites with no *a priori* selection, while MS methods are commonly employed for global and targeted profiling. Both techniques are jointly employed to provide a snapshot of the metabolism and for biomarker identification.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2010.322



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

The Role of Volatile Organic Compounds in the Indirect Defense of Plants Against Insect Herbivores Above- and Belowground

Matthias Held*, Marco D'Alessandro, Ivan Hiltpold, and Ted C. J. Turlings

*Correspondence: Dr. M. Held, Institute of Biology, University of Neuchâtel, Case postale 2, Rue Emile Argand 11, CH-2009 Neuchâtel
Tel.: +41 32 718 25 22, Fax: +41 32 718 30 01, E-Mail: matthias.held@unine.ch

Keywords: Herbivore-induced plant volatiles · Indirect defense · Modification of odor blends · Nematodes · Olfactometer · Parasitoids

Plants respond to attacks by herbivorous insects by releasing specific blends of volatile organic compounds (VOCs). These herbivore-induced VOCs are known to play a major role in the interaction between plants and insects and may directly protect the plant by being toxic or deterrent, but may also benefit the plant indirectly by attracting natural enemies of the herbivores.

The chemical composition of herbivore-induced VOC blends is known for many plant–herbivore systems. Some VOCs are taxon-specific, whereas other VOCs appear to be common to many different plant families. These common compounds mainly include 'green leaf volatiles' (C6 aldehydes, alcohols and derivatives), cyclic and acyclic terpenes, phenolic compounds and nitrogenous compounds.

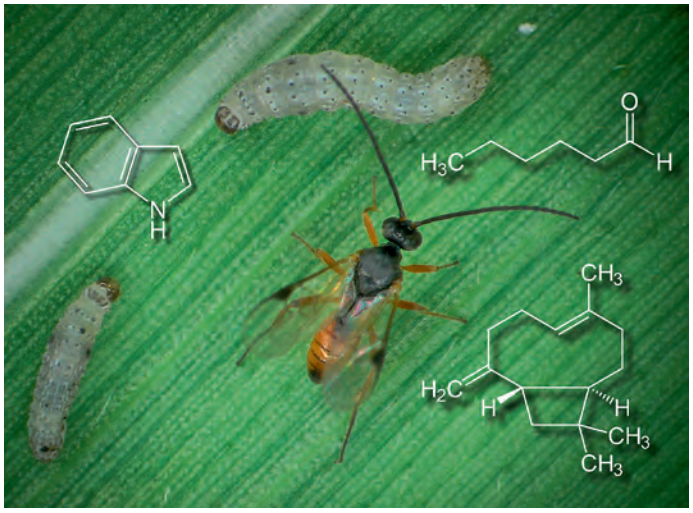
Our model plant is maize, which shows a rapid reaction to an attack by caterpillars and root feeding beetle larvae. Belowground, maize roots respond within hours to feeding of larvae by releasing the sesquiterpene (*E*)-beta-caryophyllene. The emission of this compound results in increased recruitment of entomopathogenic nematodes (tiny worms that parasitize and kill insect larvae). Similarly, after being attacked by caterpillars aboveground, maize leaves emit a complex blend of volatiles that is attractive to parasitic wasps, which use the volatiles to find and kill the caterpillars. It remains largely unclear which VOCs within the blend are the key compounds mediating this parasitoid attraction.

To study the importance of individual volatiles we combine different methods to generate and modify herbivore-induced VOC blends by manipulating the plant genotype, the plant phenotype and the headspace of volatiles produced by the plant. We focus on 'subtractive' approaches used to obtain blends differing in only few known VOCs and 'additive' approaches to generate blends of known composition. All blends are analyzed with gas chromatography/mass spectrometry and tested for attraction to the wasps in olfactometer studies. **By combining the above approaches, we aim to provide new insights into the relevance of individual VOCs involved in indirect defenses, which might help to develop ecologically sound methods to control pest insects**.

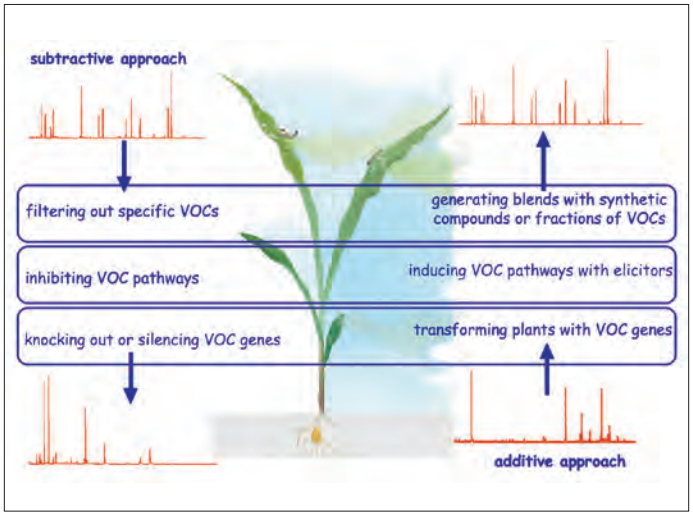
Received: March 3, 2010

References

C. Schnee, T. G. Köllner, M. Held, T. C. J. Turlings, J. Gershenzon, J. Degenhardt, *Proc. Natl. Acad. Science USA* **2006**, *103*, 1129.
S. Rasmann, T. G. Köllner, J. Degenhardt, I. Hiltpold, S. Töpfer, U. Kuhlmann, J. Gershenzon, T. C. J. Turlings, *Nature* **2005**, *434*, 732.
M. D'Alessandro, T. C. J. Turlings, *The Analyst* **2006**, *131*, 24.



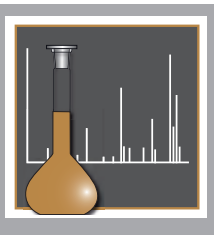
The parasitic wasp *Cotesia marginiventris* hunting for *Spodoptera littoralis* caterpillars on a maize leaf. Molecular structures illustrate some important volatiles released by maize plants after herbivore attack such as indole, hexanal and caryophyllene (photo by M. Held)



Modifying maize odor blends by manipulating plant genetics, plant physiology and plant headspace to identify the importance of individual volatile compounds for parasitoid attraction

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2010.426



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Analyses of Helium, Uranium, and Thorium in Ancient Gold Objects and Estimates of their Time of Manufacturing

Otto Eugster*

*Correspondence: Prof. Dr. O. Eugster, University of Bern, Physics Institute, Sidlerstrasse 5, CH-3012 Bern, Tel.: +41 31 631 4418, Fax: +41 31 631 4405, E-mail: eugster@space.unibe.ch

Keywords: Ancient gold objects · Helium · Thorium · Uranium · U/Th-He dating

When gold crystals are formed in the Earth's crust, other elements, such as U and Th, are incorporated into the crystal lattice. Thus, gold from mines and found in river beds always contain traces of U and Th. The three long-lived isotopes ^{238}U, ^{235}U, and ^{232}Th decay to Pb by emitting α-particles. An α-particle is the nucleus of the ^{4}He atom, so when two electrons combine with an α-particle, a ^{4}He atom is formed. Because gold is highly retentive for this gas up to about 500 °C, the He atoms remain trapped. We have studied these characteristics, beginning in 1992, in numerous natural gold samples from all over the world. In a publication on genuine and faked gold crystals of the Santa Elena gold mine in Venezuela, we mentioned that this method can also be applied to historical ancient gold objects.[1] The challenge to perform these analyses for such objects is big, because the He concentration in about 2000 year old gold is extremely low and because only very small samples are available from valuable antiquities. In 2005 we purchased a mass spectrometer specialized for low He concentration measurements from SPECTRON in St. Petersburg, Russia. Since then we determined the He, U, and Th concentrations in a large number of art objects. In the past five years we have investigated numerous gold objects in order to verify their antiquity.[2] Here we present two typical objects for which the authenticity was doubtful after art historical assessments.

A signet ring with the picture of a male bust in side-view and writing in reflected face 'HILDEBERTISREGIS'. In a comprehensive study of this ring, Weber[3] concluded that it can be attributed to one of the two kings Childebert I or II of the sixth century Merowingian dynasty of Western Europe. The weight of this gold ring (40.56 g) corresponds almost exactly to the weight of nine Byzantine *solidi* (gold coins), indicating that coins of this type were used by the goldsmith to manufacture the royal ring. Our results for He, U, and Th yield a manufacturing time of 1460 ± 400 years, in good agreement with the time when the kings Childebert I and II lived. The second object is a gold torc, purported to originate in the Hallstatt/La Tène transition period, about 5th century BC. For this torc we obtained an age of 2200 ± 1100 years confirming the authenticity of the torc.

In many cases the antiquity of a gold object can be determined using the U/Th-He dating method. Due to the extremely low He concentrations in the samples, the method is not applicable to objects younger than about 1000 years.

In samples from young objects, such as a Napoléon gold coin or commercial gold wire, the observed He concentrations were extremely low or below the detection limit of the mass spectrometer.

About one fifth of the objects purported to be genuine tested in the past years were modern forgeries.

For some gold objects we observed an excess of He resulting in an unreasonably high age. Thus, these objects were undatable. The reason for the He excess are He-rich crystalline inclusions that were included in the gold when the objects were manufactured.

Received: March 30, 2010

References

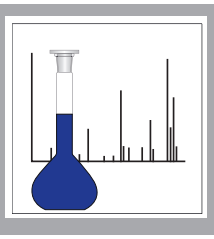
[1] O. Eugster, *Gold Bulletin* **1996** , *29*, 101, publ. by the World Gold Council, London.
[2] O. Eugster, J. Kramers, U. Krähenbühl, *Archaeometry* **2009,** *51*, 672.
[3] A. G. Weber, 'Der Childebertring und andere frühmittelalterliche Siegelringe', Ed. A.G. Weber, Gertrudenstrasse 29, D-50667 Köln, Germany, **2007**, pp. 223.

Signet ring attributed to King Childebert I or II of the sixth century Merowingian dynasty of Western Europe.

Gold torc purported to originate in the Hallstatt/La Tène transition period (5th century BC). Diameter 16.5 cm.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2010.616



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Copeptin: A New Prognostic Stress-Marker in Ischemic Stroke

Mira Katan[ab] and Mirjam Christ-Crain*[a]

*Correspondence: Dr. M. Christ-Craina, Tel.: +41 61 265 25 25, Fax: +41 61 265 51 00, E-Mail: mirjam.christ-crain@unibas.ch
[a]Department of Endocrinology, University Hospital Basel, Petersgraben 4, CH-4031 Basel
[b]Department of Neurology, University Hospital Basel, Petersgraben 4, CH-4031 Basel

Keywords: Biomarker · Copeptin · Prognosis · Stroke

Stroke is the third leading cause of death and the primary cause of long term disability. Thus, there is need to develop a credible evidence base of prognostic information for outcomes that is meaningful to patients and clinicians, including the level of independency.

Every bodily disruption – such as an ischemic stroke – evokes a stress response, which serves to restore homeostasis and to facilitate adaptation. Essential to the stress response are corticotropin-releasing hormone (CRH) with its cosecretagogue arginin-vasopressin (AVP) and other neuropeptides that drive the activity of the hypothalamic-pituitary-adrenal (HPA) axis. These stress hormones serve as a sort of on-site monitoring, and allow the endogenous information system of our body to be tapped into that accurately assesses the severity of damage and thus prognosis. An accurate prognostic assessment has the potential to guide interventions and effectively plan and monitor rehabilitation, thus optimizing the management of patients.

Unfortunately, the measurement of circulating AVP levels and CRH is challenging. Until now these stress hormones could not be used as reliable prognostic markers in stroke. However, copeptin, a glycopeptide derived from the vasopressin precursor hormone together with neurophysin II, is released in an equimolar ratio to AVP. It is more stable in the circulation and easy to determine due to a new sandwich immunoassay.

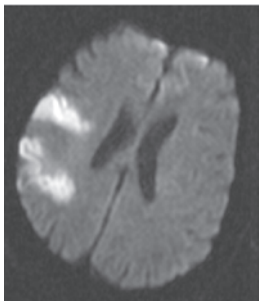
We therefore conducted a prospective cohort study at the University Hospital Basel, Switzerland, over one year. Patients presenting with an acute ischemic cerebrovascular event were included and 362 patients with an ischemic stroke were analysed. In this study, we found copeptin to be a novel, strong, and independent prognostic marker for functional outcome and death in patients with ischemic stroke. The prognostic accuracy of copeptin in stroke patients was superior to that of other commonly measured laboratory parameters. The combination of the gold standard clinical score (the National Institute of Health Stroke score) with the biomarker revealed a significantly better prognosis.

Copeptin appears to have interesting potential as a new prognostic biomarker. This may allow improved risk-stratification and allocation of targeted therapies for stroke patients in the future. A more tailored allocation of health care resources to patients at-risk is arguably the prerequisite for high quality health care in an era of limited health care resources.

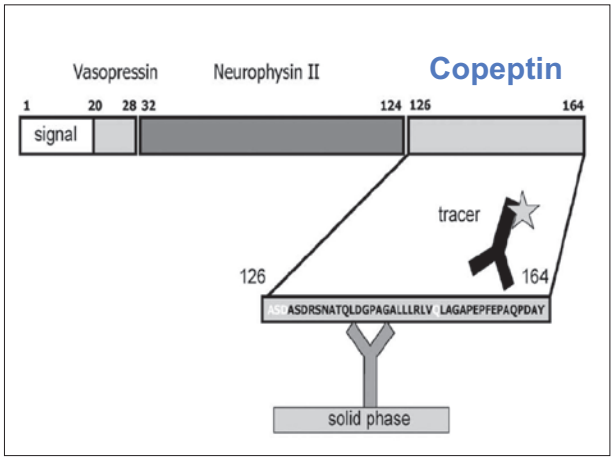
Received: May 20, 2010

References

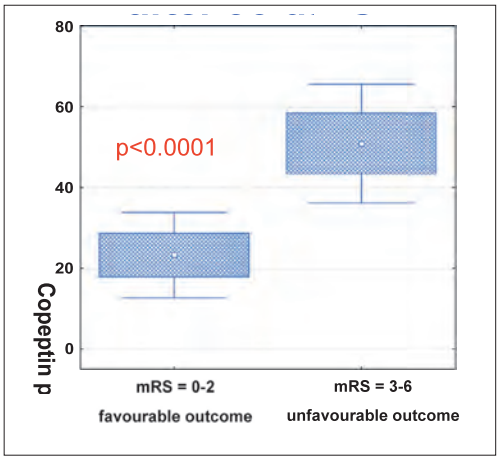
N. G. Morgenthaler, J. Struck, C. Alonso, A. Bergmann, *Clin. Chem.* **2006**, *52*, 112.
M. Katan, F. Fluri, N. G. Morgenthaler, P. Schuetz, C. Zweifel, R. Bingisser, K. Müller, S. Meckel, A. Gass, L. Kappos, A. J. Steck, S. T. Engelter, B. Müller, M. Christ-Crain, *Ann. Neurol.* **2009**, *66*, 799.



Diffusion-weighted image showing in white the ischemic area of a stroke.



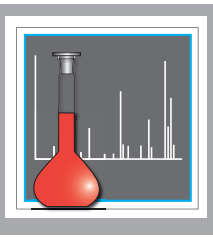
Immunoassay for copeptin (figure is partially adapted from J. Struck, N. G. Morgenthaler, A. Bergmann, *Peptides* **2005**, *26*, 2500).



Copeptin concentration in patient plasma and functional outcome after 90 days.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2010.668



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

HPLC on the Dance Floor

Daniel Allemann, Hans Pauli, André Mürner, Samuel Steiner, and Hans-Jörg Helmlin*

*Correspondence: Dr. H. J. Helmlin, Pharmaceutical Control Laboratory, Office of the Cantonal Pharmacist Berne, Baltzerstrasse 5, CH-3012 Bern, Tel.: +41 31 633 11 66, Fax: +41 31 633 11 68, E-mail: hans-joerg.helmlin@gef.be.ch

Keywords: Cocaine · Designer drugs · Drugs prevention · Ecstasy · HPLC · MDMA · Mobile laboratory · Party drugs

In the context of drug prevention projects, the mobile laboratory unit of the Cantonal Pharmacist Berne is analyzing so-called 'party drugs' at techno events. This project started in 1998 and is collaborating with 'Streetwork Zurich' and the 'Contact Net' foundation in Bern. Since then, more than 1700 samples have been investigated at more than 100 events.

The mobile laboratory – a proprietary development – is based on commercially available components. It consists of four custom-made, steel-framed racks on wheels: one is used for the balance and the documentation work, one is for sample preparation, and two are equipped with WLAN-controlled HPLC-DAD instruments. This laboratory is run on-site by two experienced technicians. Every sample is documented prior to analysis, then a simple extraction is done which yields the sample solution for qualitative and quantitative analysis. It is possible to handle about five to six samples per hour. Routinely, more than 50 compounds can be reliably characterized. In the case of unknown ingredients, dangerous mixtures or high dosages, warnings are spread during the event, if necessary also for a broader public (see *www.saferparty.ch* and *www.raveitsafe.ch*). The laboratory is the focal point of the advisory service and facilitates contact with the target group. During the laboratory analysis, a social worker conducts a conversation with a structured interview. An anonymous questionnaire is a mandatory part of the short consultation.

Besides the personal drug counseling, the twelve campaigns per year allow the illegal market to be tracked. The emergence of new compounds or changing trends of consumers' behavior can be observed and possible health risks are identified.

Some examples include:

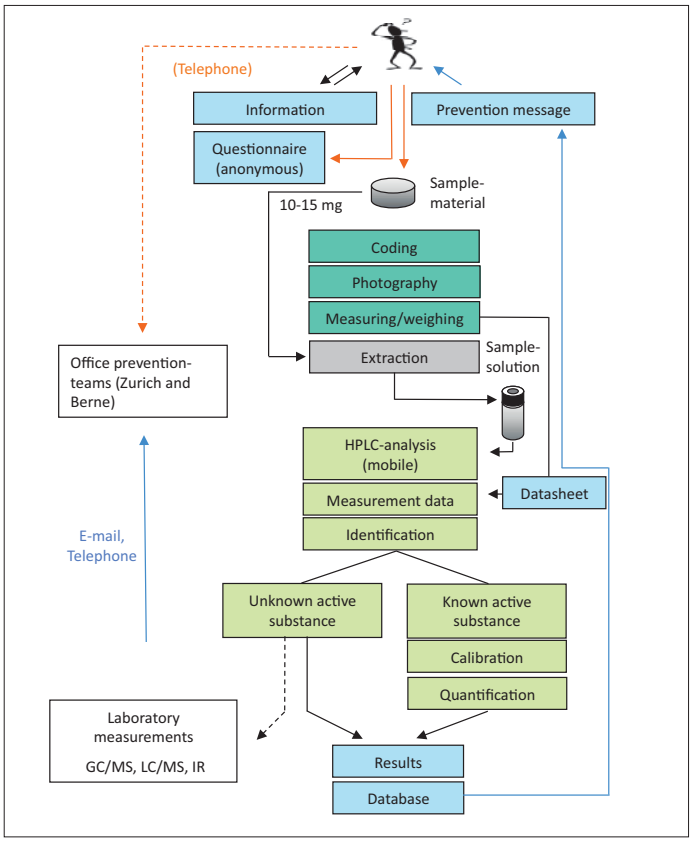
– MDMA (Ecstasy) is still the preferred party drug. Since 2005, the increased emergence of fake ecstasy pills with meta-chlorophenylpiperazine as the active ingredient has unsettled consumers.

– Since 2003, a wave-like increase of cocaine samples can be observed. Today, cocaine is the third most frequently analyzed compound, after MDMA and amphetamine. In addition, a decrease of the cocaine content from more than 50% to less than 30% mass fraction was detected over the years. A noticeable observation is the fact that pharmacologically active adulterants are now found more frequently, such as the illicit pain killer phenacetine or the anthelmintic levamisol which are dangerous to health.

– New compounds, so-called 'designer drugs', are appearing with increasing incidence at parties. This new trend emerged about two years ago. Examples are compounds such as mephedrone, methylone and butylone which could be identified recently. These drugs are derivatives of known psycho-active compounds but they are not (yet) listed as scheduled drugs with regard to controlled substances legislation.

Received: July 22, 2010

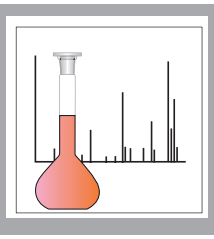
The mobile HPLC laboratory departs for the dance floor



Flow diagram: note the collaboration between the laboratory and the prevention teams

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2010.754



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Optical Detection of Endogenous Biological Cyanide

Felix Zelder* and Christine Männel-Croisé

*Correspondence: Dr. F. Zelder, Institute of Inorganic Chemistry, University of Zürich, Winterthurerstrasse 190, CH-8057 Zürich
Tel: +41 44 63 546 24, Fax: +41 44 63 568 02, E-mail: zelder@aci.uzh.ch

Keywords: Cassava · Corrinoids · Cyanide · Cyanogenic glycosides · 'Naked-eye' detection

Cyanide poisoning is well known from its murderous role in detective stories as well as from the warning labels shown on cigarette packets since October 2003.

However, it is generally unknown that cyanide in common foodstuff exhibits a daily life problem for hundreds of million of people in developing countries and continues to cause severe acute and chronic health problems. Cyanide is stored in the form of cyanogenic glycosides in more than 2000 plants such as flax seeds, bamboo or cassava and is enzymatically released after cell disruption. Cassava (*Manihot esculenta* Crantz) is one of the most popular staple foods in Africa.

For instance, in Mozambique, which is one of the poorest African countries, cassava roots are mainly produced for rural householders' consumption and sold at local markets (680 g per day and capita). Notably, the bitter cassava varieties with cyanide concentrations of up to 2.4 g/kg are widely used due to their natural defense mechanism against animal predation. Certain regions still suffer from cyanide poisoning as a consequence of non-adequately processed cassava roots.

It is astonishing that a cheap, easy-to-understand, fast and reliable test that is available to anyone is still lacking. Optical sensors that do not need expensive instrumentation are very attractive for these purposes. The research in our group focuses on the development of optical chemosensors for cyanide on the basis of vitamin B12 derivatives consisting of a corrin macrocycle with a central cobalt ion for cyanide binding. In the presence of cyanide, the cobalt-coordinated water is replaced by a cyanide anion inducing a color change from orange to violet. With this methodology in hand, the selective detection of cyanide below the guideline value of the U.S. Environmental Protection Agency of 0.2 mg/l was rendered possible by 'naked-eye' detection. Recently we demonstrated for the first time the detection of endogenous cyanide directly in biological matrices; we were able to follow the enzymatic release of cyanide in real-time directly on a biological surface using diffuse reflectance spectroscopy (DRUV-vis). **We envisage that this methodology will find further applications and will help to improve food safety control of cassava products in developing countries.**

Selling of dried cassava on a street in Zambeze Provinze/ Mozambique (courtesy of Lucas Tivana).

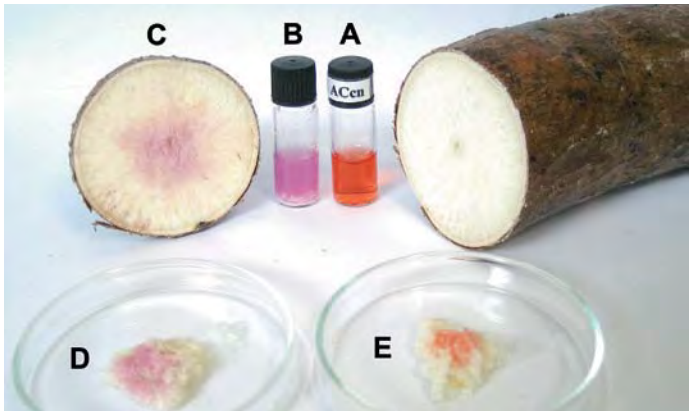
Acknowledgment

C.M.C. is grateful to financial support by the Marie Heim-Vögtlin-Programm of the Swiss National Science Foundation (Grant No. PMCDP2_129054/1) and F.Z. to the Forschungskredit of the University of Zurich. Support by R. Alberto and a generous gift of vitamin B12 from DSM Nutritional Products (Basel, Switzerland) is acknowledged.

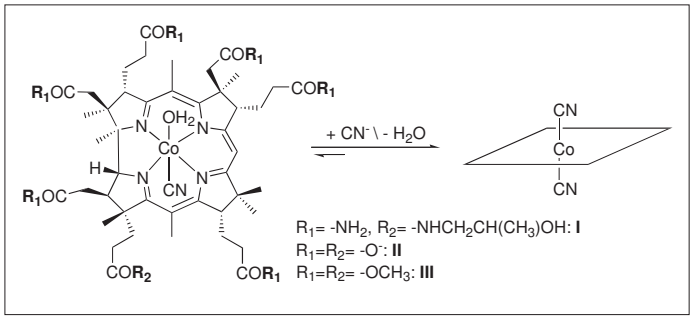
Received: August 5, 2010

Reference

C. Männel-Croisé, B. Probst, F. Zelder, *Anal. Chem.* **2009**, *81*, 9493.



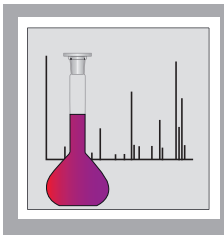
The orange corrin-based chemosensor (A) turns violet in the presence of cyanide, as in an aqueous solution of crude cassava (B), a freshly sliced cassava surface (C) or a ground cassava extract (D). No cyanide is detected after thorough washing of the ground cassava extract (E).



Structural formula of the corrin-based chemosensors I-III and a schematic representation of cyanide detection (right).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2010.825



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Enhancing the Quality and Efficiency of Analytical Method Development as Part of the Quality by Design Framework

Christoph Meyer*, Tomislav Soldo, and Undine Kettenring

*Correspondence: Dr. C. Meyer, Novartis Pharma AG, PHAD Oral Dosage Forms 2, Forum 1, Novartis Campus, CH-4056 Basel
Tel.: +41 61 696 31 43, Fax: +41 61 696 31 23, E-mail: christoph.meyer@novartis.com

Keywords: Analytical method development & validation · Design of Experiments (DoE) · Drug substance (DS) and drug product (DP) · Failure Mode Effects Analysis (FMEA) · Fishbone · HPLC · International Committee on Harmonization (ICH) guidelines · Quality by Design (QbD)

Analytical methods employed in the Pharmaceutical Industry must meet the most stringent demands in order to ensure product quality and patient safety for medicinal products that are released for clinical trials or market. Demands according ICH guidelines on analytical methods remain unchanged also with novel approaches such as QbD for method development and method validation. Contrary to traditional approaches towards method development and validation, employing QbD methodologies will allow for an earlier understanding and identification of potential variables affecting the method performance. QbD tools such as FMEA based upon fishbone evaluation followed by DoE approaches for robustness studies will enable enhanced quality to be integrated into the analytical method upfront.

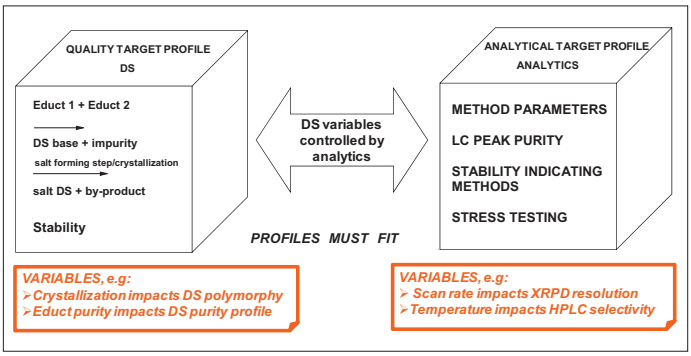
Variables affecting the method performance are included in a fishbone outline and are prioritized according to occurrence, detection, and impact leading to risk prioritization assessments. Critical method variables are employed for DoE and finally for the definition of the design space of the analytical method. Method performance is dependent on the critical method variables. Method performance per se is given by system suitability test requirements, for example limit of detection, repeatability, and resolution, for HPLC. These requirements define the analytical method target profile. On the other side, the aimed for quality target profile (technical perspective) of the DS or DP dictates what your analytical method performance must be capable of, thus the quality target profile of the DS or DP defines the analytical method target profile. This also includes the possible detection of unexpected impurities, for example new degradation products possibly arising from storage or any unforeseen impurity, for example arising from scale-up effects of the synthesis due to unpredicted hot-spot effects in your reaction vessel.

Applying QbD for analytics enables the reduction of variability of end-product and final release method to achieve the delivery of pre-defined, well-understood and constantly complying quality.

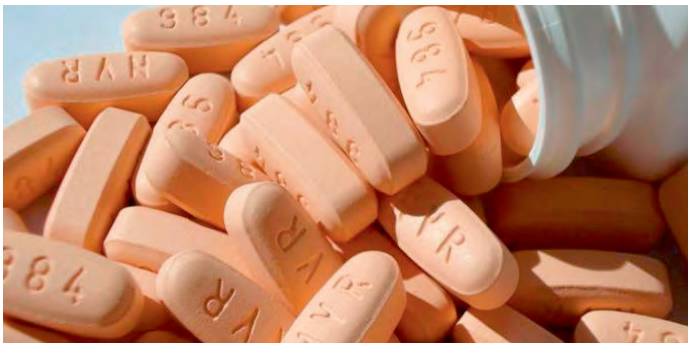
Received: September 1, 2010

Reference

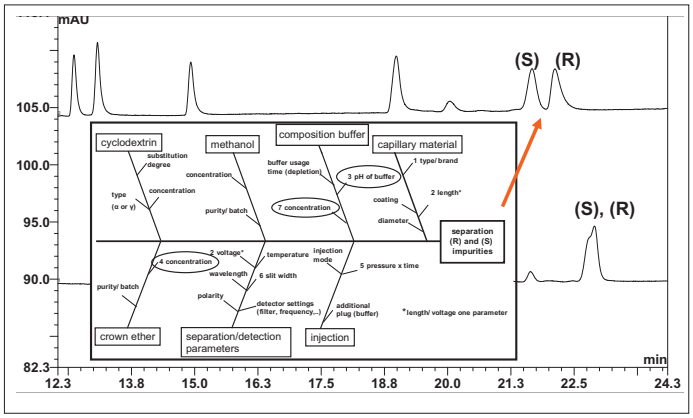
C. Meyer, F. Vogel, M. Manz, R. Heckmann, Lecture at HPLC 2009 Dresden, 'Quality by Design for HPLC – Perspective from pharmaceutical industry', **2009**.



The analytical target profile must fit the quality target profile. Knowledge-driven control of DS (or DP) variables: For example proper control of carry-over of impurities, stability and of the polymorphy of a drug substance.



In addition to the classical ICH guidelines 1–7, the ICH guidelines 8 (Pharmaceutical Development), 9 (Quality Risk Management), and 10 (Pharmaceutical Quality System) have recently been defined to holistically integrate a pharmaceutical quality system throughout the different stages of the lifetime of a product.

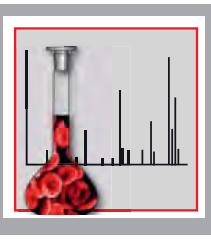


Fishbone diagram for a capillary electrophoresis method. Proper control of critical method variables and critical interactions will ensure proper method performance: Crown ether concentration increase leads to separation of (*S*) and (*R*) impurity.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2010.886



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Blood Doping Detection – A New Analytical Approach with Capillary Electrophoresis

Aline Staub[ac], Serge Rudaz[ac], Martial Saugy[bc], Jean-Luc Veuthey[ac], and Julie Schappler*[ac]

*Correspondence: J. Schappler[ac], Tel.: +41 22 379 64 77, Fax: +41 22 379 68 08, E-mail: julie.schappler@unige.ch

[a]School of Pharmaceutical Sciences, University of Geneva, University of Lausanne, Bd. d'Yvoy 20, CH-1211 Geneva 4; [b]Swiss Laboratory for Doping Analysis, University Centre of Legal Medicine, Geneva and Lausanne, Ch. des Croisettes 22, CH-1066 Epalinges; [c]Swiss Centre for Applied Human Toxicology (SCAHT), University of Geneva, CMU, Rue Michel-Servet 1, CH-1211 Geneva 4

Keywords: Blood doping · Capillary electrophoresis · HBOC · Hemoglobin-based oxygen carriers · Time-of-flight mass spectrometry

Blood doping is defined by the World Anti-Doping Agency (WADA) as the use of products and methods that enhance the uptake, transport, or delivery of oxygen to the blood. One approach uses artificial oxygen carriers, known as hemoglobin-based oxygen carriers (HBOC). These products are made of bovine or human hemoglobin (Hb) and were developed to treat some types of severe anaemia. They are claimed to provide a threefold more efficient oxygen transport and consequently to potentially improve sports performance, particularly in endurance disciplines such as long-distance running, cycling or swimming.

Capillary electrophoresis (CE) appears to be a promising technique for HBOC analysis in the context of doping control, since different CE protocols have already been developed for the analysis of Hb variants. In addition, the online combination of CE with mass spectrometry (MS) is an attractive option for intact protein analysis (*i.e.* no digestion, no derivatization step required). On the one hand, CE offers features such as high speed, great efficiency, and low solvent and sample consumptions. On the other hand, MS provides selectivity and specificity.

In this context, a complete analytical strategy based on CE was developed to detect intact HBOC in plasma samples. This methodology includes four distinct steps:

i) Plasma samples preparation based on immunodepletion to remove the most abundant proteins (*e.g.* albumin and immunoglobulin) that can interfere with CE separation and alter electrospray ionization.

ii) CE separation to obtain sufficient electrophoretic resolution between HBOC and Hb that could be released from mechanical hemolysis.

iii) Online UV-visible detection at 415 nm to selectively detect hemoproteins such as HBOC and Hb.

iv) TOF/MS detection to provide accurate mass on analytes and unambiguous determination of HBOC uptake.

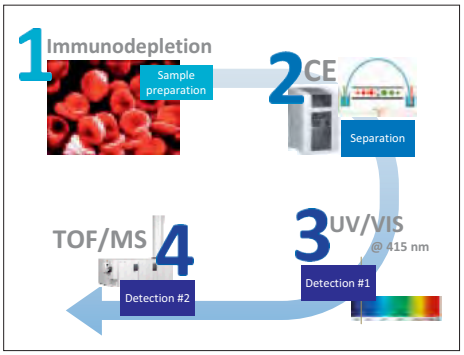
The limits of detection were in agreement with doping control requirements. This methodology thus appears suitable for implementation as a doping control screening method for HBOC analysis.

Received: September 23, 2010

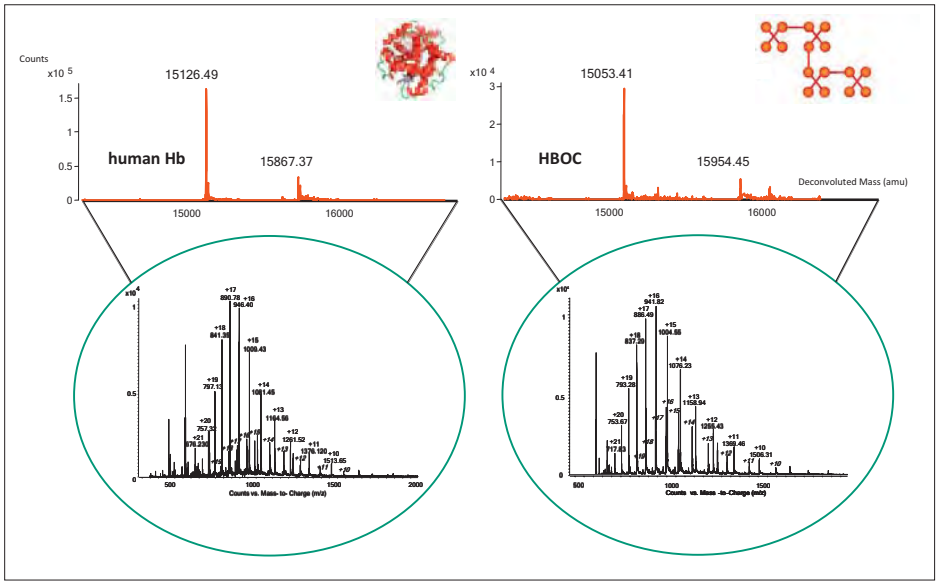
References

A. Staub, S. Rudaz, M. Saugy, J. L. Veuthey, J. Schappler, *Electrophoresis* **2010**, *31*, 1241.

A. Staub, J. Schappler, S. Rudaz, J. L. Veuthey, *Electrophoresis* **2009**, *30*, 1610.



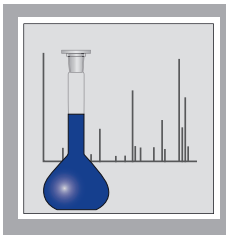
The four selectivity levels obtained with our method.



Mass spectra and deconvoluted mass spectra of Hb and HBOC by CE-TOF/MS.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2011.105



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Non-invasive Medical Diagnostic by Breath Analysis: Acetone Detection

Marco Righettoni, Antonio Tricoli, and Sotiris E. Pratsinis*

*Correspondence: Prof. Dr. S. E. Pratsinis, Department of Mechanical and Process Engineering, Particle Technology Laboratory, ETH Zürich, Sonneggstrasse 3, CH-8092 Zürich, Tel.: +41 44 632 31 80, Fax: +41 44 632 12 76, E-mail: sotiris.pratsinis@ptl.mavt.ethz.ch

Keywords: Acetone · Breath analysis · Diabetes · Nanoparticle gas sensors · Non-invasive medical diagnostic

The rising costs of medical care are pushing toward an optimization of resources and rapid integration of novel approaches. Breath analysis is a non-invasive diagnostic method offering for some applications even better performance than labor-intensive approaches such as blood analysis while drastically decreasing personnel and material costs. Breath is a mixture of nitrogen, oxygen, carbon dioxide, water, and a small fraction of other gases. The latter consists of simple gases (NO_x, NH_3) and more than 1000 trace and volatile organic compounds (VOCs) that are either generated in the body (endogenous) or are absorbed as contaminants from the environment (exogenous). These endogenous compounds can be utilized as breath markers for specific diseases.

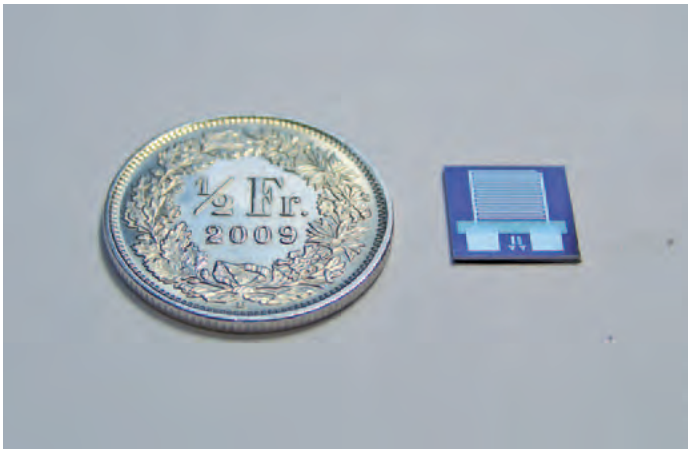
Acetone is related to type-1 diabetes and its concentration increases from 300–900 ppb for healthy humans to more than 1800 ppb for diabetic patients. Methods for breath analysis have progressed considerably over recent years. However, to achieve their use in clinical practice, the test techniques and devices need to be highly sensitive, selective, and require a fast response to the analyte; low cross sensitivity to humidity; small size and low production and maintenance costs.

Recently, we have demonstrated that Si:WO_3 nanoparticle films made by flame spray pyrolysis are able to rapidly detect down to 20 ppb of acetone in realistic breath conditions (*e.g.* 90% relative humidity). More specifically, the electrical resistance of such films drops remarkably (up to several orders of magnitude) by reaction with the analyte and thus allows a direct measurement of its concentration (chemo-resistive gas sensor). If a diabetic were to exhale on such a sensor, its resistance would suddenly drop much more (40%) than if a healthy person would do it. As a result, it would be possible to perform fast screening of potential diabetics during routine medical visits or even in pharmacies. Furthermore, this sensor prototype can be easily miniaturized to decrease power consumption and thus to improve its portability. This has potential for the monitoring of breath acetone concentration and in the future could facilitate the determination of blood glucose level. **These results demonstrate that breath analysis by chemo-resistive nanoparticle gas sensors has high potential as a rapid, non-invasive medical diagnostic. Furthermore, these portable devices can be produced at low cost while offering extremely high performance and thus could help reducing the cost of medical care while improving the quality of life of diabetic patients (no finger prick).**

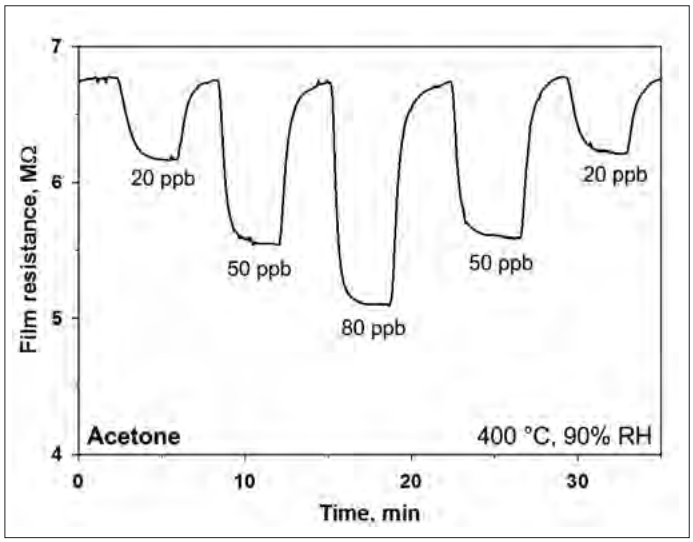
Received: December 10, 2010

References

A. Tricoli, M. Graf, F. Mayer, S. Kühne, A. Hierlemann, S.E. Pratsinis, *Adv. Mater.* **2008**, *20*, 3005.
M. Righettoni, A. Tricoli, S.E. Pratsinis, *Anal. Chem.* **2010**, *82*, 3581.
M. Righettoni, A. Tricoli, S.E. Pratsinis, *Chem. Mater.* **2010**, *22*, 3152.



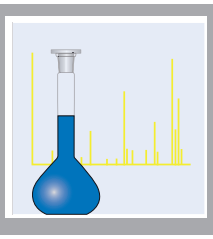
A prototype of the diabetes sensor. Thanks to its small size, it could be easily incorporated into an affordable, portable device for self-diagnosis.



WO_3 sensor resistance at realistic conditions (90% relative humidity) upon exposure of different ultra-low acetone concentrations (20, 50 and 80 ppb) at 400 °C.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2011.176



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Acesulfame: From Sugar Substitute to Wastewater Marker

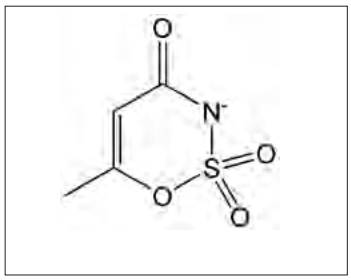
Ignaz J. Buerge* and Thomas Poiger

*Correspondence: Dr. I. J. Buerge, Agroscope Changins-Wädenswil Research Station ACW, Schloss, CH-8820 Wädenswil, Tel.: +41 44 783 63 83, Fax: +41 44 780 63 41, E-Mail: ignaz.buerge@acw.admin.ch

Keywords: Acesulfame · Artificial sweetener · Chemical marker · Domestic wastewater · Groundwater

Groundwater is an important drinking-water resource and deserves a high level of protection. Contamination may originate from various sources such as agriculture, households, industry, and traffic, and knowledge on the relative contribution of these sources is necessary to take efficient protection measures.

In search of a 'perfect chemical marker' of domestic wastewater from households in groundwater, we examined artificial sweeteners as they are consumed in considerable quantities with food and beverages. Some sweeteners pass through the human metabolism largely unaffected and thus reach the environment associated with domestic wastewater. One of these sweeteners, the sulfoamide acesulfame, was found ubiquitously in wastewater, surface waters, and groundwater from Switzerland.



Chemical structure of the artificial sweetener acesulfame. The compound is negatively charged at environmental pH values and thus very mobile.

Concentrations of acesulfame in wastewater ranged from 12 to 46 μg/L. The compound was not eliminated in wastewater treatment plants. Consequently, acesulfame was also detected in most surface waters, where concentrations correlated nicely with the actual wastewater burden. Furthermore, acesulfame was detected in 65% of the investigated groundwater samples. Thereby, the highest concentrations (up to 4.7 μg/L) were observed in areas where significant infiltration of river water with a high wastewater burden occurs. At certain pumping stations, our data suggest that up to 20% of the water indirectly stems from domestic wastewater. For drinking water production, groundwater is often not further purified in Switzerland, and acesulfame was thus also found in several tap water samples (up to 2.6 μg/L). However, acesulfame is susceptible to ozonation (elimination, ≈ 85–95%).

The sweetener is analyzed using a C_{18} reversed phase column and a triple quadrupole mass spectrometer operated in multiple reaction monitoring mode. As no off-line preconcentration step is necessary, results are obtained within 1 h or less.

Acesulfame thus meets all criteria for a 'perfect' marker of domestic wastewater in groundwater. It is source-specific, reflects contamination in a quantitative sense, and is amenable to rapid and sensitive analysis by liquid chromatography–tandem mass spectrometry. Given the currently achieved detection limit of ≈0.01 μg/L, it is possible to trace the presence of ≥0.05% wastewater in natural waters. Finally, acesulfame is sufficiently persistent and hydrophilic to reach groundwater.

Received: January 14, 2011

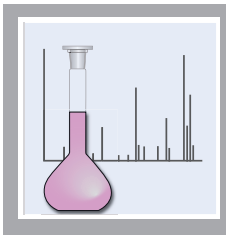
References

I. J. Buerge, H. R. Buser, M. Kahle, M. D. Müller, T. Poiger, *Environ. Sci. Technol.* **2009**, *43*, 4381.

The fate of acesulfame from its consumption as sugar substitute in light-beverages to renal excretion, passage through wastewater treatment plants, discharge to surface waters, infiltration into groundwater, and detection in tap water. Second photo from the left: 1art1 GmbH

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2011.275



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

A Tough Nut to Crack: Quantitative Analysis of Heavy Metals in Automotive Brake Linings

Renato Figi*[a], Oliver Nagel[a], Martin Tuchschmid[a], Peter Lienemann[ab], Urs Gfeller[a], and Nicolas Bukowiecki[ac]

*Correspondence: R. Figi[a], Tel.: +41 58 765 43 31, E-mail: renato.figi@empa.ch
[a]Empa, Swiss Federal Laboratories for Materials Science and Technology, Ueberlandstrasse 129, CH-8600 Dübendorf
[b]Zurich University of Applied Sciences ZHAW, Life Sciences and Facility Management, Einsiedlerstrasse 31, CH-8820 Wädenswil
[c]Paul Scherrer Institut, Laboratory of Atmospheric Chemistry, CH-5232 Villigen PSI

Keywords: Brake pads · Handheld XRF spectrometer · Heavy metals · Legal standards · Quantitative extraction

Brake linings used in automotive traffic are designed to optimally dissipate the frictional energy during the braking process with minimal loss of lining material. This is achieved by the manufacturers by using proprietary mixtures of highly temperature-resistant binder materials and metals.

The list of currently used metals also includes toxic heavy metals like chromium, antimony or lead. The abraded material ends up in the environment, where it considerably impairs the quality of roadside soils, drainage water from the roads, and the ambient air. Quantitative knowledge on the composition of brake linings is therefore important for regulating agencies to have a reliable handle on the existing legal limits for the use of heavy metals in the manufacturing process. Cracking the complex matrix of brake pads is, however, an analytical challenge; reliable analytical methods are still rather scarce.

In a recent study we presented a novel extraction method for brake pads, deploying a high-pressure asher and microwave-assisted extraction. This allowed for the quantitative analysis of the extracted elements by inductively coupled plasma optical emission spectrometry (ICP-OES) in a number of brake pad test samples from used passenger cars.

Despite the high accuracy of this method, it is not suitable for screening a large number of samples, as preferentially desired by regulating agencies. Therefore we also used our method as reference to assess the use of handheld X-ray spectrometers (ED-XRF) for *in situ* brake lining analysis, which have emerged as efficient screening tools in the last years. The comparison indicated that the applied brake pad screening procedure using the handheld ED-XRF-spectrometer provided a reliable determination of many (although not all) of the considered metals (Mo, Pb, Sb, Mn and Sn). **In future work this screening procedure will be refined by the design and validation of brake pad standard samples intended for use with handheld ED-XRF measurements.**

Acknowledgement

Financial support was granted by the Swiss Federal Office for the Environment (FOEN/BAFU).

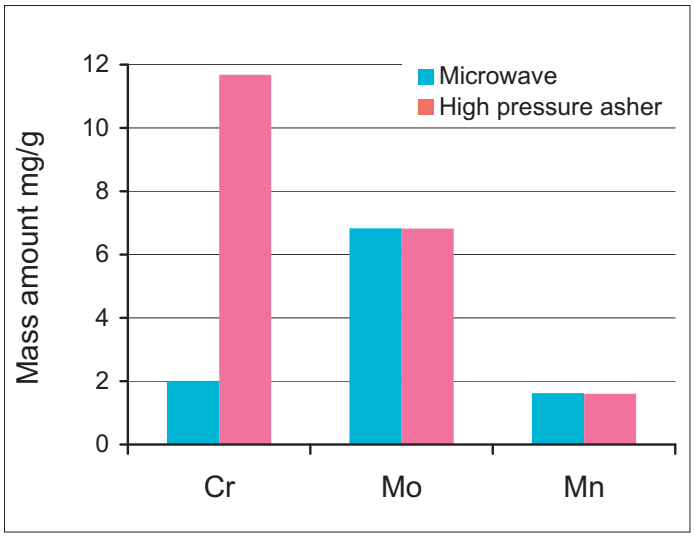
Received: February 1, 2011

References

R. Figi, O. Nagel, M. Tuchschmid, P. Lienemann, U. Gfeller, N. Bukowiecki, *Anal. Chim. Acta* **2010**, *676*, 46.

N. Bukowiecki, P. Lienemann, M. Hill, R. Figi, A. Richard, M. Furger, K. Rickers, G. Falkenberg, Y. J. Zhao, S. S. Cliff, A. S. H. Prevot, U. Baltensperger, B. Buchmann, R. Gehrig, *Env. Sci. Technol.* **2009**, *43*, 8072.

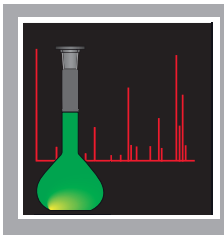
Brake pads with their temperature-resistant, hard linings composed from binder materials and heavy metals, some of them toxic.



Extraction efficiency of the microwave method vs. the high pressure asher (HPA). It is obvious that Cr with the microwave method is 6 times lower then with the HPA method. The cause is the formation of chromiumcarbide (CrC) with the microwave method.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2011.361



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Lighting-up Cancerous Cells and Tissues with Lanthanide Luminescence

Jean-Claude G. Bünzli*[a], Caroline D.B. Vandevyver[a], Anne-Sophie Chauvin[a], Martin Gijs[b], and Hans-Anton Lehr[c]

*Correspondence: Prof. Dr. J.-C. G. Bünzli[a], Tel.: +41 78 719 39 34, Fax: +41 21 693 98 25, E-mail: jean-claude.bunzli@epfl.ch
[a]Institute of Chemical Sciences and Engineering, Ecole Polytechnique Fédérale de Lausanne (EPFL), BCH 1402, CH-1015 Lausanne; [b]Microsystems Laboratory 2, EPFL, BM 3128, CH-1015 Lausanne; [c]Pathologie, Université de Lausanne, Rue du Bugnon 25, CH-1005 Lausanne

Keywords: Breast cancer cells · Immunohistochemistry · Lanthanide luminescent bioprobes · Microfluidics · Time-resolved luminescence microscopy

Time-resolved luminescence immunoassays as well as cell and tissue imaging are showcase applications of lanthanides. Novel assays are inspired by the unique emissive properties of trivalent lanthanide ions (Ln^{III}): easy-to-recognize narrow emission bands, large Stokes' shifts making facile wavelength discrimination, long excited state lifetimes allowing time-resolved detection, henceforth resulting in highly sensitive analyses, and little or no photobleaching.

New and targeted therapies for cancer treatment need rapid, specific and reliable tools to identify treatment targets on cancer cells and tissues as well as other relevant biomarkers. Lanthanide luminescent bioprobes are ideal for this type of analyses. During the past five years, we have teamed up with pathology at the University Hospital to develop practical microfluidic devices for the detection of cancerous cells *via* the biomarkers expressed by them. The lanthanide luminescent probes used are binuclear helicates, self-assembled in water under physiological conditions. The designed ligand framework yields thermodynamically stable and kinetically inert molecular entities with adequate photophysical properties and low cytotoxicity. They can be conveniently bioconjugated to avidin or monoclonal antibodies. The microfluidic device is 2.5 cm long and has a meandering 100-μm microchannel. Reactant flows are controlled by precision micropumps.

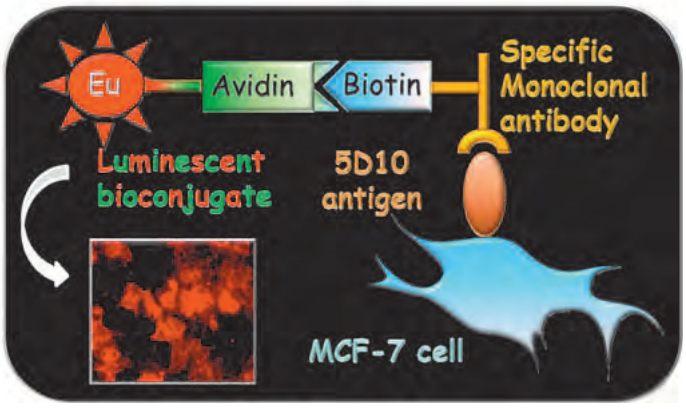
Cells such as MCF-7 breast cancer cell line can be grown in the microchannels and, after fixation, specifically be detected *via* the 5D10 antibody – which recognizes a mucin-like antigen on the cell membrane – using time-resolved luminescence microscopy. It yields bright, background-free signals, allowing high performance screening on breast cancer cells and tissues.

Two receptors expressed by these cells are relevant for treatment decisions: human epidermal growth factor receptor (Her2/*neu*) expressed on the cell membrane and estrogen receptors (ER) expressed in the nucleus. We have placed 4-μm sections of well-characterized, formalin-fixed breast carcinomas in the microchannel and visualized the two markers by dual indirect immunohistochemical luminescent assays under time-resolved conditions. Our first device allowed this test to be completed within 20 minutes versus more than 2 hours in a hospital laboratory and using 1/5 of the expensive reagents. **We are currently validating this protocol for routine diagnostic application. Test times are now down to only five minutes.**

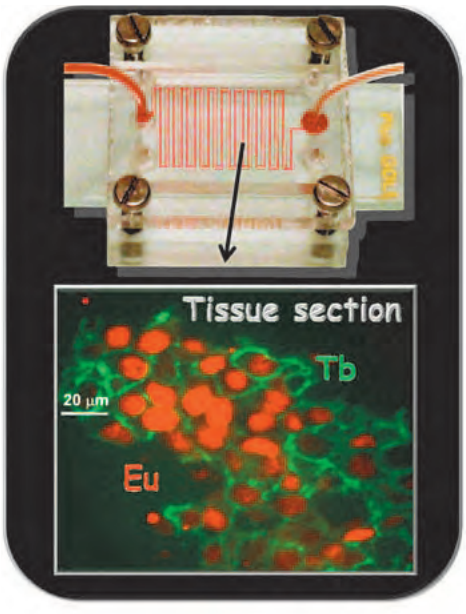
References

J.-C. G. Bünzli, *Chem. Rev.* **2010**, *110*, 2629.

V. Fernandez-Moreira, B. Song, V. Sivagnanam, A.-S. Chauvin, C. D. B. Vandevyver, M. A. M. Gijs, I. A. Hemmilä, H.-A. Lehr, J.-C. G. Bünzli, *Analyst* **2010**, *135*, 42.



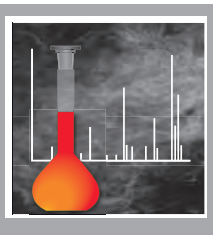
Principle of detection of MCF-7 breast cancer cells combining biochemical recognition of the 5D10 antigen they express with time-resolved luminescence microscopy of a Eu-labelled avidin and a biotinylated 5D10 antibody, taking advantage of the strong avidin-biotin interaction.



Microfluidic device and its potential for dual assays: ER (red) and Her2/*neu* (green) receptors evidenced by time-resolved luminescence microscopy. Her2/*neu* receptors: polyclonal rabbit anti-human c-erbB-2 oncoprotein antibody / Tb-labelled goat anti-rabbit IgG antibody. ER receptors: anti-human ER mouse mAb / Eu-labelled goat anti-mouse IgG Ab.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2011.438



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Continuum Between Ritual and Medicinal Use of Plants: Smoke Analysis of Ritual Plants from Southwest China

Caroline S. Weckerle*, Peter O. Staub, and Florian P. Schiestl

*Correspondence: C. S. Weckerle, Institute of Systematic Botany, University of Zurich, Zollikerstrasse 107, CH-8008 Zurich, Tel.: +41 44 634 83 52, Fax: +41 44 634 84 03, E-mail: caroline.weckerle@systbot.uzh.ch

Keywords: Ethnobotany · Headspace method · Incense · Smoke analysis · Southwest China · Volatile organic compounds

Plant-derived smoke is used in diverse cultures and regions of the world for various purposes, *e.g.* as medicine, incense, for food conservation or as insect repellent. Around 1500 plant species are known to be used to produce smoke for various uses. Beside frankincense and myrrh, only little research has been conducted on plants burnt for their fragrant fumes. It remains largely unknown which compounds of the different smokes are responsible for the various impacts smoke may have.

In Southwest China, especially in the Tibetan cultural area, the use of ritual and incense plants is very common. Incense plants are burned freshly or dried and are used to communicate with deities and spirits of the surroundings but also for the treatment of diseases such as respiratory ailments. Our research focuses on a comparative analysis of ritual plants used among different ethnic groups in this area. Since we are especially interested in the continuum between ritual and medicinal use of incense plants and aim to understand the rationale for their use as medicine, we look at the cultural context of plant use, but also analyze the volatile organic compounds (VOCs) of the smoke. So far we documented some 40 ritual plants. Foremost among the incense plants are *Juniperus*, *Cupressus*, and *Rhododendron* species. Important characteristics of incense plants are the density, color, and smell of their smoke as well as their habitat. The higher up in the mountains and hence the closer to the mountain gods the plant grows, the more effective it is thought to be.

Tibetan man worshipping the mountain gods. He burns incense plants in a ritual burner on the flat roof of the house.

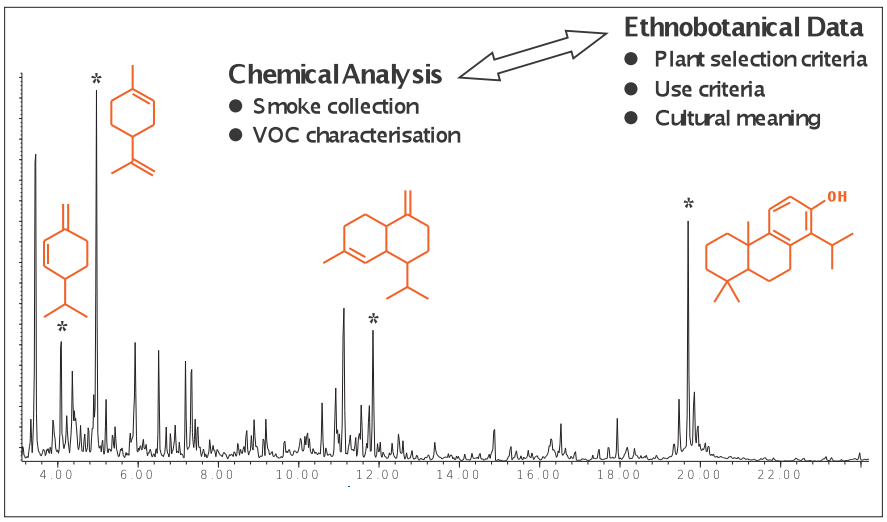
To collect VOCs of incense smoke we have used the dynamic headspace sorption method. This technique is simple to use, and smoke samples can either be collected directly in the field or from burnt dry plant material in the lab. In this method, VOCs are trapped onto an organic polymer (*e.g.* Porapak Q), eluted with solvent after collection, and subsequently analyzed using coupled gas chromatography-mass spectrometry (GC-MS). Smoke samples collected and analyzed in this way contained many typical plant secondary metabolites, such as mono- and sesquiterpenoids, benzenoids, and methoxylated phenolic compounds.

Based on the analysis of volatile organic compounds of the smoke and the cultural meaning of ritual plants, hypotheses for their successful use in health-related issues will be developed.

Received: April 13, 2011

Reference

C. S. Weckerle, F. K. Huber, Y. P. Yang, W. B. Sun. *Economic Botany* **2006**, *60*, 3.

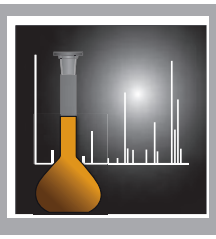


We look at the cultural context of incense plant use in Southwest China and analyze the volatile organic compounds of the smoke, in order to investigate the continuum between ritual and medicinal use of incense plants. Gas chromatogram of the smoke of *Cupressus funebris*. The peaks marked with an asterisk are, with increasing retention time: β-phellandrene, limonene, cadinene, and totarol. Their chirality was not investigated.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2011.620



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Role of Fluid Inclusion Analysis in Understanding Gigantic Selenite Crystal Growth in a Deep Karst Cave (Naica, Mexico)

Mattias B. Fricker[a], Paolo S. Garofalo[b], and Detlef Günther*[a]

*Correspondence: Prof. Dr. D. Günther[a], Tel.: +41 44 632 46 87, Fax: +41 44 633 10 71, E-mail: guenther@inorg.chem.ethz.ch
[a]ETH Zurich, Laboratory of Inorganic Chemistry, HCI G113, Wolfgang-Pauli-Strasse 10, CH-8093 Zurich; [b]University of Bologna, Department of Earth and Environmental Sciences, Piazza di Porta S. Donato 1, I-40126 Bologna

Keywords: Fluid inclusion · ICP-MS · Large crystals · Laser ablation · Naica · Selenite

The largest crystals of the world were discovered within deep karst caves of the Ag, Pb and Zn mine of Naica (Chihuahua, Mexico). These selenite crystals (for '*Cristales*' up to 11 m in length, corrected U/Th age of 155±47 ka) are as white as the moon when illuminated from the back. Due to the underground mining activities, the ground water is constantly being pumped away, which by chance led to the discovery of the cave crystals at a depth of –290 m (below entrance, b.e.). The caves are accessible for as long as the pumping is maintained for mining, but exploration conditions inside them are lethal due to the high temperature (>50 °C) and close to 100% relative humidity. Thus, special gear has been developed to enter these caves, and these impressive natural objects have been sampled and studied in detail.

To reconstruct the composition of the cave liquid at the time of crystal growth within the caves, we studied the tiny droplets of aqueous liquid entrapped (fluid inclusions, FI, tens of µm) in the crystals of three caves. These FIs were analyzed using Laser Ablation–Inductively Coupled Plasma–Mass Spectrometry and elements quantified *via* the total salt content of a FI which was obtained prior to ablation by microthermometry. Gypsum samples from the caves named '*Las espadas*' (–130 m b.e.), '*Cristales*' (–290 m b.e.) and '*Ojo de la reina*' (–290 m b.e.) were collected and the bulk composition of the FIs determined. Only Na, Mg, K and Sr were determined, other elements were either not present or below the limits of detection. Results show that major and trace element compositions of deep and shallow cave fluid are different. However, the compositions of contiguous and co-genetic FIs within a crystal are similar.

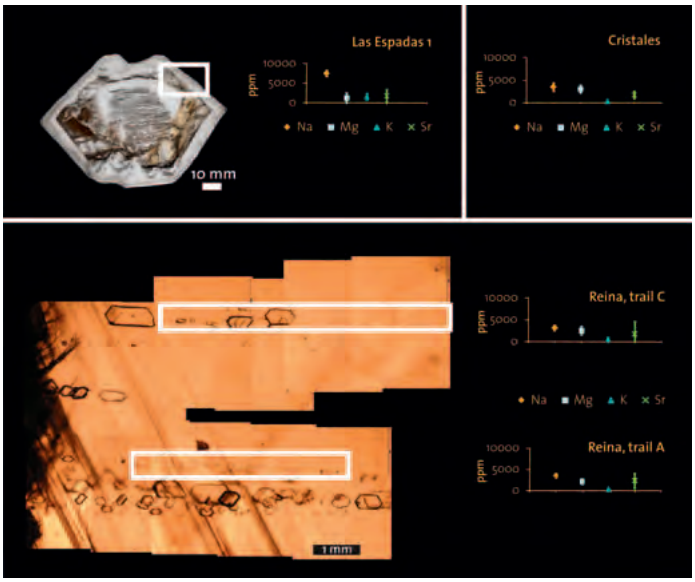
Our results indicate that the most favorable geological process which controlled the formation of such large crystals was the mixing of two chemically different cave fluids (shallow and deep). Constant mixing of these two fluids created the long-lasting supersaturation conditions necessary to grow these phenomenal crystals.

Received: May 26, 2011

References

P. S. Garofalo, M. B. Fricker, D. Günther, P. Forti, A.-M. Mercuri, M. Loreti, B. Capaccioni, *Earth Planet. Sci. Lett.* **2010**, *289*, 560.
D. Günther, A. Audétat, R. Frischknecht, C. A. Heinrich, *J. Anal. At. Spectrom.* **1998**, *13*, 236.

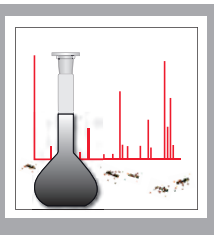
The Naica caves were explored and documented by the Italian non-profit associacion *La Venta* (photo of *'Cristales'*, courtesy of *La Venta* and *Speleoresearch and Films*), who developed the protective suit that allows safe working in the cave up to 1 hour, before escaping into the vented and cool mine galleries.



Trace element concentrations of the sample from '*Las espadas*' are different from those in '*Cristales*' (no photo) and '*Ojo de la reina*' (microscope photos of a section), whereas for the latter the concentrations are similar for two different primary FI assemblages as well as to '*Cristales*'. Presence of a selection of other elements was not detected in the FIs.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2011.744



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

A New Function of Hydrocarbons in Insect Communication: Maternal Care and Offspring Signalling in the European Earwig

Flore Mas, Joël Meunier, and Mathias Kölliker*

*Correspondence: Prof. M. Kölliker, Zoological Institute, Evolutionary Biology, University of Basel, Vesalgasse 1, CH-4051 Basel, Tel: +41 61 267 03 79, Fax: +41 61 267 03 62, E-mail: mathias.koelliker@unibas.ch

Keywords: *Forficula auricularia* · Hydrocarbons · Insects · Parental care · Social behaviour · Solicitation pheromone

An earwig mother tending her clutch of 1st instar nymphs.

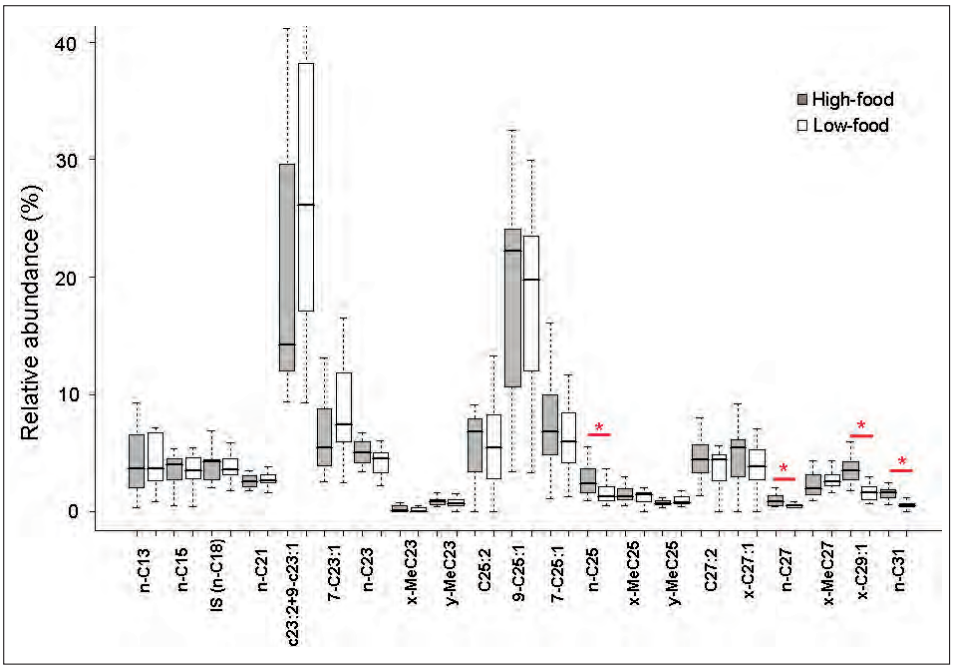
Hydrocarbons are a ubiquitous component of the insect exoskeleton (cuticle). Their primary function is to provide an effective hydrophobic barrier against water loss and desiccation. But cuticular hydrocarbons (CHCs) are also species-specific, vary with the biotic and abiotic environment, and they have been shown to often have evolved a secondary function as signals in insect communication. For instance, a sex difference in CHCs is used as sex pheromone in the fruitfly, and ants use CHCs to recognize intruders in their colony. In the context of parental care, where young insects (nymphs or larvae) interact with their parents to receive protection and/or food, we explored whether CHCs of young could have evolved to influence parental behaviour, similar to the begging calls of nestling birds or the crying of human babies.

European earwig (*Forficula auricularia:* Dermaptera) mothers care for their nymphs by defending them against predators and providing food *via* individual mouth to mouth food regurgitation. Chemical extract from CHCs of nymphs reared under different nutritional conditions (high-food versus low-food) were obtained and tested on mothers. Mothers exposed to extract from high-food nymphs foraged significantly more food and provided food to more nymphs than mothers that were exposed to extract from low-food nymphs. The identification and quantification of nymph CHCs by GC-MS revealed that the profile of CHCs is composed of 20 compounds, that the total quantity of CHCs did not differ between high- and low-food nymphs, but that there was significant variation in the relative quantities of four compounds (three alkanes: n-C25, n-C27, n-C31 and one alkene: x-C29:1). These results demonstrate that CHCs contain information about the nutritional condition of offspring to which earwig mothers respond by adjusting care behaviour. **The effect of condition-dependent CHCs of nymphs on maternal behaviour supports a new secondary function of hydrocarbons in insect communication**.

Received: July 14, 2011

References

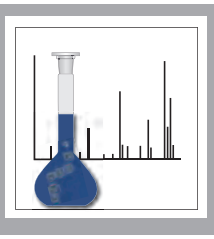
F. Mas, M. Kölliker, *Anim. Behav.* **2008**, *76*, 1121.
F. Mas, K.F. Haynes, M. Kölliker, *Proc. R. Soc. Lond. B* **2009**, *276*, 2847.



Box plots (medians and interquartile ranges) of relative quantities of the 20 hydrocarbons found on the earwig nymph cuticle, and for nymphs reared under high-food (grey) and low-food (white) conditions. IS is an internal standard. Red asterisks indicate statistically significant differences between treatments.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2011.814



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

J-based Configuration Analysis: An Enabling NMR-Spectroscopic Tool in the Synthesis and Study of Chlorinated Natural Products

Christian Nilewski and Erick M. Carreira*

*Correspondence: Prof. Dr. E. M. Carreira, ETH Zürich, HCI H335, CH-8093 Zürich, Tel.: +41 44 632 28 30, Fax: +41 44 632 13 28; E-mail: erickm.carreira@org.chem.ethz.ch

Keywords: Chlorosulfolipids · Heteronuclear coupling constants · *J*-based configuration analysis · Natural products · Organohalogens

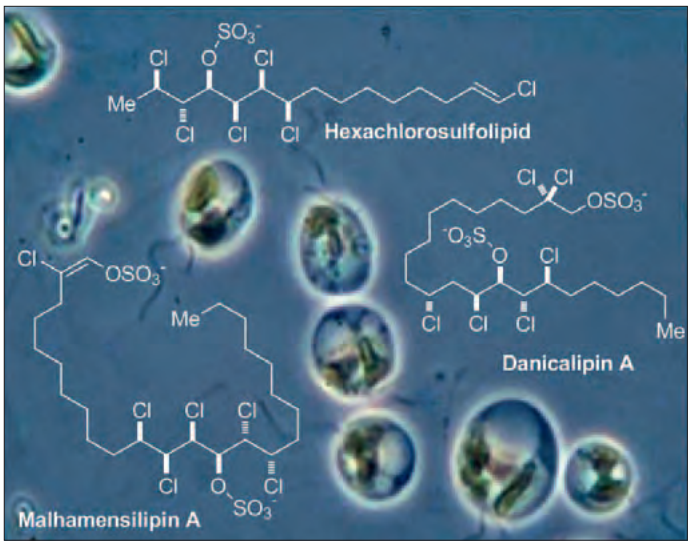
To date, more than 4700 naturally occurring organohalogens are known. Chlorosulfolipids, which are produced by sea- and freshwater microalgae alike, constitute a particularly intriguing subclass of naturally occurring organohalogens. Many interdisciplinary questions, reaching from chemistry to biology, pharmacology and toxicology – not the least of which is their association with seafood poisoning – have rendered these molecules interesting objects for study. In this context, reliable tools to secure configurational assignment are critical. As part of our synthetic program directed toward the total synthesis and study of chlorosulfolipids, we investigated the applicability of an NMR-based approach, *J*-based configuration analysis (JBCA), to chlorinated systems.

Unlike in *cyclic* entities, the analysis of vicinal (^3J) coupling constants and NOE data alone is usually insufficient to elucidate the conformation and configuration of *acyclic* systems. Key to overcome these shortcomings is the extraction and analysis of a whole set of homo- ($^3J_{H,H}$) and heteronuclear ($^2J_{C,H}$, $^3J_{C,H}$) coupling constants along two stereogenic centers bearing electronegative substituents, in addition to NOE and ROE data. For chlorinated entities, reference values for the relevant coupling constants were lacking. In order to fill the existing gap, we developed synthetic routes to a collection of trichlorinated hexane-1,3- and -1,2-diols, starting from commercially available ethyl sorbate, which served as model compounds for NMR-spectroscopic studies. All of these proved to be crystalline, which allowed us to directly correlate all NMR data with the configuration known from X-ray analysis. Extraction of the vicinal H,H-coupling constants (^{1}H-NMR) as well as the C,H-coupling constants over two and three bonds (HSQC-HECADE, PS-HMBC) allowed us to define ranges for the coupling constants as a function of the configuration and conformation. The lessons learnt in these studies are invaluable for the configurational assignment and conformational analysis of polychlorinated natural products such as chlorosulfolipids and crucial for any research directed towards the elucidation of the biological role of these molecules in the producing organisms. **In summary, we have validated JBCA for chlorinated systems by detailed NMR- and X-ray analysis of trichlorohexanediol model systems.**

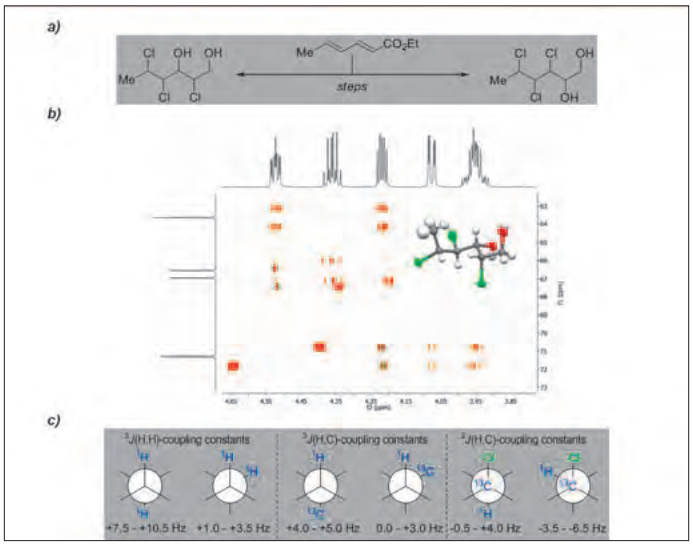
Received: August 10, 2011

References

C. Nilewski, R. W. Geisser, E. M. Carreira, *Nature* **2009**, *457*, 573.
C. Nilewski, R. W. Geisser, M.-O. Ebert, E. M. Carreira, *J. Am. Chem. Soc.* **2009**, *131*, 15866.
C. Nilewski, N. R. Deprez, T. C. Fessard, D. B. Li, R. W. Geisser, E. M. Carreira, *Angew. Chem.* **2011**, early view (DOI: 10.1002/ange.201102521); *Angew. Chem. Int. Ed.* **2011**, early view (DOI: 10.1002/anie.201102521).



Selected members of the chlorosulfolipid natural product family originating from microalga, such as the chrysophyte *Poterioochromonas malhamensis* (background taken from *http://starcentral.mbl.edu/mv/portal.php?pagetitle =assetfactsheet&imageid=22998)*.



The synthesis of trichlorinated hexanediol model systems (*a*) and subsequent X-ray-structural and NMR-spectroscopic analysis (*b*) allowed for the definition of ranges for homo- and heteronuclear coupling constants for chlorinated systems as a function of configuration and conformation (*c*).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2011.875

Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

NIR Spectroscopy to Identify Counterfeit Drugs

Simon Meyer*

*Correspondence: S. Meyer, Swissmedic, Labor OMCL Pharmazeutika, Hallerstrasse 7, Postfach, CH-3000 Bern 9, Tel.: +41 31 322 02 67, Fax: +41 31 322 05 04, E-mail: simon.meyer@swissmedic.ch

Keywords: Counterfeit medicines · NIR spectroscopy

Spam mails advertising prescription drugs for a discount price are well known to all of us. They may be just a minor irritant, but behind these mails a billion dollar market is hiding.

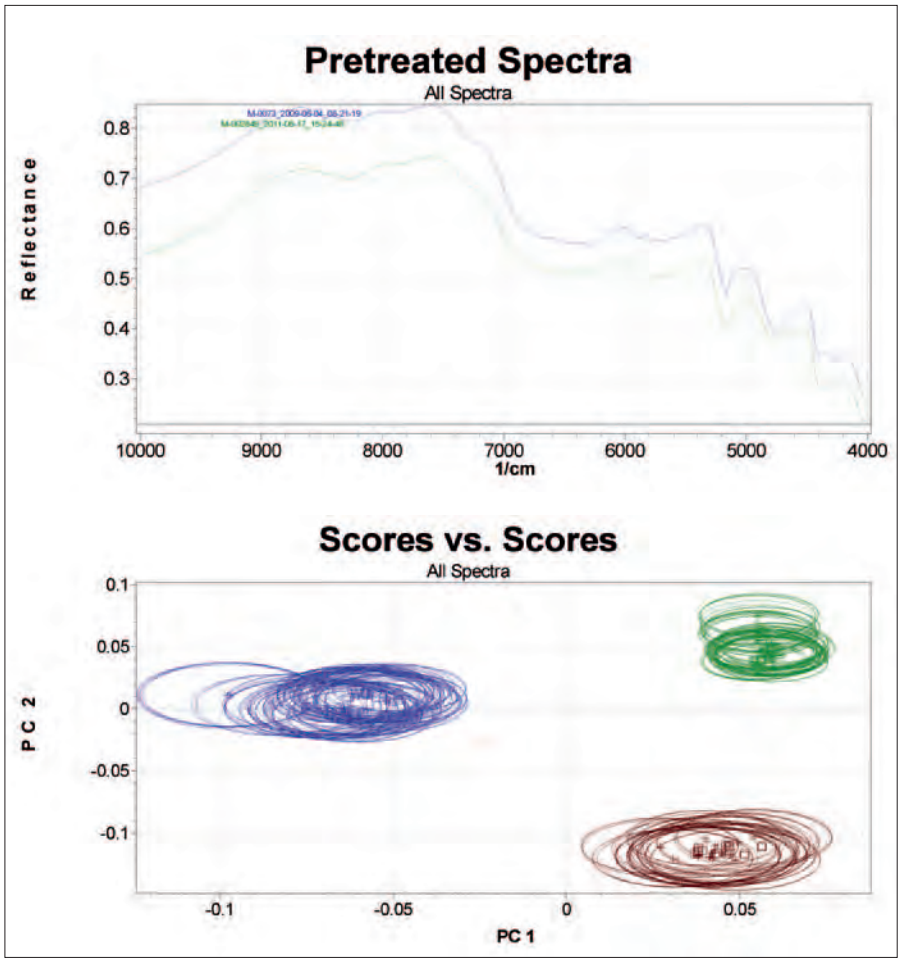
Counterfeit drugs present a substantial health risk. WHO estimates that about 50% of drugs ordered at non-licensed online pharmacies are counterfeit. However, to date no counterfeit drugs have been observed in the legal supply chain in Switzerland.

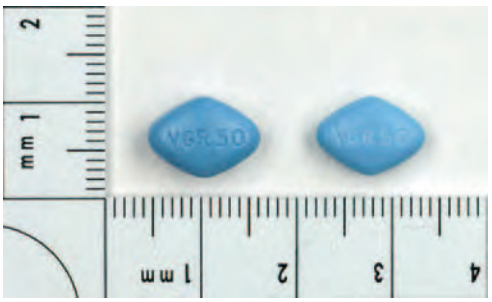
In 2010, Swissmedic (the Swiss Agency for Therapeutic Products) received more than 500 confiscated samples for further analysis from the Swiss Federal Customs. Due to the steadily increasing number of samples, new methods for rapid identification are needed. One promising approach is near infrared (NIR) spectroscopy. The high penetration depth (several millimetres) of the NIR-radiation into the surface allows for a non-destructive and extremely fast analysis. A full spectrum scan (800–2500 nm) can be acquired in less than 10 seconds.

The broad and overlapping signals in NIR spectroscopy preclude a direct interpretation of the spectra. Therefore, a chemometric model (calibration) has to be established based on data of different genuine lots. Based on statistical models, the collected data is pretreated (*e.g.* derivatives or normalisation algorithms) to eliminate spectral effects. In a second step a principal component analysis (PCA) is performed in order to reduce the data quantity to the significant differences between the samples. After validation, the chemometric model can be used to distinguish between authentic and counterfeit medical products.

The evaluation of these data showed that NIR spectroscopy is capable to rapidly and reliably distinguish between authentic and counterfeit drugs.

Received: September 8, 2011



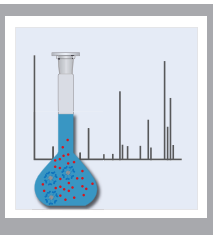


Counterfeit (left) and authentic (right) drug.

Top: Similar NIR spectra of genuine (blue) and counterfeit (green) drugs for erectile dysfunction (ED). Bottom: Chemometric modelling (PCA) is used to distinguish the counterfeited drug. Cluster calibration of three authentic medicines for ED treatment. The red square in the middle corresponds to the green spectrum in the top figure.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2011.978



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Microdroplets and Magnetic Beads: Fishing for Molecules in nL Volumes

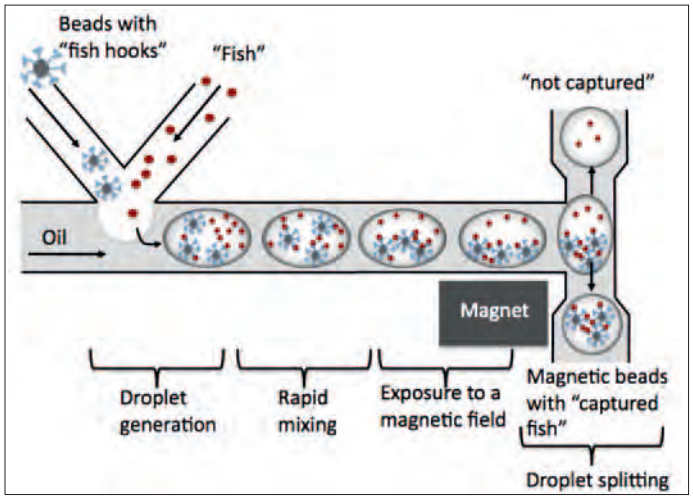
Dario Lombardi and Petra S. Dittrich*

*Correspondence: Prof. Dr. P. S. Dittrich, ETH Zurich, Wolfgang-Pauli-Str.10, CH-8093 Zurich, Tel.: +41 44 633 68 93, Fax: +41 44 633 16 21, E-mail: dittrich@org.chem.ethz.ch

Keywords: Lab-on-Chip device · Magnetic beads · Microdroplets · Microfluidics · Protein–drug interactions

Microfluidic platforms (more general: lab-on-chip devices) are nowadays widely used for applications in analytical and bioanalytical chemistry due the appealing properties they provide, *e.g.* for handling of small sample volumes and the integration of sample (pre)treatment steps. In recent years, microdevices designed for droplet-based microfluidics have attracted increasing interest, particularly for screening applications.

Microfluidic devices facilitate the continuous and robust generation of extraordinary monodisperse, aqueous droplets into a carrier stream (hydrophobic liquid or gas), having volumes as small as a few micro- to picoliters. These tiny droplets could serve as microreactors for synthesis and crystallization, or as microcarriers to provide a defined microenvironment for cells. Using chemical gradients during droplet formation, it becomes possible to screen for optimum reaction conditions, or to systematically investigate reaction kinetics or influences of chemical compounds (*e.g.* drugs) on cells. Despite their utilization in many scientific areas, it remains still challenging to integrate standard procedures such as washing and separation steps with continuous droplet microfluidics.



Scheme of the method for droplet generation and removal of molecules captured by magnetic beads.

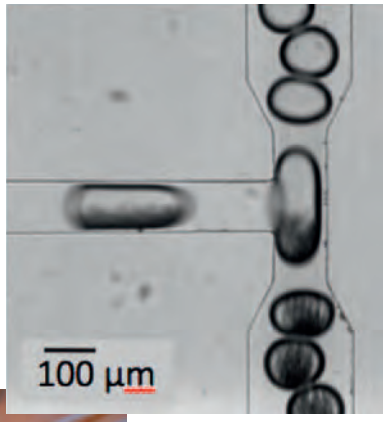
Recently, we could expand the applicability of droplet microfluidics by integrating a permanent magnet in the device and employing a magnetic bead-based assay. We used the method for characterization of drug-protein binding constants, here warfarin to human serum albumin (HSA). HSA is the most abundant protein in the human blood plasma and therefore, binding of drug molecules to HSA is an important parameter for drug characterization. Beads with surface-bound target molecules (HSA) are introduced the droplet generating microdevice together with target-binding molecules (warfarin). At the T-junction, droplets are split into two daughter droplets, one of which contain the beads and move towards the direction of the magnet, the other daughter droplets are free of beads and contain only residual unbound target molecules. Hence, the magnetic beads with bound molecules are efficiently separated from the bead-free solution. After analyzing the droplet content, we could derive the HSA-warfarin binding constant. **The continuous method lays the basis for a microfluidic droplet-based screening device aimed at investigating the interactions of drugs with specific targets including enzymes and cells. Furthermore, it could be employed for various applications, in which rapid removal of a (reactive) component or catalyst (immobilized on the magnetic beads) is required.**

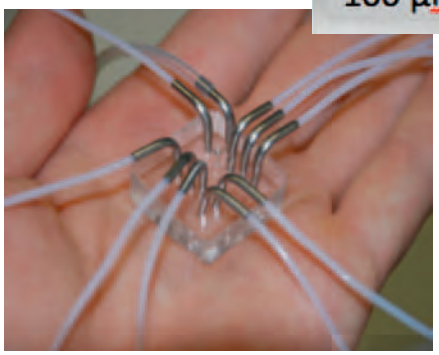
Received: September 27, 2011

Reference

D. Lombardi, P. S. Dittrich, *Anal. Bioanal. Chem.* **2011**, *399*, 347.

Micrograph of the T-junction, where droplets are split into two daughter droplets (flow from left to right). The black magnetic beads are moving towards the outlet where the magnet is placed, while the bead-free droplets are flowing towards the other outlet.

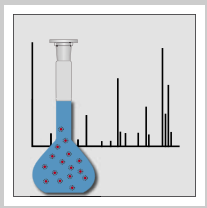




Photograph of a microdevice made of poly(dimethylsiloxane), channel inlets and outlets are connected to tubings.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2012.65



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

A Novel Tube-based Format for Dried Blood Spots Integrating Sample Collection and Sample Preparation

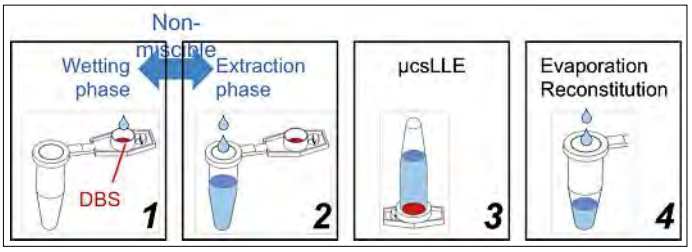
Michel Wagner, Emmanuel Varesio, and Gérard Hopfgartner*

*Correspondence: Prof. Dr. G. Hopfgartner, Life Sciences Mass Spectrometry, School of Pharmaceutical Sciences, University of Lausanne, University of Geneva, 20 Bd. d'Yvoy, CH-1211 Geneva 4, Tel.: +41 22 379 33 31, Fax: +41 22 379 68 08, E-mail: gerard.hopfgartner@unige.ch

Keywords: Dried blood spot · Liquid chromatography–mass spectrometry · Liquid–liquid extraction

Dried blood spots (DBS) are a convenient way to collect and to store small-volume blood samples. Typically, after finger pricking, a few droplets of blood are deposited onto dedicated paper cards and allowed to dry. The benefits rely especially in an easy and cheap sample storage (under ambient conditions) and shipment (in a standard envelope) and in reduced biohazard risks. DBS have been applied recently to the quantitation of drugs and metabolites for therapeutic drug monitoring and drug development. Whereas modern bioanalytics relies on the handling of liquid samples (*e.g.* in tubes) for liquid chromatography–mass spectrometry (LC–MS) analysis, DBS cards represent a sample format in the solid state, thus less compatible with the usual bioanalytical workflow. The standard approach is to punch a small DBS disk from the paper card into a tube, and analytes are extracted with the addition of an appropriate solvent.

To retain all the inherent advantages of DBS and to better match the sample collection format with the sample handling/preparation format, an alternative tube-based format was introduced, whose design consists in a tube with a paper disk immobilized in the lid for sample collection. The extraction can be then performed directly in the device by adding the extraction solvent into the tube (solid–liquid extraction, SLE).



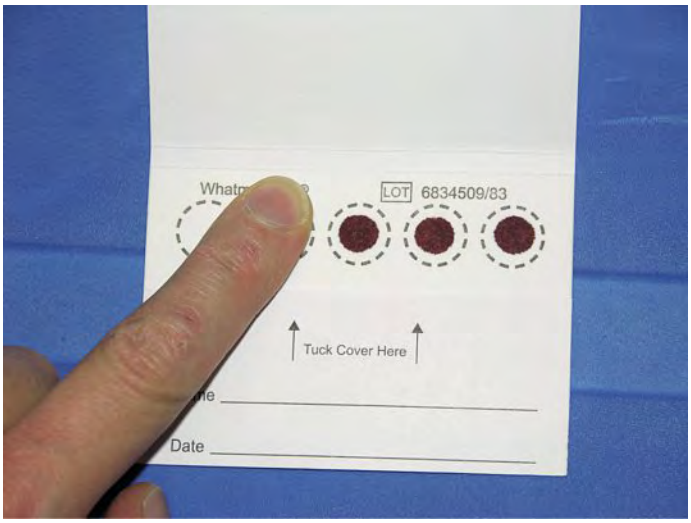
DBS tube-based format and micro cellulose-supported liquid-liquid extraction (µcsLLE).

In addition, a new sample preparation strategy specific to this format can be used, namely micro cellulose-supported liquid–liquid extraction (µcsLLE). Its concept consists in the wetting of the paper disk in the lid with an aqueous-based solvent (wetting phase), while a non-miscible, organic extraction solvent is added in the tube (extraction phase). After closing the tube, the sample is extracted under sonication upside-down. Then the extraction phase containing the analytes is easily separated from the paper patch by simply opening the tube. The extracts have shown to contain fewer endogenous blood interferences (especially phospholipids) and to generate fewer matrix effects. **Finally, this integrated device has been demonstrated as a suitable format for quantitative analysis in dried plasma and blood spots.**

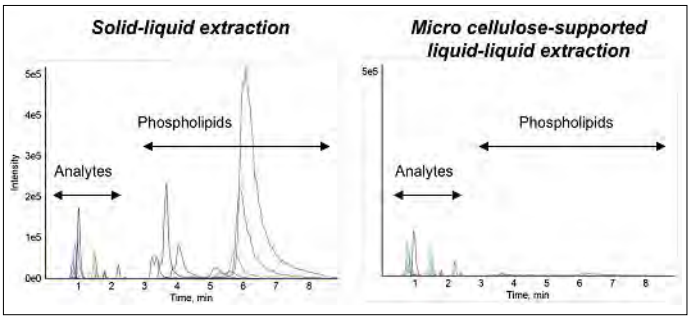
Received: December 16, 2011

Reference

M. Wagner, E. Varesio, G. Hopfgartner, priority application number EP 11153161.2 (filed on Feb 3rd, **2011**, European Patent Office).



DBS in the card format.

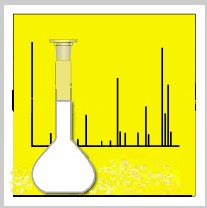


LC-MS analysis illustrating analyte extraction from DBS in the tube format and concomitant sample clean-up (phospholipid removal). Analytes consisted of 18 representative substances (amphetamines, cocaine and metabolites, benzodiazepines, tricyclic antidepressants and antiretroviral drugs).

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2012.131



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Polonium – on the Trace of a Powerful Alpha Nuclide in the Environment

Franziska Richter, Michael Wagmann, and Markus Zehringer*

*Correspondence: Dr. M. Zehringer, Kantonales Laboratorium Basel-Stadt, Kannenfeldstrasse 2, CH-4012 Basel, Tel.: +41 61 385 25 17, Fax: +41 61 385 25 09, E-Mail: markus.zehringer@bs.ch

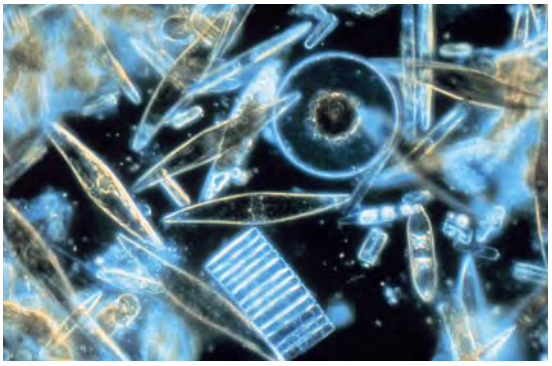
Keywords: Alpha spectrometry · Diatomaceous earth · Healing earth · Natural decay series · Polonium

Polonium-210 (^{210}Po) belongs to the natural decay series of uranium-238. It is produced at the end of the decay series as a daughter nuclide of the β-emitter lead-210 (^{210}Pb). ^{210}Po decays with a half-life of 140 days. Therefore chemical modifications and transport processes are possible. The main source of ^{210}Po is the natural fallout of the decay of radon-222 in the atmosphere. The ingestion of dust particles causes 8–10% of the natural internal radiation dose of man. ^{210}Po can accumulate especially in seafood.

Polonium is a very toxic metal. Irène Joliot-Curie died in 1957 of leukemia probably caused by the inhalation of polonium dust from a broken vial in 1946. A well-known case is the death of the ex-Soviet agent Alexander Litwinenko. He died in London weeks after drinking poisoned tea.

^{210}Po is a strong alpha emitter with an energy of 5'400 keV and has only one weak gamma ray emission at 803 keV (0.005% emission probability). Therefore the analytical method of choice is alpha spectrometry. The first two steps in every alpha spectrometry are the destruction of the matrix and the selective enrichment of the analyte. Above temperatures of 250 °C polonium is lost by evaporation. Therefore the methods of choice are wet ashing or microwave digestion. The final sample solution is set to a reducing milieu by the addition of hydroxylamine hydrochloride. The polonium is deposited onto a silver disc, which is then analyzed with alpha spectrometry.

Commercially available healing earth.



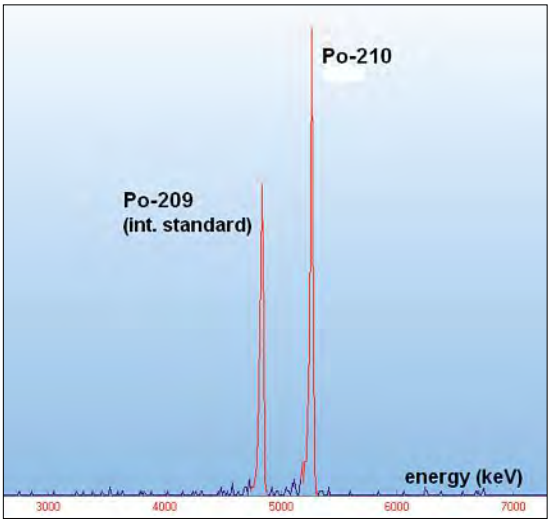
Diatoms (@ public domain).

Sediments containing the residues of diatoms are known as siliceous earths, also called diatomaceous earths or mountain flours. They find a wide spread use in industry, in cosmetics and in supplementary diet (healing earths). Our investigations of healing earths with gamma ray detection showed remarkable amounts of nuclides of the radioactive series of ^{238}U and ^{232}Th. In one sample we measured 400 Bq/kg of ^{210}Pb, the precursor of ^{210}Po. Our focus then switched to ^{210}Po. Its activity was 42 Bq/kg, so the two nuclides were not in equilibrium. Probably most of the ^{210}Po was lost during a heating step during the production process. **The yearly intake of two kg of this healing earth would result in a dose of 500 μSv, half of the annual permitted dose for non-professionals in Switzerland. ^{210}Po activity only causes 10 μSv.**

Received: January 5, 2012

Reference

M. Yamamoto, T. Abe, J. Kuwabara, K. Komura, K. Ueno, *et al.*, *J. Radioanal. Nucl. Chem.* **1994**, *178*, 81.

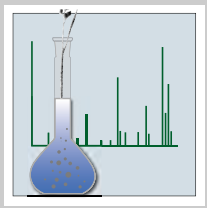


Alpha spectrum of a healing earth extract. For quantification control ^{209}Po was added (70 mBq). ^{209}Po has an alpha energy of 4'800 keV. The sample was counted for 24 h in an alpha vacuum chamber (silicon barrier detector).

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St. Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2012.257



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Carbon Isotopic Composition in the Water Column of Lake Rotsee Reveals Importance of Methane Oxidation in Aquatic Environments

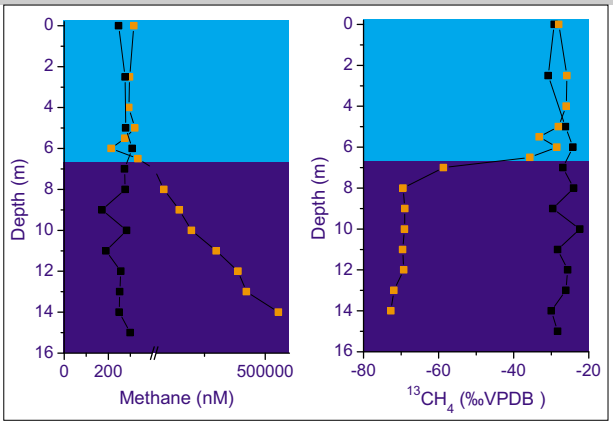
Torsten Diem, Oliver Scheidegger, and Carsten J. Schubert*

*Correspondence: Dr. C. J. Schubert, Eawag, Swiss Federal Institute of Aquatic Science and Technology, Department of Surface Waters – Research and Management, CH-6047 Kastanienbaum, Tel.: +41 58 765 21 95, Fax: +41 58 765 21 68, E-mail: carsten.schubert@eawag.ch

Keywords: Climate change · Methane emission · Methane isotopes · Trace Gas IR-MS

For estimates of global greenhouse gas emissions, the importance of lakes in carbon cycling and the emission of CO_2 and CH_4 has recently gained attention. Methane, an approximately 25 times stronger greenhouse gas than CO_2, is produced under anaerobic conditions in the sediments and oxidized in the water column. This oxidation is carried out by micro-organisms, whose enzymatic reactions strongly influence the carbon isotopic signal of product (CO_2) and substrate (CH_4), preferentially using the methane with the lighter isotope for gaining energy. The resulting isotopic fractionation can be traced by Isotope Ratio–Mass Spectrometry (IR-MS), either by measuring the enrichment of the heavy isotope in the remaining substrate or the light isotope in the product. Methane concentrations in this open system oxidation can vary from mmol/l in anoxic water layers and sediments to nmol/l in oxic waters. If concentrations are low, a sufficient amount of CH_4 for the IR-MS is achieved with a Trace Gas Pre-Concentrator unit.

To investigate the importance of methane oxidation for the carbon cycle of small, stratified lakes we studied the Rotsee, a small wind-shielded lake close to Lucerne (famous for rowing). In general, lakes are stratified in summer with warm surface water and cold deep water. However, in winter when the surface water cools down and becomes denser the lake turns over and the water column mixes. We collected water samples from various depths of the lake and measured methane concentrations, stable isotopic composition of carbon ($^{13}C/^{12}C$), oxygen concentrations, and several parameters to evaluate lake stratification (*e.g.* temperature, conductivity, pH). At the oxic/anoxic boundary we detected strong methane oxidation together with strong fractionation of the remaining methane, which became enriched in the heavy ^{13}C isotope. Whereas isotopically light methane in the deep water and isotopically heavy methane in the surface water is the normal picture during stratification, the profile changes shortly after mixing when isotopically heavy methane (higher ^{13}C content) is found in the whole water column. During stratification there was little evidence for oxidation in the oxic surface zone with only very low oxidation rates, except for times of lake mixing, when high nutrient, methane-rich and oxygenated water creates favourable conditions for very strong methane oxidation.



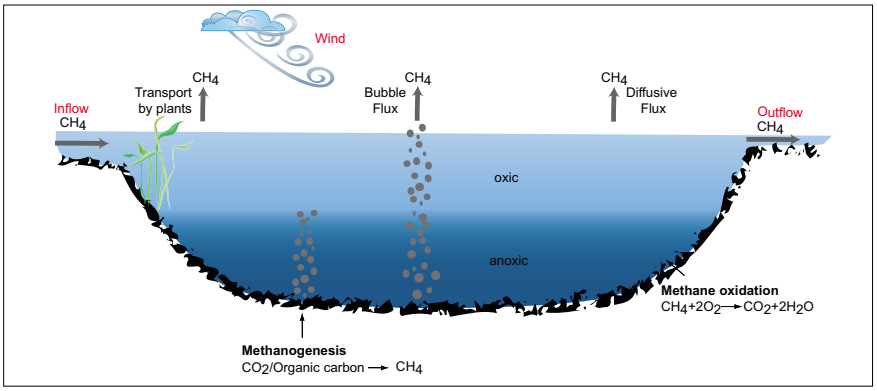
Methane concentration and isotopic composition profile of Rotsee in summer during stratification (orange dots) and in winter after the lake mixed (black dots).

Stable isotopes are a helpful tool to trace microbial processes in natural waters and were successfully used to investigate methane oxidation in a small, stratified lake.

Received: March 22, 2012

Reference

C. J. Schubert, F. Lucas, E. Durisch-Kaiser, R. Stierli, T. Diem, O. Scheidegger, F. Vazquez, B. Müller, *Aquatic Sciences – Research Across Boundaries* **2010**, *72*, 455.



Methane pathways in lakes. Depending on the specific situation, inflowing and outflowing water may contain small or larger concentrations of methane. (Artwork: Eliane Scharmin)

The Rotsee near Lucerne, prepared for a rowing regatta. (Photo: Ewi Weber)

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2012.346

Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Detection and Significance of Cocaine Traces on Swiss and Euro Banknotes

Frédéric Anglada[a], Olivier Delémont*[a], Olivier Guéniat[b], and Pierre Esseiva[a]

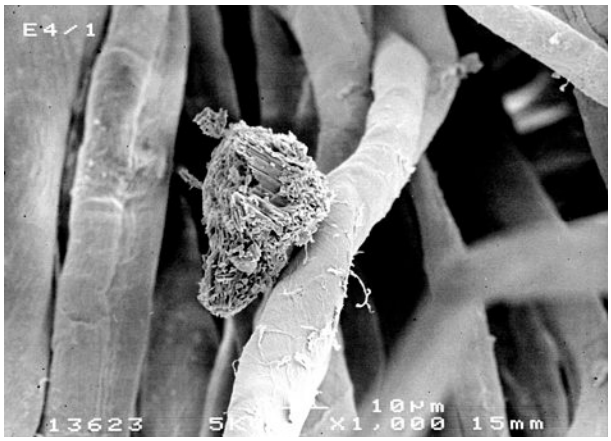
*Correspondence: Prof. Dr. O. Delémont[a], Tel.: +41 21 692 46 00, Fax: +41 21 692 46 05, E-mail: olivier.delemont@unil.ch
[a]University of Lausanne, Ecole des Sciences Criminelles, Batochime, CH-1015 Lausanne; [b]Police Cantonale Neuchâteloise, rue des Poudrières 14, CH-2006 Neuchâtel

Keywords: Banknotes · Cocaine · Discrimination · Distribution · Ion mobility spectrometry

In the fight against illicit drug trafficking, police investigations cannot solely rely on the seizure of illicit drugs to determine the involvement of people in such activities. More often than not, investigators have to collate information from different sources (testimonies, intelligence database, observations, *etc.*) in order to gather intelligence that could serve to reveal the structure of a network. Among other means, the detection of traces of illicit drugs on banknotes was proposed in the middle of the 90s to be used as an indicator of money related to trafficking. Banknotes coming in contact or being close to illicit drugs may become contaminated by such substances. Many studies showed that cocaine may be commonly detected on banknotes, but there is a lack of knowledge concerning the value of such a detection: does it really reveal an involvement in illicit drug trafficking or is it just background noise?

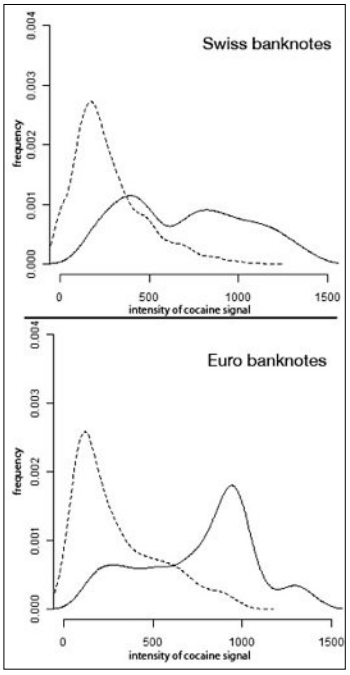
Cocaine seizures on Swiss banknotes.

The study of significance of cocaine traces on banknotes encompasses sampling issues, analytical developments, and data treatments. Two distinct populations were considered: one composed of banknotes in circulation (Swiss francs and Euros), put at our disposal by financial institutions (n_{CHF} = 900; n_{EUR} = 992), the other one by banknotes originating from police seizures linked to illicit drug trafficking (n_{CHF} = 640; n_{EUR}=462). New Swiss banknotes were also studied as control. Detection of cocaine traces was undertaken by Ion Mobility Spectrometry after swabbing on the banknotes' surfaces. For both Swiss and Euros banknotes, the results indicate that the detection of cocaine traces cannot be used to discriminate between the two populations as more than 90% of all specimens are contaminated with cocaine. However, significant differences are observed considering the intensity of cocaine signals between banknotes in circulation and banknotes seized by the police. Distribution curves of the intensity of cocaine signals in these populations were computed both for Swiss francs and Euros. A model was then constructed taking into account the measured distributions that could be used to discriminate between the two populations (ROC – receiver operating characteristic – curve area: 0.86). This model can serve as a support for the decision to assess the significance of cocaine detection intensities on a specific batch of banknotes in comparison to the two considered populations.



Cocaine grain adhering to the paper fibres of a banknote (viewed by scanning electron microscopy).

The model raised from these findings has a decisive potential for the detection of banknote batches related to cocaine trafficking.



Distributions of cocaine signal intensities for the two populations (dotted line: banknotes in circulation; plain line: banknotes seized in cases of illicit drug trafficking).

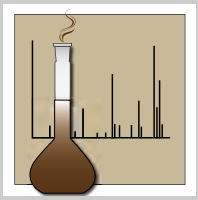
Received: March 14, 2012

References

F. Anglada, O. Delémont, O. Guéniat, P. Esseiva, Revue international de criminologie et de police technique et scientifique **2011**, *LXIV(2)*, 213 and 231.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2012.443



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

On-Line Process Control of the Roast Degree of Coffee

Flurin Wieland[a], Alexia N. Gloess[a], Marco Keller[b], Andreas Wetzel[b], Stefan Schenker[b], and Chahan Yeretzian*[a]

*Correspondence: Dr. C. Yeretzian[a], Tel.: +41 58 934 55 26, Fax: +41 58 934 50 01, E-mail: chahan.yeretzian@zhaw.ch
[a]Zurich University of Applied Sciences, Institute of Chemistry and Biological Chemistry, CH-8820 Wädenswil; [b]Bühler AG, Gupfenstrasse 5, CH-9240 Uzwil

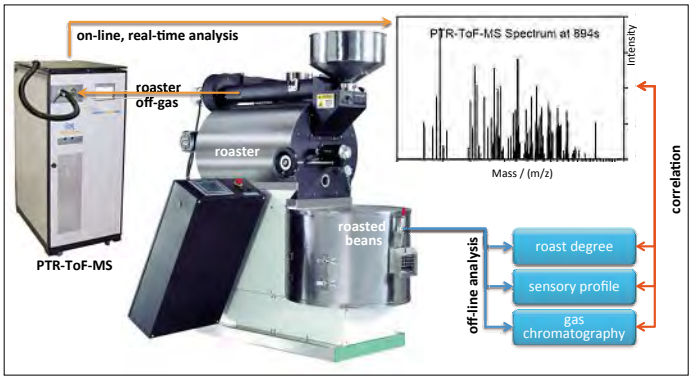
Keywords: Coffee · On-line process control · Principle Component Analysis (PCA) · Proton-transfer-reaction time-of-flight mass spectrometry (PTR-ToF-MS) · Roasting

The flavour of roasted coffee.
Photo: *http://mi9.com/wallpaper/i-love-coffee-wallpaper_80513/*

The flavour of a freshly prepared cup of coffee is the final expression and perceptible result of a long chain of transformations. Along this journey from the seed to the cup, roasting is without doubt the most significant processing step. First, from a quality perspective, it is the very step where the coffee aroma is unlocked and formed from the precursors in the green bean. Second, from an economic perspective, it defines whether the potential in the green beans is expressed in the cup and materializes also in economic terms – even the best crop can be spoiled if not properly roasted.

Here we report on the development of a fast on-line process control technology for a consistent roast, batch after batch. It involves the on-line monitoring of the roaster off-gas using Proton-Transfer-Reaction Time-of-Flight Mass-Spectrometry (PTR-ToF-MS) and the analysis of the PTR-ToF-MS data *via* principle component analysis (PCA) to predict the roast degree in real time. The PCA was calibrated in advance with a large number of roasting trials, to develop the predictive model.

During each roasting cycle, the roaster off-gas is analysed on-line by PTR-ToF-MS, as a means to follow the evolution of the roasting process. Furthermore, the roast degree, the sensory profile (human panel) and the profile of volatile flavour compounds (gas chromatography) are measured off-line. To link the time-dependent PTR-ToF-MS mass profile with off-line measured quality attributes of coffee, a large number of 'calibration experiments' were performed. This allowed in a first study the development of a predictive model for the roast



Experimental strategy implemented for a real-time process control of the roast degree by on-line monitoring roaster off-gas *via* PTR-ToF-MS.

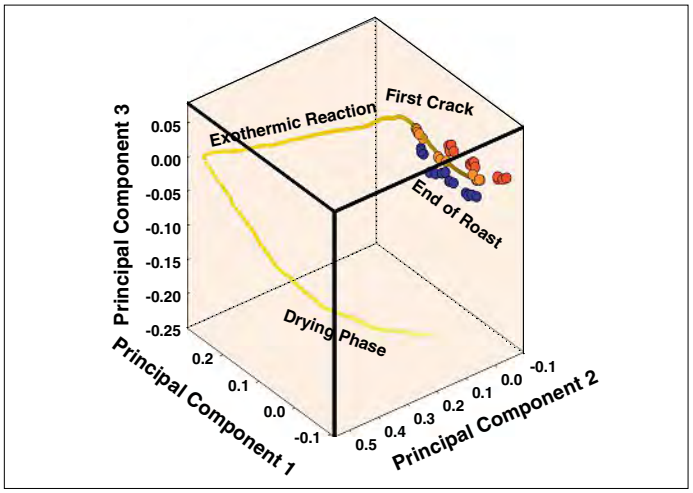
degree based on on-line monitored PTR-ToF-MS profiles. More specifically, the off-line determined roast degree was calibrated against the PTR-ToF-MS data (intensity of a series of relevant ion masses) at the end point of each roasting cycle, using multivariate statistical analysis, and a predictive model was derived. These ion masses were subsequently monitored on-line and the roast degree predicted during a roasting cycle.

This research demonstrates that a time-resolved analysis of the roaster off-gas by PTR-ToF-MS provides a detailed picture of the evolution of the roasting process and allows establishing a real-time process control tool to ensure highest consistency of the roast degree.

Received: March 27, 2012

Reference

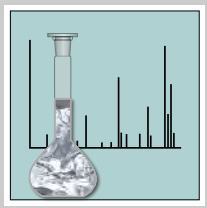
F. Wieland, A.N. Gloess, M. Keller, A. Wetzel, S. Schenker, C. Yeretzian, *Anal. Bioanal. Chem.* **2012,** *402,* 2531.



Principal component analysis to predict the roast degree of coffee. Experimental data of different roasting temperatures are shown (red: high, orange: medium, blue: low) in the 3D-space of the three most important principal components. The predicted roasting degree in real-time is shown as a yellow trace, here for a specific roasting process at medium temperature.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2012.644



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

POPs – A Haunting Legacy

Peter Schmid*[a], Christian Bogdal[b], Nancy Blüthgen[c], and Flavio S. Anselmetti[d]

*Correspondence: P. Schmid[a], Tel.: +41 58 765 46 51, Fax: +41 58 765 46 14, E-mail: peter.schmid@empa.ch
[a]Empa, Swiss Federal Laboratories for Materials Science and Technology, Überlandstrasse 129, CH-8600 Dübendorf
[b]Institute for Chemical and Bioengineering, ETH Zurich, Wolfgang-Pauli-Strasse 10, CH-8093 Zürich
[c]School of Life Sciences, University of Applied Sciences Northwestern Switzerland, Gründenstrasse 40, CH-4132 Muttenz
[d]Eawag, Swiss Federal Institute of Aquatic Science and Technology, Überlandstrasse 133, CH-8600 Dübendorf

Keywords: Glacier · POPs · Sediment · Trace analysis

Industrial chemicals such as polychlorinated biphenyls (PCB) and dichlorodiphenyltrichloroethane (DDT) have been produced and used in large quantities more than 50 years ago. During the phase of application they were released to the environment and mainly distributed by atmospheric transport. Today, due to their hazardous properties these chemicals are apostrophized as persistent organic pollutants (POPs) and are banned worldwide by the Stockholm Convention. However, they are still circulating in the environment. Actual and historical atmospheric input of chemicals can be calculated from investigations of dated lake sediments. Trace analyses of POPs in sediments from Swiss plateau lakes using gas chromatography-high resolution mass spectrometry show decreasing input in the last 40 years. In strong contrast, we observed increasing input in proglacial lakes. This surprising phenomenon led us to the 'glacier hypothesis' claiming that POPs deposited in the past on glaciers are now released from the melting ice. This hypothesis has been corroborated by findings from sediment analyses of several mountain lakes. In these investigations we observed that not only the long-term behavior of glacier movement and ablation but also short-term based growth and decline are reflected in the sediment input of a proglacial lake.

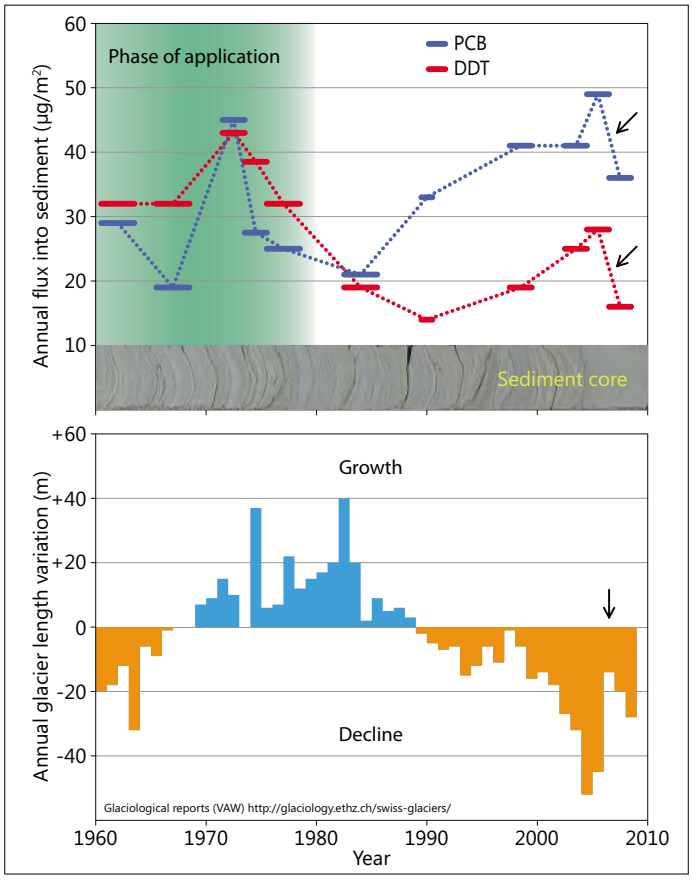
Stein glacier and Lake Stein in the Bernese Alps. (Photo: Ruedi Keller 2009)

Comparison of length variations of Stein glacier and annual fluxes of DDT and PCB into the same-named lake show that fluxes increased during the application phase of these POPs (highlighted in green). Thus, input into the lake in the 1970s is assigned mainly to direct atmospheric input, which decreased rapidly due to phase-out of these chemicals later on. After 1990, fluxes increased again due to release from the glacier by melting of ice in which the chemicals had been stored for more than two decades. The renewed decrease observed in the last sediment layer (*ca.* 2007, arrows) is attributed to an intermediate stagnation of the accelerated decline of the glacier after 2005 (arrow). **The findings are a piece of jigsaw to the knowledge how POPs are still circulating in the environment, even if phased out decades ago. Thus, the haunting legacy of POPs calls for the development of more sustainable chemical products and a careful assessment of their properties prior to widespread use.**

Received: May 8, 2012

References

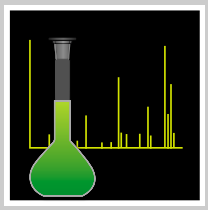
C. Bogdal, P. Schmid, M. Zennegg, F. S. Anselmetti, M. Scheringer, K. Hungerbühler, *Environ. Sci. Technol.* **2009**, *43*, 8173.
P. Schmid, C. Bogdal, N. Blüthgen, F. S. Anselmetti, A. Zwyssig, K. Hungerbühler, *Environ. Sci. Technol.* **2011**, *45*, 203.



Annual fluxes of PCB and DDT into the sediment of Lake Stein and annual length variation of Stein glacier.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St. Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2012.714



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Cell Growth Processes in *Arabidopsis thaliana* are Modified by Flavonols

Christoph Ringli*[a], Benjamin M. Kuhn[ac], and Laurent Bigler*[b]

*Correspondence: C. Ringli[a], Tel.: +41 44 634 82 33, E-mail: chringli@botinst.uzh.ch; L. Bigler[b], Tel.: +41 44 635 42 86, E-mail: lbigler@oci.uzh.ch

[a]Institute of Plant Biology, University of Zürich, Zollikerstrasse 107, CH-8008 Zürich

[b]Institute of Organic Chemistry, University of Zürich, Winterthurerstrasse 190, CH-8057 Zürich

[c]Present address: Energy Biosciences Institute, University of Berkeley, CA, USA

Keywords: Arabidopsis · Auxin · Epidermal cells · Flavonols · UHPLC-HR-MS/MS

The phenylpropanoid pathway (PPP) is a biosynthetic process ubiquitously found in plants. A large array of compounds is produced by the PPP including lignin for wood formation, phytoalexins which serve as a line of defense against pathogens, or anthocyanins (a group of flavonoids) which protect the plant from UV-induced damage. Flavonols form a second subgroup of flavonoids and are attracting increasing attention due to their suggested health-beneficial effects.

Most of the flavonols accumulating in the model plant *Arabidopsis thaliana* are glycosylated with either glucose or rhamnose. The mutant plant *rol1-2* is affected in the synthesis of rhamnose, shows a modified flavonol glycoside accumulation, and exhibits a distorted cell growth phenotype. UHPLC-HR-MS/MS analysis was used to identify and quantify the exact flavonol glycoside composition. The biological significance of this change in the flavonol glycosylation profile was assessed by genetic means. Blocking flavonol biosynthesis in the *rol1-2* mutant, by introducing mutations in genes coding for enzymes active in the PPP pathway, leads to suppression of the *rol1-2* cell growth phenotype. Hence, flavonols accumulating in the *rol1-2* mutant interfere with proper cell development. One of several potential modes of action of flavonols is to modify the transport activity of auxin, a major plant hormone that affects numerous plant developmental processes. Auxin is not produced by all but only a restricted number of cells and must be transported to the target tissues. While the *rol1-2* mutant shows altered transport and accumulation of auxin in the plant shoot, this effect is reverted to wild-type levels by blocking flavonol biosynthesis.

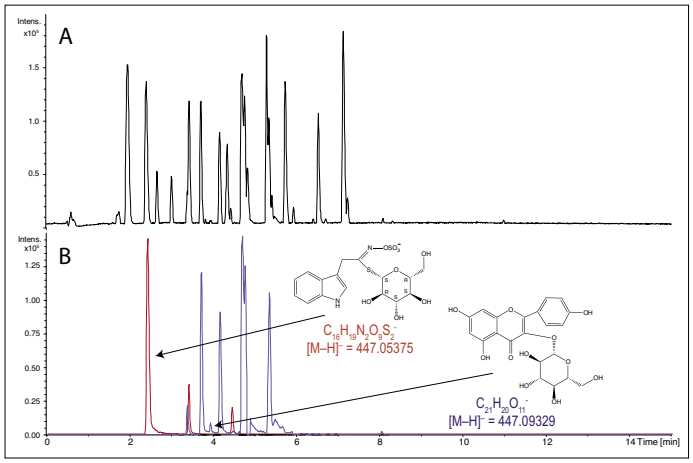
Hence, the *rol1-2* mutant of *Arabidopsis thaliana* shows an alteration in the flavonol glycoside accumulation profile which was analyzed in detail by UHPLC-HR-MS/MS. The observed changes have a direct effect on cell growth processes in the *rol1-2* mutant, which thus can serve as a model system to investigate in detail the mode of action of flavonols on plant development.

Received: June 7, 2012

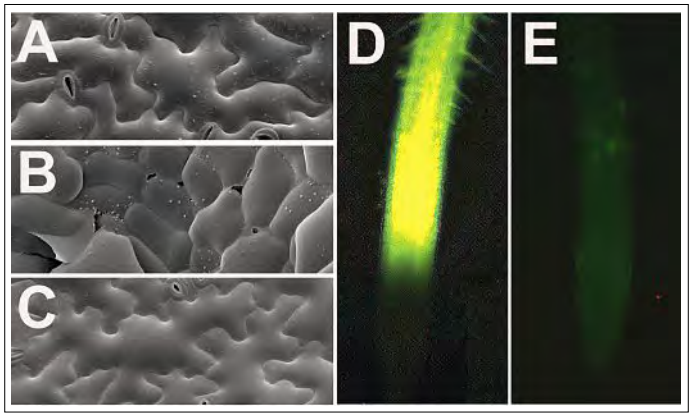
References

C. Ringli, L. Bigler, B. M. Kuhn, R. M. Leiber, A. Diet, D. Santelia, B. Frey, S. Pollmann, M. Klein, *Plant Cell* **2008**, *20,* 1470.

B. M. Kuhn, M. Geisler, L. Bigler, C. Ringli, *Plant Physiol.* **2010**, *156,* 585.



UHPLC-HR-ESI-MS of *A. thaliana* shoot extract. (A) Base peak chromatogram of the extract. (B) Selected high-resolution extracted ion chromatograms (± 0.005 m/z width) of glucosinolates (red, m/z 447.05375; 477.06431) and flavonoids (blue, m/z 431.09837; 447.09329; 463.08820; 477.10385; 489.10385; 577.15628; 593.15119; 609.14611; 623.16176; 739.20910; 755.20402; 771.19893) used for quantitative determination.



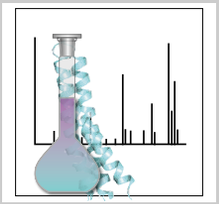
Flavonol-induced cell growth phenotype. Wild-type cotyledons of *A. thaliana* develop puzzle-shaped epidermal cells (A). In *rol1-2* mutants, they are brick-shaped (B), an effect that is suppressed in the *rol1-2 tt4* double mutant (C) which lacks chalcone synthase, one of the enzymes of the PPP essential for flavonoid biosynthesis. Flavonoids can be visualized in planta by staining with diphenylboric acid 2-aminoethyl ester in the root of the *rol1-2* (D) but not in the flavonoid-less *rol1-2 tt4* mutant (E).

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen

Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2012.802



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

X-Ray Structure of a Heterodimeric ABC Transporter Crystallized in its Inward-Facing Conformation

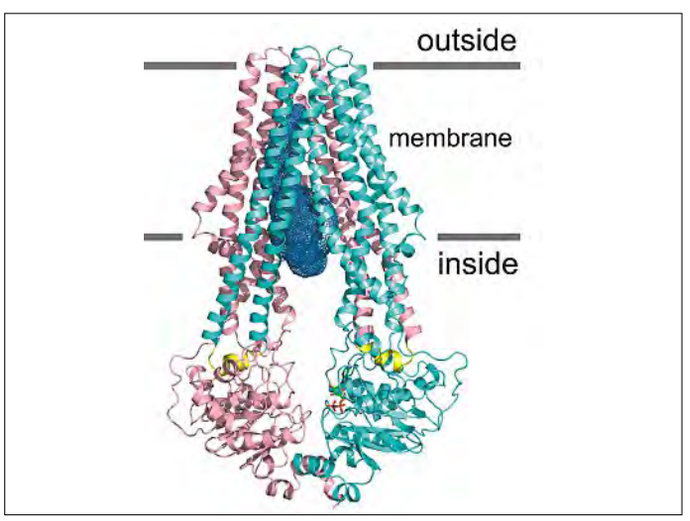
Michael Hohl, Markus G. Grütter*, and Markus A. Seeger*

*Correspondence: Prof. M. G. Grütter, Dr. M. A. Seeger
University of Zurich, Department of Biochemistry, CH-8057 Zürich
Tel.: +41 44 635 55 80, +41 44 635 55 52, E-mail: gruetter@bioc.uzh.ch, m.seeger@bioc.uzh.ch

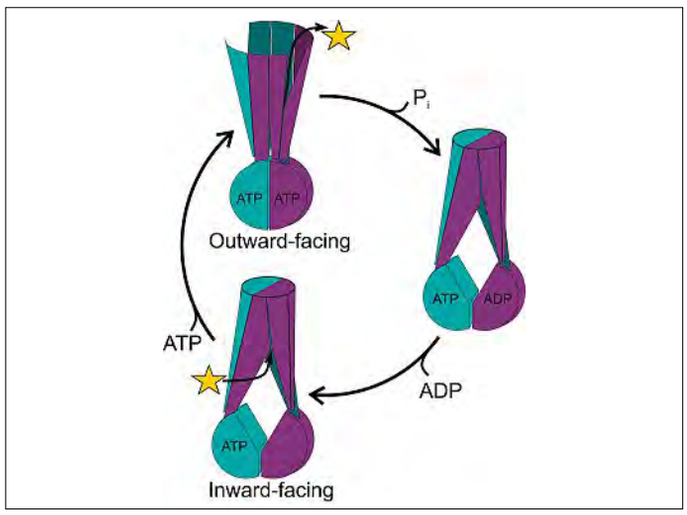
Keywords: ABC transporter · Alternating access model · Drug efflux · Membrane proteins · Structural biology

ATP-binding cassette transporters (ABC transporters) are found in all living organisms and use the energy from ATP binding and hydrolysis to shuttle a wide variety of substrates across cellular membranes. Many ABC transporters actively extrude drugs and thereby contribute to the development of multidrug resistance in cancers and pathogenic microorganisms which causes severe problems in chemotherapy and in the treatment of bacterial infections. In order to understand the molecular mechanism how ABC transporters recognize and transport their substrates, three-dimensional structures determined by X-ray crystallography are of critical importance. Unfortunately, most ABC transporters are reluctant to crystallize and currently only few structures are available for this clinically important class of membrane proteins.

The extrusion of drugs from the cell is accomplished based on an alternating access mechanism. The transmembrane domains of ABC transporters alternately form an inward- and an outward-facing substrate binding cavity which allows drug binding at the cytoplasmic side and its release to the external environment. This requires large conformational changes that are coupled to ATP binding and hydrolysis at highly conserved cytoplasmatic nucleotide binding domains. Until recently, structures of the inward-facing state of ABC transporters have been determined only at low resolution whereas the outward-facing state is well described by X-ray structures.



TM287/288 viewed along the membrane plane. The membrane boundary is indicated by gray lines. The two different polypeptide chains, which assemble to an asymmetric heterodimer, are colored cyan and pink. TM287/288 confines an inward-facing cavity shown as a blue mesh.



Alternating access mechanism of transport for heterodimeric ABC transporters. The transport cycle starts (lower left) with TM287/288 in its inward-facing conformation with one ATP bound. Upon binding of *e.g.* an antibiotic (yellow star) and a second molecule of ATP, the transporter adopts the outward-facing conformation. The substrate is released and ATP is hydrolyzed, which resets the transporter to its inward-facing state and a new transport cycle can begin.

We have succeeded in solving the X-ray structure of TM287/288, a heterodimeric ABC transporter which originates from the thermophilic bacterium *Thermotoga maritima,* at a resolution of 2.9 Å. The structure of TM287/288 reveals a large hydrophobic cavity formed by twelve transmembrane helices that is accessible for drugs from the inside of the cell and therefore represents the inward-facing state. Recombinantly expressed TM287/288 is capable of transporting the anticancer drug daunomycin.

An important feature of TM287/288 is its heterodimeric assembly. In the human body, more than 40 ABC transporters fulfill vital duties, and their malfunction due to inherited mutations may lead to severe diseases. Interestingly, about half of the human ABC transporters are heterodimers like TM287/288. Among these are CFTR, whose failure leads to cystic fibrosis, and SUR1, which is associated with neonatal diabetes. **In summary, we have solved the first X-ray structure of a heterodimeric ABC transporter homologous to medically important transporters connected to cystic fibrosis and multi-drug resistance.**

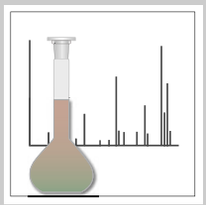
Received: July 10, 2012

Reference

M. Hohl, C. Briand, M. G. Grütter, M. A. Seeger, *Nat. Struct. Mol. Biol.* **2012**, *19,* 395.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2012.877



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Synchrotron-based Spectroscopy Reveals First Evidence for Organic Sulfur-coordinated Arsenic in Peat

Peggy Langner, Christian Mikutta*, and Ruben Kretzschmar

*Correspondence: Dr. C. Mikutta, Institute of Biogeochemistry and Pollutant Dynamics, Soil Chemistry Group, ETH Zurich, Universitätsstrasse 16, CH-8092 Zurich, Tel.: +41 44 633 60 24, Fax: +41 44 633 11 18, E-mail: christian.mikutta@env.ethz.ch

Keywords: Arsenic · Iron · Natural organic matter · Peatland · Sulfur · X-ray absorption spectroscopy

Arsenic is recognized as a toxic contaminant and a threat to some of the world's water resources. Accumulating in organic-rich soils and sediments, As is typically associated with Fe-oxyhydroxide, silicate, and sulfide minerals. Natural organic matter (NOM) has also been suggested as a potential sorbent for As, but the binding mechanisms are still elusive. Since our understanding of the biogeochemical As cycle is therefore essentially incomplete, the major goal of this study was to (1) identify the major mechanism of As binding to NOM and (2) assess its quantitative importance relative to well-established As sequestration pathways involving mineral phases. To this end, we studied the solid-phase speciation of As and Fe in a groundwater-fed peatland (*Gola di Lago*, canton Ticino, Switzerland) containing high natural As concentrations. Anoxic peat samples were analyzed by bulk As and Fe K-edge X-ray absorption near edge structure (XANES) and extended X-ray absorption fine structure (EXAFS) spectroscopy. We focused our speciation analyses on shallow (<0.4 m) and deep (1.5–2.6 m) peat layers.

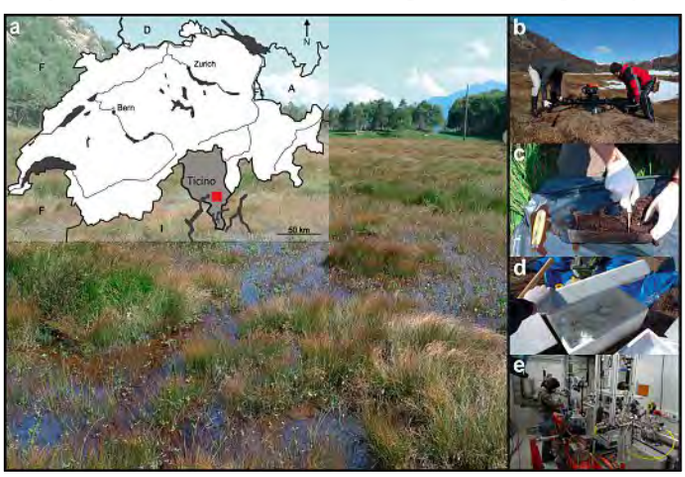


Fig. 1. The field site *Gola di Lago* (red square) is situated in canton Ticino, Switzerland (a). In order to preserve the element speciation in the samples, retrieved peat cores were rapidly cut into slices, shock-frozen, and stored on dry ice for transportation to the laboratory (b–d). After anoxic sample preparation, selected samples were measured at beamline BM29 of the European Synchrotron Radiation Facility (ESRF, Grenoble, France) (e).

With up to 1800 mg As kg^{-1}, both depth intervals showed high As concentrations but differed significantly in the contents of Fe and sulfur (S). Speciation analyses of As revealed that close to the peat surface As was mainly present as As sulfide, and As(III)/(V) sorbed to Fe(III)-oxyhydroxides. In the deep peat layers, however, As was almost entirely coordinated in its trivalent oxidation state to 2–3 S atoms of NOM. The Fe speciation was dominated by chlorite, Fe(III)-oxyhydroxides, Fe(III)-NOM complexes, and Fe sulfides. Although the latter three phases were shown or hypothesized to immobilize As(III), nearly all As was associated with NOM.

Our results thus imply that the binding of As to sulfhydryl groups of NOM impairs As sequestration pathways involving reactive Fe species, and suggest that this mechanism is the major mode of As-NOM interactions in moderately anoxic and S-rich environments.

Acknowledgements

We acknowledge the European Synchrotron Radiation Facility in Grenoble, France (ESRF) for provision of synchrotron radiation facilities, and would like to thank M. Chorro for assistance in using beamline BM29.

Received: August 22, 2012

Reference

P. Langner, C. Mikutta, R. Kretzschmar, *Nature Geoscience* **2012**, *5*, 66.

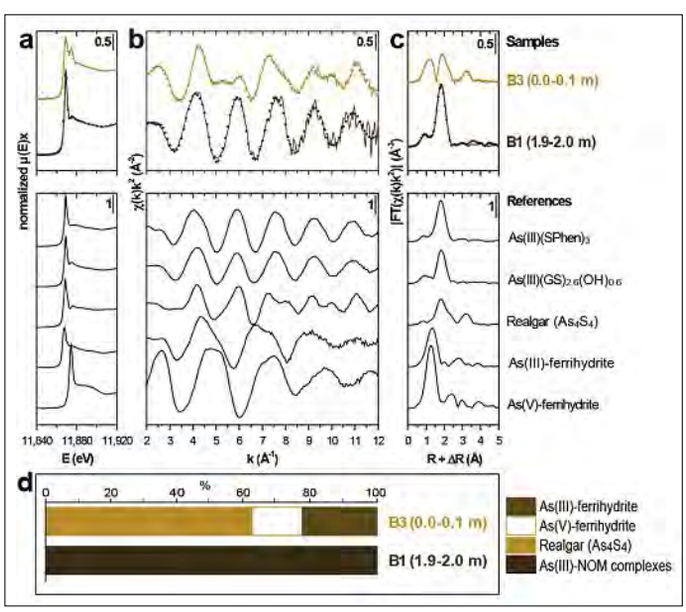
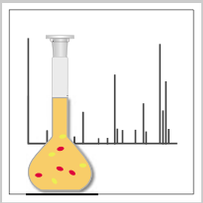


Fig. 2. Arsenic K-edge XANES (a) and k^2-weighted EXAFS spectra (b) as well as Fourier-transform magnitudes (c) of two representative peat samples and selected reference compounds. The displayed reference spectra were used to model the EXAFS spectra of the peat samples. Solid lines are experimental data and filled circles represent best model fits. Results of the As speciation analysis are summarized in (d). Tris(phenyl)thioarsine ($As^{(III)}(SPhen)_3$) and a mixture of di- and tri(glutamylcysteinylglycinyl)-thioarsenite ($As^{(III)}(GS)_{2.6}(OH)_{0.6}$) were used as references for organic S-coordinated As(III).

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2012.950



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry
A Division of the Swiss Chemical Society

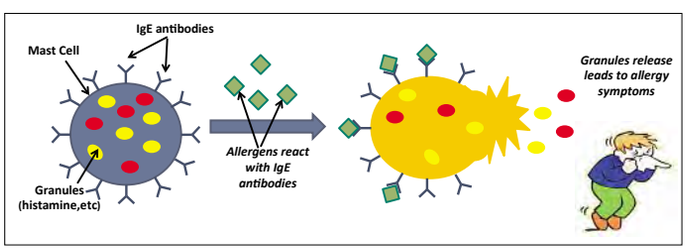
Allergy Diagnostics Using Magnetic Beads in a GRAVI™-*Cell* Microfluidic Device

Natalia Gasilova, Gaëlle Proczek, Anne-Laure Gassner, Jean-Marc Busnel, and Hubert H. Girault*

**Correspondence:* Dr. H. H. Girault, Laboratoire d'Electrochimie Physique et Analytique, Ecole Polytechnique Fédérale de Lausanne, Station 6, CH-1015 Lausanne, Tel.: +41 21 693 31 45, Fax: +41 21 693 36 67, E-mail: hubert.girault@epfl.ch

Keywords: Allergy · Immunoassay · Magnetic beads · Microfluidic device

Allergy is a widespread immunological disorder often related with Western lifestyles in which sterile environments deprive the immune system of factors stimulating its proper development. Allergic diseases, for example allergic rhinitis and asthma, are mediated by histamine (and other substances) released from mast cells due to their interaction with special type of antibody, so-called IgE antibodies, in response to normally harmless substances, allergens. IgE antibodies recognize allergens and activate mast cells, thus a high level (>200 µg/L for adults) of IgE in blood serum is an allergy indicator.

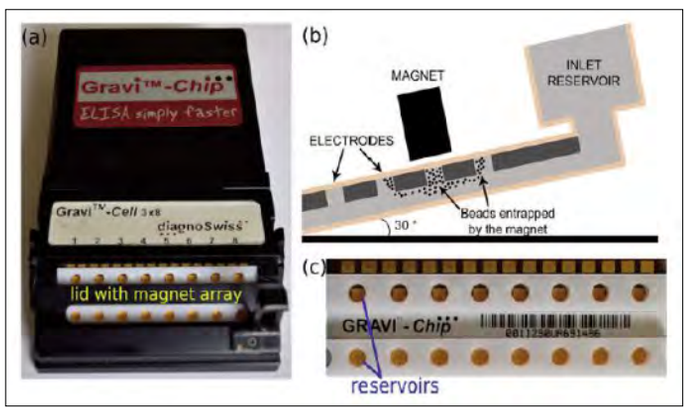


Schematic representation of allergic reaction: IgE antibodies fixed on the surface of mast cell recognize the allergen and provoke the release of histamine and other mediators leading to the development of allergy symptoms.

Measurement of total IgE concentration is one of the methods of allergy diagnostics in clinics. Analytical techniques employed for such routine analysis should therefore be fast and cheap. Herein, a fast immunoassay of IgE antibodies in human blood serum was developed using magnetic beads and the commercial device GRAVI™-*Cell* from DiagnoSwiss (Monthey, Switzerland).

A GRAVI™-Chip placed inside the device at an angle of 30° allows introduced liquids to flow under gravity and capillary forces only. It comprises of eight microchannels and each microchannel possesses two reservoirs and a microelectrode for electrochemical detection. IgE quantification is performed as one-step sandwich ELISA (enzyme-linked immunosorbent assay) with the immunocomplex formed on the surface of the magnetic beads which are trapped inside the microchannels by integrated permanent magnets.

The developed analysis shows good sensitivity (limit of detection 17.5 µg/L) suitable for effective allergy diagnosis.

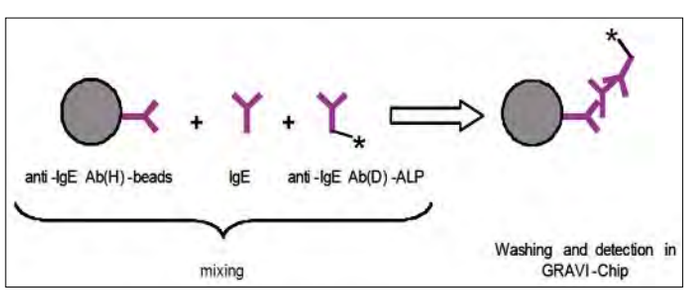


a) GRAVI™-*Cell* device with an 8-microchannel chip tilted at 30°. b) Cross-section along the microchip showing magnetic beads trapping. c) GRAVI™-*Chip* comprising 8 microchannels, inlet reservoirs at the top and outlet ones at the bottom.

Due to the miniaturized format and the application of magnetic beads as a support for the immunoassay the entire analysis can be performed in less than 1 hour and only 1.5 µl of sample is required. As each GRAVI™-Chip possesses eight parallel microchannels it is possible to perform calibration and sample analysis simultaneously with good inter- and intra-chip reproducibility (RSD <10%).

The presented technique for IgE analysis combines the sensitivity and selectivity of immunoassay performed on magnetic beads with advantages of microfluidics, of gravity force-driven fluidics and of electrochemical detection, offering an opportunity of process automation for cheap and high throughput clinical analysis.

Received: October 10, 2012



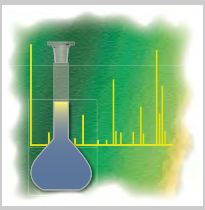
One-step sandwich ELISA: immunocomplex is formed by secondary anti-human-IgE antibodies Ab(H) immobilized on magnetic beads surface, IgE antibodies present in the sample, and by secondary anti-human-IgE antibodies Ab(D) labeled with enzyme alkaline phosphatase (ALP). The electrochemically active substrate of ALP is used for detection.

Reference

G. Proczek, A. L. Gassner, J. M. Busnel, H. H. Girault, *Anal. Bioanal. Chem.* **2012**, *402*, 2645.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.86



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Structure Elucidation in Water Analysis – A Need?

Jean-Daniel Berset*[a], Markus Godejohann*[b], and Daniel Muff[a]

*Correspondence: Dr. J.-D. Berset[a], Tel.: +41 31 634 23 83, E-mail: jean-daniel.berset@bve.be.ch; Dr. M. Godejohann[b], Tel.: +49 721 5161 0, E-mail: Markus.Godejohann@bruker-biospin.de; [a]Water and Soil Protection Laboratory, Office of Water and Waste Management (AWA), Schermenweg 11, CH-3014 Bern; [b]Bruker Biospin GmbH, Silberstreifen 4, D-76287 Rheinstetten

Keywords: HPLC-time slice-SPE-NMR/TOF-MS · Non-target analysis · Structure elucidation · Wastewater effluents

Wastewater treatment plants (WWTP) are important point sources for environmental, organic micropollutants (OMPs) such as pesticides, drugs, artificial sweeteners and personal care products due to incomplete or no degradation at all. Once released, they can be found in river water, ground water and even in low ng/L levels in drinking water samples. Among the myriad of OMPs, transformation products (TPs) have attracted a broad scientific interest as evidence is increasing that OMPs are only slightly modified, frequently to more polar, hydrophilic compounds which seem to be persistent in the aquatic environment. In recent years, efforts have been made to establish the ecotoxicological risks of such complex mixtures of compounds in water samples taking into account also their environmental concentration. As it is not possible to perform an analysis of all possible compounds in a targeted approach by predefining each component and analyzing them by traditional HPLC-tandem mass spectrometry (MS/MS) using the multiple reaction monitoring technique, complementary analytical tools are essential to track such new substances.

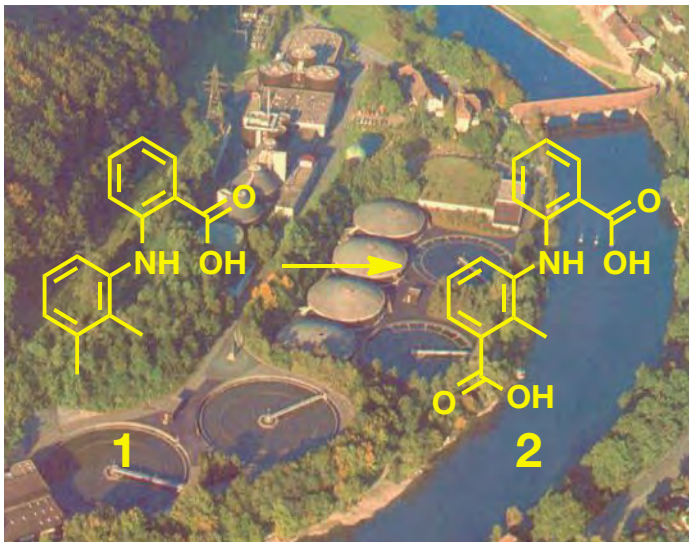
Proton detected nuclear magnetic resonance (^{1}H-NMR) represents the most powerful spectroscopic technique for structure elucidation and has been used in the past in a non-targeted approach for the investigation of environmental water samples. Its combination with HPLC is meanwhile well known and applied in natural product and pharmaceutical analysis. Due to technical improvements such as cryogenically cooled NMR probe heads and post-column solid-phase extraction (SPE) trapping, detection limits have dramatically improved to the mid- to upper ng-range of analyte injected on the column.

HPLC-time slice-SPE-NMR/TOF-MS was applied to 2-weeks WWTP effluent composite samples by injecting 4 × 12.5 µL of a concentrated extract onto a 250 × 4 mm C18 column using a shallow gradient and performing 1-minute post column SPE fractions. Many pesticides such as linuron, metazachlor, ethofumesate, metamitron and propazine could be confirmed by NMR. Among the non-targets, a TP of mefenamic acid, a drug used to treat pain, namely 3-carboxymefenamic acid, could unambiguously be identified using TOF-MS and NMR. **To summarize, the combined HPLC-SPE-NMR/TOF-MS shows great potential for the structure elucidation of unknowns, particularly of transformation products of organic micropollutants.**

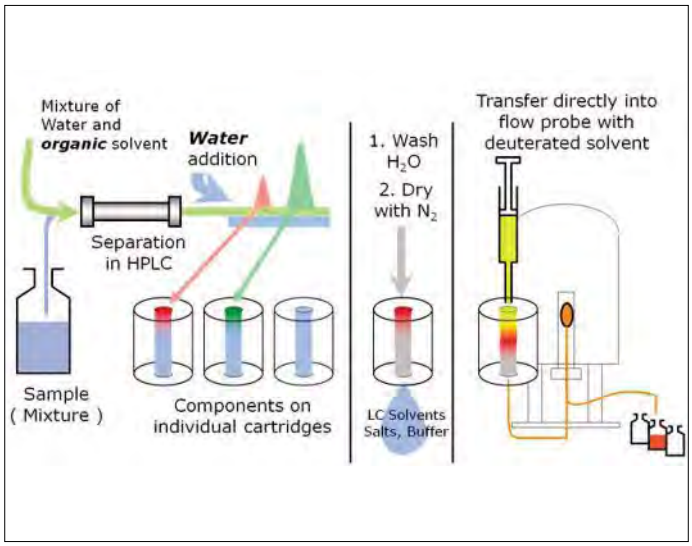
Received: November 23, 2012

Reference

M. Godejohann, J. D. Berset, D. Muff, *J. Chromatogr. A* **2011**, *1218*, 9202.



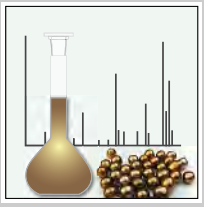
Identification of 3-carboxymefenamic acid (**2**), a transformation product of mefenamic acid (**1**); in the background WWTP Bern.



Basic steps of time-slice SPE-NMR (kindly provided by the Bruker company).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.188



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

The Story of Pearls – An Elemental Perspective

Steffen Allner[a], Francesca Peretti[b], Kathrin Hametner[a], Mattias B. Fricker[a], Adolf Peretti[b], and Detlef Günther*[a]

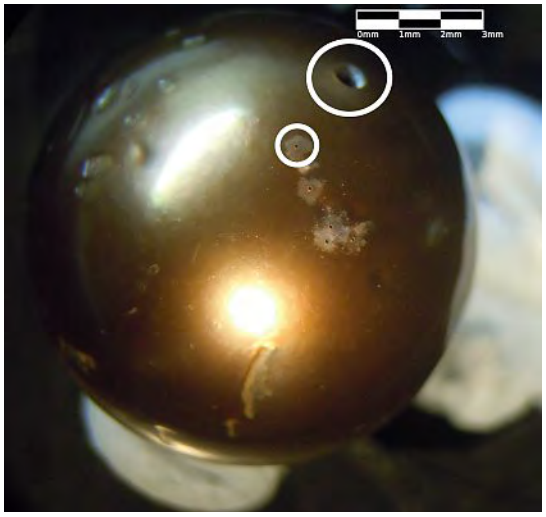
*Correspondence: Prof Dr. D. Günther, Tel.: +41 44 632 46 87, Fax: +41 44 633 10 71, E-mail: guenther@inorg.chem.ethz.ch. [a]ETH Zurich, Laboratory of Inorganic Chemistry, HCI G113, Wolfgang-Pauli-Strasse 10, CH-8093 Zurich. [b]GRS Gemresearch Swisslab AG, Sempacherstrasse 1, CH-6002 Luzern

Keywords: Concentration maps · ICPMS · Laser ablation · Pearl

Pearls are one of the important sectors in the gem market. They are originally a product in the shell of a mollusk. The cause of natural pearl formation was long attributed to small grains of sand or other dirt particles inside mollusks. Today a major reason for their formation is seen as a measure of defense due to enclosure of small intruding organisms. Before the 20th century, the demand of pearls was mainly satisfied by river pearls in Europe and the pearls of the Persian Gulf, also known as oriental pearls. In the 1910s the first pearl farms evolved and cultured pearls emerged on the gem market. The availability of cultured pearls in combination with the Great Depression led to a sharp drop in the prize of pearls.

Besides being less expensive, cultured pearls also have the advantage of a more spherical shape and more desirable color or luster, depending on the growing conditions. The color can be altered in another step after the pearl is removed from the oyster. As this influences the prize of a pearl, it would be most valuable to have a method to distinguish between different origins and treatments of pearls.

In our study, we analyzed 110 cultured pearls from various origins by laser ablation inductively coupled plasma mass spectrometry (LA-ICPMS) and determined the concentration of 45 different elements. The concentrations were analyzed in dependence on water condition of culturing (sea/freshwater) and on the region of origin. For Ba, Mn, and P significant higher concentrations were found in freshwater pearls, whereas Na, K, Mg, B, S, and Sr concentrations are lower than in seawater pearls. However, a significant tracing back of the origin was not possible within this set of pearls.



An analyzed pearl from Tahiti. The tiny craters (middle) produced by the laser are small (60 µm) compared to the hole for the string of a necklace (*ca.* 1 mm) (top).

Additionally, elemental mapping was performed on a pearl cut in half, where growth rings could be seen.

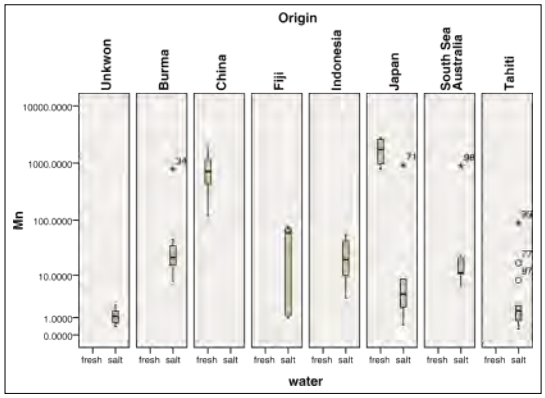
LA-ICPMS has been shown to be a valid method for the distinction of seawater from freshwater pearls and to perform a mapping of concentration down to single rings from different growth periods.

Received: December 18, 2012

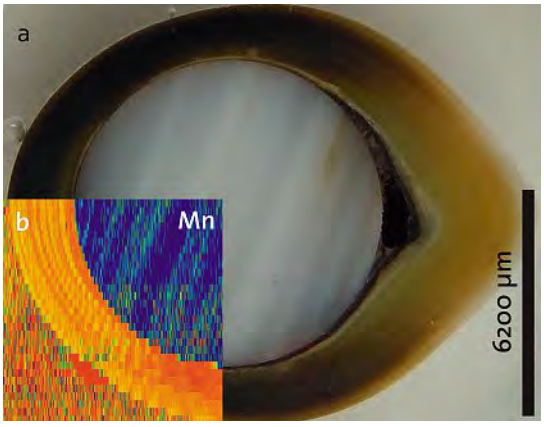
References

S. Allner, F. Peretti, D. Günther, SCS Fall Meeting **2012**, Zurich, Switzerland.

M. B. Fricker, ETH-Diss. No. 20780, 'Design of ablation cells for LA-ICP-MS: from modeling to high spatial resolution analysis applications', **2012**.



Box plots (showing medians and interquartile ranges) of the Mn concentration categorized by region of origin and water condition. Higher levels are seen for fresh water pearls. A similar trend is seen for Ba and P, an inverse trend for Na, K, Mg, B, S, and Sr.

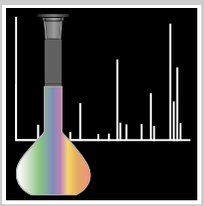


Photograph of the pearl section (a) with the Mn distribution represented with false colors (b). Several layers in the nacre and the inner bead are clearly visible.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.296



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Mass Spectrometric Imaging Applied to Biomedical Research

Dieter Staab, Gregory Morandi, and Markus Stoeckli*

*Correspondence: Dr. M. Stöckli, Novartis Institutes for BioMedical Research, WSJ-155.2.27, Fabrikstrasse 10, Novartis Campus, CH-4056 Basel, Tel.: +41 61 324 77 43, E-mail: markus.stoeckli@novartis.com

Keywords: Compound and metabolites · Mass spectrometric imaging · Molecular imaging · MSI

Mass spectrometric imaging (MSI) stands out from the available molecular imaging technologies due to its ability to simultaneously map multiple analytes without the need for labeling. This makes it the method of choice for applications where labeling is not amenable, or where many (up to hundreds) analytes are to be monitored in one sample. Since the technology is based on the identification of the analyte molecules by their exact mass and/or fragmentation pattern, it also allows the imaging of a wide mass range without the need to know the analytes *a priori* to the measurement. While the potential of this technology was recognized early on, it was not till recently that new technological advances made it routinely applicable to biomedical research.

In our laboratory, the optimized mass spectrometric imaging process starts with whole-body tissue sections which are mounted on metal plates and coated with matrix which is required for the subsequent matrix-assisted laser desorption/ionization (MALDI) process. A reproducible matrix layer is achieved by spray-deposition using an in-house developed coater. The prepared samples are transferred to a temperature and humidity controlled store holding up to 110 plates. A robot distributes these plates to two MALDI mass spectrometers (FlashQuant, AB SCIEX) which acquire the image data from pre-defined regions, either for multiple analytes or whole mass ranges.

A typical experiment where compound and metabolite distributions are analyzed in rodents after administration involves five time points, with analysis of twelve sections per animal (triplicates from four positions). The resulting data shows the time-dependent distribution of the compound and its metabolites from one experiment, delivering mechanistic information in early drug discovery.

We proved the value of MS imaging for compound and metabolite distribution studies and demonstrated it to be an alternative to existing technology in cases where micromolar tissue concentrations are achieved. By applying a normalization strategy with internal standards, quantification accuracy of better than thirty percent was achieved.

Received: January 22, 2013

References

The authors maintain a website at *http://maldi.ms* with information related to MSI and free software.

B. Prideaux, M. Stoeckli, *J. Proteom.* **2012**, *75*, 4999.

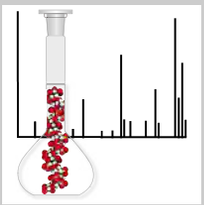
Mass spectrometric imaging platform at the Novartis campus. Tissue sections are prepared in a wet-lab and transferred to the mass spec lab using an elevator (right side). Two high sensitive mass spectrometers with a robotic system analyze the samples in automatic mode. Due to the novelty of this technology, it is on display in the Novartis showcase lab on the Novartis campus in Basel where visitors can learn about the process and see the system in action.

Mass spectrometric imaging data depicting the compound and metabolite distributions in rat after dosage. Higher intensity in the picture correlates to higher analyte concentration. From one animal, up to four sections are analyzed, covering the 50 organs of interest (z-axis). From one section, the compound (Cpd) and multiple metabolites (M1 to M3) are analyzed simultaneously. The time (t) dependent distribution information is acquired from different animals.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.350



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

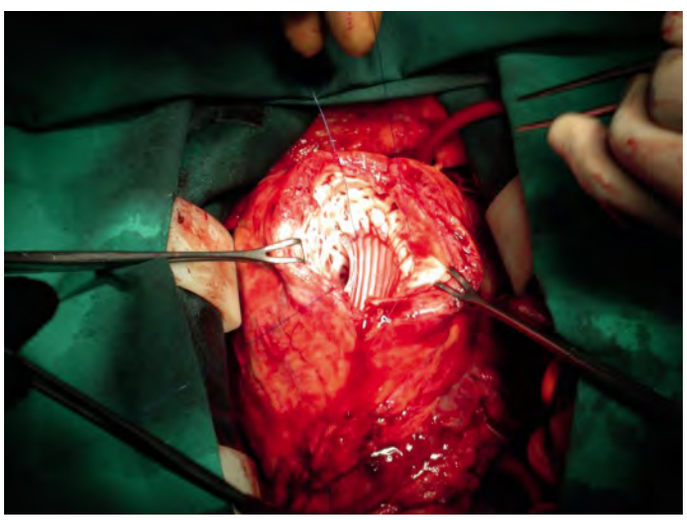
A Division of the Swiss Chemical Society

Detecting Heparin in Whole Blood for Point of Care Anticoagulation Control During Surgery

Eric Bakker*, Gastón A. Crespo, Majid Gharhaman Afshar, Till Saxer, and Karim Bendjelid

*Correspondence: Prof. E. Bakker, University of Geneva, Department of Inorganic and Analytical Chemistry, Quai Ernest-Ansermet 30, CH-1211 Geneva, Tel.: +41 22 379 64 31, E-mail: eric.bakker@unige.ch

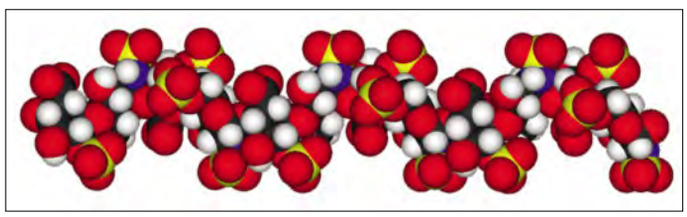
Keywords: Chronopotentiometry · Heparin · Membrane electrodes · Protamine · Surgery



Cardiac surgery, where the heparin detection principle will be applied (Photo A. Kühn, Bad Oeynhausen).

High molecular weight polyanionic heparin (standard heparin) is the anticoagulant of choice in many surgical procedures because of its fast onset of action and since its effects can be effectively and rapidly reversed by its antidote, the polycationic protamine. Accurate reversal of heparin requires knowledge of its concentration after surgery, which is accomplished on the plasma sample with a colorimetric assay performed centrally in the clinical laboratory. Unfortunately, this assay is not available around the clock and exhibits a long turnaround time of more than one hour, during which time the heparin concentration in the patient may no longer reflect the reported value. A direct and rapid detection of heparin at the point of care would hold great promise for delivering better anticoagulation care to millions of patients around the world.

Our group has recently reported on an electrochemical approach to detect the antidote protamine in whole blood samples with a precision of the order of 1%. A supported liquid membrane containing dinonylnaphthalene sulfonate partially paired with tetradodecylammonium is used to detect protamine in blood. An applied cathodic current forces the extraction of protamine from the blood sample into a membrane, and the potential at the same membrane is monitored over time. As protamine is depleted at the membrane surface in a diffusion-limited process, the potential changes at a precise transition time. This time is taken as the analytical signal and gives a linear calibration curve when plotted as square root of transition time *vs.* concentration.



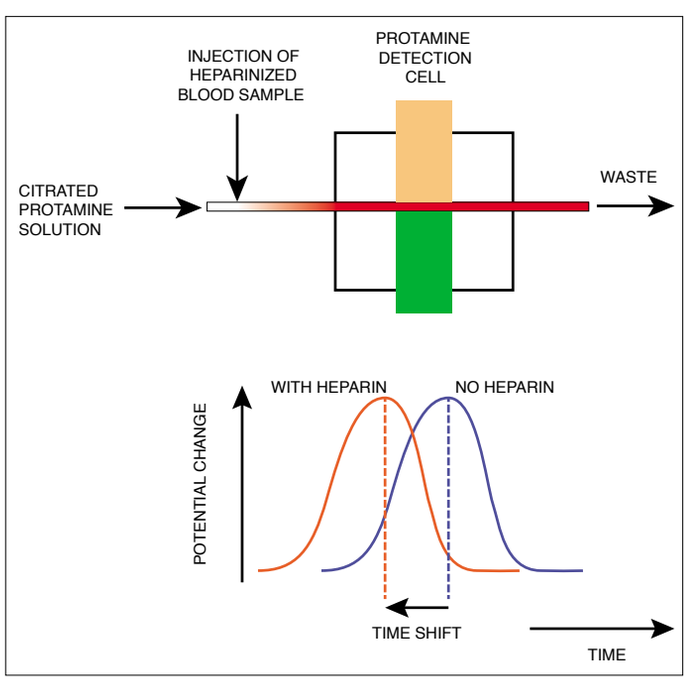
Substructure of the highly charged heparin.

Heparin is quantified by adding a known concentration of protamine to a sample aliquot and measuring the excess protamine that is not lost by interacting with heparin. The binding between heparin and protamine is diffusion-controlled, allowing for a rapid measurement time in the order of seconds after mixing. The liquid membranes exhibit excellent reproducibilities for repeated measurements. Work is currently underway at the University Hospital of Geneva to validate the technology in clinical settings. **In conclusion, we present here a new and convenient electrochemical methodology to quantify heparin in blood that may improve on the current state of the art in patient care.**

Received: March 19, 2013

Reference

G. A. Crespo, M. G. Afshar, E. Bakker, *Angew. Chem. Int. Ed.* **2012**, *51*, 12575.

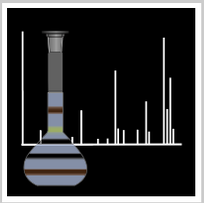


Schematic of the measurement and detection signal.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.428



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Determination of PCR Products by Capillary Electrophoresis with Contactless Conductivity Detection

Marko Stojkovic[a], Narasimha Rao Uda[a], Peter Brodmann[b], and Peter C. Hauser*[a]

*Correspondence: Prof. Dr. P.C. Hauser[a], Tel.: +41 61 267 10 03, Fax: +41 61 267 10 13, E-mail: peter.hauser@unibas.ch. [a]Department of Chemistry, University of Basel, Spitalstrasse 51, CH-4056 Basel. [b]Biosafety Laboratory, State Laboratory Basel City, Kannenfeldstrasse 2, CH-4012 Basel

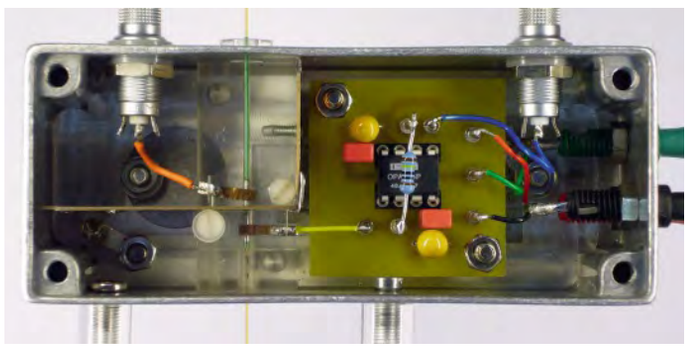
Keywords: Capillary electrophoresis · Contactless conductivity detection · PCR

The detection of polymerase chain reaction (PCR) products is widely used in DNA analysis for such diverse tasks as the determination of paternity, genetic fingerprinting in forensics, identification of pathogens, diagnosis of genetic diseases, recognition of banned genetically modified food items or the identity of meat samples. The standard method for this analysis is planar gel electrophoresis in which the DNA fragments are separated by their size. This method is well established, but it is hard to automate, time consuming, and requires staining for visualization on the plate. Data processing requires awkward optical scanning of the plate.

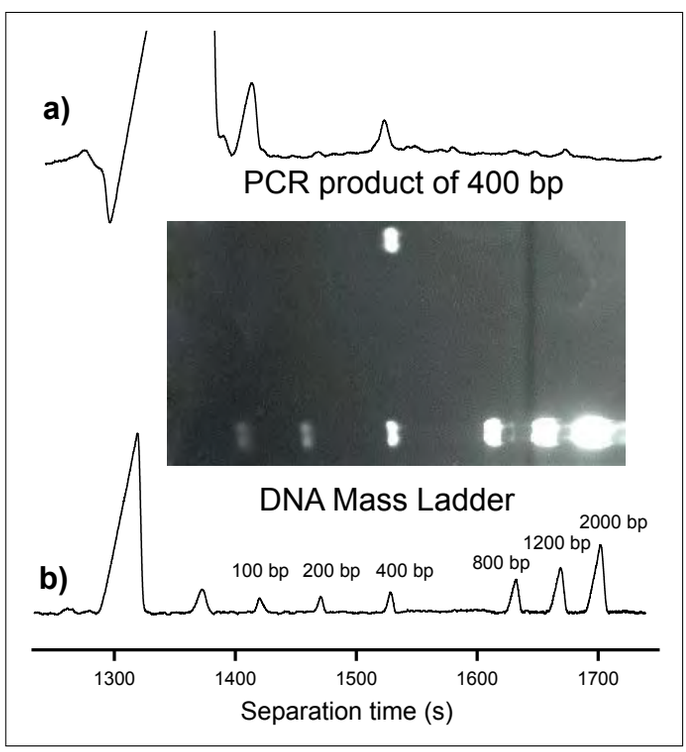
Capillary electrophoresis (CE) is an alternative which allows faster separations and the direct electronic acquisition of electropherograms with characteristic peaks whose areas are directly related to the amount of the species in question. The method is relatively simple as only the application of a high voltage is required and high pressure pumps as in column chromatography are not needed. Contactless conductivity detection is a fully electronic universal technique which is much easier to implement than optical detection on the narrow capillaries needed in electrophoresis which have inner diameters of typically 50 µm. The electrodes are placed on the outside of the capillary and thus cannot deteriorate by contact with solutions. The conductivity measurement of the solution inside the tubing is enabled by capacitive coupling of an AC-voltage into the capillary and the similar coupling of the resulting current out of the capillary on a pair of tubular electrodes. The term C^4D, for capacitively coupled contactless conductivity detection, has become widely accepted for this technique. Due to the low power requirements it also possible to construct complete portable CE-C^4D instruments which can be run from batteries.

As an example of the application, the identification of genetically modified soybean (Roundup Ready), which is banned from importation into Switzerland, was carried out. PCR primers were designed to yield a fragment of 400 base-pairs for the GM-soybeans.

The method allows the relatively fast analysis of PCR products yielding the results in a standard electropherogram on a simple and inexpensive instrument.



In-house constructed C^4D-cell.



Electropherograms obtained by CE-C^4D for the PCR-product of the Roundup Ready soybean (a) and a mixture of mass standards (ladder) (b), shown together with a picture of the stained plate for the separations carried out by conventional planar gel electrophoresis.

Received: April 16, 2013

References

M. Stojkovic, N. R. Uda, P. Brodmann, M. Popovic, P. C. Hauser, *J. Sep. Sci.* **2012**, *35,* 3509.

T. D. Mai, T. T. T. Pham, H. V. Pham, J. Sáiz, C. García Ruiz, P. C. Hauser, *Anal. Chem.* **2013**, *85,* 2333.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.610

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Volatile Sulphur Compounds in Cheeses – An Odorous Analytical Challenge

Pascal Fuchsmann*, Stefan Irmler, and Katharina Breme

*Correspondence: P. Fuchsmann, Agroscope, Schwarzenburgstrasse 161, CH-3003 Bern
Tel.: +41 31 323 82 60, E-mail: pascal.fuchsmann@agroscope.admin.ch

Keywords: Cheese · Flavour analysis · GC/PFPD · Volatile sulphur compounds

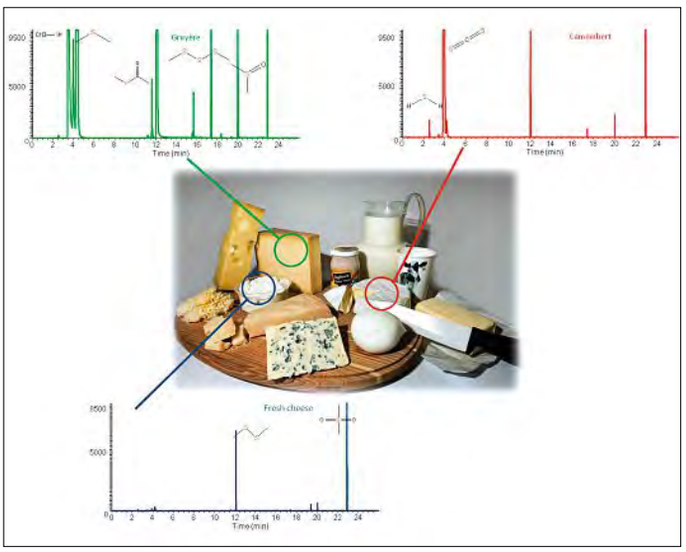
Cheese flavour is mainly the result of bacterial metabolic activities. Not only the starter culture, but also the non-starter lactic acid bacteria used to manufacture cheeses contribute to flavour formation, and cheese flavour is primarily determined by degradation of proteins to peptides and free amino acids, degradation of milk fat, and degradation of lactate and citrate.

Volatile sulphur compounds (VSCs) contribute essentially to the characteristic flavour of many foods, and in numerous cheeses, VSCs such as methanethiol, hydrogen sulphide, and methylsulphides (which are mainly derived from the decomposition of the sulphur-containing amino acids cysteine and methionine) are amongst the key flavour compounds. Due to their frequent low odour thresholds, their presence and sensory properties can significantly influence cheese flavour even when present at low quantities. As a consequence, a variation in VSC concentration can profoundly change cheese flavour. Since VSCs are highly volatile and reactive compounds, their analysis, mostly by gas chromatography (GC), remains an analytical challenge. Carefully chosen and state-of-the-art analytical tools in sampling, extraction, analysis and detection are needed.

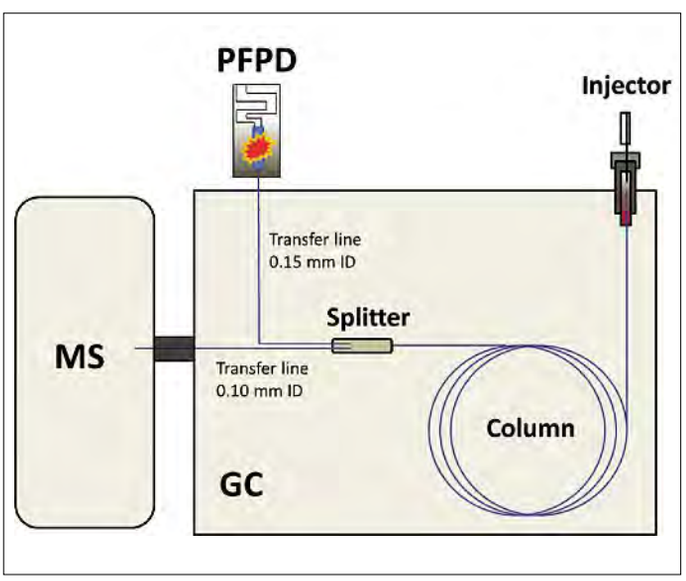
In addition to universal physical detectors such as the mass selective detector (MSD) which allow the structural identification of chemicals, specific detectors targeting heteroatomic compounds are used to increase sensitivity. Pulsed-flame photometric detection (GC/PFPD) can be used for the detection of sulphur and various other heteroatoms; the detection being based on the combustion of compounds eluting from the GC in a hydrogen-rich flame leading to the generation of excited species and consequently photomultiplied light emission (sulphur emission wavelength: 393 nm).

Samples of different cheese varieties produced in Switzerland were analysed by GC-MSD/PFPD, and VSC profiles were found to be very different. Extraction of VSCs was done by headspace solid-phase microextraction where volatile compounds from the gaseous space above the sample in a closed vial are ab- and/or adsorbed on a polymer matrix and thermally desorbed into the GC.

GC-MSD/PFPD allows the efficient and reliable analysis of volatile sulphur compounds which are often present in very low concentrations and nevertheless influence cheese flavour due to their low sensory thresholds.



Pulsed-flame photometric detector sulphur-specific trace comparison between three different cheeses produced in Switzerland: Gruyère, Camembert, and fresh cheese.



The GC-MS/PFPD experimental setup used at Agroscope's flavour analytical laboratory in Bern: A GC (Thermo Finnigan Trace GC) is equipped with a mass spectrometer (Thermo Scientific DSQ II Single Quadrupole) and a PFPD (O.I. Analytical, detector model 5380) to simultaneously measure the MS trace and the sulphur-specific response chromatogram.

Received: June 12, 2013

Reference

B. Bogicevic, P. Fuchsmann, K. Breme, R. Portmann, B. Guggenbühl, S. Irmler, *Int. Dairy J.* **2013**, DOI: 10.1016/j.idairyj.2013.05.005.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.684

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences
A Division of the Swiss Chemical Society

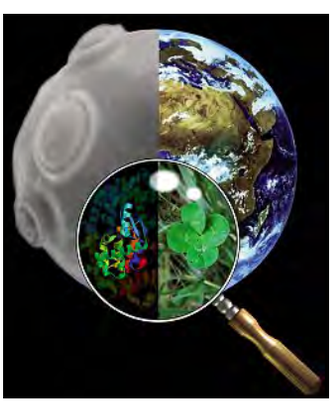
A Complete Mass-spectrometric Map of a Eukaryotic Proteome

Martin Soste and Paola Picotti*

*Correspondence: Prof. Dr. P. Picotti, ETH Zurich, Department of Biology, Institute of Biochemistry, Schafmattstrasse 18, CH-8093 Zurich, Tel.: +41 44 633 66 27, E-mail: paola.picotti@bc.biol.ethz.ch

Keywords: Mass spectrometry · Protein quantification · Proteomics · Quantitative trait analysis · *S. cerevisiae* · Selected reaction monitoring

The ability to quantify any protein or set of proteins of interest is an essential task in the life sciences. In terms of total mass, proteins are the second most abundant molecules in human cells, second only to water, and are crucial effectors and regulators of virtually all cellular processes. A eukaryotic cell contains more than 5,000 different proteins, which span a broad range of abundances, and thereby challenge current analytical techniques that aim to reliably measure proteins of interest. Measuring proteins is a crucial requirement in biomedicine, as they can change their abundance in response to stimuli such as an infection or during disease progression (*e.g.* as in cancer). Quantifying proteins is also extremely important in the biological sciences to understand basic cellular processes since proteins directly or indirectly supervise all reactions occurring in cells.



A proteome map enables the extraction of mass-spectrometric coordinates for proteins of interest. The sensitivity of the developed SRM assays enables the reliable detection of low-abundance proteins in yeast (~50 copies/cell), a challenge of dynamic range analogous to finding a four-leaf clover from outer space.

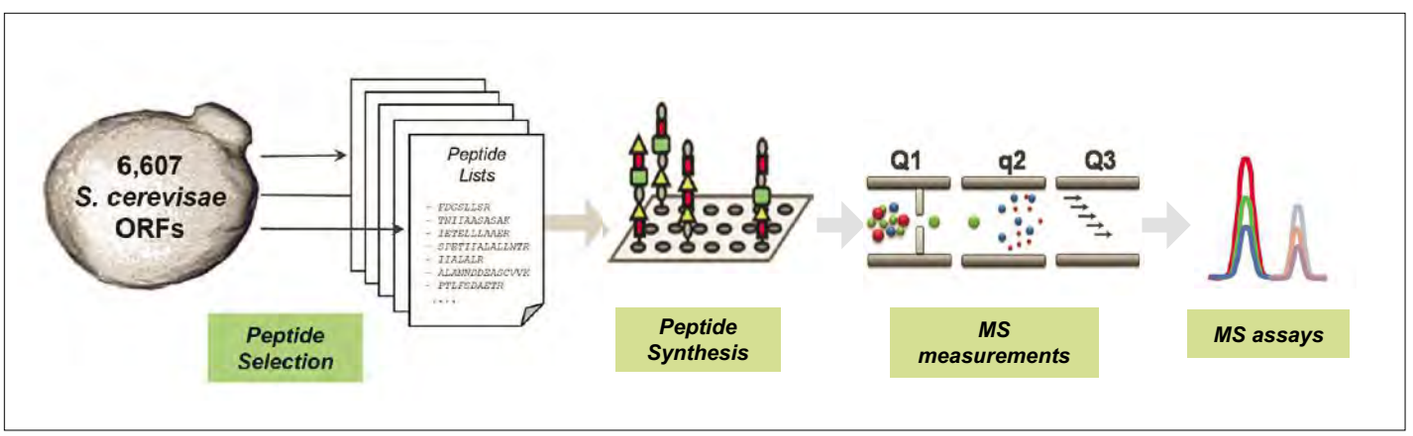
In the analytical sciences, complete gold-standard reference maps or datasets describing the properties of the compounds under study (*e.g.* libraries for the spectroscopic properties of molecules) are commonly used to reliably probe any sample for the presence of the molecule(s) of interest. Attempts to generate such maps for a proteome, the ensemble of all proteins contained in a given organism, have so far failed to reach complete coverage.

To generate a complete (97%) reference map for the proteome of *S. cerevisiae*, a model eukaryotic organism commonly used in biological research, a strategy based on high-throughput peptide synthesis and mass spectrometry (MS) was used. Two versions of this MS map were generated, one supporting discovery experiments and the other hypothesis-driven (targeted) proteomic measurements based on selected reaction monitoring (SRM) assays. As a proof of principle, high coverage of the protein abundance range (~50 – 1E6 copies/cell) was achieved in total cell lysates using SRM assays. The MS map was later coupled to the complete genomic information available for *S. cerevisiae* in a quantitative trait locus (QTL) analysis to unravel the complex relationships that exist between genes and protein abundances in yeast.

This mass-spectrometric proteome map constitutes the first complete set of quantitative proteomic assays for more than 6,000 proteins and can be used to support most contemporary proteomic studies in the model eukaryote, yeast. The same approach can be applied to the human proteome.

Received: July 16, 2013

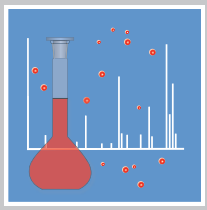
References
P. Picotti, R. Aebersold, *Nature Methods* **2012**, *9*, 555.
P. Picotti, M. Clément-Ziza, H. Lam, D. S. Campbell, A. Schmidt, E. W. Deutsch, H. Röst, Z. Sun, O. Rinner, L. Reiter, Q. Shen, J. J. Michaelson, A. Frei, S. Alberti, U. Kusebauch, B. Wollscheid, R. L. Moritz, A. Beyer, R. Aebersold, *Nature* **2013**, *494*, 266.



Schematic representation of the workflow used to create a reference mass-spectrometric map of the yeast proteome.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.739



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Analytical Strategy to Characterize Drug–Plasma Interactions: From High Throughput to In-depth Analysis

Karine Vuignier*, Jean-Luc Veuthey, Pierre-Alain Carrupt, and Julie Schappler

*Correspondence: Dr. K. Vuignier, School of Pharmaceutical Sciences, University of Geneva, University of Lausanne, 20 Bd. d'Yvoy, CH-1211 Geneva 4, Tel.: +41 22 379 64 77, E-mail: karine.vuignier@unige.ch

Keywords: Affinity chromatography · Capillary electrophoresis · Pharmacokinetics · Protein interaction · Surface plasmon resonance

Launching a drug is a complex and time-consuming process that requires 15–20 years. It usually costs around 1 billion dollars and is rather risky: only one out of 10,000 studied compounds will eventually reach the market. Among the different challenges the pharmaceutical industry has to face to produce better drug candidates, it is essential to reduce the attrition rates during drug development by developing compounds with improved pharmacokinetics. Plasma protein binding (PPB) is an important drug characteristic that has strong implications for *in vivo* performance. It is widely accepted that only the free drug fraction can cross membrane barriers, be distributed to tissues, and elicit a pharmaceutical response. Moreover, the effect of a drug (pharmacological or toxicological) is related to the exposure of a patient to the free drug in plasma rather than to the total drug concentration. The binding of a drug to plasma proteins (albumin and α_1-acid glycoprotein), by regulating the free drug fraction, is thus considered an important parameter to be determined during the drug research process. Nowadays, the most widely used techniques for PPB measurement are equilibrium dialysis and ultrafiltration. However, these techniques have some limitations, which narrow their application in the current high-throughput pharmaceutical environment.

Our proposed methodology takes into account the requirements and specificity of the different stages of the drug research process. During the early stages of the drug discovery phase, the number of compounds to test is huge and detailed analysis cannot be performed on every molecule. Therefore, a screening step by affinity chromatography is first applied to identify strongly bound compounds (>85%) that are likely to cause drug safety issues or severe adverse effects. Affinity chromatography requires only a single analysis per compound to obtain an estimation of its affinity for a protein. Moreover, using a highly selective detector, such as mass spectrometry, compound pooling can be performed to further enhance the throughput. In a second step, the strong binders are studied with techniques that produce more information on the binding process (*i.e.* affinity constant, stoichiometry, kinetics of the interaction), even though they are more time-consuming. For this purpose, surface plasmon resonance biosensor and capillary electrophoresis, for drug-albumin and drug–α_1-acid glycoprotein, respectively, are particularly well adapted. **The developed strategy shows great potential to enhance the pharmacokinetic profile of drug candidates.**

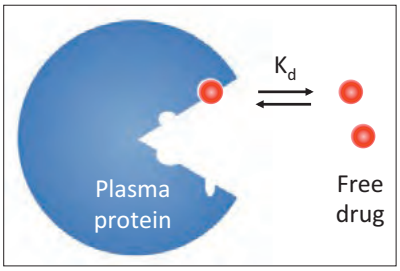


Fig. 1. Binding equilibrium between a plasma protein and a drug. K_d represents the dissociation constant.

Received: August 14, 2013

Reference

K. Vuignier, J.-L. Veuthey, P.-A. Carrupt, J. Schappler, *Drug Discovery Today* **2013**, in press.

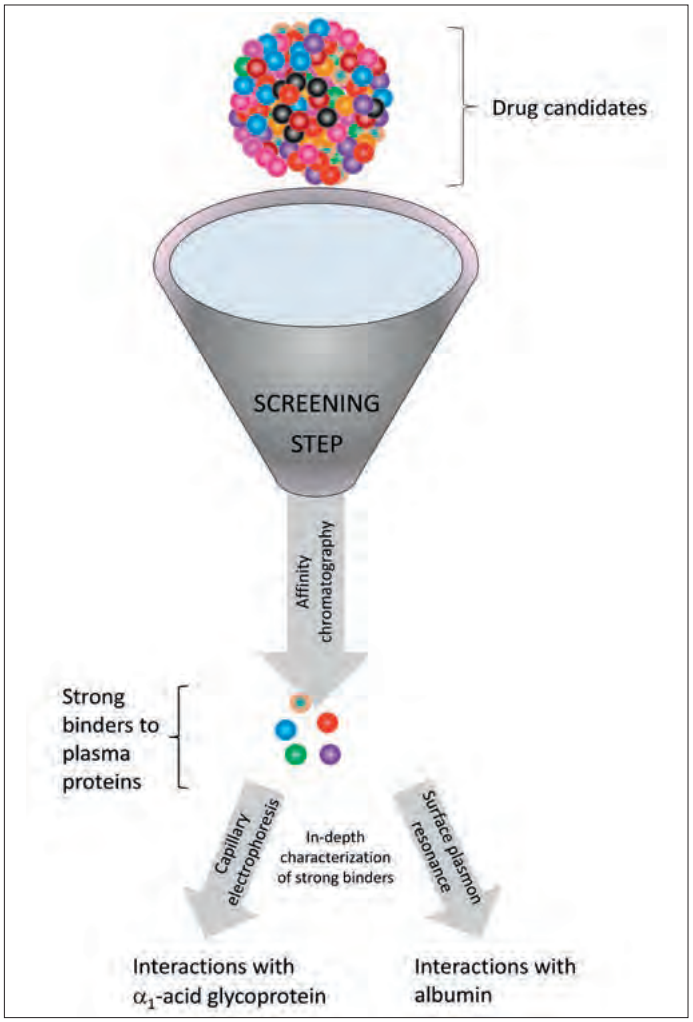
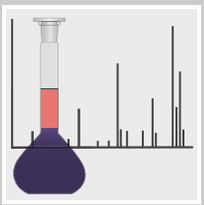


Fig. 2. Proposed methodology to assess drug–plasma protein interactions.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.828



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Neutron Activation Analysis – Another Approach to Uranium and Thorium Analysis in Environmental Samples

Markus Zehringer*[a], Jan Mazacek[b], Reto Dolf[b], Giuseppe Testa[c], and Jürg Jourdan[c]

*Correspondence: Dr. M. Zehringer[a], Tel.: +41 61 385 25 17, Fax: +41 61 385 25 09, E-Mail: markus.zehringer@bs.ch. [a]Kantonales Laboratorium Basel-Stadt, Kannenfeldstrasse 2, CH-4012 Basel. [b]Amt für Umweltschutz und Energie Basel-Stadt, Neuhausstrasse 31, CH-4019 Basel. [c]Departement Physik, Universität Basel, Klingelbergstrasse 82, CH-4056 Basel

Keywords: Neutron activation analysis · Suspended matter · Thorium · Uranium

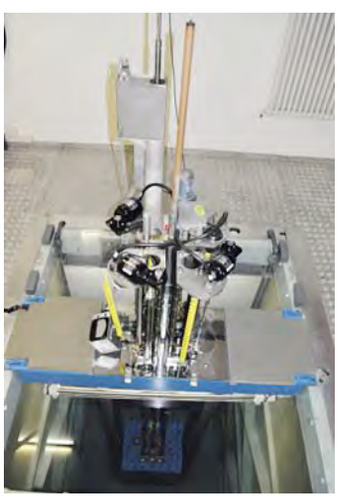
Uranium (U) and thorium (Th) are the starting elements of two natural decay series. The isotopic abundance in the Earth's crust for ^{238}U and for ^{232}Th is 2 and 7 mg/kg, respectively; however, in suspended matter they are enriched (30–40 mg/kg uranium; 30–60 mg/kg thorium). Normally, these isotopes are analysed with spectroscopic methods, such as ICP/MS or ICP/OES, alpha spectrometry, or by means of gamma ray detection *via* either their daughter nuclides (^{234}Th for ^{238}U, at 92.4 keV) or by analysing directly the weak low-energy gamma line of ^{232}Th at 63.8 keV.

Another possibility is to use instrumental neutron activation analysis (INAA). The analytes are irradiated with neutrons produced in a nuclear reactor. The activation processes are as follows:

$^{238}U + n \rightarrow {}^{239}U \rightarrow {}^{239}Np + \beta + \gamma \rightarrow {}^{239}Pu + \beta + \gamma$ (half-life of 2.4 d)

$^{232}Th + n \rightarrow {}^{233}Th \rightarrow {}^{233}Pa + \beta + \gamma \rightarrow {}^{233}U + \beta + \gamma \rightarrow \ldots$ (half-life of 27 d)

The international monitoring station Weil am Rhein, Germany (photo by S. Zehringer).



Nuclear reactor core at the University of Basel. The AGN-211-P is a light-water moderated swimming pool reactor with a power of 2 kW and a neutron flux of 3.8E+10 neutrons/cm^2/s (photo by G. Testa).

The gamma rays of the irradiated samples are analysed with high-purity germanium detectors. Gold is used as an internal standard (activated to ^{198}Au, half-life: 65 h).

Suspended matter collected with the centrifuge at the international monitoring station Weil am Rhein. Collecting time depends on the turbidity of the river water, typically, it is 24–48 h (photo by R. Dolf).

At the international monitoring station Weil am Rhein, Germany, the main task is the daily control of the Rhine water. As a completion, suspended matter is collected and analysed for substances of environmental concern, such as heavy metals, polychlorinated biphenyls and last but not least, artificial and naturally occurring radionuclides. Periodically, suspended matter is extracted by means of a centrifuge. After freeze-drying and grinding, the sample is ready for INAA. 1 g sample is irradiated for 30 min by means of the nuclear reactor at the Department of Physics, University of Basel. After a cool-down period of 2 hours the sample is counted at the Kantonales Laboratorium by means of a gamma spectrometer for at least 2000 s.

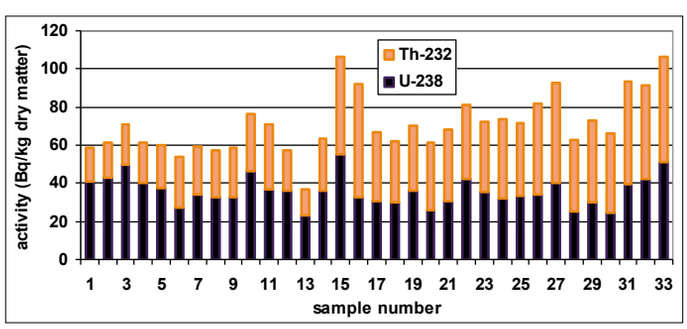
Recently, discussion started about elevated uranium concentrations in ground- and river waters. Phosphate fertilisers are a natural source of uranium and other actinides. For this reason, the treatment of agricultural soils with phosphate fertilisers can lead to an accumulation of uranium and other actinides in the soils. Uranium-VI is soluble and can be leached from the soils into ground- and river waters.

INAA is an alternative method for the determination of U and Th in soil, sediment and suspended matter samples. The method omits interferences from the γ-decay of natural nuclides in the measured gamma ray spectra.

Received: September 2, 2013

References

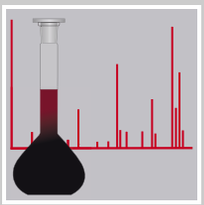
S. Landsberger, R. Kapsimalis, *J. Environmental Radioactivity* **2013**, *117*, 41.
E. Schnug, B.G. Lottermoser, *Environ. Sci. Technol.* **2013**, *4*, 2433.



Activities of uranium and thorium in suspended matter of the River Rhine at Weil, 2011–2012.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.922



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

New Calibration System for Breath-Alcohol Analysers Based on SI

Martin Stalder, Daniel Schwaller, Bernhard Niederhauser, Hanspeter Andres, and Samuel Wunderli*

*Correspondence: Dr. S. Wunderli, Eidgenössisches Institut für Metrologie METAS, Lindenweg 50, CH-3003 Bern-Wabern, Tel.: +41 58 387 03 83, E-mail: samuel.wunderli@metas.ch

Keywords: Breath-alcohol · Calibration · Traceability · Uncertainty

Based on a new ordinance, the Swiss police have been using verified breath-alcohol test instruments for official controls since January 1st 2012. Such instruments are increasingly used for medical prevention and occupational security. The measurement stability cannot be solely left to the manufacturer or his representatives.

Drink and drive…

For the yearly verification, type approval test, and conformity assessment of breath-alcohol devices, wet breath is generated by a saturation system. The traceability is given by a recommendation of the International Organisation of Legal Metrology (OIML) only,[1] which is heavily disputed and partly modified nationally. For the OIML generation method, the 'Physikalisch-Technische Bundesanstalt' in Germany reports a bias of 1% to 2%.[2]

The traceability of the breath-alcohol mass concentration is effected by gravimetrically prepared gas mixtures in pressure cylinders or by a wet generation with bubble trains using the convention of Dubowski:[3] $\beta_{gas}(EtOH) = \beta_{liquid}(EtOH) \cdot A_{Dub} \cdot \exp(B_{Dub} \cdot t)$.

β is the mass concentration β_{gas}, β_{liquid} in (mg/L); t is the temperature in °C; the constants of the Dubowski formula are $A_{Dub} = 0.04145 \cdot 10^{-3}$, $B_{Dub} = 0.06583\ °C^{-1}$.

The SI-traceability of the breath-alcohol tests results is desirably ensured without the OIML-convention.[1,3,4]

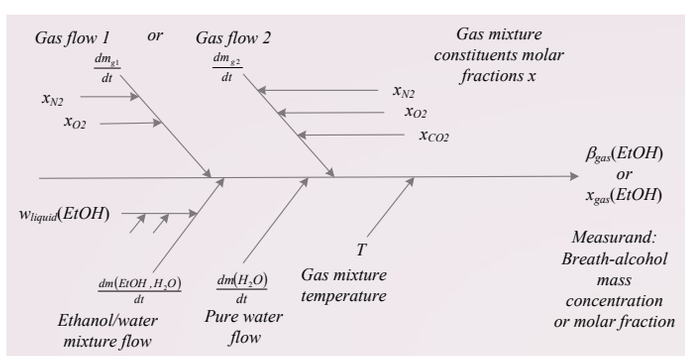
The generator for wet breath-alcohol analysis built at METAS.

A generator for wet breath-alcohol was built and is now tested at METAS. Using low-pressure, programmable micro annular gear pumps, water and water/ethanol mixtures are mixed dynamically in an evaporator with calibrated gas mass flows of certified air-like gas mixtures. Breath-alcohol of 0.5 mg/L to 1 mg/L, at 34 °C, 95% relative humidity and 1 atm results. First-order influence parameters are displayed in the fish-bone diagram. Gravimetrically calibrated liquid mass flows of pure water are accumulated in tared vials containing silica gel.

A preliminary uncertainty evaluation based on empirical input quantity data showed that a combined relative uncertainty better than 1% can be achieved. As a consequence, the Dubowski formula constants can be made traceable to the SI.

Received: October 12, 2013

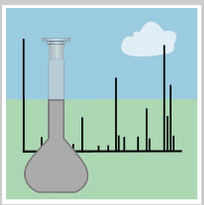
[1] a) International Organisation of Legal Metrology, 'OIML R 126: Evidential breath analyzers', **1998**.
[2] S. Pratzler, D. Knopf, P. Ulbig, S. Scholl, *Chemie Ingenieur Technik* **2010**, *82,* 1753.
[3] K. M. Dubowski, *J. Anal. Toxicol.* **1979**, *3*, 177.
[4] DIN VDE 0405, 'Ermittlung der Atemalkoholkonzentration', **1995**.



Cause-and-effect diagram of breath-alcohol analysis.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.86



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

OMA & OPA – A Software Tool for Mass Spectrometric Sequencing of Nucleic Acids

Yvonne Hari, Silvan R. Stucki, Adrien Nyakas, Lorenz Blum, Jean-Louis Reymond, and Stefan Schürch*

*Correspondence: PD Dr. S. Schürch, Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern, Tel.: +41 31 631 43 89, E-mail: stefan.schuerch@dcb.unibe.ch

Keywords: Modified nucleic acids · Oligonucleotide sequencing · Software-assisted spectra analysis · Tandem mass spectrometry

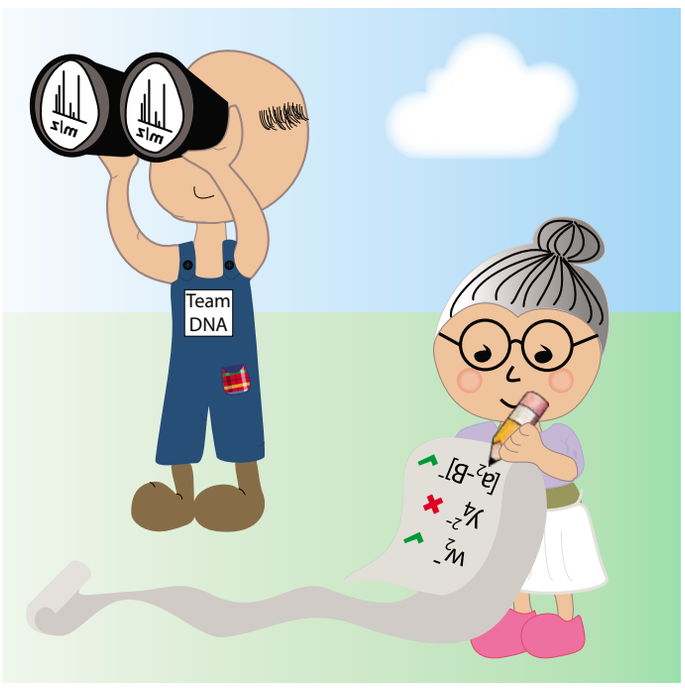
Oligonucleotides comprising unnatural building blocks, which interfere with the translation machinery, have gained increased attention for the treatment of gene-related diseases (*e.g.* antisense, RNAi). Due to structural modifications, synthetic oligonucleotides exhibit increased biostability and bioavailability upon administration. Consequently, classical enzyme-based sequencing methods are not applicable to their sequence elucidation and verification. Tandem mass spectrometry is the method of choice for performing such tasks, since gas-phase dissociation is not restricted to natural nucleic acids. However, tandem mass spectrometric analysis can generate product ion spectra of tremendous complexity, as the number of possible fragments grows rapidly with increasing sequence length. The fact that structural modifications affect the dissociation pathways greatly increases the variety of analytically valuable fragment ions. The gas-phase dissociation of oligonucleotides is characterized by the cleavage of one of the four bonds along the phosphodiester chain, by the accompanying loss of nucleobases, and by the generation of internal fragments due to secondary backbone cleavage. For example, an 18-mer oligonucleotide yields a total number of 272'920 theoretical fragment ions.

In contrast to the processing of peptide product ion spectra, which nowadays is highly automated, there is a lack of tools assisting the interpretation of oligonucleotide data. The existing web-based and stand-alone software applications are primarily designed for the sequence analysis of natural nucleic acids, but do not account for chemical modifications and adducts.

Consequently, we developed a software to support the interpretation of mass spectrometric data of natural and modified nucleic acids and their adducts with chemotherapeutic agents. The software package consists of two parts: (i) The Oligonucleotide Mass Assembler (OMA) and (ii) the Oligonucleotide Peak Analyzer (OPA). The OMA represents a tool for calculating all possible fragment ions of a given nucleic acid sequence. The OPA subsequently matches the m/z of the theoretical dissociation products with the experimental data. The library of oligonucleotide building blocks can be expanded by the user in order to address any structural modification.

The OMA & OPA software is programmed in the platform-independent language Java and it therefore runs on all major operating systems. It can be downloaded for free from: *http://schuerch.dcb.unibe.ch/omaopa/*.

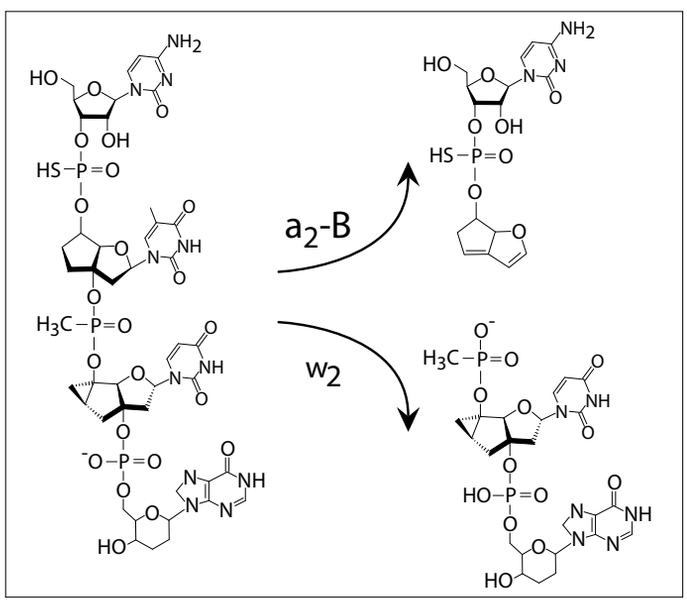
Received: November 22, 2013



A successful team: The Oligonucleotide Mass Assembler (OMA) and the Oligonucleotide Peak Analyzer (OPA) calculate and match the fragment ions of nucleic acids, respectively.

Reference

A. Nyakas, L. C. Blum, S. R. Stucki, J. L. Reymond, S. Schürch, *J. Am. Soc. Mass Spectrom.* **2013**, *24*, 249.

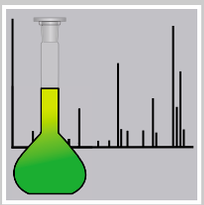


The functionality of the software package is independent of the customized introduction of chemical modifications.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.184



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Mass Spectrometric Characterization of Disulfide Bridges in Snake Venom Proteins

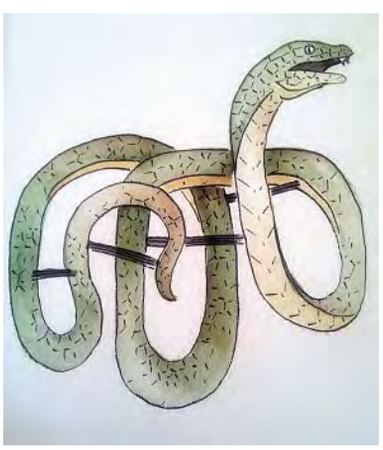
Miriam S. Goyder*, Marc E. Pfeifer, and Franka Kálmán

*Correspondence: Dr. M. S. Goyder, Institute of Life Technologies, University of Applied Sciences Western Switzerland, Route du Rawyl 47, CH-1950 Sion, Tel.: +41 27 606 86 40, E-mail: miriam.goyder@hevs.ch

Keywords: Disulfide bridges · Mass spectrometry · Protein analysis · Snake venom proteins

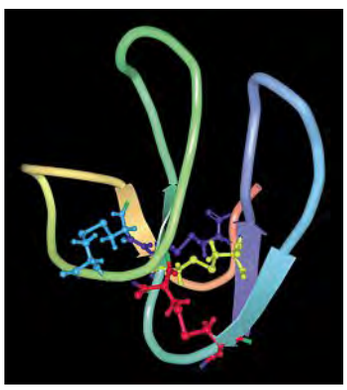
Venoms from snakes, spiders, scorpions *etc.* offer an Aladdin's cave of proteins and peptides for drug discovery. Within the venom of these species are numerous proteins and enzymes designed to kill or immobilise prey and aid digestion, including neurotoxins, cardiotoxins and muscarinic toxins. The individual proteins can be isolated (or produced recombinantly) and used for therapeutic effect.

Disulfide bridges are covalent bonds formed between the thiol groups of two cysteine residues. Many venom proteins contain a proportionally large number of such bridges, which play a fundamental role in defining their structure and specialized functionality. For many proteins, disulfide assignment can be achieved fairly simply by mass spectrometry (MS) analysis of bridged fragments following proteolytic digestion under non-reducing conditions. In venom proteins, elucidation of disulfide connectivities is often much more challenging due to the interwoven arrangement of bridges, which means that a simple proteolytic digest will not cut the protein in such a way that the connectivity can be determined unambiguously. Thus a variety of techniques are required to yield fragments that will reveal the disulfide connectivity.



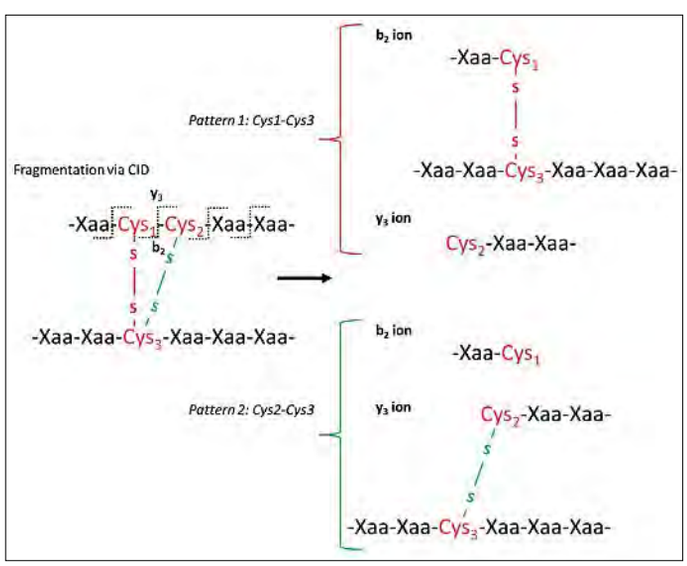
Artist's representation of mambaglin-1, a pain-relieving peptide from the venom of the black mamba snake. The peptide contains four disulfide bonds in the positions Cys1–3, 2–4, 5–6, and 7–8, as shown by the grey lines. Image reproduced with permission of John Wiley and Sons, from C. J. Craik, C. I. Schroeder, *Angew. Chem. Int. Ed.* **2013**, *52*, 3071.

At HES-SO Valais, recombinant snake venom proteins are being developed for use as new drugs. Part of the analytical strategy is to verify that disulfide bridges are correctly formed. To confirm their number, a high mass accuracy QTOF mass spectrometer is used to observe the mass difference of 1 Da between a disulfide bonded and free cysteine. The presence of disulfide isoforms (proteins with identical sequence but different disulfide connectivities) is determined *via* MS following their separation with RP-(U) HPLC. To assign bridges, proteins are digested using carefully selected combinations of proteolytic enzymes such as trypsin and pepsin to give proteolytic fragments which consist of several peptide chains linked by disulfide bridges. MS/MS with collision-induced dissociation is then used to cleave along the polypeptide backbone to give peptide fragments joined together by single disulfides, from which the bonding pattern can be deduced. This enables us to study challenging proteins containing interwoven disulfides and vicinal cysteines as are often an occurrence in venom proteins. **Verifying disulfide bonding in venom protein-based drugs is a key element in assuring Active Pharmaceutical Ingredient safety and efficacy.**



3D model of the three-finger toxin, mambin. Disulfide bonds are shown in red, yellow, light blue and dark blue. Image of PDB ID: 2LA1 (C.H. Cheng *et al., Protein Sci.* **2012,** *21,* 1872) created using RCSB PDB Protein workshop (L. Moreland *et al., BMC Bioinformatics* **2005**, *6*, 1472).

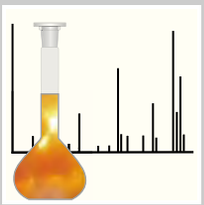
Received: December 19, 2013



MS/MS disulfide connectivity determination strategy. Xaa represents any amino acid in a hypothetical protein, which has undergone enzymatic digestion to yield disulfide bridged chains with two possible disulfide connectivities: Cys1-Cys3 or Cys2-Cys3. In this case, b2 and y3 ions from fragmentation on the first chain elucidate the connectivity. Reproduced with permission of John Wiley and Sons, from M. S. Goyder, F. Rebeaud, M. E. Pfeifer, F. Kálmán, *Exp. Rev. Proteomics* **2013**, *10*, 489.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.272



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

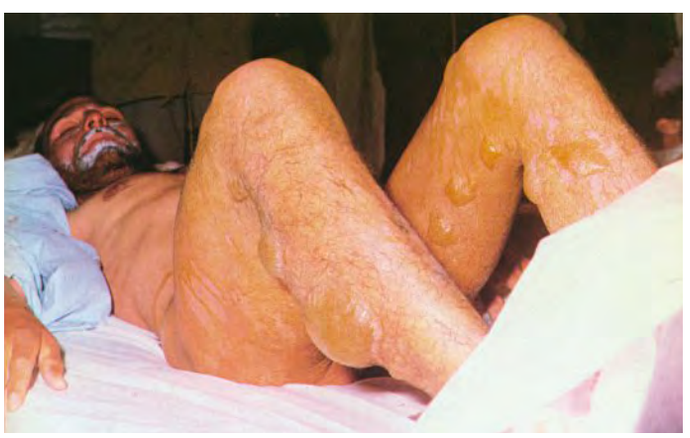
Identification of Sulfur Mustard Hydrolysis Products by LC-UV-SPE NMR

Urs C. Meier*

Correspondence: Dr. U. Meier, Swiss NBC Defence Establishment, Spiez Laboratory, CH-3700 Spiez, Tel.: +41 33 228 16 92, E-Mail: urs.meier@babs.admin.ch

Keywords: Environmental sample · LC-UV-SPE NMR · Solid phase extraction · Sulfur mustard

Sulfur mustards (SM) are strong vesicants which form blisters on the skin and in the lung. Full body protection is required as countermeasure against SM. SM were first used during World War I (WWI) in 1917 near Ypres by the German military. Since WWI SM or other chemical warfare agents (CWA), notably organophosphorus nerve agents like Sarin, have been used on a large scale repeatedly, most recently in the civil war in Syria. The remaining CWA stockpiles are mostly made of organophosphorus nerve agents and SM.



Iranian victim of exposure to sulfur mustard. 'A short documentation on the Iraqi army's use of chemical weapons', published by the Embassy of the Islamic Republic of Iran, Stockholm, Cultural Section, April 1984.

Analytical methods for the detection and unambiguous identification of CWA are needed for the verification of the chemical weapons convention, for the protection of the population, and for the medical treatment of victims. However, the analysis in case of an alleged use of chemical weapons cannot be restricted to the CWA themselves as the CWA undergo degradation in the environment. As an example, SM can be hydrolyzed. These degradation/hydrolysis products must be included in the scope of analysis.

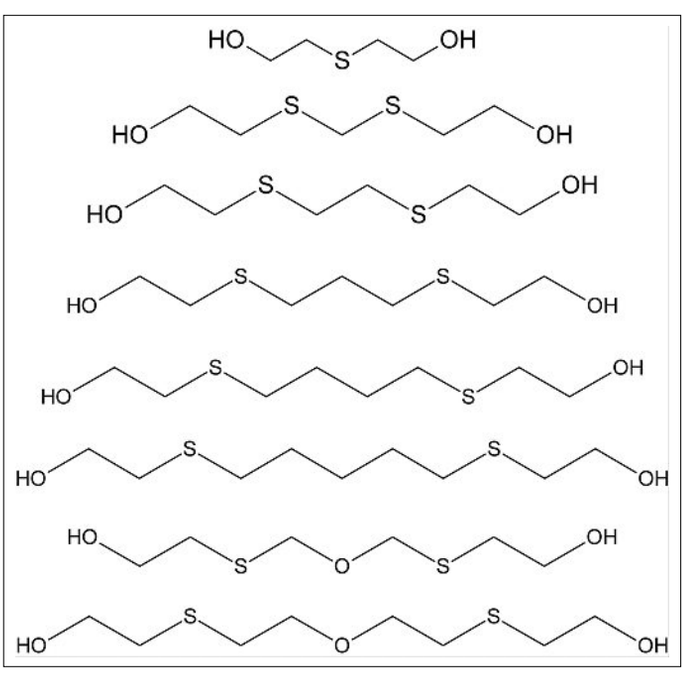
^{1}H NMR is a powerful spectroscopic method for the identification of chemicals. The application of ^{1}H NMR to the analysis of environmental samples is in most cases not limited by its sensitivity but by the signals from the background chemicals present in the sample which partially or completely obscure the analyte signals. This necessitates a sample preparation step to isolate the analytes from the background chemicals. In the liquid chromatography–UV detection-solid phase extraction–NMR technique, the SM hydrolysis products are separated from the background chemicals by LC, detected by UV, trapped and concentrated on a SPE cartridge and after elution in an NMR tube identified by ^{1}H NMR. Detection limits of 200–450 ng of analyte injected on the column are obtained for ^{1}H NMR spectra recorded at 500 MHz using a cryoprobe and an acquisition time of 15 min. **LC-UV-SPE NMR is a powerful method to identify SM hydrolysis products in environmental samples.**

Samples suspected of contamination with sulfur mustard.

Received: February 4, 2014

Reference

Urs C. Meier, *J. Chromatogr. A* **2013**, *1286*, 159.

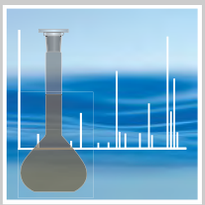


Sulfur mustard hydrolysis products.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2014.333



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Lake Sediments Tell the Story of Climate Change

Sebastian Naeher[ab], Ryan P. North[bc], Adrian Gilli[d], David M. Livingstone[c], and Carsten J. Schubert*[a]

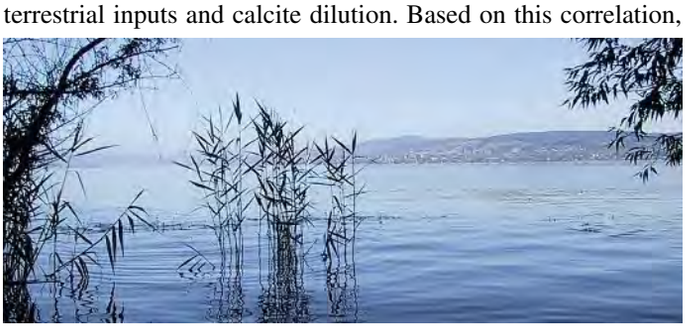
*Correspondence: Dr. C. J. Schubert[a], Tel.: +41 58 765 21 95, E-mail: carsten.schubert@eawag.ch

[a]Eawag – Swiss Federal Institute of Aquatic Science and Technology, Seestrasse 79, CH-6047 Kastanienbaum. [b]ETH Zurich, Institute for Biogeochemistry and Pollution Dynamics, Universitätsstrasse 16, CH-8092 Zurich. [c]Eawag, Ueberlandstrasse 133, CH-8600 Dübendorf. [d]ETH Zurich, Geological Institute, Sonneggstrasse 5, CH-8092 Zurich

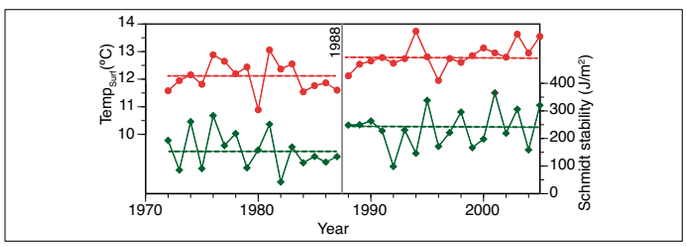
Keywords: Lake Zurich · Mn/Fe ratio · Oxygen · Redox-sensitive elements · Time series

Climate change and eutrophication may both contribute to a dramatic decline in oxygen (O_2) concentrations in lakes and oceans. An analysis of Lake Zurich's 70-year dataset of monthly water column measurements revealed a clear impact of rising air temperature on the lake's water temperature and O_2 concentration. A pronounced shift to higher air temperature in the late 1980s corresponded with an increase in water temperature. Warming was greater in the lake's surface water than in the deep water, leading to an increase in water column stratification, which resulted in a general decline in bottom water O_2 concentrations.

In an attempt to extend Lake Zurich's O_2 record further back in time, a sediment core from the lake's deepest region (137 m) was analysed with non-destructive X-ray fluorescence (XRF) core scanning to obtain high-resolution manganese (Mn) and iron (Fe) element profiles. As the sediment core contains semi-annual laminations (*i.e.* similar to tree rings) dating back to 1895, the XRF data, which have a sampling resolution of 0.3 mm, provide high-resolution trace metal records. Because Mn and Fe differ with respect to their redox behaviour, the Mn/Fe ratio in sediment cores has been considered a proxy for anoxic conditions for decades, but this has never before been validated with monitoring data. Using the Lake Zurich core, we could show that the Mn/Fe ratio is moderately correlated with the measured maximum annual bottom-water O_2 concentration ($R^2 = 0.6$; $n = 66$; $p < 0.01$; 1936–2010). Sedimentary processes like the deposition of turbidites ('underwater mass movements') or diatom blooms reduce the consistency of this relationship. Although the elemental profiles are relative, normalising the Mn signal with Fe corrected for differences in porosity, water content, terrestrial inputs and calcite dilution. Based on this correlation, bottom-water O_2 concentrations from 1895 to the present were reconstructed to gain insight into the impact of high external phosphorus loading on bottom-water O_2. Applying this method to cores from shallower water depths revealed a breakdown of the Mn/Fe ratio that most likely resulted from the lateral transport of redox-sensitive elements and their subsequent enrichment in the deepest part of the lake.



Lake Zurich (copyright Zürichsee Tourismus).



The effects on Lake Zurich of a sudden climate shift in the late 1980s included increases in the mean annual surface temperature (upper curve) and in the thermal stability of the water column (Schmidt stability, lower curve).

The Mn/Fe ratio was shown to be useful as a semi-quantitative proxy for past bottom-water oxygen concentration in Lake Zurich. Combined with monthly monitoring data, the method shows the long-term impact of eutrophication and climate on bottom-water oxygen concentrations.

Acknowledgements

The lake data used in this study were kindly provided by the City of Zurich Water Supply (WVZ). This research forms part of project 'HYPOX', funded under the European Commission's Seventh Framework Programme (contract no. 226213).

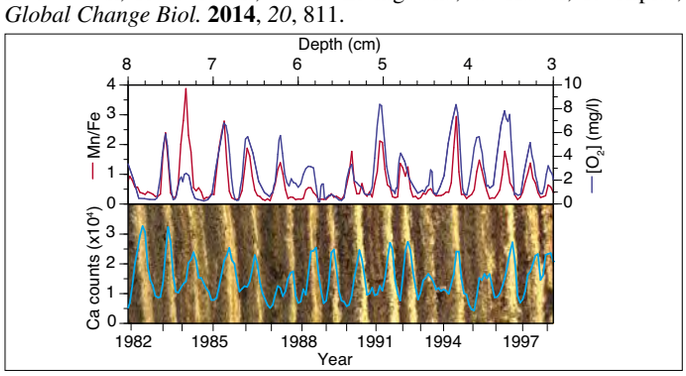
Received: March 12, 2014

References

S. Naeher, A. Gilli, R. P. North, Y. Hamann, C. J. Schubert, *Chem. Geol.* **2013**, *352*, 125.

R. P. North, D. M. Livingstone, R. E. Hari, O. Köster, P. Niederhauser, R. Kipfer, *Inland Waters* **2013**, *3*, 341.

R. P. North, R. L. North, D. M. Livingstone, O. Köster, R. Kipfer, *Global Change Biol.* **2014**, *20*, 811.

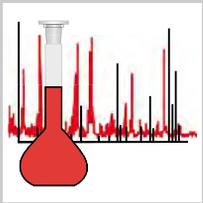


XRF profiles of Ca (lower panel, light blue curve) and of the Mn/Fe ratio (upper panel, red) for sediments deposited in Lake Zurich from 1982 to 1998. The light sediment layers consist of $CaCO_3$ precipitated during summer. This seasonal deposition allows the Mn/Fe ratio to be aligned with the bottom-water O_2 concentration (upper panel, dark blue), which is highest during water-column turnover in spring. The Mn/Fe record captures semi-quantitatively the oxygenation of the deeper lake basin. Note that the Mn/Fe peak (in spring) precedes the Ca peak (in summer).

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.453



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

When Time-to-Result Matters: Identification of Microbes Based on MALDI-TOF Protein and Peptide Profiling

David Drissner[a], Maria-Theresia Gekenidis[a], Ralph Schlapbach[b], and René Brunisholz*[b]

*Correspondence: PD Dr. R. Brunisholz[b], Tel.: +41 44 635 39 03, E-Mail: rene.brunisholz@fgcz.ethz.ch

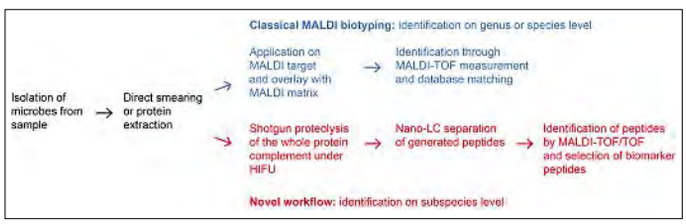
[a]Agroscope, Institute for Food Sciences, Schloss 1, CH-8820 Waedenswil

[b]Functional Genomics Center Zurich, ETH Zurich and University of Zurich, Winterthurerstrasse 190, CH-8057 Zurich

Keywords: Discrimination · HIFU · MALDI biotyping · Pathogenic microbes · Peptide biomarker · Trypsin digest

Rapid and reliable microbial identification is of utmost importance – whether in clinical and veterinary diagnostics or in food safety control and outbreak tracking. Conventional methods assessing phenotypic traits of isolated microbes based on biochemical reactions, Gram staining, colony morphology, or growth pattern are often time-consuming. Molecular biological techniques for assessment of genotypic traits are often expensive. Identification of microbes by MALDI-TOF mass spectrometry (MALDI biotyping), based on profiling of mainly ribosomal proteins and comparison to a reference mass spectra database, has developed from an emerging to a robust leading-edge diagnostic technology and has revolutionized work in microbiological laboratories in recent years. This is due to its short time-to-result, streamlined protocol allowing a cost-effective identification within less than 20 minutes. With MALDI biotyping, an accurate and reliable identification of bacteria and fungi is possible down to genus and species level**.** For the accurate identification of individual subspecies or serovars, modified methods need to be applied**.**

In order to further advance the analytical method, the Functional Genomics Center Zurich (FGCZ) and Agroscope have entered a collaboration and developed jointly a novel and ultra-fast workflow that combines the classical MALDI biotyping approach with shotgun trypsin digestion of proteins under High-Intensity-Focused-Ultrasound (HIFU) and subsequent nano-LC separation of resulting peptides. The latter are subsequently identified by MALDI-TOF/TOF mass spectrometry. The use of peptides as biomarkers extends the usable mass range and type of proteins potentially identified as compared to classical MALDI biotyping, resulting in an increased discrimination power to the subspecies level. The established workflow is currently used for the identification of several pathogenic microbes and will be applied in the near future to selected reaction monitoring (SRM) experiments for an even more rapid identification of microbial strains. **The new combined analytical method will contribute to a more accurate and more sensitive pathogen identification on subspecies level in a multitude of disciplines, such as clinical diagnostics and food safety.**



Classical MALDI biotyping and novel workflow.

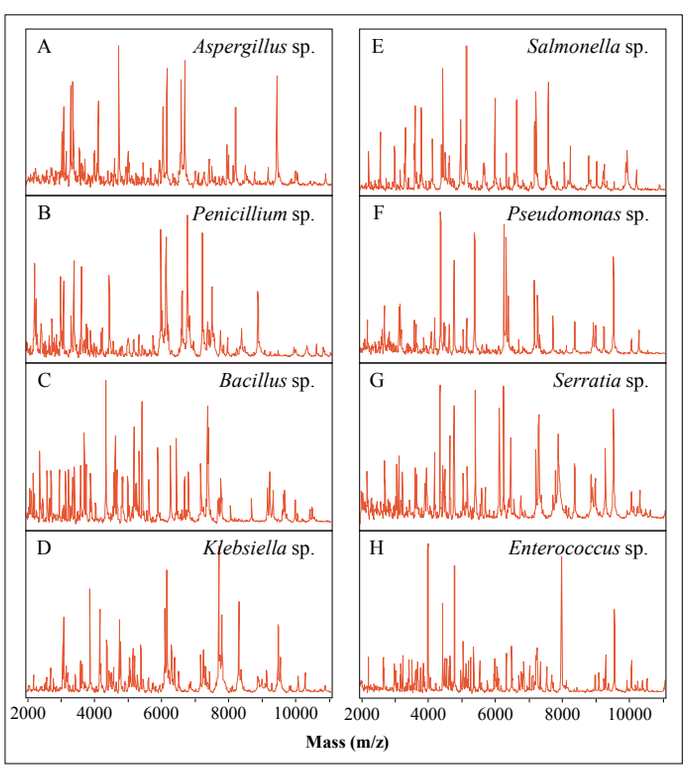
Onion seeds, agar plate with colonies of *Salmonella* sp. isolated thereof and single *Salmonella* cells under the microscope (from left to right).

Received: March 27, 2014

References

M. T. Gekenidis, P. Studer, S. Wüthrich, R. Brunisholz, D. Drissner, *Appl. Environ. Microbiol*, **2014**, doi:10.1128/AEM.00740-14.

D. Drissner, U. Zürcher, in 'Encyclopedia of Food Safety', Eds. Y. Motarjemi, E. Todd, G. Moy, **2014**. Elsevier, Oxford, UK.



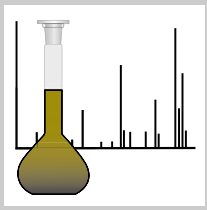
MALDI-TOF MS spectra of foodborne spoilage and pathogenic microbes isolated from beans (A), apple juice (B), and onion seeds (C – H).

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen

Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2014.567



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences
A Division of the Swiss Chemical Society

Organic Acids Exuded by Pioneering Fungi from a Glacier Forefield Help to Weather the Granitic Sediments

Ivano Brunner* and Alessandro Schlumpf

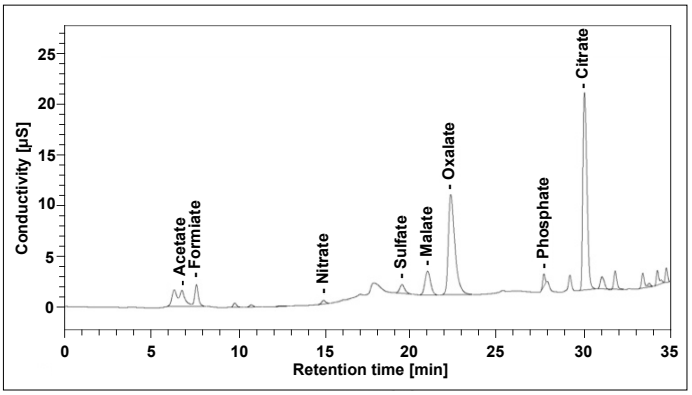
*Correspondence: Dr. I. Brunner, Swiss Federal Institute for Forest, Snow and Landscape Research WSL, Zürcherstrasse 111, CH-8903 Birmensdorf, Tel.: +41 44 739 22 84, E-Mail: ivano.brunner@wsl.ch

Keywords: Glacier forefield · Organic acids · Pioneering fungi · Weathering granitic materials

Glaciers are retreating worldwide due to global climate change. In Europe, alpine glaciers lost about half of their total surface area and their total volume within the last 150 years. Consequently, fresh rock sediments are exposed at the surface and subjected to weathering processes.

Rock surfaces that are freshly exposed to the atmosphere become rapidly colonized by microbial communities as the first settlers. In particular, granitic sediments of glacier forefields are inhabited by a large variety of microorganisms, such as bacteria, cyanobacteria, archaea, green algae and fungi. As no plants grow during the first years after the glacier has retreated, the carbon found does not originate from autochthonous plants. Cell-wall remnants and exudates of green algae and cyanobacteria are most likely the major primary carbon source in this environment, in addition to deposition (*e.g.* pollen) and the ancient recalcitrant organic matter.

Damma Glacier with forefield, situation of October 2007: 1 Glacier tongue, 2 side moraine, 3 frontal moraine from 1992, 4 glacier forefield younger than 15 years, 5 glacier forefield older than 50 years. The studies were conducted in association with the 'BigLink' project of the Competence Center Environment and Sustainability of the ETH Domain (CCES), S. M. Bernasconi *et al*., *Vadose Zone J.* **2011**, *10*, 867. Photo by G. Furrer



Ion chromatogram of exuded organic and inorganic anions of *Mucor hiemalis*. The fungus was raised in a solution which contained the cell-wall component pectin as the only carbohydrate source.

A set of fungal species isolated from fine granitic sediment of the non-vegetated forefield of the Damma Glacier in the central Swiss Alps showed a high potential to weather powdered granite material in batch experiments. In particular, the zygomycete fungi *Mucor hiemalis, Mortierella alpina, Umbelopsis isabellina* and the ascomycete fungus *Penicillium chrysogenum* dissolved the granite powder most efficiently. It was shown that the high concentrations of Ca, Fe, Mg and Mn in the solutions were the result of the release of high amounts of organic acids, mainly citrate, malate and oxalate.

Concentrations of the organic acids in the treatment solutions were analyzed by ion chromatography on a Dionex ICS-3000, using an IonPac AS19 analytical column. An IonPac AG19 guard column and an IonPac AG11-HC guard column were used as pre-columns to improve run quality. Cell temperature of the conductivity detector was set to 35 °C and column temperature to 30 °C. Separation of the organic acids in the columns was achieved using a NaOH gradient, with a detection limit of 0.15 mg l^{-1}.

In a consecutive study we showed that the patterns of released organic acids are dependent on the sources of carbohydrate. **In particular, pollen and remnants of algal cells can trigger the exudation of organic acids of fungi in order to promote the weathering of minerals and to make nutrients available.**

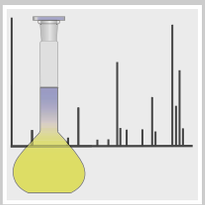
Received: May 8, 2014

References

I. Brunner, A. Goren, A. Schlumpf, *Environ. Res. Lett.* **2014**, *9*, 025002.
I. Brunner, M. Plötze, S. Rieder, A. Zumsteg, G. Furrer, B. Frey, *Geobiology* **2011**, *9*, 266.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2013.665



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Non-aqueous Capillary Electrophoresis for the Analysis of Pharmaceutical Acidic Compounds Using Negative ESI-MS

Grégoire Bonvin, Julie Schappler, and Serge Rudaz*

*Correspondence: Prof. S. Rudaz, School of Pharmaceutical Sciences, University of Geneva, University of Lausanne, Boulevard d'Yvoy 20, CH-1211 Geneva 4
Tel.: +41 22 379 63 36, E-mail: serge.rudaz@unige.ch

Keywords: Capillary electrophoresis · CE-MS · NACE · Negative ESI · Sheathless interface · Sheath liquid interface

Non-aqueous capillary electrophoresis (NACE) is an attractive capillary electrophoresis (CE) mode in which the conventional aqueous background electrolyte (BGE) is replaced by organic solvents. This substitution modifies several physicochemical properties (pK_a, dielectric constant, viscosity, zeta potential, and conductivity) resulting in a modification and often an improvement of the CE separation performance. NACE is particularly well adapted to mass spectrometry (MS) detection due to the high volatility of solvents that improves the formation of easily evaporable droplets with the electrospray ionization (ESI) source, increasing ionization efficiency while ensuring a stable spray.

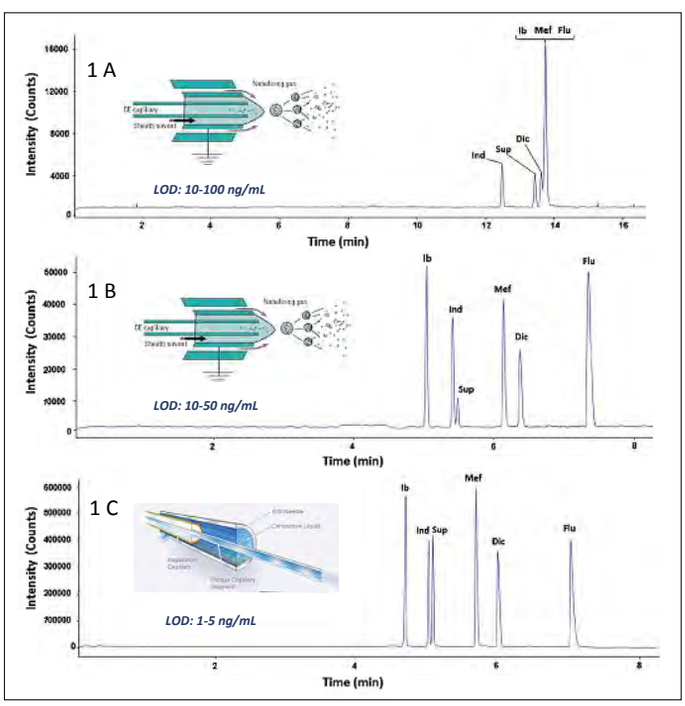


Fig. 1. CE-MS separation of non-steroidal anti-inflammatory drugs with aqueous electrolyte and sheath liquid interface (A), with organic electrolyte and sheath liquid interface (B), and with organic electrolyte and sheathless interface (C).

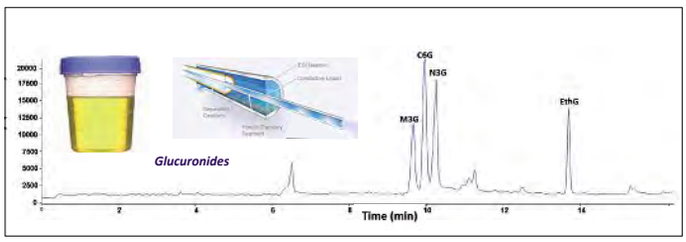


Fig. 2. CE-MS separation of four glucuronides in diluted urine with organic electrolyte and sheathless interface.

We studied the use of NACE coupled to negative ESI-MS for the analysis of acidic compounds with two CE-MS interfaces (sheath liquid and sheathless). First, the NACE mode was compared to the aqueous CE mode for the analysis of non-steroidal anti-inflammatory drugs (NSAIDs) that represent an important pharmacological class commonly used for their analgesic and antipyretic properties. As shown in Fig. 1A, the NSAIDs were not separated when an aqueous BGE was used, whereas an organic BGE (acetonitrile, methanol and ammonium acetate) allowed a complete separation (Fig. 1B) and led to a 1–10-fold improvement of the detection sensitivity. Separation performance as well as detection limit could be further improved using the sheathless interface without modifying the BGE composition (Fig. 1C).

These results indicate that the NACE-ESI-MS method could be considered an attractive tool for the analysis of very polar phase II metabolites such as glucuronides. The latter are infrequently analyzed using aqueous BGE due to their amphoteric properties. Additionally, glucuronides are present at low concentrations in urine (ng/mL range); therefore, NACE-ESI-MS with the sheathless interface could provide the benefit of increased sensitivity, particularly when a minimal sample preparation such as simple urine dilution is used. As presented on the Fig. 2, a complete separation of four glucuronides was achieved using a sheathless interface. Concentration limits down to 500 ng/mL in urine (corresponding to 25 ng/mL injected concentration) were obtained without the presence of any significant matrix effect, while a simple and rapid sample pre-treatment (dilution 1:20 with the BGE) was applied.

NACE is an interesting alternative to the CE aqueous mode, especially because of the improved selectivity, sensitivity, and spray stability when used in combination with ESI-MS.

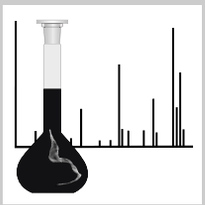
Received: July 1, 2014

References

G. Bonvin, J. Schappler, S. Rudaz, *J. Chromatogr. A* **2012,** *1267,* 17.
G. Bonvin, J. Schappler, S. Rudaz, *J. Chromatogr. A* **2014,** *1323,* 163.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2014.749



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences
A Division of the Swiss Chemical Society

Parasite Reveals Mitochondrial Inheritance Machinery

André Schneider* and Felix Schnarwiler

*Correspondence: Prof. A. Schneider, Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern, Tel.: +41 31 631 42 53, E-mail: andre.schneider@dcb.unibe.ch

Keywords: Beta-barrel protein · Mitochondrial inheritance · Trypanosomes

Mitochondria are double membrane bounded organelles that together with the nucleus define the eukaryotic cell. Their main function is energy production by oxidative phosphorylation. Mitochondria derive from bacteria, which during evolution have gradually been converted into organelles. The bacterial descent of mitochondria is reflected by their genome which encodes a small number of essential proteins. Every eukaryote therefore needs mechanisms that during cell division correctly distribute mitochondria and their genomes to the daughter cells. In a typical eukaryotic cell this distribution process is however difficult to study because it contains many dozens of mitochondria each of which carries multiple mitochondrial genomes.

The unicellular flagellar parasite *Trypanosoma brucei*, best known for causing African sleeping sickness, provides a way out: unlike other eukaryotes it has a single mitochondrion with a single unit genome, which can easily be observed with a microscope. This genome is physically linked, across the two membranes, to the base of the flagellum. Prior to cell division a new flagellum is produced which subsequently is segregated to the daughter cell. Due to its linkage to the flagellum this leads to simultaneous segregation of the replicated mitochondrial genome.

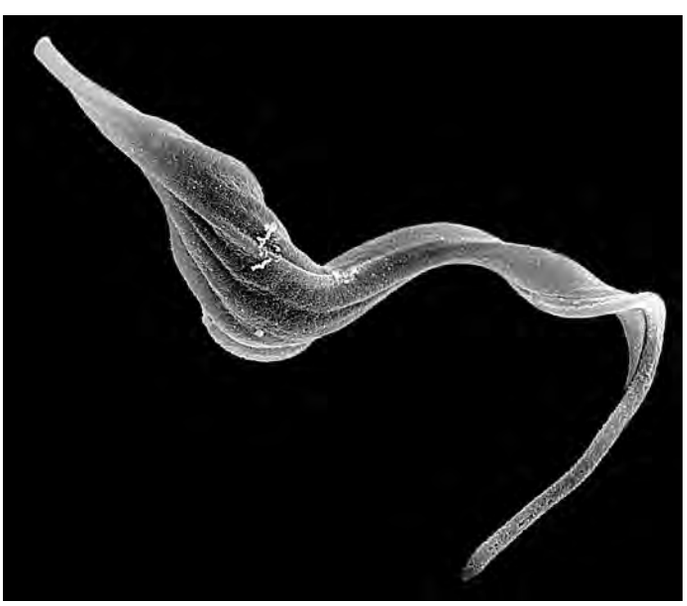
Using a combination of organellar proteomics, biochemistry, and molecular genetics we have discovered a protein, termed TAC40, that mediates this linkage. Removing TAC40 by genetic tricks interrupts the linkage causing a failure of segregation which results in unviable daughter cells that lack mitochondrial DNA. Thus, TAC40 is a key component required for mitochondrial inheritance in trypanosomes. But there is more: A bioinformatic analysis shows that TAC40 defines a novel trypanosome-specific subclass of the mitochondrial porin protein family that is conserved in all eukaryotes. Mitochondrial porins are beta-barrel structured membrane proteins that have been implicated in many different functions including mitochondrial inheritance.

In summary, the discovery of the mitochondrial outer membrane protein TAC40 in the tropical parasite *Trypanosoma brucei* has revealed that mitochondrial genome inheritance is likely the main and ancestral function of this group of mitochondrial porins.

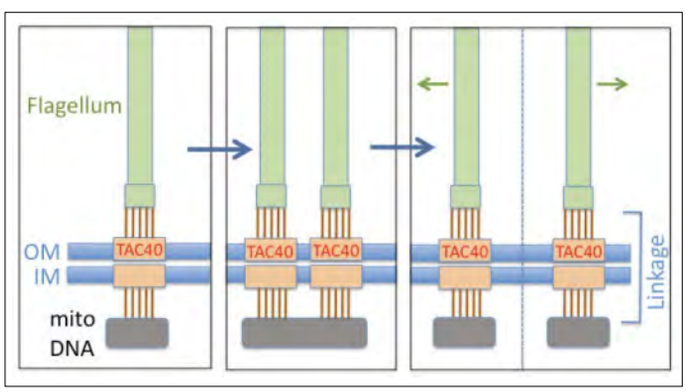
Received: July 18, 2014

Reference

F. Schnarwiler, M. Niemann, N. Doiron, A. Harsman, S. Käser, J. Mani, A. Chanfon, C. E. Dewar, S. Oeljeklaus, C. B. Jackson, M. Pusnik, O. Schmidt, C. Meisinger, S. Hiller, B. Warscheid, A. C. Schnaufer, T. Ochsenreiter, A. Schneider, *Proc. Natl. Acad. Sci. USA* **2014**, *111*, 7624.



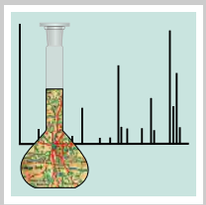
Scanning electron micrograph of the bloodstream form of the parasitic protozoa *Trypanosoma brucei*. The single flagellum is laterally attached to the cell body and extends the cell on the right side. The length of the cell is approximately 30 μm (image courtesy of Christopher P. Jackson).



Schematic diagram of the mitochondrial DNA-flagellum linkage and position of the TAC40 protein (red) in *T. brucei*. The three pictures show different stages of the cell cycle. In the left panel the cell has a single mitochondrial genome and a single flagellum. In the middle panel the mitochondrial DNA has been replicated but not segregated yet. It is linked to both the old and the newly produced flagella. The right panel shows how the replicated mitochondrial DNA and the flagella co-segregate (green arrows). The broken line indicates the position where the mitochondrion will be divided. OM, mitochondrial outer membrane; IM, mitochondrial inner membrane.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2014.818



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

A Close Look at the Fate of Compounds we are Exposed to

Bertrand Rochat*, Julia Bilat, and Baptiste Grund

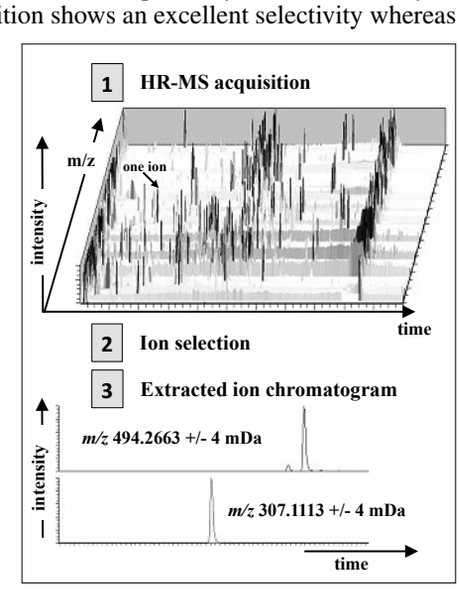
*Correspondence: Dr. B. Rochat, Quantitative Mass Spectrometry Facility, University of Lausanne, Centre Hospitalier Universitaire Vaudois, Rte du Bugnon 46, CH-1011 Lausanne, Tel.: +41 21 314 41 58, E-mail: bertrand.rochat@chuv.ch

Keywords: Biotransformation enzymes · Blood · Drug metabolism · Exposome · High-resolution mass spectrometry · Tamoxifen

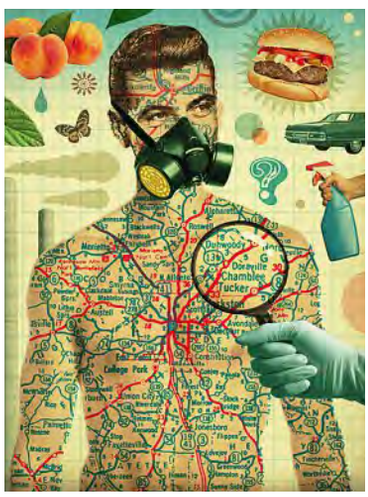
The exposome was defined by C. P. Wild as non-genetic and encompasses "every exposure to which an individual is subjected from conception to death". An exposome can be endogenous microbes, physical activity, infectious agents, stress, xenobiotics such as pollutants or drugs and so forth and is a new term rather than a new concept. The capacity of new liquid-chromatography mass-spectrometry (LC-MS) to detect, in the same analysis, a large number of molecules (100s to 1000s) at low levels has advanced our understanding of the exposome. These new detectors are LC-high-resolution mass-spectrometers (HR-MS) and are mainly composed of Orbitrap- and Time-Of-Flight-MS.

HR-MS allows for the discrimination between very close ionized molecular masses (m/z for mass-over-charge ratio). For instance, $C_{15}H_{14}O_3N$ or $C_{16}H_{16}OS$, ionized by an H^+ adduct, would easily be discriminated by their m/z values: 257.10464 and 257.09946 Da (delta = 5 mDa), respectively. LC-HRMS analysis with full scan acquisition shows an excellent selectivity whereas 1000s of ions are recorded in a LC-MS analysis. HR-MS has shown similar quantitative capabilities in comparison to traditional quantification technology, triple-quadrupole-MS.

We studied the fate of a drug, tamoxifen, taken for three months or more by women with breast cancer. We discovered over 44 tamoxifen metabolites in their blood that are the result of different biotransformation enzymes, with up to seven biotransformation steps. This underscores that, when we are exposed to one molecule chronically, the body can eventually be exposed to a lot of different derived molecules. We revealed the inter-individual differences in the levels of some tamoxifen metabolites, demonstrating that the effect of a xenobiotic and its metabolites can strongly vary from person to person.



Typical LC–high-resolution mass-spectrometry analysis. 1) A high resolution (HR) full scan is acquired from sample extracts. 2) The ionized molecules of interest are selected based on their accurate m/z ratio. 3) The extracted ion chromatograms are constructed.



Michael Waraksa's illustration shows how our environment shapes our health and underscores the concept of the exposome.

Today, using high-resolution mass-spectrometry, the fate of drugs and pollutants in humans can be studied more in-depth and with ease. From a single compound we are chronically exposed to, there are tens of metabolites produced that could have adverse reactions. Although our body is armed to cope with most exposures, a more in-depth analysis allows to relate toxic events, *e.g.* in a sub-population, and xenobiotic and its various metabolites.

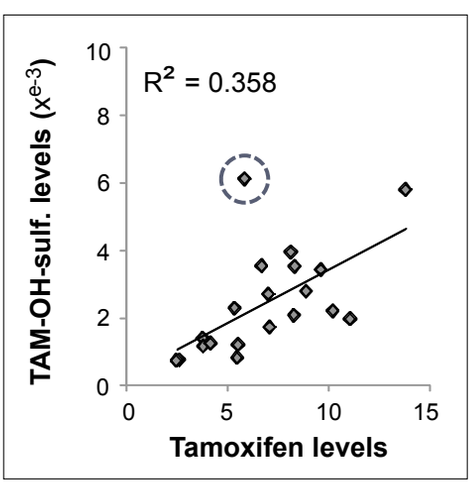
Received: August 28, 2014

References

C. P. Wild, *Int. J. Epidemiol*. **2012**, *41*, 24.

B. Rochat, E. Kottelat, J. McMullen, *Bioanalysis* **2012**, *4*, 2939.

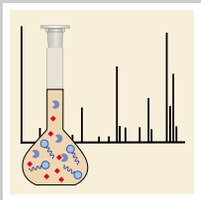
E. Dahmane, J. Boccard, C. Csajka, S. Rudaz, L. Décosterd, E. Genin, B. Duretz, M. Bromirski, K. Zaman, B. Testa, B. Rochat, *Anal. Bioanal. Chem.* **2014**, *406*, 2627.



Determination coefficient (R^2) between relative levels of tamoxifen metabolites and tamoxifen) in 20 patients treated with tamoxifen (TAM). TAM-OH-sulf.: Tamoxifen-hydroxy-sulfate. Data reveal high inter-individual variability of tamoxifen metabolite levels with potential outliers (dashed circle).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2014.899



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Advancing Schwarzenbach's Complexometry: Nanoscale Titration Reagents Based on Heterogeneous Reactions

Jingying Zhai, Xiaojiang Xie, and Eric Bakker*

*Correspondence: Prof. Dr. E. Bakker, Department of Inorganic and Analytical Chemistry, University of Geneva, 30 Quai Ernest Ansermet, CH-1211 Geneva 4, Tel.: +41 22 379 64 29, E-mail: Eric.Bakker@unige.ch

Keywords: Calcium-selective colloidal suspensions · Complexometric titrations · Heterogeneous reactions · Ion-exchange nanospheres

Gerold Schwarzenbach's treatise on complexometric titrations established that for a titration reagent to be successful, the complexation reaction must be rapid, proceed stoichiometrically, and must be accompanied by a large change in free energy. The model reagent for this methodology has of course been EDTA, which forms stable complexes of a defined 1:1 stoichiometry with a wide range of metal ions. Chelating agents must be water soluble, and the associated ionizable groups necessitate a careful control of pH.

Our group recently introduced colloidal titration reagents that may dramatically increase the available chemical toolbox, alleviate the need for pH control and eliminate the requirement of a defined and singular reaction stoichiometry. The principle of this nanoscale reagent is shown in Fig. 1. The hydrophobic core of the suspended particles is doped with a lipophilic ion-exchanger and a chemical receptor molecule (ionophore) known from electrochemical and optical ion sensors. The ion of interest will spontaneously ion-exchange with the counter ion initially present in the particle core. This extraction is driven by the lipophilicity difference between the two ions and the ion-receptor binding energy. For a sufficient molar excess of receptor, the binding capacity is dictated by the ion-exchanger concentration, and a fixed complex stoichiometry is no longer required. The receptors do not need to be water soluble and therefore do not require protonatable groups.

Fig. 2 demonstrates the titration of two different water samples using calcium-selective colloidal suspensions doped with cation-exchanger and a calcium-selective receptor. The titration was performed without pH control (titration with EDTA requires pH 10), detecting pCa with a calcium-selective electrode. The observed concentrations (5.2 ± 0.1 mM for Swiss Alpina and 2.1 ± 0.1 mM for Evian) agree quantitatively with the expected calcium levels (5.2 mM and 2.0 mM). The nanosphere suspensions are clear to the eye, simple to fabricate, and have been found stable for a number of weeks. Doping with different reagents will allow one to obtain binding affinities and selectivities that have been very difficult to achieve so far with traditional homogeneous reagents.

In conclusion, nanoscale titration reagents that work on the basis of extraction and complexation equilibria may overcome numerous limits imposed by water-soluble chelators that work in homogeneous phase.

Received: October 15, 2014

References

G. Schwarzenbach, H. Flaschka, 'Complexometric Titrations', Methuen, London, **1969**.

J. Zhai, X. Xie, E. Bakker, *Chem. Commun.* **2014**, *50*, 12659.

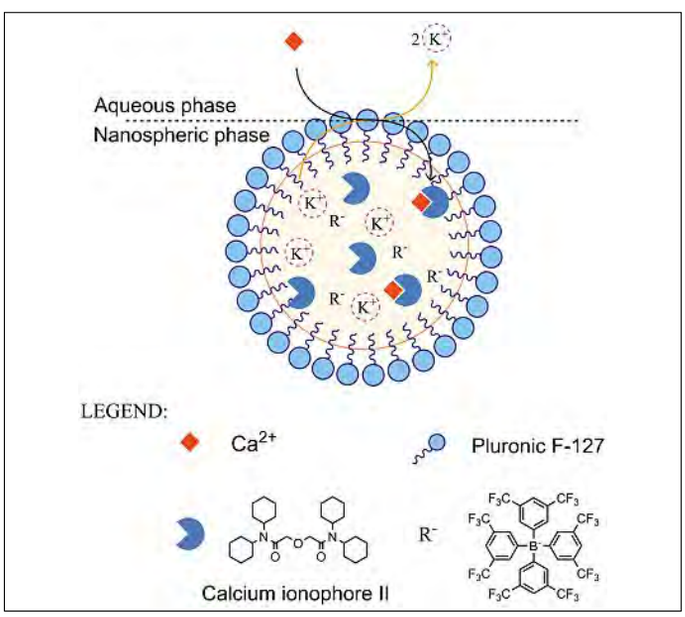


Fig. 1. Ion-selective nanospheres as complexing agent and structures of the compounds used in this work.

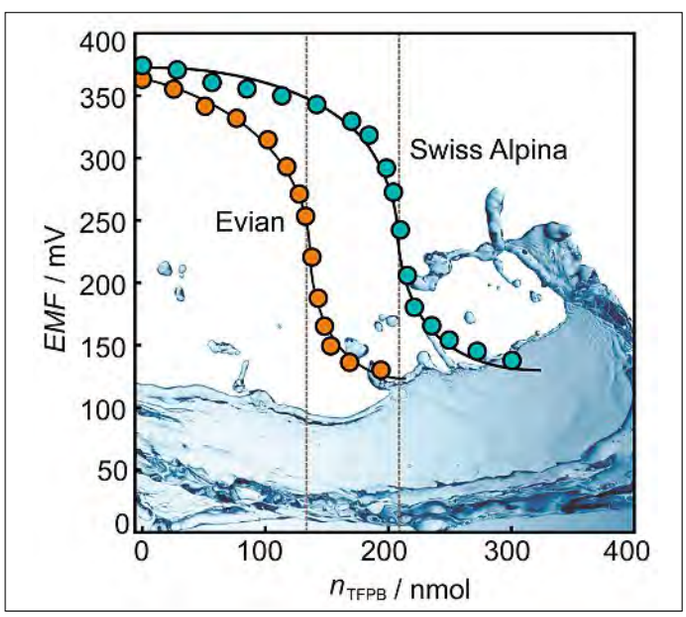
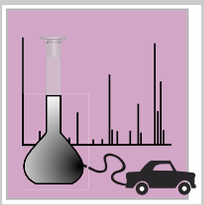


Fig. 2. Titration of Ca^{2+} in diluted mineral water Evian® and Swiss Alpina®, detection by calcium-sensitive electrode.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2015.68



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

A Fast and Reliable *in vitro* Method for Screening of Exhaust Emission Toxicity in Lung Cells

Christoph Bisig[a], Sandro Steiner[a], Jan Czerwinski[b], Pierre Comte[b], Andreas Mayer[c], Alke Petri-Fink[a], and Barbara Rothen-Rutishauser*[a]

*Correspondence: Prof. B. Rothen-Rutishauser[a], Tel.: +41 26 300 95 02, E-mail: barbara.rothen@unifr.ch
[a]Adolphe Merkle Institute, Université de Fribourg, Ch. de Verdiers 4, CH-1700 Fribourg; [b]Bern University of Applied Sciences, Automotive Engineering, Gwerdtstrasse 5, CH-2560 Nidau; [c]TTM, Technik thermischer Maschinen, Fohrhölzlistrasse 14b, CH-5443 Niederrohrdorf

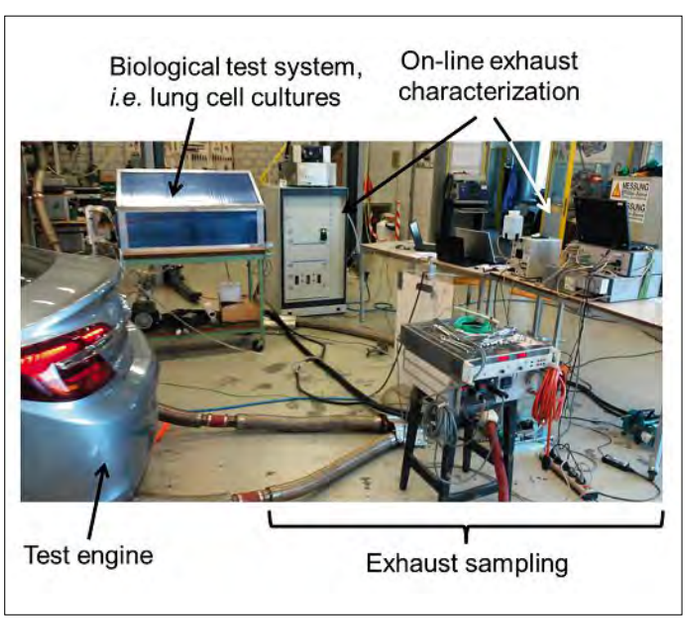
Keywords: 3D lung cell model · Adverse effects · Exhaust emission · Exposure system · Physicochemical properties of exhaust

Pollution by vehicles is a major problem for the environment due to the various components in the exhaust gases, *i.e.* gaseous and non-gaseous compounds such as particulate matter. Epidemiological studies demonstrate the profound impact of vehicle emissions upon human health.[1] Such studies, however, cannot attribute an adverse effect to a certain exhaust component, which renders decision-making difficult when defining which emission sources should be regulated more stringently.

Reduction in emission of certain exhaust constituents and increased engine efficiency can be measured by technical means (see the Analytical Highlight of Heeb *et al.* in the next issue of CHIMIA). Standardized protocols for exhaust toxicity assessment are lacking and rely in many aspects on epidemiological and *in vivo* studies. Reasonable alternatives are *in vitro* studies using highly standardized cell cultures such as a 3D model of the human airway epithelium composed of epithelial cells and two types of immune cells, *i.e.* macrophages and dendritic cells. They can be used in combination with an exhaust system for exposure of lung cells to complete engine exhaust. The emission samples of an engine of choice can be taken directly at the exhaust and brought onto the lung cell surface with exhaust characterisation being performed on-line.

The system was established for scooter exhaust and has also been adapted for diesel cars.[2] It yields reproducible results, provides the needed sensitivity for detecting differences in biological responses, and allows for differentiation between effects induced either by gaseous or by particulate components of the complete exhaust.[3]

This advanced exposure system is well suited for risk assessment of exhaust emissions as well as for investigations on how engine type, exhaust after-treatment technologies, fuel additives, and fuel types affect acute exhaust toxicity.



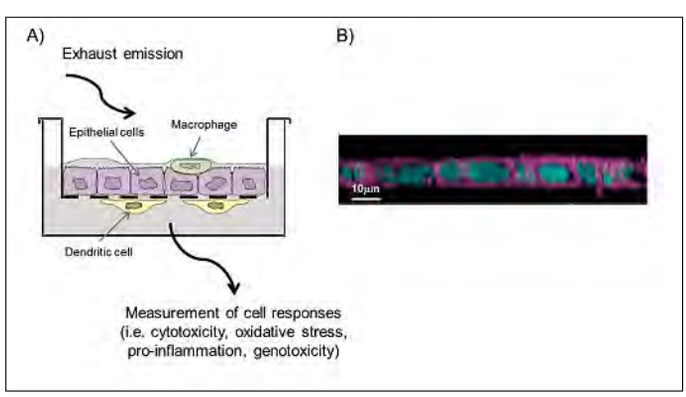
Overview of the exposure system with the engine on the chassis dynamometer, the measuring units and the exposure box.

Acknowledgements

This work is financially supported by the Swiss Federal Office for the Environment, Erdölvereinigung EV and VSS lubes, Bern University of Applied Sciences as well as the Adolphe Merkle Foundation.

Received: December 11, 2014

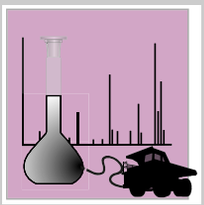
[1] A. J. Ghio, M. S. Carraway, M. C. Madden, *J. Toxicol. Environ. Health B* **2012**, *15*, 1.
[2] L. Müller, P. Comte, J. Czerwinski, M. Kasper, A. C. R. Mayer, A. Schmid, L. Rosinus, M. J. D. Clift, S. Steiner, P. Gehr, B. Rothen-Rutishauser, *Toxicol. Env. Chem.* **2012**, *94*, 164.
[3] S. Steiner, J. Czerwinski, P. Comte, O. Popovicheva, E. Kireeva, L. Müller, N. Heeb, A. Mayer, A. Fink, B. Rothen-Rutishauser, *Atmos. Env.* **2013**, *81*, 380.



Exposure of lung cell cultures with the exhaust emissions. A) Schematic drawing of the 3D cellular model of the human airway epithelium composed of epithelial cells, macrophages and dendritic cells. The cells as well as the cell culture medium can be sampled to assess various cell responses. B) Laser scanning micrograph (xz-projection) of the epithelial cells grown on a porous filter insert. F-actin is shown in violet, the cell nuclei in light blue.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2015.152



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Benefit-Risk Assessment of Diesel Particle Filters (DPFs): An Analytical and a Toxicological Challenge

Norbert Heeb*[a], Regula Haag[a], Peter Schmid[a], Cornelia Seiler[a], Adrian Wichser[a], Markus Zennegg[a], Peter Honegger[a], Kerstin Zeyer[a], Lukas Emmenegger[a], Yan Zimmerli[b], Jan Czerwinski[b], and Andreas Mayer[c]

*Correspondence: Dr. N. Heeb[a], Tel.: +41 58 765 42 57, E-Mail: norbert.heeb@empa.ch

[a]EMPA, Swiss Federal Laboratories for Materials Testing and Research, Ueberlandstrasse 129, CH-8600 Dübendorf. [b]UASB, University of Applied Sciences Biel, Gwerdtstrasse 5, CH-2560 Nidau. [c]TTM, Technik Thermischer Maschinen, Fohrhölzlistrasse 14b, CH-5443 Niederrohrdorf

Keywords: Diesel particle filters · Genotoxicity · Heavy duty vehicles · Nitro-PAHs · PAHs · PCDD/Fs

Filter or no filter is not the question anymore, except perhaps in the Swiss parliament which voted against a retrofit program for heavy duty vehicles in May 2014. In R&D, one asks if catalyzed or non-catalyzed filters are the best available technology for detoxification of diesel exhaust. Assessing the impact of filters on exhaust composition and toxicity is challenging for analytical chemists and toxicologists (see the Highlight of Bisig *et al.*, *Chimia* **2015**, *69*, 68). Are toxic compounds reactive species triggering oxidative stress and inflammation, are they genotoxic inducing cancer or do they provoke other cell responses?

The endeavor 'NEAT' (Neue Alpentransversale, the new transalpine rail link) triggered various activities, among them the VERT project (Verminderung der Emissionen von Realmaschinen im Tunnelbau) – a joint effort from SUVA, BAFU, filter and catalyst manufacturers, TTM, and EMPA – to evaluate suitable filter technology for construction machinery to fulfill air quality standards in these long tunnels (Fig. 1).

Fig. 1. Construction machinery in Switzerland has to be equipped with filters since 2009, but most trucks on roads are not.

By now all construction machinery in Switzerland has to be equipped with efficient filters fulfilling the VERT standards (efficiencies >98%). Approved filters must convert genotoxic compounds such as polycyclic aromatic hydrocarbons (PAHs) but must not support a *de novo* formation of other pollutants such as nitro-PAHs and polychlorinated dibenzodioxins/furans (PCDD/Fs). Fig. 2 displays sampling filters, exposed to 7 m^3 exhaust (3 min operation) of a heavy duty engine (6.1 L). A VERT-approved diesel particle filter was used in one case. The other sample represents untreated heavy duty vehicle exhaust (94% of the Swiss HDV fleet).

Fig. 2. Glass sampling devices exposed to 7 m^3 exhausts of a heavy duty engine (3 min operation) with and without filter.

Obviously, particles are removed with filters, but semi-volatile compounds including genotoxic PAHs and nitro-PAHs are not necessarily converted. An assessment of filters, now described in the Swiss Norm 277206, also includes an evaluation of genotoxic compounds. EMPA has contributed congener-specific PAH, nitro-PAH and PCDD/F analyses for >40 diesel particle filters with GC-HRMS.

Fig. 3 compares pyrene and 1-nitro pyrene penetration of filters with high, low and no oxidation potential. Catalyzed filters convert pyrene (75–97%). The non-catalyzed filter stored pyrene when new, but released it when soot-loaded. Such storage-release phenomena may occur when changing from cold to hot conditions (*e.g.* urban vs. highway driving). Emissions of 1-nitropyrene even increased for the non-catalyzed filter. A secondary formation of nitro-PAHs affects the exhaust genotoxicity. **We conclude that filtration *per se* is not sufficient to lower genotoxicity. Genotoxic compounds must be combusted in filters with efficient catalysts.**

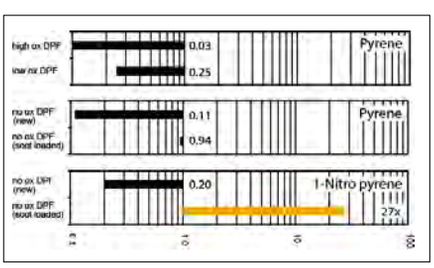


Fig. 3. Pyrene and 1-nitro pyrene penetration of filters with high, low and no oxidation potential (new and soot loaded) are compared.

Received: December 23, 2015

References

N. V. Heeb, P. Schmid, M. Kohler, E. Gujer, M. Zennegg, D. Wenger, A. Wichser, A. Ulrich, U. Gfeller, P. Honegger, K. Zeyer, L. Emmenegger, J. L. Petermann, J. Czerwinski, T. Mosimann, M. Kasper, A. Mayer, *Environ. Sci. Technol.* **2008**, *42*, 3773.

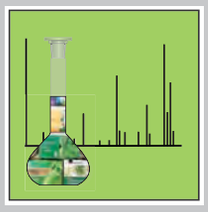
N. V. Heeb, P. Schmid, M. Kohler, E. Gujer, M. Zennegg, D. Wenger, A. Wichser, A. Ulrich, U. R. S. Gfeller, P. Honegger, K. Zeyer, L. Emmenegger, J. L. Petermann, J. Czerwinski, T. Mosimann, M. Kasper, A. Mayer, *Environ. Sci. Technol.* **2010**, *44*, 1078

N. V. Heeb, M. Zennegg, R. Haag, A. Wichser, P. Schmid, C. Seiler, A. Ulrich, P. Honegger, K. Zeyer, L. Emmenegger, P. Bonsack, Y. Zimmerli, J. Czerwinski, M. Kasper, A. Mayer, *Environ. Sci. Technol.* **2013**, *47*, 6510.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: +41 58 765 77 87, Fax: +41 58 765 77 62, Mail to: veronika.meyer@empa.ch

doi:10.2533/chimia.2015.231



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

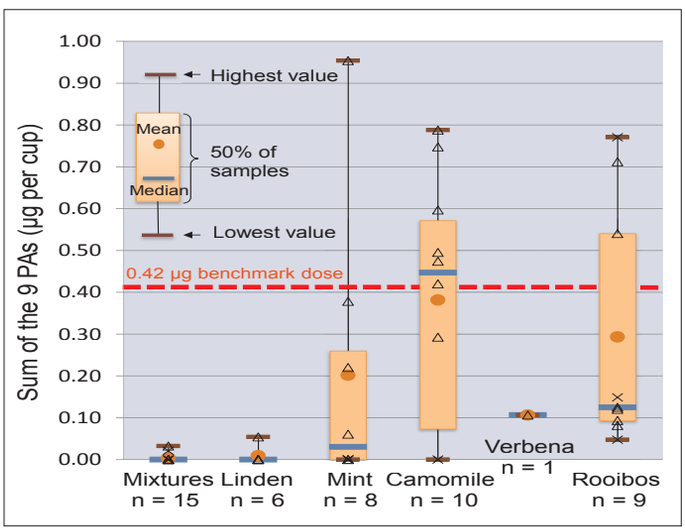
Occurrence of Natural Hepatotoxins in Herbal Teas

Stefan Bieri*[a], Caroline Mathon[ab], Patrick Edder[a], and Philippe Christen[b]

*Correspondence: Dr. S. Bieri, Tel.: +41 21 415 97 19, E-mail: stefan.bieri@vd.ch
[a]Official Food Control Authority of Geneva, Quai Ernest-Ansermet 22, CH-1211 Geneva; [b]School of Pharmaceutical Sciences, EPGL, University of Geneva, University of Lausanne, Quai Ernest-Ansermet 30, CH-1211 Geneva

Keywords: Food safety · Herbal teas · HPLC-MS/MS · Pyrrolizidine alkaloids

Pyrrolizidine alkaloids (PAs) are a large class of secondary metabolites naturally occurring in many botanicals worldwide. PAs that contain a 1,2-unsaturated necine base and are esterified on the hydroxymethyl group at C(1) and/or C(7) cause hepatotoxicity. Thus, consumption of PA-contaminated food or beverages may lead to acute or chronic hepatic veno-occlusive disease. Herbal-derived food products are probably the major source of exposure but data are still very scarce. Following several cases of intoxications and toxicological studies, risk assessment agencies have proposed various limits for maximal daily PA intake. Up to now, legal limits for PAs in food exist neither within the EU nor in Switzerland. The generally accepted benchmark dose for an adult corresponds to about 0.42 µg of unsaturated PAs per day. In our study dealing with 70 teas and herbal teas, 24 beverages were found to contain PAs >LOQ: 0.02 µg/cup (200 mL). The identity of the natural toxins was confirmed by high-resolution MS. Quantification of the nine 1,2-unsaturated PAs varied from 0.02 to up to 0.95 µg. Analysis were conducted with a validated UHPLC-MS/MS method implementing sub 2-µm core-shell particles. Results indicated that the sum of screened PAs was higher than the recommended maximum dose in 10 samples. All rooibos samples were positive suggesting that small amounts of PAs are occurring naturally. In the other contaminated samples, the presence of PAs is possibly due to cross-contamination with PAs-containing botanicals during harvesting, storage and/or transport.



Box plot of PA amounts measured in one cup of tea or herbal tea preparation.

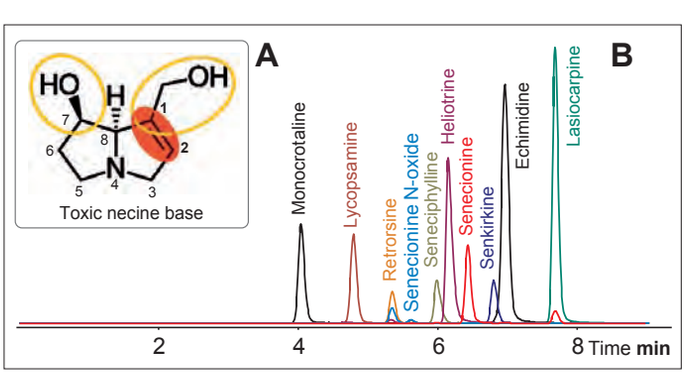
Results of this survey show that the long-term consumption of highly contaminated herbal tea exposes consumers, and particularly pregnant women and infants, above the reference level of possible health impairment. Consequently, the herbal infusion industry is urged to monitor contamination levels and to find solutions to secure an acceptable margin of exposure.

Received: February 18, 2015

Reference

C. Mathon, P. Edder, S. Bieri, P. Christen, *Anal. Bioanal. Chem.* **2014**, *406*, 7345.

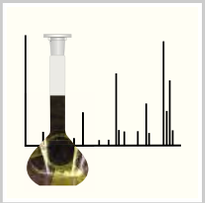
Samples of selected teas and herbal teas from the Swiss market.



A, Structure of the hepatotoxic moiety of PAs; B, UHPLC-MS/MS chromatogram of a standard mixture at 50 µg/L.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2015.301



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Gamma Ray Spectrometry of Sewer Sludge – A Useful Tool for the Identification of Emission Sources in a City

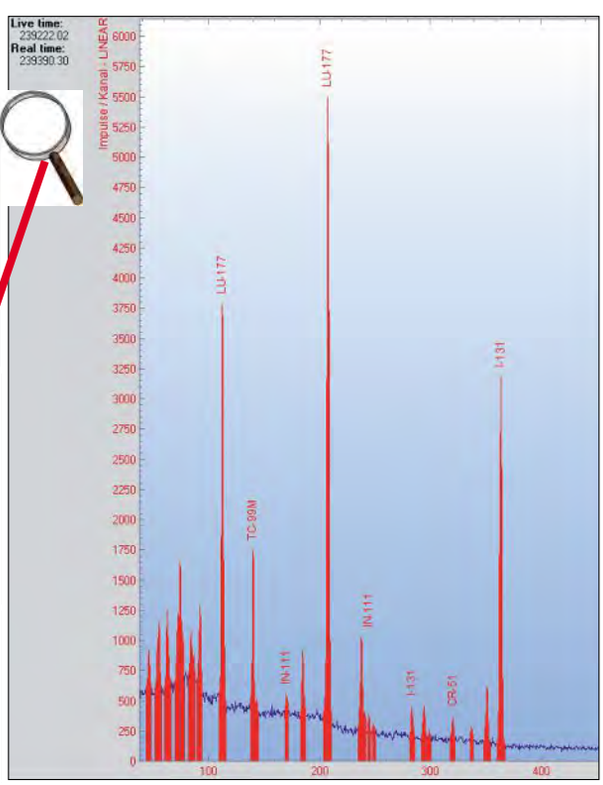
Natascha Rumpel, Franziska Kammerer, Michael Wagmann, and Markus Zehringer*

*Correspondence: Dr. M. Zehringer, Kantonales Laboratorium Basel-Stadt, Kannenfeldstrasse 2, CH-4012 Basel, Tel.: +41 61 385 25 17, E-mail: markus.zehringer@bs.ch

Keywords: Gamma ray spectrometry · Radiopharmaceuticals · Sewer sludge

Sewer sludge stands for the biofilm, which forms between the wastewater and concrete in a sewage water system. It consists of bacteria, algae and fungi and has powerful adsorbent properties for many chemicals and is therefore the remainder or 'memory' of the past load of wastewater running through. The analysis of sewer sludge can provide reference to and can lead to the identification of point sources, such as emissions of heavy metals, organochlorine compounds or radionuclides.

The photo on the lower left shows the object of study, *i.e.* the base of a wastewater tube with wastewater and sewer sludge. Below: Gamma ray spectrum of a sewer sludge sample. 5 g dry weight was counted for three days on a high-resolution germanium detector (extracted spectrum from 50 to 1000 keV). Quantifiable short-lived radionuclides were ^{99m}Tc, ^{177}Lu, ^{111}In, and ^{131}I.



Hospitals are a main source of radiopharmaceutical emissions. Short-lived radionuclides, such as iodine-131, lutetium-177 or technetium-99M, are used in high doses for the diagnosis and treatment of thyroid cancers or neuroendocrine tumours (DOTATOC therapies). After such treatments, patients show high doses of the incorporated radionuclides accompanied by high amounts of radiation in the form of beta and gamma rays. Therefore faeces, urine and all other waste products have to be collected in special wastewater containment units at hospitals and are left to cool down. Due to their short half-lives (technetium-99m: 6.0 hours, iodine-131: 8.0 days, lutetium-177: 6.7 days) the collected waste water can only be discharged into the wastewater system after a number of weeks when its activity is below a certain contamination limit.

Sewer sludge was collected in the wastewater system above and below the discharge point of the radioactive wastewater of a hospital. The sludge was transferred to a calibrated geometry (Petri dish of 12 mm height and 60 mm diameter) and then counted on a gamma ray spectrometer (high-resolution germanium detector) for 24 hours.

Sewer sludge and the running wastewater collected at the same place and time did not provide the same results. A random sample only shows the momentary load of the wastewater, whereas the sewer sludge offers an overview of short-lived radionuclides from the past few days.

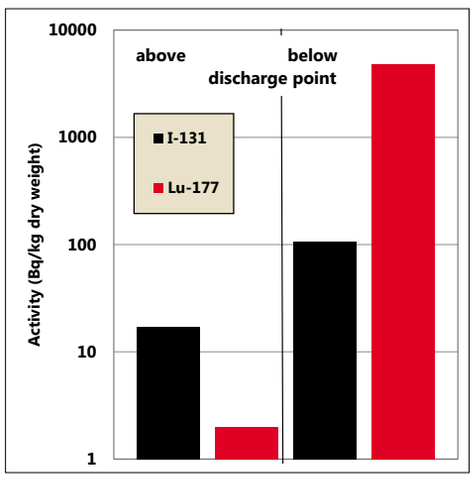
Gamma ray analysis of the sewer sludge of a wastewater system can be a powerful instrument for the identification of gamma emitters. Due to the adsorptive properties of the sewer sludge, emissions of short-lived radionuclides can be detected even after a few days.

Received: March 11, 2015

References

B. Gutekunst, Sielhautuntersuchungen zur Einkreisung schwermetallhaltiger Einleitungen, Diss. Karlsruhe, **1988**.

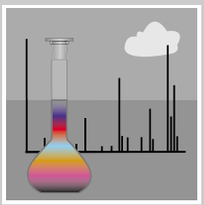
J. Sauer, E. Antusch, C. Ripp, *Vom Wasser* **1997**, *88*, 49.



Load of sewer sludge in the vicinity of a hospital centre (notice the logarithmic y-axis).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2015.368



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

What are the Sources of Aerosols during Haze Events in China?

Sönke Szidat*[a] and André S. H. Prévôt[b]

*Correspondence: PD Dr. S. Szidat[a], Tel.: +41 31 631 43 08, E-Mail: szidat@dcb.unibe.ch
[a]Department of Chemistry and Biochemistry & Oeschger Centre for Climate Change Research, University of Bern, Freiestrasse 3, CH-3012 Bern; [b]Paul Scherrer Institute, CH-5232 Villigen PSI

Keywords: Aerosol mass spectrometry · Air pollution · Radiocarbon · Source apportionment

Air-borne aerosols have an influence on human health and the global climate. Very high concentrations of particulate matter with a diameter <2.5 µm ($PM_{2.5}$) are frequently observed in Central and East Asia during winter. In China, such haze episodes often result in exceedances of the Chinese pollution standard for $PM_{2.5}$ of 75 µg m^{-3} by up to a factor of 10, which cause poor visibility and air quality and increase in respiratory diseases. To define strategies to reduce $PM_{2.5}$ concentrations, the factors governing its abundance and composition have to be elucidated.

During severe pollution episodes in January 2013, aerosols were collected on quartz filters in four major cities of China, *i.e.* Beijing, Xi'an, Shanghai and Guangzhou. Here, we show results from Beijing as one example. For a unique chemical analysis, several chromatographic and mass spectrometric techniques were combined. The two most important methods were a newly developed offline application of aerosol mass spectrometry, which identifies major aerosol components and their general emission processes, and measurement of the radioactive carbon isotope ^{14}C (radiocarbon) with accelerator mass spectrometry, which allows the distinction of emissions from fossil sources (mainly traffic and coal burning) and non-fossil sources (mainly biomass burning and natural aerosol emissions).

Beijing (here at Tiananmen Square) is one of the Chinese cities with severe air quality problems during haze events in winter. Photo by Paul Scherrer Institute.

All measurement data were evaluated using several statistical models and interpreted in two different ways due to the complexity of the atmospheric processes. First, the combination of all methods allowed quantification of the inorganic and organic composition as well as the contribution of seven main sources of aerosol emission or formation. Second, emphasis was laid upon a detailed source apportionment of the organic aerosol using radiocarbon analysis as the key method for a deeper understanding of the role of fossil-fuel usage and biomass burning for the bad air quality.

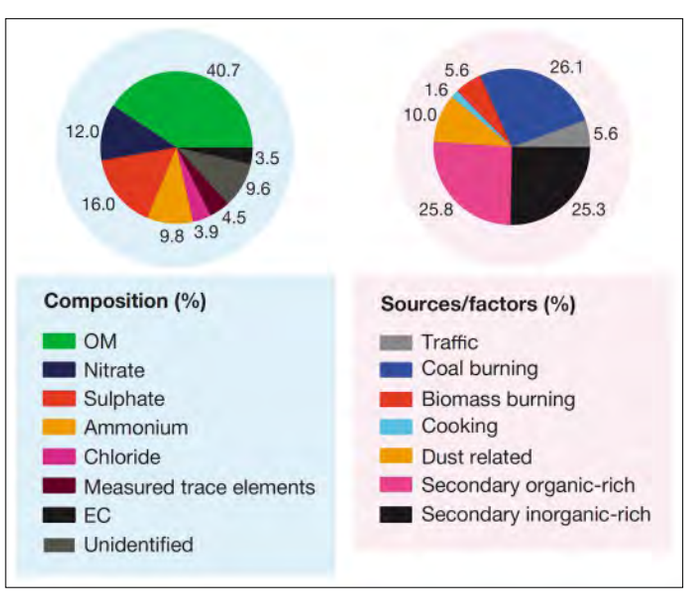
Both approaches showed that haze events in China are driven to a large extent by so-called secondary aerosols, which were formed in the atmosphere by oxidation of gaseous precursors, rather than by direct aerosol emissions. This suggests that the reduction of precursor gases from fossil-fuel combustion and biomass burning, which form secondary aerosols, is as important as the decrease of direct aerosol emissions for air quality improvement in China.

Received: April 3, 2015

References

R. J. Huang, Y. Zhang, C. Bozzetti, K. F. Ho, J. J. Cao, Y. Han, K. R. Daellenbach, J. G. Slowik, S. M. Platt, F. Canonaco, P. Zotter, R. Wolf, S. M. Pieber, E. A. Bruns, M. Crippa, G. Ciarelli, A. Piazzalunga, M. Schwikowski, G. Abbaszade, J. Schnelle-Kreis, R. Zimmermann, Z. An, S. Szidat, U. Baltensperger, I. El Haddad, A. S. Prévôt, *Nature* **2014**, *514*, 218.

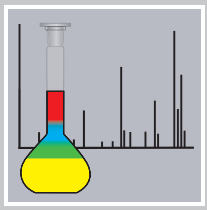
Y. L. Zhang, R. J. Huang, I. El Haddad, K. F. Ho, J. J. Cao, Y. Han, P. Zotter, C. Bozzetti, K. R. Daellenbach, F. Canonaco, J. G. Slowik, G. Salazar, M. Schwikowski, J. Schnelle-Kreis, G. Abbaszade, R. Zimmermann, U. Baltensperger, A. S. H. Prévôt, S. Szidat, *Atmos. Chem. Phys.* **2015,** *15,* 1299.



Chemical composition and source apportionment of fine aerosols at Beijing during the high pollution event in January 2013. OM and EC define organic matter and elemental carbon, respectively. Modified from Huang *et al.*, *Nature* **2014**, *514*, 218.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2015.494



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Mass Spectrometric Proteome Analysis of Small Three-Dimensional Microtissues Allows for the Quantitative Description of Toxic Effects of Drugs

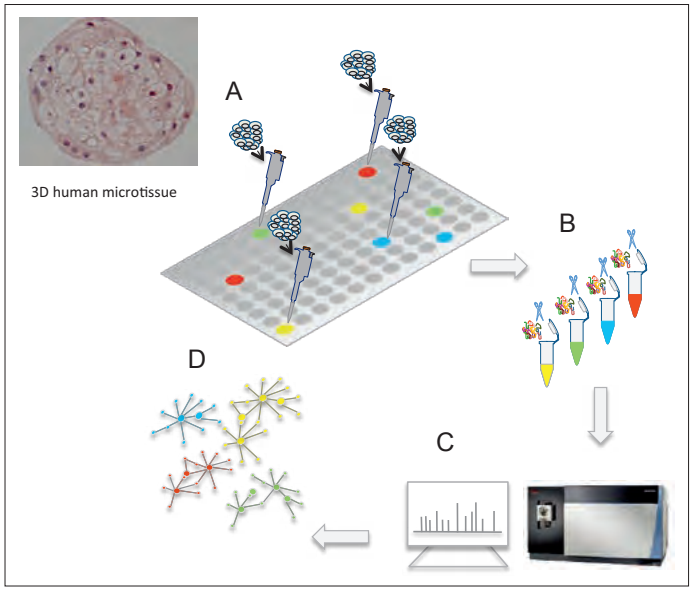
Nathalie Selevsek* and Ralph Schlapbach

*Correspondence: Dr. N. Selevsek, Functional Genomics Center Zurich, ETH Zurich and University of Zurich, Winterthurerstrasse 190, CH-8057 Zurich, Tel: +41 44 635 39 61, E-Mail: selevsek@fgcz.ethz.ch

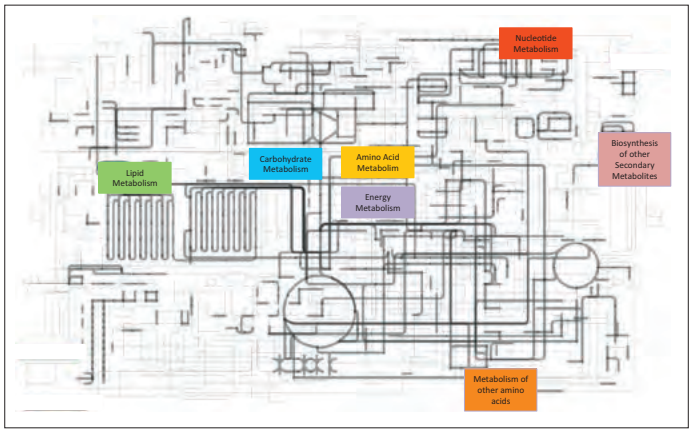
Keywords: Chemical safety · Drug toxicity · Human 3D cells · Mass spectrometer · Protein networks · Proteomics

In vitro tissue models are essential for safety testing of novel candidate molecules developed in the pharmaceutical, cosmetic, and chemical industries. Recently, 3D cellular tissue models have been established for improved testing of chronic exposure toxicity, featuring longer lifespans and greater stability compared to 2D monolayer cultures. Besides, their 3D architecture displays more organ-like function than conventional monolayer cell cultures and are often referred to as spheroids, due to their spherical shape.

In the context of a European research project aiming at developing integrative *in silico* tools for predicting human liver and heart toxicity after drug administration, corresponding spheroid tissues are challenged with prototypical hepato- or cardiotoxicants to reveal the biomolecules, such as proteins, involved in the toxic phenotype.



Highly sensitive analytical workflow for the proteomics analysis of drug-treated human spheroids. A: Treatment of liver and cardiac spheroids with prototypical hepato- or cardiotoxicants. B: Protein extraction from drug-treated human spheroids and preparation for proteomics analysis. C: Mass spectrometric analysis of digested proteins for proteome identification and quantitation. D: Protein network analysis.



Metabolic protein pathways identified by MS-based proteomics in liver spheroids (*http://pathways.embl.de/iTuby/*).

Thanks to the rapid development of robust and sensitive mass spectrometers together with computational tools, mass spectrometry-based proteomics has become a powerful analytical approach to study large numbers of proteins up to rather complete proteomes isolated from living cells and organs. Using a latest generation proteomics approach, our analyses were carried out by digesting the protein extracts by trypsin, separation of the resulting peptides by hydrophilic interaction liquid chromatography, and finally mass spectrometric analysis using a Thermo Orbitrap Fusion system. In the mass spectrometer, the peptides are fragmented by collision with a neutral gas and the resulting precursor and fragment-ion spectra are analyzed. Using this method, 3000 proteins can be identified and quantified from as little as the protein equivalent of 1000 cells per measurement. Combining the data from multiple treated spheroids allows to quantitatively map out more than 5000 proteins of the spheroid proteome.

Currently ongoing work focuses on the in-depth analysis of the drug dosage effects on proteomes from drug-exposed liver and cardiac spheroids revealing their drug-specific toxic responses. **The generated data illustrates that with new spheroid fabrication techniques together with sensitive and accurate MS-based technologies and sophisticated bioinformatics methods, the comprehensive analysis of drug mechanisms and toxicity is feasible at the proteome scale and can be applied to various types of 3D tissue model systems in the future.**

Received: April 21, 2015

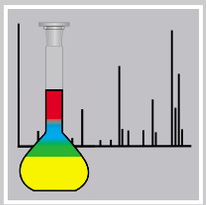
Reference

Hecatos (Hepatic and Cardiac Toxicity Systems Modeling), Framework Programme (HEALTH-F4-2013-602156).

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2015.547



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Using Multiple Geochemical Techniques to Investigate Rainfall as a Potential Source of Selenium to Soils

Tim Blazina and Lenny Winkel*

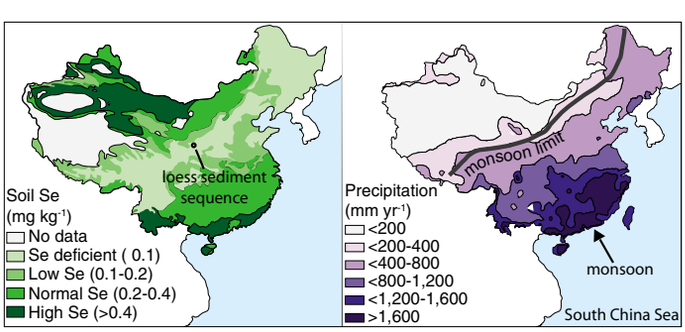
*Correspondence: Prof. Dr. L. Winkel, Eawag – Swiss Federal Institute of Aquatic Science and Technology, Überlandstrasse 133, CH-8600 Dübendorf and ETH Zurich, Universitätsstrasse 16, CH-8092. Tel.: +41 58 765 56 01, E-mail: lenny.winkel@eawag.ch

Keywords: Climate · Environmental archives · Geochemistry · Selenium · Trace element distribution

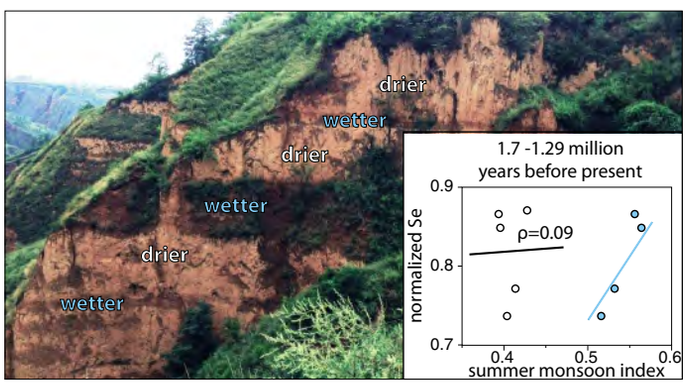
The trace element selenium (Se) is a micronutrient required by humans for important biological functions. Despite its importance for human health, the sources and processes that control the large-scale spatial distribution of Se in the environment remain unclear. Similar patterns of rainfall and soil Se concentrations, *e.g.* in Southern China, suggest that rainfall may be an important source of Se to soils.

With the goal of exploring rainfall as a source of Se to soils, we examined climatic and geochemical variables in a sediment sequence from the Loess Plateau of Central China. We used multiple analytical methods to investigate Se concentrations and speciation, which is a main factor controlling environmental Se mobility.

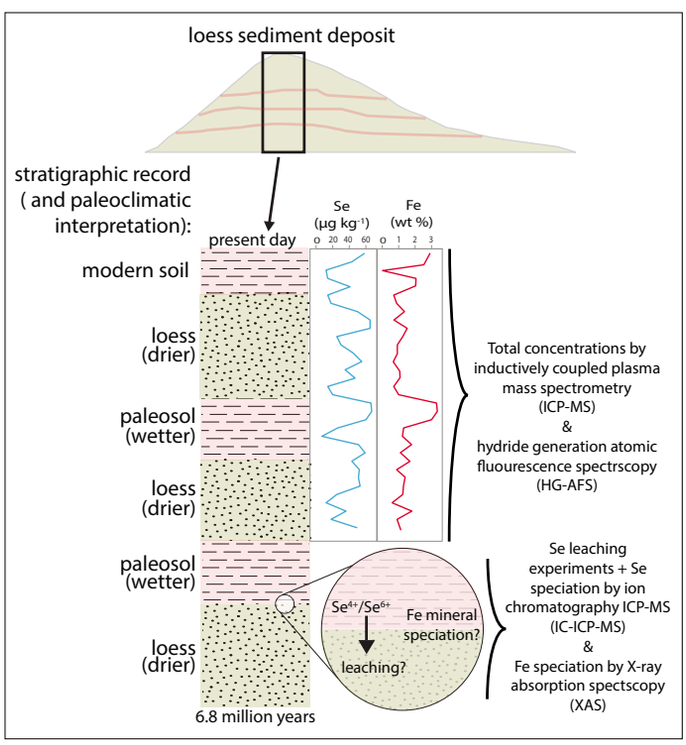
Speciation of Se could not be directly measured due to the low concentrations (< 70 mg Se per kg sediment). However by carrying out batch leaching experiments, followed by ion chromatography-inductively coupled plasma mass spectrometry analysis, we could quantify the maximum concentrations of Se species that could have been removed from these sediments by natural leaching processes. This amount was low, indicating that these sediments are a suitable environmental archive. Furthermore, speciation of iron was analyzed using X-ray absorption spectroscopy, since different iron minerals can have different binding capacities for Se, which influences the mobility of Se. Comparisons between results from geochemical analyses and climate variables



Distribution of Se in soils and rainfall in China. Also shown is the location of the studied sediment section, and the monsoon limit (present-day northern extent of the monsoon) (modified from Blazina *et al.*, **2014**).



A sediment sequence in the Chinese Loess Plateau. Inlay shows relationship of Se to the monsoon index (a proxy for precipitation) in wetter/drier times.



Schematic of loess section (modified from *http://gec.cr.usgs.gov/archive/eolian/images/11a.gif*) and overview of geochemical analyses and techniques employed in this study.

showed that in wetter time periods there was a relationship between Se and the strength of the monsoon, which was less pronounced in drier time periods.

By combining multiple geochemical techniques we could identify rainfall as a likely source of Se to soils. This finding is important in future efforts to predict the distribution of this vital trace element in soils.

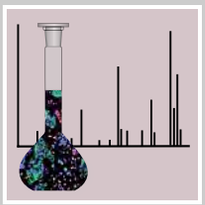
Received: 15 June, 2015

Can you show us your analytical highlight?
Please contact:
Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

Reference

T. Blazina, Y. Sun, A. Voegelin, M. Lenz, M. Berg, L. H. E. Winkel, *Nat. Commun.* **2014,** *5,* 4717.

doi:10.2533/chimia.2015.637



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

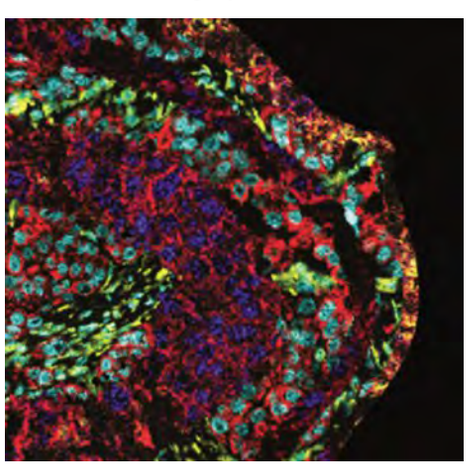
Laser Ablation ICP-MS for Single-Cell-based Tissue Imaging

Gunnar Schwarz[a], Hao A. O. Wang[a], Charlotte Giessen[b], Denis Schapiro[b], Bodo Hattendorf[a], Bernd Bodenmiller*[b] and Detlef Günther*[a]

*Correspondence: Prof. Dr. B. Bodenmiller[b], E-Mail: bernd.bodenmiller@imls.uzh.ch or Prof. Dr. D. Günther[a], E-Mail: guenther@inorg.chem.ethz.ch. [a]Laboratory of Inorganic Chemistry, ETH Zurich, Vladimir-Prelog-Weg 1, CH-8093 Zurich; [b]Institute of Molecular Life Sciences, University of Zurich, Winterthurerstrasse 190, CH-8057 Zurich

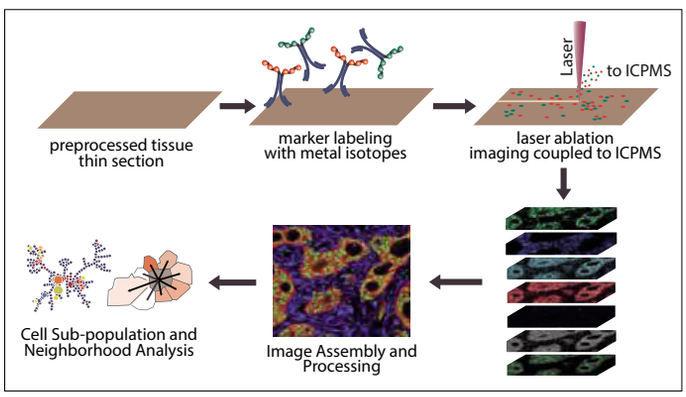
Keywords: Imaging mass cytometry · Laser ablation ICPMS · Multiplexed tissue analysis · Subcellular resolution · Tumor cell heterogeneity

The cell heterogeneity of tumor tissues drives tumor pathogenesis and progression and is currently of particular interest in biomedical research. Adapting and combining mass cytometry workflows with laser ablation techniques brings with it the opportunity to visualize this tumor cell heterogeneity, and cell-to-cell interactions in the so-called microenvironment, on the single-cell level in tissue thin sections. Similar to immunohistochemistry, tissue sections are treated with distinct rare earth isotope-tagged antibodies. Subsequently, the tissue is analyzed by scanning using a high-energy pulsed laser across the surface and transfer of the so generated aerosol into an inductively coupled plasma mass spectrometer (ICPMS) for detection of the metal labels. In addition to a novel ICP-TOFMS, a dedicated laser ablation system was developed, facilitating high spatial resolution, fast image acquisition, high sensitivity and multiplexed elemental analyses. A laser spot size of 1 µm diameter enables recognition and distinction of features at subcellular resolution. Specific markers can be employed to enable the detection of individual cells for automated, software-based data evaluation. The imaging mass cytometry approach allows labeling of potentially more than 100 different markers for highly multiplexed tissue analyses.



The tumor microenvironment in breast cancer tissues can be investigated by the combination of laser ablation imaging and mass cytometry (artistic design and copyright Nicole Seidel).

In a pilot study, 32 different protein markers and protein modifications could successfully be localized in tissue samples from 20 patients in an automated and high throughput manner at a limit of detection of approx. 500 marker molecules per pixel. The analysis revealed a variety of cancer cell subtypes in groups of patients, which had been classified as similar using classical histology schemes.



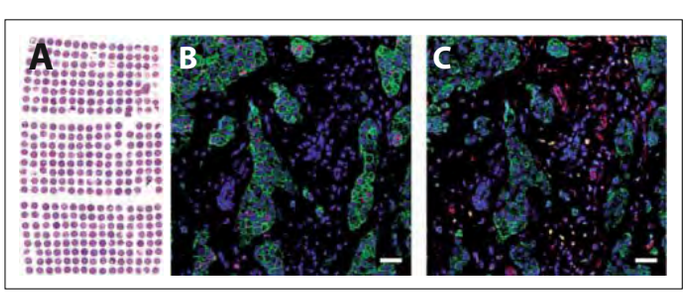
Workflow for imaging mass cytometry, based on mass cytometry and laser ablation ICPMS imaging.

The laser ablation ICPMS imaging and in combination with element labels is now routinely used for imaging mass cytometry studies at the University of Zurich. Of special interest is the interplay of particular cells, their regulatory circuits and how processes in the tumor microenvironment are induced and maintained.

Received: August 21, 2015

References

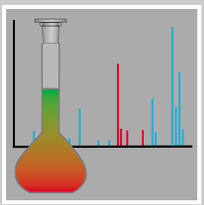
O. I. Ornatsky, R. Kinach, D. R. Bandura, X. Lou, S. D. Tanner, V. I. Baranov, M. Nitz, M. A. Winnik, *J. Anal. At. Spectrom.* **2008**, *23*, 463.
C. Giesen, H. A. O.Wang, D. Schapiro, N. Zivanovic, A. Jacobs, B. Hattendorf, P. J. Schuffler, D. Grolimund, J. M. Buhmann, S. Brandt, Z. Varga, P. J. Wild, D. Gunther, B. Bodenmiller, *Nat. Meth.* **2014**, *11*, 417.
H. A. O. Wang, D. Grolimund, C. Giesen, C. N. Borca, J. R. H. Shaw-Stewart, B. Bodenmiller, D. Gunther, *Anal Chem.* **2013**, *85*, 10107.



(A) On a typical tissue microarray each sample has a diameter of about 0.7 mm. (B and C) Mass cytometry images of breast cancer tissue. (B) Overlay of markers Ki-67 (red), H3 (blue) and HER2 (green). (C) Overlay of cytokeratin 8/18 (green), H3 (blue), vimentin (red), and CD68 (yellow). The white size bars indicate 25 µm.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2015.708



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Multi-Component Trace Gas Spectroscopy Using Dual-Wavelength Quantum Cascade Lasers

Lukas Emmenegger*[a], Jana Jágerská[b], Rolf Brönnimann[a], Jérôme Faist[c], Pierre Jouy[c], Herbert Looser[d], Patrik Soltic[a], and Béla Tuzson[a]

*Correspondence: Dr. L. Emmenegger, E-mail: Lukas.Emmenegger@empa.ch
[a]Empa, Swiss Federal Laboratories for Materials Testing and Research, CH-8600 Dübendorf; [b]Department of Physics and Technology, UiT The Arctic University of Norway, NO-9037 Tromsø; [c]Institute for Quantum Electronics, ETH, CH-8093 Zürich; [d]Institute for Aerosol and Sensor Technology, FHNW, CH-5210 Windisch

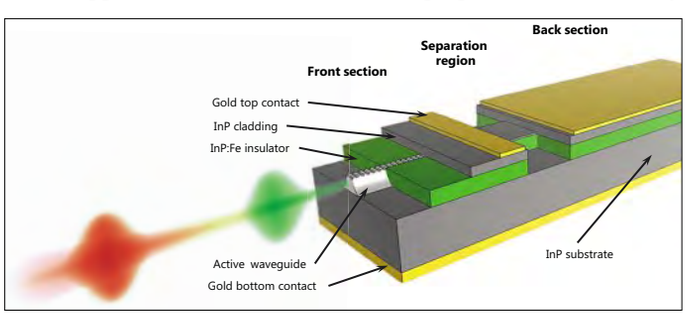
Keywords: Mid-IR spectroscopy · Nitrogen oxides · Quantum cascade lasers · Trace gas analysis

Simultaneous detection of multiple gas species using mid-infrared laser spectroscopy is highly desired for numerous applications ranging from air quality monitoring, medical breath analysis or drug and explosive detection to industrial process control. Since it is often impossible to address the high-resolution spectra of different gases with a single laser, state-of-the-art multi-wavelength spectrometers have to rely on the use of several lasers and elaborate beam combining solutions. This makes them bulky, costly, and highly sensitive to optical alignment.

We explored a new concept for multi-component spectroscopy based on a Dual-Wavelength Quantum Cascade Laser (DW-QCL). Such a laser can emit at two spectrally well-separated wavelengths, which share a common waveguide to produce one output beam. Thereby, it is possible to detect multiple gases without the need for any beam-combining optics.

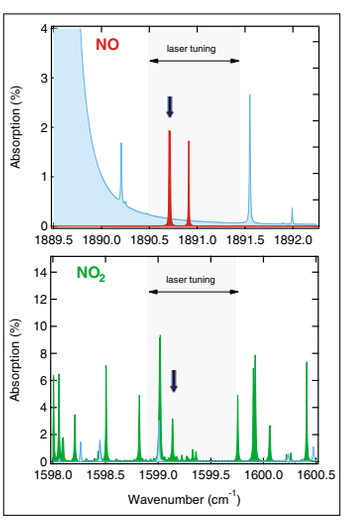
The active region of the DW-QCL consists of two different active layers stacked on top of each other, optimized for a broadband emission at 1600 cm^{-1} and 1900 cm^{-1}. These two spectral windows are ideally suited for the detection of nitrogen oxide (NO) and nitrogen dioxide (NO_2). Single-mode emission at the desired wavelengths is ensured by a succession of two distributed-feedback (DFB) gratings with different periodicities. Electrical separation of the respective laser sections makes it possible to address each wavelength independently and integrate the laser easily in a spectroscopic setup for gas analysis.

The spectrometer reached a precision (1σ) of 0.5 ppb for NO_2 and 1.5 ppb for NO after 100 s of averaging. It was successfully



Schematic drawing of the dual-wavelength laser. The laser is approximately 200 µm wide and 5 mm long. It emits at 5.26 µm (1900 cm^{-1}) and 6.25 µm (1600 cm^{-1}) as indicated by the two-colored beam.

Diesel engines are deployed in heavy-duty and passenger cars. Modern engines include both de-NO_x systems and particle filters. This allows maximum efficiency (*i.e.* high NO_x during combustion) and low tailpipe emission.



Simulated transmission spectrum of NO_2 (green), NO (red) and water vapor (blue), and the tuning range of the DW-QCL. The targeted absorption peaks are indicated with a blue arrow.

used for ambient air monitoring at a suburban site of the Swiss air pollution network (NABEL), as well as for fast, 10 Hz operation in harsh environment during automotive exhaust emission measurements. The latter is an excellent example for the value of multi-component detection, because the simultaneous measurement of both NO and NO_2 is needed to study and optimize modern diesel engines, which have nowadays complex exhaust gas treatment systems, such as selective catalytic reduction.

This analytical approach can be applied to the whole mid-infrared region which comprises the strongest, fundamental absorption features of molecules. Current developments aim to combine and optimize the concept to obtain simple and cost-effective spectrometers for the simultaneous measurement of multiple trace gas species.

Acknowledgements

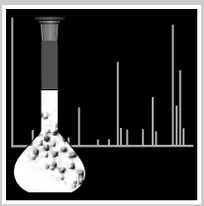
We acknowledge funding by Nanotera.ch, the Swiss National Research Foundation (SNF) and the Federal Office for the Environment (FOEN).

References

J. Jágerská, P. Jouy, A. Hugi, B. Tuzson, H. Looser, M. Mangold, M. Beck, L. Emmenegger, J. Faist, *Appl. Phys. Lett.* **2014**, *105*, 161109.
J. Jágerská, P. Jouy, B. Tuzson, H. Looser, M. Mangold, P. Soltic, A. Hugi, R. Brönnimann, J. Faist, L. Emmenegger, *Optics Express* **2015**, *23*, 1512.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2015.806



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Deep UV-LED Based Absorbance Detectors for Narrow-Bore HPLC and Capillary Electrophoresis

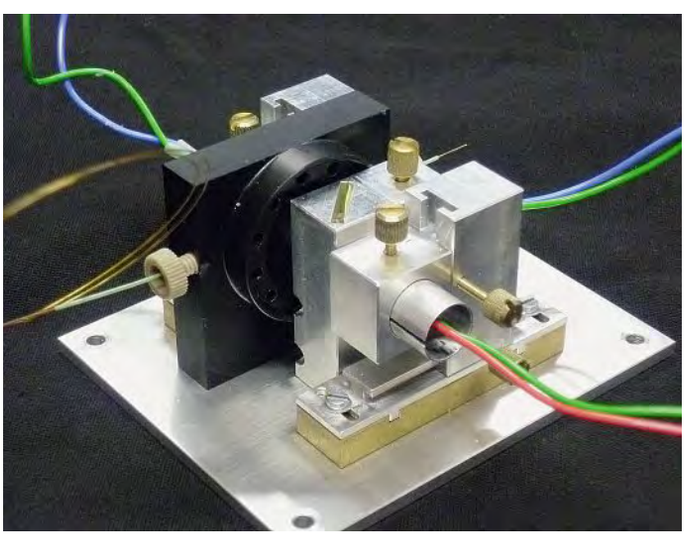
Duy Anh Bui and Peter C. Hauser*

*Correspondence: Prof. P.C. Hauser, Department of Chemistry, University of Basel, Spitalstrasse 51, CH-4051 Basel, E-mail: Peter.Hauser@unibas.ch

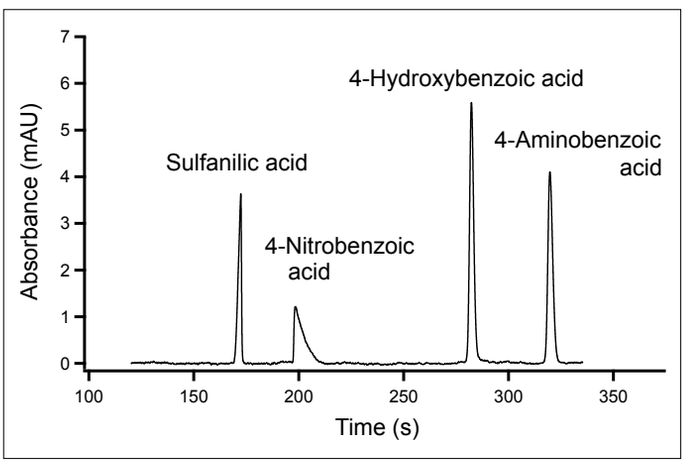
Keywords: Capillary detection · CE · Deep UV-LED · HPLC · UV photodiode

The most common detection method for the analytical separation techniques of HPLC and capillary electrophoresis (CE) is absorbance measurement in the deep-UV range (below 300 nm) as a large number of organic species absorb in this wavelength region. Conventional UV detectors are based on deuterium discharge lamps coupled to a monochromator for wavelength selection. Light-emitting diodes (LEDs) for this wavelength range have been produced in recent years. They have bandwidths of typically 30 nm, which makes them well suited for direct absorbance measurements of molecules without requiring a monochromator. Only UV-photodiodes and a log-ratio amplifier integrated circuit for emulating Lambert-Beer's law are required to complete the electronic circuitry.

Narrow-bore HPLC has primarily been developed for use with mass-spectrometric detection, for which only small amounts of analytes are sufficient. However, the savings in eluent consumption makes this approach also attractive for use with optical detection when ultimate sensitivity is not required. In CE narrow channels are essential to limit the Joule heating associated with the ionic current along the separation path.



The detector cell for capillary electrophoresis.



Detection of aromatic acids in capillary electrophoresis using a 50 µm ID capillary with a 255 nm LED.

The design of LED-based detectors for these narrow gauge methods is more challenging than for standard HPLC. Due to the small available volumes, the construction of dedicated Z-shaped flow cells is not possible and the measurement has to be made transverse to the flow path. The narrowness of the necessary apertures requires careful attention to efficient light coupling and avoidance of stray light. High mechanical stability is also required in order to minimize noise due to mechanical fluctuations. Despite these hurdles excellent performance with regard to baseline noise (low µAU range), reproducibility of peak areas (~1%), and linearity of calibration curves (correlation coefficients >0.999) could be obtained with LEDs of the commonly used wavelengths of 255 and 280 nm for both, narrow-bore HPLC (250 mm ID) and CE (50 mm ID).

The inexpensive LED-based devices display a capability comparable to standard commercial detectors. Their compact size and low power requirements make them also suitable for portable battery-powered instruments.

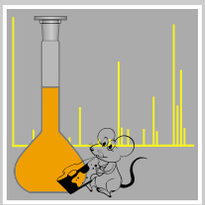
Received: September 30, 2015

References

B. Bomastyk, I. Petrovic, P. C. Hauser, *J. Chromatogr. A* **2011**, *1218*, 3750.
D. A. Bui, B. Bomastyk, P. C. Hauser, *J. Sep. Sci.* **2013**, *36*, 3152.
D. A. Bui, P. C. Hauser, *J. Chromatogr. A*, **2015**, *1421*, 203..

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2016.109



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Investigating the Relationship between Colour Code, Odour, and Flavour Analytics in Swiss Tilsit Cheeses

Pascal Fuchsmann*, Mireille Tena Stern, Yves-Alain Brügger, and Katharina Breme

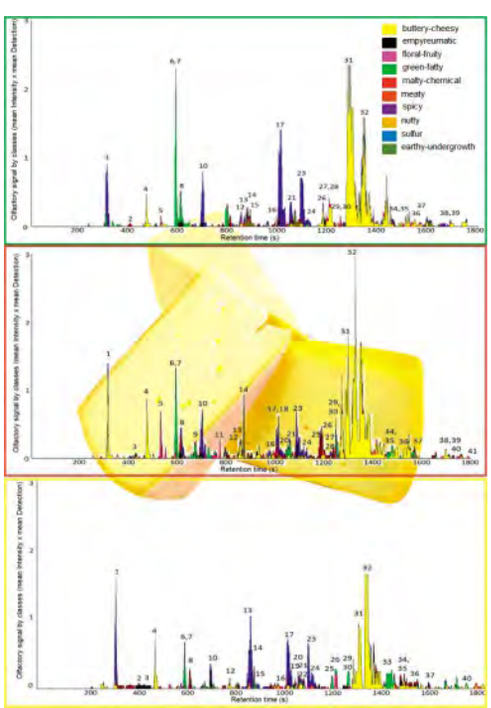
*Correspondence: P. Fuchsmann, Agroscope Institute for Food Sciences IFS, Schwarzenburgstrasse 161, CH-3003 Bern,
E-Mail: pascal.fuchsmann@agroscope.admin.ch

Keywords: Cheese · GC-Olfactometry · Headspace SPME · PFPD · Swiss Tilsit cheese · Volatile sulphur compounds

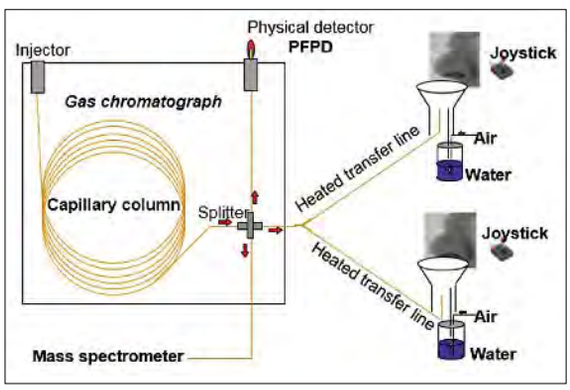
Swiss Tilsit is a semi-hard cheese manufactured in the eastern part of Switzerland. Three main types, differing in fat content, raw material, and ripening time and sold with coloured labels, are well known: green, red and yellow Swiss Tilsit (Table 1). Each dairy has its own fabrication recipe, but sensory aspects also depend on the raw material: Especially cheeses made from raw/partially thermised milk are known for a more multifaceted flavour, possibly due to microbial diversity. Volatile sulphur compounds (VSCs) are amongst other chemical compounds reported as key flavour constituents in various cheeses. Due to low odour thresholds, they have pronounced sensory properties and can influence cheese flavour even at low concentrations.

In order to evaluate odorant compounds and their impact in a (food) sample, gas chromatography (GC) employs the human nose as an analytical physiological detector (GC-Olfactometry, GC-O), often in combination with physical detectors such as a mass spectrometer (MS) or pulsed-flame photometric detection (PFPD) for specific detection of VSCs.

With the aim to conduct a comparative study between the odour and VSC profiles of the Tilsit varieties, green, red, and yellow Swiss Tilsit cheeses were analysed by GC-MS/PFPD-O on a two-way-GC-O system where two odour assessors ('panellists') work simultaneously on one sample in order to guarantee reliable results and time gains. VSCs were quantitated by GC-MS/PFPD. Volatile (odorant) compounds and VSCs were extracted by headspace solid-phase microextraction (HS-SPME) prior to analysis. Olfactometry data were recorded and processed using an olfactometry method that combines information on the number of panellists (n = 8) able to smell a specific odour ('detection frequency'), odour intensity, and the vocabulary used by the panellists to describe the odours they smell during analysis (VIDEO-Sniff: vocabulary-intensity-duration of elementary odours by sniffing). Results are displayed in coloured 'aromagrams', indicating the main odour families.



Aromagrams of Swiss Tilsit cheeses (bottom: yellow Tilsit, middle: green Tilsit, top: red Tilsit) obtained by GC-Olfactometry using the VIDEO-Sniff-method and AcquiSniff® software with eight panellists and a two-way-GC-O setup.



Scheme of the two-way GC-olfactometry set-up with mass spectrometer and pulsed-flame photometric detector PFPD used at the Agroscope Institute for Food Sciences in Bern.

GC-O and VSC profiles show a clear difference between the Tilsit cheeses. GC-O results revealed that the samples' odour is mainly influenced by buttery-cheesy and sulphury odour notes and confirmed that the overall flavour of Tilsit made from partially thermised milk is more intense and diverse than the one of Tilsit made from pasteurised milk.

Received: November 7, 2015

Reference

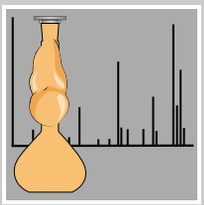
P. Fuchsmann, M. Tena Stern, Y.-A. Brügger, K. Breme, *J. Agric. Food Chem.* **2015**, *63*, 7511.

Table 1. Description of Swiss Tilsit cheeses (*www.tilsiter.ch*, 2015)

	Green Tilsit	Red Tilsit	Yellow Tilsit
Thermal treatment	Pasteurised milk	Partially thermised milk	Pasteurised milk with higher fat content
Fat in dry matter (FDM)	at least 45% FDM	at least 45% FDM	at least 55% FDM
Approx. fat content in 100 g	28 g	29.5 g	33 g
Ripening time	30–60 days	70–110 days	30–75 days
Taste perception	Mild aroma, slightly sour	Rich, spicy, and pungent	Creamy, slightly sour, mild aroma

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2016.208



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Longitudinal Monitoring of Endogenous Blood Steroids as a Tool to Detect Testosterone Abuse in Sport

Federico Ponzetto[a], Julien Boccard[b], Norbert Baume[a], Serge Rudaz[b], Martial Saugy[a], and Raul Nicoli*[a]

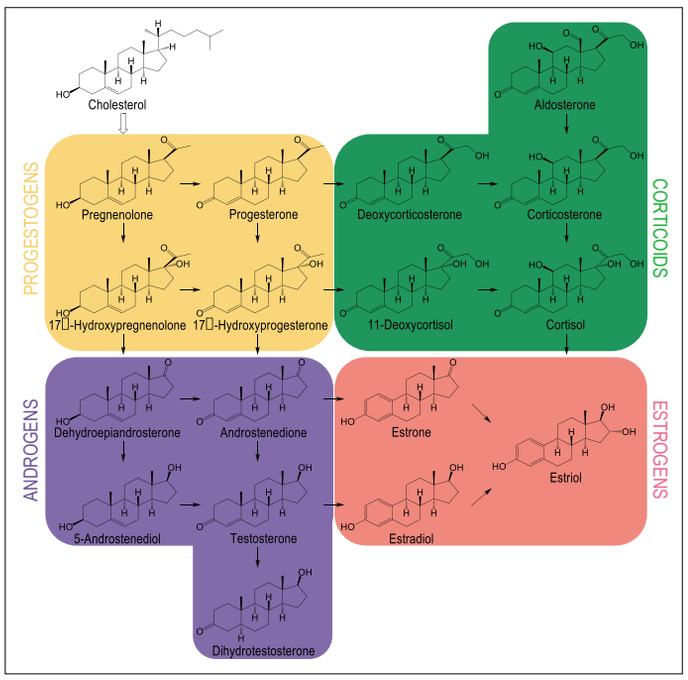
*Correspondence: Dr. R. Nicoli, E-mail: raul.nicoli@chuv.ch; [a]Swiss Laboratory for Doping Analyses, Chemin des Croisettes 22, CH-1066 Epalinges; [b]School of Pharmaceutical Sciences, University of Geneva, Boulevard d'Yvoy, CH-1211 Genève

Keywords: Doping · Longitudinal follow-up · Steroid profiling · Steroidal passport · Testosterone

Testosterone, as the major sex hormone secreted by endocrine glands, constitutes the key male endogenous anabolic androgenic steroid. Nowadays, this compound still represents one of the most widely used doping agents in strength and endurance sports, mainly due to its anabolic action on skeletal muscles. Quantification of testosterone and its major precursors and metabolites in an athlete's urine samples by GC-MS(/MS) is routinely achieved in anti-doping laboratories. To detect testosterone abuse in sport, the most sensitive biomarker is obtained by the glucuronidated testosterone over epitestosterone (T/E) concentration ratio. The latter is monitored over time using 'intra-individual reference values' for a more accurate evaluation of abnormal fluctuations that may indicate steroid misuse. This approach constitutes the so-called 'steroidal module' of the Athlete Biological Passport.

To overcome well-known weaknesses of this 'urinary steroid profile', such as genetic polymorphism (lack of enzyme responsible for testosterone glucuronidation), the monitoring of biosynthetic and metabolic pathways of testosterone in blood matrix could constitute a complementary approach. In this research, pills and patches of testosterone have therefore been administered to healthy volunteers and, after serum sample collection, selected endogenous blood steroid levels were monitored by LC-MS(/MS) with the aim of highlighting relevant biomarkers of exogenous testosterone abuse in the blood matrix. By applying multivariate data analysis, testosterone and especially dihydrotestosterone concentrations in serum were highlighted as significantly influenced by testosterone administration. Monitoring these two hormone levels in a longitudinal manner demonstrated that intra-individual reference values were clearly exceeded following testosterone administration compared to negative control (same person in the absence of administration).

Testosterone doping and its anabolic action.



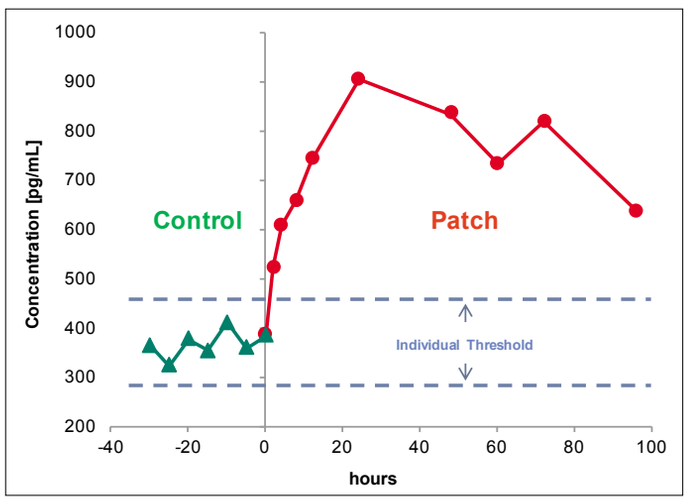
Steroidogenesis: processes by which cholesterol is converted to biologically active steroid hormones.

Results of this work show how the future implementation of a longitudinal follow-up of endogenous steroids in the blood matrix could increase the capabilities of anti-doping laboratories for detecting exogenous testosterone administration.

Received: December 14, 2015

Reference

F. Ponzetto, F. Mehl, J. Boccard, N. Baume, S. Rudaz, M. Saugy, R. Nicoli, *Anal. Bioanal. Chem.* **2016**, *408*, 705.

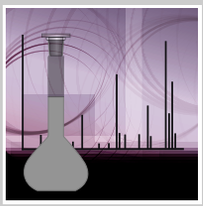


Example of a longitudinal profile in serum in the presence (red) or absence (green) of testosterone patch administration.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2016.293



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Dedicated Software Enhancing Data-independent Acquisition Methods in Mass Spectrometry

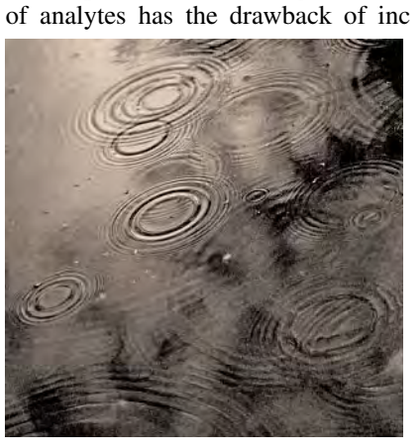
Aivett Bilbao[ab], Frédérique Lisacek*[bc], and Gérard Hopfgartner*[a]

*Correspondence: Prof. Dr. G. Hopfgartner[a], E-mail: Gerard.Hopfgartner@unige.ch; Dr. F. Lisacek[b], E-mail: Frederique.Lisacek@isb-sib.ch; [a]Life Sciences Mass Spectrometry, Department of Inorganic and Analytical Chemistry, University of Geneva, 30, quai Ernest-Ansermet, CH-1211 Geneva 4; [b]Proteome Informatics Group, SIB Swiss Institute of Bioinformatics, CMU, rue Michel Servet, CH-1211 Geneva; [c]Computer Science Department, University of Geneva, Geneva

Keywords: Data-independent acquisition · Interference removal · Metabolomics · Proteomics · SWATH · Variable-precursor-isolation-window widths

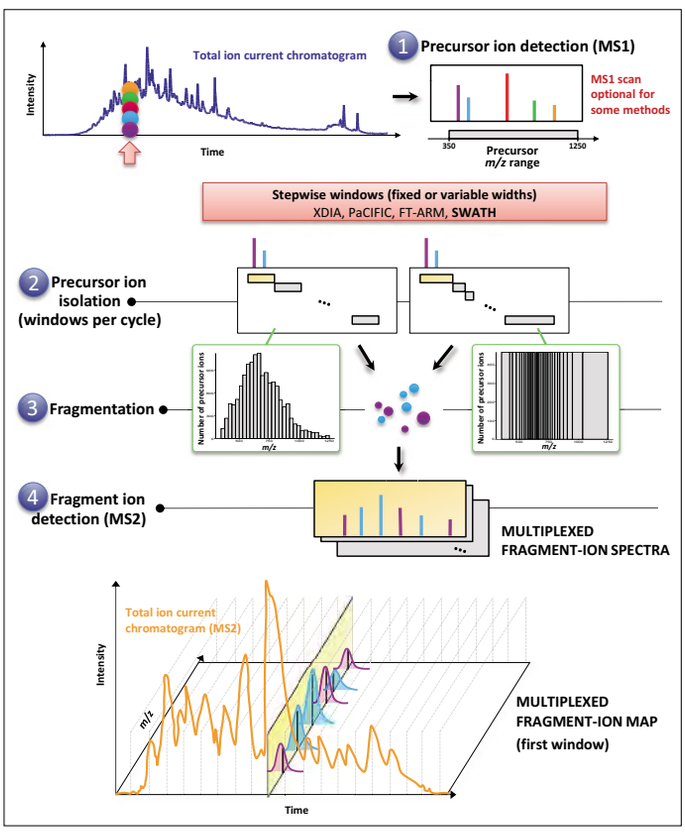
Mass spectrometry combined with liquid chromatography has become the main analytical platform to characterize proteins and low-molecular-weight compounds in complex samples. In proteomics and metabolomics, samples are commonly analyzed by data-dependent acquisition (DDA) methods. However, the intensity-based semi-stochastic selection of precursor ions favors highly abundant analytes while under-sampling the low-abundance ones. In contrast to this sequential detection, selection, and analysis of individual ions, alternative data-independent acquisition (DIA) methods systematically parallelize the fragmentation of all detectable ions within a wide mass range regardless of their intensity. The mass spectra recorded by DIA are a continuous map of multiplexed fragment chromatographic profiles of all detectable analytes. Therefore, DIA integrates qualitative and quantitative information, providing broader dynamic range of detected signals, improved reproducibility for identification, and better sensitivity and accuracy for quantification.

Despite these advantages, the concurrent fragmentation of analytes has the drawback of increasing the likelihood of interference due to the overlap of fragment ions from different precursors. We developed two solutions to tackle this issue and further expand the benefits of DIA.



Analogy for cross fragment ion interference. Several waves causing interference to each other. Photo: quapan (*https://www.flickr.com/photos/hinkelstone/7001475448*), sepia recolor.

The first solution comprises a program called SwathTUNER, implemented to design and optimize different DIA methods using stepwise isolation windows (*e.g.* SWATH). The benefits of utilizing acquisition methods with variable-precursor-isolation-window widths were demonstrated for the profiling of proteomic and metabolic samples.



Data-independent acquisition using stepwise isolation windows. Green boxes show examples of the frequency distribution of all detected precursor ions in a run for methods using fixed or variable widths optimized with SwathTUNER.

The second solution is the 'non-outlier fragment ion' (NOFI) ranking algorithm. NOFI assigns low priority to fragment ions affected by interference during DIA acquisition. The optimal subset of high-priority fragment ions defined by NOFI effectively excludes interfered fragment ions from quantification. Improvement for label-free quantification was illustrated on a well-defined quantitative dataset and on a biologically relevant cell digest.

DIA methods coupled with adequate software solutions deliver comprehensive information in a single-shot analysis to study the full range of small to large molecules and unravel biological processes.

References

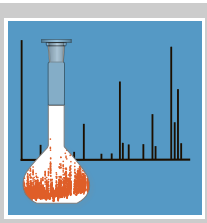
A. Bilbao, E. Varesio, J. Luban, C. Strambio-De-Castillia, G. Hopfgartner, M. Müller, F. Lisacek, *Proteomics* **2015**, *15,* 964.

Y. Zhang, A. Bilbao, T. Bruderer, J. Luban, C. Strambio-De-Castillia, F. Lisacek, G. Hopfgartner, E. Varesio, *J. Proteome Res.* **2015**, *14,* 4359.

A. Bilbao, Y. Zhang, E. Varesio, J. Luban, C. Strambio-De-Castillia, F. Lisacek, G. Hopfgartner, *J. Proteome Res.* **2015**, *14,* 4581.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2016.365



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Tracking New Halogenated Alkenes in the Atmosphere

Martin K. Vollmer*, Stefan Reimann, Matthias Hill, Brigitte Buchmann, and Lukas Emmenegger

*Correspondence: Dr. M. K. Vollmer, Empa, Swiss Federal Laboratories for Materials Science and Technology, Überlandstrasse 129, CH-8600 Dübendorf, E-mail: martin.vollmer@empa.ch

Keywords: Gas chromatography/mass spectrometry · Greenhouse gases · Ozone depletion · HFC-1234yf

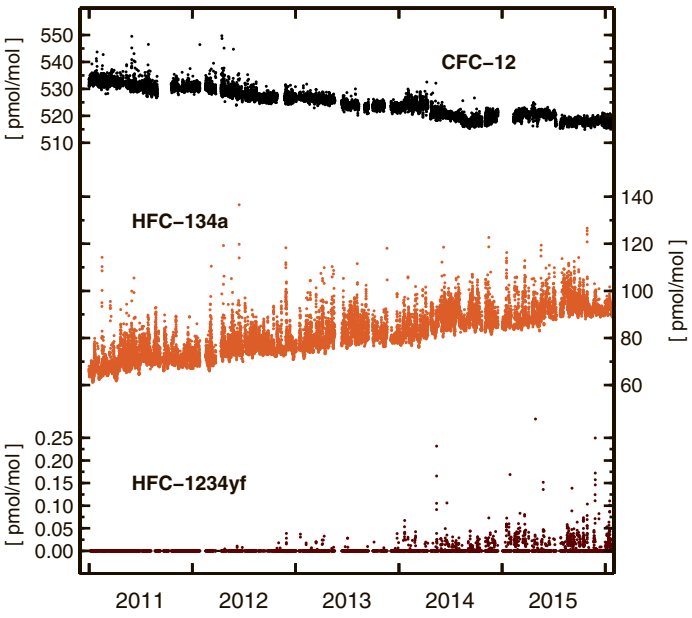
Many halogenated trace gases in the atmosphere are potent stratospheric ozone-depleting substances and greenhouse gases. For many of them, international regulations on their usage and emissions are in place such as the Montreal and Kyoto Protocols. Consequently, over the last decades some compound classes were phased out from usage while others were newly introduced.

At Jungfraujoch we started world-wide first measurements of newly-produced halogenated alkenes (also referred to as hydrofluoroolefins, HFOs), a subgroup of the hydrofluorocarbons (HFCs). These compounds were recently marketed for replacing currently-used HFCs in refrigeration, foam blowing, and as solvents. In comparison to currently-used HFCs, halogenated alkenes have shorter atmospheric lifetimes (days vs years) and lower Global Warming Potentials (GWP_{100}, <10 vs 100s to 1'000s).

We measure HFC-1234yf (2,3,3,3-tetrafluoroprop-1-ene), HFC-1234ze(E) (E-1,3,3,3-tetrafluoroprop-1-ene), and HCFC-1233zd(E) (E-1-chloro-3,3,3-trifluoroprop-1-ene) along with ~50 other halogenated trace gases using gas chromatography coupled with quadrupole mass spectrometry (GC-MS) in selected ion mode. Every two hours, a fully-automated ambient air measurement is conducted and bracketed by similar calibration measurements using whole air working standards, which are linked to absolute calibration standards. Two liters of sample are preconcentrated on cold traps held at –150° C. The traps are subsequently heated to 100° C to release the compounds of interest into the GC-MS.

An example is the highly-debated replacement of HFC-134a (1,1,1,2-tetrafluoroethane) by HFC-1234yf as refrigerant in mobile air conditioners. We have captured the phase-in of HFC-1234yf usage within the air-mass footprint at Jungfraujoch, which covers large parts of Europe. At the same time we track the phase-out of the oldest generation refrigerant CFC-12 (dichlorodifluoromethane) and we monitor the currently used HFC-134a in the atmosphere.

High-altitude research station Jungfraujoch, Switzerland. Image source: jungfrau.ch



Time series at Jungfraujoch of three generation refrigerants used in mobile air conditioning. HFC-1234yf (2,3,3,3-tetrafluoroprop-1-ene), a newly marketed compound, is still undetectable (<0.003 picomol/mol) in most air samples arriving at the site.

A widespread use of HFC-1234yf and other halogenated alkenes may be expected in the near future. While the short atmospheric lifetimes of these halogenated alkenes are favorable from a climate perspective, little is currently known about the fate of the decay products of these compounds.

Continuous atmospheric monitoring of halogenated alkenes is necessary to estimate regional emissions and distribution patterns of these compounds and their decay products in the atmosphere.

Acknowledgements

We acknowledge funding by the Federal Office for the Environment (FOEN), the Swiss National Science Foundation (SNF) and support by the International Foundation High Altitude Research Stations Jungfraujoch and Gornergrat (HFSJG).

Received: March 11, 2016

References

M. K. Vollmer, S. Reimann, M. Hill, D. Brunner, *Environ. Sci. Technol.* **2015**, *49*, 2703.

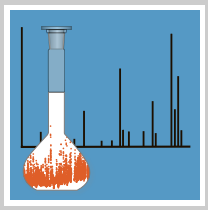
M. K. Vollmer, T. S. Rhee, M. Rigby, D. Hofstetter, M. Hill, F. Schoenenberger, S. Reimann, *Geophys. Res. Lett.* **2015**, *42*, 1606.

F. Schoenenberger, M. K. Vollmer, M. Rigby, M. Hill, P. J. Fraser, P. B. Krummel, R. L. Langenfelds, T. S. Rhee, T. Peter, S. Reimann, *Geophys. Res. Lett.* **2015**, *42*, 7817.

M. K. Vollmer, M. Rigby, J. C. Laube, S. Henne, T. S. Rhee, L. J. Gooch, A. Wenger, D. Young, L. P. Steele, R. L. Langenfelds, C. A. M. Brenninkmeijer, J.-L. Wang, C.-F. Ou-Yang, S. A. Wyss, M. Hill, D. E. Oram, P. B. Krummel, F. Schoenenberger, C. Zellweger, P. J. Fraser, W. T. Sturges, S. O'Doherty, S. Reimann, *Geophys. Res. Lett.* **2015**, *42*, 8702.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2016.456



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

RASPP, a Fully Automated Platform Preparing Analytical Samples

Inken Plitzko*, Josef Schneider, Tom Kissling, Christian Bartelmus, Thomas Zumstein, and Roger Steiner

*Correspondence: Dr. I. Plitzko, Roche Pharma Research and Early Development, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd, Grenzacherstrasse 124, CH-4070 Basel, E-mail: Inken.Plitzko@Roche.com

Keywords: Automation · Robotics · Sample Preparation · SiLA

Up to now automation of laboratory workflows has rarely included preparation of NMR samples. Therefore we developed RASPP (Roche Automated Sample Preparation Platform), a system which prepares three analytical samples (NMR, GC-MS, LC-MS) from one delivery sample (Fig. 1).

A setup of third-party components and in-house developed elements, running on a SiLA-conform scheduling software (Standardization in Lab Automation), allows all steps and challenges of this process to be addressed and to prepare several samples in parallel for optimal time efficiency.

In a first step the sample is identified by its barcode, which connects to the electronic lab notebook (ELN) and to the AWM (Analytical Workflow Manager, Waters®) LIMS system (Fig. 2). In parallel, weighing indicates if the sample comes with (enough) solvent. This allows samples to be processed that are already dissolved, for example those needing solvents other than $CDCl_3$ or d_6-DMSO, as they are not provided by RASPP. According to the information extracted, deuterated solvent is then added up to a fixed volume. d_6-DMSO is dispensed under N_2 flow, since the following high-impact ultrasound treatment which facilitates the dissolution otherwise leads to line-broadening in the NMR spectra. A potential cause is the formation of oxygen radicals and subsequent degradation of DMSO.[1,2]

Photo documentation of the dissolved sample takes place before the solution is distributed to NMR tubes and GC-/LC-MS vials – the LC-MS samples being diluted with MeCN/H_2O. Noteworthy is that the (de)cappers for those vials were developed in-house and an NMR tube capper is unprecedented (Fig. 3).

A printer labels the prepared samples with their unique LIMS number as they are distributed to respective autosampler racks. This ensures reliable tracking of samples at all times. In the end a CSV (comma-separated values) file is created and (*via* pipeline pilot script) translated directly into spectrometer work-lists.

Key to the success of this system is the efficient integration of the information flow, providing all information needed for set-up and interpretation of spectra from the ELN of the sample provider to the instrument software and to the LIMS system, in which submissions and finally the results are filed. **RASPP has replaced labor-intensive and error-prone manual sample preparation by a reliable and fully documented process.**

Received: April 5, 2016

References

[1] C. Mésangeau, S. Yous, B. Pérès, D. Lesieur,, T. Besson, *Tetrahedron Lett.* **2005**, *46,* 2465.

[2] A. Weissler, *J. Am. Chem. Soc.* **1959**, *81,* 1077.

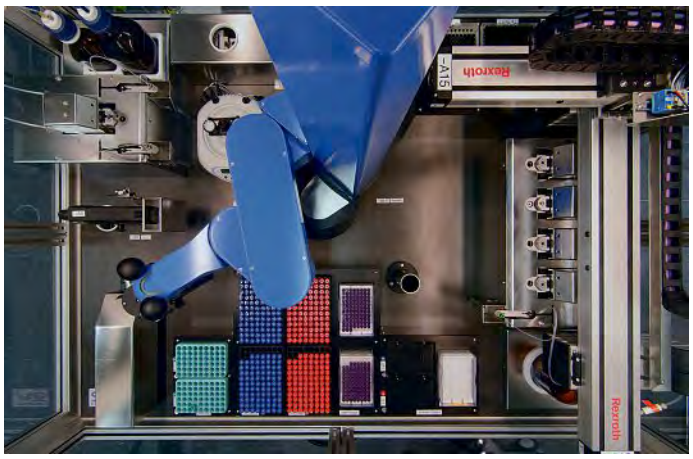


Fig. 1. Birds-eye view of RASPP.

Fig. 2. Barcode reading, weighing, and photo documentation.

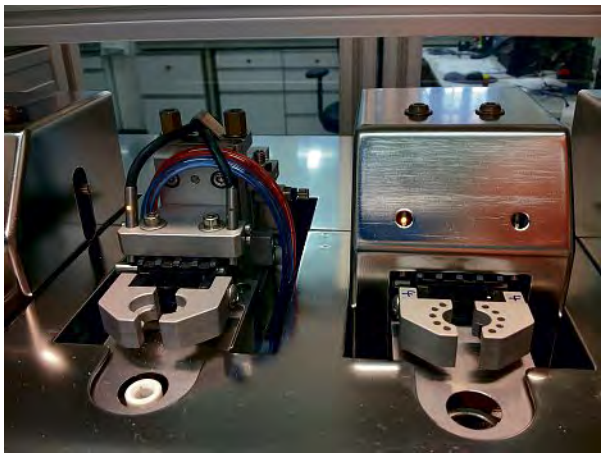
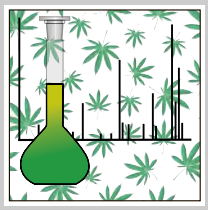


Fig. 3. In-house developed (de)cappers for vials and NMR tubes.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2016.554 Chimia 70 (2016) 554



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Assessing Cannabis Consumption Frequency: Is the Quantification of Free and Glucuronidated THCCOOH in Blood the Key?

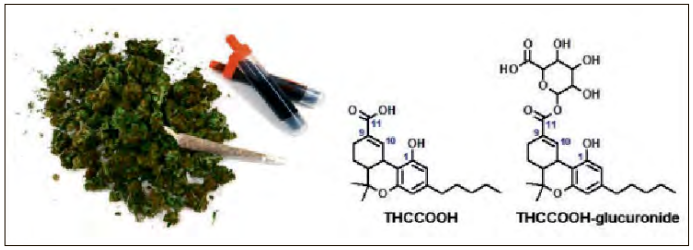
Marianne Hädener*, Wolfgang Weinmann, and Stefan König

*Correspondence: M. Hädener, Institute of Forensic Medicine, University of Bern, Bühlstrasse 20, CH-3012 Bern, E-Mail: marianne.haedener@irm.unibe.ch

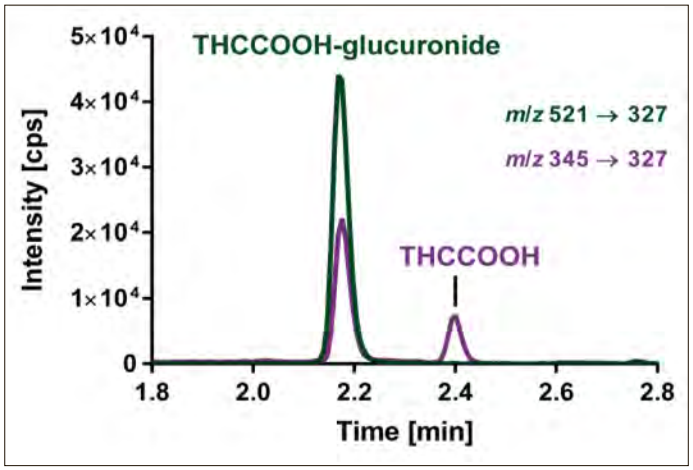
Keywords: Blood analysis · Cannabis consumption frequency · Column-switching chromatography · LC-MS/MS

Knowledge of the consumption behavior of cannabis consumers is important in many forensic and clinical circumstances, for example for deciding on medical treatment or administrative and legal consequences, such as suspension of the driver's license. The concentration of the cannabis metabolite 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (THCCOOH) serves as a diagnostic marker to distinguish between occasional and frequent smokers. In Switzerland, a THCCOOH blood level of 40 µg/L is currently used by forensic experts as decision limit for regular consumption. However, this threshold concentration was found to be correlated with a low sensitivity. Therefore, an additional and/or enhanced indicator of cannabis consumption frequency would be beneficial. Since THCCOOH in blood is extensively glucuronidated, we assume that the blood level of THCCOOH-glucuronide could serve as an additional parameter for assessing the frequency of cannabis use. To verify this assumption, we have developed a column-switching LC-MS/MS method for the simultaneous quantification of free and glucuronidated THCCOOH in whole blood.

The use of a trapping column for on-line sample enrichment and purification and an analytical column for separation and detection allows us to prepare blood samples by a simple protein precipitation step without sample preconcentration by evaporation and reconstitution. Employing two columns, each containing a different stationary phase, provides the needed selectivity to obtain excellent separation of the two analytes within a total run time of only 4.5 min. Detection of the analytes is accomplished by electrospray ionization in positive ion mode and selected reaction monitoring using a triple-stage quadrupole mass spectrometer.



11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (THCCOOH) and its glucuronide conjugate are metabolites of Δ^9-tetrahydrocannabinol (THC), the major psychoactive component of cannabis. Their quantification in whole blood is of interest for interpreting cannabis consumption behavior.



Chromatogram of an authentic whole blood specimen from a cannabis consumer (THCCOOH, 97.6 µg/L; THCCOOH-glucuronide, 296 µg/L). The purple peak at 2.16 min corresponds to the THCCOOH fragment originating from in-source decay of the glucuronide.

This method was used to analyze blood samples from a controlled cannabis administration study and therefore provided the required pharmacokinetic data for investigating the suitability of free and glucuronidated THCCOOH as indicators of cannabis consumption frequency.

Column-switching chromatography combined with tandem mass spectrometry allows for simultaneous and ultra-rapid quantification of THCCOOH and THCCOOH-glucuronide in whole blood, requiring only minimal sample pre-treatment, and offers new possibilities for assessing cannabis consumption behavior.

Received: May 13, 2016

Reference

M. Hädener, W. Weinmann, S. Schürch, S. König, *Anal. Bioanal. Chem.* **2016**, *408*, 1953.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2016.660 Chimia 70 (2016) 660

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Real Time Read-Out of Plant Metabolism

César Barrios-Collado[abc], Diego García-Gómez[a], Renato Zenobi[a], Guillermo Vidal-de-Miguel[ad], Alfredo J. Ibáñez[ae], and Pablo Martinez-Lozano Sinues*[a]

*Correspondence: PD Dr. P. Martinez-Lozano Sinues[a], E-Mail: pablo.mlsinues@org.chem.ethz.ch

[a] ETH Zurich, Department of Chemistry and Applied Biosciences, D-CHAB, HCI E 331, CH-8093 Zurich; [b] SEADM S.L., Valladolid, Spain; [c] Department of Energy Engineering and Fluid Dynamics, University of Valladolid, Spain; [d] Fossil Ion Technology S.L., Madrid, Spain; [e] Instituto de Ciencias Ómicas y Biotecnología Aplicada - Pontificia Universidad Católica del Perú, Lima, Perú

Keywords: Begonia plant · Mass spectrometry · Plant metabolism · Real-time analysis

To overcome the fact that they cannot move, plants have developed over years of evolution a chemical arsenal that enables them to communicate with each other and to defend themselves against external insult, such as pests. Such compounds are released to the ambient air and eventually reach their target (*e.g.* other plant, insect, *etc.*). Elucidating the underlying mechanisms of plant communication and defense is crucial, for example, to improve crop production. In order to do so, one needs to elucidate the metabolites released by plants upon certain stimuli.

The traditional way to do so is to sample the air surrounding the plant and analyzing the gaseous compounds by gas chromatography-mass spectrometry (GC-MS). GC-MS has been the workhorse for decades to decipher plants' volatile communications. However, the fact that GC-MS requires sample collection and further manipulation limits the opportunities to capture the highly dynamic processes in their full extent. Complementary to GC-MS, secondary electrospray ionization-mass spectrometry (SESI-MS) enables the analysis of gases in real time, down to parts-per-trillion (ppt) and without sample preparation. We have recently deployed SESI-MS to investigate the emissions of a *Begonia semperflorens* during three entire days, before as well as after mechanically damaging the leaves. As a result, hundreds of species could be tracked with an unparalleled time resolution of 2 min. Diurnal and nocturnal compounds can be clearly identified, as well as chemicals emitted upon piercing the leaves, mimicking insect attack.

The capability of SESI-MS to capture highly dynamic emissions of chemical species and its wide analyte coverage makes it an attractive tool to complement GC-MS in plant studies. SESI-MS provides valuable complementary real-time chemical information of plants metabolism without any sample manipulation.

Acknowledgements

We gratefully acknowledge Dr. Juan Zhang (Novartis AG) for the donation of the LTQ Orbitrap instrument used in this study and the European Community's Seventh Framework Programme (FP7-2013-IAPP) for funding the project 'Analytical Chemistry Instrumentation Development' (609691).

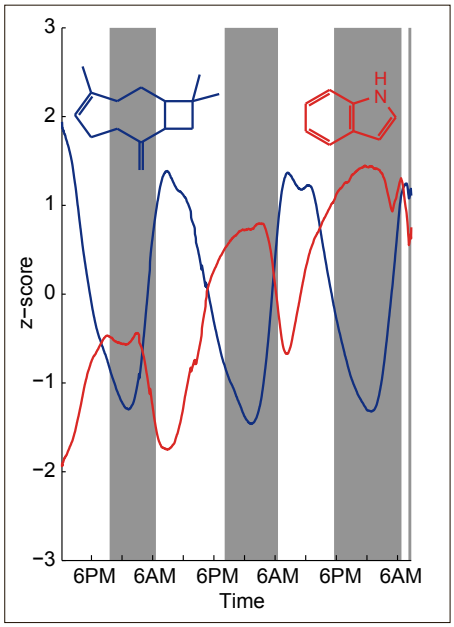
References

C. Barrios-Collado, G. Vidal-de-Miguel, P. Martinez-Lozano Sinues, *Sensors Actuators B: Chem.* **2016**, *223*, 217.

C. Barrios-Collado, D. García-Gómez, R. Zenobi, G. Vidal-de-Miguel, A. J. Ibáñez, P. Martinez-Lozano Sinues, *Anal. Chem.* **2016**, *88*, 2406.

Video link: *https://www.youtube.com/watch?v=UZyN1beyKjA*

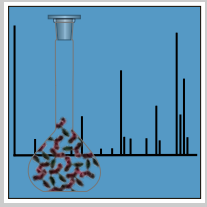
Begonia semperflorens within the container used to study its chemical emissions. During daylight it produces caryophyllene, among hundreds of other molecules.



Time profiles of caryophyllene (blue) and indole (red) illustrate typical diurnal and nocturnal patterns, respectively.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2016.731 Chimia 70 (2016) 731



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Rapid and Straightforward Quantification of Recombinant Proteins Using Fluorescence Polarization

Enrico Condemi[a], Denis Prim[a], Rebecca Brönnimann[b], Jonathan Fusco[a], Simon Crelier[a], Olimpia Mamula Steiner[b], and Jean-Manuel Segura*[a]

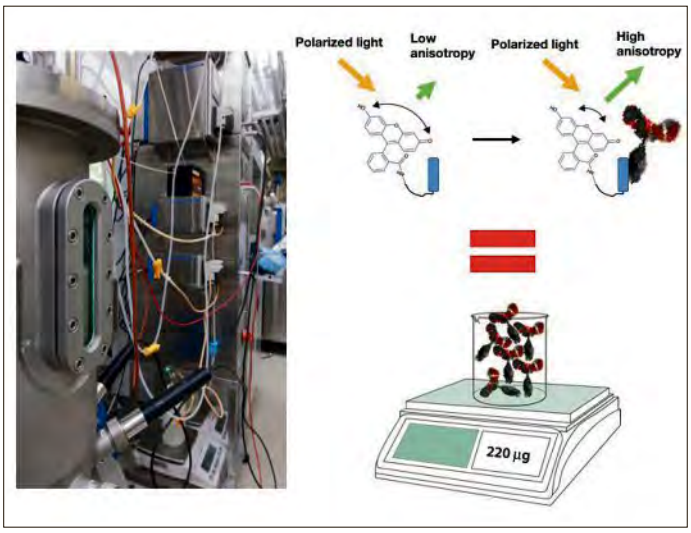
*Correspondence: Prof. Dr. J.-M. Segura, E-mail: jmanuel.segura@hevs.ch; [a]Institute of Life Technologies, University of Applied Sciences and Arts Western Switzerland Valais, Route du Rawyl 64, CH-1950 Sion; [b]Institute of Chemical Technology, School of Engineering and Architecture, University of Applied Sciences and Arts Western Switzerland Fribourg, Bd de Pérolles 80, CH-1705 Fribourg

Keywords: Antibodies · Assays · Biotechnology · Fluorescence · Recombinant proteins

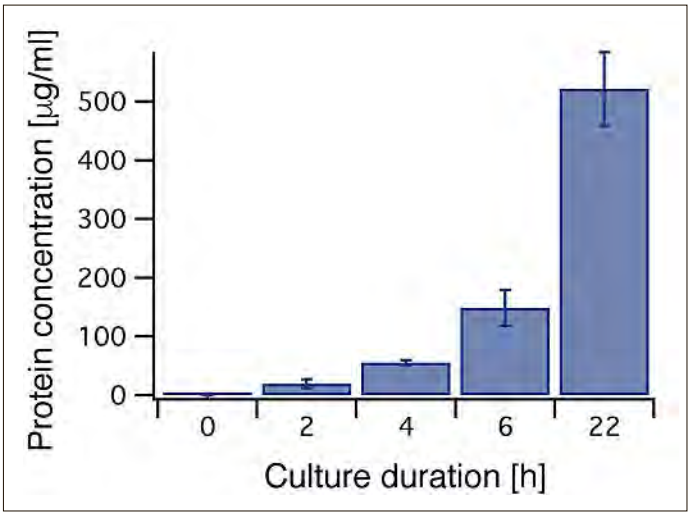
Biotechnology enables the production and commercialization of recombinant proteins for diagnostic, therapeutic and research applications. For instance, monoclonal antibodies nowadays represent a fast growing market that accounts for almost half of the biopharmaceutical compounds business with $75 billion turnover in 2013.

Quantification of proteins is an important task in order to optimize cell culture conditions and ensure that every step of the production process is in line with the specifications. For therapeutics, precise and reliable dosage is mandatory to avoid adverse effects for the patients. Current analytical techniques such as ELISA or HPLC are time-consuming and often require purification prior to analysis. In this context, there is a strong demand for a technology that would be to protein quantification what a balance is to weight measurement: rapid, precise, accurate, robust, and straightforward.

To this effect, we have developed an assay for the rapid quantification of recombinant proteins. It is based on fluorescence polarization and requires little or no pretreatment of samples.



Fluorescence anisotropy of a small specific fluorescent ligand increased upon binding to its recombinant target protein, *e.g.* a monoclonal antibody, enabling quantification. The assay did not require prior separation of biotechnological cultures making it as straightforward as weighing using a balance.



Monitoring of the production of a representative His-tagged protein during *E.coli* fermentation was obtained by regular sampling and assaying using the fluorescence polarization assay.

The technique makes use of the relationship between the size of a fluorescent molecule and the degree of polarization of its fluorescence when excited using polarized excitation light. Two small fluorescent ligands were designed and synthetized that specifically bind onto two particularly important recombinant protein classes, antibodies and His-tagged proteins. When these small ligands bound to their large recombinant target protein, a concomitant increase in fluorescence polarization anisotropy was recorded and enabled quantification. The assay did not require prior purification: For antibodies it was performed directly in the culture medium, while for His-tagged proteins it was done after the lysis of the bacterial cells. The measurement only required mixing of the specific ligand with typically 100 µL of cell culture in 96-well format, and enabled the concentration in target protein to be assessed within less than 15 min using fluorescence readers. Production of prototypical recombinant proteins could be monitored by regular sampling of the culture medium.

Rapid quantification using fluorescence polarization could be a key tool in the future for the efficient optimization and monitoring of bioprocesses.

Received: July 27, 2016

References

D. M. Ecker, S. D. Jones, H. L. Levine, *mAbs* **2015**, *7*, 9.
D. M. Jameson, J. A. Ross, *Chem. Rev.* **2010**, *110*, 2685.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2016.816 Chimia 70 (2016) 816

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Fast Survey of Radiostrontium after an Emergency Incident involving Ionizing Radiation

Johannes Abraham, Franziska Kammerer, Michael Wagmann, and Markus Zehringer*

*Correspondence: Dr. M. Zehringer, Kantonales Laboratorium Basel-Stadt, Kannenfeldstrasse 2, CH-4012 Basel, E-Mail: markus.zehringer@bs.ch

Keywords: Beta spectrometry · Emergency analysis · Radio strontium

Radiostrontium (mainly ^{90}Sr) is one of the radionuclides that is emitted when nuclear fission gets out of control. The main source is from bomb fallout. Radiostrontium was released to the environment from 1945 to 1970, when over 600 bombs were tested in the atmosphere. Nuclear accidents, such as the nuclear power plants of Chernobyl or Fukushima-Daiji, are another source of this artificial radionuclide. ^{90}Sr has a half-life of 30 years and is known as a bone seeker. Therefore, it is important to obtain ^{90}Sr-data within a short time after an emergency incident. The focus is then on analyzing the drinking water.

We extract the ^{90}Sr directly from the water sample with an organic solvent. It contains the crown ether dicyclohexano-18-crown-6 as an extracting agent and didodecylnaphthalene sulfonic acid as a scintillator. It is commercially available as STRONEX. 8 mL of this extracting solvent are sufficient to extract more than 70% of radiostrontiumfrom a 1L water sample. Interfering β-nuclides (such as ^{140}Ba) are eliminated by a scavenge with barium chromate prior to the extraction. Three hours after sampling, the first ^{90}Sr results are available. Twenty samples can be analyzed within 24 hours when using one liquid scintillation counter. With this method, it is possible to detect ^{90}Sr at a level of 0.1 Bq/L and higher. The working range is linear up to over 1'000 Bq/L.

Analysis of ^{90}Sr in drinking water by liquid/liquid extraction and β-spectrometry is fast and sensitive enough for emergency analyses. It is a reliable tool for the fast survey of drinking water after an emergency.

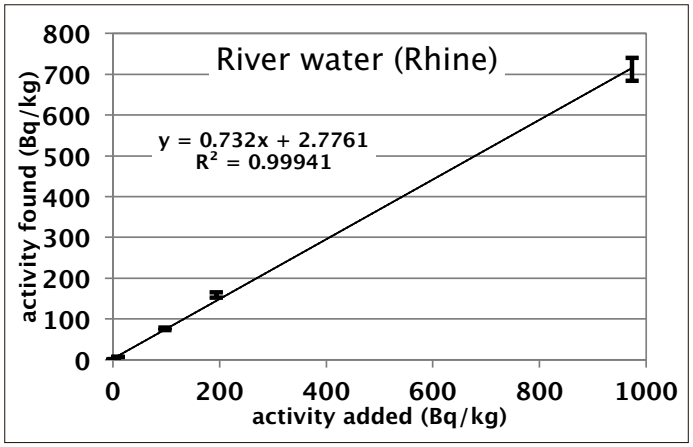
Nuclear power plant Fukushima-Daiji after the accident (photo TEPCO)

References

W. McDowell, *Sep. Sci. Technol.* **1988**, 22, 1251.

W. McDowell, 'Proposed separation and analysis scheme for strontium', ETRAC Inc., **1995**, *www.ordela.com.*

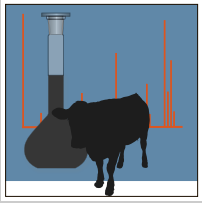
Microseparator system for the separation of the upper STRONEX phase from the water sample (yellow). The STRONEX is drained with the valve to the right.



Recoveries of ^{90}Sr in river water (error bars are the relative standard deviation of the liquid scintillation counting).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2016.899 Chimia 70 (2016) 899



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Soil Contamination with Trace Metals: Quantification, Speciation, and Source Identification

Moritz Bigalke*, Lorenz Schwab, Sebastian Gygax, and Adrien Mestrot

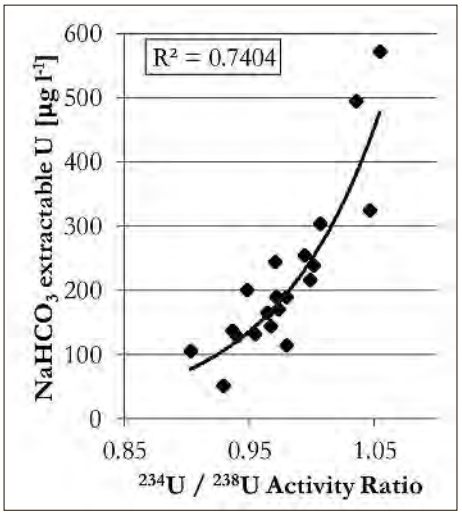
*Correspondence: Dr. M. Bigalke, Institute of Geography, University of Bern, Hallerstrasse 12, CH-3012 Bern, E-Mail: moritz.bigalke@giub.unibe.ch

Keywords: High performance liquid chromatography (HPLC) · Inductively coupled plasma-mass spectrometry (ICP-MS) · Soil contamination · Speciation · Stable isotopes · Trace metal

Trace metals can naturally occur in soils or become enriched by anthropogenic activities. These compounds can be transferred to plants and ground or surface waters and therefore reach humans. However, only measuring total concentrations is not sufficient to assess and control exposure pathways of trace metals. New analytical tools such as speciation and heavy stable isotope ratios are also essential. Indeed, identification of sources and tracing of pollutants using isotopes are important for legal reasons and also to understand their fate while identification and quantification of the different forms of trace elements are necessary since they possess different toxicity and mobility.

As one example we investigated the role of mineral-phosphate fertilizers for uranium concentrations and isotope ratios in agricultural soils by ICP-MS analysis. We could show that arable sites and surface soils of arable sites show significantly higher concentrations than grasslands and subsoils. Finally, a correlation of mobile ($NaHCO_3$ extractable) uranium with the $^{234}U/^{238}U$ activity ratio (AR; fertilizer-derived U has an AR ≈ 1–1.05) implies that fertilizers significantly add to mobile uranium.

We also analysed the speciation of mercury (Hg) in a contaminated agricultural floodplain in Valais, by coupling HPLC to ICP-MS. We developed and validated a new method to easily screen soils, biota and sediments for methylmercury (MeHg) concentrations above 1 µg/kg. We found that in our studied area, MeHg concentrations in soils vary between <LOD and 8 µg/kg. We could also show that these concentrations can be multiplied by a factor of 5 when agricultural sites are flooded in the presence of organic matter (cow dung).



Relationship between the mobile U fraction and the U activity ratio in arable soils.

Developing new analytical techniques to measure heavy stable isotope ratios or to quantify the different species of trace metals present in the environment is essential to understand, ultimately prevent, and limit trace metal pollution in the environment.

Acknowledgement

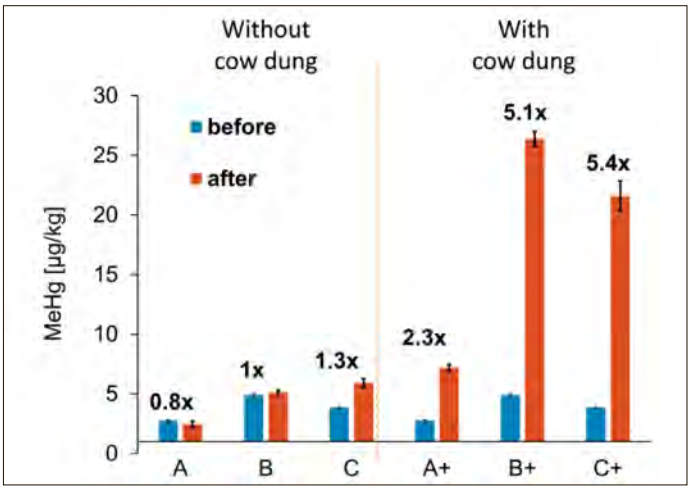
A.M. acknowledges funding from BAFU and from the IEF MCA of the EU's FP7/2007-2013/ n°[326736]: BIOMETA.

Received: October 4, 2016

Reference

M. Bigalke, A. Rehmus, A. Keller, 'Belastung mineralisch gedüngter Böden mit Schadelementen (Arsen, Blei, Cadmium, Uran)', Bundesamt für Landwirtschaft, Bern, **2016**.

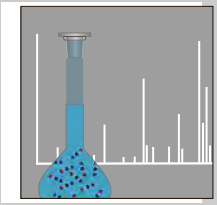
Sampling of arable soil for U isotope analysis.



Concentration of methylmercury (MeHg) in soils before and after an 11-day incubation under flooded conditions.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2017.46 Chimia 71 (2017) 46



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Using Isotopic Fingerprints to Trace Nitrous Oxide in the Atmosphere

Eliza Harris*[a], Lukas Emmenegger, and Joachim Mohn*

*Correspondence: Dr. E. Harris[a], Dr. J. Mohn, Laboratory of Air Pollution/ Environmental Technology, Empa Dübendorf, Überlandstrasse 129, CH-8600 Dübendorf, E-Mail: Eliza.Harris@uibk.ac.at, Joachim.Mohn@empa.ch. [a]Present address: Plant, Soil and Ecosystems Processes Research Group, Institute for Ecology, University of Innsbruck, Steinwartstr. 15, A-6020 Innsbruck

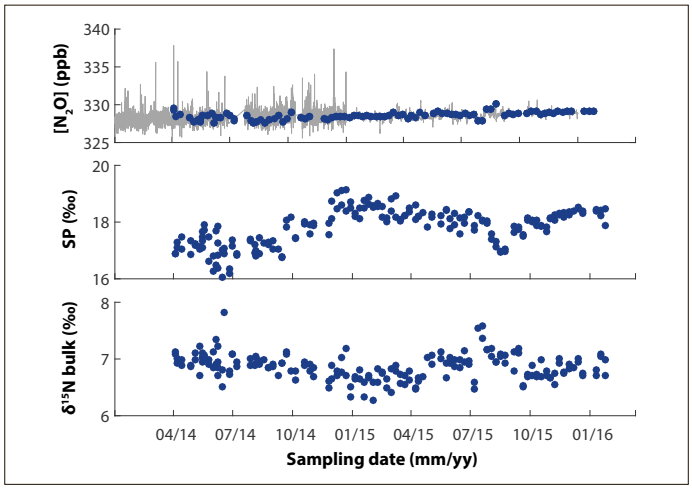
Keywords: Greenhouse gas · Isotope · Nitrous oxide · Spectroscopy

Nitrous oxide (N_2O) is an important greenhouse gas and a dominant contributor to stratospheric ozone destruction. Anthropogenic N_2O emissions arise from a range of activities, in particular, agriculture, fertilizer use, wastewater treatment, and energy production. The variability and partitioning of N_2O emissions between different source types is poorly understood, making it difficult to develop policies to efficiently reduce emissions.

Isotopic composition of N_2O is a tracer to distinguish between different emission processes and pathways, as well as constraining the stratospheric N_2O sink. N_2O is a linear molecule with four different 'isotopocules': $^{14}N^{14}N^{16}O$ (99%), $^{14}N^{15}\mathbf{N}^{16}O$ (α, 0.4%), $^{15}\mathbf{N}^{14}N^{16}O$ (β, 0.4%) and $^{14}N^{14}N^{\mathbf{18}}\mathbf{O}$ (0.2%). $N_2O(\alpha)$ and $N_2O(\beta)$ differ only in the position of the ^{15}N atom, and the difference in their abundance – known as site preference (SP) – can be a particularly powerful indicator for different N_2O production mechanisms.

We developed a quantum cascade laser absorption spectroscopy (QCLAS)-based technique for N_2O isotope measurements. QCLAS is inherently selective due to differences in fundamental rovibrational bands, even for molecules with the same mass. This technique thereby surpasses isotope ratio mass spectrometry, which does not allow for direct measurement of site-specific ^{15}N isotopic composition.[1] QCLAS allows real-time measurement and can be coupled to preconcentration for field-deployable monitoring of ambient air.

We applied QCLAS to measure N_2O isotopic composition in a number of studies, *e.g.*, to identify N_2O production pathways from a pilot-scale partial nitritation-anammox wastewater treatment system.[2] If N_2O production from these systems is minimized, wastewater treatment can be carbon-neutral. Since April 2014, we have been measuring N_2O isotopic composition at the high alpine site Jungfraujoch using QCLAS with preconcentration. The results show unexpectedly strong seasonal variability in site preference at this remote site, which is not captured by current models. Within an ongoing project, we plan to confirm this intra-annual variability by continuing the measurements.



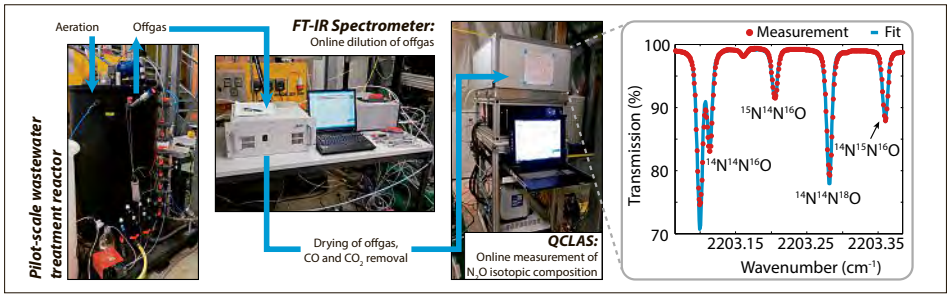
Top panel: Mole fraction of N_2O at Jungfraujoch. *In situ* measurements using GC-ECD (2014: Agilent 6890N) and off-axis ICOS (2015–16: LGR-23r, Los Gatos Research) are shown in grey (data credit: M. Steinbacher, Empa, Global Atmospheric Watch). Flask measurements made using QCLAS (Aerodyne Research, Inc.) are in blue. *Lower panels*: N_2O isotopic composition measured in flask samples using preconcentration coupled to QCLAS.

QCLAS offers the potential for high-precision analysis of N_2O isotopic composition in a wide range of applications, to trace emission and consumption pathways.

Received: November 10, 2016

[1] J. Mohn, B. Wolf, S. Toyoda, C. T. Lin, M. C. Liang, N. Brüggemann, H. Wissel, A. E. Steiker, J. Dyckmans, L. Szwec, N. E. Ostrom, K. L. Casciotti, M. Forbes, A. Giesemann, R. Well, R. R. Doucett, C. T. Yarnes, A. R. Ridely, J. Kaiser, N. Yosida, *Rapid Commun. Mass Sp.* **2014**, *28*, 1995.

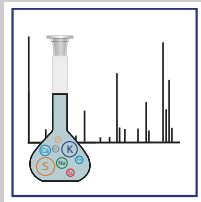
[2] E. Harris, A. Joss, L. Emmenegger, M. Kipf, B. Wolf, J. Mohn, P. Wunderlin, *Water Res.* **2015**, *83*, 258.



A schematic view of the analytical set-up used for online monitoring of isotopic composition in the off-gas from a pilot-scale partial nitritation-anammox reactor: Offgas from the wastewater treatment reactor is diluted online, using measurements from the FT-IR to scale the dilution, before continuous measurement of isotopic composition with QCLAS. At the right hand side, an example of a QCLAS spectrum is shown, illustrating the simultaneous quantification of all four isotopocules.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2017.131 Chimia 71 (2017) 131



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

A Powerful Tool to Better Understand Cement Hydration

Francesco Caruso*, Sara Mantellato, Marta Palacios, and Robert J. Flatt*

*Correspondence: Dr. F. Caruso, Prof. Dr. R. J. Flatt, ETH Zürich, Institut für Baustoffe (IfB), Physical Chemistry of Building Materials, Stefano-Franscini-Platz 3, CH-8093 Zurich, E-mail: francesco.caruso@iakh.uio.no, flattr@ethz.ch

Keywords: Cement · Chemical admixtures · ICP-OES

Concrete is the most widely used material in the world, after water, and is essential in the current society in terms of infrastructure and housing. Cement is the main binding component of concrete and its production represents more than 4 billion tons per year. In presence of water, cement hardens, conferring to concrete its excellent mechanical properties. Furthermore, polymeric dispersants, so-called superplasticizers, are widely used in concrete to increase its fluidity or reduce its permeability, thus enhancing its durability. These dispersants also decrease the environmental impact of concrete as they allow the reduction of cement content per unit volume. Despite such wide use, cement hydration involves a complex dissolution/precipitation process that has not been fully elucidated yet.

The elemental characterization of the cement pore solution is important for gaining insight into the thermodynamics and kinetics of cement hydration, and predicting the durability of concrete. Eight elements are of crucial interest: calcium, potassium, sodium, sulfur, aluminum, iron, magnesium, and silicon. The first four are present at a concentration in the order of several g/L, while the others are at a level of microtraces (µg/L), thus constituting a major analytical challenge.

Researchers and operators working in the field of cement broadly use Inductively Coupled Plasma – Optical (or Atomic) Emission Spectrometry (ICP-OES), because of its versatility and relative ease of use. Yet, an easy and robust ICP-OES method for characterizing cement pore solutions has been missing and awaited for a long time.

By properly accounting the matrix effects and the careful analysis of the spectral lines, our study provides for the first time experimental guidelines and analytical performances for a highly accurate and versatile ICP-OES method for the elemental characterization of cement pore solutions with and without the presence of admixtures. The quantification of some elements is improved by a factor 34 when compared with what is generally reported.

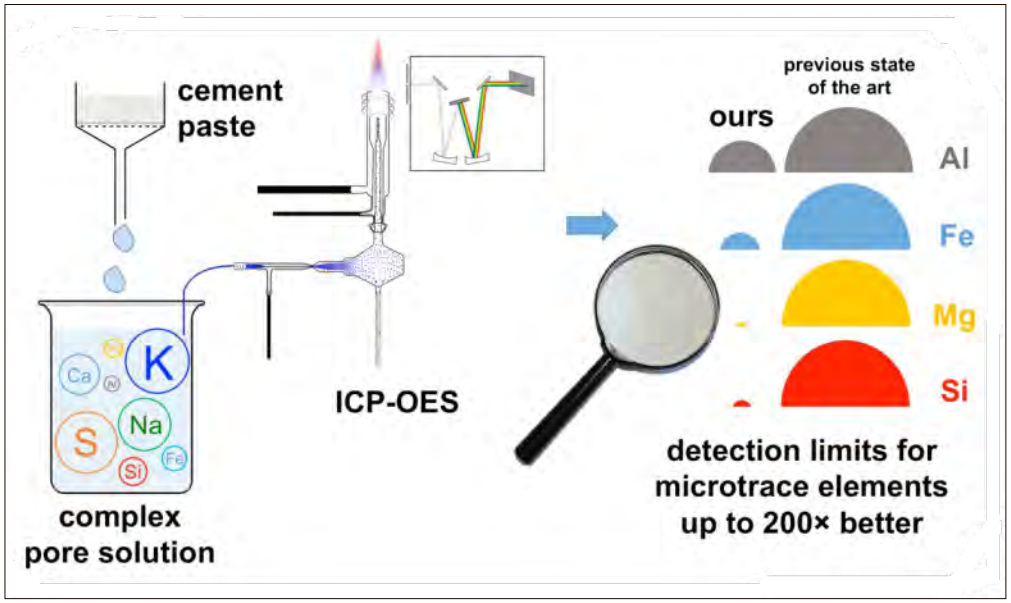
In pore solutions from admixed cement pastes, our ICP-OES method allowed us to accurately observe an increase of the microtrace elements. This could be due to the formation of nanoparticles that may consist of intramolecular complexes between the polymeric admixtures and polyvalent cations, as aluminum, iron, and magnesium. The formation can be expected to have important consequences on the working mechanisms of chemical admixtures such as superplasticizers.

Received: December 14, 2016

References

F. Caruso, S. Mantellato, M. Palacios, R. J. Flatt, *Cem. Concr. Res.* **2017**, *91*, 52.

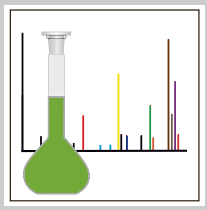
'Science and Technology of Concrete Admixtures', Eds.: P.-C. Aïtcin, R. J. Flatt, Woodhead Publishing, Cambridge, **2015**.



The proposed ICP-OES method allows the simultaneous, very accurate determination of high- (Ca, K, Na, S) and low-concentration (Al, Fe, Mg, Si) elements of the pore solutions from cement pastes, with and without superplasticizers.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2017.242 Chimia 71 (2017) 242



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Multimode Separation for Metabolomics and Complex Environmental Samples

Adrian A. Ammann[a] and Marc J.-F. Suter*[ab]

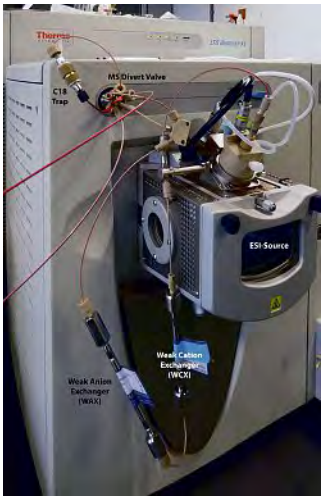
*Correspondence: Dr. M. J.-F. Suter, E-mail: marc.suter@eawag.ch; [a]Eawag, Swiss Federal Institute of Aquatic Science and Technology, Überlandstrasse 133, CH-8600 Dübendorf; [b]ETH Zurich, Swiss Federal Institute of Technology, Department of Environmental Systems Science, CH-8092 Zurich

Keywords: HILIC · Ion exchange · Multimode separation · Reversed phase · Universe of chemicals

To understand how organisms, for instance green algae, react to external stimuli, such as drugs, environmental pollutants or other stressors, it is necessary to monitor changes in their metabolome. Additionally, it is very often unknown what chemical in the environment caused an adverse effect on the physiological level. In both situations, the analytical method used should capture and analyze the 'universe of chemicals', since depending on the pH, both the endogenous metabolites and the environmental chemicals range from ionic and very polar to lipophilic with log K_{ow} greater than five. While a mixed-mode solid phase extraction allows this multitude of chemicals to be captured, there is today only a limited combination of different separation mechanisms available in one chromatographic run. By combining a C18 trap with two analytical columns, consisting of a mixture of C18 and weak anion (WAX) or cation exchange material (WCX), four separation mechanisms become available during the same run, including hydrophobic interaction (HILIC) at the beginning of the run. First, the injected sample is loaded onto the C18 trap which retains the non-polar part of the chemicals, while ionic and very polar material is passed on to the analytical columns. The gradient starts with 97% acetynitrile (ACN) and aqueous NH_4HCO_3 (3 mM) and ends at 10% ACN and 30 mM aqueous NH_4HCO_3. HILIC conditions are maintained down to 70% ACN followed by ion exchange chromatography given with the increasing ionic strength of the two eluents. At 21 min. the MS divert valve switches and now guides the eluents through the C18 trap, which starts the reversed phase chromatography with again increasing organic content. The chromatogram shows a nice separation of a standard mixture of 18 compounds, detected with a triple quadrupole mass spectrometer in multiple reaction monitoring mode.

The combination of two commercially available mixed-mode ion exchange/reversed phase columns together with a trap column allows separating complex chemical mixtures of metabolites and environmental pollutants in one run.

Batch culture of the green algae *Chlamydomonas reinhardtii*, grown in an incubator.



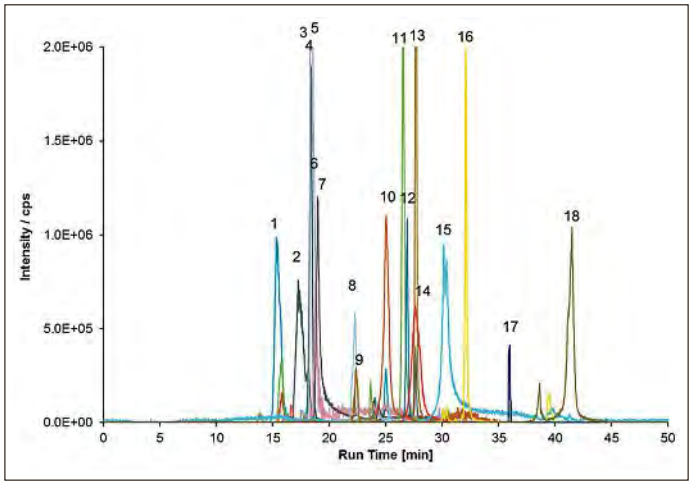
Front end of an Orbitrap MS with the trap column and the two ion exchange columns clearly visible.

Received: January 20, 2017

References

A. A. Ammann, M. J.-F. Suter, *J. Chromatogr. A* **2016**, *1456*, 145.

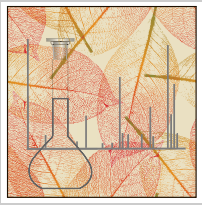
A. A. Ammann, P. Macikova, K. J. Groh, K. Schirmer, M. J.-F. Suter, *Anal. Bioanal. Chem.* **2014**, *406*, 7653.



Multimode separation chromatogram obtained from 18 standard compounds on a triple quadrupole mass spectrometer (multiple reaction monitoring): 1 phenylalanine, 2 ascorbic acid, 3 galacturonic acid, 4 glutamic acid, 5 cystine, 6 hexanoic acid, 7 glutathione, 8 glucose-1-phosphate, 9 glutathione disulfide, 10 lysine, 11 tryptophan, 12 sucralose, 13 fluconazole, 14 arginine, 15 cysteine, 16 clotrimazole, 17 tocopherol, 18 dodecyl sulfate.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2017.310 Chimia 71 (2017) 310



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

How Do Plants Know When to Let Go?

Sebastian Augustin and Julia Santiago*

*Correspondence: Dr. J. Santiago, University of Lausanne, Department of Plant Molecular Biology, UNIL-Sorge, CH-1015 Lausanne, E-mail: julia.santiago@unil.ch

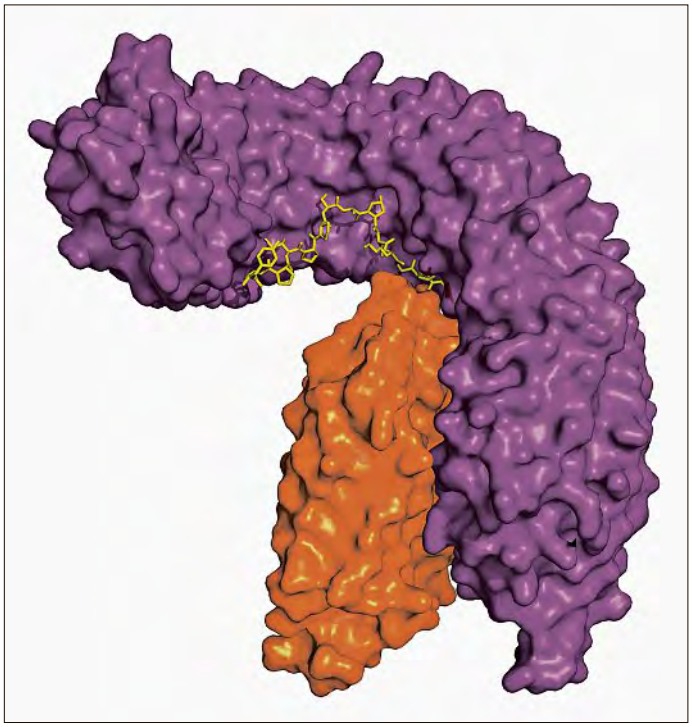
Keywords: Membrane receptor · Organ separation · Peptide hormone · Signaling complex · Structural biology

Plants have the capacity to renew themselves and get rid of damaged or no longer needed organs. By this mechanism plants conserve energy, spread their seeds and avoid the spread of pathogen infections. But when does a plant know when is the right time to let go? This process is specifically controlled by the receptor protein HAESA, located at the surface of specific cells that form a layer around the future break point. When it is time to shed an organ, a small hormone called IDA instructs HAESA to trigger the shedding event. Elucidating the underlying mechanism of this communication process will be crucial, for example, to optimize crop production by reducing fruit loss and synchronizing fruit harvesting.

Using protein biochemistry, structural biology and genetics we have uncovered the molecular details of this process. Our experiments show that the hormone IDA binds directly to a canyon-shaped pocket in HAESA. IDA binding to HAESA generates a new surface of interaction that is then recognized by another receptor protein called SERK1. SERK1 binding to the HAESA-IDA complex leads to the release of signals inside the cell that trigger the shedding of organs.

With the chemical mechanism at the atomic level at hand, we can now use this information to carry out rational drug design to generate compounds that mimic or antagonize the IDA hormone. This will represent a very powerful tool allowing us to control the process from the outside, for example, by watering or spraying with these compounds. The next step following on from this work is to identify and dissect what are the signals produced when IDA activates HAESA.

Activation of the HAESA receptor triggers the shedding of leaves in the fall.



Overall view of the three-dimensional structure of the active receptor complex. The receptor HAESA is depicted in deep purple, the hormone IDA in yellow, and SERK1 is highlighted in orange.

The combined use of protein biochemistry, structural biology and genetics offers a powerful combination to dissect and understand communication events in plants. This approach provides valuable information to allow for rational drug design to regulate physiological processes in plants.

Acknowledgement

We thank C. Henzler and L. Broger for technical assistance, and the staff at beam lines PXII and PXIII of the Swiss Light Source (Villigen, CH). We would also like to thank Paula Santiago for donating the 'forest in the fall' original picture. This work was supported by the Swiss National Science Foundation (grant no: 31003A_156920) and a long-term fellowship from EMBO.

Received: March 6, 2017

References

J. Santiago, B. Brandt, M. Wildhagen, U. Hohmann, L. A. Hothorn, M. A. Butenko, M. Hothorn, *eLife* **2016**, doi: 10.7554/eLife.15075.

M. A. Butenko, S. E. Patterson, P. E. Grini, G. E. Stenvik, S. S. Amundsen, A. Mandal, R. B. Aalen, *Plant Cell* **2003**, *15*, 2296.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen

Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2017.385 Chimia 71 (2017) 385

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Precision Diagnostics for Mobile Health Using Capillary-driven Microfluidics

Emmanuel Delamarche*, Yuksel Temiz, Onur Gökçe, and Yulieth Arango

*Correspondence: Dr. E. Delamarche, IBM Research – Zurich, Säumerstrasse 4, CH-8803 Rüschlikon, E-mail: emd@zurich.ibm.com

Keywords: Immunoassays · Microfluidics · Point-of-care diagnostics · Smartphone

Microfluidic technology may revolutionize point-of-care (POC) diagnostics owing to the precision with which small volumes of samples can be analyzed outside of centralized healthcare infrastructures. However, this potential will only be fully harnessed if biochemical reactions can be implemented on microfluidics in a way that supports (i) simple use, (ii) scalability to many types of assays, and (iii) interactivity with electronic devices such as smartphones and with the 'Internet of Things'. Our research has mostly focused on implementing immunoassays on capillary-driven microfluidic chips and led to creating a library of microfluidic functional elements and integrating reagents (capture antibody and detection antibody) to such chips. The assay methodology maps the approach used for lateral flow assays wherein biochemical reactions occur sequentially as a sample progressively wets a flow path and reconstitutes reagents.

We recently devised microfluidic chips having patterned electrodes for trapping microbeads functionalized with receptors using dielectrophoresis or monitoring flow in the chips. In this later case, wetting of parallel Pd electrodes affects the capacitance across the electrodes due to the ionic double layer. The capacitance is measured by a small peripheral and transmitted to a smartphone for real-time monitoring of flow conditions in the chip with sub-nanoliter precision.

Disposable, simple-to-use microfluidic chips for immunoassays represent a powerful enabling technology in combination with chip peripherals, smartphones, and modern information technology infrastructures such as cloud computing/storage and cognitive analytics, opening the door to game-changing strategies for health technologies on a global scale.

Acknowledgements

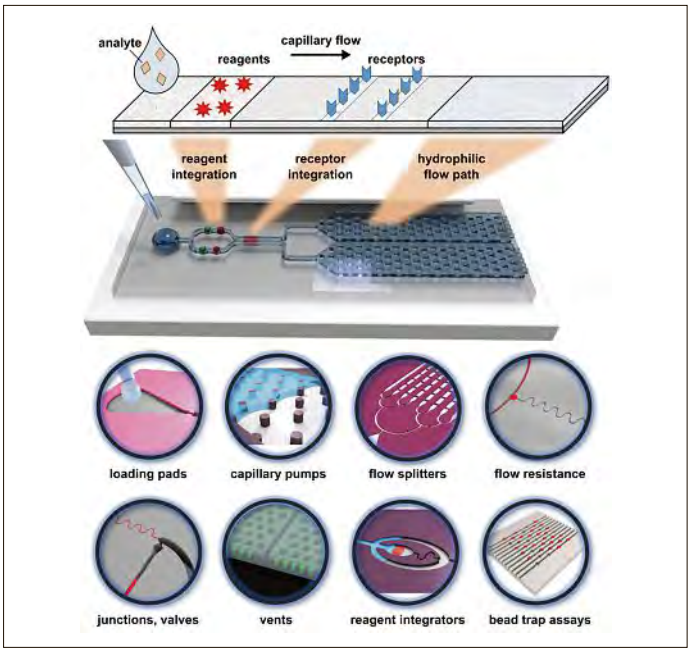
This work has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie Grant Agreement No. [701690].

Received: March 28, 2017

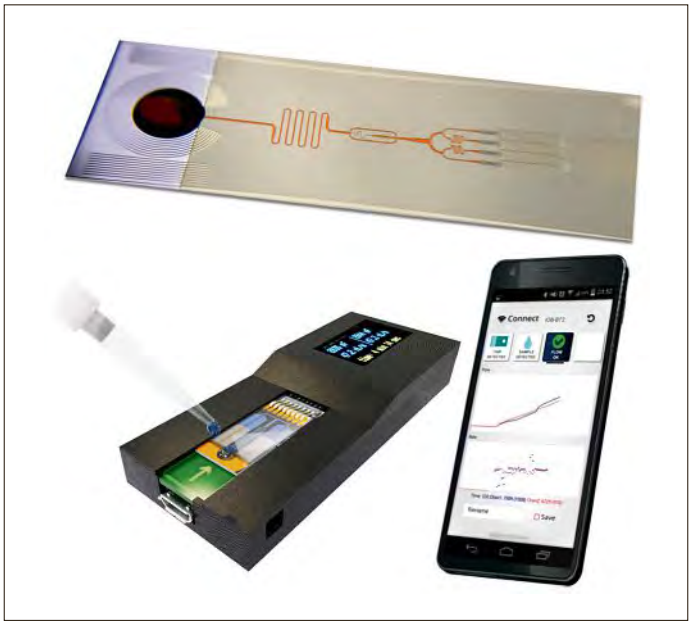
References

L. Gervais, E. Delamarche, *Lab Chip* **2009**, *9*, 3330.

Y. Temiz, M. Lim, E. Delamarche, *Proc. SPIE 9705, Microfluidics, BioMEMS, and Medical Microsystems XIV*, **2016**, 97050Z.



Immunoassays are implemented in capillary-driven microfluidic chips by defining a hydrophilic flow path through which a sample passes, dissolves detection antibodies, and forms an antigen–antibody complex on downstream capture antibodies. The flow path is modular and can be created using various assortments of microfluidic functional elements.



A microfluidic chip having patterned electrodes can be inserted on a small, low-cost peripheral for monitoring flow and reading assay results. Such a peripheral has a Bluetooth module, a microcontroller, and can communicate with a smartphone. This technology is broadly applicable to any ligand–receptor type of assay for the generation and analysis of precise data.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2017.507 Chimia 71 (2017) 507

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

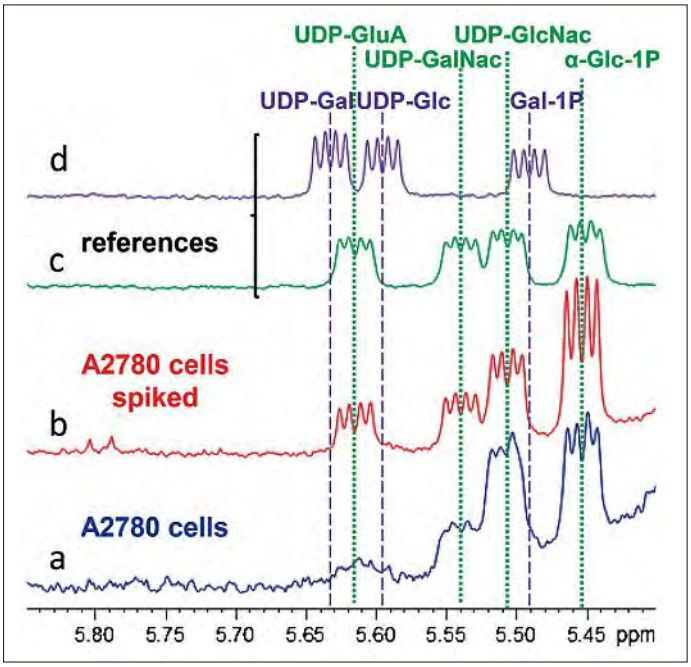
^{1}H High-resolution Magic-Angle-Spinning NMR Spectroscopy to Determine Phosphate Sugars in Biological Tissues and Cell Cultures

Gaëlle Diserens*[a], Martina Vermathen[b], Ilche Gjuroski[b], Sandra Kurth[c], Christina Precht[d], and Peter Vermathen[a]

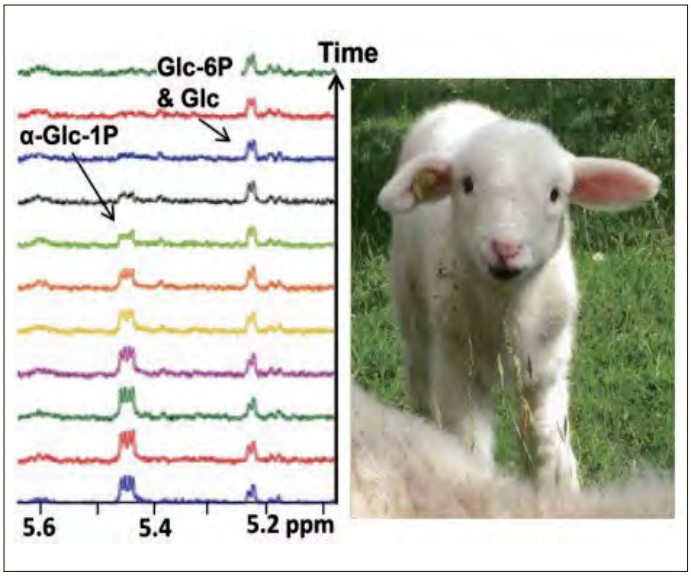
*Correspondence: Dr. G. Diserens[a], E-mail: gaelle.diserens@insel.ch; [a]Departments of Radiology and Clinical Research, University of Bern, Erlachstr. 9a, CH-3012 Bern; [b]Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern; [c]University Institute of Clinical Chemistry, Inselspital, CH-3010 Bern; [d]Department of Clinical Veterinary Medicine, University of Bern, Länggassstrasse 124, 3012 Bern

Keywords: Glucose phosphates · ^{1}H HR-MAS NMR · Nucleotide sugars · UDP-X

Nucleotide sugars, mainly those containing uridine diphosphate (UDP-X), are key players in glycosylation processes. Glucose phosphates (Glc-1P and Glc-6P) are intermediate metabolites of the glycogen cycle and as such important for storage and transfer of energy. Tissue biopsies and cells can be metabolically characterized by high-resolution magic-angle-spinning (HR-MAS) NMR. Temporal metabolite changes can be monitored by this technique, thus enabling metabolic pathway activities to be followed. ^{1}H HR-MAS NMR allows these phosphate sugars to be assessed qualitatively and quantitatively as a minimally invasive analytical tool, preserving the cell and biopsy integrity, as no extraction or separation steps are required.



Cell NMR spectra spiked with different phosphate sugars, confirming the presence of UDP-GluA, UDP-GalNAc, UDP-GlcNAc and α-Glc-1P. Reprinted with permission from Springer, Diserens *et al.*



Sheep cardiac muscle NMR spectra acquired over 3.5 h after biopsy, showing the evolution of the α-Glc-1P content.

Anomeric sugar protons bound to phosphate show the typical doublet of doublet resonances between 5.4 and 5.7 ppm. Due to similar patterns and only slight chemical shift differences of those peaks originating from different sugar phosphates, a correct assignment can be challenging. Therefore, the metabolite assignment was supported by spiking experiments.

The results of our study clearly demonstrated that sugar phosphates can be determined quickly and non-destructively in living cells and in biopsies by HR-MAS, including their quantitative estimation, without extraction processes. Considering the importance of phosphate sugars in cell metabolism for nucleic acid synthesis, HR-MAS measurements may prove valuable. Different phosphate sugars could be clearly separated from each other. In skeletal and cardiac muscle, the presence of α-Glc-1P and Glc-6P could be unambiguously assigned. The α-Glc-1P kinetics proves exemplarily the possibility of monitoring metabolic processes dynamically by ^{1}H HR-MAS NMR. As suggested by the kinetic analysis, the initial α-Glc-1P increase and subsequent decrease may be due to glycogen breakdown, followed by enzymatic conversion into Glc-6P and finally Glc through phosphoglucomutase. **^{1}H HR-MAS NMR allows the assessment of phosphate sugars contained *e.g.* in cells and skeletal and cardiac muscle biopsies, and facilitates the study of their kinetics for monitoring metabolic pathways.**

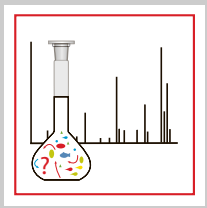
Received: May 22, 2017

Reference

G. Diserens, M. Vermathen, I. Gjuroski, S. Eggimann, C. Precht, C. Boesch, P. Vermathen, *Anal. Bioanal. Chem.* **2016**, *408*, 5651.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2017.601 Chimia 71 (2017) 601



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Quantification of Quaternary Ammonium Compounds Against Surrogate Matrix by HILIC-MS/MS

Christian Steuer*[a], Philipp Schuetz[b], Luca Bernasconi[c], and Andreas R. Huber[c]

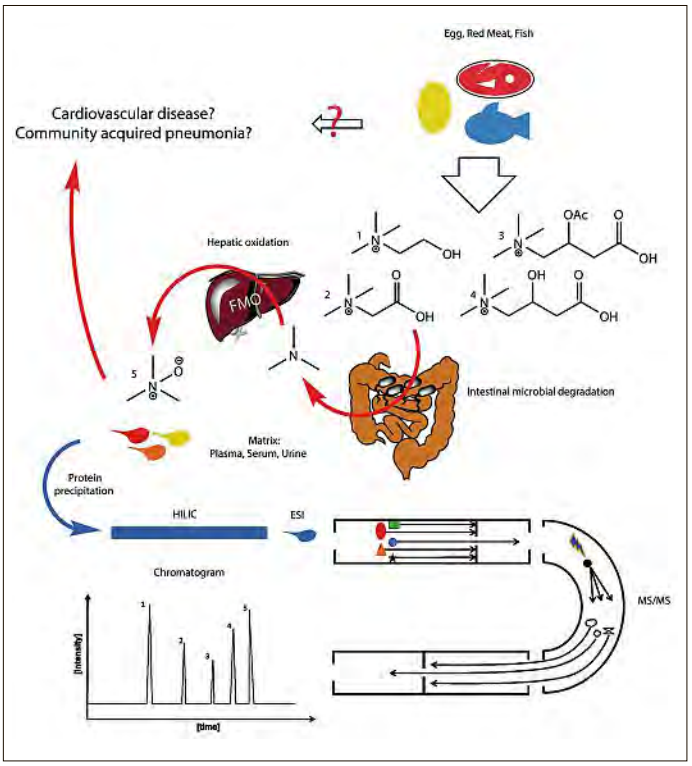
*Correspondence: Dr. C. Steuer, E-mail: christian.steuer@pharma.ethz.ch; [a]ETH Zurich, Institute of Pharmaceutical Sciences, Vladimir-Prelog-Weg 1-5/10, CH-8093 Zurich; [b]Kantonsspital Aarau, Medical University Department, Tellstrasse 1, CH-5001 Aarau; [c]Kantonsspital Aarau, Institute of Laboratory Medicine, Tellstrasse 1, CH-5001 Aarau

Keywords: Community acquired pneumonia (CAP) · HILIC · HPLC · MS/MS · Surrogate matrix · Trimethylamine-*N*-oxide (TMAO)

Metabolites like choline and its oxidized form betaine as well as other closely related quaternary ammonium compounds like L-carnitine and *O*-acetyl-L-carnitine, play a pivotal role in the synthesis of membrane phospholipids, energy metabolism, and as methyl group donators in a number of biosynthetic reactions. Choline, betaine, L-carnitine, and *O*-acetyl-L-carnitine are the main ingredients found in red meat, fish and many life-style products. Numerous studies have highlighted the protective effect of L-carnitine, choline and betaine on cardiac metabolism and performance. However, recent publications described the intestinal breakdown of choline, betaine and L-carnitine to trimethylamine by intestinal microorganism and subsequent oxidation to trimethylamine-*N*-oxide (TMAO) by flavin-monooxygenases (FMO) in the liver. Several researchers investigated the importance of TMAO in predicting cardiovascular events.

Due to the high polarity and low volatility of TMAO and its precursor, analysis is predominantly done by HPLC. As solid support, mostly hydrophilic interaction liquid chromatography (HILIC-), C4- or Phenyl-columns are used. In our opinion, HILIC chromatography seems to be the best method for the separation of the above-mentioned analytes. As solvent, a mixture of acetonitrile and water was used with ammonium formiate as buffer showing less background noise compared to ammonium acetate. After protein precipitation with acetonitrile and centrifugation, the supernatant was directly injected. Method validation was done according to international guidelines showing good results for selectivity, recovery and matrix effects. Calibration and quality control samples were prepared in water as surrogate matrix. Standard addition control experiments were performed to assure accuracy for non-matrix-matched calibration. The final calibration model was linear for all analytes.

The method was developed for analysis of plasma, serum and urine samples after overnight fasting. For urine samples, a 5-fold pre-dilution was necessary. In a well-defined study group, we could highlight a close association of TMAO with long-term fatal outcomes in CAP patients without coronary artery disease.



"You are what you eat": from plate to reader.

This LC-MS/MS multi-analyte approach allows the simultaneous and precise quantification of TMAO and its precursors in selected human fluids. Standard addition experiments for all matrices showed good correlation with calibrators prepared in water as surrogate matrix.

Received: June 30, 2017

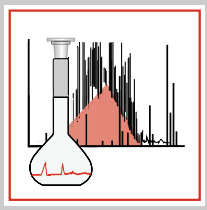
References

C. Steuer, P. Schuetz, L. Bernasconi, A. R. Huber, *J. Chromatogr. B* **2016**, *1008*, 206.

M. Ottiger, M. Nickler, C. Steuer, J. Odermatt, A. Huber, M. Christ-Crain, C. Henzen, C. Hoess, R. Thomann, W. Zimmerli, B. Mueller, P. Schuetz, *Eur. J. Intern. Med.* **2016**, *36*, 67.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2017.732 Chimia 71 (2017) 732



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Mineral Oil in Food – The Development of an Issue

Koni Grob*

*Correspondence: Dr. K. Grob, Kantonales Labor Zürich, P.O. Box, CH-8032 Zurich, E-mail: koni@grob.org

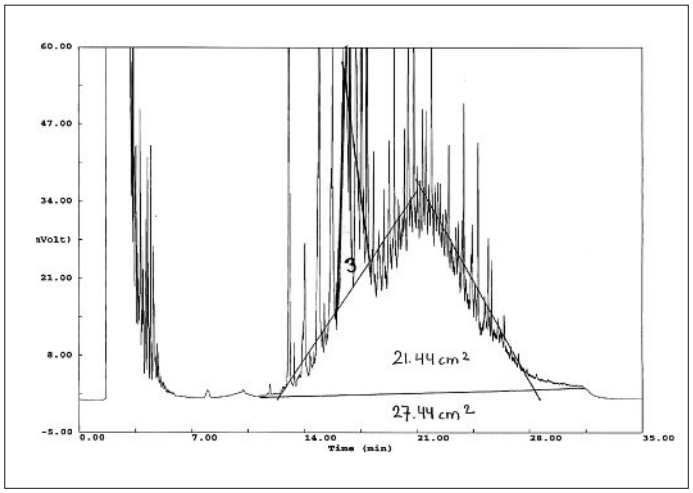
Keywords: Mineral oil saturated hydrocarbons (MOSH) · Mineral oil aromatic hydrocarbons (MOAH)

For many decades, 'clean' or 'food grade' mineral oil products were used rather carelessly, even though granuloma attributed to ingested mineral oil were widely observed in human tissues as far back as around 1950. This has changed dramatically: today mineral oil hydrocarbons are primarily considered as contaminants.

In 1989, it was detected that hazelnuts were contaminated from jute- and sisal bags made of fibers batched with rather crude mineral oils; chocolate sometimes contained several 100 mg/kg mineral oil. Typical batching oils included more than 30% mineral oil aromatic hydrocarbons (MOAH), among which genotoxic, largely alkylated polyaromatic hydrocarbons. Rice was sprayed with (white) mineral oil just to make it shiny (*ca.* 3000 mg/kg); industrial bakeries consumed truckloads of mineral oil products as release agents; used motor oils found their way into used frying oils added to animal feed and returned onto our plates with the meat or eggs. Milk powders for babies were contaminated from the recycled paperboard they were packed in. Over the years, all these contaminants were stopped or at least strongly reduced. There is, however, little that can be done against diesel oil and lubricating oil from diesel engines as well as debris from tires and bitumen contaminating our food.

For almost 20 years, the subject found little attention outside the Kantonales Labor Zurich (KLZ), mainly because of the demanding chemical analysis: on-line coupled HPLC-GC is the method of choice, a technique developed in the KLZ and until recently available only in few laboratories. Even the detection of mineral oil saturated hydrocarbons (MOSH) in human milk and human adipose tissue did not attract much attention. In 2008, mineral oil was added to Ukrainian sunflower oils, and all of sudden numerous laboratories had to analyze for mineral oils. This incidence was still not considered particularly serious, since only a further development of the on-line HPLC-GC method revealed the MOAH it contained but it triggered the EFSA opinion on mineral oils (completed in 2012).

Mineral oil contamination became an issue when the German BfR dealt with migration from recycled paperboard (at levels of 10–50 mg/kg food). The German ministry immediately drafted a regulation to get this migration under control, but did not succeed up to today. At this point, the issue heated up. Media reported



Mineral oil hydrocarbons in chocolate analyzed in 1993 by on-line HPLC-GC-FID and the graphical peak integration commonly used at that time. The narrow triangle (with inserted '3') primarily represents natural hydrocarbons in milk. Without these, the concentration corresponded to 42 mg/kg, which was typical by then, high values reaching hundreds of mg/kg.

and many laboratories bought HPLC-GC instrumentation to start analysis; ever-lower concentrations were considered critical.

The toxicity of MOSH was underestimated owing to strong accumulation in human tissues (determined in 2014): concentrations in livers and spleens are 100–1000 times higher than extrapolated from animal experiments. For the MOAH it was assumed that they include genotoxic constituents. This is confirmed for rather crude oils like those used for jute bags, but is questionable for better refined ones. This calls for a revision of the current reference values.

Mineral oil is the most common food contaminant, but still awaits adequate evaluation to conclude whether the strongly reduced present occurrence in foods can be tolerated.

Received: July 27, 2017

References

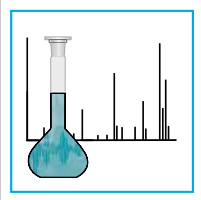
EFSA (European Food Safety Authority), CONTAM Panel, 2012. *EFSA J.* **2012**, *10*, 1 (2704). *http://www.efsa.europa.eu/en/efsajournal/pub/2704.htm*.

L. Barp C. Kornauth, T. Wuerger, M. Rudas, M. Biedermann, A. Reiner, N. Concin, K. Grob, *Food Chem. Toxicol.* **2014**, 72, 312.

L. Barp, M. Biedermann, K. Grob, F. Blas-Y-Estrada, U. C. Nygaard, J. Alexander, J. P. Cravedi, *Sci. Total Environ.* **2017**, 583, 319.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2017.778 Chimia 71 (2017) 778



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

ReGaS: SI-traceable Reference Mixtures of Reactive Trace Gases Produced by Mobile Generators

Céline Pascale, Daiana Leuenberger, Myriam Guillevic, Andreas Ackermann, and Bernhard Niederhauser*

*Correspondence: B. Niederhauser, Eidgenössisches Institut für Metrologie METAS, Lindenweg 50, CH-3003 Bern-Wabern, E-Mail: bernhard.niederhauser@metas.ch

Keywords: Dynamic generation · Expanded uncertainty · Permeation · Reference gas mixture · SI-traceability

To answer the needs of air quality and climate monitoring networks, three reference gas generators were developed and manufactured at METAS, dynamically producing reference gas mixtures for reactive compounds at atmospheric concentrations which are traceable to the international system of units (SI). These generators (Reactive Gas Standard ReGaS) can be applied for on-site calibrations of instruments in laboratories as well as in air quality monitoring stations. The technical features of the mobile generators allow the realization of such gas standards for reactive compounds (*e.g.* NO_2, NH_3, volatile organic compounds) in the nmol·mol^{-1} range (ReGaS1 and ReGaS2), and halogenated gases in the pmol·mol^{-1} range (ReGaS3).

The generation method is based on permeation and dynamic dilution. The purpose-built, multi-chamber permeation ovens of generators ReGaS2 and ReGaS3 allow for the generation of mixtures containing up to five different compounds. This mixture is then diluted using thermal mass flow controllers (MFC), thus making the production process easily adaptable to generate the required concentrations. All parts of ReGaS1 and ReGaS2 in contact with the gas mixture have been treated with a silica-based coating to reduce adsorption/desorption processes. Every input parameter relevant for the generation of the reference gas mixtures is calibrated with traceable standards at METAS. Therefore the molar fraction of the reference gas mixture with its associated uncertainty is traceable to the SI.

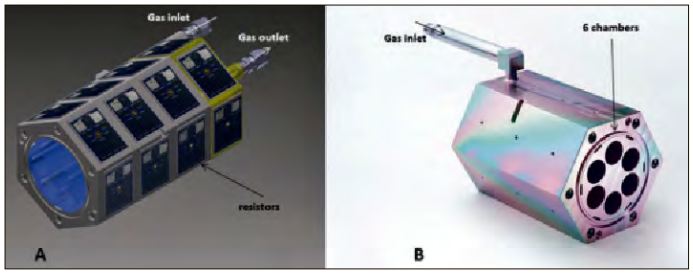
The stability and reproducibility of the generated amount fractions were tested with NH_3 for ReGaS1, NO_2 for ReGaS2 and HFC-125 for ReGaS3. They demonstrate stability over days better than 0.2%, 0.4% and 0.8%, respectively, and reproducibility better than 0.5%, 0.7% and 1%, respectively. Finally, depending on the analyte and concentration, the relative expanded uncertainty of the generated concentration is between 1.5% and 4% with the major contributions coming from the uncertainty of the permeation rate and/or of the purity of the matrix gas.

The reference gas mixtures can be used on-site for the calibration of measurement instruments at the relevant atmospheric amount fractions. The relative expanded uncertainties are sufficiently low for distinguishing long-term atmospheric trends recorded with high-resolution and high-precision instrumentation.

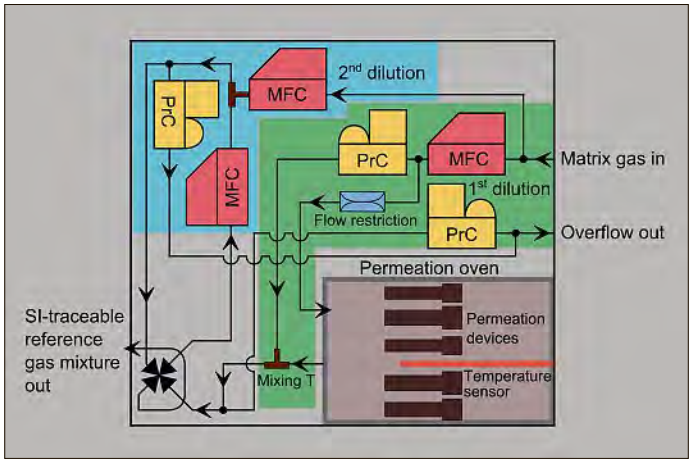
Received: September 11, 2017

Reference

C. Pascale, M. Guillevic, A. Ackermann, D. Leuenberger, B. Niederhauser, *Meas. Sci. Technol.* **2017**, in press: *https://doi.org/10.1088/1361-6501/aa870c*



(A) CAD design and (B) picture of the multi-chamber permeation oven in ReGaS2 and ReGaS3 with Silconert2000 coating allowing for the generation of up to five compounds simultaneously.



Scheme of ReGaS3. ReGaS3 has two dilution steps and a multi-chamber permeation oven for the generation of halogenated compounds at pmol/mol level. (MFC: mass flow control, PrC: pressure control.)

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2017.860 Chimia 71 (2017) 860

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

The Beginnings of Alpine Transhumance? Isotopic Insights into Neolithic Cattle Herding

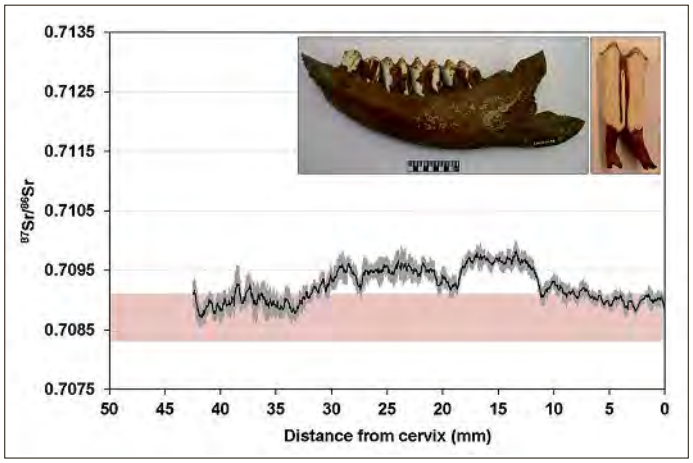
Claudia Gerling*[a], Thomas Doppler[a], Alistair W. G. Pike[b], Corina Knipper[c], Volker Heyd[d], Thomas Kuhn[e], Moritz F. Lehmann[e], and Jörg Schibler[a]

*Correspondence: Dr. C. Gerling, E-mail: claudia.gerling@unibas.ch. [a]Department of Environmental Sciences, University of Basel, Spalenring 145, CH-4055 Basel; [b]Department of Archaeology, University of Southampton, Avenue Campus, Highfield Road, Southampton SO17 1BF, UK; [c]Curt-Engelhorn Centre Archaeometry, D6,3, D-68159 Mannheim; [d]Department of Archaeology & Anthropology, University of Bristol, 43 Woodland Road, Bristol BS8 1UU, UK; [e]Department of Environmental Sciences, University of Basel, Bernoullistrasse 30, CH-4056 Basel

Keywords: High-resolution laser-ablation multi-collector inductively-coupled plasma mass spectrometry (LA-MC-ICP-MS) · Strontium and carbon isotopes · Wetland archaeology

The Neolithic period marks the initiation of sedentary lifestyles in central Europe and animal husbandry becomes one of the key elements of human society. In (sub)alpine environments, the development of the animal economy is tightly linked to the advent and rise of transhumance, *i.e.* the seasonal translocation of animals to grazing grounds above the timber line. The latter implies wide-ranging economic and social consequences.

To investigate early cattle husbandry and animal mobility in the Neolithic wetland sites of Switzerland, we applied strontium isotope analysis ($^{87}Sr/^{86}Sr$) to solid tooth enamel samples. The $^{87}Sr/^{86}Sr$ ratios in the tooth material reflect the $^{87}Sr/^{86}Sr$ of the geological environment and feeding grounds during different life periods of individual cattle. In order to obtain samples at the spatial and hence temporal resolution required to identify seasonal movements of cattle, we employed laser ablation (LA) inductively coupled plasma mass spectrometry (ICP-MS). A homogenized Ar-F 213nm laser with a spot size of 120 µm, fired at 10 Hz, is focused on the sample, which is then ablated continuously, while it is moved in the growth axis of the tooth. The ejecta are swept into the MS, where the Sr isotope ratio ($^{87}Sr/^{86}Sr$) is determined.



5400 year old cattle mandible, second molar extracted for strontium and carbon isotope analysis (Photo: C. Gerling) and $^{87}Sr/^{86}Sr$ cattle mobility pattern 2 (seasonal movement) at the Neolithic wetland site of Arbon Bleiche 3, Lake Constance (Gerling *et al. PLoS ONE* **2017**, *12*, e0180164, Fig. S1, Detail).

This allows many hundreds of analyses per cm of tooth, and in turn the assessment of Sr isotopic composition variations at a very high temporal resolution.

The combination of carbon and high-resolution strontium isotope analyses provided conclusive evidence for transhumance in the Neolithic. We were able to distinguish between three concurrent patterns of animal mobility and husbandry in the settlement of Arbon Bleiche 3 at Lake Constance (middle 4th Millennium BC), which suggest differential access to grazing resources: 1) localised cattle herding, 2) seasonal movement, and 3) herding away from the site year-round. We argue that the densely forested environment created pressure on local fodder capacities, making alternative herding strategies (*i.e.* transhumance) necessary. As a consequence, cattle had an increasing importance in the local landscape and were likely to have contributed to the progress of socio-economic differentiation in early agricultural societies in Europe.

The combined application of new and established analytical techniques thus provides high-resolution insights into prehistoric subsistence economies and people's way of life.

Alpine cattle economy (Photo: J. Schibler).

Acknowledgements

This work was supported by the Swiss National Science Foundation (CR12I2_143815/1) and enabled through the kind provision of sample material by the Archaeological Services of the Cantons Thurgau and Zurich.

Received: September 22, 2017

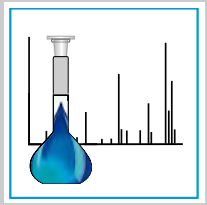
Reference

C. Gerling, T. Doppler, V. Heyd, C. Knipper, T. Kuhn, M.F. Lehmann, A.W.G. Pike, J. Schibler, *PLoS ONE* **2017**, *12*, e0180164.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2018.69 Chimia 72 (2018) 69



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

How to Apply Compound-Specific Isotope Analysis to Complex Environmental Samples

Violaine Ponsin*[a], Timothy E. Buscheck[b], and Daniel Hunkeler[a]

*Correspondence: Dr. V. Ponsin[a], E-mail: violaine.ponsin@unine.ch; [a]Centre for Hydrogeology and Geothermics (CHYN), University of Neuchâtel, Emile Argand 11,CH-2000 Neuchâtel; [b]Chevron Energy Technology Company, 6001 Bollinger Canyon Road, San Ramon, California 94583, United States

Keywords: BTEX · CSIA · Heart-cutting · Isotope ratio mass spectrometry · Multidimensional GC · Stable isotope

Compound-Specific isotope analysis (CSIA) is an increasingly applied tool to evaluate the origin and fate of volatile organic compounds such as benzene, toluene, ethylbenzene, and xylenes (BTEX), which are widespread contaminants in the environment. CSIA is commonly performed using a gas chromatograph coupled to an isotope-ratio mass spectrometer (GC-IRMS). The compounds eluting from the GC column are transformed into a single analyte before entering the source of the mass spectrometer (CO_2 for carbon, H_2 for hydrogen). Thus, an excellent chromatographic resolution is crucial for GC-IRMS to obtain accurate isotope measurements. BTEX present a great challenge for GC-IRMS because they occur as part of a complex mixture of hydrocarbons at most contaminated field sites. The objective of this study was to implement a two-dimensional heart-cutting GC hyphenated to an IRMS detector to analyze carbon isotope in BTEX in complex environmental samples (groundwater and gas-phase samples), *i.e.* with a high load of non-targeted compounds.

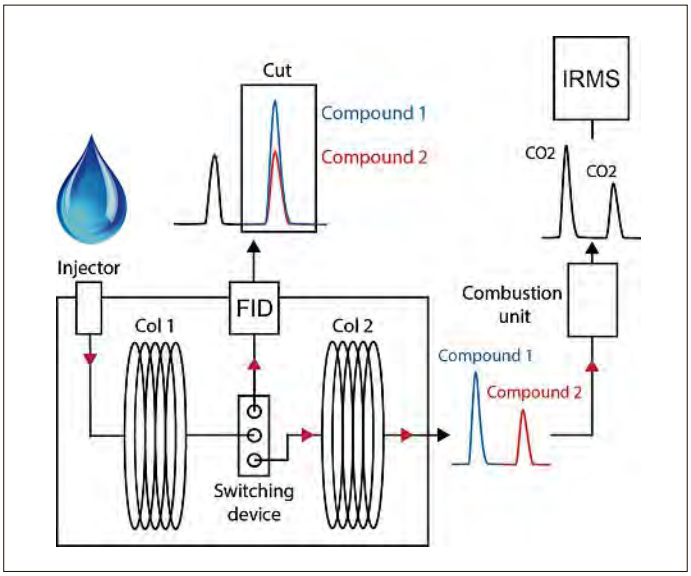
Accuracy of carbon isotope values measured with the newly implemented 2D-GC-IRMS system remained comparable to classic 1D-GC-IRMS whilst precision was still very high. Samples from two field sites were successfully analyzed, and substantial enrichment of ^{13}C in toluene was shown in some samples, which is a proof of *in situ* biodegradation by indigenous microorganisms. The final 2D-GC oven program was shorter than programs previously implemented for 1D-GC for similar compounds for a much better resolving capacity. Furthermore, there was no need for an additional oven for the second column as both columns lie within the same GC oven.

2D-GC-IRMS was successfully applied to groundwater and gas-phase samples that could not be analyzed by classic 1D-GC-IRMS for the determination of carbon isotope ratios in BTEX. This technique expands the spectrum of environmental samples suitable for isotope ratio measurements, and will provide new insights into attenuation processes of BTEX in contaminated sites.

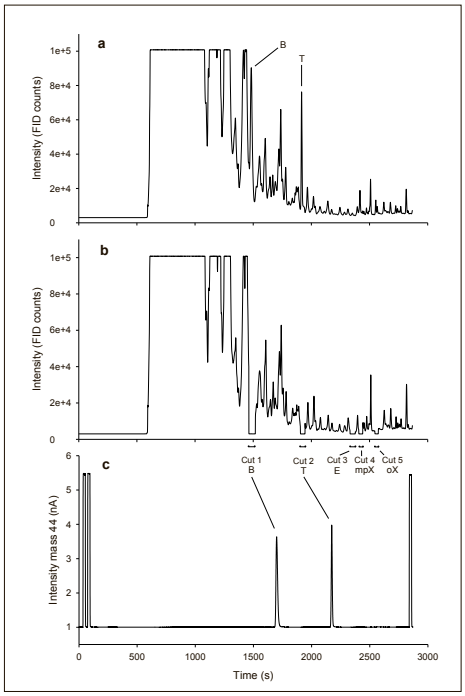
Received: November 29, 2017

Reference

V. Ponsin, T. E. Buscheck, D. Hunkeler. *J. Chromatogr. A* **2017**, *1492*, 117.



2D-GC-IRMS configuration for carbon isotope analysis. The switching device after the first column directs by default the flow to the FID detector. Compounds of interest are sent to the second column by heart-cuts defined according to their retention time on the first column, and then to the IRMS detector.

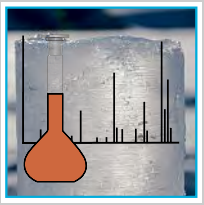


2D-GC–IRMS analysis of a gas-phase sample. a) FID chromatogram without heart-cuts, b) FID chromatogram with heart-cuts for BTEX and c), the corresponding IRMS chromatogram. Only benzene (B) and toluene (T) were sent to the IRMS. Reprinted with permission from Elsevier, Ponsin *et al.*, *J. Chromatogr. A* **2017**, *1492*, 117.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2018.152 Chimia 72 (2018) 152



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Ice-Core Evidence of Earliest Extensive Copper Metallurgy in the Andes 2700 Years ago

Anja Eichler*[ab], Gabriela Gramlich[abc], Thomas Kellerhals[ab], Leonhard Tobler[ab], Thilo Rehren[de], and Margit Schwikowski[abc]

*Correspondence: Dr. A. Eichler[ab], E-mail: anja.eichler@psi.ch. [a]Laboratory of Environmental Chemistry, Paul Scherrer Institute, CH-5232 Villigen; [b]Oeschger Centre for Climate Change Research, University of Bern, CH-3012 Bern; [c]Department of Chemistry and Biochemistry, University of Bern, CH-3012 Bern; [d]UCL Institute of Archaeology, 31-34 Gordon Square, London WC1H 0PY, UK; [e]College for Humanities and Social Sciences, HBKU Doha, Qatar

Keywords: Andes · Copper · Ice core · Metallurgy · South America

Access to metal is considered as a main driving force for the socioeconomic development of cultures and countries. Advances in agriculture, warfare, transport, cookery, and the entire Industrial Revolution would have been impossible without metal. Historically, Andean copper (Cu) in particular was an essential resource of wealth for pre- and post-colonial societies and still plays a central economic role in many South American countries today. Despite of this importance the onset of extensive Cu metallurgy in South America is still debated. Comprehensive archaeological findings point to first sophisticated Cu metallurgy during the Moche culture ~200–800 AD.

In 1999, a 138.7 m long ice core was retrieved from Nevado Illimani, the highest mountain of the eastern Bolivian Andes. In the −20 °C cold room at PSI, inner core sections (~2.2 × 2.2 × 70 cm) were cut out using a stainless steel band saw. Trace element concentrations were determined in the inner sections with continuous ice melting inductively coupled plasma-sector field-mass spectrometry (CIM-ICP-SF-MS). Based on the resulting highly time-resolved ice-core data from Illimani glacier, we reconstructed a 6500-years Cu emission history for the Andes, providing the first complete record of large-scale Cu smelting activities in South America.

Ice-core Cu originates from two different sources, namely wind erosion of Cu-containing mineral dust and anthropogenic emissions from mining and metallurgical processing. Cu enrichment factors above the natural dust background were derived by normalizing the Cu concentration with the concentration of cerium (Ce), a geogenic element present in mineral dust.

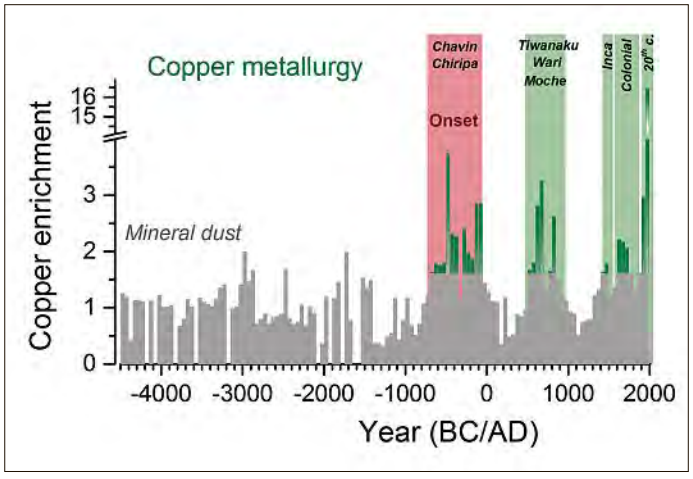
We find earliest anthropogenic Cu pollution during the Early Horizon period ~700–50 BC, and attribute the onset of intensified Cu smelting in South America to the activities of the central Andean Chiripa and Chavin cultures about 2700 years ago. Maxima in Cu enrichment factors were similarly observed during the times of later South American high cultures such as the Moche, Tiwanaku, Wari, and Inca, as well as during the colonial period and in the 20th century, matching the archaeologically known periods of increased metal production during the last two millennia. **Our study is the first one to provide substantial evidence for extensive Cu metallurgy in the Andes starting already 2700 years ago**.

Received: January 9, 2018

Reference

A. Eichler, G. Gramlich, T. Kellerhals, L. Tobler, T. Rehren, M. Schwikowski, *Nature Sci. Rep*. **2017**, *7*, 41855.

Earliest extensive Cu artefacts are known so far from the Moche culture in South America. Shown is a Moche belt ornament (Peru, 2nd–7th century AD), Credit: The Metropolitan Museum of Art, *www.metmuseum.org*, bequest of Jane Costello Goldberg, from the Collection of Arnold I. Goldberg, 1986.

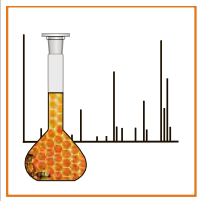


Illimani ice-core record of anthropogenic Cu emissions over the past 6,500 years in the Bolivian Altiplano. Shown are Cu enrichment factors (green) above the natural background from mineral dust (grey) during the flourishing of the pre-Columbian Chavin/Chiripa cultures (onset of Cu metallurgy), Tiwanaku/Wari/Moche cultures, the Inca, colonial times, and the 20th century.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2018.254 Chimia 72 (2017) 254



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Three-quarters of World's Honey Contain Neonicotinoids

Aline Mutabazi, Blaise Mulhauser, Matthieu Mulot, Alexandre Aebi, Edward A. D. Mitchell, and Gaétan Glauser*

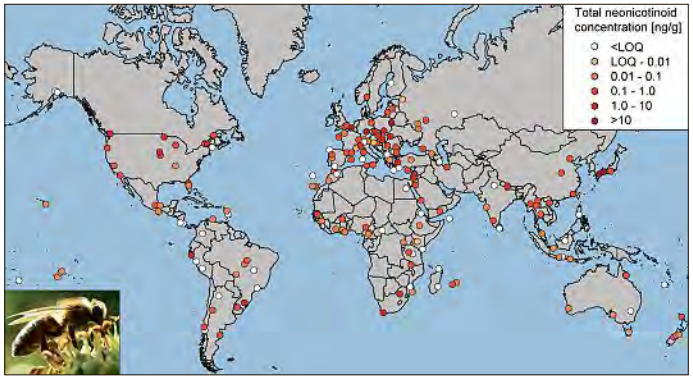
*Correspondence: Dr. G. Glauser, Neuchâtel Platform of Analytical Chemistry, Faculty of Sciences, University of Neuchâtel, Avenue de Bellevaux 51, CH-2000 Neuchâtel, E-mail: gaetan.glauser@unine.ch

Keywords: Bees · Honey · Neonicotinoids · UHPLC-MS/MS

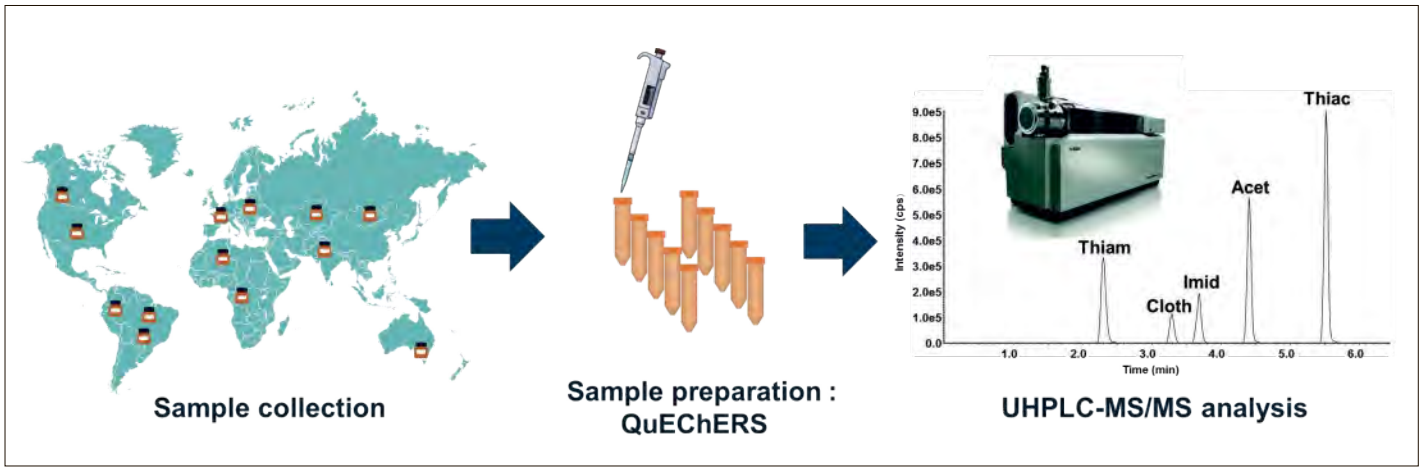
Since the discovery of imidacloprid in the late 1980s, neonicotinoids have become the most widely used insecticides in agricultural crop protection. Yet, in recent years there has been growing concern about the impact of these systemic pesticides on non-target organisms, especially on pollinators such as bees. Indeed, due to their physicochemical properties, neonicotinoids are translocated to all plant organs and can thus be found in pollen and nectar which are the only sources of nutrition for bees. To assess the risk posed by neonicotinoids for biodiversity and ecosystems, it is urgent to obtain a global view of their distribution in our environment.

In this study, we measured neonicotinoid concentrations in 198 honey samples collected from all around the world through a citizen science project led by the Botanical Garden of Neuchâtel. We focused on the five most commonly used neonicotinoids: acetamiprid, clothianidin, imidacloprid, thiacloprid and thiamethoxam. First, we developed and validated a stable isotope ultra-sensitive method able to quantify levels of neonicotinoids in the ppt range in honey. For this, a QuEChERS-based sample preparation followed by ultra-high performance liquid chromatography-tandem mass spectrometry was employed. Second, we determined the levels of each neonicotinoid in our honey samples. This revealed that 75% of the samples contained quantifiable amounts of at least one neonicotinoid, and that 45% contained more than one. While concentrations were in all cases below admissible limits for human consumption according to current EU and US regulations, they were in a range where significant detrimental effects on bees have been demonstrated. **Our results illustrate that advances in analytical techniques allow the detection of traces of pesticides which would have previously remained undetected, but are within the range now known to affect bees and other insects, thereby profoundly transforming our vision of ecological questions.**

Received: February 7, 2018



Worldwide distribution of honey contamination by neonicotinoids (reproduced from reference Mitchell *et al. Science*, **2017**, *358,* 109 with modifications). Picture of bee: Blaise Mulhauser.



Analytical workflow for the determination of neonicotinoid concentrations in honey.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2018.339 Chimia 72 (2018) 339

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

High-resolution, Non-destructive X-ray Tomography

Mirko Holler*, Manuel Guizar-Sicairos, Esther H. R. Tsai, Michal Odstrcil, Roberto Dinapoli, Elisabeth Müller, Ana Diaz, Oliver Bunk, Jörg Raab, and Gabriel Aeppli

*Correspondence: Dr. M. Holler, Paul Scherrer Institut, CH-5232 Villigen PSI, E-mail: mirko.holler@psi.ch

Keywords: Integrated circuits · Nano tomography · Ptychography · X-ray imaging

Ptychographic X-ray Computed Tomography (PXCT) is a lens-less microscopy technique that can fill the imaging gap between electron microscopy and conventional X-ray microscopy, *i.e.* imaging at high resolution in the 10 nm range in combination with tens of microns thick samples. The method provides quantitative information of the spatially resolved electron density in the sample in 3D. PXCT was pioneered at the Paul Scherrer Institut, and by now two dedicated microscopes have been constructed and are employed by internal and external users of the Swiss Light Source for scientific projects ranging from materials science to biology.

Many projections of the sample are acquired at different rotation angles by scanning it through a coherent X-ray beam and collecting far-field diffraction images. There is no imaging lens between the sample and the detector, the image is formed computationally from the diffraction images using iterative algorithms explicitly developed for this purpose. As a lens-less imaging method, PXCT bypasses limitations of X-ray optical systems, making it currently the X-ray microscopy technique with the highest spatial resolution.

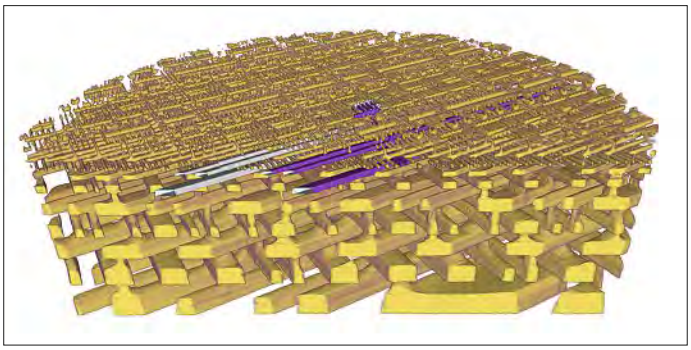
We are continuously exploring new fields of application of PXCT, one of them being non-destructive imaging of integrated circuits. As an example we show here the imaging of an Intel® processor (G3260) manufactured in a 22 nm node. Conventionally such samples are measured destructively in a FIB-SEM (focused ion beam, scanning electron microscope combination) using the slice-and-view technique. We extracted a 10 micron diameter pillar from the chip and using non-destructive PXCT achieved a resolution of 15 nm in 3D which allowed the identification of all electrical connections in the circuit down to the transistor layer. This measurement took 22 h, but with next generation synchrotron sources, improved X-ray optics and detectors, we expect the measurement speed to increase by orders of magnitude. In preparation we are currently building a new instrument in laminography geometry which will no longer require the extraction of a small pillar from the initially flat sample, such that the imaging volume will be purely determined by measurement time.

X-ray ptychography in laminography geometry and foreseeable improvements in imaging speed and resolution may make a significant contribution to chip inspection and lead to rapid and non-destructive imaging of integrated circuits for optimization of production processes, failure analysis and validation of chips used in critical application fields such as healthcare and aviation.

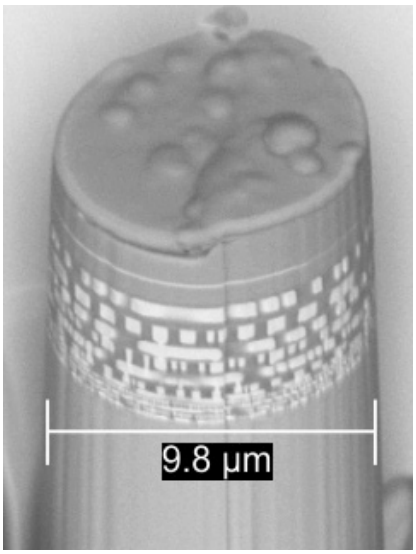
Received: February 27, 2018

Reference

M. Holler, M. Guizar-Sicairos, E. H. R. Tsai, R. Dinapoli, E. Müller, O. Bunk, J. Raabe, G. Aeppli, *Nature* **2017**, *543*, 402.



3D rendering of the internal structure of a microchip (metal components in an Intel processor). A piece of a G3260 processor of around 10 µm diameter was investigated. The layer at the top level shows where the transistors are located. The material in yellow is copper showing the processor's connections between individual transistors.



Chip sample pillar prepared by FIB-SEM for the X-ray measurement.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2018.425 Chimia 72 (2018) 425

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Analyzing Breath with Chemical Sensors

Jan van den Broek and Andreas T. Güntner*

*Correspondence: Dr. A. T. Güntner, Particle Technology Laboratory, Department of Mechanical and Process Engineering, ETH Zürich, Sonneggstrasse 3, CH-8092 Zurich, E-mail: andreas.guentner@ptl.mavt.ethz.ch

Keywords: Gas sensors · Medical diagnostics · Non-invasive · Volatile compounds

Non-invasive breath analyzers could facilitate rapid and routine disease screening for early stage detection and improved therapies. In fact, elevated breath concentrations of key molecules have been associated to physiological and pathological states, such as ammonia to kidney failure, acetone to diabetes and enhanced fat metabolism or NO to asthma, the latter being applied actively in today's clinical practice. Especially promising to detect these 'breath markers' are solid-state gas sensors due to their compact design and low cost, making them ideal for incorporation into wearable devices.

In specific, gas sensors based on chemo-resistive metal-oxides nanoparticles offer sufficiently low detection limits in the part-per-billion (ppb) range, fast response and recovery times (seconds to few minutes), however, they lack selectivity. This can be tackled for some tracers by material design (*e.g.* Si-doped WO_3 for acetone, Si-doped MoO_3 for ammonia), microporous filter membranes or the combination of sensors to arrays.

Recently, a filter-sensor system was developed for fast and highly selective breath isoprene detection. Isoprene is a promising marker for high blood cholesterol levels. The sensor system consists of a filter of activated alumina in combination with a non-specific but highly sensitive Pt-doped SnO_2 sensor. Isoprene is hydrophobic, in contrast to other major breath compounds including acetone, ammonia, ethanol and methanol. The filter exploits this by ab-/adsorbing and retaining them while isoprene passes unhindered and is registered by the sensor without interference. That way, isoprene is detected quickly (< 5 s) down to 5 ppb with selectivities >100 over other compounds in simulated breath mixtures, unprecedented by state-of-the-art sensors. As a result, this sensor-filter system is promising as breath isoprene detector for non-invasive monitoring of high blood cholesterol levels.

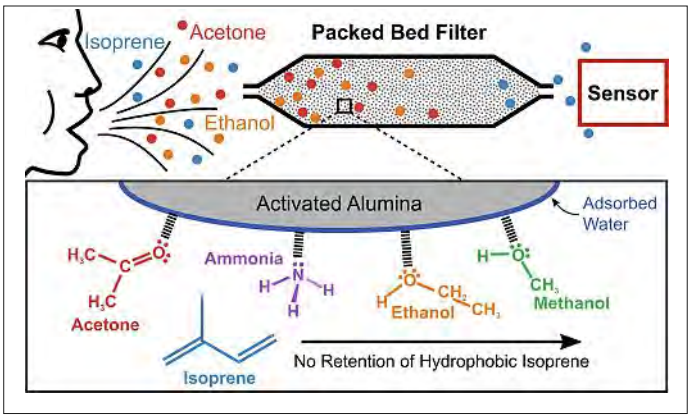
Such sensors can be integrated readily into portable breath analyzers for individualized health monitoring at home. This was demonstrated recently with breath acetone sensors that monitored individual fat burn rates in 20 volunteers during exercise and rest.

Acknowledgement

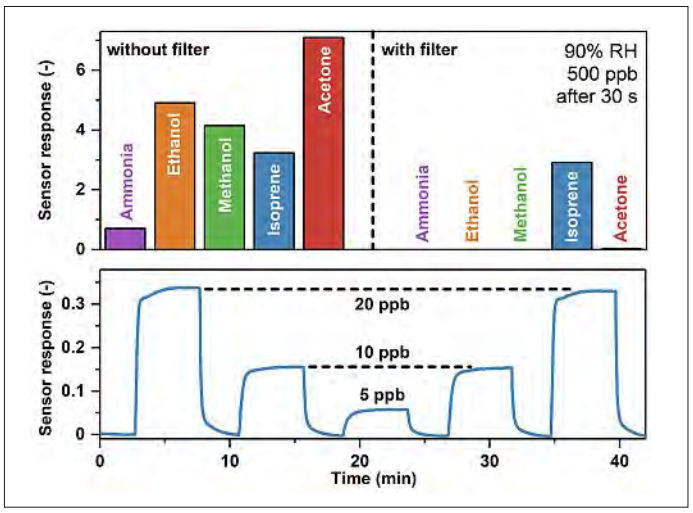
The authors thank Prof. S. E. Pratsinis (ETH Zurich) for his support and guidance during this research. Financial support by the SNF Grant #159763, 170729, and 175754 is kindly acknowledged.

References

J. van den Broek, A. T. Güntner, S. E. Pratsinis, *ACS Sens.* **2018**, *3*, 677.
A. T. Güntner, S. Abegg, K. Wegner, S. E. Pratsinis, *Sens. Actuators B* **2018**, *257*, 916.
A. T. Güntner, N. A. Sievi, S. J. Theodore, T. Gulich, M. Kohler, S. E. Pratsinis, *Anal Chem.* **2017**, *89*, 10578.
A. T. Güntner, N. J. Pineau, P. Mochalski, H. Wiesenhofer, A. Agapiou, C. A. Mayhew, S. E. Pratsinis, *Anal. Chem.* **2018**, *90*, 4940, doi: 10.1021/acs.analchem.8b00237.



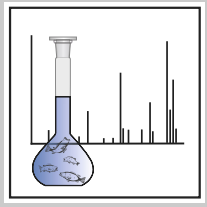
Isoprene detector based on an alumina-powder filter to retain hydrophilic compounds and a highly sensitive Pt-doped SnO_2 sensor to quantify isoprene concentrations. Adapted with permission from van den Broek *et al.*, *ACS Sens*. **2018**, *3*, 677. Copyright (2018) American Chemical Society.



Response of the Pt-doped SnO_2 sensor without (top left) and with activated alumina filter (top right) to 500 ppb of breath-relevant analytes at 90% RH. Response of the filter-sensor system to ultra-low isoprene concentrations of 5, 10 and 20 ppb at 90% RH (bottom). Adapted with permission from van den Broek *et al.*, *ACS Sens*. **2018**, *3*, 677. Copyright (2018) American Chemical Society.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2018.547 Chimia 72 (2018) 547



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Detective Work on the Rhine River in Basel – Finding Pollutants and Polluters

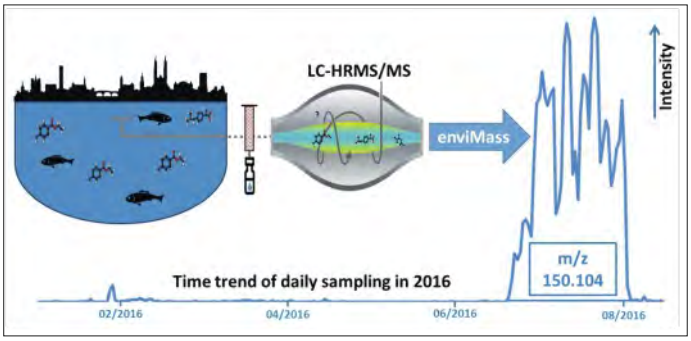
Steffen Ruppe*[a], Dorrit S. Griesshaber[a], Ingrid Langlois[a], Heinz P. Singer[b], and Jan Mazacek[a]

*Correspondence: Dr. S. Ruppe[a], E-mail: steffen.ruppe@bs.ch. [a]AUE-BS, Agency for Environment and Energy Canton Basel-City, Hochbergstr. 157, CH-4019 Basel; [b]Eawag, Swiss Federal Institute of Aquatic Science and Technology, CH-8600 Dübendorf

Keywords: enviMass · HR-LCMS/MS · Micropollutants · Non-target screening · Rhine · Water analysis

Around 58 million people live along the Rhine, and many are dependent upon the Rhine for drinking water and wastewater disposal. The riverside industrial activity is among the highest in the world. In order to monitor the Rhine water quality, the countries using the Rhine operate a network of monitoring stations. The first such station, the *RÜS*, was built in Weil a.R. (Germany) in 1993. This station and the associated laboratory are operated by the Agency for Environment and Energy of the Swiss canton Basel-Stadt.

Every day, the laboratory monitors over 350 substances and also performs screening of unknown compounds (non-targets). The non-target screening is based on high resolution mass spectrometry coupled with liquid chromatography (LC-HRMS/MS) detection. The LCMS data is processed by the cutting-edge, automated trend-detection software enviMass, which can recognize patterns in periodic time-series data. This software was developed in cooperation with the Eawag (Swiss Federal Institute of Aquatic Science and Technology) and it red-flags features (characterized by mass fingerprint, retention time, and signal intensity) with a suspicious temporal trend or unusually high intensities. Various compound databases (like Pubchem or Chemspider) are then queried to obtain a molecular structure. Ideally, the identification of the compound is confirmed via reference standards.



enviMass is a data-mining workflow based on LC-HRMS/MS data and extraction of mass profiles in time. In June 2016, enviMass reported an unusual profile pattern of a substance with m/z 150.104 which subsequently could be identified as *N*-(chloromethyl)-triethylammonium cation.

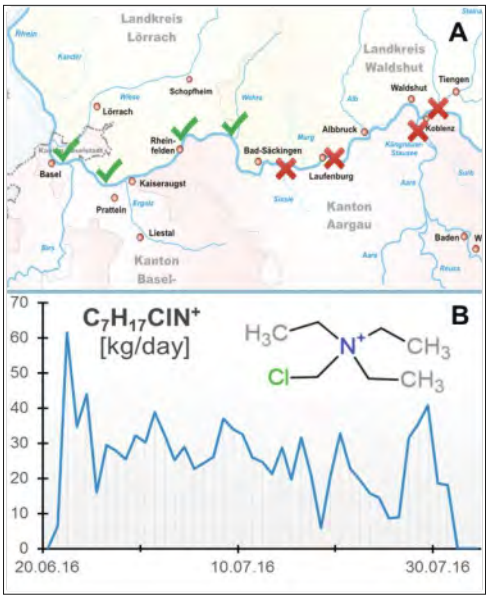
At times, the structural search is inconclusive. Additional meta information can help to identify an unknown substance. The usefulness of such complemental information can be illustrated with a feature red-flagged by enviMass in June 2016. Identification efforts suggested the structure of *N*-(chloromethyl)-triethylammonium cation, but no reference standard was available for confirmation. An upriver sampling campaign, including *e.g.* tributaries and wastewater treatment plants, revealed a point source in an adjacent canton. The company in question assisted the effort greatly by synthesizing a reference standard for the previously unknown byproduct of an industrial process. The calculated load of that byproduct into the Rhine over the period of one month was 1.1 tons. Since then the company has managed to eliminate the compound *via* process modifications.

Daily non-target-screening is essential for detecting the presence of unknown pollutants in our rivers; however, collaboration with industry and local authorities can be crucial in the enduring effort to eliminate sources of pollution and to protect our waters.

Received: May 22, 2018

References

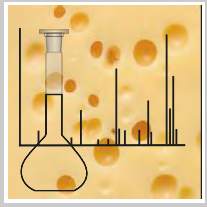
J. Hollender, E. L. Schymanski, H. P. Singer, P. L. Ferguson, *Environ. Sci. Technol.* **2017**, *51*, 11505.
M. Ruff, M. S. Mueller, M. Loos, H. P. Singer, *Water Res.* **2015**, *87*, 145.
M. Loos, **2018**, *enviMass version 3.5 LC-HRMS trend detection workflow – R package*. Zenodo. *https://doi.org/10.5281/zenodo.1213098*.



A: Sampling sites along the Rhine with positive (green marks) and negative results (red crosses) of the substance N-(chloromethyl)-triethylammonium cation. B: Based on these findings, the source was identified and the emission stopped. The total load in the Rhine was 1.1 t.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2018.647 Chimia 72 (2018) 647



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Enlightening the Lactate Degradation Processes in Cheese and Bacterial Cultures Using Phenylboronic Esterification and GC-MS

René Badertscher*, Carola Freiburghaus, Daniel Wechsler, and Stefan Irmler

*Correspondence: R. Badertscher, Agroscope, Schwarzenburgstrasse 161, CH-3003 Bern, E-mail: rene.badertscher@agroscope.admin.ch

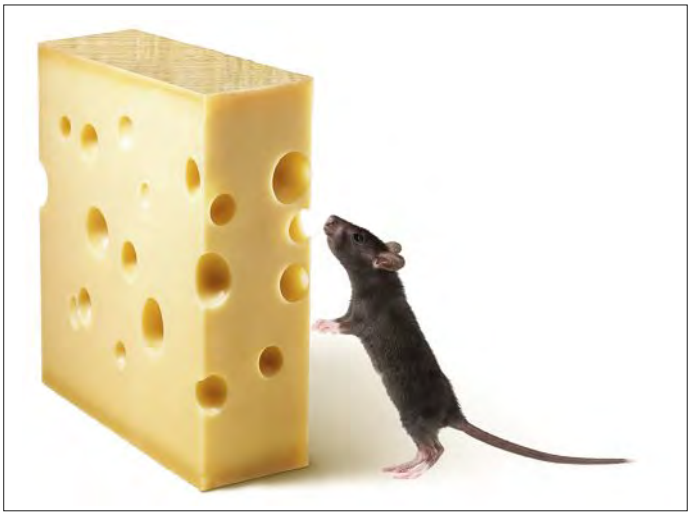
Keywords: Bacterial cultures · Butane-2,3-diol · Cheese · GC-MS · Propane-1,2-diol · Propane-1,3-diol

In food production, fermentation plays a key role for preserving food. At the same time, the process can be used to achieve the desired qualities of aroma, taste and texture. For example, for various cheeses, the eye formation is important, which is caused by the release of carbon dioxide during the ripening process. The bacteria used for this have a multitude of metabolic activities that can also release other gases. Some of the degradation pathways lead to the formation of diols. *Lactobacillus parabuchneri* is an interesting example for such a pathway, because it can metabolize lactate to propane-1,2-diol with simultaneous release of acetate and carbon dioxide. *Lactobacillus buchneri*, on the other hand, produces propane-1,3-diol during the co-fermentation of carbohydrates and glycerine. The 2,3-butanediol fermentation is a way of breaking down carbohydrates to produce energy under anoxic conditions. The pathways that convert lactate into acetate under anaerobic conditions are not well understood at the molecular level. A sensitive method was therefore developed and validated for the simultaneous quantitative measurement of the metabolites propane-1,2-diol, butane-2,3-diol, and propane-1,3-diol in cheese and bacterial cultures. In a first step, the diols are extracted in water and esterified directly in the extract with the aid of phenylboronic acid. After extraction with toluene, the resulting phenylboronic esters are measured directly using GC-MS in selected-ion monitoring (SIM) mode with an external calibration using butane-1,2-diol as the internal standard. **The method is simple, fast, robust, allows precise measurements in the mg/kg range and can be used in complex matrices due to selective double extraction and is therefore also of interest for plant and non-dairy food fermentation.**

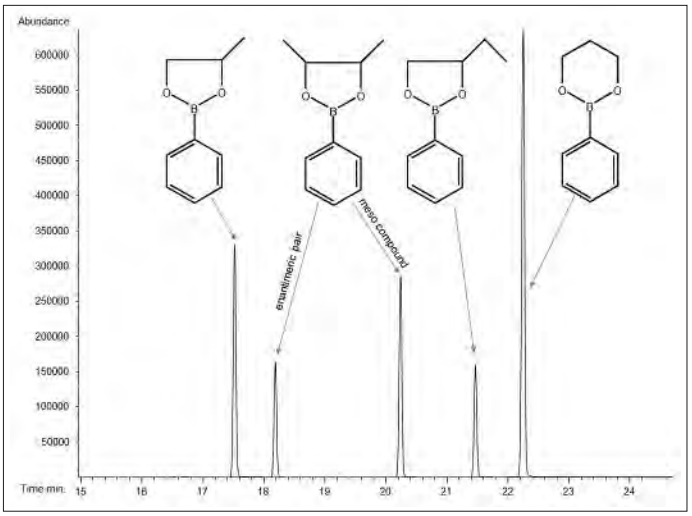
Received: July 25, 2018

Reference

R. Badertscher, C. Freiburghaus, D. Wechsler, S. Irmler. *Food Chemistry* **2017**, *230,* 372.



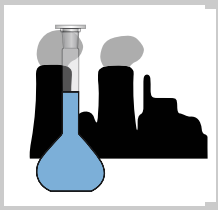
Eye formation in cheese, a quality feature.



Selected-ion mode chromatogram of a standard diol calibration sample. From left to right: Phenylboronic esters of propane-1,2-diol, butane-2,3-diols, butane-1,2-diol (internal standard), and propane-1,3-diol.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2018.726 Chimia 72 (2018) 726



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

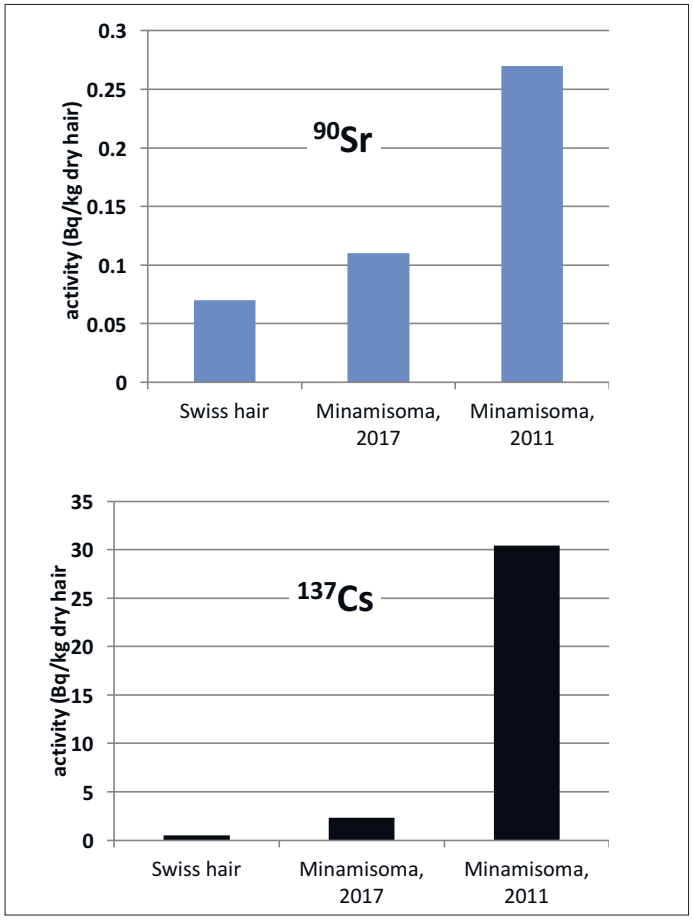
Radionuclides in Human Hair of Swiss People

Franziska Kramer, Franziska Kammerer, Michael Wagmann, and Markus Zehringer*

*Correspondence: Dr. M. Zehringer, Kantonales Laboratorium Basel-Stadt, Kannenfeldstrasse 2, CH-4012 Basel, E-mail: markus.zehringer@bs.ch

Keywords: Beta spectrometry · Gamma spectrometry · Human hair · Radiocaesium · Radiostrontium

Radiocaesium (^{134}Cs and ^{137}Cs) and radiostrontium (^{90}Sr) belong to the radionuclides, which are emitted to the environment when nuclear fission gets out of control. Their main source is from bomb fallout, when over 600 bombs were tested in the atmosphere from 1945 to 1970. Additionally, they originate from nuclear accidents, such as the reactor fire at the nuclear power plant (NPP) of Chernobyl or the core melting of three reactors at Fukushima Dai-ichi in 2011. In Switzerland, the fallout from bomb tests and from the Chernobyl reactor-fire contributes to the internal dose mainly by consumption of food.



Mean activities in hair from Swiss people compared to contaminated Japanese hair from the exclusion zone of Fukushima Dai-ichi.

One possibility to investigate these internal doses is by whole-body counting (mainly gamma rays are detectable) or analysing urine and faeces. Scientists often use the analyses of teeth or bones to estimate the amount of incorporated radiostrontium. The analysis of hair offers another approach. Hair is a common matrix to test for drug abuse or for intoxications (*e.g.* with a toxic metal). Yet, little is published about hair analysis for the determination of radio contamination in man.

In 2017, we investigated the pooled hair samples collected by hairdressers of the city of Basel and surrounding villages. The hair was washed with detergents and water. After drying the hair, it was ashed at 600 °C. The ashes were analysed with gamma spectrometry (radiocaesium). Then, after several clean-up steps, the extracts were analysed with beta spectrometry (radiostrontium).

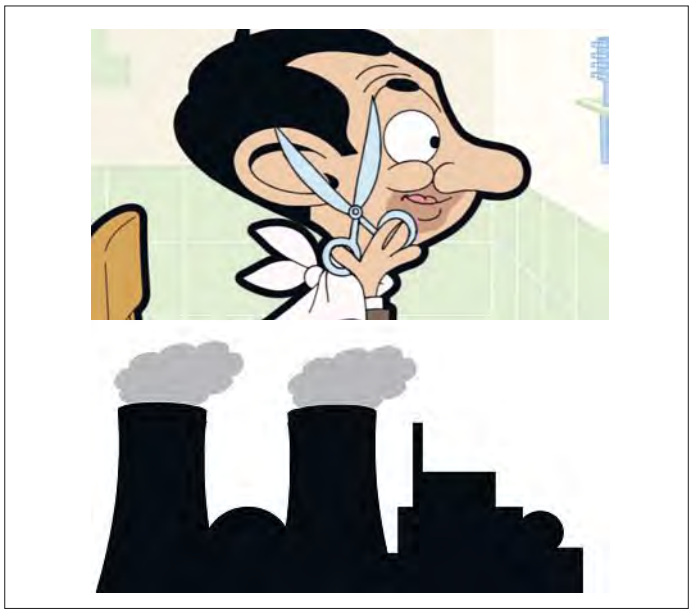
We compared the results to human hair of Japanese people from Minamisoma City (a town in the exclusion zone of the NPP Fukushima Dai-ichi) collected by a hairdresser in 2011 and 2017.

Today, the Swiss hair show little radio contamination. While the hair from Japanese people who were exposed directly to the fallout from the NPP Fukushima Dai-ichi showed significantly higher contamination. Seven years after the NPP accident, the radio contamination of the hair dropped to about 10% (^{137}Cs) and 30% (^{90}Sr), respectively, of the original contamination level.

Received: August 13, 2018

Reference

A. A. Kist, R. I. Radyuk, L. I. Zhuk, V. P. Pikul, A. D. Belyaev, *J. Alloys Compounds* **1994**, *213/214*, 81.



Radioactive fallout, which is incorporated with food and *via* air, is deposited in human hair to some extent.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2018.816 Chimia 72 (2018) 816

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Genome Mining-guided and MALDI Imaging-assisted Discovery of New Antibiotics

Silke I. Probst, Christine Vogel, Julia A. Vorholt, and Jörn Piel*

*Correspondence: Prof. Dr. J. Piel, Institute of Microbiology, ETH Zurich, Vladimir-Prelog-Weg 1-5/10, CH-8093 Zurich, E-mail: jpiel@ethz.ch

Keywords: Antibiotic discovery · *Arabidopsis thaliana* · Genome mining · MALDI imaging

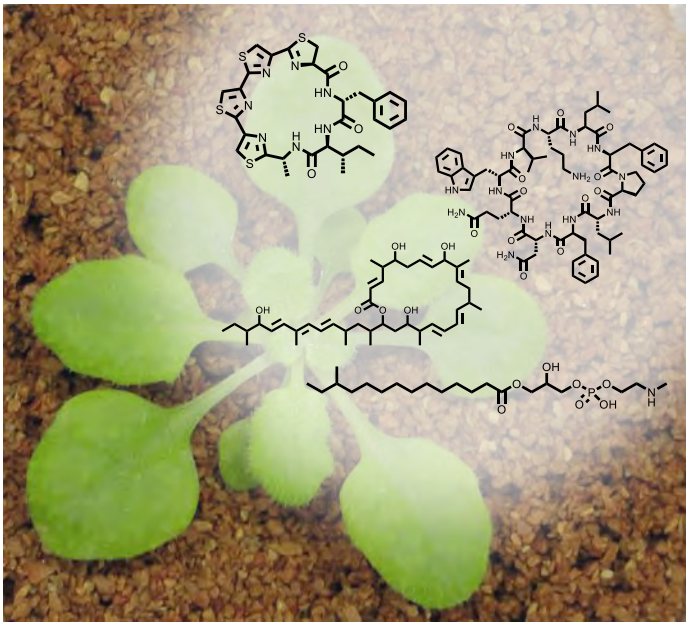
Despite rapid technological progress, the discovery of new antibiotics has stalled. Meanwhile, long-term prescription and misuse of antibiotics has resulted in increased resistances culminating in the current antibiotic resistance crisis. Most therapeutically relevant antibiotic classes are based on natural products discovered from bacteria. Traditionally, 'talented' natural product producers such as soil Actinomycetes were used as sources for antibiotics discovery. However, the focus on taxonomically related bacteria from similar habitats increasingly results in the re-isolation of known compounds.

A powerful discovery strategy is based on the computational prediction of biosynthetic products from microbial genome sequences. Natural products are generated by enzymes encoded in clustered sets of genes called biosynthetic gene clusters (BGC). Knowledge of their function allows prediction of natural product structures for some compound classes. Advanced bioinformatic tools are used to identify BGCs in bacterial genomes and compare these to known biosynthetic pathways, thus providing insights into the biosynthetic potential for novel natural products in a bacterium.

These *in silico* dereplication techniques can be applied to bacteria from as-yet chemically poorly explored taxa and ecosystems. We studied bacteria associated with leaves of the model plant *Arabidopsis thaliana* as bacteria colonizing this nutrient-poor habitat might employ antimicrobial warfare against competitors. A large collection of leaf bacteria were subjected to genomic analysis in combination with thousands of binary interaction assays, which revealed a large number of novel BGCs and antagonistic interactions. For bacteria showing potential in both analyses, Matrix Assisted Laser Desorption Ionization Imaging Mass Spectrometry (MALDI IMS) was used to scan the spatial distribution of ions around colonies grown on sensitive strains. It allows metabolic changes to be detected, such as an increased secretion of metabolites when confronting the producer strain with a competing organism. Moreover, it suggests which ions belong to an antibiotic by comparing the shape of the inhibition zone around the colony with the distribution of the detected compounds. Compounds of interest were purified guided by the *in silico*, analytical, and activity data, followed by full structure elucidation. This resulted in the identification of two novel antibiotics from a single producer.

This combinatorial approach of interaction data, genome mining and MALDI IMS streamlines the identification of new talented producers and simplifies the HPLC purification and elucidation of novel molecules.

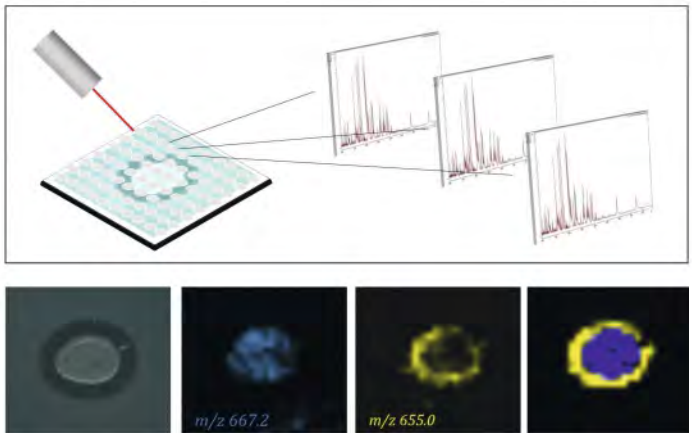
Received: September 24, 2018



Arabidopsis thaliana overlaid by bioactive compounds from the isolated *Brevibacillus* sp. Leaf182.

Reference

E. J. N. Helfrich, C. M. Vogel, R. Ueoka, M. Schäfer, F. Ryffel, D. B. Müller, S. Probst, M. Kreuzer, J. Piel, J. A. Vorholt, *Nature Microbiol.* **2018**, *3.8,* 909.



MALDI IMS of a bacterial colony forming an inhibition zone on a lawn of competing bacteria. The intensities of color-coded masses correspond to two isolated secondary metabolites, the antibiotics macrobrevin (*m/z* 667.2) and marthiapeptide A (*m/z* 655.0).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2018.901 Chimia 72 (2018) 901

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Micro- and Nanoplastic Analysis in Soils

Moritz Bigalke*[a], Montserrat Filella[b], Daniela Fischer[a], Anna Muntwyler[a], Michael Scheurer[a], and Benjamin Watts[c]

*Correspondence: Dr. M. Bigalke[a], E-mail: moritz.bigalke@giub.unibe.ch. [a]Institute of Geography, Hallerstrasse 12, CH-3012 Bern; [b]Department F.-A. Forel, University of Geneva, Boulevard Carl-Vogt 66, CH-1205 Geneva; [c]Paul Scherrer Institute, CH-5232 Villigen PSI.

Keywords: Microplastic · Nanoplastic · Soil

Microplastic (MP) and nanoplastic (NP) pollution in the environment are of great concern. Even though the amount of MP applied to soils is greater than the yearly load to the ocean, terrestrial systems are much less studied in terms of MP and NP concentrations and characteristics. The main reason for the very limited number of MP analyses in soils is the lack of an established method to perform this kind of analysis. We separate the 1–5 mm sized MP particles by sieving the dry sample and identifying the plastics by attenuated total reflection Fourier transform infrared spectroscopy (ATR-FTIR). The particles of <1 mm size are separated by wet chemical methods, *i.e.* by density separation from the mineral soil matrix. Natural organic substances (with a similar density) are oxidized and a second density separation is used for the final cleanup. Finally, the sample is filtered – on a filter transparent at wavelengths between 1250 and 4000 cm^{-1} – and the single particles are analyzed by FTIR microscopy in transmission mode. The quantification is done by precisely measuring the size of the single particles and calculating their weight using an empirical relationship between particle size and weight.

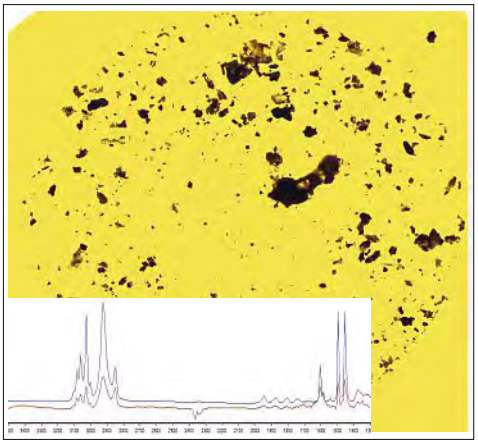
While the number of MP analyses in soils is limited, there is no single publication that analyses NP in soils. The lack of NP research is mostly due to the fact that the analytical techniques applied to MP research (*e.g.* FTIR and Raman spectroscopy) do not work for nanoscale particles, and that other methods established for nanoparticles (*e.g.* transmission electron microscopy) cannot distinguish plastic from natural soil organic matter. We have recently begun testing the use of scanning transmission X-ray microscopy (STXM) to analyze NP in soils. The STXM method can display NP with a resolution of about 30 nm and identify the plastics *via* near edge X-ray absorption fine spectra (NEXAFS) at the carbon K-edge.

MP and NP particles in soils can be analyzed by wet chemical sample preparation, FTIR microscopy and STXM to investigate their occurrence and fate in the environment.

Received: October 12, 2018

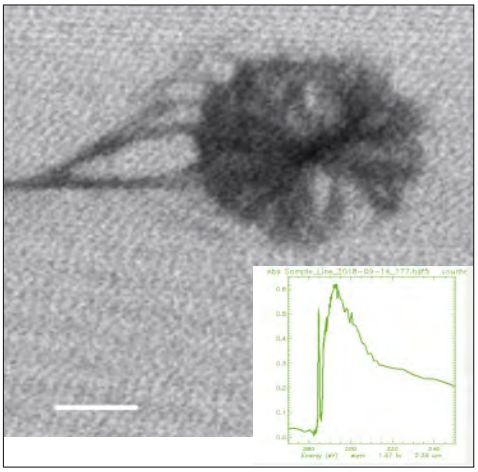
Reference

M. Scheurer, M. Bigalke, *Env. Sci. Technol.* **2018**, *52*, 3591.



Filter with particles <1 mm from a Swiss floodplain soil with FTIR spectra of a particle from the soil (in red) and of polystyrene from a polymer database (in blue). Size of the filter = 13 mm.

Sieve with particles >1 mm from Swiss floodplain soils. Many of the particles are plastics, as confirmed by ATR-FTIR spectroscopy.



STXM image of polystyrene fibers recorded at 320 eV and corresponding NEXAFS spectra from 270–350 eV. Scale bar = 1 μm.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2019.91 Chimia 73 (2019) 91

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Hazardous Plastics in Swiss Lakes?

Montserrat Filella*[a] and Andrew Turner[b]

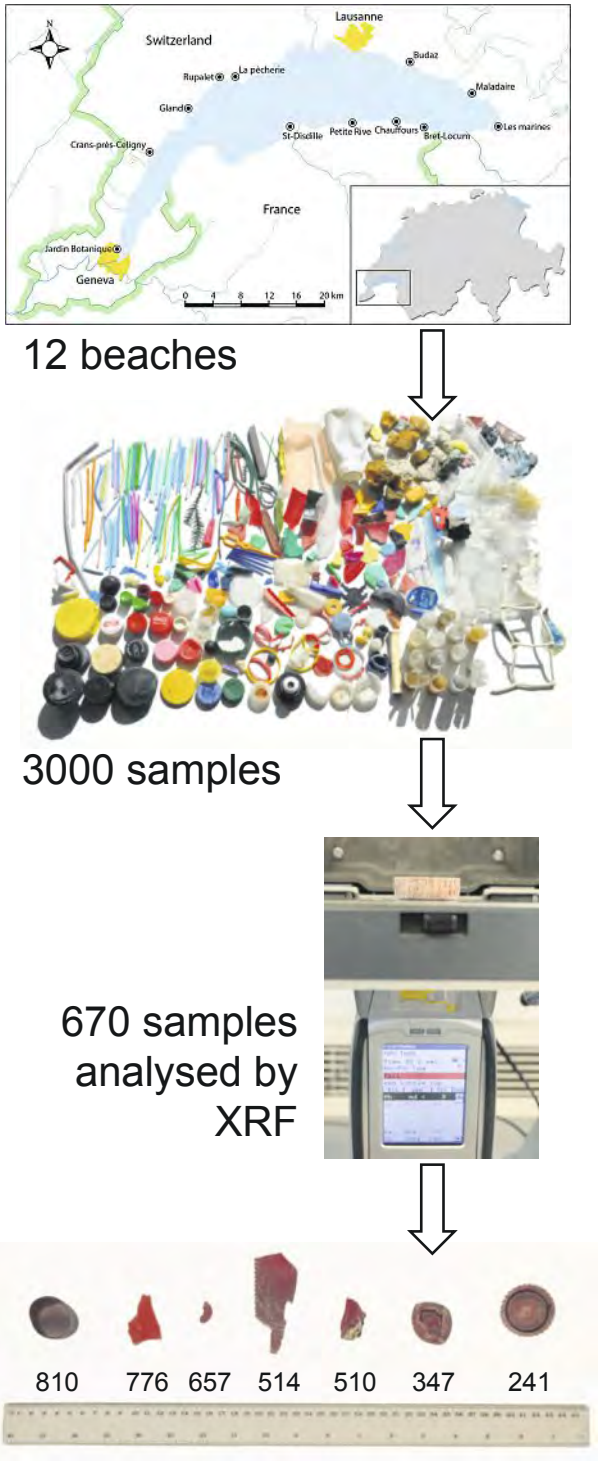
*Correspondence: Dr. M. Filella, E-mail: montserrat.filella@unige.ch
[a]Department F.-A. Forel, University of Geneva, Boulevard Carl-Vogt 66, CH-1205 Geneva;
[b]School of Geography, Earth and Environmental Sciences, Plymouth University, Drake Circus, Plymouth PL4 8AA, UK

Keywords: Hazardous elements · Lakes · Plastics · X-ray fluorescence spectrometry

The accumulation and impacts of plastic litter in marine environments has received extensive attention over the past decade. In contrast, littering in the freshwater environment has received relatively little study, despite the presence of plastics on the shores and beds of lakes and suspended in the lentic water column that are likely to pose the same problems to wildlife as marine plastics. Regardless of the type of water system, the majority of research in this area has targeted the presence of plastics themselves and, sometimes, their accumulation of persistent organic micropollutants (*e.g.* PCBs, PAHs). Only very recently attention has been paid to the occurrence of chemical elements, like metals, metalloids and halogens, that are either adsorbed to the plastic surface or incorporated into the polymer itself as an additive.

Following initial work on beached marine plastics,[1] we have turned our attention to the presence of chemical elements in plastics on lake beaches.[2] The sampling and measuring workflow is illustrated in the Figure. The plastic stock was collected from the shores of Lake Geneva and consisted of pieces or blocks of expanded polymer (polystyrene or polyurethane foam), identifiable primary objects of various size and color (*e.g.* bottles, bottle tops, cotton buds, pens, toys, straws) and an heterogeneous assortment of secondary fragments whose origin was either discernible or unknown. Several hundred samples were analyzed by energy-dispersive portable X-ray fluorescence (XRF) spectrometry, a technique that is perfectly adapted to this type of study because of its non-destructive nature and high throughput capacity. Significantly, the results revealed high concentrations of hazardous elements or compounds among many of the plastics analyzed; specifically, Cd, Hg, Sb, Pb and Br were frequently detected with maximum concentrations of 6760, 810, 27.100, 23.500 and 27.400 ppm, respectively. The abundance of hazardous elements in beached plastics that have been restricted or banned point to a high residence time of the plastic stock in lakes. **The migratability of hazardous elements from the polymeric matrix is likely to determine their environmental impacts and is recommended as a future area of research**.

Received: November 26, 2018

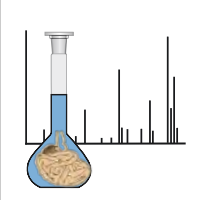


Workflow of the study in Lake Geneva, Switzerland, showing samples with high Hg contents.

[1] A. Turner, K. R. Solman, *Talanta* **2016**, *159*, 262.
[2] M. Filella, A. Turner, *Front. Environ. Sci.* **2018**, *6*, 1. doi:10.3389/fenvs.2018.00001.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2019.206 Chimia 73 (2019) 206



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Piperine Analogs as Modulators of the Central Nervous System

Mouhssin Oufir*[a], Volha Zabela[a], Timm Hettich[b], Götz Schlotterbeck[b], Laurin Wimmer[c], Marko D. Mihovilovic[c], Fabrice Guillet[d], Belkacem Bouaita[d], Bénédicte Shevchenko[e], and Matthias Hamburger[b]

*Correspondence: Dr. M. Oufir[a], E-mail: mouhssin.oufir@unibas.ch. [a]Pharmaceutical Biology, Department of Pharmaceutical Sciences, University of Basel, Klingelbergstrasse 50, CH-4056 Basel; [b]Institute for Chemistry and Bioanalytics, School of Life Sciences, University of Applied Sciences Northwestern Switzerland, Gründenstrasse 40, CH-4132 Muttenz; [c]Institute of Applied Synthetic Chemistry, Vienna University of Technology, Getreidemarkt 9, A-1060 Vienna, Austria; [d]Eurosafe, Parc d'Affaires La Bretêche, F-35760 Saint Grégoire, France; [e]Biopredic International, Parc d'Affaires La Bretêche, F-35760 Saint Grégoire, France

Keywords: $GABA_A$ · *In vitro* metabolism · Piperine analogs · Silensomes · UHPLC-MS/MS · UHPLC-QTOF-MS

Central nervous system-active drugs such as benzodiazepines or the so-called Z-drugs act *via* an allosteric modulation of $GABA_A$ receptors. However, these drugs have well-known side-effects which largely result from their lack of $GABA_A$ receptor subtype selectivity. Therefore, drug discovery efforts in this field are directed towards identifying subtype-selective $GABA_A$ receptor modulators to overcome the limitations of existing drugs. In a library screening for $GABA_A$ modulatory natural products, we identified some years ago piperine as a positive allosteric modulator which interacted with a benzodiazepine-independent binding site, which was compliant with Lipinski's rule of five, and which showed *in vivo* activity in rodents. Given that piperine is also an activator of TRPV1 (transient receptor potential vanilloid type 1) receptors involved in pain signaling and thermoregulation, systematic structural modifications of the parent structure were carried out in several cycles of optimization, aiming at separating $GABA_A$ modulatory from TRPV1 activity.

To guide further structural modifications, biopharmaceutical properties of selected compounds from three cycles of optimization were assessed. Using fit-for-purpose bioanalytical UHPLC-MS/MS methods and UHPLC-QTOF-MS, we evaluated i) metabolic stability and metabolite formation in microsomal incubations, ii) performed CYP450 (cytochrome P450) reaction phenotyping in Silensomes, and iii) determined unbound fraction in whole blood using rapid equilibrium dialysis.

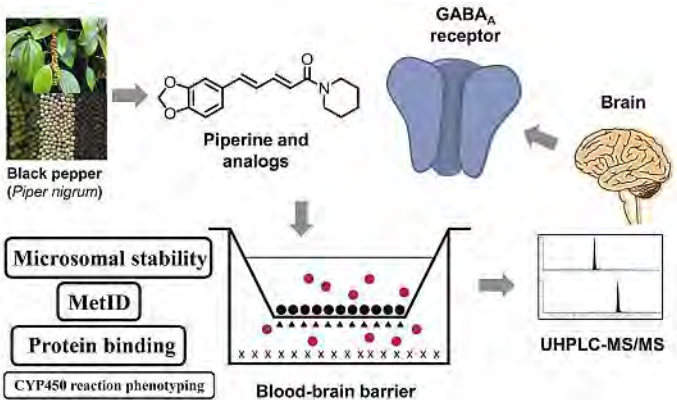
Piperine analogs (SCT-29, LAU 397, and LAU 399) were rapidly metabolized, with a significant contribution of the highly polymorphic CYP2C9 (which would lead to a highly varying drug response between individuals) and showed strong binding to blood constituents (which in turn would result in a low hepatic extraction ratio).

Therefore, the next cycle of medicinal chemistry optimization focuses on lowering lipophilicity, in order to decrease metabolic liabilities and extensive protein binding.

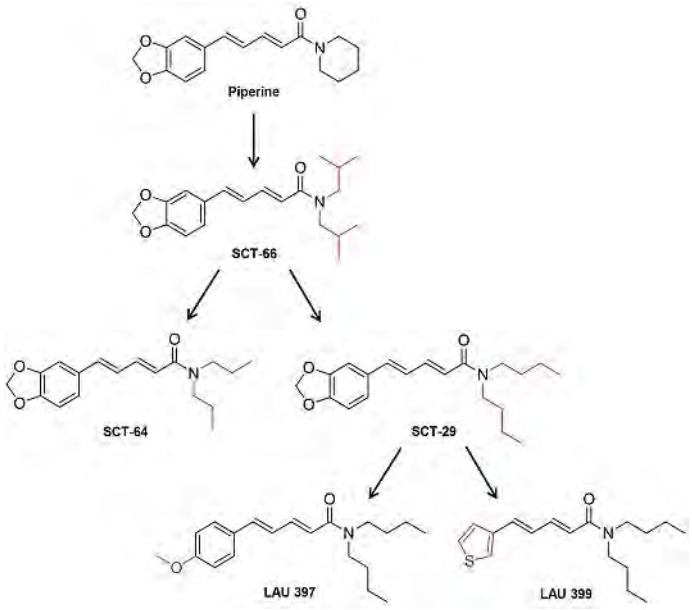
Received: January 4, 2019

Reference

V. Zabela, T. Hettich, G. Schlotterbeck, L. Wimmer, M. O. Mihovilovic, F. Guillet, B. Bouaita, B. Shevchenko, M. Hamburger, M. Oufir, *J. Chromatogr. B* **2018**, *1072*, 379.



Drug-like properties optimization of piperine (from *Piper nigrum*) and analogs as $GABA_A$ receptor modulators using various drug metabolism and pharmacokinetics assays.

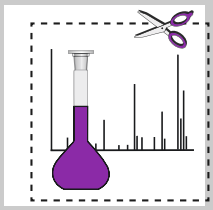


Chemical structures of piperine and selected analogs from three cycles of optimization.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2019.330 Chimia 73 (2019) 330



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Revealing Pre-analytical Pitfalls in Concentration Determination of Peptides by Quantification of Amino Acid Fluorescence

Martina D. Allenspach, Jens A. Fuchs, and Christian Steuer*

*Correspondence: Dr. C. Steuer, Department of Chemistry and Applied Biosciences, Institute of Pharmaceutical Sciences, Swiss Federal Institute of Technology (ETH), Vladimir-Prelog-Weg 4, CH-8093 Zürich, E-mail: christian.steuer@pharma.ethz.ch

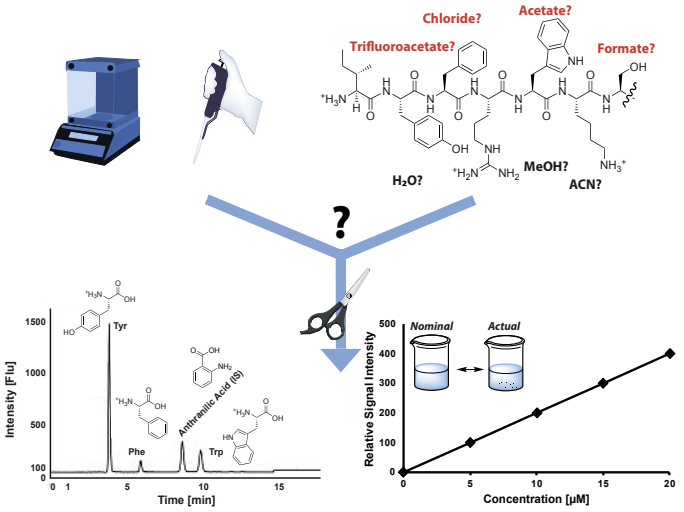
Keywords: Antioxidant · Fluorescence · HPLC · Method development · Peptides · Validation

Synthetic peptides are important for drug discovery and have been identified as hit and lead compounds. There is a growing interest in developing simple, fast and accurate analytical assays for the quantification of peptides and proteins in the early drug discovery process. Most peptides are purified by reversed phase (RP)-HPLC by using an acidic modifier such as formic acid, acetic acid or trifluoroacetic acid (TFA). The peptides form salts with the acidic modifier, which binds specifically to free NH_2 termini and to the side chains of exposed basic residues. Given the molecular weight of the TFA molecule (114 Da), the association of a single molecule to a peptide of 500 Da would increase the formula weight by more than 20%. The evaluation of the concentration of the peptides prior to biological activity testing is therefore crucial to avoid a source of error in concentration-dependent biological activity assays. However, the question is which molecular weight – either of the formed salts resulting from the purification process or the neutral form – is used for the calculation. Furthermore, other pre-analytical pitfalls such as weighing errors, pipetting performance or solubility issues can lead to false interpretation of the activity data. An analytical approach which allows to identify pre-analytical differences between the nominal and actual concentration is needed.

Therefore an easy, accurate and broadly applicable HPLC-fluorescence-detection method for the quantitative determination of the aromatic amino acids (AAA) tyrosine (Tyr), phenylalanine (Phe) and tryptophan (Trp) using an isocratic elution was developed and validated. The peptides are hydrolyzed under heated and acidic conditions to yield the monomeric AAAs. To prevent the AAAs from oxidative decomposition, cysteine as protective agent is applied. The separation of the three AAAs and the internal standard was performed using ion-pair chromatography. The AAAs and the internal standard anthranilic acid are clearly separated. The power of the method was confirmed by the correct quantification of a protein reference standard to 98.6% over all fluorescence traces.

Interestingly, for a peptide which contains five basic AAs, the method yielded an 85% lower concentration than expected. The observed value was confirmed independently on Tyr and Trp traces. Considering five TFA counter ions, one would expect only a 40% lower amount of the indicated concentration. We speculate that the observed lower amount resulted from other impurities like fluorescent or UV-inactive organic species or residual solvents. The presented method requires only a few pre-analytical steps and can be implemented with standard laboratory equipment. Furthermore, only one solution is needed to perform quantification, UV-purity tests, and subsequent activity testing.

The developed fluorescence-based method is able to quantify peptides and proteins and is applied to determine accurately the concentration of peptides to limit the risk of erroneous activity data in drug discovery projects.



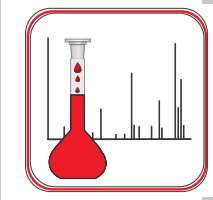
Salt formation, weighing errors, pipetting errors or solubility issues can lead to false declaration of peptide concentration. After chemical cleavage, the actual concentration of peptides can be determined by quantification of amino acid fluorescence.

Reference

M. D. Allenspach, J. A. Fuchs, N. Doriot, J. A. Hiss, G. Schneider, C. Steuer, *J. Pept. Sci.* **2018**, *24*, e3113.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2019.416 Chimia 73 (2019) 416



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

A Generic Approach for High-throughput Blood Analysis

Sophie Bravo-Veyrat and Gérard Hopfgartner*

*Correspondence: Prof. Dr. G. Hopfgartner, University of Geneva, Life Sciences Mass Spectrometry, Department of Inorganic and Analytical Chemistry, 24 Quai Ernest-Ansermet, CH-1211 Genève 4, E-mail: gerard.hopfgartner@unige.ch

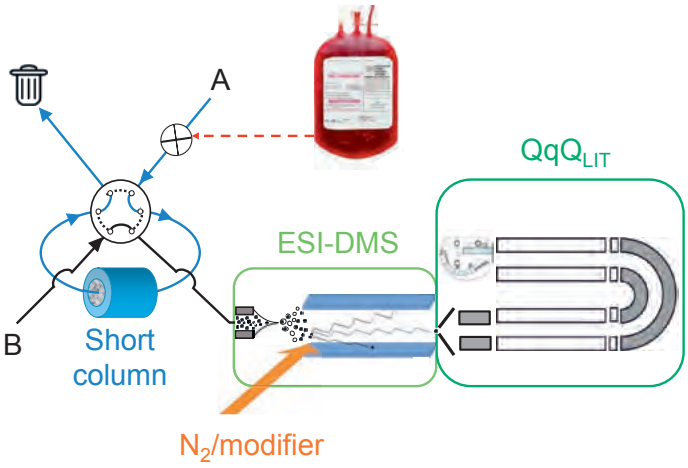
Keywords: Blood · Differential mobility spectrometry · MRM · Quantification · Trap/Elute LC

During the 42 days of legal storage of blood bags, red blood cells can be altered due to an increase of oxidative stress degrading blood quality prior to transfusion. Oxidative stress can be measured by the ratio between the accurate concentrations of reduced and oxidized glutathione (respectively GSH and GSSG).

Donated blood is precious and should be of highest possible quality.

Quantitative liquid chromatography coupled to multiple reaction monitoring mass spectrometry (LC-MRM/MS) is the current gold standard for quantitative bioanalysis, and different assays have been reported for the quantification of GSH and GSSG. However, analysis times of 5 to 10 minutes limit their application for high-throughput analysis. Flow-injection analysis in MRM is not an alternative as matrix effects during ionization alter the limit of quantification, and non-separated endogenous analytes affect the selectivity of the assay. A decrease of analytical time while maintaining good precision and accuracy passes by the shortening of the column length. Replacing a 50 mm Hypercarb column for a 10 mm C18 column (short LC) gives a 1-minute runtime but inaccurate and non-precise quantitative results. As blood cannot be injected directly into an LC column a protein precipitation (PP) step is mandatory. The use of organic solvent would require an additional evaporation/reconstitution step. Perchloric acid is an efficient PP agent and allows to inject a large volume onto a trapping column. In the present work a short LC column was used in trap/elute mode, with an in-line front flush preconcentration performed with ion-pairing trifluoroacetic acid. MS sensitivity was improved by backflush elution with formic acid. One-dimensional separation with the short LC column allowed to control suppression effects but selectivity was still lacking for GSH and GSSG. Modifier-assisted differential mobility spectrometry (DMS) was added as a second dimension of separation without compromising analysis time. This 'in-space' separation of GSH and GSSG, based on their compensation voltage (CoV) in the DMS cell, was tuned with the addition of modifiers. Thereby, the best resolution was obtained with ethanol, allowing to separate GSH and GSSG with different CoV values. With this 2D separation, oxidative stress could be measured in 10 human donors in 1.5 min per sample with accuracy and precision.

This generic approach combining perchloric protein precipitation, multidimensional trap/elute short LC column, and differential mobility spectrometry with MS detection is an alternative to LC for high-throughput bioanalysis with the capability to quantify 400 samples in 10 hours.



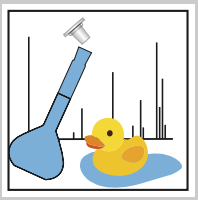
Generic bioanalytical workflow of whole blood sample combining short LC column-switching and differential mobility spectrometry assisted by modifier, with a QqQ_{LIT} mass spectrometer.

References

D. Giustarini, D. Tsikas, G. Colombo, A. Milzani, I. Dalle-Donne, P. Fanti, R. Rossi, *J. Chromatogr. B* **2016**, *1019*, 21.
G. Hopfgartner, E. Bourgogne, *Mass Spectrom. Rev.* **2003**, *22*, 195.
S. Bravo-Veyrat, G. Hopfgartner, *Anal. Bioanal. Chem.* **2018**, *410*, 7153.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2019.504 Chimia 73 (2019) 504



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Mass Spectrometric Analysis of Short-Chain Chlorinated Paraffins in Plastic Consumer Products

Lena Schinkel*[a], Elia Canonica[a,b], Peter Lienemann[b], Davide Bleiner[a], and Norbert Heeb[a]

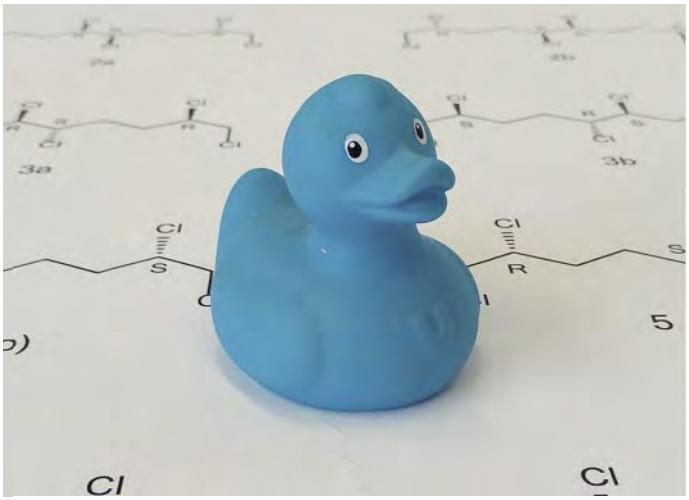
*Correspondence: L. Schinkel[a], E-mail: lena.schinkel@empa.ch. [a]Empa, Laboratory for Advanced Analytical Technologies, Überlandstrasse 129, CH-8600 Dübendorf; [b]ZHAW, Institute of Chemistry and Biotechnology, Grüentalstrasse 14, CH-8820 Wädenswil

Keywords: Chlorinated paraffins · High-resolution mass spectrometry · Persistent organic pollutants

Chlorinated paraffins (CPs) are industrial chemicals with a production volume of more than 1 million tons per year. Technical CPs are complex mixtures of thousands of isomers, covering a range of carbon chain lengths (C_{10}–C_{30}) and degrees of chlorination (30–70% Cl by mass). They are applied in plastic consumer products as plasticizers or flame retardants. In 2017, short-chain chlorinated paraffins (SCCPs, C_{10}–C_{13}) were listed under the UN Stockholm Convention on Persistent Organic Pollutants (POPs) for global elimination. Accordingly, acceptable SCCP levels in consumer products have been recently lowered to 0.15% by mass (EU and Switzerland).

Mass spectrometry is the method of choice to analyze CPs. Due to high degrees of chlorination, CPs have many isotopologues (^{35}Cl, ^{37}Cl) resulting in broad isotope clusters that overlap for different CP homologues. If mass resolution is low (R < 7,000), these clusters interfere, which impedes a correct quantification of CPs. We could show that high-resolution mass spectrometry (HRMS, R > 100,000) is required to resolve mass interferences of (a) different CP homologues, (b) transformation products (*e.g.* chlorinated olefins), (c) other chlorinated organic compounds (*e.g.* polychlorinated biphenyls), and (d) fragment ions formed in the ion source. If mass resolution is insufficient, mathematical deconvolution procedures can be applied to derive non-interfered data.

In a pilot study, we tested whether SCCP levels in selected plastic consumer products are below the limit of 0.15%. Samples were cut and extracted with solvent (dichloromethane). Processed extracts were analyzed using HRMS. SCCP levels ranged between 1% and 4.4%. Hence, the tested plastic products exceeded the legal limit by 7 to 29 times. Many plastic products are imported from countries that do not have legal limits for SCCPs. Monitoring of SCCPs in imported goods is therefore an important but challenging task. **High-resolution mass spectrometry is the preferred tool for the accurate quantification of SCCP levels in consumer products and other samples.**



CPs are applied as plasticizers or flame retardants in various plastic consumer products.

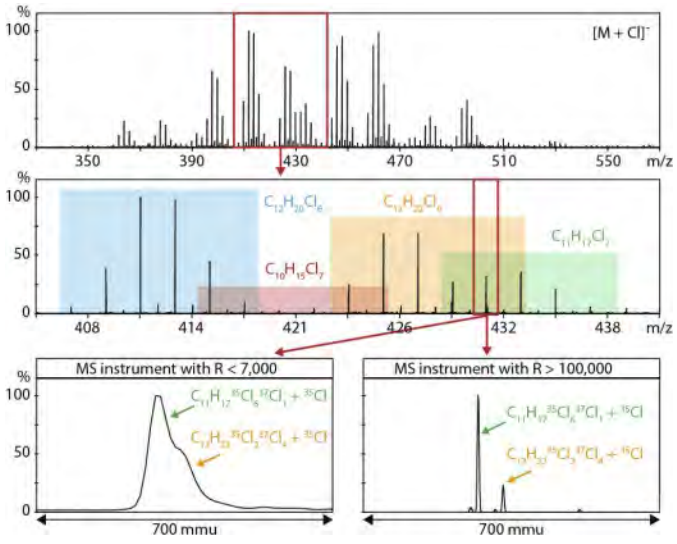
Acknowledgement

The Swiss Federal Office for the Environment (BAFU) is acknowledged for financing Empa's research on chlorinated paraffins.

Received: April 4, 2019

Reference

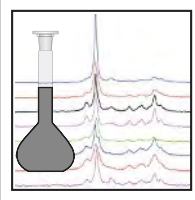
L. Schinkel, S. Lehner, N. Heeb, P. Marchand, R. Cariou, K. McNeill, C. Bogdal, *Trends Anal. Chem.* **2018**, *106*, 116, doi: 10.1016/j.trac.2018.07.002.



Mass spectrum of a SCCP mixture. Chloride-adducts $[M+Cl]^-$ are forced under the given ionization conditions. Isotope clusters of different CP homologues overlap and interfere in case of insufficient mass resolution (R), but can be resolved with HRMS.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2019.635 Chimia 73 (2019) 635



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

CMOS and 3D Printing for NMR Spectroscopy at the Single Embryo Scale

Marco Grisi[a], Enrica Montinaro[a], Franck Vincent[b], Laszlo Pethö[c], Maria Cristina Letizia[a], Beatrice Volpe[a], Nicola Harris[a], Armin Beck[b], Roberto Guidetti[d], Martin Gijs[a], Johann Michler[c], Jürgen Brugger[a], and Giovanni Boero*[a]

*Correspondence: Dr. G. Boero[a], E-mail: giovanni.boero@epfl.ch; [a]Institute of Microengineering, Ecole Polytechnique Fédérale de Lausanne (EPFL), Station 17, CH-1015 Lausanne; [b]Bruker BioSpin AG, CH-8117 Fällanden; [c]Swiss Federal Laboratories for Materials Science and Technology (EMPA), CH-3602 Thun; [d]University of Modena and Reggio Emilia, I-41121 Modena, Italy

Keywords: 3D printing · CMOS · NMR · Sub-nL

Nuclear magnetic resonance (NMR) allows, among many other applications, for non-invasive studies of intact living entities. In particular, NMR is successfully employed for imaging and to obtain detailed information on the chemical composition of large living animals. NMR experiments at the volume-scale of single microorganisms and single cells are hindered by the limited sensitivity of the detector and the difficulties in positioning such small samples in proximity of the detector. Many interesting biological entities (*e.g.* the human ovum and those of other mammalians) have typical volumes below 1 nL. Commercial NMR probes have a too low sensitivity for the investigation of such small important entities.

Recently, we introduced an innovative generation of NMR probes, based on the combination of single-chip CMOS integrated electronics together with high-resolution 3D printed microfluidic structures. The CMOS technology is used to implement miniaturized probes, where a multilayer microcoil is co-integrated on the same chip with the transceiver electronics. The microfluidic structures are fabricated using a two-photon polymerization 3D printing technique having a resolution better than 1 μm^3. The adopted 3D printing approach allows to fabricate complex microfluidic structures tailored to position and feed biological samples in the most sensitive region of the CMOS-integrated microcoil. Using a probe having a sensing volume of 200 pL and a sensitivity of 2×10^{13} spins/$Hz^{1/2}$, we demonstrated direct reading of endogenous compounds in sub-nL eggs of microorganisms and in sub-sections of worms. In the figures we report spectra of body sections and eggs of small animals (which show differences among species and heterogeneities among individuals) and of a test liquid solution (which demonstrates a spectral resolution of 2 Hz). **The proposed combination of CMOS and 3D printing technologies achieves state-of-the-art sensitivity for the NMR studies of nanoliter and subnanoliter living biological entities.**

Received: May 13, 2019

References

M. Grisi, F. Vincent, B. Volpe, R. Guidetti, N. Harris, A. Beck, G. Boero, *Sci. Rep.* **2017**, *7*, 44670.

E. Montinaro, M. Grisi, M. C. Letizia, L. Pethö, M. A. M. Gijs, R. Guidetti, J. Michler, J. Brugger, G. Boero, *Plos One* **2018**, *13*, e0192780.

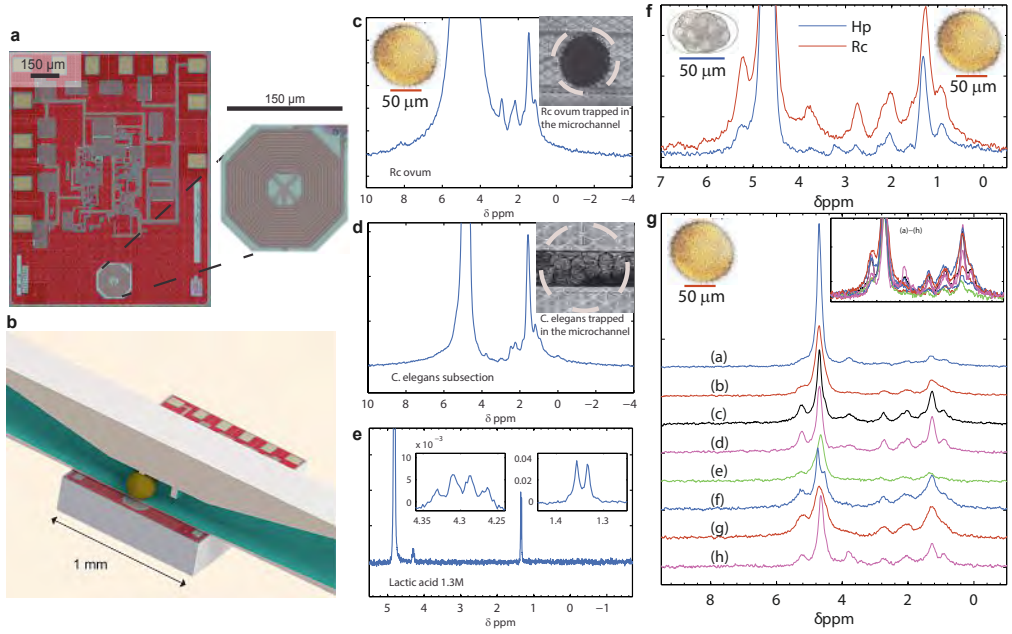
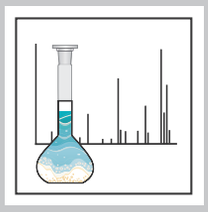


Fig. 1. (a) Single-chip CMOS transceiver with co-integrated microcoil, and (b) assembled with a 3D printed microchannel. (c) ^{1}H NMR spectrum of a single tardigrade ovum, belonging to *Richtersius coronifer* (Rc), in H_2O. (d) ^{1}H NMR spectrum of an intact *Caenorhabditis elegans* worm subsection in PBS. (e) ^{1}H NMR spectrum of 1.3 M lactic acid in H_2O. (f) ^{1}H NMR spectra of single sub-nL ova (*Richtersius coronifer* (Rc) and the parasitic nematode *Heligmosomoides polygyrus bakeri* (Hp)). (g)^{1}H NMR spectra of eight, visually identical, Rc ova in D_2O.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2019.759 Chimia 73 (2019) 759



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Micropollutants in Bernese Waters

Claudia Minkowski*, Matthias Ruff, and Rico Ryser

*Correspondence: Dr. C. Minkowski, Water and Soil Protection Laboratory, Office of Water and Waste Management of the Canton of Berne (OWW), Schermenweg 11, CH-3014 Bern, E-mail: claudia.minkowski@bve.be.ch

Keywords: Micropollutants · Plant Protection Products (PPP) · Wastewater

Micropollutants such as residues of pharmaceuticals, ingredients of products for daily use or plant protection products (PPP) occur in the aquatic environment in concentrations of microgram to nanogram per liter. Some of them can be harmful for water organisms even at such low concentrations. Micropollutants enter the water bodies either by discharge of wastewater, as so-called point sources, or as diffuse entrances directly from the site of application into the water, *e.g.* by run-off of PPPs. Major rivers are mainly affected by point sources from urban wastewater, with pollution increasing the higher the percentage of wastewater. Due to the large water amounts, these micropollutants are diluted to lower concentrations, thus reducing the ecotoxicological risk for water organisms. But the high load of micropollutants in these major waters is a matter of concern. Diffuse inputs account quantitatively less than point sources. But since they affect all sizes of water bodies, especially in small rivers and lakes, they are often responsible for enhanced concentrations. In these cases, the associated risk increases with the intensity of land use in the catchment area. The main source for diffuse inputs is agriculture, especially the use of PPPs. It is therefore not surprising that peaks of high concentrations of critical substances are found mainly during the application period.

Micropollutants, especially if they are persistent and mobile, are also found in groundwater aquifers. Concentrations are usually very low and mostly non-hazardous for humans and animals. However, these micropollutants in the groundwater lead to a potential contamination of our drinking water. For precautionary reasons we should strive to keep this important resource free of impurities. Besides, groundwater aquifers tend to being inert and having a long lasting memory. It will take ages to decades for showing improvements, even if measures are implemented today.

Micropollutants are ubiquitous in Bernese Waters and can be detected in running waters, in lakes, and in groundwater. Pollution increases with population density and intensity of agricultural activities in the catchment area. For precautionary reasons, especially water bodies being used for the production of drinking water deserve special protection.

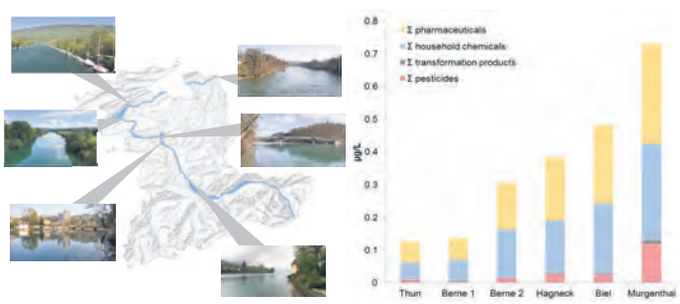
Acknowledgement

A special thanks goes to the collaborators of the Water and Soil Protection Laboratory.

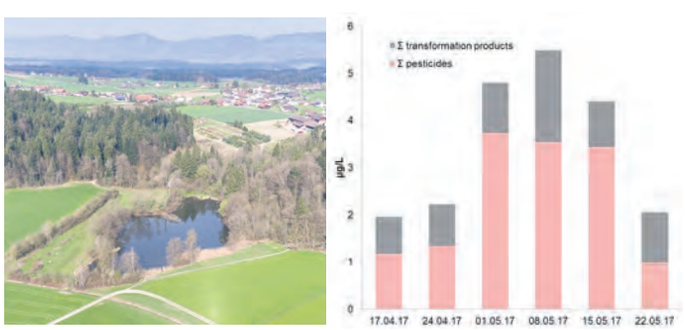
Received: June 3, 2019

Reference

Further information on the Water and Soil Protection Laboratory or the water quality of bernese waters can be found on *https://www.bve.be.ch/bve/de/index/wasser/wasser/gewaesserqualitaet.html.*



Micropollutants in the river Aare at six downstream measuring points with increasing population density and intensity of agricultural activities in the catchment area. The concentrations are not critical for water organisms, but the load at Murgenthal (top right) of 16.2 kg micropollutants per day is very high.



Micropollutants in the Wolferbach, a tributary to a small lake in a rural area, show concentration peaks at the beginning of May, a period that correlates well with the application time of PPPs. This results in a strong risk for water organisms.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2019.836 Chimia 73 (2019) 836

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

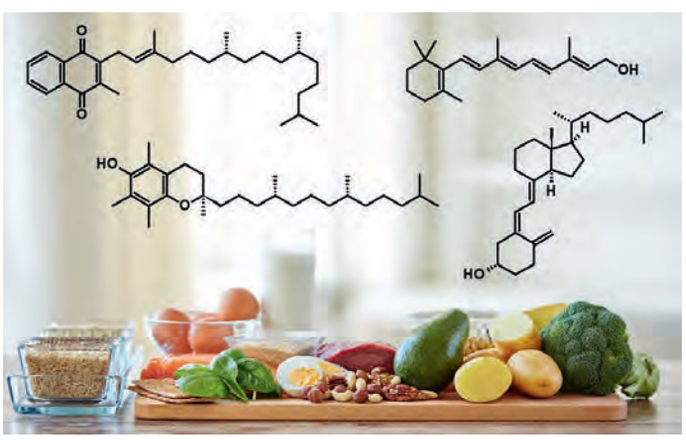
Fat-soluble Vitamins in Foods: Analysis by Supercritical Fluid Chromatography Coupled to Mass Spectrometry

Esther Campos-Giménez* and Jean-Marie Oberson

*Correspondence: E. Campos-Giménez, Nestlé Research, Vers-chez-les-Blanc, CH-1000 Lausanne 26, E-mail: esther.campos-gimenez@rdls.nestle.com

Keywords: Fat-soluble vitamins · Supercritical fluid chromatography · Vitamin A · Vitamin D · Vitamin E · Vitamin K

Fat-soluble vitamins are essential to maintain metabolic functions in humans and other species. Vitamin A is vital to maintain normal vision and healthy skin. Vitamin E's primary action in the human body is the protection of the cellular membranes from oxidation. Vitamin D is required to maintain healthy bones and muscles. Vitamin K plays an important role in blood coagulation.



Fat-soluble vitamins are essential to maintain health. Vitamin A (retinol) is found in eggs, milk and meat. Vitamin E (α-tocopherol) is naturally present in oils and nuts. Vitamin K (phylloquinone) can be found in leafy greens and oils, while vitamin D (calciferol) in the diet originates mainly from eggs and milk.

Fat-soluble vitamins, due to their physicochemical properties, are frequently extracted from the food matrix using large volumes of organic solvents. The different compounds are then analyzed using liquid chromatography, most of the times in normal-phase mode using organic solvents as the main mobile phase.

Supercritical Fluid Chromatography (SFC) uses a fluid in supercritical condition as mobile phase. Different fluids have been historically used, which presented several health, safety, and environmental concerns. In the past decades, SFC has evolved into modern SFC, based on the use of CO_2, with enhanced safety and environmental advantages. CO_2 is safe and nontoxic. Additionally, when compared to liquid chromatography, SFC separations are faster and provide sharper peaks and improved resolution.

A new method for the analysis of fat-soluble vitamins using SFC-MS/MS was developed aiming to decrease the use of organic solvents. The extraction solvents used are aqueous papain solution, methanol, and isooctane. The extraction procedure allows the simultaneous isolation of vitamin A (as retinyl acetate, palmitate or retinol), vitamin E (as α-tocopherol or α-tocopheryl acetate), vitamin K (as phylloquinone or menaquinone-4) and vitamin D (cholecalciferol and ergocalciferol). The method is successfully applied in daily routine work.

The application of supercritical fluid chromatography coupled to mass spectrometry allows the simultaneous analysis of fat-soluble vitamins in foods. The method shows enhanced safety and reduced cost as compared with previous methodologies. Its application in control laboratories dramatically increases sample throughput and reduces solvent consumption.

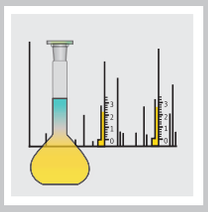
Received: July 12, 2019

Reference

J. M. Oberson, E. Campos-Giménez, J. Rivière, F. Martin, *J. Chromatogr. B* **2018**, *1086,* 118.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2019.944 Chimia 73 (2019) 944



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Equipment-free Detection of K^+ on Paper

Yoshiki Soda[a], Daniel Citterio*[b], and Eric Bakker*[a]

*Correspondence: Prof. Dr. E. Bakker[a], E-mail: Eric.Bakker@unige.ch;
Prof. Dr. D. Citterio[b], E-mail: citterio@applc.keio.ac.jp
[a]Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, CH-1211Geneva, [b]Department of Applied Chemistry, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, 223-8522 Yokohama, Japan,

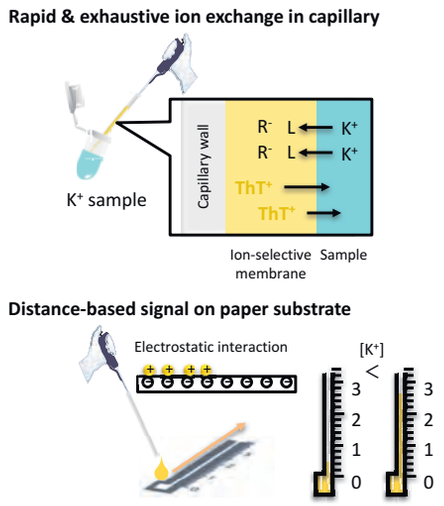
Keywords: Equipment-free analysis · Ion-selective membrane · Point-of-care diagnosis · Serum sample analysis

Microfluidic paper-based analytical devices (μPAD) have been introduced as simpler variants of lab-on-a-chip (LOC) devices, aiming at point-of-care (POC) diagnostics of various analytes. While colorimetric detection is a promising signal output principle, it has difficulty meeting the requirements of the World Health Organization and associated feasibility of commercialization.

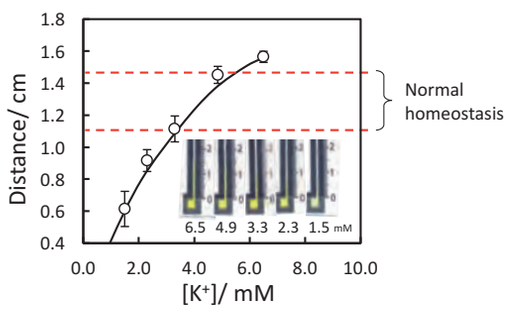
This work describes μPADs for the equipment-free detection of K^+ in a 10 μL serum sample where K^+ concentration is translated to a distance-based signal. This goal is achieved by separating recognition and detection steps. The recognition part uses an ion-selective film solvent-cast into a glass capillary. This coating contains a charged dye, thioflavin T (ThT^+), along with the K^+ ionophore valinomycin. Once a 10 μL sample volume is aspirated into the capillary by a commercial pipette, K^+ in the sample is allowed to be exhaustively exchanged with ThT^+, thereby releasing a quantity of ThT^+ that reflects the original amount of K^+. To allow for a distance-based detection, this ThT^+ is discharged into a paper channel defined by hydrophobic wax barriers. As the sample flows, ThT^+ binds electrostatically to anionic functionalities of the cellulose substrate, which is further enhanced by a polyanionic coating. Higher amounts of K^+ translate into a higher quantity of ThT^+, in turn resulting in an increased distance of the perceivable color band on the μPAD.

The exhaustive depletion of K^+ makes it possible to detect K^+ with high sensitivity in a narrow concentration range, suitable for serum diagnostics (3.5~5 mM). In comparison with traditional ion optodes, this readout principle does not depend on the sample pH and gives a more sensitive response while maintaining a high selectivity. The distance-based readout is more robust than colorimetric detection, which is notoriously difficult to quantify, and does not require any readout equipment. **This device principle may pave the way for the practical realization of μPADs for the detection of ions.**

Apply a drop of serum through a special capillary into a paper channel and get the result!



Schematic illustration of the distance-based analysis of potassium ions with an ion-selective capillary film (top) that exhaustively exchanges potassium ions for the cationic dye ThT^+. This dye is in turn detected on paper *via* electrostatic interactions, giving a distance-based visual readout (bottom). Adapted with permission from Y. Soda *et al*., *ACS Sensors* **2019**, *4*, 670. Copyright (2019) American Chemical Society.



Result of distance-based analysis of K^+ in pooled serum samples. Adapted with permission from Y. Soda *et al*., *ACS Sensors* **2019**, *4*, 670. Copyright (2019) American Chemical Society.

Received: September 9, 2019

References

Y. Soda, D. Citterio, E. Bakker, *ACS Sensors* **2019**, *4*, 670.
B. H. Weigl, O. S. Wolfbeis, *Anal. Chem*. **1994**, *66*, 3323.
X. Xie, J. Zhai, E. Bakker, *Anal. Chem.* **2014**, *86*, 2853.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2019.1033 Chimia 73 (2019) 1033

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

SU-8 Micropipettes for Gentle Single-cell Manipulation

Vincent Martinez, Hana Han, János Vörös, and Tomaso Zambelli*

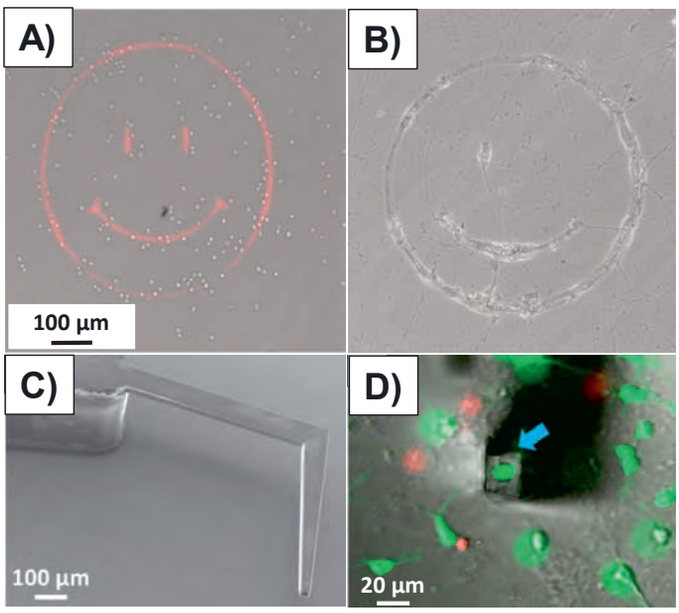
*Correspondence: Prof. Dr. T. Zambelli, E-mail: ztomaso@ethz.ch, Laboratory of Biosensors and Bioelectronics, Institute for Biomedical Engineering, ETH Zurich, Gloriastrasse 35, CH-8092 Zurich,

Keywords: AFM cantilever · Microfabrication · Micropipette · Neuronal circuit · Single cell

In 1904, Marshall Barber reported about the invention of glass micropipettes for bacterial isolation and inoculation. A century afterward, glass pipettes are a standard tool for single-cell manipulation. As they are rigid, the technical challenge is to implement a feedback to enable a controlled and thus gentle approach onto a cell.

We established a microfabrication process to produce atomic force microscopy (AFM) cantilevers with an embedded microchannel in order to take advantage of the force feedback. They are bendable because they are entirely made of the resin SU-8. With these devices, we are able to determine the adhesion force of hundreds of yeast cells on glass and chemically coated glass enlarging the statistical relevance of such experiments. The tough issue was to find the right material compatible with the SU-8 processing as sacrificial layer for the formation of the microchannel. We used an electrochemically deposited copper film which allows for a flexible choice of its thickness up to tens of micrometers. In this way, we can load the probe with a solution containing live cells and utilize it as a tool to pattern single-cells on a substrate with micrometric precision. We defined two main protocols: the direct deposition (additive patterning) and the selective removal of cells (subtractive patterning). Cells can be placed in elastomeric wells and on flat adhesive surfaces by physical confinement and mechanical squeezing upon application of a positive pressure. On the other hand, detachment and removal of chosen cells from a cell layer is achieved by exerting a negative pressure depending on the chemical functionalization of the substrate (adhesive or repulsive). In this way, we realized complex networks of neurons that could be tracked after several days. Such patterns can be eventually adjusted by subsequent *in situ* deposition or removal of mature cells. They represent the first milestone for the bottom-up approach of engineering neuronal circuits with controlled topology to investigate basic mechanisms in neuroscience such as signal transmission and neurocomputation.

Our sideways microfabrication scheme offers the possibility of designing various types of cantilevers with different shapes and lengths within a single wafer. We are now envisaging the fabrication of AFM SU-8 pipettes with embedded self-sensing aiming at a system with several micropipettes, each one having a different task and thus driven independently, for applications not only in sequential single-cell manipulation but in multimaterial 3D printing.



A) Subtractive patterning of primary hippocampal neurons on pre-patterned surfaces: Neurons before and B) after removing the unwanted cells from the pattern. By 12 days *in vitro*, neuronal processes originating from the cells on the left side of the smiley closed the loop by following the pattern. C) SEM image of a side-view SU-8 micropipette with a 500-µm long tip. D) Superposition of a bright field optical image and of the corresponding fluorescent one showing a pipette approached onto the selected neuron in matrigel for the isolation process (the blue arrow indicates the rectangular probe apex).

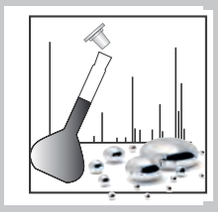
Received: October 17, 2019

References

V. Martinez, P. Behr, U. Drechsler, J. Polesel Maris, E. Potthoff, J. Vörös, T Zambelli, *J. Micromech. Microeng.* **2016**, *26*, 055006.
V. Martinez, C. Forró, S. Weydert, M. Aebersold, H. Dermutz, O. Guillaume-Gentil, T. Zambelli, J. Vörös, L. Demkó, *Lab Chip* **2016**, *16*, 1663.
H. Han, V. Martinez, M. J. Aebersold, I. Lüchtefeld, J. Polesel-Maris, J. Vörös, T. Zambelli, *J. Micromech. Microeng.* **2018**, *28*, 095015.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2020.58 Chimia 74 (2020) 58



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Reactivity of Soil Mercury by Stable Isotope Dilution

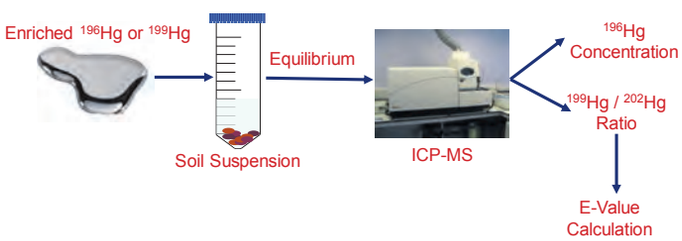
Waleed H. Shetaya[ab] and Jen-How Huang*[a]

*Correspondence: PD Dr. J. H. Huang[a], E-mail: jen-how.huang@unibas.ch
[a]Environmental Geosciences, University of Basel, Bernoullistrasse 30, CH-4056 Basel; [b]Air Pollution Research Department, National Research Centre, 33 El-Bohouth St., Dokki, Giza 12622, Egypt

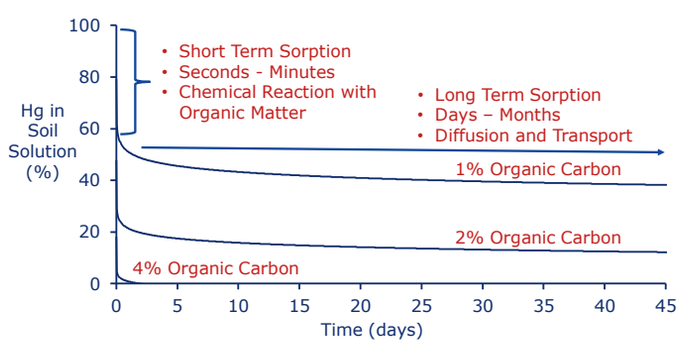
Keywords: ICP-MS · Kinetic Modelling · Metal Availability · Soil Mercury · Stable Isotopes

Recognition of global mercury (Hg) pollution has prompted research and policy development that led to the 2013 UN's Minamata Convention aiming to reduce human exposure to this neurotoxin.

Soil plays a key role in the global cycle of Hg. The bioavailability of soil Hg, and consequently its potential health risks, are a function of its reactivity. Traditionally, the reactive fraction of soil Hg has been determined by chemical extraction; however, extraction methods are prone to many inaccuracies resulting from the enforced release of solid-phase Hg to the extraction solution.



Isotopic dilution procedure.



Temporal reduction in the solution phase concentration of Hg added to soil microcosms. The sorption kinetics of Hg were modelled using a parameterized Elovich expression fitted to the experimental data of $^{196}Hg^{+2}$ sorption in soils with different properties. Modelled lines are displayed for a range of soil organic carbon values at a fixed pH of 4.4.

Stable isotope dilution (SID) has recently become the most promising approach to estimate the reactivity of soil metals due to the greater availability and abilities of Inductively Coupled Plasma Mass Spectrometry (ICP-MS). However, the logistical and analytical complexities resulting from the multiple stable isotopes and chemical forms of Hg has made it very challenging to apply SID on Hg.

We have developed, for the first time, a SID protocol to quantify Hg lability (Hg-E) in soils using enriched ^{199}Hg (spike isotope) and ^{202}Hg (reference isotope). Application of the developed protocol on soil samples collected from Visp, Switzerland, delivered novel knowledge in comparison to the conventional extraction methods. The reactive Hg pools estimated by CH_3COONH_4 and $MgCl_2$ extractions were considerably lower than the Hg-E values. However, the limited range of Hg-E (12–25% of total Hg), as opposed to the wide range of total Hg concentrations (0.37–310 mg kg^{-1}), demonstrated the capability of soils to stabilise large amounts of Hg, and therefore diminishing the risks of Hg transfer to humans and animals.

The temporal change in the solubility of newly added Hg to soils was also followed and modelled using trace levels of $^{196}Hg^{+2}$ spikes. The very low natural abundance of ^{196}Hg (0.15%) rendered it a perfect candidate to study the reactivity of Hg in soil under almost natural conditions. Kinetic simulations of the obtained results predicted that in organic-rich soils Hg is immobilised within minutes of contact, whereas in alkaline arid soils Hg may remain reactive for many years.

Our investigations demonstrated the viability and versatility of stable isotope dilution methods to study and predict the fate of Hg in soil and to assess its potential risks with high precision and with minimum disturbance to the natural soil equilibrium.

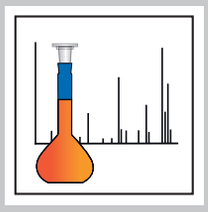
Received: December 9, 2019

References

W. H. Shetaya, S. Osterwalder, M. Bigalke, A. Mestrot, J. H. Huang, C. Alewell, *Env. Sci. Technol. Lett.* **2017**, *12*, 556.
W. H. Shetaya, J. H. Huang, S. Osterwalder, A. Mestrot, M. Bigalke, C. Alewell, *Chemosphere* **2019**, *221*,193.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2020.193 Chimia 74 (2020) 193



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

An Introduction to Analytics for Autologous Cell and Gene Therapies

Christoph Meyer*, Erik Rutjens, and Thomas Merlin

*Correspondence: Dr. Chr. Meyer, Novartis Pharma AG, Cell and Gene Therapies, Schaffhauserstrasse 101, CH-4332 Stein, E-mail: christoph.meyer@novartis.com

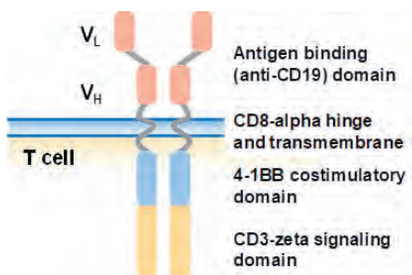
Keywords: Autologous cell and gene therapy · Bioassay · CAR-T · IFNγ

Autologous cell and gene therapies, such as the Chimeric Antigen Receptor Therapy (CAR-T), use the patient's own immune system to fight certain types of cancers. A patient's T cells are reprogrammed with a viral vector to express a transgene receptor, CAR, enabling them to destroy the cancer cells which express a particular antigen: B cells expressing CD19 (Cluster of Differentiation 19).

Leukapheresis material is collected and cryopreserved at the clinical site and then sent to the manufacturing facility where the enrichment and activation is taking place, making use of CD3/CD28 antibody-coated beads before T cell transduction with a lentiviral vector for genetic reprogramming. T cell expansion is the next step before bead removal, formulation and cryopreservation. Then, the cells are shipped back to the clinical site and the administration is taking place. In the patient, the antigen-binding domain recognizes CD19 on B cells. The CD3-zeta signaling domain initiates T cell activation and mediates antitumor activity.

Cell and gene therapy cell processing at the manufacturing site.

The quality control of such a therapy is very specific and 'customized', with biological/molecular methodologies being essential. For Identity testing, a Polymerase Chain Reaction (PCR) based test confirms the presence of the CAR transgene. Safety testing is key, to confirm there is no microbiological contamination and no residual virus DNA in the final product. Tested parameters are: bacterial endotoxins, sterility, mycoplasma, and determination of virus DNA by quantitative PCR. Purity testing includes cellular phenotyping by flow cytometry testing for viable T-cell percentage, transduction efficiency tested by CAR, quantitative PCR and cell viability test. For Impurity testing, residual beads are tested by microscopy, and CD19 B-cells are determined by flow cytometry. For Quantity, the cell count is measured and used together with the purity analysis to calculate viable cell number and dose. Finally, for Potency, CAR-expression by flow cytometry and release of IFNγ in response to CD19-expressing target cells is determined.



Mode of action: CAR-T cells express chimeric antigen receptors. V_L, V_H: light and heavy chain variable domain, respectively.

The laboratories for the execution of quantitative PCR test methods and the rooms for the cell-based assays are to be clearly separated from each other to avoid cross-contamination. Stability is necessary to assure the shelf life of the product. In addition, an important point to consider is the stability of samples and critical analytical reagents in the laboratory.

Cell and gene therapies offer the potential to transform medicine. Analytical tools and technology are key for ensuring the quality of the treatment being produced.

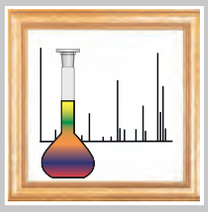
Definitions

T-cell: Type of lymphocyte that develops in the thymus gland.
B-cell: Type of white blood cell of the small lymphocyte subtype.
B-lymphocyte antigen CD19: Transmembrane protein encoded by the gene CD19.
The CD3 protein complex is composed of polypeptide chains. With the T-cell receptor (TCR) and the zeta chain, they form the TCR-CD3 complex, used to activate T lymphocytes.
CD28 is one of the proteins expressed on T cells that provide co-stimulatory signals required for T cell activation.
IFNγ: Dimerized soluble cytokine that is the only member of the type II class of interferons. Interferon-γ is involved in inflammatory processes. It has antiviral, immunostimulating and anti-tumor properties.

Received: January 15, 2020

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2020.299 Chimia 74 (2020) 299



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Age and Provenance Analysis from Micrograms of Artwork Pigments

Stefan Kradolfer*[a], Laura Hendriks[b], Tiziana Lombardo[c], Vera Hubert[c], Markus Küffner[d], Narayan Khandekar[e], Irka Hajdas[b], Bodo Hattendorf[a], Arno Synal[b], and Detlef Günther[a]

*Correspondence: S. Kradolfer[a], E-mail: stefan.kradolfer@inorg.chem.ethz.ch.
[a]Department of Chemistry and Applied Biosciences, ETH Zurich, Vladimir-Prelog-Weg 1, CH-8093 Zurich; [b]Department of Physics, ETH Zurich, Otto-Stern-Weg 5, CH-8093 Zurich; [c]Laboratory for Conservation Research, Collection Centre, Swiss National Museum, Lindenmoosstrasse 1, CH-8910 Affoltern am Albis; [d]Swiss Institute for Art Research (SIK-ISEA), Zollikerstrasse 32, CH-8008 Zurich; [e]Straus Center for Conservation and Technical Studies, Harvard Art Museums, 32 Quincy Street Cambridge, MA 02138, USA

Keywords: ^{14}C-dating · AMS · Art · Lead isotopes · MC-ICPMS · Paintings

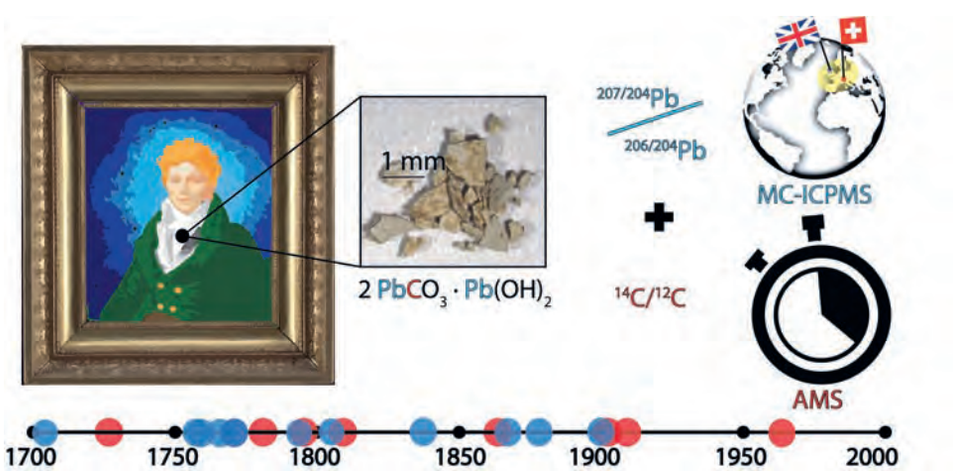
Generally, it is possible to make a lot of money in the business of selling art, and art forgery is a direct consequence. However, no art buyer wants to be fooled, thus in the puzzle of artwork authentication the demand for scientific evaluation is continuously rising. Isotopic analysis is a very promising approach to tackle these problems by providing insights into the age and the provenance of specific materials. In this study, we focused on lead white ($2PbCO_3 \cdot Pb(OH)_2$), a widely used pigment from ancient times up till the middle of the 20th century. Accelerator mass spectrometry (AMS) allows us to measure the ^{14}C age of the pigment carbonate anion, while multi-collector inductively coupled plasma mass spectrometry (MC-ICPMS) yields highly precise lead isotope ratios for a geographical classification, as shown by Fortunato *et al.* This study had only become possible due to recent advances in AMS allowing accurate age determination from µg-levels of carbonate – hereby allowing to minimize the sample size.

Twenty paintings with signed dates covering the 17th up to the 20th century, originating either from Switzerland or Great Britain, were investigated. Sample amounts ranging from a few hundred µg's to a maximum of 1.5 mg allowed the Pb isotope ratios of the carbonates as well as the corresponding ^{14}C ages of both the carbonates and the oil binders to be determined. The results of all paintings, except one, allowed the conclusion that the used pigment was produced following a traditional production process incorporating atmospheric CO_2 and allowed to give a time range for the production of the used pigment. The lead isotope measurements showed no clear distinction between the artworks' origins but corresponded to lead ore deposits located in Europe. **In conclusion, these results illustrate the great potential of combining isotope analyses from a minute piece of lead white in the mg-range, allowing for insights into its age and provenance.**

Received: January 28, 2020

References

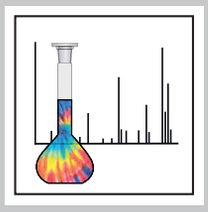
G. Fortunato, A. Ritter, D. Fabian, *Analyst* **2005**, *130*, 898.
L. Hendriks, S. Kradolfer, T. Lombardo, V. Hubert, M. Küffner, N. Khandekar, I. Hajdas, H. A. Synal, B. Hattendorf, D. Günther, *Analyst* **2020**, *145*, 1310.



Lead white samples are taken directly from paintings and further analyzed by AMS (radiocarbon age) and by MC-ICPMS (lead isotope signature). The ^{14}C ages allow conclusions to be drawn about the production process of the pigment and give a time-range of its production. The lead isotope signatures are used for geographical classification and are in agreement with European ore sources.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2020.419 Chimia 74 (2020) 419



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Simultaneous Quantification of 58 Hazardous Aromatic Amines and Positional Isomers in Textiles by LC-MS/MS

Patrick Kämpfer*[a], Stéphanie Crettaz[a], Susanne Nussbaumer[a], Michael Scherer[b], Scott Krepich[b], and Otmar Deflorin[a]

*Correspondence: P. Kämpfer[a], E-mail: patrick.kaempfer@be.ch. [a]Official Food Control Authority of the Canton of Berne, Muesmattstrasse 19, CH-3012 Berne; [b]Sciex, Stadtturmstrasse 19, CH-5401 Baden

Keywords: Aromatic amines · Azo dyes · Clothing textiles · Isomeric amines · LC-MS/MS

Azo dyes are best suited for coloring textiles, however, they have the disadvantage of the potential occurrence of aromatic amines (AAs) used in the manufacturing process of these colors. AAs can be released upon physical skin contact through skin bacteria by wearing textiles. Due to their carcinogenic and mutagenic characteristics, 22 of these AAs are regulated by the European Union (REACH regulation). The regulated amines may be emitted by reductive cleavage of the textiles with a maximum of 30 mg kg^{-1}. A normalized test method used in laboratories worldwide to determine these amines is the DIN EN 14362-1.

The most powerful method to determine the AAs is HPLC-MS/MS. Unfortunately, some of these amines (*e.g.* toluidine) have different isomers that can lead to false-positive findings. These isomers cannot be separated by mass spectrometry, however, so the chromatography parameters had to be optimized. Choosing a modern stationary phase with a biphenyl modification, the interaction with the aromatic functional group of the amines works best. By finding the optimal pH conditions at 3.5, the isomers can be baseline separated. To enhance the sensitivity of some amines, *e.g. o*-toluidine, a post-column addition with formic acid is used. In addition, more amines suspected as carcinogenic or mutagenic were implemented in the analytical method. For better identification and differentiation of all 58 amines, a combination of retention times, MRM-transitions, ion ratios and enhanced product ion scans (EPI) showed excellent information. The linearity of the system was tested with eight points. The very good regression coefficient (>0.99) allowed calibration of the system with only one point. The method was completely validated and presented excellent quantitative performance.

Finally, the described method was applied on 150 different textile samples from local stores. The results show that about 50% of the samples contain one or even more AAs, but only in three samples regulated amines were found. The study shows that even more amines than the 22 regulated are present in textiles. **The developed method is a powerful tool to differentiate important positional isomers from regulated AAs and to analyze additional, non-regulated AAs of interest.**

Textiles with different colors and fibers were analyzed.

Acknowledgement

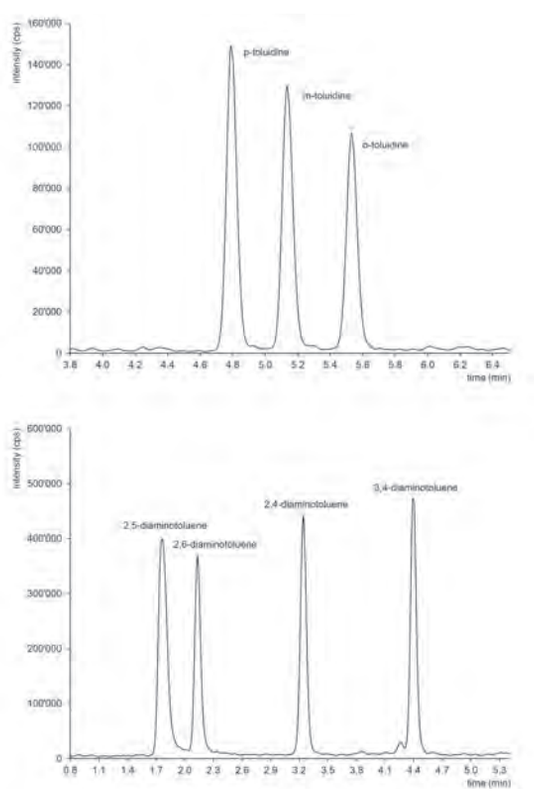
The Swiss Federal Food Safety and Veterinary Office (FSVO) is acknowledged for financing and supporting this study.

Received: March 6, 2020

References

P. Kämpfer, S. Crettaz, S. Nussbaumer, M. Scherer, S. Krepich, O. Deflorin, *J. Chromatogr. A* **2019**, *1592*, 71, doi: 10.1016/j.chroma.2019.01.039.

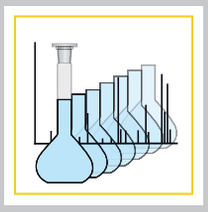
S. Crettaz, P. Kämpfer, B. J. Brüschweiler, S. Nussbaumer, O. Deflorin, *J. Consum. Prot. Food Saf.* **2019**, doi: 10.1007/s00003-019-01245-1.



Positional isomers of toluidine and diaminotoluene are separated by chromatography at pH 3.5.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2020.506 Chimia 74 (2020) 506



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Ultrasensitive Quantification of Pyrethroid and Organophosphate Insecticides in Surface Water

Michael Patrick[a], Andrea Rösch[a], Birgit Beck[a], Tobias Doppler[b], and Heinz Singer*[a]

*Correspondence: H. Singer[a], E-mail: heinz.singer@eawag.ch;
[a]Eawag, Swiss Federal Institute of Aquatic Science and Technology, CH-8600 Dübendorf; [b]VSA, Swiss Water Association, CH-8152 Glattbrugg

Keywords: GC-APCI-MS/MS · Picogram per liter · Pyrethroids · Organophosphates

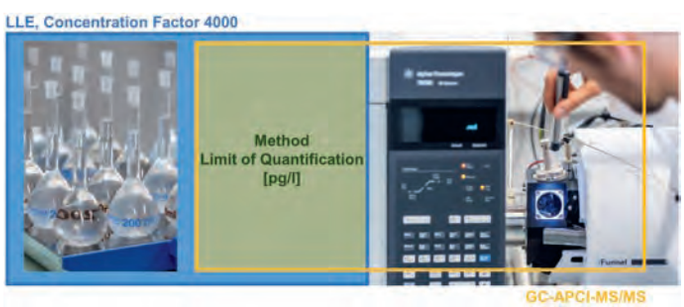
Pesticides, including herbicides, fungicides and insecticides, are frequently found in surface waters in agricultural areas, where these bioactive substances can pose a threat to the aquatic ecosystem. In particular, pyrethroid and organophosphate insecticides can be detrimental to aquatic organisms already in the pg/l range. Only recently, a quantitative analytical method able to reach these very low, but ecotoxicologically relevant concentration ranges has been developed[1] in consultation with the Swiss intercantonal laboratory group 'Task-Force Pyrethroids'.[2]

To determine the dissolved and particulate-bound pyrethroid and organophosphate insecticide concentrations, unfiltered water samples were extracted by liquid–liquid extraction using n-hexane up to an enrichment factor of 4000. Gas chromatography coupled to tandem mass spectrometry by means of chemical ionization under atmospheric pressure was used for ultrasensitive (pg/l) detection of these insecticides. With this approach, method limits of quantification (MLOQ) between 2.5 and 125 pg/l were achieved, thus reaching chronic environmental quality standards (AA-EQS) for pyrethroids and organophosphates for the first time. Using this method, concentrations of these insecticides were determined in six small- to mid-sized Swiss streams with agricultural land use from mid March to the beginning of October 2018. A total of 84 two-week time proportional composite samples were analyzed.

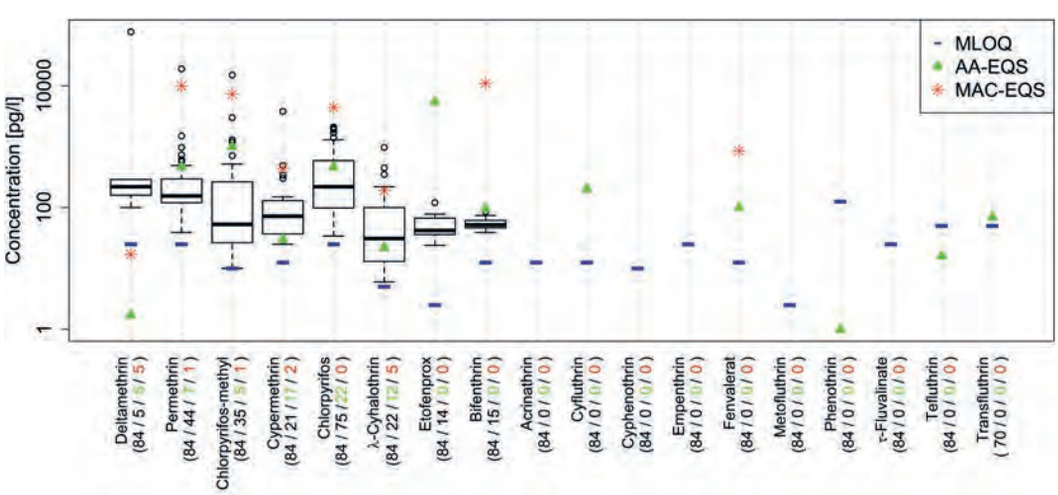
The concentrations of the individual insecticides with positive detection ranged between 6 and 77000 pg/l, with a median value of 110 pg/l. Acute environmental quality standards (MAC-EQS) were exceeded for 5 out of the 18 investigated insecticides, whereas AA-EQS were exceeded for 6 out of the 18 investigated insecticides. At least one MAC-EQS was exceeded in 15% of the samples and at least one AA-EQS was exceeded in 55% of the samples. **These results indicate at times unsatisfactory water quality in the six investigated Swiss streams, as the measured pyrethroid and organophosphate concentrations pose a risk to invertebrates, the most vulnerable aquatic organism group to these insecticides.**

Received: March 30, 2020

[1] A. Rösch, B. Beck, J. Hollender, H. Singer, *Anal. Bioanal. Chem.* **2019**, *411*, 3151.
[2] C. Moschet, *Aqua & Gas* **2019**, *99*, 2.
[3] A. Rösch, B. Beck, J. Hollender, C. Stamm, H. Singer, T. Doppler, M. Junghans, *Aqua & Gas* **2019**, *99*, 54.



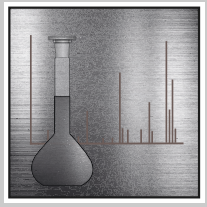
The combination of gas chromatography (GC) with chemical ionization under atmospheric pressure (APCI) and tandem mass spectrometry (MS/MS) allows for ultrasensitive quantification (pg/l) of insecticides. Photos: Alessandro della Bella, Eawag.



Concentration ranges of positively detected pyrethroid and organophosphate insecticides measured in two-week composite samples taken from six Swiss streams in 2018. The method limits of quantification (MLOQ; blue line) as well as chronic (AA-EQS; green triangle) and acute environmental quality standards (MAC-EQS; red asterisk) are indicated for each analyte. The numbers under the analyte names indicate in succession the number of composite samples analyzed (black) / number of detections (black) / number of detections > AA-EQS (green) / number of detections > MAC-EQS (red). The achieved MLOQ slightly varied between analytical runs. Here illustrated are the lowest MLOQ observed.[3]

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen, Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2020.611 Chimia 74 (2020) 611



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Innovative Approaches towards a Green and Sustainable Metal Conservation

Edith Joseph*[ab], Magdalena Albelda-Berenguer[a], Emilie Cornet[b], Luana Cuvillier[b], Sarah James[a], Lidia Mathys[a], Mathilde Monachon[a], Arianna Passaretti[b], and Silvia Russo[b]

*Correspondence: Prof. Dr. E. Joseph[ab], E-mail: edith.joseph@unine.ch/ edith.joseph@he-arc.ch
[a]Laboratory of Technologies for Heritage Materials, University of Neuchâtel, Avenue de Bellevaux 51, CH-2000 Neuchâtel; [b]Haute Ecole Arc Conservation-Restauration, University of Applied Sciences and Arts HES-SO, Espace de l'Europe 11, CH-2000 Neuchâtel

Keywords: Biotechnology · Chemical imaging · Metal conservation · Green methods

Our research topics integrate innovative aspects and inventive interdisciplinary approach at the boundaries between art conservation and natural sciences, with the aim to act against corrosion on metal artefacts (*i.e.* sculptures, archaeological items) or composite objects, such as painted metals. Thanks to advanced chemical imaging techniques, we study interactions between metals and their environment, and aspire to propose alternative green approaches in metal conservation.

For example, the application of biopassivation processes result in the formation of biogenic layers whose performances are assessed through stratigraphy studies and ageing procedures. Not only copper-based substrates are successfully treated but also iron and modern alloys, such as zinc and aluminum.

In addition, extraction methods based on siderophores or specific bacterial metabolisms are developed to remove iron or sulfur species from archeological iron objects or waterlogged wood with iron parts. Siderophores and sulfur-oxidizing bacteria solubilize harmful Fe/S species without damaging the wood structure. Also, iron-reducing bacteria are able to reduce iron(III) compounds and to form biogenic minerals.

Finally, fungal-induced translocation is applied to successfully remove rust, demonstrating high potential to develop biocleaning methods for altered and tarnished surfaces from iron but also copper and silver artworks.

In the case of painted metals, the use of spectral imaging techniques allows to provide end-users with a non-destructive diagnostic tool.

Applying the latest advances in chemical imaging and biotechnology to conservative perspectives, significant steps are achieved toward going beyond the boundaries and preconceived ideas allowing to solve the complex and multifaceted issues of heritage degradation.

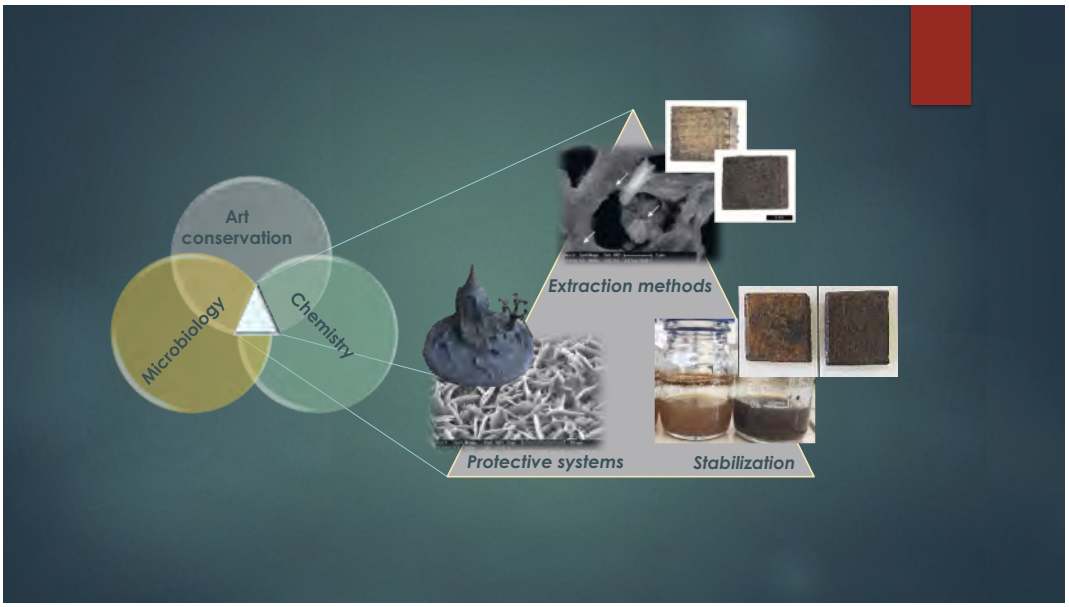
Acknowledgements

These works were supported by the Swiss Commission for the Technology and Innovation; the Swiss National Science Foundation; the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement; the Gebert Rüf Stiftung; the Stiftung zur Förderung der Denkmalpflege; and the Réseau de Compétences Design et Arts visuels, University of Applied Sciences Western Switzerland HES-SO.

Received: June 5, 2020

Reference

E. Joseph, P. Junier, *New Biotechnology* **2020**, *56*, 21.



Research topics applied to the preservation of cultural heritage.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2020.733 Chimia 74 (2020) 733

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Assessment of the Chemical Evolution of E-Cigarette Droplets

Grégory David*[a], Evelyne A. Parmentier[a], Irene Taurino[b], and Ruth Signorell[a]

*Correspondence: Dr. G. David[a], E-mail: gregory.david@phys.chem.ethz.ch. [a]Department of Chemistry and Applied Biosciences, ETH Zurich, Vladimir-Prelog-Weg 2, CH-8093, Zurich; [b]PMI R&D, Philip Morris Products S.A., Quai Jeanrenaud 5, CH-2000, Neuchâtel

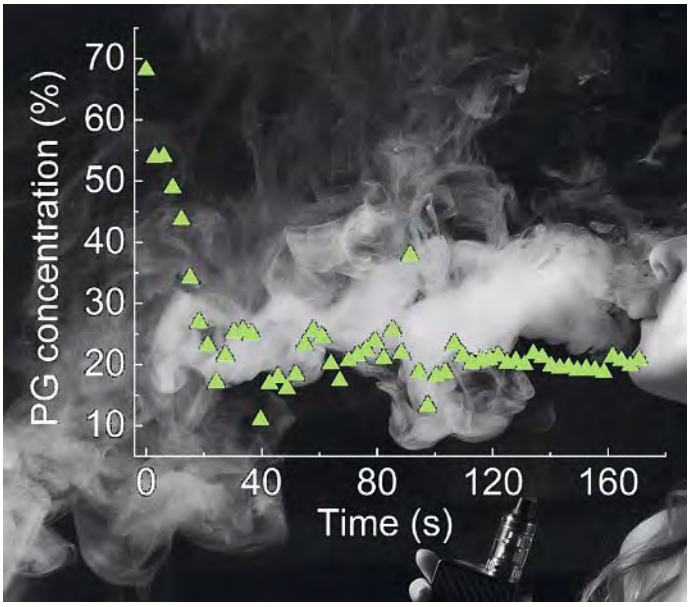
Keywords: Condensation · E-cigarette droplets · Evaporation · Nicotine · Optical trapping · Raman scattering

The electronic cigarette (e-cigarette) industry is a fast-growing industry, already representing a multi-billion-dollar market. E-cigarettes deliver nicotine to the user through droplets generated from an e-liquid. E-cigarettes hence represent an alternative to conventional tobacco products. The health impact of e-cigarettes is still debated among scientists. Despite numerous studies on e-cigarette droplets, certain aspects remain largely unexplored.

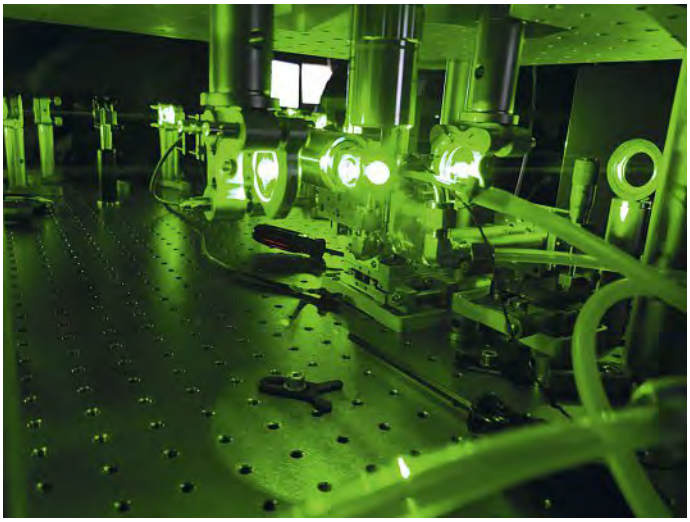
In this study, we addressed two key aspects of e-cigarette droplets: the time evolution of their chemical composition and the partitioning of their main constituents between the droplet and gas phase. For this, *in situ* Raman scattering measurements were performed on single e-cigarette droplets isolated in air by using an optical trap. Thereby, we were able to measure the time evolution of the concentrations of the main compounds in the e-cigarette droplet phase separate from those in the gas phase. The results demonstrated that the chemical composition of the e-cigarette droplets undergoes major changes on a time scale of a few to some 10 s. More than 50% of the total mass of the e-cigarette droplets evaporates within 20 s. Moreover, the pH of the e-liquid dictates the time evolution of the nicotine concentration inside the generated e-cigarette droplets. When an e-liquid with acidic pH is used, nicotine remains in the generated e-cigarette droplets, while, under basic pH, nicotine completely evaporates from the droplets within ~20 s.

Such destruction-free *in situ* measurements of single particles are opening up new perspectives for further research on e-cigarette droplets and e-liquid manufacturing. **The measured partitioning of the main e-cigarette compounds between the droplet and gas phase as a function of time will improve our understanding of their deposition in the respiratory tracts and hence of their impact on health.**

Received: July 9, 2020



The foreground graph of the figure shows the typical time evolution of the propylene glycol (PG) concentration in e-cigarette droplets isolated in air. Most of the PG in the droplets is evaporating within 20 s and its concentration then stabilizes around 20%. The background shows a person vaping an e-cigarette and the droplets generated from it.



Picture of the optical setup used for trapping single e-cigarette droplets.

Reference
G. David, E. A. Parmentier, I. Taurino, R. Signorell, *Sci. Rep.* **2020**, *10*, 7929.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2020.820 Chimia 74 (2020) 820

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Chemical and Functional Complexity in Flower Fragrance

Florian P. Schiestl*

*Correspondence: Prof. Dr. F. P. Schiestl, E-mail: florian.schiestl@systbot.uzh.ch
Institute of Systematic and Evolutionary Botany, University of Zurich, Zollikerstrasse 107, CH- 8008 Zürich,

Keywords: Bees · Mimicry · Pollination · Signaling · Volatiles

Beside colorful displays, flowers also attract pollinators by using volatile chemicals. Since the invention of high-resolution capillary gas chromatography, thousands of flower bouquets have been analyzed chemically, with the insight that floral scent is stunningly complex, with thousands of floral scent compounds known today. But what are the functions of this chemical diversity? Important advances in answering this question were gained by the coupling of gas chromatography with electrophysiology, enabling the screening of volatile blends for those compounds that are actually detected by pollinators. This led to the discovery of novel, pollinator-attracting compounds, and indirectly showed that many floral chemicals have other functions, such as anti-microbial or herbivore deterrence. Floral scent works in combination with color, and often encodes highly specific signals, because plants usually emit chemically unique bouquets of volatiles.

An example is the unusual floral scent compound 1,4-benzoquinone, specifically emitted, together with more common compounds, by *Echium* flowers. This compound, which is known as a deterrent compound in other insects, is used by *Hoplitis adunca* bees (viper's bugloss mason bee) specialized on *Echium* (viper bugloss) for pollen collection, together with the blue color of the flowers, to reliably identify their host plants.

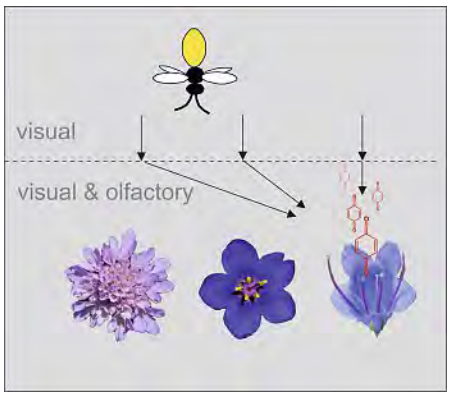
Floral scent also enables floral mimicry, the imitation of attractive but deceptive signals.[1] Some flowers imitate the intraspecific sexual signals of pollinators, and trick them into attempted copulations with the flowers, thereby enabling pollination. An Australian orchid employs a unique compound, chiloglottone, for such sexual mimicry. Upon its discovery in 2003, chiloglottone represented a new class of natural products and its biosynthesis is currently still unknown, but interestingly dependent on UV-B light.[2]

An example for an 'honest signal' is the relatively common compound phenylacetaldehyde, synthesized in plants from phenylalanine. The amount of this compound is associated with the volume of nectar available in flowers, and therefore encodes information about the profitability of a given plant for pollinators.[3] **In conclusion, the combination of high resolution gas chromatography with electrophysiological detection has led to the identification of new, unexpected compounds and gave new insights into the role of chemical signals in pollinator attraction in general.**

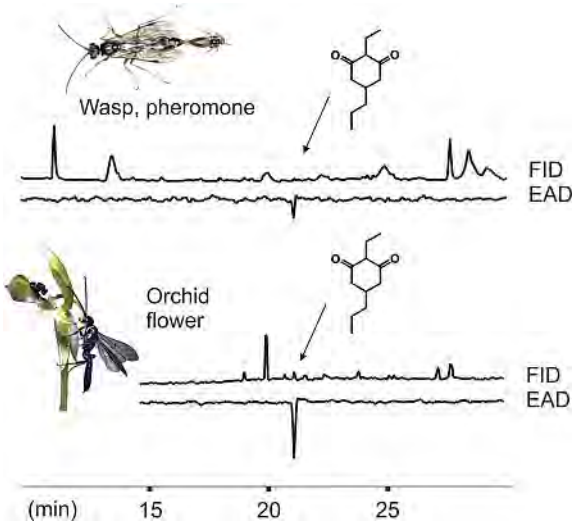
Received: August 19, 2020

References

[1] S. D. Johnson, F. P. Schiestl, 'Floral Mimicry', Oxford University Press, Oxford, **2016**.
[2] V. Falara, R. Amarasinghe, J. Poldy, E. Pichersky, R. A. Barrow, R. Peakall, *Ann. Bot.* **2013**, *111*, 21.
[3] A. C. Knauer, F. P. Schiestl, *Ecol. Lett.* **2015**, *18*, 135.



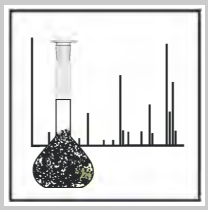
Specificity in pollinator attraction through floral scent in *Echium* flowers. The specialized bee *Hoplitis adunca* is attracted by the blue color of the flowers from a distance, but uses the specific scent compound, 1,4-benzoquinone to identify its host plants at close range.



Sexual mimicry through floral scent in the Australian orchid genus *Chiloglottis*. The pollinator of this orchid, the wasp *Neozeleboria cryptoides,* uses a single compound, 2-ethyl-5-propylcyclohexan-1,3-dione ('chiloglottone'), as sex pheromone. The females of this wasp are wingless and call with the pheromone for a male, which picks them up and mates with them (photograph above). The orchid *Chiloglottis trapeziformis* produces the same chemical to lure the males into attempted copulations with its flowers, leading to pollination (photograph below). The figure shows gas chromatograms (FID, flame ionization detector) with electroantennographic detection (EAD) using a male wasp antenna.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2020.906 Chimia 74 (2020) 906



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Microfluidics and Electron Microscopy: A Powerful Couple

Luca Rima[ac], Andri Fränkl[bc], Anastasia Syntychaki[ac], Paola Oliva[b], M. Zimmermann[a], Xavier Wildermuth[a], Rosemarie Sütterlin[a], and Thomas Braun*[ab]

*Correspondence: Dr. Th. Braun, [a]Center for Cellular Imaging and Nanoanalytics, Biozentrum, University of Basel, Mattenstrasse 26, CH-4058 Basel, E-mail: thomas.braun@unibas.ch; [b]Swiss Nanoscience Institute, University of Basel, CH-4056 Basel; [c]Equally contributed

Keywords: Cryo-EM · Microfluidics · Nanoanalytics · Single particle analysis · Single-cell analysis · Visual Proteomics

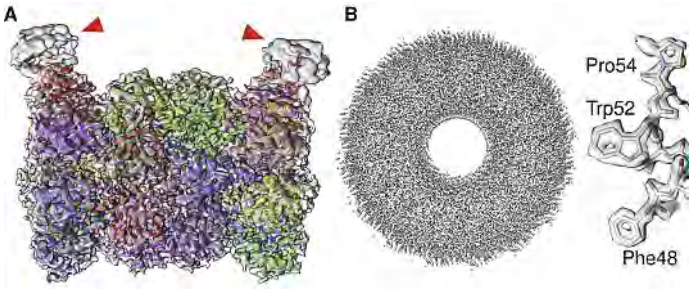
Cryogenic electron microscopy (cryo-EM) enables the determination of protein structures without crystallization using a single particle analysis (SPA) approach. Unfortunately, classical protein preparation strategies are a bottleneck in this workflow. Furthermore, EM is rarely used as an analytical tool. Here we present a modular, microfluidic toolchain called *cryoWriter* for EM sample preparation. We will discuss (i) microfluidic protein isolation coupled to EM specimen preparation for structure determination, and, (ii) single-cell lysis connected to EM sample preparation for the proteome-wide detection of structural rearrangement of protein complexes.

In SPA, a thin layer of isolated protein complexes in vitrified ice is imaged. Only several thousand to a few million recorded particles are needed to calculate a high-resolution structure. We show that this amount of protein can be prepared using our microfluidic approach. We isolated the human proteasome 20S from < 1 µL cell lysate using a combination of immuno extraction and photo elution.[1] The structures of all 14 subunits of the proteasome 20S at 3.5 Å resolution are shown. Additionally, the tobacco mosaic virus (TMV, added as resolution control) was resolved at 1.9 Å.

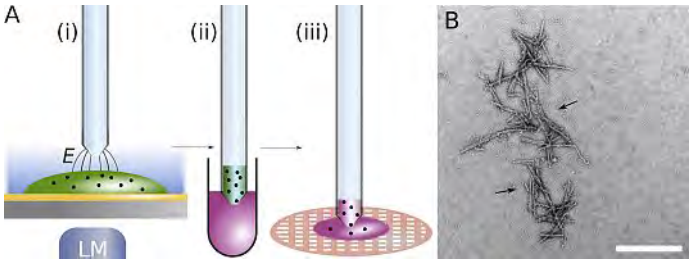
The microfluidic EM sample preparation system can be directly combined with a single-cell lysis device. The cell is disrupted by electroporation, and the cell content is aspirated into the microcapillary and subsequently used for lossless EM grid preparation.[2] Finally, the total cell lysate is imaged by EM. A *differential visual proteomics* algorithm allows for the detection of rearranged protein complexes on a proteome-wide scale.[3] While this method is still in its infancy, we demonstrate the power of microfluidic sample preparation combined with the single-molecule detection limit of EM.

We show the application of microfluidic sample preparation methods for high-resolution structure determination and single-cell nano analytics.

Received: September 11, 2020



Microfluidic protein isolation and sample preparation for high-resolution cryo-EM.[1] A) Isolation of the human proteasome 20S from less than 1 µL cell lysate. Resolution at 3.5Å. An atomic model for all 14 subunits was built. Antibody fragments (red arrowheads) were used for the isolation of the endogenous protein. B) TMV. Resolution at 1.9 Å, note the holes in the aromatic rings.



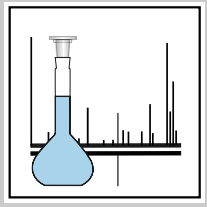
Single-cell lysis and lossless EM sample preparation for *differential visual proteomics*.[2,3] A) Principles: (i) Single-cell lysis observed by light-microscopy; aspiration of lysate into microcapillary. (ii) Conditioning of the 3 to 5 nL lysate plug. (iii) Dispensing on EM sample-carrier. B) Typical image of the cell lysate. Here, amyloid fragments (arrows) are visible from a single neuron-like cell (scalebar: 500 nm).

References

[1] C. Schmidli, S. Albiez, L. Rima, R. Righetto, I. Mohammed, P. Oliva, L. Kovacik, H. Stahlberg, T. Braun, *PNAS USA* **2019**, *116*, 15007.
[2] S. A. Arnold, S. Albiez, N. Opara, M. Chami, C. Schmidli, A. Bieri, C. Padeste, H. Stahlberg, T. Braun, *ACS Nano* **2016**, *10*, 4981.
[3] A. Syntychaki, L. Rima, C. Schmidli, T. Stohler, A. Bieri, R. Sütterlin, H. Stahlberg, D. Castaño-Diez, T. Braun, *J. Prot. R.* **2019**, *18*, 3521.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2020.1021 Chimia 74 (2020) 1021



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Ultra-Sensitive Measurement of Ocean pH

Pitchnaree Kraikaew and Eric Bakker*

*Correspondence: Prof. Dr. E. Bakker, E-mail: Eric.Bakker@unige.ch
Department of Inorganic and Analytical Chemistry, University of Geneva, 30, quai Ernest-Ansermet, CH-1211 Geneva

Keywords: Capacitive readout · Capacitor · Ion-selective electrode · pH measurement · Seawater

When S. Sørensen started to quantify solution acidity in 1909 by introducing the now ubiquitous concept of pH, he did so on the basis of a potentiometric measurement cell. From the Nernst equation this gives a change of the electromotive force that depends on the logarithmic hydrogen ion activity. Because this earliest link between pH and resulting potential has existed from the start, the practical pH scale is still based on the output of a properly calibrated potentiometric pH probe. Today, glass electrodes measured against a standardized reference electrode containing a 3M KCl electrolyte in contact with the sample through a liquid junction are most often used, but other electrode materials are also established.

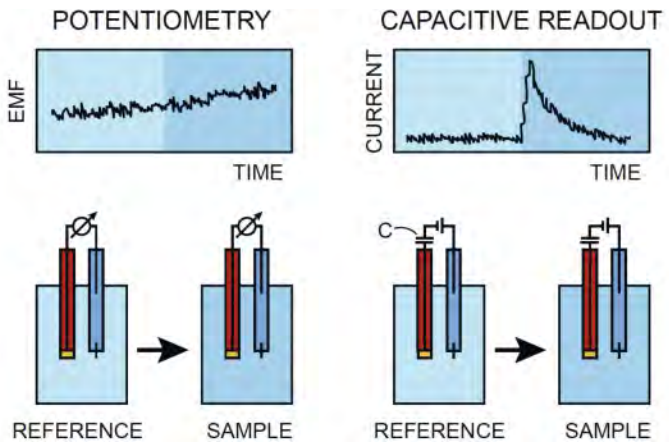
Unfortunately, potentiometric probes give reproducibilities on the order of mpH units and are therefore not adequate for some applications where exquisite sensitivities are required. One such example is the reliable monitoring of ocean acidification, an anthropogenic problem of potentially enormous significance that requires ultra-high resolution data. In the past 30 years, ocean pH has decreased by 0.035 units, about 1.2 mpH per year or just 97 µpH per month. This is a difficult measurement science problem.

We have recently reported that pH measurements from potentiometric probes can be made dramatically more sensitive by operating in a capacitive detection mode.[1,2] It requires a cell potential that is held constant while the sample pH is compared with that of a reference solution. The unique feature relative to earlier work is the use of an electronic capacitive component placed in series with the pH probe (labeled as C in the Figure). Any small pH deviation between the reference and sample solution still results in the same potential change, but since the cell potential is held constant it must be compensated by an opposite voltage change over the capacitive element. This gives rise to a current spike that is more easily identifiable than the underlying potential change. The current is background-subtracted and integrated to give the corresponding charge, which serves as signal because it is directly proportional to the change of pH. In our initial work with membrane electrodes containing an aqueous inner solution, a reproducibility (standard deviation) of 28 µpH in buffer and 67 µpH in stabilized seawater samples was achieved, which is orders of magnitude better than with direct potentiometry.[1]

More recently, the concept has been extended to all solid-state membrane electrodes that are pressure-insensitive and therefore more practical for environmental use.[2] The inner ion-to-electron transducing material is already characterized by a capacitance. It is, however, non-ideal and gives rise to sluggish current transients that are very difficult to quantify if no additional external capacitor is added. Kirchhoff's law is useful to choose the appropriate value for the external capacitor as it needs to be chosen to dominate the capacitance of the entire cell. We now aim to make this principle applicable for the electrochemical *in situ* monitoring of ocean pH with unsurpassed precision. **A capacitive readout method is orders of magnitude more sensitive than direct potentiometry**.

Received: November 4, 2020

Humpback whale off Sydney Harbour. © Eric Bakker, 2020.



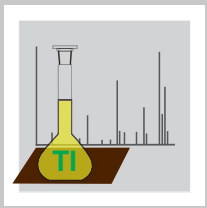
Principles of potentiometry and capacitive readout. Left: With established potentiometric pH probes, a small pH change from a reference to a sample solution (bottom) results in a potential change that is often difficult to distinguish from baseline drift (top). Right: With the new methodology the cell potential is held constant and the potential change at the pH probe results in a charging of the capacitive element C placed in series (bottom). This results in a current spike that is more easily identified and isolated (top). The final sensor signal is the charge from the integrated current, which is proportional to the capacitance value and the pH change.

References

[1] P. Kraikaew, S. Jeanneret, Y. Soda, T. Cherubini, E. Bakker, *ACS Sensors* **2020**, *5*, 650.
[2] P. Kraikaew, S. K. Sailapu, E. Bakker, *Anal. Chem.* **2020**, *92*, 14174.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2021.103 Chimia 75 (2021) 103



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Exploring the Geochemistry of Thallium in Soils by X-ray Absorption Spectroscopy and Chemical Soil Extractions

Silvan Wick[a], Bart Baeyens[b], Maria Marques Fernandes[b], Numa Pfenninger[a], and Andreas Voegelin*[a]

*Correspondence: Dr. A. Voegelin[a], E-Mail: andreas.voegelin@eawag.ch.
[a]Eawag, Swiss Federal Institute of Aquatic Science and Technology, Überlandstrasse 133, CH-8600 Dübendorf; [b]Paul Scherrer Institute, CH-5232 Villigen

Keywords: Chemical soil extractions · Clay minerals · ICP-MS · Manganese oxides · Soils · Thallium · XAS

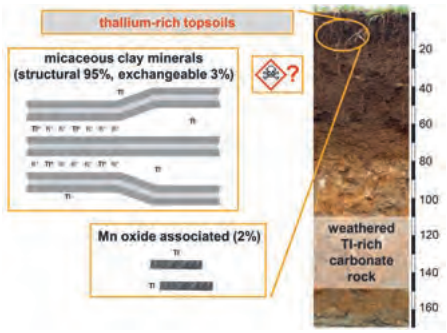
Thallium (Tl) is a toxic trace element. From Tl-contaminated soils, Tl may enter the food chain or leach into groundwater, and may therefore also threaten human health. However, mechanistic studies on the geochemical behavior of Tl in soils are still scarce. In the Swiss Jura mountains, on the Erzmatt near the village Buus (BL), soils with high Tl contents have developed on carbonate rock that hosts a hydrothermal mineralization.

In a first study, we used synchrotron-based X-ray absorption spectroscopy (XAS; Tl L_{III}-edge) to show that Tl in topsoil horizons was mainly monovalent Tl(I) associated with micaceous clay minerals (illite and muscovite) and only to a minor extent trivalent Tl(III) associated with manganese (Mn) oxides. In subsequent work, we examined the extent and mechanisms of Tl sorption onto illite and Mn oxides. In our most recent study, we used XAS to characterize the speciation of geogenic Tl in numerous topsoil samples from the Erzmatt, and performed chemical extractions to determine the concentrations of Tl in soil porewater and the amounts of exchangeable and Mn oxide-associated Tl, using inductively coupled plasma-mass spectrometry (ICP-MS) for solution analysis. From our results, we derived the following conclusions: (i) Most of the geogenic Tl in topsoils from the Erzmatt (~95%) is fixed in the structure of micaceous clay minerals. (ii) Only ~3% of the total Tl is adsorbed onto micaceous clay minerals in readily exchangeable form, and the solubility of this fraction can be described with a model for Tl adsorption onto illite. (iii) About 2% of the total Tl is associated with Mn oxides.

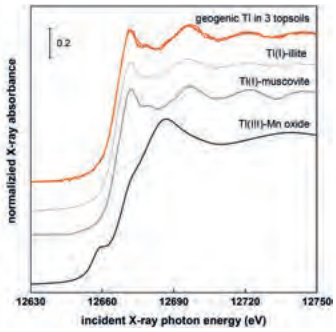
Our results allow to explain the observation of the local authorities that Tl transfer from soils to plants on the Erzmatt is limited and to better predict the effects of variations in soil chemical conditions on the solubility of Tl in soils. **In conclusion, synchrotron-based XAS together with chemical soil extractions is a powerful approach to advance the mechanistic understanding of the behavior of potentially toxic elements in soils.**

Acknowledgement

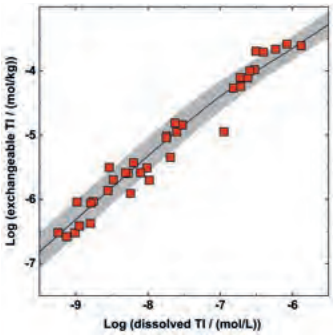
We acknowledge the Swiss National Science Foundation for funding parts of this research (contract no. 200021-162364), Daniel Schmutz and Iwan Fankhauser (Kanton Basel-Landschaft) for providing soil samples, and the Swiss Light Source, the European Synchrotron Radiation Facility, and the French National Synchrotron Soleil for access to XAS beamlines.



Geogenic Tl in topsoils from the Erzmatt (Buus, BL).



X-ray absorption spectra (at the Tl L_{III}-edge) of Tl in 3 topsoil samples with ~10 to 1000 mg/kg geogenic Tl in comparison to reference spectra of Tl(I) adsorbed onto illite, Tl(I) incorporated into muscovite, and Tl(III) sorbed onto Mn oxide.



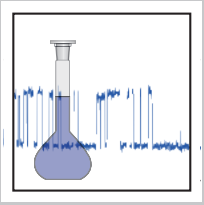
Exchangeable soil Tl (1 M NH_4-acetate extract) dissolved Tl in soil solution (0.01 M $CaCl_2$ extract) (red squares), compared to the relationship predicted using a cation exchange model for Tl adsorption onto illite (black line, gray area).

Received: December 10, 2020

References

A. Voegelin, N. Pfenninger, J. Petrikis, J. Majzlan, M. Plötze, A. C. Senn, S. Mangold, R. Steininger, J. Göttlicher, *Environ. Sci. Technol.* **2015**, *49*, 5390.
S. Wick, B. Baeyens, M. Marques Fernandes, J. Göttlicher, M. Fischer, N. Pfenninger, M. Plötze, A. Voegelin, *Geochim. Cosmochim. Acta* **2020**, *288*, 83.

doi:10.2533/chimia.2021.210 Chimia 75 (2021) 210 © Swiss Chemical Society



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Single-Molecule Analytics of Reaction Products of Guanine Oxidation in Oligonucleotides

Jens Sobek*and Ralph Schlapbach

*Correspondence: Dr. J. Sobek, E-mail: jens.sobek@fgcz.ethz.ch, Functional Genomics Center Zurich, ETH Zurich/University of Zurich, Winterthurerstrasse 190, CH-8057 Zurich

Keywords: CY3 · Dyes · Electron transfer · Fluorescence · Guanine · Oligonucleotides · Oxidation · Single molecules

We are using a modified RSII+ DNA sequencer to study molecular interactions and chemical reactions at the single-molecule level. Molecules are immobilised on a chip containing 150'000 nanostructures of about 150 nm in diameter and well depth, respectively. The small dimensions create a zero-mode waveguide through which light cannot pass but becomes evanescent. For this reason, only fluorescent molecules near the surface can be excited and thus perfectly discriminated from bulk solution.[1] Typically, some 10'000 single molecules can be monitored in parallel with a time resolution of 13 ms resulting in a large number of single-molecule fluorescence traces to give an excellent statistics for determination of binding kinetics.

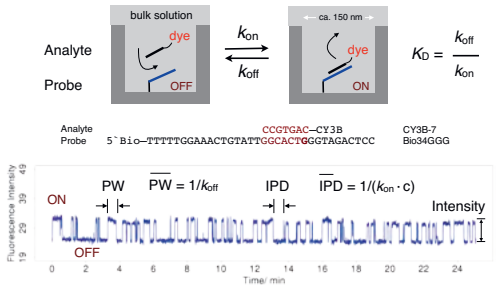


Fig. 1. Experimental setup and a resulting pulse sequence.

We investigated the hybridisation of immobilised probes (7–93 nucleotides, nt) with short oligonucleotides labelled with CY3 dye derivatives whose fluorescence is very sensitive to the stacking base pair.[2,3] Hybridisation reveals a sequence of pulses which can be monitored over a long period. The pulse sequence creates a pattern characterised by pulse width (PW), interpulse duration (IPD), and fluorescence intensity, from which kinetic constants can be calculated.[2] In many fluorescence traces, pulse pattern changes were observed that indicate chemical reactions take place at the immobilised probe which are initiated by a photoinduced electron transfer from a guanine (G) donor to the dye (Fig. 2).[4] The G radical cation can react with water, oxygen, and reactive oxygen species, respectively, leading to a large number of oxidation products, of which we so far identified 8-oxoG, and products of secondary reactions. Product formation was confirmed by SPR measurements using oligonucleotides modified with the respective oxidation product of G, and static fluorescence spectra since CY3 fluorescence strongly depends on the local environment, *i.e.* the stacking base pair.[3]

After hybridisation to a cyclic 93 nt oligonucleotide, the RSII+ allows the chemically converted molecules to be sequenced. The nature of lesions can be determined by the delay of polymerase activity (IPD ratio) that is specific for a base modification.[5]

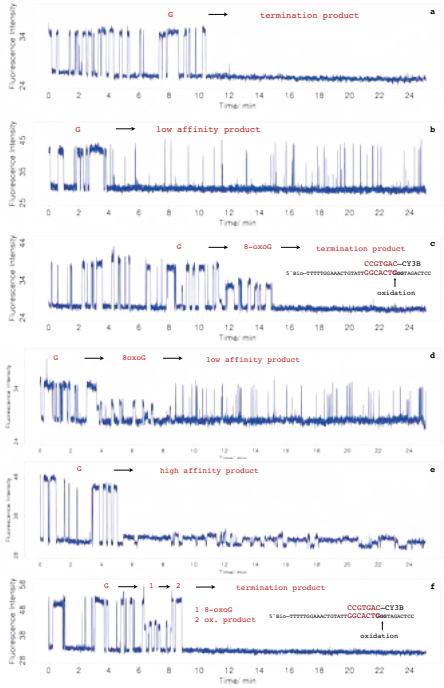


Fig. 2. Hybridisation of a 34 nt probe with CY3B-7 in the presence of oxygen. a) Formation of a product characterised by a loss of affinity (termination), b) formation of a low affinity product (short pulses), c) formation of short-lived 8-oxoG followed by termination, d) formation of 8-oxoG followed by creation of a low affinity product, e) formation of a product that is strongly quenching CY3 fluorescence, f) formation of 8-oxoG in the guanine *adjacent* to the hybrid region, further oxidation does not influence hybridisation kinetics. c) and d) feature different reaction pathways of 8-oxoG oxidation.

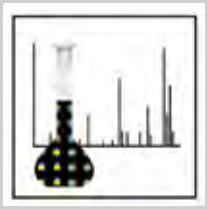
Monitoring the fate of single molecules over a long period enables us to follow sequences of chemical reactions, to analyse reaction pathways, to detect short-lived intermediates, and to determine product yields.

Received: January 20, 2021

[1] J. Korlach *et al.*, *Methods Enzymol.* **2010**, *472*, 431.
[2] J. Sobek, H. Rehrauer, S. Schauer, D. Fischer, A. Patrignani, S. Landgraf, J. Korlach, R. Schlapbach, *Methods Appl. Fluoresc.* **2016**, *4*, 015002.
[3] J. Sobek, R. Schlapbach, *Molecules* **2020**, *25*, 5369.
[4] J. Sobek, M. Schmidt, J. Grossmann, H. Rehrauer, L. Schmidt, R. Schlapbach, *Methods Appl. Fluoresc.* **2020**, *8*, 035010.
[5] J. Korlach, S. Turner, *Curr. Opin. Struct. Biol.* **2012**, *3*, 251.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2021.437 Chimia 75 (2021) 437



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

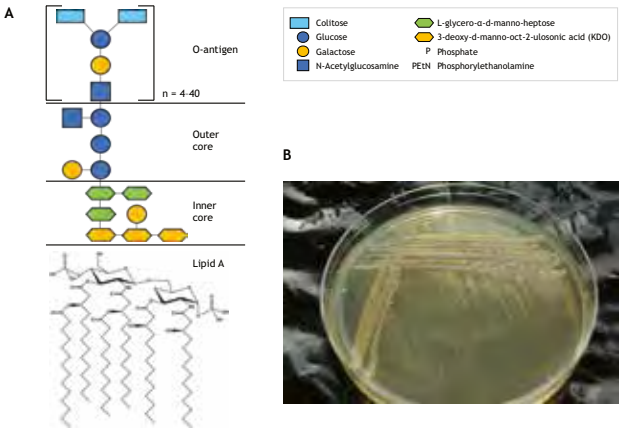
A Lipopolysaccharide Microarray for Analysis of Human Antibodies

Lisa Crone*[a], Thierry Hennet[a], and Jens Sobek[b]

*Correspondence: L. Crone[a], E-mail: lisa.crone@uzh.ch
[a]Institute of Physiology, University of Zurich, and [b]Functional Genomics Center Zurich, ETH Zurich/University of Zurich, Winterthurerstrasse 190, CH-8057 Zurich

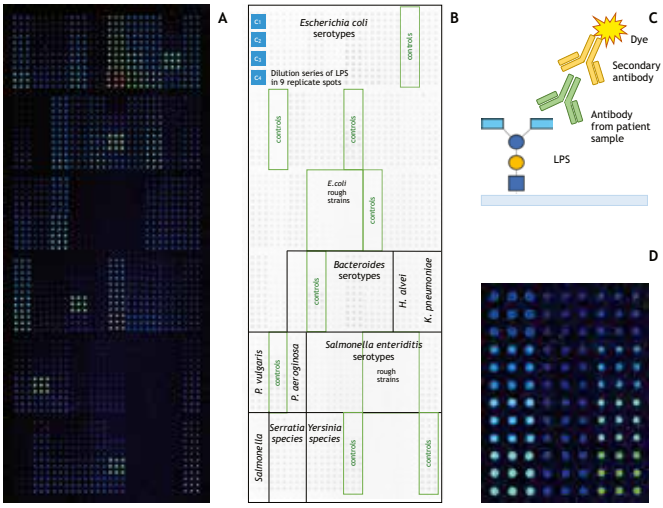
Keywords: Antibodies · Bacterial infections · Clinical studies · Lipopolysaccharides · Microarrays

During a lifetime, the immune system is challenged by a large number of bacterial infections, but also by the trillions of commensal bacteria that colonize the gastrointestinal tract. Protective antibodies are produced upon contact with bacterial antigens which specifically bind and control bacterial expansion. The surfaces of Gram-negative bacteria are almost entirely covered with lipopolysaccharides (LPS), providing membrane integrity and stability. Exposed on the cell surface, LPS interact with the surroundings and protect the bacterium from environmental threats, and are known to induce strong immune reactions. The outermost part of the LPS, the O-antigen, is highly diverse structurally and in sugar composition; the basis for bacterial serotyping. About 176 O-antigens are known for *Escherichia coli* alone.



A Schematic overview of *E. coli* O111 LPS, **B** colonies of *Hafnia alvei*.

The tremendous diversity of O-antigens on bacterial lipopolysaccharides contributes to the generation of a vast repertoire of protective antibodies. Analysis of antibody reactivity to LPS in human samples such as blood or breast milk provide an indication about infection history but also confirm the presence of protective antibodies. Microarrays displaying a library of LPS are ideally suited for this kind of analyses. The limiting factor of LPS microarrays is the availability of probes that must be extracted from bacteria in an elaborate process since only a few are commercially available.



A Scan of a microarray incubated with blood plasma, **B** LPS spotting scheme, **C** scheme of a sandwich assay, **D** enlarged part of the array visualizing spot morphology (spotted volume: 1.5 nL).

From the analytical point of view, the limit of detection of a microarray is determined by the affinity of the probe–analyte pair at the surface which is lower compared with solution. The quality of analysis critically depends on spot morphology, *i.e.* the homogeneity of probe distribution within the spot that determines the variability of the fluorescence signal as an essential part of the experimental error. For microarray production, we optimised spotting conditions, buffer composition, pH and ionic strength, and immobilisation conditions for 50 LPS. Array processing conditions were optimised regarding surface blocking (8 h, 23 °C), incubation time and temperature (16 h, 10 °C), including the subsequent reaction with a secondary fluorescence labelled antibody (1 h, 23 °C).

LPS microarrays are convenient tools to study bacterial antigen–antibody interactions and past exposure of an individual to pathogenic and commensal bacteria.

Received: March 30, 2021

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2021.550 Chimia 75 (2021) 550

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

High-throughput Quantification of Cheese Bacteria

Matthias Dreier* and Daniel Wechsler

*Correspondence: M. Dreier, E-mail: matthias.dreier@agroscope.admin.ch
Agroscope, Schwarzenburgstrasse 161, CH-3003 Bern

Keywords: Cheese quality · High-throughput · Microfluidics · Raw milk · Real-time qPCR

Raw milk cheeses are considered richer in flavor than cheeses made from pasteurized milk due to the beneficial impact of the microbial community in raw milk. However, the impact of starter and non-starter lactic acid bacteria (NSLAB) on cheese quality in terms of flavor, texture and ripening stability is still incompletely understood in Swiss cheese varieties. So far, mainly culture-dependent methods with a limited set of selective media were used to study microbial communities of Swiss raw milk cheeses. Quantitative real-time PCR (qPCR) is a well-established method for detecting and quantifying bacteria. High-throughput qPCR (HT-qPCR) using microfluidics brings further advantages by providing fast results and by decreasing the cost per sample.

Recently, we validated our new HT-qPCR system targeting 24 bacterial species relevant for cheese quality in collaboration with the Genetic Diversity Centre (GDC, ETH Zurich). The developed qPCR assays were highly specific for the target species under identical amplification conditions. The HT-qPCR system offers a fast, accurate, and cost-efficient monitoring of desired and undesired microorganisms in cheese. As for example, with a 192.24 Dynamic array integrated fluidic circuit (IFC, Fluidigm Corporation) chip, a simultaneous screening of the 24 species in 56 cheese DNA samples in technical triplicates in a single run is possible.

Microfluidics brings many advantages, allowing thousands of reactions to be performed in parallel in very small volumes (nanoliter-scale) and thus consuming massively less material and reagents in comparison to standard qPCR. However, there is also a trade-off in terms of significantly higher detection limits. This disadvantage can be partially compensated by a multiplex-PCR step with a low number of cycles to selectively enrich the target DNA sequences. This preamplification step can be used to qualitatively detect bacterial species with low abundance (< 8×10^4 genome equivalents/g cheese).

The use of the new HT-qPCR approach will provide more comprehensive data on the growth and succession of microbial species during cheese ripening, thus providing a better understanding of the influence of individual species on cheese quality. Moreover, we see a great potential for new diagnostic possibilities regarding the identification and monitoring of microbially induced cheese quality defects.

In conclusion, HT-qPCR is a fast, reliable and economic approach to quantify quality-relevant bacterial species in cheese and has promising applications, such as monitoring the composition of the bacterial microbiome of raw milk cheeses to ensure consistent product quality.

Received: April 15, 2021

Fig. 1. Raclette du Valais AOP, a smear-ripened, full-fat semi-hard cheese made from raw milk. The cheese microbiome and thus also the quality of raw milk cheeses is influenced by environmental factors as well as manufacturing and ripening conditions.

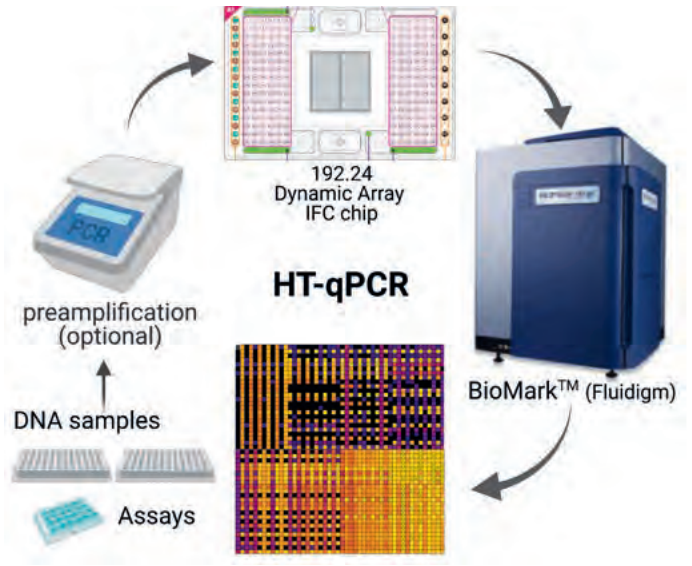
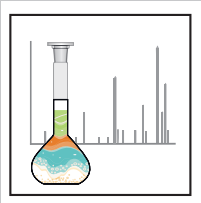


Fig. 2. Overview of the HT-qPCR workflow (created with BioRender.com). DNA samples and qPCR assays were loaded on the Dynamic Array integrated fluidic circuit (IFC, Fluidigm Corporation) chip. The Biomark instrument (Fluidigm Corporation) performed qPCR for the 4608 singleplex-qPCR reactions on the chip in parallel and recorded the fluorescence signal with a high sensitivity camera. Quantification cycle values were compared to qPCR standard dilution series and the number of copies in the DNA samples was calculated.

Reference
M. Dreier, H. Berthoud, N. Shani, D. Wechsler, P. Junier, *Front. Microbiol.* **2021**, *11*, 619166. https://doi.org/10.3389/fmicb.2020.619166.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2021.675 Chimia 75 (2021) 675



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Uranium – Lead Geochronology by ID-TIMS at Highest Precision and Reproducibility

Urs Schaltegger*

*Correspondence: Prof. Dr. U. Schaltegger, E-mail: urs.schaltegger@unige.ch, Université de Genève, Département des Sciences de la Terre, Rue des Maraîchers 13, CH-1205 Genève,

Keywords: Geochronology · Isotope dilution · Thermal ionization mass spectrometry · U-Pb dating

Age determination utilizing the radioactive decay of ^{238,235}U into ^{206,207}Pb is one of the backbones of modern Earth sciences. Precise and accurate temporal correlations are needed to understand the interaction of geosphere, hydrosphere, atmosphere, and life in the geological past. A timely example are periods of dramatic biodiversity loss ('mass extinctions') in the geological past that can be related to largest-scale volcanism (Large Igneous Provinces or LIPs), triggering profound disturbance of the carbon cycle and the climate, and affecting life. The geological record is mostly restricted to marine life, which has repeatedly suffered near-extinction. The most pronounced one at the Permian-Triassic boundary (252 million years ago) coincides with volcanic activity in the Siberian LIP. Precise U-Pb dating of these volcanic products, as well as of volcanic ash beds within marine sedimentary sections, allows for temporal correlation between volcanic activity, changes in biodiversity and marine biomass, and seawater temperature at a precision of a few 10'000 years.

The dating employs isotope-dilution techniques using a ^{202,205}Pb–^{233,235}U mixed tracer solution, which is distributed by the EARTHTIME consortium. This solution is precisely known for concentration and isotope composition of U, Pb and its U/Pb ratio, and allows for precise Pb, U isotope analysis of individual, 100-µm-sized zircon ($ZrSiO_4$) crystals through thermal ionization mass spectrometry. One such sample contains 2–5 pg (10^{-12}g) of radiogenic ^{206,207}Pb, which is isotopically analyzed in an ultraclean environment at a total procedural background level of 0.1–0.3 pg Pb. However, the U-Pb system in zircon presents two main challenges: (1) zircon crystallized in a magmatic system over several 100'000 years, therefore 10 to 20 analyses of carefully selected zircon grains are needed per sample to identify the youngest products of crystallization; (2) the radioactive alpha-decay of U, Th in zircon creates profound damage of the zircon crystal lattice that no longer behaves as a closed system for radiogenic nuclides. Therefore, an empirical 'chemical abrasion' treatment removes domains that have undergone >2 x 10^{18} alpha-decays/g prior to dissolution and analysis.

The precision, accuracy and repeatability of a U-Pb laboratory is controlled *via* isotope-dilution analysis of a synthetic EARTHTIME isotope calibration solution, which allows intra- and interlaboratory calibration at the 0.01% level of uncertainty for an apparent ^{206}Pb/^{238}U date.

Long-term analysis of this calibration solution has confirmed that high-precision ^{206}Pb/^{238}U dates are reproducible between different laboratories at a precision level of 0.01% (2s), providing a temporal resolution of 25'000 years for the correlation of environmental and biotic crisis at the Permian-Triassic boundary 252 million years ago.

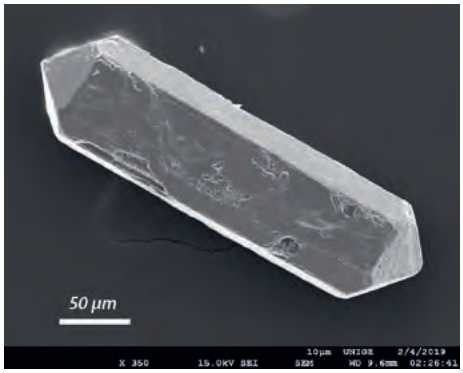


Fig. 1. Secondary electron image of a zircon ($ZrSiO_4$) in a volcanic ash bed used to date the age of deposition in a sedimentary rock.

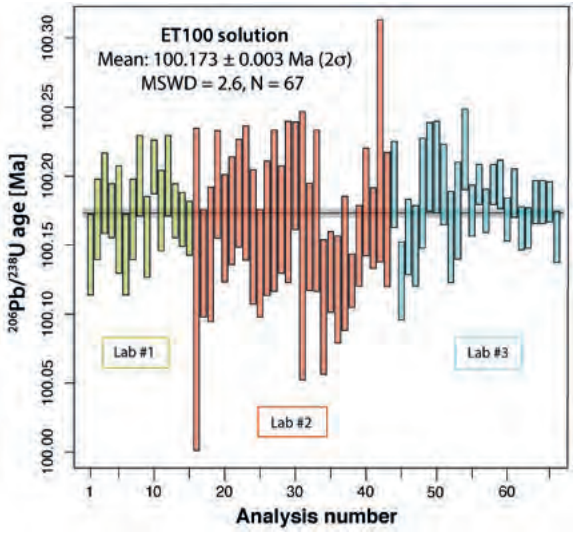


Fig. 2. Measured apparent ^{206}Pb/^{238}U dates for the EARTHTIME ET100 calibration solution in three laboratories applying identical analytical techniques and using the EARTHTIME ^{202,205}Pb-^{233,235}U tracer for isotope dilution.

Acknowledgement

The long-standing financial support of the Swiss National Science Foundation to US is highly acknowledged (projects CRSII5_180253, 200020_182007). The author thanks all former and present members of the Geochronology group at University of Geneva for their contributions.

Reference

U. Schaltegger, M. Ovtcharova, P. S. Gaynor, J. H. F. L. Davies, J. F. Wotzlaw, N. Greber, F. Farina, D. Szymanowski, C. Chelle-Michou, *J. Anal. Atom. Spectrom.* **2021**, *36*, 1466; https://doi.org/10.1039/D1JA00116G

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer,
Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2021.802 Chimia 75 (2021) 802

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Bird's-eye View of Localized Methane Emission Sources

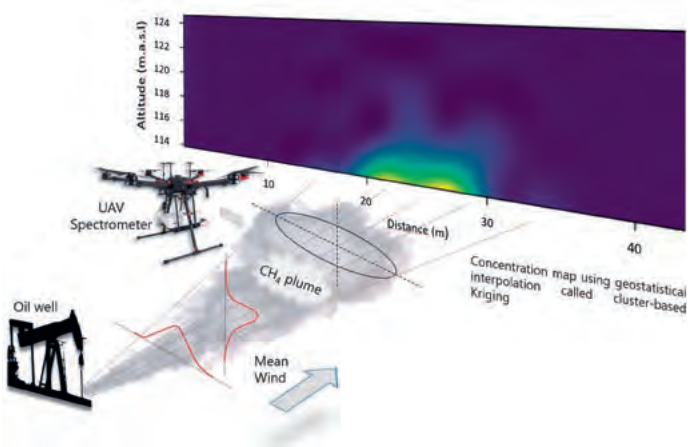
Béla Tuzson*, Randulph Morales, Manuel Graf, Philipp Scheidegger, Herbert Looser, André Kupferschmid, and Lukas Emmenegger

*Correspondence: Dr. B. Tuzson, E-mail: bela.tuzson@empa.ch
Laboratory for Air Pollution/Environmental Technology, Empa – Swiss Federal Laboratory for Materials Science and Technology, Überlandstrasse 129, CH-8600 Dübendorf

Keywords: Drone · Laser spectroscopy · Methane · Quantum cascade laser

The increase of greenhouse gas emissions from anthropogenic activities and its negative impact on the Earth's climate is an urgent issue for our civilization. Beside the widely discussed carbon dioxide, methane (CH_4) represents the second most important anthropogenic greenhouse gas. Its relatively short lifetime in the atmosphere creates unique opportunities for effective mitigation of climate change, especially with short-term benefits. Detailed and accurate knowledge about its sources, spatial distribution, and temporal variation are, as yet, lacking, and the partitioning of CH_4 emissions by region and processes is currently not sufficiently constrained. To improve this situation, we developed laser-based sensing technologies that enable the tracking and identification of methane sources at local scale, regardless of terrain complexity. This is achieved by a dedicated lightweight and high-precision CH_4 sensor based on mid-infrared laser absorption spectroscopy. Using a quantum cascade laser as light source, a narrow spectral range around a specific absorption line of methane is rapidly scanned, while the transmitted signal is used to retrieve the atmospheric concentration. The instrument is lightweight enough to be carried by commercial drones, thus yielding in a fully autonomous and highly mobile analytical system.

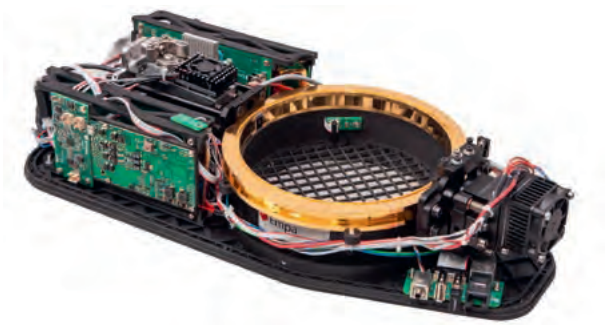
For quantification of localized CH_4 emission sources, the mobile analyzer is combined with 3D sonic wind measurements, and the emission fluxes are estimated by mass balance. This approach is performed by flying the drone-integrated system through a vertical cross section, downwind of a given source, perpendicular to the main wind direction at several altitudes. A refined (cluster-based) Kriging framework was developed to spatially map individual CH_4 measurement points into the measurement plane, while taking into account the different spatial scales between background and enhanced methane values in the plume. Emission rates are derived by multiplying the CH_4 fields with a corresponding wind field, *i.e.* by taking the net difference between fluxes into and out of a volume containing the source.



Scheme of CH_4 emission source quantification using the mass balance approach.

We recently applied this method to support the ROmanian MEthane Emissions from Oil and gas (ROMEO) campaign, which quantified methane emissions from oil- and gas-production facilities in Romania using various techniques and approaches. Hundreds of facility scale observations were conducted to generate a robust quantification of individual sources, from which bottom-up estimates can then be derived.

In conclusion, mapping trace gas emission plumes using *in-situ* spectroscopic measurements from unmanned aerial vehicles (UAV) is an emerging and attractive possibility to quantify emissions from localized sources.



Picture of the CH_4 laser spectrometer. The main parts are the quantum cascade laser, the segmented circular multipass cell, and a thermoelectrically cooled infrared detector.

Acknowledgements

This research has received funding under the Marie Skłodowska-Curie grant agreement No. 722479, through the Swiss National Science Foundation grant No. 157208, and by ABB Switzerland.

Received: June 23, 2021

Reference

B. Tuzson, M. Graf, J. Ravelid, P. Scheidegger, A. Kupferschmid, H. Looser, R. P. Morales, L. Emmenegger, *Atmos. Meas. Tech.* **2020**, *13*, 4715, https://doi.org/10.5194/amt-13-4715-2020

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2021.888 Chimia 75 (2021) 888

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Vacuum and Headspace – An Efficient and Fast Combination for the Extraction of Volatile Compounds

Pascal Fuchsmann*

*Correspondence: P. Fuchsmann, E-Mail: pascal.fuchsmann@agroscope.admin.ch. Agroscope, Schwarzenburgstrasse 161, CH-3003 Bern

Keywords: Gas chromatography – mass spectrometry · In-tube extraction · Reduced pressure sampling · Vacuum-transfer in trap

Different methods of extraction of volatile compounds from the headspace are known. Most of these techniques are carried out at a pressure higher than atmospheric pressure due to the heating of the sample in a closed space. For these techniques, the sample has to be heated in order to quickly reach an equilibrium state in the headspace. Reduced pressure extraction techniques have also been shown to extract compounds over a wide molecular weight range.

The Flavour Research Laboratory of the Swiss Federal Competence Centre for Agricultural Research, Agroscope, has developed an innovative and cost-effective method for the extraction of volatile compounds for gas chromatography (GC) analysis under the name of Dynamic Headspace Vacuum Transfer In Trap Extraction (DHS-VTT).[1,2] The technique also limits artefact formation during the extraction process thanks to reduced temperature and extraction time.

The aim is to combine Headspace In-tube Extraction (ITEX) with a vacuum pump to obtain a dynamic extraction at reduced pressure.

Volatile compounds from the sample are trapped in an ITEX-filled needle using a vacuum of around 5–10 mbar. The extraction time depends on the compounds to be extracted but varies between 5 and 30 minutes. A temperature-programmed injector (PTV) completes the set-up perfectly to optimise the separation of volatile compounds in the GC-MS.

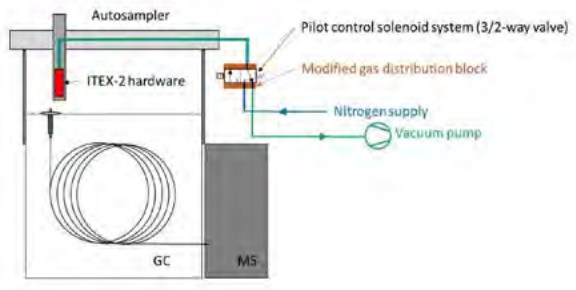


Fig. 1 Diagram of the GC–MS instrument with the autosampler and ITEX-2 hardware. Connection of the original nitrogen line to the new distribution block (in orange) and the solenoid valve. The vacuum and nitrogen lines are coloured green and blue, respectively.

The DHS-VTT technique significantly improves the extraction of volatile compounds from a complex matrix such as fermented dairy products in comparison with the ITEX and solid phase microextraction (SPME) method. The modification of the sampler is fast, economical and allows the use of commercial ITEX equipment. The method allows rapid extraction of target compounds using vacuum with little artefact formation or sample degradation. In addition, it is possible to extract large quantities of samples without having to replace the extraction equipment due to premature wear of the extraction parts or polymer. The results showed that the extraction equipment can be used for more than 850 injections without being modified; their relative standard deviation (total peak areas of 43 target volatile compounds over two weeks) was 9.6%. The technology is commercially available from CTC Analytics AG (www.ctc.ch).

DHS-VTT has many applications, such as working on projects requiring a large number of samples for metabolomic analysis.[3] The high extraction capacity of the ITEX needle polymer allows olfactometric analysis to be carried out with several panelists simultaneously without the limitations of the extraction media.

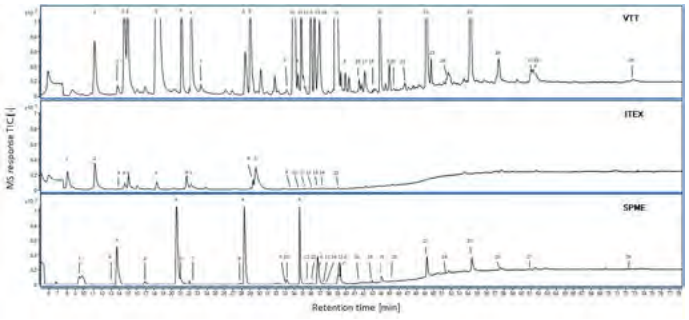


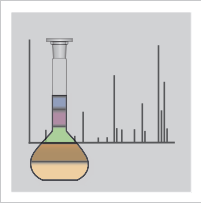
Fig. 2 Chromatograms corresponding to the volatile fraction of plain yoghurt extracted by DHS-VTT, HS-ITEX, and HS-SPME methods. Analytes from left to right: acetaldehyde, acetone, ethylacetate, butan-2-one, butane-2,3-dione, pentane-2,3-dione, hexanal, heptan-2-one, octanal, 3-hydroxy-butan-2-one, 2-methylpentan-3-ol, 2-hydroxy-3-pentanone, nonan-2-one, nonanal, acetic acid, propanoic acid, 2-methylpropanoic acid, undecan-2-one, butanoic acid, 2-phenylacetaldehyde, pentanoic acid, hexanoic acid, 6,10-dimethylundeca-5,9-dien-2-one, 2-phenylethanol, octanoic acid, nonanoic acid, δ–decalactone, decanoic acid, δ-dodecalactone. A = artifact.

Received: August 27, 2021

[1] P. Fuchsmann, M. Tena Stern, P. Bischoff, R. Badertscher, K. Breme, B. Walther, *J. Chromatogr. A* **2019**, *1601*, 60, https://doi.org/10.1016/j.chroma.2019.05.016
[2] Patent N° WO2020160686 A1, **2020**.
[3] P. Fuchsmann, M. Tena Stern, L. H. Münger, G. Pimentel, K. J. Burton, N. Vionnet, G. Vergères, *J. Proteome Res.* **2020**, *19*, 4019, https://doi.org/10.1021/acs.jproteome.0c00324.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical.highlights@chimia.ch

doi:10.2533/chimia.2021.981 Chimia 75 (2021) 981



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Key Odorants of Cocoa

Irene Chetschik*

*Correspondence: Prof. Dr. I. Chetschik, E-mail: irene.chetschik@zhaw.ch, Institute of Food and Beverage Innovation, Zurich University of Applied Sciences, Grüentalstrasse 14, CH-8820 Wädenswil

Keywords: Cocoa · Gas chromatography – olfactometry · Key odorants

The flavour of cocoa and chocolate is beloved all over the world and can be regarded as the final result of many different processing steps along the cocoa value chain, such as the cultivation, the post-harvest treatment, and last but not least the technological processing such as roasting and conching. All these steps impact the flavour properties of the final product, the chocolate. For this reason, many different research groups started already more than 30 years ago to gain insights into the molecular composition of cocoa flavour. Thereby, a high number of volatile compounds (>500) could be identified in cocoa products and chocolate intermediates.[1] However, more recent research studies could show that only a small percentage of these volatiles significantly contribute to the overall aroma of cocoa.[2] The so-called key odorants of cocoa were also recently identified in Swiss dark chocolates[3] and cocoa beans deriving from different post-harvest treatments[4] by gas chromatography – olfactometry, a technique that allows the differentiation between odourless volatiles and odour-active compounds. Based on the findings of our research and of other research groups, the key odorants of cocoa can be grouped in different categories based on their generation

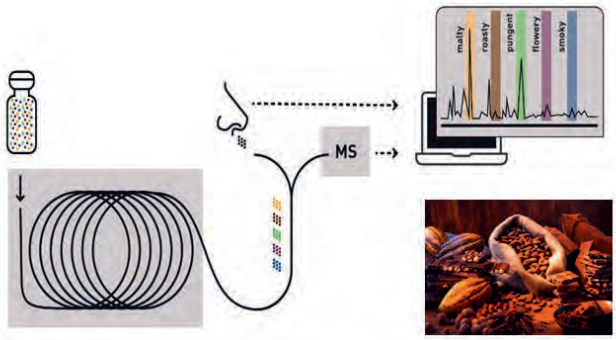


Fig. 1. Analysis of cocoa key odorants by gas chromatography – olfactometry.

along the cocoa value chain. There are some compounds which are already present in raw and unfermented cocoa beans, others arising during the post-harvest treatment, and further compounds mainly formed during thermal processing. Interestingly, there is no odorant which elicits the odour of cocoa or chocolate itself, it is more the combination of odorants with different odour qualities which have to be present in specific concentrations in order to evoke the aroma of cocoa or chocolate. These compounds have been recently compiled to a sensory kit, a cocoa aroma library containing 25 most important cocoa odorants, with the aim to give insights into the cocoa odour constitution and to be used as a training tool for the sensory evaluation of cocoa.[5]

Although a lot of research has been done in the past in order to decode the cocoa flavour on a molecular level, there is still a lot to do to understand the flavour properties of cocoa as a result of its variety and origin. This knowledge might also help to promote biodiversity and fair cocoa farming and ensure the quality of cocoa products in the future.

Received: September 6, 2021

[1] online VCF. Volatile Compounds in Food 16.8; available from: http://www.vcf-online.nl
[2] F. Frauendorfer, P. Schieberle, *J. Agric. Food Chem.* **2008**, *56*, 10244; https://doi.org/10.1021/jf802098f
[3] I. Chetschik, V. Pedan, K. Chatelain, M. Kneubühl, T. Hühn, *J. Agric. Food Chem.* **2019**, *67*, 3991; https://doi.org/10.1021/acs.jafc.8b06800
[4] A. Schlüter, T. Hühn, M. Kneubühl, K. Chatelain, S. Rohn, I. Chetschik, *J. Agric. Food Chem.* **2020**, *68*, 10336; https://doi.org/10.1021/acs.jafc.9b06119
[5] https://www.zhaw.ch/en/lsfm/institutes-centres/ilgi/food-chemistry/translate-to-english-zhaw-aroma-kit-kakao-eine-geruchsbibliothek-fuer-kakao-und-schokolade/

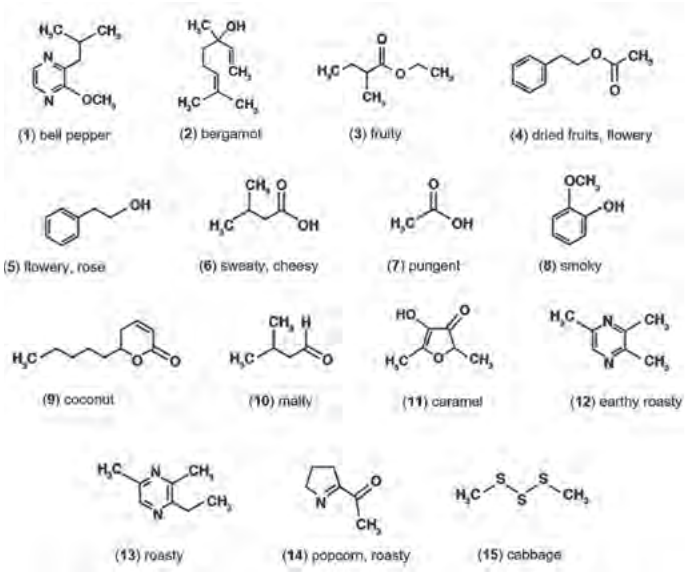
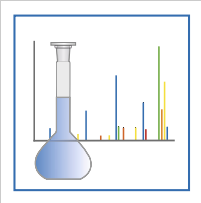


Fig. 2. Key odorants of cocoa. Compounds present in raw and unfermented cocoa beans: (**1**) 2-isobutyl-3-methoxypyrazine, (**2**) linalool; compounds deriving from fermentation: (**3**) ethyl-2-methylbutanoate, (**4**) 2-phenylethyl acetate, (**5**) 2-phenylethanol, (**6**) 3-methylbutanoic acid, (**7**) acetic acid, (**8**) guaiacol, (**9**) δ-decenolactone; compounds deriving from thermal processing: (**10**) 3-methylbutanal, (**11**) furaneol, (**12**) 2,3,5-trimethylpyrazine, (**13**) 2-ethyl-3,5-dimethylpyrazine, (**14**) 2-acetyl-1-pyrroline, (**15**) dimethyl trisulfide.

doi:10.2533/chimia.2021.1047 Chimia 75 (2021) 1047



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Moving Standardization of HPTLC to the Next Level

Thi Kieu Tiên Do* and Eike Reich

*Correspondence: Dr. T. Do, E-mail: tien.do@camag.com, CAMAG, Sonnenmattstrasse 11, CH-4132 Muttenz

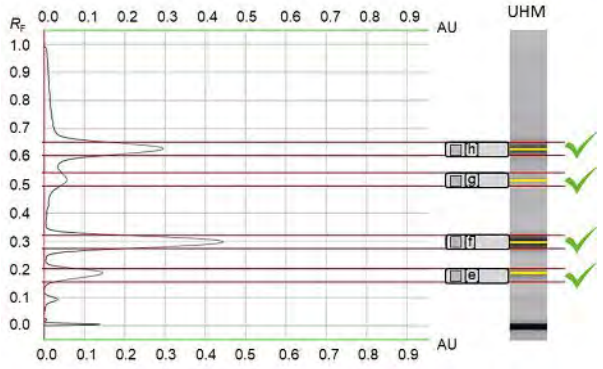
Keywords: HPTLC · System suitability test · Universal HPTLC mix (UHM)

High Performance Thin Layer Chromatography (HPTLC) is a well-known chromatographic separation technique applied in a large number of methods, particularly for generating chemical fingerprints of herbal drugs. Standardized HPTLC methods, focused on reproducibility and qualification of the chromatogram, are the ticket to reliable analytical results in daily routine.

Traditionally, qualification is performed on each plate using an appropriate system suitability test (SST). For that, nearly all methods rely on the chromatographic behavior of specific chemical reference substances, typically related to the target analytes. The search for individual substances is often cumbersome and expensive. Therefore, a generally applicable, cost- and time-efficient alternative for use in the SST was sought.

This led to the development of a novel approach using the Universal HPTLC Mix (UHM), a pre-defined mixture of eight substances. The selection of the substances started with considerations of minimum environmental and health hazards. Then, detectability, stability, availability and price were taken into account. The final mixture includes compounds from a broad polarity range featuring different functional groups.

A large number of chromatographic systems separate the UHM into a defined and unique pattern of zones with specific response characteristics to changes of the activity of the plate, composition of the mobile phase, and degree of saturation of the developing chamber. The use of these patterns in the SST allows checking whether a method was performed appropriately. Based on assigned R_F values and their respective windows obtained during method validation, such SST can be performed automatically. Furthermore, the SST can be used as reference point for adjustments of R_F shifts caused by differences in plate batches and for the normalization of signal intensities between plates. The UHM is now commercially available.



System Suitability Test (SST) view using the UHM consisting of [e]: phthalimide; [f]: 9-hydroxyfluorene; [g]: thioxanthen-9-one; [h]: 2-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol. Note: the other four substances of the mixture, namely guanosine, sulisobenzone, thymidine, and paracetamol stay at the application position. HPTLC Silica Gel F_{254} glass plate developed in the HPTLC PRO Module DEVELOPMENT, using toluene as developing solvent, and scanned at 254 nm.

The future of standardized HPTLC.

The Universal HPTLC mix opens the door to the next level of standardization of HPTLC methods. Software-based system suitability tests and normalization of data are getting within reach, meaning that in the future, results will be highly comparable in-between different laboratories and time periods. This is the first step towards a data-driven HPTLC with focus on artificial intelligence.

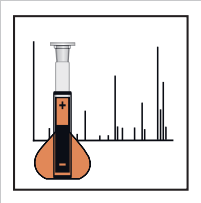
Received: October 5, 2021

Reference

T. K. T. Do, M. Schmid, M. Phanse, A. Charegaonkar, H. Sprecher, M. Obkircher, E. Reich, *J. Chromatogr. A* **2021**, *1638,* 461830, https://doi.org/10.1016/j.chroma.2020.461830.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2022.153 Chimia 76 (2022) 153 © Swiss Chemical Society



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

High-Precision Micro/Macro-Analysis with Laser-Induced XUV Spectroscopy (LIXS)

Di Qu and Davide Bleiner*

*Correspondence: PD Dr. D. Bleiner, E-mail: Davide.Bleiner@empa.ch
Laboratory for Advanced Analytical Technologies, Empa – Swiss Federal Laboratories for Materials Science and Technology, Ueberlandstr. 129, CH-8600 Dübendorf

Keywords: Laser-induced breakdown spectroscopy · Laser-induced plasma · Lithium battery · LIXS · Plasma emission · XUV spectroscopy

Laser-induced breakdown spectroscopy (LIBS) is a direct method for elemental analysis of solid materials thanks to no sample preparation, trace to major element sensitivity, and the spatially resolved acquisition. However, conventional LIBS in the optical range (UV to IR) suffers from low precision originating from

(i) high continuum background,

(ii) low repeatability of the plasma optical emission.

It has been reported that the plasma emission shows poor reproducibility, as a consequence of the hydrodynamic expansion. Indeed, the expansion is dominated by flicker noise, which is particularly critical for spatially resolved analysis in inhomogeneous samples. Fig. 1 shows the qualitative temperature evolution of laser-induced plasmas. The plasma temperature determines the range of spectral emission (kT = 1 eV corresponds to approx. 11'600 K).

In the irradiation phase, the plasma is very hot and dense, such that it emits soft X-rays. After a few ns of expansion and cooling (end of laser pulse), the emission is dominated by a strong continuum, so that one must delay the collection for this background to drop. Soft X-ray and extreme ultraviolet (XUV) emission from the dense laser-induced plasma shows high reproducibility and consistency.[1] Therefore, laser-induced XUV spectroscopy (LIXS), as an evolution of LIBS, can mitigate the flicker noise and substantially improve the precision.

The potential of LIXS was investigated in a quantitative analysis of Li-Mn oxide samples, as shown in Fig. 2. Their use as energy materials requires homogeneity. One should be able to detect impurities and heterogeneities from the same shot. Indeed, increased sensitivity may shrink the dynamic range. In LIXS, the dynamic range is substantially extended while the sensitivity is reduced (Fig. 3a). This does not hinder the detection limits because the background noise is negligible.

Finally, a fingerprint for oxidation was also demonstrated; where the oxidative pockets showed the same three O-VI emission lines at 12.99 nm, 15.01 nm, and 17.31 nm, which was not observed in LiF (see Fig. 3b). **In short, LIXS is a novel evolution to LIBS microanalysis with high precision and wide dynamic range.**

Received: November 24, 2021

[1] D. Qu, N. Ohannessian, C. Wyder, M. Trottmann, A. Wichser, T. Lippert, D. Bleiner, *Spectrochim. Acta – Part B At. Spectrosc.* **2021**, *181*, 106214.

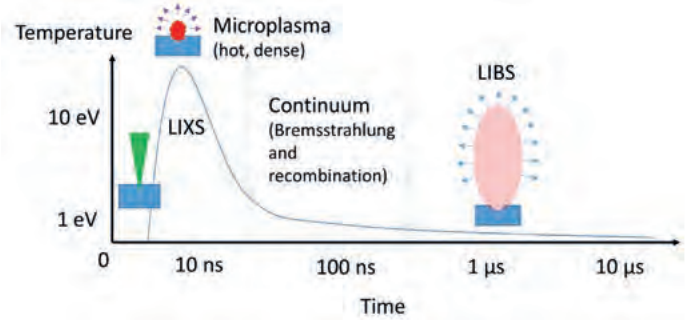


Fig. 1. Qualitative temperature evolution of laser-induced plasma.

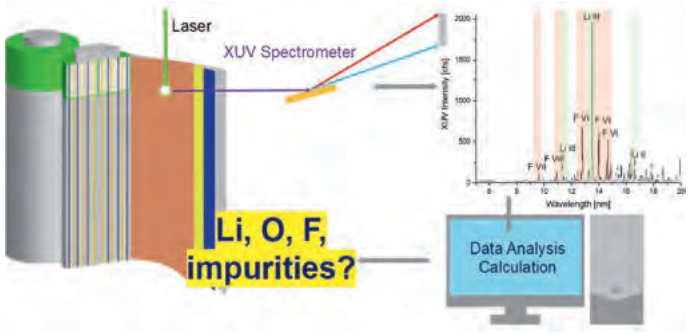


Fig. 2. Depth profiling analysis in batteries using laser-induced spectroscopy (LIXS).

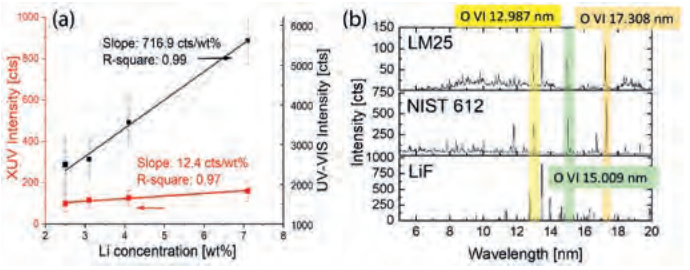


Fig. 3. (a) Calibration curves of LIXS (red) and LIBS (black) showing the different sensitivity and dynamic range. (b) LIXS spectra of three standard materials: Li_2O/Mn_xO_y standard sample (LM25), NIST 612 multielemental glass and a LiF crystal. Fingerprint lines of oxidation are observed at O VI 12.987 nm, O VI 15.009 nm, O VI 17.308 nm (LIXS spectral range).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2022.257 Chimia 76 (2022) 257

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Back to the Moon – *in situ* Chemical Analysis on the Lunar Surface using LIMS

Peter Keresztes Schmidt*, Andreas Riedo, and Peter Wurz

*Correspondence: P. Keresztes Schmidt, E-mail: peter.keresztes@unibe.ch
Physics Institute, Space Research & Planetary Sciences, University of Bern, Sidlerstrasse 5, CH-3012 Bern

Keywords: LIMS · Moon · Space Instrumentation · TOFMS

Swiss instrumentation has a long history in lunar science exploration, making its debut on the lunar surface as part of the Apollo 11 mission in the form of the Solar Wind Composition experiment (SWC), developed at the Physics Institute of the University of Bern. Comprising an ultra-pure aluminum foil sail, the SWC collected solar wind ions and was subsequently returned to Earth for analysis. With the renewed interest in human lunar landings, *e.g.* within NASA's Artemis program, which serves also as a precursor program for Mars exploration, new opportunities to perform more complex scientific experiments on the Moon arise. Such *in situ* experiments are of high interest to the field of planetary sciences, since they can contribute to answering fundamental questions *e.g.* about the evolution of our solar system. Therefore, new precise instrumentation, which *e.g.* can determine the element and isotope composition of lunar rock, is required that would also support the astronauts' on-site work. Such an instrument can facilitate pre-classification and prioritization studies of samples selected for sample return to Earth, as well as *in situ* analysis of samples for which sample return is infeasible (*e.g.* volatiles in lunar permanently shadowed regions).

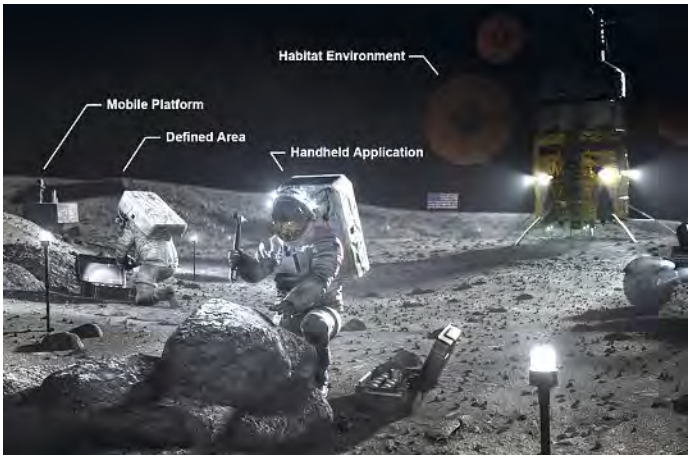
At the University of Bern, we have been developing a Laser Ablation Ionization Mass Spectrometer (LIMS) that is a candidate instrument for the Artemis program. LIMS offers advantages over currently routinely used chemical analysis techniques on planetary surfaces such as X-ray fluorescence, γ-ray or neutron spectroscopy. One major advantage is the achievable dynamic range, allowing for detection and quantification of main but also trace elements. In combination with high lateral resolution at the micrometer level, this yields a unique parametric set, which currently cannot be replicated by other methods used in planetary research. We present the preliminary flight design of our miniature LIMS system suited to operate on the lunar surface. A cage system containing all relevant components of a flight design was designed and realized to facilitate the evaluation of the laser and optical setup. In anticipation of deployment on the Moon, this setup is currently being used for characterization studies of the system to ensure optimal preparation.

After more than 50 years of Switzerland having been present on the Moon, the next chapter in Lunar exploration is right around the corner.

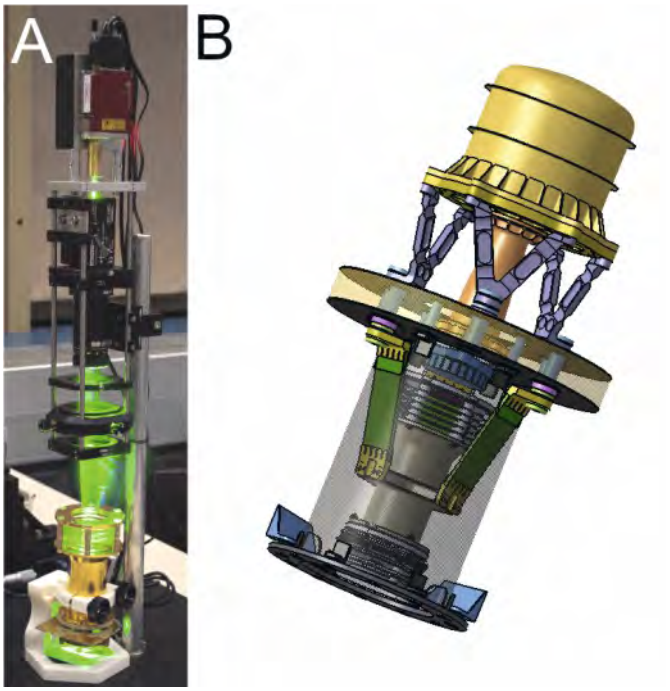
Received: January 7, 2022

Reference

A. Riedo, V. Grimaudo, J. W. Aerts, R. Lukmanov, M. Tulej, P. Broekmann, R. Lindner, P. Wurz, P. Ehrenfreund, *Front. Astron. Space Sci.* **2021**, *8*, 726373.



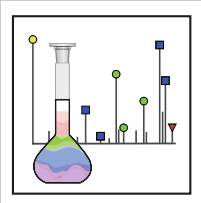
Lunar landing site of a manned mission within NASA's Artemis program. Scientific instruments can be operated within the pressurized habitat or while performing Extravehicular Activities on mobile platforms. Adapted from NASA Artemis III SDT Report.



Laboratory setup to test the laser and optical components of the LIMS (A) and instrument flight design as shown by the CAD drawing (B). For illustrative purposes the TOF mass analyzer has been placed directly under the optical cage. Under operating conditions, it is mounted in a vacuum compartment. The sample introduction system will be attached to the bottom of the flight design.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical.highlights@chimia.ch

doi:10.2533/chimia.2022.363 Chimia 76 (2022) 363



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

A New Approach for Identifying Positional Isomers of Glycans Cleaved from Monoclonal Antibodies

Irina Dyukova*[a], Ahmed Ben Faleh[a], Stephan Warnke[a], Natalia Yalovenko[a], Vasyl Yatsyna[ab], Priyanka Bansal[a], and Thomas R. Rizzo*[a]

*Correspondence: I. Dyukova[a], E-mail: irina.diukova@epfl.ch
[a]Laboratoire de Chimie Physique Moléculaire, École Polytechnique Fédérale de Lausanne, EPFL SB ISIC LCPM, Station 6, CH-1015 Lausanne; [b]University of Gothenburg, Department of Physics, S-412 96 Gothenburg, Sweden

Keywords: Cryogenic infrared spectroscopy · Ion mobility separation · Positional isomers of glycans

Glycosylation patterns in monoclonal antibodies (mAbs) can vary significantly between different host cell types, and these differences may affect mAbs safety, efficacy, and immunogenicity. Recent studies have demonstrated that glycan isomers with the terminal galactose position on either the Man α1-3 or the Man α1-6 branch have an impact on the effector functions and dynamic structure of mAbs. One of the most powerful techniques for glycan investigation is the combination of liquid chromatography (LC) with mass spectrometry (MS), however, even this method cannot distinguish all the various forms of isomerism. The development of a robust technology to distinguish positional isomers of glycans is thus critical to guarantee mAb quality.

Our group has recently demonstrated that cryogenic infrared (IR at 45 K) spectroscopy provides unique vibrational spectra of glycans. Since spectroscopic fingerprints can be extremely sensitive to the slightest differences between molecules, we can distinguish all the various types of isomerism present in glycans. We apply the combination of IR spectroscopy with ultrahigh-resolution ion mobility separation (IMS) based on structures for lossless ion manipulation (SLIM) technology.

On the example of N-linked glycan G1F, we demonstrated the ability of our technique to assign the mobility-separated positional isomers (G1(α1-3)F and G1(α1-6)F) based on their unique IR fingerprint spectra. We then used these results to investigate the influence of the host cell line (CHO and HEK-293) on the G1F profile at the isomer level.

Our results demonstrate that the combination of high-resolution ion mobility and cryogenic ion spectroscopy provides a fast and reliable method for glycan isomer identification. It can be used to complement, or even replace, existing methods for establishing the similarity of glycan profiles between biological drugs and their biosimilars.

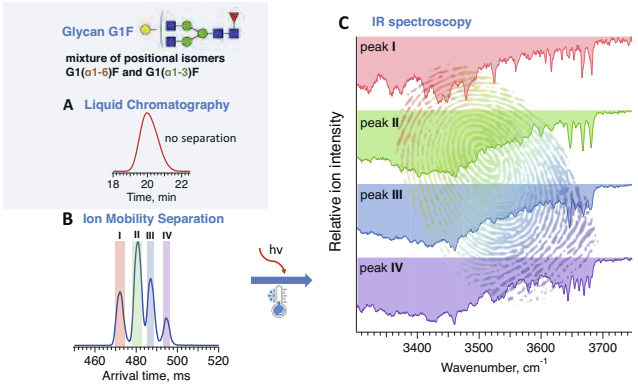


Fig. 1. Comparison of liquid chromatography (A) with our three-dimensional IMS-MS-IR approach (B, C) on the example of the N-linked glycan G1F which consists of nine monosaccharide units. Yellow circle: galactose; green circle: mannose; blue square: N-acetylglucosamine, red triangle: fucose.

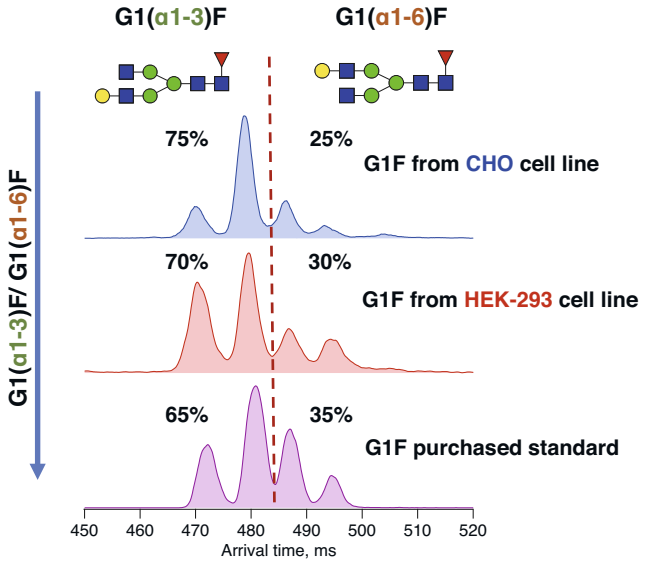


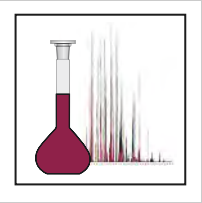
Fig. 2. Arrival time distributions of a G1F standard and G1F released from IgG antibody produced in CHO and HEK-293 cell lines.

Reference

I. Dyukova, A. Ben Faleh, S. Warnke, N. Yalovenko, V. Yatsyna, P. Bansal, T. R. Rizzo, *Analyst* **2021**, *146*, 4789, https://doi.org/10.1039/D1AN00780G.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical.highlights@chimia.ch

doi:10.2533/chimia.2022.476 Chimia 76 (2022) 476



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Robinia pseudoacacia (Black Locust) – An Invasive Species with Unsuspected Potential in Grappa Ageing

Pascal Fuchsmann*[a], Mireille Tena Stern[a], Sonia Petignat-Keller[a], Jonas Inderbitzin[a], Mark Bertogliati[b], Marilyn Cléroux[c], and Benoit Bach[c]

*Correspondence: P. Fuchsmann[a], E-Mail: pascal.fuchsmann@agroscope.admin.ch
[a]Agroscope, Schwarzenburgstrasse 161, CH-3003 Bern; [b]Swiss Federal Institute for Forest, Snow and Landscape Research WSL, a Ramél 18, CH-6593 Cadenazzo; [c]Haute école de viticulture et œnologie HES-SO Changins, Route de Duillier 50, CH-1260 Nyon

Keywords: Black Locust · Gas chromatography - mass spectrometry · Grappa · Olfactometry · Robinia pseudoacacia · Spirits

The use of different types of wood for the manufacture of barrels for the maturing of wines has been used since the 5th century BC. Wood has several physical and chemical properties that allow gas exchange between the external environment and the wine while conferring typical aromas to the species used. Spirits such as whiskies, cognacs, armagnacs, grappas and others are matured in wooden barrels giving aroma and color to their coveted nectars.

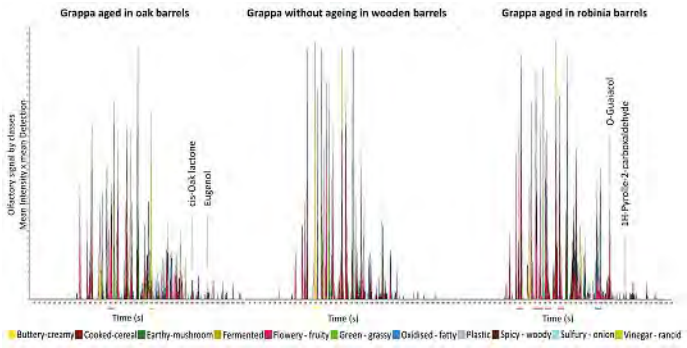
The wine and spirits industry focuses on a range of well-known species such as oak or chestnut in the production process. However, the environment and climate change make the accessibility and use of these species increasingly complex. In this context, the characteristics of the Black Locust (false acacia – *Robinia pseudoacacia*) (an ubiquitous and invasive species with excellent drought resistance and few specific pathogens) make it potentially resilient. Since the end of the 19th century Robinia trees were widely planted in the Ticino for the production of poles and beams. A project to develop the use of Robinia for the production of barrel-aged Grappa in partnership with the Swiss Federal Agricultural Research Institute (Agroscope) in Wädenswil and the Swiss Federal Institute for Forest, Snow and Landscape Research (WSL) in Birmensdorf has highlighted the aromatic qualities of this species in the production of quality distillates.

The project consisted of the manufacture of several 50-litre Robinia barrels for the controlled ageing of Grappa produced from typical Ticino Merlot marc. Regular samples of the distillates during a 6-month ageing period were evaluated by a sensory panel as well as by gas chromatography – mass spectrometry – olfactometry to identify aromatic characteristics throughout the maturation period. Very promising results showed that the maturation in Robinia barrels had more intense floral, fruity, and herbal aromatic characteristics than in oak barrels. However, the maturation period is slower than in oak. It takes about 50 days for the Robinia when the oak requires only 28 days (according to sensory evaluation). This can be explained by the denser wood fiber than in oak which limits exchanges with the outside environment.

The analyses showed a slightly different diversity of volatile compounds than with oak. Some aromatic compounds come exclusively from oak (*e.g. cis*-Oak lactone or Eugenol) and give spicy and fruity notes to the distillates that Robinia cannot generate. However, other compounds are present in both wood species but are extracted more rapidly in Robinia than in oak (O-guaiacol and 1H-pyrrole-2-carboxaldehyde). These compounds are therefore found in greater quantities in the distillates and bring unique aromatic variations to them.

In the future, Robinia barrels could offer a more diverse range of aromas to the grappa producers.

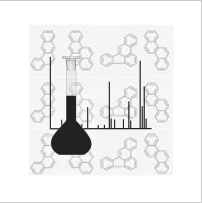
Merlot grape, distillation, and ageing of the grappa distillates in Robinia barrels.



Olfactometric profile (N=8) of grappa distillates aged in oak barrels versus in Robinia barrels after 180 days.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2022.596 Chimia 76 (2022) 596



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

METAS UncLib – A Measurement Uncertainty Calculator in Chemical Analysis

Simon Lobsiger[a]*, Michael Wollensack[b], and Markus Zeier[b]

*Correspondence: Dr. Simon Lobsiger, E-Mail: simon.lobsiger@metas.ch
[a]Laboratory Chemical and Biological References and [b]Laboratory Radio Frequency and Microwave, Federal Institute of Metrology METAS, Lindenweg 50, CH-3003 Bern-Wabern

Keywords: GC-MS/MS · Measurement uncertainty · METAS UncLib · PAH

Evaluation of measurement uncertainty (MU) in chemical analysis is essential to make measurement results comparable and to fulfill the requirement of metrological traceability to reference values obtained by agreed realizations of the SI units. It is therefore also a requirement for all accredited laboratories working under ISO/IEC 17025:2017. With the Guide to the Expression of Uncertainty in Measurement (GUM)[1], an internationally accepted and uniform procedure for the evaluation of MU was established. However, without the help of an uncertainty propagation software, it can be very challenging and time-consuming to implement this approach in a mathematically correct way, especially for complicated analytical methods.

METAS UncLib[2], a software library that facilitates the linear propagation of uncertainties through a measurement model is in full accordance with the GUM and is one of the most versatile MU calculators available. METAS UncLib can be downloaded free of charge at [3]. It is written in C#, and MATLAB and Python wrappers exist. So far, METAS UncLib has been mainly known in the physical community. We think that it can be of great use for chemists as well for establishing their MU budgets.

In our laboratory, we use METAS UncLib together with Python for the evaluation of the MU in the determination of polycyclic aromatic hydrocarbons (PAHs) in food matrices, for example. The analytical method is composed of solvent extraction of the test material, multi-stage purification by solid-phase extraction (SPE) and/or gel permeation chromatography (GPC), and measurement with GC-MS/MS using isotopically labelled internal standards. It currently includes the 16 PAHs listed in EPA610. For each PAH, our measurement model relates more than 45 input quantities, each exhibiting uncertainties, to the output quantity, the mass fraction of the PAH in the tested food. As an example, the figure shows the results of a measurement of contaminated infant formula. While for PAH4 (sum of benz[a]anthracene (BaA), benzo[a]pyrene (BaP), benzo[b]fluoranthene (BbF), and chrysene (Chr)), the lower bound of the MU at the 95 % level (k = 2) is clearly above the regulated maximum level, there is an overlap of the MU range for BaP. In this case, MU is a key factor for conformity assessment.

In conclusion, METAS UncLib is perfectly suited as a measurement uncertainty calculator in chemical analysis, especially for complicated analytical methods including a large number of chemical compounds.

Received: May 7, 2022

[1] BIPM, IEC, IFCC, ILAC, ISO, IUPAC, IUPAP, OIML, Evaluation of Measurement Data - Guide to the Expression of Uncertainty in Measurement, *JCGM/WG1* **2008**, *100*.
[2] M. Zeier, J. Hoffmann, M. Wollensack, *Metrologia* **2012**, *49*, 809, https://doi.org/10.1088/0026-1394/49/6/809.
[3] https://www.metas.ch/unclib

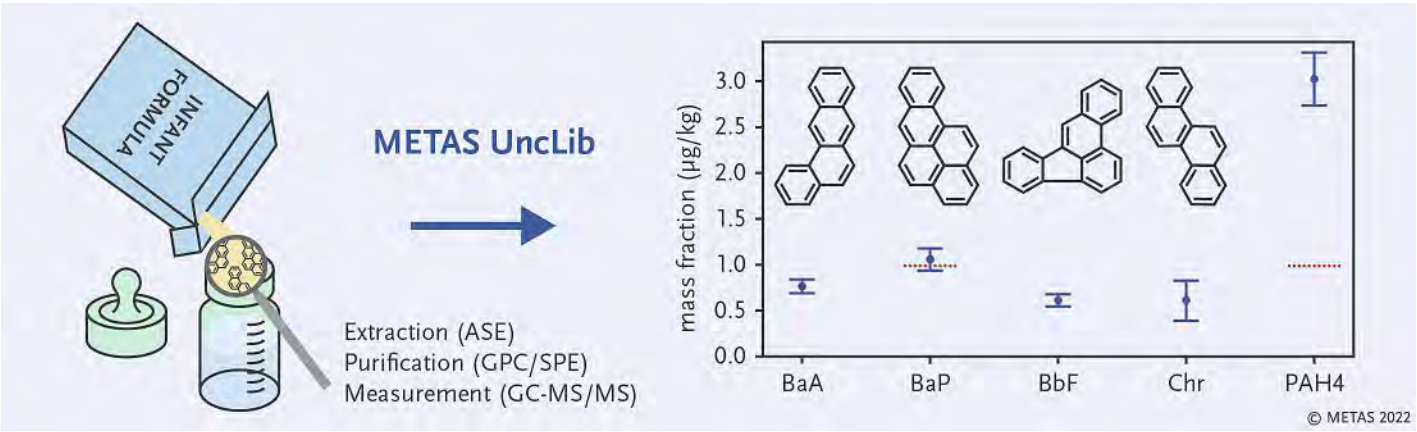
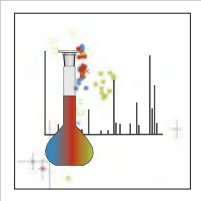


Fig. 1: Selected mass fractions and uncertainties (95 %, k = 2) for the PAHs benz[a]anthracene (BaA), benzo[a]pyrene (BaP), benzo[b]fluoranthene (BbF) and chrysene (Chr) determined in contaminated infant formula (proficiency test material, BIPEA 09-2344). Maximum levels (1 µg/kg) of BaP and the sum of BaA, BaP, BbF and Chr (PAH4) listed in the Swiss contaminants regulation (SR 817.022.15) are indicated with red dotted lines.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2022.702 Chimia 76 (2022) 702



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Dietary Changes in Bronze Age Switzerland

Alessandra Varalli[a] and Mireille David-Elbiali[*b]

*Correspondence: Dr. M. David-Elbiali[b], E-mail: mireille.david-elbiali@unige.ch
[a]CaSEs Research Group, Department of Humanities, Universitat Pompeu Fabra. Barcelona, Spain; [b]Laboratory of Prehistoric Archaeology and Anthropology, University of Geneva, Blvd. Carl-Vogt 66, CH-1211 Genève 4

Keywords: Bronze Age • Farming • Human diet • Prehistory

Stable isotope analyses applied to archaeological remains allow to reconstruct aspects of prehistoric human lifestyle that were completely inaccessible until recently. Particularly, carbon, nitrogen, and sulfur stable isotopes from cereal and legume seeds ($\delta^{13}C$, $\delta^{15}N$), animal bone collagen ($\delta^{13}C_{coll}$, $\delta^{15}N$, $\delta^{34}S$), human bone and dentin collagen ($\delta^{13}C_{coll}$, $\delta^{15}N$, $\delta^{34}S$), and tooth enamel ($\delta^{13}C_{enamel}$) provide essential information in the reconstruction of human diet, mobility, and subsistence strategies.

The analysis of carbon isotopic ratios ($\delta^{13}C$) allows to distinguish the environment where humans acquired their resources (terrestrial vs aquatic) and notably the type of plants consumed: C_3 type plants (wheat, barley) are typical of a temperate environment, whereas C_4 type plants (millet, sorghum) usually reflect an open and warm environment. The nitrogen isotopic ratios ($\delta^{15}N$) detect the trophic level occupied by an organism within a food chain: plants present lower values than animals and humans that, as consumers, show higher nitrogen ratios. The sulfur isotopic ratios ($\delta^{34}S$) provide information on the origin of food sources – from a terrestrial, marine, or freshwater ecosystem – and contribute to detect human mobility.

In this study we considered three cemeteries located on the Lake Geneva Basin and dated from the Early to the Late Bronze Age (2200–800 BC). Our results show that these human groups mainly consumed terrestrial foodstuffs, despite the proximity of Lake Geneva. Furthermore, a change in the main staple crops along the Bronze Age is highlighted due to the transition from a diet mainly based on C_3 plants during the Early (2200–1500 BC) and Middle/Recent (1500–1100 BC) Bronze Age to the significant consumption of C_4 plants at the Final Bronze Age (1100–800 BC). The millets, first domesticated in China, are more resistant to aridity and were cultivated in Switzerland especially from the 11th century BC onwards. They could have contributed to the prosperity of the Late Bronze Age. Dietary differences according to sex, age-at-death or graves goods were not detected. Moreover, soil fertilization seems to have been increased along the Bronze Age, suggesting changes in agriculture strategies.

The use in archaeology of techniques from the natural sciences, such as chemistry, contributes significantly to our knowledge of the human way of life in the past.

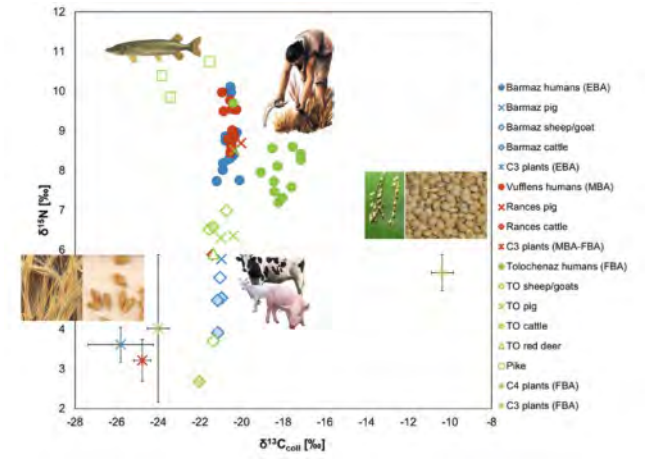


Fig. 1. Scatter plot of $\delta^{13}C$ and $\delta^{15}N$ bone collagen values for humans, animals, and botanical remains according to their chronological periods (C_3 plants include wheat and barley, C_4 plants include broomcorn and foxtail millet; representation of mean and sd for the plants). TO = Chens sur Léman, Tougues. EBA = Early Bronze Age, MBA = Middle Bronze Age, FBA = Final Bronze Age.

Fig. 2. Tolochenaz (Vaud) La Caroline. Map of the Final Bronze Age (1050–800 BC) cemetery with indication of funerary rituals, grave goods, sex/gender, class age, and sampled individuals.

Acknowledgements

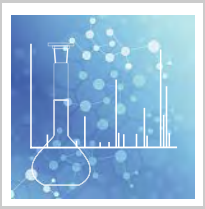
The authors thank M. Honegger (Univ. Neuchâtel), A. Gallay (Archéodunum), J. Studer (Muséum Genève), E. Néré, M. Cabanis (INRAP), L. Pernet, J. Bullinger, G. Keller (Musée d'archéologie et d'histoire Lausanne), C. Brunetti, E. Evéquoz and F. Mariéthoz (Office cantonal d'Archéologie du Valais), P. Chapuis, C. Laroche, M.P. Feuillet (DRAC-ARA) for granting permits and access to the human, faunal, and botanical collections. Thanks to the LAP (M. Besse, J. Desideri - Univ. Genève) and LAMPEA (G. Goude – CNRS, Univ. Aix-Marseille), for providing the facilities to perform the isotopic analysis. This research was funded by the Fyssen, the Schmidheiny and the Boninchi and the Institut Danone France/Fondation pour la Recherche Médicale 2015.

Reference

A. Varalli, J. Desideri, M. David-Elbiali, G. Goude, M. Honegger, M. Besse, *Plos One* **2021**, https://doi.org/10.1371/journal.pone.0245726.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer,
Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2022.794 Chimia 76 (2022) 794



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

A Challenge: Controlling the Quality of Cell and Gene Therapies

Christoph Meyer*, Alexander Sandoval, Allyson Decker, Sophia Nguyen, Susan Barr, and Andreas Wirth

*Correspondence: Dr. Chr. Meyer, E-mail: christoph.meyer@lonza.com
Lonza Pharma AG, Cell and Gene Therapies, Hochbergerstrasse 60A, CH-4057 Basel

Keywords: Cell and gene therapy · Good manufacturing practice · Quality control

Cell and gene therapies are revolutionizing the treatment of patients with cancers or genetic diseases, but they are complex: The respective starting materials, *e.g.* blood cells, have an impact on the quality and variability of the final product. Tailored analytical methods need to properly control and understand the starting materials, the process, and final product. In order to adhere to commercial current Good Manufacturing Practice, CQAs (Critical Quality Attributes) must be identified and their dependence from the CMAs and CPPs (Clinical Process Parameters) must be clear. Safety and efficacy requirements must be met and quality controlled.

Viral vectors (VVs) are the key vehicles to introduce therapeutic benefit into human cells. Various types can be employed such as Adeno-Associated Viruses (most common vectors used), Lentiviruses, or oncolytic viruses. Functional and potency assays need to be tailored for the respective virus types. Testing the strength includes cell count and viability, physical titer ddPCR and qPCR, HPLC titer, optical density titer, and infectious titer. Identification is done with cell line identification, Sanger sequencing, next generation sequencing, and restriction enzyme mapping. Purity testing includes residual Benzonase, Triton testing. For potency, ddPCR and ELISA are employed as well as *in vivo* testing. Safety testing includes methods for detection of retrovirus, adventitious agents, sterility, mycoplasma, endotoxin, and bioburden.

Autologous therapies use the patient's own T-cells which are reprogrammed making use of VVs. The patient is at the beginning and end of the supply chain. The quality of cells differs, so even though it is not possible to produce a standard, the product must meet certain specifications. Process comparability is more frequently required with a more complex design, which requires adequate analytical methodologies capturing the CQAs. Rapid disease progression may be an issue, and product shelf-life can be short: quality control release testing is time-critical. A step-wise release process, *e.g.* interim sterility, may be needed. Automated plate-reading technologies allow faster turn-around times (TAT). Generally, methods applied include: Identity: PCR testing for transgene presence. Safety: Endotoxin, sterility, mycoplasma, and virus DNA qPCR. Purity: Cellular phenotyping by flow cytometry for viable T-cell percentage. Transduction efficiency is tested by CAR, qPCR, and cell viability test. Impurities: Microscopy to check for residual beads. Potency: Release of Interferon Gamma in response to CD19-expressing target cells (Cluster of Differentiation 19, B-lymphocyte antigen).

Fig. 1. The Lonza Cocoon® system for the manufacturing of autologous cell therapies.

Allogenic therapies allow for off-the-shelf centralized manufacturing. They stand out for their scalability with challenges similar to those of traditional biologics. Induced pluripotent stem cells can differentiate into any of the 220 plus cell types found in the human body. This allows for tissue material standardization and analytical method standardization. Allogenic CAR-T has the potential to solve the major CAR-T challenge of donor variability with a pool of well-characterized reference donors. CQAs to be tested are less variable. There are multiplex gene editing options, and a combination of viral and non-viral methods can be employed.

Exosomes function as intercellular messengers and are key mediators of cell-to-cell communication by transfer of nucleic acids, proteins, and lipids and accordingly influence functional aspects of recipient cells. All cells produce and absorb these round nanovesicles. They play fundamental roles in altering the activity of recipient cells as a response to physiological stress and disease. Tailored functional assays are required for Exosome quality control testing.

Generally, analytical quality control methods must be capable of testing for safety, identity, strength, purity, and overall quality (SISPQ). The methods must be validated for specificity, accuracy, precision, linearity, range, limit of detection, and limit of quantitation in accordance to the regulatory guidances. Robustness criteria need to be met.

All main areas in cell and gene therapy are unique and with specific needs for both manufacturing and the analytical sciences. The requirements on product quality and the analytical methodologies remain the same as with traditional treatments.

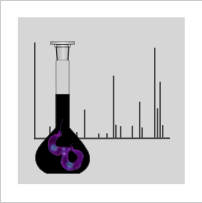
Received: June 15, 2022

References

EudraLex Vol. 4, 'Guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal Products', **2017**.
ICH Guidances: www.ich.org (International Conference on Harmonization).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2022.863 Chimia 76 (2022) 863



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Ultrastructure Expansion Microscopy to Uncover Novel Features of the Parasite *Trypanosoma brucei*

Ana Kalichava and Torsten Ochsenreiter*

*Correspondence: Prof. Dr. T. Ochsenreiter,
E-mail: torsten.ochsenreiter@izb.unibe.ch
Institute of Cell Biology, University of Bern, Baltzerstrasse 4, CH-3012 Bern

Keywords: Protein localization · *Trypanosoma brucei* · Ultrastructure expansion microscopy

Trypanosoma brucei is a single-celled eukaryotic parasite causing human African sleeping sickness and nagana in cattle. The parasite is transmitted by the tsetse fly in sub-Saharan Africa and infections in humans are fatal if left untreated. Aside from the medical and also veterinarian relevance, *T. brucei* has been developed into a model system for a number of basic biological questions including flagellum- and mitochondrial biogenesis.

The flagellum is required for the propulsion of the cell and attaches alongside the cell body. Biogenesis of the highly conserved flagellar structure initiates at the basal body inside the cell, which itself is also a very conserved organelle in biology. In *T. brucei* the basal body is in proximity to the mitochondrial genome, which is termed kinetoplast or kDNA. In fact, the kDNA is physically linked to the basal body *via* the unique protein-based tripartite attachment complex. Since this structure is essential for the parasite and is not present in the human or animal host it provides a potential avenue for therapeutic interventions.

In order to better characterize this ~200 nm wide structure inside the cell we require high-resolution microscopy techniques. Ultrastructure Expansion Microscopy (U-ExM) is a powerful novel approach to overcome resolution limits in microscopic imaging by increasing the size of the sample rather than increasing the resolution of the microscope.[1] We recently adapted the previously developed approach to trypanosomes.[2,3] For this the *T. brucei* cells are incubated in an anchoring solution to link all cell components to a gel polymer at nanometer scale. After the polymerization of the gel, the sample is heated to 95 °C in a solution with detergent to prepare the cell for the expansion step, which is followed by standard immunofluorescence staining to identify the molecular components of interest. The U-ExM method is compatible with epifluorescence or confocal microscopy, resulting in ~ 50 nm to 10 nm spatial resolution. In this our study the cells were isotropically expanded to 4.5 times their original size, which allowed us to closely observe the mitochondrial kDNA and its associated protein factors.

U-ExM enables the localization of individual cell components at nanometer scale, thus bridging the gap between light- and electron microscopy.

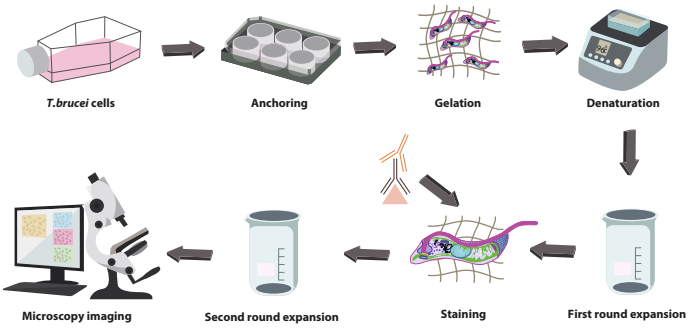


Fig. 1. U-ExM workflow in *T. brucei*.

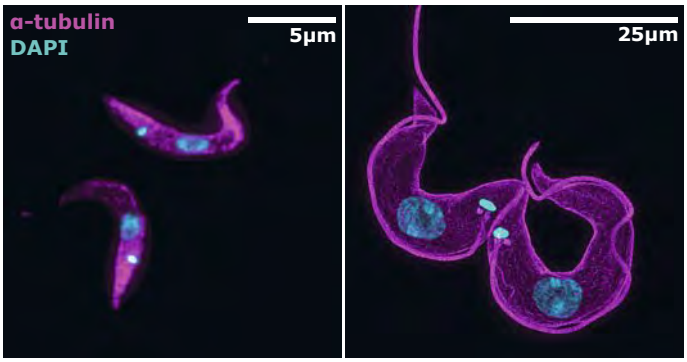


Fig. 2. Representative images of non-expanded and expanded *T. brucei*. Cells stained with anti alpha-tubulin antibodies (magenta; Alexa 647) and DAPI (cyan; kDNA and nucleus).

Acknowledgements

We would like to acknowledge Prof. Paul Guichard for training and help with reagents. We also acknowledge the Swiss National Science Foundation for their long-standing support.

Received: July 9, 2022

[1] F. Chen, P. W. Tillberg, E. S. Boyden, *Science* **2015**, *347*, 543, https://doi.org/10.1126/science.1260088.

[2] S. Amodeo, A. Kalichava, A. Fradera-Sola, E. Bertiaux-Lequoy, P. Guichard, F. Butter, T. Ochsenreiter, *J. Cell Sci.* **2021**, *134*, jcs254300, https://doi,org/10.1242/jcs.254300.

[3] A. Kalichava, T. Ochsenreiter, *Open Biol.* **2021**, *10*, 210132, https://doi.org/10.1098/rsob.210132.

doi:10.2533/chimia.2022.966 Chimia 76 (2022) 966

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

A Novel Chemical Assay that Brings Endotoxin Analysis into the 21st Century

Anika Hoffmann*[a], Blanka Bucsell[b], Brian Frank[c], and Franka Kalman[a]

*Correspondence: A. Hoffmann[a], E-mail: anika.hoffmann@hevs.ch
[a]University of Applied Sciences and Arts Western Switzerland Valais, Institute of Life Technology, Rue de l'Industrie 23, CH-1950 Sion; [b]Lonza AG, Lonzastrasse 2, CH-3930 Visp; [c]FILTROX AG, Moosmühlestrasse 6, CH-9000 St. Gallen

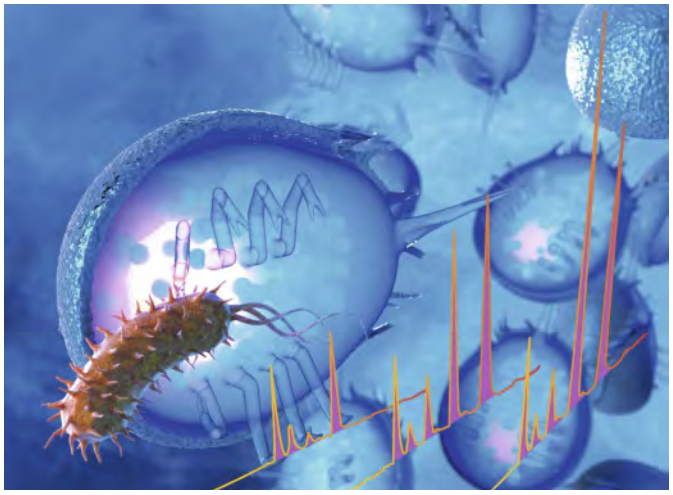
Keywords: Endotoxin quantification · Endotoxin testing · Kdo · LAL

Endotoxins (ETs) cover, non-covalently bound, to about 75% the outer cell wall of all Gram-negative bacteria. These are ubiquitously found in our environment, *e.g.* in non-sterile pharmaceutical preparations and bioprocesses, nutrition, and at working places like butcheries or cotton fields. If ETs enter the human blood stream, they initiate at very low concentrations a strong immune response with potentially fatal outcome. In consequence, health authorities worldwide regulate strictly the maximal ET content in pharmaceutical preparations at very low levels, *e.g.* 0.25 EU (0.025 ng)/mL for water of injection.

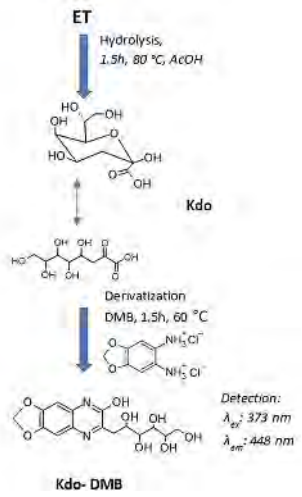
Today, ET testing is performed with biological assays; the gold standard is the 1977 FDA-accepted Limulus Amoebocyte Lysate (LAL) assay. However, for the widely used LAL test, the blood of horseshoe crabs (*Limulus polyphemus*) is needed, a marine species that is highly endangered. Those biological assays are very sensitive and specific to the complex, heterogeneous, and large molecular weight distribution of ET molecules. But they are expensive and show inherent poor reproducibility and recovery. Results are strongly dependent on sample handling and composition. That may lead to false negative test results as shown for certain ET-spiked monoclonal antibody (MAB) formulations, endangering patient safety.

In the framework of an ET-removal depth filter development project, our group established a reproducible, automatable, low-cost chemical ET assay. Every ET molecule contains one to three units of 3-deoxy-D-manno-oct-2-ulsonic acid (Kdo), which is almost only found in ETs. Kdo is quantitatively released by mild acidic hydrolysis. To reach sensitive detection, Kdo is derivatized with the fluorophore 1,2-diamino-4,5-methylenedioxybenzene-2 HCl (DMB) which recognizes specifically its α-keto-acid functionality. That circumvents matrix effects of, *e.g.*, neutral sugars from the ET molecule or proteins, present in complex bioreactor matrices. DMB increases Kdo's hydrophobicity, making it suitable for reversed-phase HPLC separation, *e.g.*, from sialic acids. The Kdo content is converted to ET content. LAL and Kdo-DMB-HPLC assay results show a strong correlation even in crude bioreactor ET samples.

The Kdo-DMB-HPLC assay opens the transition of endotoxin analytics to the 21st century.



Art picture of an *E. coli* bacteria cell in front of a horseshoe crab whose harvested blue blood is used to extract the enzymes needed to perform the conventional LAL assays. In the foreground on the right, an exemplary chromatogram is visible as it is obtained for Kdo-DMB separation from sialic acids in a Gram-negative bacterium bioreactor matrix.



Scheme of the Kdo-DMB-LC assay workflow. The first step is mild acidic hydrolysis of the ET molecule followed by derivatization of the released Kdo sugar acid with the fluorophore DMB. The mixture is separated by RP-(U)HPLC from matrix compounds, and Kdo-DMB is detected *via* fluorescence detection.

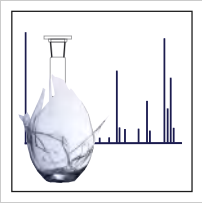
References

B. Bucsella, A. Hoffmann, M. Zollinger, F.Stephan, M. Pattky, R. Daumke, F. J. Heiligtag, B. Frank, M. Bassas-Galia, M. Zinn, F. Kalman, *Anal. Methods* **2020**, *12*, 4621; https://doi.org/10.1039/d0ay00872a.

A. Hoffmann, K. Pacios, R. Mühlemann, R. Daumke, B. Frank. F. Kalman, *Front. Bioeng. Biotechnol. Sec. Bioproc. Eng.* **2022** (submitted July 2022).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2022.1070 Chimia 76 (2022) 1070



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Forensic Analysis of Glass Fragments

Pascal Becker and Detlef Günther*

*Correspondence: Prof. Dr. D. Günther, E-mail: guenther@inorg.chem.ethz.ch
Department of Chemistry and Applied Biosciences, Laboratory of Inorganic Chemistry, ETH Zurich, Vladimir-Prelog-Weg 1, CH-8093 Zürich

Keywords: Forensics · Glass fragments · Laser ablation · Mass spectrometry

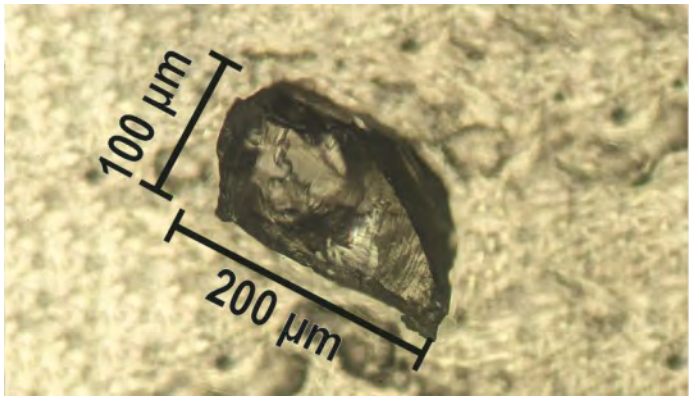
Broken glass is a common piece of evidence in burglaries, car crashes, and violent crime. When a glass object breaks, fragments are spread in the surrounding area and can be found in the clothes and skin of people who were in the vicinity at the time of the object breaking. If glass fragments found on a suspect are from the same source as the fragments at a crime scene, it can link the suspect to that crime scene.

In order to determine whether two fragments originate from the same source, different glass properties are analyzed and compared. The most successful application so far is the use of Single-Pulse Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICPMS) to quantify the concentrations of a set of elements in samples of known and unknown origin and compare them to one another. The court-approved established method makes use of sequential mass analyzers and high-dispersion ablation cells, using long and stable signals for quantification. Six measurements are made using large spot sizes and 500–600 laser pulses for each data point. However, this method requires larger samples of the size of 400 µm x 200 µm x 100 µm (20 µg), while most of the fragments found on suspects are smaller.

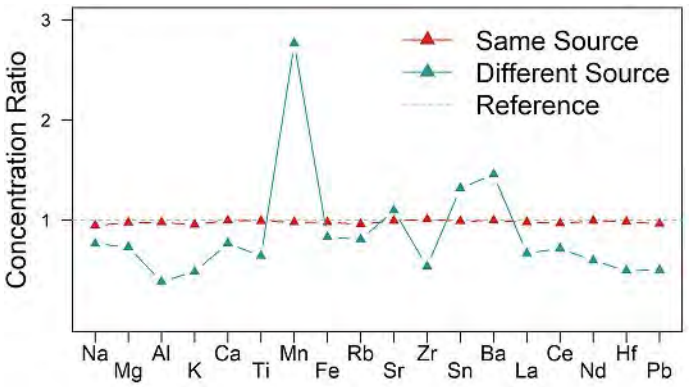
Changing to fast-washout low-dispersion ablation cells, individual laser pulses can be resolved and the sample is analyzed layer by layer with each pulse representing an independent measurement. This allows to get more information out of the small samples and to quantify using less material. As sequential mass analyzers are too slow for multi-elemental analysis of the faster transient signals, a (quasi-) simultaneous time-of-flight mass analyzer was used instead. Furthermore, it was possible to significantly increase the amount of data points, allowing for more sophisticated options with the statistical treatment of the measurements.

This approach allowed for a 25-fold reduction in the amount of sample material required to 100 µm x 100 µm x 33 µm (0.8 µg) while offering comparable matching and mismatching capabilities.

Received: October 17, 2022



Photograph of a typically sized glass fragment found as evidence on a suspect, placed on tape.

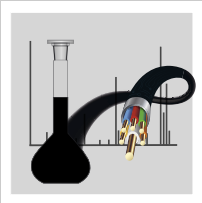


Ratios of concentrations for glass fragments when compared to fragments of the same source or a different source.

References:
P. Becker, C. Neff, S. Hess, P. Weis, D. Günther, *J. Anal. At. Spectrom.* **2020**, *35*, 2248, https://doi.org/10.1039/D0JA00284D.
C. Neff, P. Becker, D. Günther, *J. Anal. At. Spectrom.* **2022**, *37,* 677, https://doi.org/10.1039/D1JA00421B.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2023.68 Chimia 77 (2023) 68 © Swiss Chemical Society



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

RASER – A Tool for Rapid Mass Spectra Analysis of Chlorinated Paraffins

Marco C. Knobloch[ab], Jules Hutter[ac], Adriana Tell[ac], Oscar Mendo Diaz[ab], Flurin Mathis[ac], Urs Stalder[b], Laurent Bigler[b], Susanne Kern[c], Norbert V. Heeb[a]*, and Davide Bleiner[ab]

*Correspondence: Dr. N. Heeb[a], E-Mail: norbert.heeb@empa.ch
[a]Empa, Laboratory for Advanced Analytical Technologies, Überlandstrasse 129, CH-8600 Dübendorf; [b]University of Zürich, Department of Chemistry, Winterthurerstrasse 190, CH-8057 Zürich; [c]Zürich University of Applied Sciences ZHAW, Institute of Chemistry and Biotechnology, Einsiedlerstrasse 31, CH-8820 Wädenswil

Keywords: Automatic spectra evaluation · Chlorinated paraffins · High-resolution mass spectrometry · Persistent organic pollutants

Chlorinated paraffins (CPs) are complex mixtures of polychlorinated alkanes with carbon chain-length n_C between 10 to 30 (C-homologues) and chlorine numbers n_{Cl} between 2 to 14 (Cl-homologues). CP materials are widely used in metalworking fluids and in plastic. Short-chain CPs (SCCPs, $C_{10\text{-}13}$) are restricted and classified as persistent organic pollutants (POPs) under the Stockholm Convention. Medium-chain CPs (MCCPs, $C_{14\text{-}17}$) are under evaluation for legal restrictions as well, while information about environmental hazards of long-chain (LCCPs, $C_{\geq 18}$) is scarce. Technical CP mixtures can contain hundreds of homologues and millions of constitutional isomers and stereoisomers. This analytical complexity increases even more when CP transformation products, such as chlorinated olefins (COs), are present.

We developed a method based on liquid chromatography coupled to atmospheric pressure chemical ionization and Orbitrap mass spectrometry (LC-APCI-Orbitrap-MS) with mass resolution of ≥100'000 that allows to study complex CP mixtures. Respective mass spectra can contain up to 7'300 ions from 384 homologues. Manual data processing of this vast number of ions consumes several weeks.

Therefore, we developed an R-based automatic spectra evaluation routine (RASER) to identify and read-out MS-signals and report here data from a plastic insulation. The algorithm identifies signals by comparing simulated isotope clusters with measured ones. With RASER, CP-distributions of such materials were obtained within hours only. The workload to evaluate such mass spectra was reduced by a factor of 75. In total, 2'225 signals from 163 CP-homologues were identified in the spectrum of the plastic material. The distribution is bimodal with respect to the C-homologues and unimodal with respect to the Cl-homologues. MCCPs (52%) were the major CP-class, with relevant contributions of SCCPs (23%) and LCCPs (25%). **Therefore, LC-APCI-Orbitrap-MS in combination with RASER is a selective and time-efficient method to study complex CP mixtures from plastic materials and environmental samples.**

Received: December 5, 2022

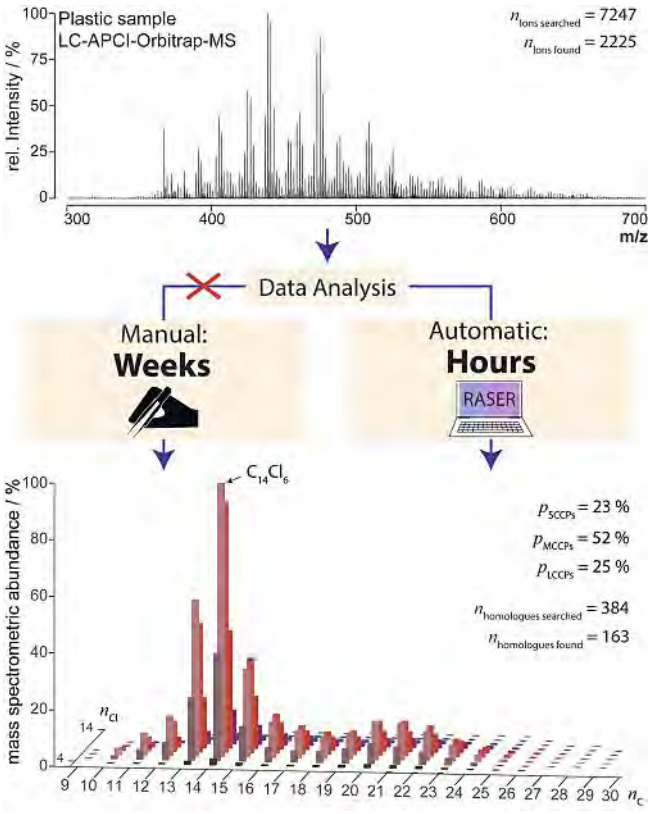
Acknowledgement

We thank the Federal Office for the Environment (FOEN) for the financial support (Grant 19.0011.PJ/S113-1600).

Reference

M. Knobloch, F. Mathis, O. Mendo Diaz, U. Stalder, L. Bigler, S. Kern, D. Bleiner, N. Heeb, *Anal. Chem.* **2022**, *94*, 13777, https://doi.org/10.1021/acs.analchem.2c02240

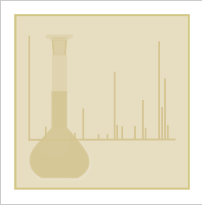
Technical CP mixtures are applied in plastic materials as plasticizers and flame-retardants. Photo by Marco C. Knobloch.



Evaluation of complex CP mass spectra from LC-APCI-Orbitrap-MS can take weeks when done manually. RASER reduces the workload to hours and provides C- (n_C= 9 to 30) and Cl- (n_{Cl} = 4 to 14) homologue distributions of CPs as found in the plastic coating of various electric cables.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2023.163 Chimia 77 (2023) 163



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Zwischgold – The Secret Nanomaterial of Medieval Gilding

Qing Wu[a], Karolina Soppa[b], Tiziana Lombardo[c], Katharina Schmidt-Ott[c], Frithjof Nolting[d], and Benjamin Watts*[d]

*Correspondence: Dr. B. Watts[d], E-mail: benjamin.watts@psi.ch
[a]Haute École Arc Conservation-restauration, HES-SO University of Applied Sciences and Arts Western Switzerland, Espace de l'Europe 11, CH-2000 Neuchâtel; [b]Institute Materiality in Art and Culture, Bern Academy of the Arts, Fellerstrasse 11, CH-3027 Bern; [c]Conservation Research, Collection Centre, Swiss National Museum, Lindenmoosstrasse 1, CH-8910 Affoltern am Albis; [d]Swiss Light Source, Paul Scherrer Institute, Forschungsstrasse 111, CH-5232 Villigen PSI

Keywords: Medieval gilding · Nanotomography · PXCT · Zwischgold

Zwischgold is a bi-layer metal leaf made from a thin gold layer atop a silver base. Since it uses less gold to present an actual gold surface than simple gold leaf, its application was popular on medieval sculptures and altarpieces, and was strictly regulated by guilds. However, information about the materials and production of medieval Zwischgold is scarce. In addition, the chemical instability of the silver component has been an obstinate problem for the conservation of Zwischgold artefacts. Difficulties in identifying well-preserved examples[1] and the need for nanoscale measurements[2] have also hindered modern research of Zwischgold.

We used an advanced imaging technique, Ptychographic X-ray computed tomography (PXCT), to measure nanoscale, quantitative 3D images of a Zwischgold micro-sample taken from the central figure *Mary* of the 1420-dated Leiggern Altar, which is on permanent exhibition in the Swiss National Museum, Zurich. The PXCT measurements clearly demonstrate a decreasing density (increasing porosity) of the leaf materials and the development of corrosion products within this 800-year-old sample. The voids at the underside of the metal leaf that reach over 50% of the total leaf area indicate a delamination tendency of the leaf from its substrate, which may be a critical issue for the future conservation of Zwischgold-applied artefacts.[3]

The PXCT measurements show that the *Mary* sample has an average gold layer of *ca.* 127 nm and full leaf thickness of *ca*. 252 nm, which stand at the higher end of the thickness range observed in our previous SEM measurements of 74 medieval samples.[2] The nanoscale thickness range (*ca*. 20–50 nm) of the gold layer of medieval Zwischgold strongly supports its competitive market price compared to gold leaf (*ca.* 160 nm thick on average[4]).

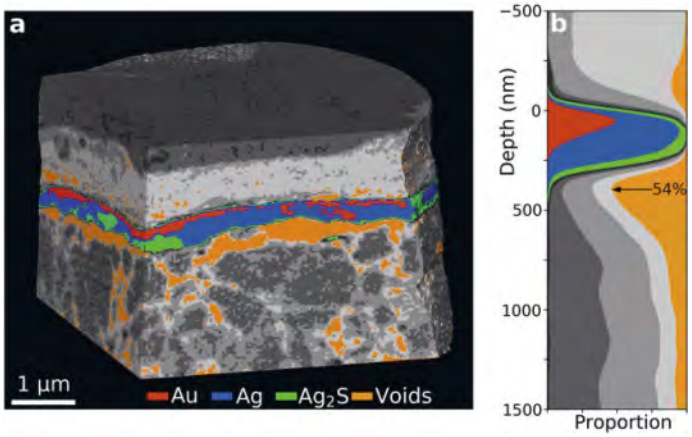
The revelation of nanomaterials in Zwischgold demonstrates that the Middle Ages was not the Dark Ages but rather a climax epoch that produced exquisite art technologies.

Acknowledgements

We thank the Swiss National Museum – Collection Centre, the Basel Historical Museum, and the Institute Materiality in Art and Culture at the Bern Academy of the Arts for support and access to sample materials. The PXCT measurements were performed at the cSAXS beamline of the Swiss Light Source at the Paul Scherrer Institute.

The central altar figure *Mary* (Inv. No. LM16701.2) in the Leiggern Altar (Inv. No. LM16701.1), 1420, Swiss National Museum. The sample-taking position is indicated by a green arrow. Reproduced from Wu *et al*.[3] Copyright: Schweizerisches Nationalmuseum, (source: Inv. No. LM16701.1, DIG-2195).

Received: January 18, 2023



(a) Segmented PXCT 3D image of the *Mary* sample showing the locations of Au (red), Ag (blue), silver corrosion products (green), voids (orange), and other segments in shades of grey. (b) Stack plot of the depth profile of the sample, aligned to the Au segment. Reproduced from Wu *et al*.[3]

[1] Q. Wu, T. Lombardo, V. Hubert, E. Hildbrand, P. Wyer, F. Nolting, D. Ganz, *Microchem. J.* **2020**, *156*, 104810. https://doi.org/10.1016/j.microc.2020.104810.
[2] Q. Wu, B. Watts, M. Döbeli, J. Müller, B. Butz, T. Lombardo, K. Schmidt-Ott, R. Fink, F. Nolting, D. Ganz, *J. Cult. Herit.* **2021**, *49*, 211. https://doi.org/10.1016/j.culher.2021.01.010.
[3] Q. Wu, K. Soppa, E. Müller, J. Müller, M. Odstrcil, E. H. R. Tsai, A. Späth, M. Holler, M. Guizar-Sicairos, B. Butz, R. H. Fink, B. Watts, *Nanoscale* **2022**, *14*, 15165. https://doi.org/10.1039/d2nr03367d.
[4] Q. Wu, M. Döbeli, T. Lombardo, K. Schmidt-Ott, B. Watts, F. Nolting, D. Ganz, *Herit. Sci*. **2020**, *8*, 119. https://doi.org/10.1186/s40494-020-00456-2.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2023.256

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Nanoparticles Are Everywhere, Even Inside Trees

Paula Ballikaya*[ab], Ivano Brunner[a], Claudia Cocozza[c], Daniel Grolimund[d], Ralf Kaegi[e], Maria E. Murazzi[a], Marcus Schaub[a], Leonie C. Schönbeck[af], Brian Sinnet[e], and Paolo Cherubini[abg]

*Correspondence: P. Ballikaya[ab], E-mail: paula.ballikaya@wsl.ch

[a]WSL Swiss Federal Institute for Forest, Snow and Landscape Research, CH-8903 Birmensdorf; [b]Department of Geography, University of Zurich, CH-8057 Zurich; [c]Department of Agriculture, Food, Environment and Forestry (DAGRI), University of Florence, I-50145 Florence; [d]Swiss Light Source, PSI Paul Scherrer Institute, CH-5232 Villigen PSI; [e]Eawag Swiss Federal Institute of Aquatic Science and Technology, CH-8600 Dübendorf; [f]Department of Botany & Plant Sciences, University of California Riverside, 2150 Batchelor Hall, Riverside, CA, 92521-0124; [g]Department of Forest and Conservation Sciences, Faculty of Forestry, University of British Columbia, 2004-2424 Main Mall, V6T 1Z4, Vancouver BC

Keywords: Gold nanoparticles · Leaf and root uptake · Pollution · Stem accumulation · Stomatal pathway · Tree species

The presence of natural nanomaterials in the Earth system has always been abundant since billions of years. Since the Industrial Revolution and the advent of nanotechnology, new types of nanomaterials are released into the atmosphere, water and soil as a byproduct from human activities and as engineered nanoparticles (NPs) from NP-based products. To understand the consequences of NP pollution, numerous studies are assessing the fate, transport and interaction of NPs in humans, organisms and environmental systems.

Trees have been used for phytoremediation and as bio-monitors of current and past pollution as they can store various contaminants in the roots, stems and leaves. Seemingly, trees must have been exposed to naturally occurring NPs since they first evolved. Recent evidence of foliar uptake and transport of silver NPs in trees increased the attention on understanding the interactions between NPs and trees. Today, still not much is known about the mechanisms of uptake of these particles, neither the risks related to their exposure, as a function of size and chemical properties of the NPs. This assessment will contribute to enlighten the potential role of trees in mitigating the NP pollution and related impacts.

In the framework of studying trees as bioindicators of pollution, we used gold (Au) NPs as model NPs to investigate their uptake and transport in European beech and Scots pine trees. We found that Au NPs were taken up by roots and leaves, while a small fraction was transported to the stem in both species. Gold was transported from leaves to roots but not *vice versa*. 2D X-ray fluorescence imaging of a beech leaf, complemented by 3D confocal XRF microscopy, revealed Au NPs hotspots sparsely distributed over the entire scanned part of the leaf. While several Au NPs were mostly trapped on the leaf surface, abundantly associated with trichomes along the midrib and lateral veins, a small number of Au NPs could penetrate the leaf, probably through the stomata.

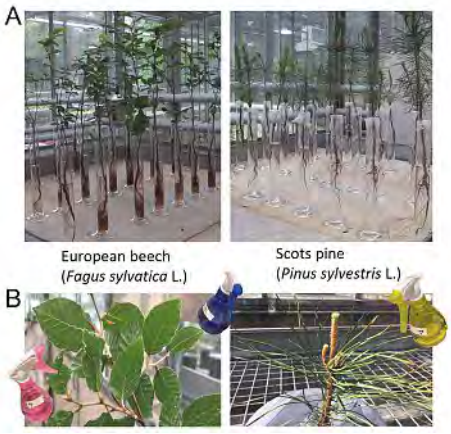
Our results show that trees can absorb NPs. Now we need to understand how they translocate them to different tree compartments.

Received: February 14, 2023

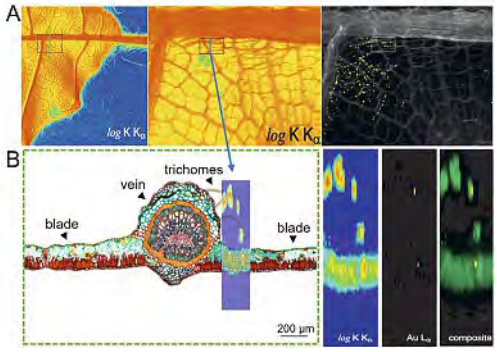
References

P. Ballikaya, *et al., Tree Physiol*. **2023**, *43*, 262, https://doi.org/10.1093/treephys/tpac117.

P. Ballikaya, J. M. Mateos, I. Brunner, A. Kaech, P. Cherubini, *Front. Environ. Sci*. **2023**, *10*, 1107005. https://doi.org/10.3389/fenvs.2022.1107005.



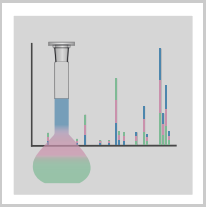
Experimental design to investigate the (A) root and (B) leaf uptake and transport of Au NPs in European beech and Scots pine trees. The NPs were hydrophonically applied to the roots and sprayed to the leaves in a greenhouse chamber at the WSL Swiss Federal Research Institute.



Microscopic, two- and three-dimensional chemical imaging. 2D XRF images show the distribution of gold nanoparticles on leaf and petiole of European beech (top row). A tomographic sub-volume (indicated by the square), obtained by confocal X-ray microscopy, revealed two isolated gold nanoparticles, one in the leaf blade and one inside/on a trichome (bottom, right). The schematic representation of the section of beech leaf indicates the position of the tomographic slice shown in both panels. The 2D/3D chemical imaging was conducted at the microXAS beamline at the Swiss Light Source of the Paul Scherrer Institute.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2023.348 Chimia 77 (2023) 348



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Visualizing a Carbon-Fixing Nanowire Inside Bacteria

Ricardo D. Righetto* and Benjamin D. Engel*

*Correspondence: Dr. R. D. Righetto, E-mail: ricardo.righetto@unibas.ch; Prof. Dr. B. D. Engel, E-mail: ben.engel@unibas.ch

Biozentrum, University of Basel, Spitalstrasse 41, CH-4056 Basel

Keywords: Anaerobic bacteria · Carbon fixation · Cryo-electron microscopy · Electron transfer · Enzyme · Nanowire

Bacteria have evolved unusual ways to obtain energy in extreme environments with no oxygen. The hydrogen-dependent CO_2 reductase (HDCR) enzyme from acetogenic bacteria is one particularly ingenious example. HDCR performs the reversible conversion of molecular hydrogen and CO_2 into formic acid much more efficiently than any other known chemical catalyst. To understand how HDCR achieves such an impressive turnover rate, we sought to visualize its molecular structure.

Working in collaboration with the research groups of Volker Müller (University of Frankfurt) and Jan Schuller (University of Marburg), we used cryo-electron microscopy to obtain a high-resolution 3D structure of purified HDCR proteins. This advanced imaging technique, pioneered by Swiss Nobel laureate Jacques Dubochet, involves rapidly freezing the sample in vitreous ice to preserve its structure under the electron beam. The results revealed that HDCR is a novel type of biological nanowire, which is decorated by hydrogenase and formate dehydrogenase enzymes. The enzymes and nanowire proteins are all interconnected by a chain of iron-sulfur clusters, which efficiently shuttle electrons between the catalytic subunits, thereby coupling the hydrogen-splitting and carbon-fixation reactions.

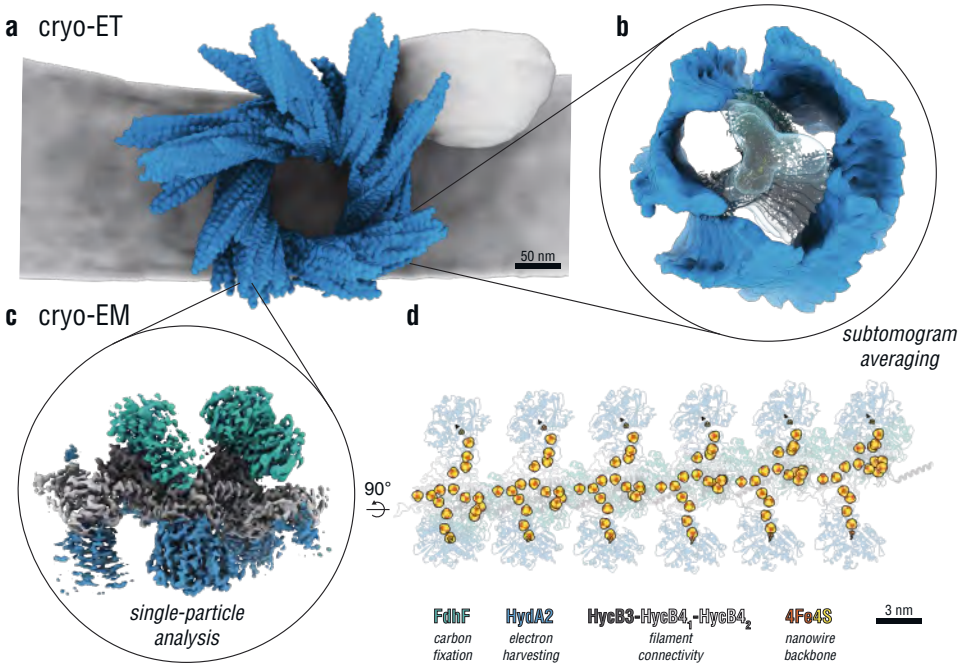
Furthermore, we also used cryo-electron tomography to visualize the HDCR filaments in their native biological context inside *Thermoanaerobacter kivui* cells. These cells were preserved in vitreous ice and then thinned by focused ion beam (FIB) milling before tomographic imaging. The 3D reconstructions showed that around 100 HDCR nanowires bundle together to form ~200 nm circular superstructures attached to the cell membrane. This ordered bundling of HDCR filaments in the cell may be a concentration mechanism that further explains how these organisms are so efficient at carbon fixation. How the HDCR nanowires attach to the plasma membrane and interact with the other components in the acetogenic metabolic pathway are questions that remain to be explored.

Understanding the molecular architecture of HDCR paves the way towards its use in biotechnological applications. For example, it could be used to store hydrogen fuel in a more efficient and safer way as formate, or in carbon-capture technologies aimed at mitigating global warming.

Received: March 17, 2023

Reference

H. M. Dietrich, R. D. Righetto, A. Kumar, W. Wietrzynski, R. Trischler, S. K. Schuller, J. Wagner, F. M. Schwarz, B. D. Engel, V. Müller, J. M. Schuller, *Nature* **2022**, *607*, 823, https://doi.org/10.1038/s41586-022-04971-z.



Visualizing HDCR filaments using cryogenic electron microscopy techniques. a) Using cryo-electron tomography (cryo-ET) on FIB-milled *T. kivui* bacteria, we observed bundles of HDCR filaments (blue) attached to the cellular membrane (gray). b) These native HDCR filaments were resolved to 17 Å with subtomogram averaging. c) Single-particle cryo-electron microscopy (cryo-EM) of purified HDCR filaments resolved the structure to 3.4 Å. d) Combining the structural data from cryo-EM and cryo-ET at different scales, we built an atomic model for the HDCR filaments, showing that a nanowire of iron-sulfur clusters (orange and yellow) connects the catalytic centers of the hydrogen-splitting (HydA2) and carbon-fixing (FdhF) enzymes.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights©chimia.ch

doi:10.2533/chimia.2023.444

Chimia 77 (2023) 444

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Drug Checking: Glimpse into the Recreational Drug Market in Switzerland

Manuela Carla Monti*[a], Jill Zeugin[b], Natasa Milenkovic[c], Eva Scheurer[a], and Götz Schlotterbeck[a]

*Correspondence: Dr. M. C. Monti[a], E-mail: manuela.monti@unibas.ch
[a]Institute of Forensic Medicine, Department of Biomedical Engineering, University of Basel, Pestalozzistrasse 22, CH-4056 Basel; [b]Addiction Support, Region Basel (Suchthilfe Region Basel); [c]Addiction Services (Abteilung Sucht), Health Department Kanton Basel-Stadt

Keywords: Cocaine · Drug Checking · Harm reduction · Scheduled drugs

Drug checking services (DCS) allow recreational drug users to have drug samples chemically characterized. For the DCS *Drogeninfo Basel* (DIBS) analyses are conducted at the Institute of Forensic Medicine Basel. During sample collection, the visitors, who remain anonymous throughout, are obligated to conduct a nationwide questionnaire and professional counseling. After three days, the visitors are informed about the identity and purity of the sample. During the pilot phase (mid-2019 to mid-2022), 744 samples have been issued for analysis at the DIBS with cocaine being the most commonly analyzed drug (25%).

For the analysis, high-performance liquid chromatography coupled to a diode array detector (HPLC-DAD) is used. This method is validated for the quantification of over 20 analytes, spanning most important scheduled drugs (*e.g.* amphetamines and cocaine) and adulterants (*e.g.* caffeine, levamisole, phenacetin). In cases of 'designer drugs', further technologies are often required. Thus, gas chromatography coupled to mass spectrometry, GC coupled to vapor phase infrared spectroscopy (GC-IR), HPLC coupled to high-resolution mass spectrometry (HPLC-HRMS), and attenuated total reflectance IR (ATR-IR) are regularly applied.

In 2020, the emergence of low-tetrahydrocannabinol (THC) cannabis treated with synthetic cannabinoids (SCs) was observed in Switzerland. Such products were sold to users who believe that they are purchasing regular marihuana. SCs are potent synthetically produced compounds which act at the same target in the human brain as THC (the main active ingredient of cannabis) but have significantly aggravated risk profiles. Consequently, these novel adulterated products raised serious public health concerns. DCS enabled the rapid detection and monitoring of this trend, which has recently seen a significant drop in numbers. In 2020, a comprehensive qualitative screening method targeting over 60 SCs was developed and validated using HPLC-HRMS.

State-of-the-art technologies (*e.g.* GC-IR and HPLC-HRMS) and continuous development efforts are needed to react to the ever-changing illicit drug market in the context of DCS.

Received: April 11, 2023

Reference

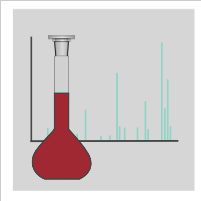
M. C. Monti, J. Zeugin, K. Koch, N. Milenkovic, E. Scheurer, K. Mercer-Chalmers-Bender, *Drug Testing and Analysis* **2022**, *14*, 1026, https://doi.org/10.1002/dta.3220.

MDMA-tablet containing 167 mg MDMA. Thorough documentation of tablets is required to be able to issue warnings that are made publicly available through diverse channels.

Cannabis and hashish samples found to contain the synthetic cannabinoid MDMB-4en-PINACA. To distinguish treated from untreated products, chemical analysis is required.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights©chimia.ch

doi:10.2533/chimia.2023.536 Chimia 77 (2023) 536



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Biomarker-based Diagnostics for Mild Traumatic Brain Injury (mTBI) at POC – Rising to the Challenges

Marc E. Pfeifer*, Milica Jović, and Denis Prim

*Correspondence: Prof. Dr. M. E. Pfeifer, E-mail: marc.pfeifer@hevs.ch
University of Applied Sciences and Arts Western Switzerland (HES-SO Valais-Wallis), School of Engineering, Institute of Life Technologies, Diagnostic Systems Research Group, Rue de l'Industrie 19, CH-1950 Sion

Keywords: Mild traumatic brain injury (mTBI) · Point-of-Care (POC) diagnostics · Spatially resolved electrochemiluminescence immunoassay (SR-ECLIA)

Every year 56 million people worldwide experience mild traumatic brain injuries (mTBI, concussion), and there are plenty of unreported cases. Contrary to moderate or severe forms of head injuries, mTBI is difficult to detect with imaging techniques (CT, MRI) and patients often have only unspecific or no apparent symptoms. Repetitive mTBI from multiple head impact events (*cf.* sports accidents) has been associated with greater severity of symptoms, longer recovery times, and with early onset of neurodegenerative diseases.

A laboratory *in vitro* diagnostic (IVD) test for mTBI developed by Banyan Biomarkers was approved by the FDA in 2018. The test is based on a chemiluminescent ELISA for determining two biomarkers, glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase isozyme L1 (UCH-L1) in blood samples. Early 2021 Abbott pioneered the first handheld POC diagnostic test based on their i-STAT™ Alinity™ device to measure these two biomarkers amperometrically. Other companies, such as Medicortex, NanoDx, and ABCDx followed the same path, developing POC diagnostic tests based on other analytical techniques and (partially) different biomarkers. However, all these approaches are limited by the number of biomarkers that can be measured simultaneously.

Aiming to develop a 'next-generation' POC multiplex IVD device for mTBI, our group established both a demonstrator device and a sensitive 3-plex assay to simultaneously quantify the biomarkers GFAP, human fatty acid-binding protein (h-FABP), and S100 calcium-binding protein B (S100β). The test is based on a spatially resolved electrochemiluminescence immunoassay (SR-ECLIA), supported by a low-cost screen-printed carbon electrode (SPCE) that can be integrated into a disposable cartridge. Signal generation occurs at distinct areas of the electrode functionalized with capture antibodies, via a tripropylamine-mediated redox process with $Ru(bpy)_3^{2+}$-luminophores attached to detection antibodies. At the current development stage, the demonstrator is a compact tabletop device that includes a specifically designed light collection module and an sCMOS detector. The three mTBI biomarkers can reproducibly be quantified in 50% diluted serum in the pg mL^{-1} range.

The demonstrator device and assay signify milestone achievements towards a future high-sensitivity multiplex IVD system for mTBI testing at the POC.

Received: June 7, 2023

References
M. Jović, D. Prim, E. Saini, M. E. Pfeifer, *Biosensors* **2022**, *12*, 172, https://doi.org/10.3390/bios12030172.
M. Jović, D. Prim, O. Righini, D. Tagan, M. Stäuble, M. Pignat, S. Gallay, M. Geiser, M. E. Pfeifer, *Sens. Diagn.* **2023** (accepted May 2023), https://doi.org/10.1039/D3SD00090G.

Fig. 1. Simulated use case scenario with a person having suffered a TBI and first responders providing *ad hoc* patient care at the site of an accident. At the bottom right, on the foldable patient stretcher, a model of the envisioned POC diagnostic device for multi-biomarker detection with inserted sample preparation cartridge is depicted. The five bars on the display represent results from a putative 5-plex SR-ECLIA. Device designed by MADI comunicazione and Marc E. Pfeifer. Copyright HES-SO Valais-Wallis (based on Shutterstock photo).

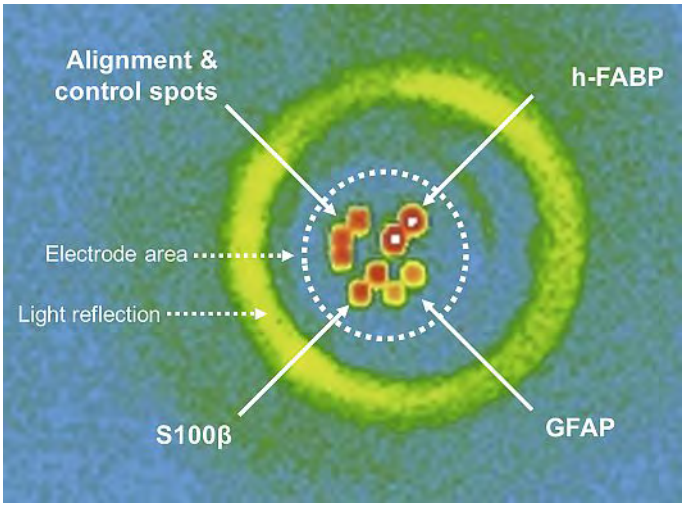
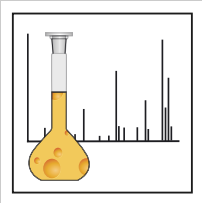


Fig. 2. Early proof-of-principle of the spatially resolved electrochemiluminescence immunoassay (SR-ECLIA) experiment for the concurrent detection of the mTBI biomarkers h-FABP, GFAP and S100β in duplicate spots.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2023.622 Chimia 77 (2023) 622



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

A Simple, Rapid and Validated Method for the Determination of Free Volatile Carboxylic Acids in Cheese by GC-FID

René Badertscher, Grégory Pimentel*, Carola Blaser, and Priska Noth

*Correspondence: Dr. G. Pimentel, E-Mail: gregory.pimentel@agroscope.admin.ch
Federal Department of Economic Affairs, Education and Research EAER, Agroscope, Schwarzenburgstrasse 161, CH-3003 Bern

Keywords: Bacterial cultures · Cheese · Flavour · Free volatile carboxylic acids · Free volatile fatty acids · GC-FID · Headspace

Free volatile fatty acids, or more precisely free volatile carboxylic acids (FVCA), are formed during cheese ripening by microorganisms *via* heterofermentative lactic acid fermentation or amino acid deamination. FVCAs content varies greatly from a cheese to another, depending on the type of bacteria or yeasts present, and contributes significantly to the final taste and flavor of each cheese. While the presence of some FVCAs is associated with desirable typical flavors (*e.g.* propionic acid in Emmental cheese), other FVCAs, resulting from fermentations by undesirable microorganisms, can lead to unpleasant flavors or eye formation. Therefore, the quantification of FVCAs is of great interest in cheese manufacturing as it can reveal ripening defects.

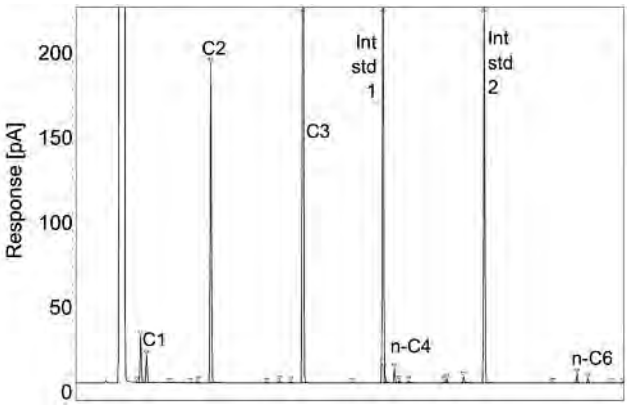
Many different approaches for FVCAs quantification have been proposed over the years, improving sensitivity, but remaining complex to implement. Such methods combine extraction (with polar or apolar solvents, dynamic headspace, solid phase (micro)extraction), pre-purification with various adsorbents, conversion into sodium salts, drying, esterification and analysis using gas-chromatography coupled with flame ionization (GC-FID), thermal conductivity or mass spectrometry detectors.

Our new method allows the simultaneous quantitative determination of FVCAs, and has been validated for eight target analytes. It uses a weakly basic aqueous extraction, followed by an esterification with ethanol directly from the aqueous phase in a headspace vial. The ethyl esters thus formed are then analyzed by GC-FID. The conditions for the extraction, esterification, and headspace (amount of ethanol, sodium hydroxide concentration, time and temperature) were optimized over the years. The limits of detection (LOD) in cheese were less than 0.3 µmol kg^{-1}. The lower limits of quantitation (LOQ) were better than 0.001 mmol kg^{-1}. The upper LOQ varied from 39 to 136 mmol kg^{-1} depending on the analyte. The Horwitz ratio showed good precision for all analytes (less than 0.77).

Our new method is simple and rapid to implement. The validation parameters of trueness, specificity, precision, LOD, and LOQ demonstrate that it is sensitive, robust and suitable for accurate quantification of FVCAs over a wide range of measurements in cheese, in bacterial culture, and potentially in other type of matrices.

Reference
R. Badertscher, C. Blaser, P. Noth, *Food Chemistry* **2023**, *398*, 133932, https://doi.org/10.1016/j.foodchem.2022.133932.

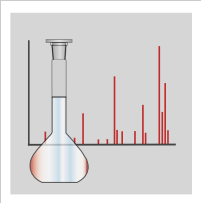
Agroscope's experimental cheese factory (A), Agilent 8890 gas chromatograph coupled with a flame ionization detector and a PAL3 autosampler in headspace mode (B).



Chromatogram of the free volatile carboxylic acids in their ethyl ester form in a hard cheese sample. Formic acid (C1), acetic acid (C2), propionic acid (C3), isobutyric acid (i-C4), n-butyric acid (n-C4), isovaleric acid (i-C5), isocaproic acid (i-C6) and n-caproic acid (n-C6). Samples' headspace were analyzed with an Agilent 8890 GC-FID equipped with an Agilent HP-5 cross-linked phenyl methyl silicone fused silica capillary column, using helium as the carrier gas. The GC temperature program was 40 °C (4 min), 8 °C.min^{-1} to 144 °C, then 30 °C.min^{-1} to 279 °C (0.5 min).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights©chimia.ch

doi:10.2533/chimia.2023.693 Chimia 77 (2023) 693



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Operando Surface Hydrogen Analysis by Plasmon Spectroscopy

Andreas Borgschulte*, Emanuel Billeter, and Selim Kazaz

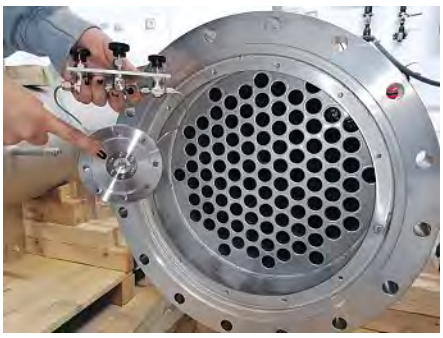
*Correspondence: PD Dr. A. Borgschulte, E-mail: andreas.borgschulte@empa.ch, Laboratory for Advanced Analytical Technologies, Empa – Swiss Federal Laboratories for Materials Science and Technology, Überlandstrasse 129, CH-8600 Dübendorf

Keywords: Hydrogen · Membrane · Pressure composition isotherm · Reflecting electron energy loss spectroscopy · Surface

Hydrogen is a ubiquitous element in the environment. The element plays a key role in biology, chemistry, and physics: It is involved in numerous chemical reactions, from photosynthesis to the combustion of its products, and plays an essential role in the chemical industry and corrosion. The fast diffusion of hydrogen in most materials, including nonorganic matter such as metals and oxides, makes hydrogen an omnipresent impurity. Hydrogen is used on large scale as a process gas in chemical industry. Understanding the interaction of hydrogen with matter is crucial for any technology, with hydrogen involved as reactant, intermediate, or product. Needless to say that hydrogen-solid interactions gain relevance with the upcoming renewable hydrogen energy technology.

Hydrogen quantification in bulk materials is relatively straightforward. However, the analysis of hydrogen at the surface is much more difficult but no less important as it is the precursor of bulk hydrogen. Electron spectroscopy is the usual tool to characterize surfaces; however, the most common one, X-ray photoelectron spectroscopy, is a suboptimal technique for hydrogen detection due to the lack of a hydrogen core electron. The dependence of plasmon excitation on the hydrogen content as measured by reflecting electron energy loss spectroscopy (REELS) was found to be a reliable method to determine the sub-surface hydrogen concentration, from which the surface hydrogen-pressure composition isotherms are determined. The stability of hydrogen at the surfaces of hydrogen selective membranes is still controversially debated and thus the ideal system to be studied by the method. The Figure below shows the surface hydrogen pressure composition isotherms of vanadium membranes as a proof of principle of the technique. The energy dependence of REELS reveals that the VH_x layer formed at higher pressures exhibits a hydrogen concentration gradient at the surface. The experimental results deliver the input parameters to model and eventually improve hydrogen-selective membranes.

Apart from hydrogen membranes, the laboratory-based REELS method to analyze hydrogen at the surface of metals and alloys is highly relevant for additional applications such as hydrogen storage and hydrogen sensing.

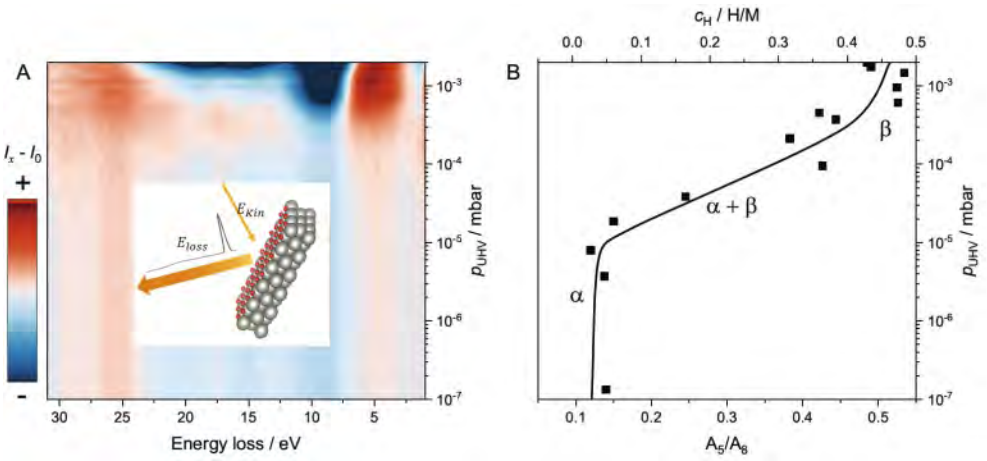


Size comparison between a test device for measuring the permeability of hydrogen selective membranes and a small industrial reactor. In industrial membrane reactors, the membranes are designed as tube bundles, while a flat design (a flat membrane is inserted at the location indicated by index finger) is chosen for scientific characterisation. The need for cheap membrane materials is obvious.

Received: August 28, 2023

Reference

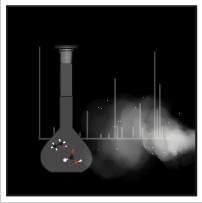
E. Billeter, S. Kazaz, A. Borgschulte, *Adv. Mater. Interf.* **2022**, *9*, 2200767, https://doi.org/10.1002/admi.202200767.



Left: Principle of reflecting electron energy loss spectroscopy (REELS) inset. Left and right: REELS difference spectra of the downstream surface of a vanadium membrane at 100 °C exposed to incrementally increased hydrogen pressure as 2D-contour plot showing the continuous change of the spectra upon hydrogen uptake particularly strong at 5 and 8 eV. The corresponding pressure surface composition isotherms are derived from the area ratio at these loss energies and the measured permeate pressure.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights©chimia.ch

doi:10.2533/chimia.2023.785 Chimia 77 (2023) 785–785



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Analysis of Breath-related Volatile Organic Compounds with Laser Absorption Spectroscopy

Miloš Selaković[ab], Raphael Brechbühler[a], Philipp Scheidegger[a], Herbert Looser[a], André Kupferschmid[c], Stéphane Blaser[d], Lukas Emmenegger[a], Renato Zenobi[b], and Béla Tuzson*[a]

*Correspondence: Dr. B. Tuzson[a], E-mail: bela.tuzson@empa.ch
[a]Laboratory for Air Pollution/Environmental Technology, Empa, Überlandstrasse 129, CH-8600 Dübendorf; [b]Department of Chemistry and Applied Biosciences, ETH Zürich, Vladimir-Prelog-Weg 1–5/10, CH-8093 Zürich; [c]Transport at Nanoscale Interfaces Laboratory, Empa, Überlandstrasse 129, CH-8600 Dübendorf; [d]Alpes Lasers SA, Avenue des Pâquiers 1, CH-2072 St-Blaise

Keywords: Extended-tuning quantum cascade laser (QC-XT) · Methanol quantification · On-line breath analysis · Volatile organic compounds (VOCs)

On-line breath analysis has gained much interest in recent years as it has great potential for non-invasive point-of-care diagnostics and personalized medicine. Mass spectrometry is the most frequently used technique, mainly for the untargeted analysis of exhaled breath and the identification of volatile organic compounds (VOCs) as biomarkers. For routine monitoring of established biomarkers, however, there is a need for a method that can provide fast and accurate response in a compact, easy-to-use, and cost-effective instrumentation. Here, mid-infrared laser absorption spectroscopy (LAS) is a promising alternative technique, as already demonstrated by the wide range of monitoring applications, especially for small inorganic gaseous compounds.

Optical analysis of VOCs is, however, far more challenging, because these compounds often exhibit broad, congested, and spectrally overlapped absorption spectra. Consequently, there is a stringent requirement on the laser source to provide broad spectral coverage and high spectral resolution for a selective and accurate multi-VOC analysis.

Our proposed solution to cope with this requirement is the extended-tuning quantum cascade laser (QC-XT). Using this device, we developed a spectrometer that can access six spectral windows spanning over 40 cm^{-1} and provide high-resolution scans (~10^{-4} cm^{-1}) within the individual windows. Custom-built electronics allow rapid switching between and tuning within the six windows (~3300 scans/s), resulting in the measurement of one complete spectrum every 360 ms. With this approach, we can quantify VOCs at amount fractions down to tens of ppb. The broad measuring range and the high spectral resolution of the spectrometer, combined with the unique spectral fingerprints of the investigated VOCs assure excellent selectivity of the method and enable multi-compound measurements in the breath.

This approach allows for the simultaneous measurement of concentration profiles of several VOCs, water vapor and CO_2 in one breath stroke with a relative expanded uncertainty (k = 2) of <2 %.

Received: September 28, 2023

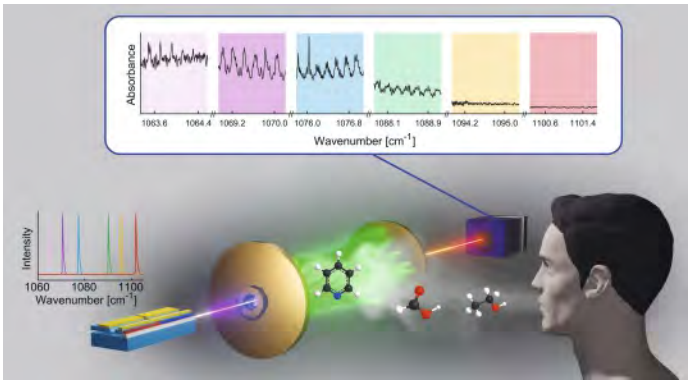
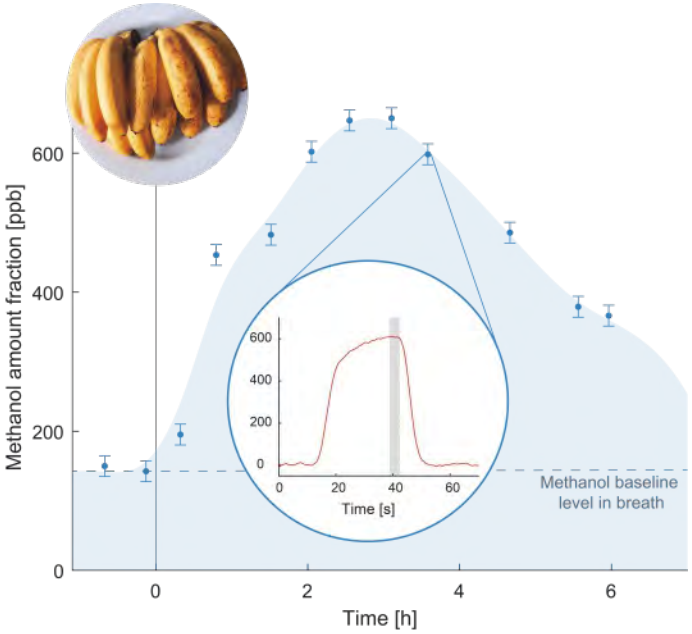


Illustration of the measurement concept. The multi-frequency mid-IR light beam (around 9.25 µm) emitted by the QC-XT laser is coupled into a multi-pass absorption cell (76 m optical path) before reaching the IR detector. A recorded spectrum of pyridine, on top, is shown as a typical example of a broad and congested absorption spectra of VOCs. The spectrometer targets on-line VOC analysis of human breath samples.

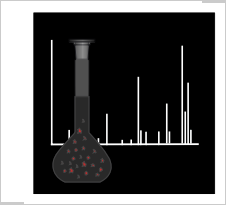


Methanol profile in breath before and after consumption of baby bananas measured on-line with the laser spectrometer. Methanol level was expressed as a mean value of measured amount fractions in the last part of a single breath stroke as indicated by the gray bar in the inset.

Reference
R. Brechbühler, M. Selaković, P. Scheidegger, H. Looser, A. Kupferschmid, S. Blaser, J. Butet, L. Emmenegger, B. Tuzson, *Anal. Chem.* **2023**, *95*, 2857, https://doi.org/10.1021/acs.analchem.2c04352.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: VRMeyer@bluewin.ch

doi:10.2533/chimia.2023.874 Chimia 77 (2023) 874



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Fluorescently Labelled Tau Protein

Saurabh Awasthi*[ab], Liviana Mummolo[b], Yuanjie Li[b], Louise Bryan[b], Peter Niraj Nirmalraj[c], Sandor Balog[b], Jerry Yang[d], and Michael Mayer*[b]

*Correspondence: Dr. S. Awasthi[ab], E-mail: rf.saurabh.awasthi@niperrbl.ac.in; Prof. M. Mayer[b], E-mail: michael.mayer@unifr.ch

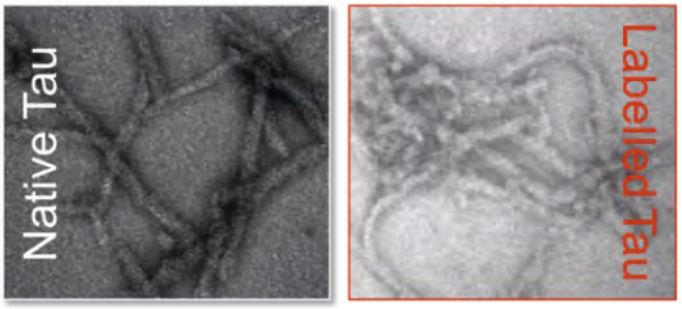
[a]Department of Biotechnology, National Institute of Pharmaceutical Education and Research-Raebareli (NIPER-R), Lucknow, Uttar Pradesh, India; [b]Adolphe Merkle Institute, University of Fribourg, Chemin des Verdiers 4, CH-1700 Fribourg; [c]Transport at Nanoscale Interfaces Laboratory, Swiss Federal Laboratories for Materials Science and Technology, CH-8600 Dübendorf; [d]University of California San Diego, Department of Chemistry and Biochemistry, La Jolla, CA, 92093-0358, USA

Keywords: Alzheimer's disease · Sortase A · Tau aggregation

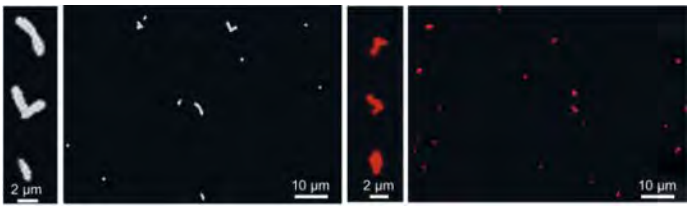
Aggregation of microtubule-associated protein Tau (MAP-Tau) is involved in the progression of Alzheimer's disease and other neurodegenerative disorders. Collectively, these diseases are termed tauopathies and affect millions of people worldwide. Therefore, monitoring the aggregation of Tau protein is critical for a better understanding of the pathological mechanisms of neurodegenerative disorders. In this framework, single-molecule fluorescence microscopy provides a compelling tool for studying the formation of Tau aggregates. One challenge, however, is that labeling Tau monomers with a fluorescent dye may interfere with the regions involved in aggregation. The two hexapeptide hydrophobic regions in the microtubule-binding repeats R2 and R3, which are responsible for Tau aggregation, and the cysteine residue Cys-322, which is involved in the formation of dimers that putatively drive the formation of fibrils, should not be perturbed. Conventional approaches for preparing fluorescent derivatives of Tau protein are, however, targeted to cysteine or lysine residues and may hence perturb these essential regions of Tau.

Here, we designed a strategy to label Tau at its C-terminus, using an approach mediated by the enzyme Sortase-A. We added a short peptide sequence (LPETGG) to the C terminus of full-length Tau, which enables Sortase-A to bind to the threonine (T), forming a thioester. Then, a histidine-tagged fluorophore (GGGH6C-Alexa647) is conjugated to Tau, with the terminal glycine replacing the thioester with an amide bond and cleaving off Sortase-A. We chose the fluorophore Alexa647 for its photostability and for its strong fluorescence emission in the far-red region of the visible spectrum, which prevents its excitation and emission spectra to overlap with those of Thioflavin T (ThT), a commonly used fluorophore for monitoring Tau aggregation. Results from circular dichroism (CD) spectroscopy and from monitoring ThT fluorescence revealed that these Alexa647-labeled Tau monomers have similar secondary structures to native Tau and that the presence of the fluorophore exhibits minimal effect on aggregation kinetics. Characterization of the morphology of Tau fibrils by transmission electron microscopy (TEM) and atomic force microscopy in a liquid cell revealed no difference between fibrils from native (wildtype) Tau and the C-terminally-labelled Tau introduced here.

This approach provides an effective way to prepare fluorescently labeled Tau protein while minimizing possible effects on its aggregation kinetics and fibril morphology. Since site-specific labeling by Sortase-A can also be carried out inside living cells, the resulting Alexa647-labeled Tau protein may be useful for studying Tau aggregation *in vivo* and for carrying out single-molecule fluorescence microscopy studies.



Transmission electron microscopy images of amyloid fibrils formed by native and Alexa647-labelled Tau protein. Sortase-mediated C-terminal labeling of Tau does not affect the overall morphology of amyloid fibrils.



Fluorescence microscopy images of amyloid oligomers, protofibrils and fibrils formed by native and labelled Tau protein. Left: Native Tau protein labeled with thioflavin T (ThT) in solution. Right: Alexa647-labeled Tau protein without ThT in solution.

Received: November 6, 2023

L. Bryan, S. Awasthi, Y. Li, P. N. Nirmalraj, S. Balog, J. Yang, M. Mayer, *ACS Omega* **2022**, *7*, 47009. https://doi.org/10.1021/acsomega.2c06139.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2024.61 Chimia 78 (2024) 61

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Harvesting at Night or During the Day – What is the Impact on the Sauvignon Blanc's Varietal and Aroma Profiles?

Pascal Fuchsmann*, Thierry Wins, Ágnes DienesNagy, Stefan Bieri, and Andreas Bühlmann

*Correspondence: P. Fuchsmann, E-mail: pascal.fuchsmann@agroscope.admin.ch
Agroscope, Schwarzenburgstrasse 161, CH-3003 Bern

Keywords: Aroma compounds · Day versus night harvest · Gas chromatography · Sauvignon Blanc · Wine

Grape harvesting at night is often used as a marketing argument. It gives it a romantic edge. But what about the advantages of these methods on aroma generation in wine production?

One of the main reasons for harvesting at night is to preserve the quality of the grapes and thus increase the quality of the resulting wine. Harvesting at night allows the grapes to be picked at a lower temperature than during the day. What about the impact of temperature on the grapes? Uncontrolled fermentation by microorganisms naturally present on the grapes can lead to lower quality wines. Higher temperatures additionally lead to chemical changes and in particular oxidation of aroma compounds and their precursors, and the risk of the production of off-flavours due to spontaneous microbiological processes in defective grapes.

A comparative study carried out in collaboration between Agroscope and the Weinbauzentrum in Wädenswil (Switzerland) was carried out with Sauvignon Blanc grapes harvested on the shores of the Lake of Zürich (Switzerland). The aim of the project was to demonstrate the impact of harvest time (day or night) on Sauvignon Blanc quality. The night harvest was carried out between 00h00 and 06h00 in the morning. The daytime harvest took place between 06h00 and 13h00.

The thiol analysis shows that the 3-mercaptohexanol (3MH) and 4-mercapto-4-methylpentan-2-one (4MMP) thiols typical of Sauvignon Blanc are in greater concentration in the wines obtained after night-time harvesting. These results indicate that the precursors of these compounds are generally better preserved with night harvests. Additionally, the analysis of the volatile compounds showed significant differences between the two harvests. C6-volatile compounds and esters showed the greatest differences.

Numerous external parameters influence aroma formation in the juice prior to fermentation, and subsequently in the resulting wine. Of course, the yeasts selected for fermentation make a major contribution to the final aroma. Apart from economic and ecological reasons, the negative impact of too high a temperature at harvest is an important factor in the formation of aromatic precursors in grape juices. This study also raises new questions. Would night harvesting also have a positive effect on other grape varieties? Does night harvesting in a hot climate or a temperate climate show the same results? Does natural light during harvest also have an impact?

Received: December 19, 2023

Fig. 1. Night harvesting of Sauvignon Blanc grapes on the shores of Lake of Zurich (K. Mackie-Haas, Agroscope).

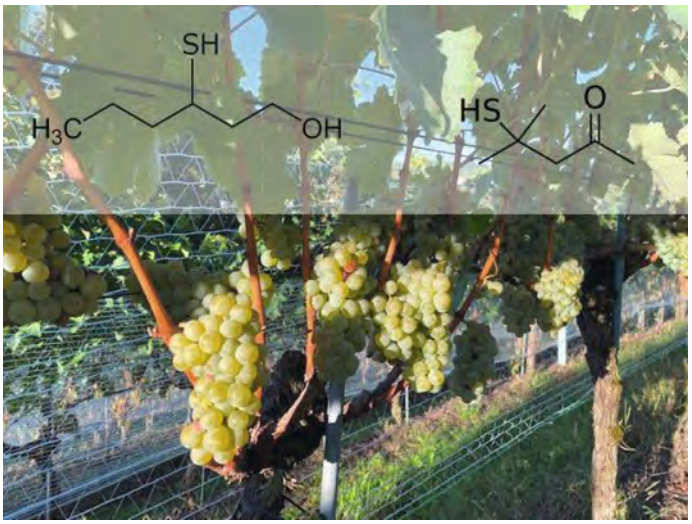
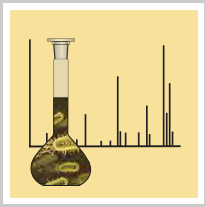


Fig. 2. 3-mercaptohexanol and 4-mercapto-4-methylpentan-2-one in Sauvignon Blanc grapes (K. Mackie-Haas, Agroscope).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2024.164 Chimia 78 (2024) 164



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Reducing Endotoxin Contamination in Biopharmaceuticals for Happier Biotechnologist?

Anika Hoffmann, Kevin Pacios, and Franka Kalman*

*Correspondence: Prof. Dr. F. Kalman, E-mail: franka.kalman@hevs.ch, HES-SO Valais-Wallis, University of Applied Sciences, Institute of Life Technologies, CH-1950 Sion

Keywords: Cultivation conditions · Dry cell weight · Endotoxins · Escherichia coli

Bacterial bioreactors are frequently used in the biopharmaceutical industry. About 30% of approved therapeutic proteins are produced in *Escherichia coli* strains and include products such as human insulin or antibodies, *e.g.* Ranibizumab marketed as Lucentis® by Genentech. *E. coli* is a Gram-negative bacterium. Hence, it has endotoxin molecules integrated in its outer membrane. During cell growth, lysis, and environmental adaptation processes, these molecules are released into the culture media. Therefore, endotoxins are widespread contaminations in antibodies, bioplastics, or plasmid DNA produced by bacterial cultivations. They are very potent fever-inducing immunostimulants that can cause organ failure at pg mL^{-1} concentrations when inside the human blood stream. Consequently, products such as injectables or biomaterials for medical applications need to undergo very costly, time-consuming, and tedious downstream processing.

Could the endotoxin contamination of the product be minimized by changing cultivation conditions, thus leading to lower manufacturing costs and increased product safety? To answer this question one needs a method to measure their concentration in a simple and economic way.

The Kdo-DMB-LC assay allows endotoxin quantification in challenging bioreactor matrices in a straightforward way. The sugar acid 3-deoxy-D-manno-2-ulosonic acid (Kdo) is used as an endotoxin marker. Released under mild acid hydrolytic conditions, Kdo is derivatized with the fluorophore 1,2-diamino-4,5-methylenedioxybenzene (DMB), and separated by HPLC from matrix compounds. The endotoxin concentration was analysed in lab- and pilot-scale bioreactors of *E. coli* K12 cultivated under different conditions: one using glucose as the carbon source and the other using a carbon source mix of glucose and arabinose. A comparison of the ratio between the endotoxin concentration in the cell culture media and the dry cell weight of samples at different cultivation times showed that less biomass was produced with the mixed carbon source and more endotoxin was released by the bacteria. Bacteria that grow on their preferred food, *i.e.* in glucose medium, have less adaptation pressure and release less endotoxins.

Our results show that changing bioreactor cultivation conditions can change the endotoxin contamination levels to deal with during downstream processing. Material costs and time expenses can be lowered in the future. **Or: Happy bacteria lead to happy biotechnologists.**

Received: January 20, 2024

Fig. 1. Lab scale bioreactor with an *Escherichia coli* K12 culture. This bacterial strain is used to produce injectables such as antibiotics that need to be endotoxin-free.

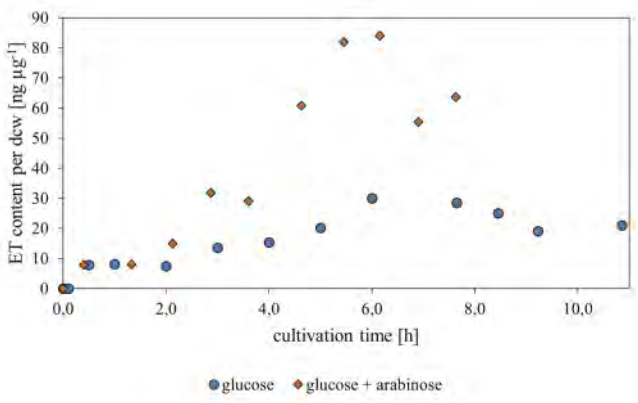


Fig.2. Ratio of released endotoxin amount [ng] per bacterial biomass [µg] for *E. coli* K12 grown on different carbon sources as glucose (blue dots) and glucose / arabinose (orange diamonds).

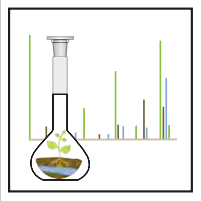
Reference

A. Hoffmann, K. Pacios, R. Mühlemann, R. Daumke, B. Frank, F. Kalman, *J. Chromatogr. B* **2023** *1228*, 123839, https://doi.org/10.1016/j.jchromb.2023.123839.

Can you show us your analytical highlight?

Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2024.263 Chimia 78 (2024) 263



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

An Innovative Approach for Analyzing Phytotoxins as Micropollutants in the Environment

Xiaomeng Liang*[a,b], Thomas D. Bucheli[c], Jan H. Christensen[a], and Nikoline Juul Nielsen[a]

*Correspondence: Dr. X. Liang, E-mail: x.liang@lbl.gov
[a]Department of Plant and Environmental Sciences, University of Copenhagen, DK-1871 Frederiksberg C, Denmark; [b]Lawrence Berkeley National Laboratory, Biological Systems and Engineering, Berkeley, CA, USA, [c]Environmental Analytics, Agroscope, Reckenholzstrasse 191, CH-8046 Zürich.

Keywords: Alkaloid · Flavonoid · Lupin · Micropollutant · Phytotoxin · Source supported suspect screening

Phytotoxins (PTs) are bioactive compounds originating from plants. Typically, they are small molecules (<1000 Da) acting as secondary metabolites to support plant growth and development. When released into the environment, PTs are recognized as a new category of environmental micropollutants and can lead to adverse effects when the exposure levels exceed the tolerance thresholds for humans and animals.[1] To date, only a small number of PTs have been investigated in terrestrial and aquatic environments. Consequently, our understanding of their environmental occurrence, transport, fate, and eco-toxicological risk remains limited.

Detecting and monitoring PTs in terrestrial and aquatic environments is challenging. This is due to their structural diversity, spatial variability influenced by *e.g.* vegetation and land use, and fluctuating loads tied to seasonal and climatic factors. The lack of reference standards and informational databases further complicates their qualitative and quantitative analysis.

To tackle the challenge, we suggest *Source Supported Suspect Screening* (4S), a liquid chromatography-mass spectrometry based analytical strategy in combination with knowledge on plant secondary metabolites to detect and identify specific source-related chemicals. The 4S approach enables fingerprinting analysis of PTs along their temporal and spatial trajectories, from plant origin to environmental occurrence and fate in soil and water. Demonstrated in a five-month crop field experiment in Switzerland with blue lupin (*Lupinus angustifolius* L) (Fig. 1), the 4S approach successfully enabled the detection of 41 flavonoids and 12 alkaloids in agricultural soil, drainage water or surface water, linking them to the lupin plant (Fig. 2).[2] The study also revealed that the occurrence and abundance of PTs in terrestrial soil and aquatic environments can be influenced by both the stage of plant growth and weather conditions. The successful application of the 4S approach in the lupin field study suggests a great potential for using source-supported strategies in investigations of PTs in aquatic and terrestrial environments.

The 4S approach can be an efficient and reliable strategy for analyzing PTs in plant, soil and water, elucidating their occurrence from downstream environments back to the plant's origin.

Fig. 1. Photo of the lupin plant. Lupins are a popular European legume crop. The seeds are rich in protein content, making them a promising substitute for soybeans. However, the plant produces alkaloids and flavonoids which can become toxic when exceeding certain thresholds. © Agroscope, Gabriela Brändle

Received: February 26, 2024

[1] T. D. Bucheli, *Env. Sci. Technol.* **2014**, *48*, (22), 13027, https://doi.org/10.1021/es504342w.
[2] X. Liang, J. H. Christensen, T. D. Bucheli, N. J. Nielsen, *Env. Sci. Technol.* **2023**, *57* (6), 2333, https://doi.org/10.1021/acs.est.2c05387.

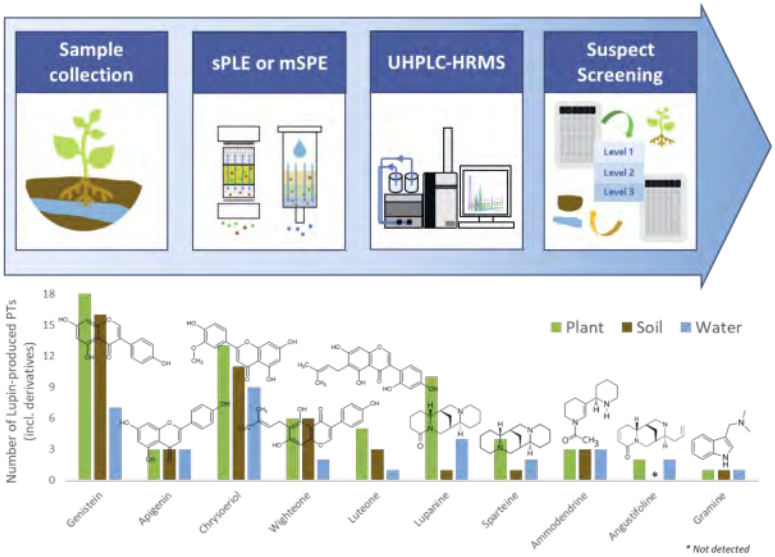
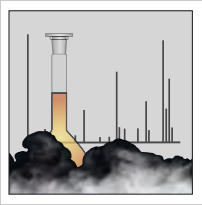


Fig. 2. Illustration of using 4S strategy to identify lupin-produced phytotoxins (PTs; flavonoids and alkaloids) in the downstream terrestrial and aquatic environments. sPLE, selective pressurized liquid extraction; mSPE, multi-layer solid phase extraction; UHPLC, ultrahigh-performance liquid chromatography; HRMS, high resolution mass spectrometry.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2024.351 Chimia 78 (2024) 351



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Towards Elimination of Aircraft Soot Emissions

Georgios A. Kelesidis*[a,b], Amogh Nagarkar[a], Una Trivanovic[a], and Sotiris E. Pratsinis*[a]

*Correspondence: Dr. G. A. Kelesidis, E-mail: georgios.kelesidis@rutgers.edu
[a]Particle Technology Laboratory, Institute of Energy and Process Engineering, Department of Mechanical and Process Engineering, ETH Zürich, Sonneggstrasse 3, CH-8092 Zürich; [b]Nanoscience and Advanced Material Center, Environmental and Occupational Health Science Institute, School of Public Health, Rutgers University, Frelinghuysen 170, 08854 Piscataway, NJ, USA

Keywords: Aviation · Jet fuel combustion · Oxidation · Soot emissions

About a million tons of carbonaceous (soot) nanoparticles are released every year by aviation through incomplete combustion of jet fuel. Such nanoparticles are rather toxic affecting the health of airport employees and nearby communities. Furthermore, aircraft soot emissions contribute to global warming mainly through the formation of contrail cirrus clouds that make up more than half of the total climate impact from aviation. Climate models have revealed that a 90 % reduction of soot emissions can halve the climate effect as a result of contrail cirrus clouds.

Such a reduction can be attained through judicious injection of air downstream of aircraft combustors. In fact, the design of quite a few of these combustors are based on the rich-quench-lean (RQL) concept where swirling and cross-flow jets of air are used in the primary (rich) zone of the combustor to burn the fuel and generate the required energy for aviation resulting in high concentrations of soot (Fig. 1). This is followed by a lean zone where additional air is injected to oxidize that soot. However, only a fraction of it is removed in current RQL combustors. This is attributed to the inhomogeneity of oxygen concentration and high temperature particle residence time (HTPRT) there. As a result, some soot survives oxidation and escapes into the atmosphere.

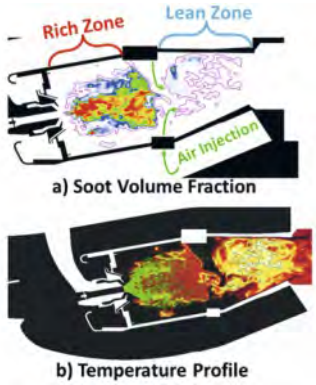


Fig. 1. Cross-sections of an RQL aircraft combustor along with the soot volume fraction (a) and temperature (b) profiles obtained during jet fuel combustion (adapted from Mueller & Pitsch, ref. [1]).

Here, an enclosed unit for spray combustion of jet fuel following the RQL concept is used that emulates soot emissions from aviation. The elimination of such emissions is explored by systematic swirl-injection of O_2-containing N_2 through 12 jets using a torus ring. This unit has been designed by computational fluid dynamics (CFD) to optimize the mixing between particles and gases and closely control the HTPRT. It has been shown that increasing the O_2 concentration to 20 vol % in its dilution zone of this unit enhances soot oxidation, cutting the emitted concentration of soot by about 90% and its mass by 98% (Fig. 2).

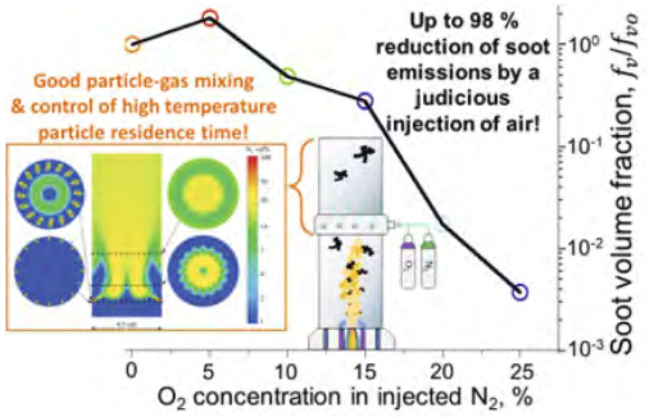


Fig. 2. Reducing soot emissions by swirl-injection of O_2-containing N_2 downstream of an enclosed unit for spray combustion of jet fuel (inset) that has been designed for optimal mixing between particles and gases, as well as the HTPRT (orange-framed inset; adapted from Teleki *et al.*, [2]). The emitted soot volume fraction, f_v, is measured at the exhaust of the unit as a function of O_2 concentration in the injected gas and normalized with the f_{vo} obtained at 0 vol % O_2 (solid line & symbols; adapted from Kelesidis *et al.*, [3]).

Thus, a clever control of the HTPRT and particle-gas mixing is essential for judicious injection of air in the dilution zone of RQL aircraft combustors to reduce drastically their soot emissions and minimize their impact on health and climate.

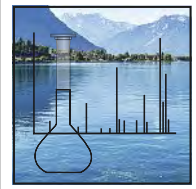
Received: March 07, 2024

References

[1] M. E. Mueller, H. Pitsch, *Phys. Fluids* **2013**, *25*, 110812, https://doi.org/10.1063/1.4819347.
[2] A. Teleki, B. Buesser, M. C. Heine, F. Krumeich, M. K. Akhtar, S. E. Pratsinis, *Ind. Eng. Chem. Res.* **2009**, *48*, 85, https://doi.org/10.1021/ie800226d.
[3] G. A. Kelesidis, A. Nagarkar, U. Trivanovic, S. E. Pratsinis, *Environ. Sci. Technol.* **2023**, *57*, 10276, https://doi.org/10.1021/acs.est.3c01048.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2024.445 Chimia 78 (2024) 445



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Improving the Sensitivity of pH Glass Electrodes Towards Ultrasensitive Environmental Monitoring

Robin Nussbaum and Eric Bakker*

*Correspondence: Prof. Dr. E. Bakker, E-mail: eric.bakker@unige.ch
University of Geneva, Department of Inorganic and Analytical Chemistry, CH-1211 Geneva 4

Keywords: Capacitive readout · Ion-selective electrodes · Natural waters · pH glass electrode · Voltage follower

pH measurements are routinely performed with the well-known glass electrode, which is regarded as the gold standard. Its output is accepted as the practical pH value, traceable across laboratories, when combined with a reference electrode containing 3M KCl in contact with the sample through a liquid junction. Unfortunately, the potentiometric readings suffer from limited measurement reproducibility, making it difficult to use in applications that require very high precision. One example is anthropogenic oceanic acidification owing to increasing atmospheric carbon dioxide levels. The resulting pH change is estimated to –1.7 mpH per year and may have important adverse consequences if not properly monitored.

Fig. 1. Submersible probe platform developed by our group at the University of Geneva. Photo Credit: Eric Bakker.

Our group previously reported an increased sensitivity and reproducibility using constant potential coulometric readout with polymeric membrane-based pH electrodes.[1] In this protocol, the cell potential is kept constant and a capacitor (C in Fig. 2) is placed in series of the pH electrode. The sample pH is then compared to that of a reference solution. Because the cell potential is fixed, any potential change at the pH electrode induces an opposite potential change over the capacitor and consequently a transient current is observed. The latter is integrated to obtain the charge, which is used as the analytical signal. Unfortunately, however, as the current needs to flow through the pH electrode, it was impossible to use glass electrodes owing to their high impedance of tens of MΩ.

This problem has now been overcome.[2] We recently reported on a novel electronic circuit that uses a high-impedance input voltage follower (VF in Fig. 2) that separates the capacitive current entirely from the electrochemical cell. Thus, even glass electrodes can now be used in this configuration for enhanced sensitivity. The work resulted in an attractive measurement reproducibility of just 64 µpH for steps of 10 mpH units. pH determination was also achieved over the entire pH range, which was not previously possible. We now aim to implement this principle in a submersible probe to achieve *in situ* ultrasensitive pH sensing in natural waters. This increased precision may also be correlated with *in situ* trace metal detection developed in our group and could provide new insights on metal speciation. **This novel experimental setup is appropriate for high precision pH sensing with a glass electrode, but may be applied to any other ion-selective electrode for enhanced sensitivity.**

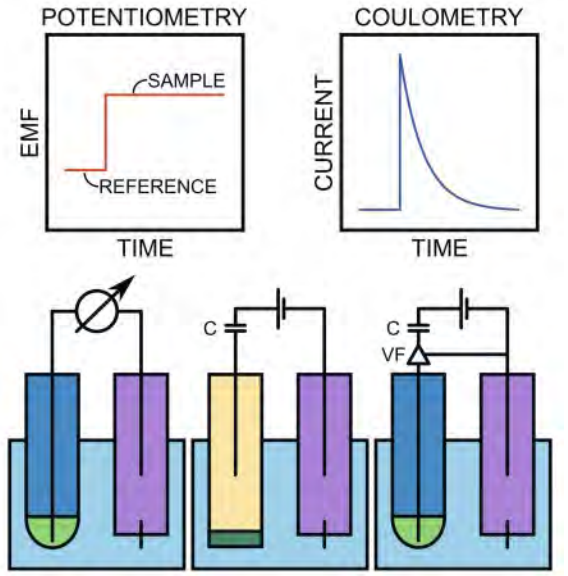


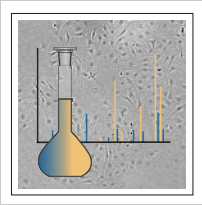
Fig. 2. Increasing the sensitivity of pH glass electrodes by constant potential coulometry. Left: Traditional potentiometric setup. The potential between the two electrodes is recorded over time, making very small potential steps difficult to distinguish from background drift. Center: Original experimental setup for coulometric readout with membrane-based pH electrodes. The cell potential is held constant, forcing a capacitive element to charge. This allows one to record current spikes that are easier to identify than potential changes, resulting in increased sensitivity. Unfortunately, a transient current must pass through the measurement cell. Right: Novel arrangement using a voltage follower, achieving constant potential coulometry without passing any current through the cell. Highly resistive membranes such as the pH glass electrode can now be used in this mode for the first time.

Received: April 23, 2024

[1] P. Kraikaew, S. Jeanneret, Y. Soda, T. Cherubini, E. Bakker, *ACS Sens.* **2020**, *5*, 650, https://doi.org/10.1021/acssensors.0c00031.
[2] R. Nussbaum, S. Jeanneret, E. Bakker, *Anal. Chem.* **2024**, *96*, 6436, https://doi.org/10.1021/acs.analchem.4c00592.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2024.558 Chimia 78 (2024) 558



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Exploring Zebrafish Embryonic Cell Line PAC2 by Proteomics Profiling

Mihai-Ovidiu Degeratu[a,b], René Schönenberger[a], Nikolai Huwa[a], and Ksenia Groh[a]*

*Correspondence: Dr. K. Groh, E-mail: ksenia.groh@eawag.ch
[a]Eawag, Swiss Federal Institute of Aquatic Science and Technology, Überlandstrasse 133, CH-8600 Dübendorf; [b]ETH Zurich, Department of Environmental Systems Science, Universitätstrasse 16, CH-8092 Zurich

Keywords: Animal testing alternative · Bottom-up global proteomics · Cell line-based models · Cell morphology markers · Fish toxicity · Zebrafish

Over 350'000 synthetic chemicals are currently used in commerce and this number continues to increase. As many chemicals end up contaminating the aquatic environment, concerns over their effects on the organisms living in water are growing as well. Fish toxicity tests provide crucial data for chemical risk assessments, which in turn are necessary to guide environmental protection efforts. However, these tests sacrifice millions of fish and require ample resources, raising both the ethical and cost-related concerns.

Alternative methods, such as fish-derived permanent cell lines, represent promising animal-free toxicity test models, but their properties need to be better understood to enable broader uptake in research and regulation. For this, molecular profiling could allow insights into both the general characteristics and the functional capacity of these cell lines.

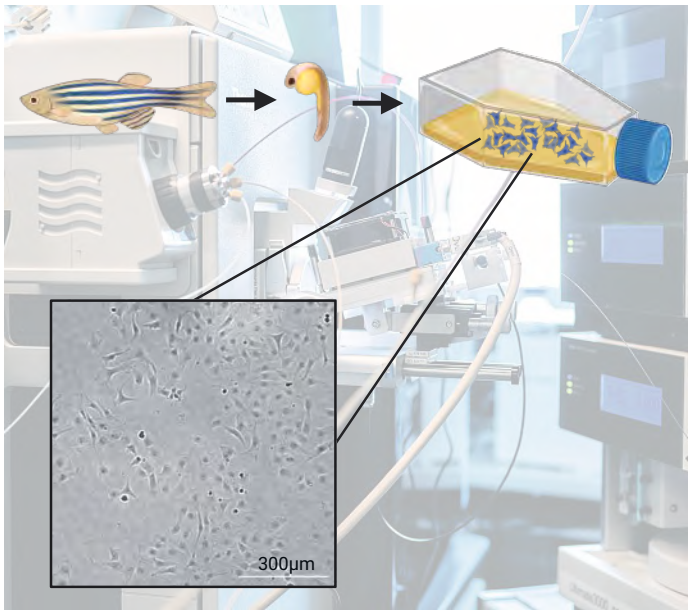


Fig. 1. Permanent fish cell line PAC2 was derived from early embryos of zebrafish (*Danio rerio*) in the 1990s and originally classified as fibroblast-like. Phase contrast image shows recent culture of PAC2 cells from our lab, displaying heterogeneous appearance and notable presence of cells with epithelial-like morphology.

Here, we focused on the PAC2 cell line derived from early embryos of zebrafish (*Danio rerio*). PAC2 was originally classified as 'fibroblast-like' based on cell morphology, but currently, PAC2 cultures in ours and others' laboratories exhibit a heterogeneous appearance with pronounced epithelial-like features instead. Therefore, we set out to validate the initial classification by examining the presence of protein markers characteristic of different cellular origins. For this, we relied on a mass spectrometry-based bottom-up global proteomics approach, an analytical method that not only overcomes the absence of specific antibodies for some of the fish proteins, but also enables simultaneous detection and quantification of multiple proteins without prior knowledge.

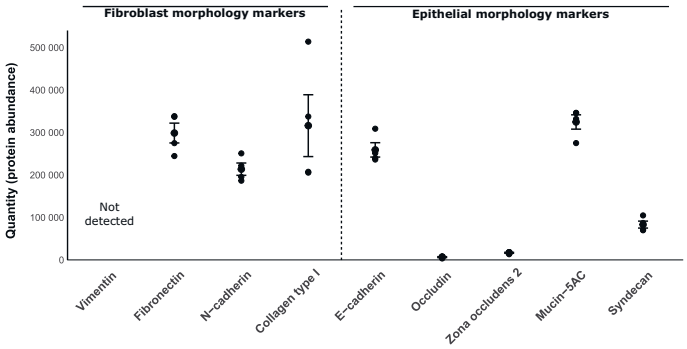


Fig. 2. Protein markers associated with fibroblast and epithelial morphology, measured in actively growing PAC2 cells by bottom-up global proteomics, acquired with nanoLC-MS/MS on Orbitrap Fusion™ Lumos™ Tribrid™ mass spectrometer in data-independent acquisition (DIA) mode. Each dot represents a biological replicate.

Among the *ca.* 7000 proteins covered by our method, we could observe fibronectin, N-cadherin, and collagen type I, known as fibroblast-associated proteins, but not the most specific fibroblast marker, vimentin. We also detected multiple proteins related to epithelial-like morphology, including E-cadherin, syndecan, mucin-5AC, and tight junction proteins, occludin and zona occludens 2. Our evidence thus suggests that PAC2 cell line harbors mixed cell populations, which questions its official classification as 'fibroblast' only. **This work demonstrates the power of mass spectrometry-based global proteomics analysis for studying non-mammalian cell models.**

Acknowledgement

This research is funded by the Swiss National Science Foundation through National Research Programme 79 'Advancing 3R – Animals, research and society', project number 407940_206439, 'Expanding the fish invitrome towards a modular, socio-technical framework for animal-free prediction of chemical toxicity to fish'.

Received: May 22, 2024

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2024.615 Chimia 78 (2024) 615

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Microdroplet Arrays for High-Throughput Analysis and Biochemical Assays

Maximilian Breitfeld, Claudius L. Dietsche, Friederike-L. Born, and Petra S. Dittrich*

*Correspondence: Prof. Dr. P. S. Dittrich, E-mail: petra.dittrich@bsse.ethz.ch
ETH Zürich, Department of Biosystems Science and Engineering, Schanzenstrasse 44, CH-4056 Basel

Keywords: Droplet microfluidics · Drug testing · High-throughput analysis · Microdroplet arrays

Students and technicians working in a biochemical, pharmaceutical, or biology-oriented lab know very well the tedious procedure of filling multi-well plates (*e.g.* with 96 or 384 wells) for biochemical analyses or for cell assays. Repeating the same pipetting steps again and again is laborious, boring and produces often experimental mistakes. For large numbers of experiments, robotic systems are replacing humans to fill the wells faster, more precise and in a systematic way. For very high throughput, it is still time-demanding as well as compound- and resource-consuming.

We developed microdroplet arrays as an efficient alternative, enabling automated sample handling and miniaturisation of sample volumes in the sub-nanolitre range.[1] Moreover, the number of experiments that can be done on a single platform can be massively increased. Fig. 1 shows such a glass platform which can hold up to 7'200 droplets. Upscaling is straightforward – we already fabricated plates for up to 100'000 droplets. The key is the surface of the glass which is hydrophilic where the aqueous sample droplets will be placed, and hydrophobic everywhere else. The hydrophilic areas are comparable to the wells on a multi-well plate; however, no walls surround the droplets. Instead, they are covered by an oil to prevent evaporation. We use these microdroplet arrays for a variety of biochemical assays and long-term studies with cells, where we monitor the droplets by brightfield or fluorescence microscopy. We also use mass spectrometry to assess the content (usually, matrix-assisted laser desorption/ionization (MALDI) mass spectrometry).

The ultra-high throughput is essential in many applications such as single-cell analysis or testing a large library of compounds. For example, aiming at antibiotic drug testing, bacteria growth is monitored while the cells are exposed to several compounds in varying concentrations. We can perform experimental series with a single compound but also combinations of two or more compounds in a systematic way within a single experiment. The effect of the compounds (*e.g.* bacteriostatic or bactericidal) can be derived within hours as well as the minimal inhibitory concentration (MIC). **Further automation and integration of data analysis is currently on the way to increase the number of compounds that can be tested and make use of the full potential of a 100'000-well plate, which drastically reduces time and consumables for high throughput analysis.**

Received: July 10, 2024

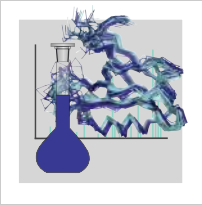
Reference

[1] R. Strutt, B. Xiong, V. F. Abegg, P. S. Dittrich, *Lab Chip* **2024**, *24*, 1064, https://doi.org/10.1039/D3LC01024D.

Fig. 1. Photograph of a microdroplet array next to a 96-well plate. The glass plate carries picoliter droplets in high density (inset). When used in an experiment, these droplets are covered by oil to prevent evaporation. The platform is used to test the effect of antibiotic compounds on bacteria (data left side), achieved by assessing viability and morphology of the cells.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2024.685 Chimia 78 (2024) 685



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Probing the Dynamic Nature of Protein Allostery *via* NMR

Henry Wetton, Olivia Gampp, and Roland Riek*

*Correspondence: Prof. R. Riek, E-mail: roland.riek@phys.chem.ethz.ch
Institute of Molecular Physical Science, Vladimir-Prelog-Weg 2, CH-8093 Zurich

Keywords: Allostery · Dynamics · NMR · Protein · Structural biology

Since the cooperative interaction between haemoglobin and oxygen was first described over 60 years ago, protein allostery – two ligands binding to a protein at different sites influencing each other's binding affinities – has fascinated structural biologists due to its potential in understanding enzyme regulation, elucidating biological mechanisms, and developing new therapeutics.

Studies of allosteric systems began using only static X-ray crystal structures and have now progressed to simulated trajectories of atomic motion to provide insights into changes in structural dynamics. Thanks to developments in NMR methods, it is also possible to analyse protein motion directly using experimental data in the proteins' native environment.

Fig. 1. Two-state structure of the PDZ2 domain of the protein human tyrosine phosphatase 1E, determined using eNOE NMR spectroscopy (PDB ID 7QCX). State A is shown in cyan and state B in blue. Each state is represented by 20 conformers, highlighting the quality of the data (root mean square deviation).

Many NMR techniques used for allostery studies are based on differences in spectra upon addition of a known allosteric ligand to a protein. Others use specific pulse programs to capture structural changes on a long timescale. Our eNOE (exact Nuclear Overhauser Effect) technique takes a different approach by building on the standard NOESY method of protein structure determination by NMR and significantly increasing the number and precision of distance restraints extracted from the primary data. This allows structure calculation of multiple states from a single set of measurements, thus enabling experimental investigation of allostery at an atomic level. For example, applying this method to the PDZ2 domain of human tyrosine phosphatase 1E in a recent study yielded detailed insights into its allosteric regulation mechanism upon binding of a peptide ligand.

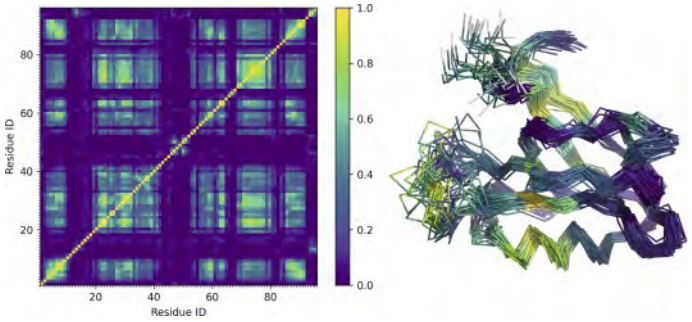


Fig. 2. **Left**: Inter-residue correlation values obtained from distance-based PDBCor analysis of multi-state PDZ2, representing the allosteric network. **Right**: Average correlation between each residue and its neighbours projected onto the 7QCX protein structure using the same colour scheme.

An additional challenge is the detection of correlated motion or allosteric networks given an ensemble of protein structures. Many approaches originate in the molecular dynamics field and require 3D superposition of each available structure prior to analysis. Our software package PDBCor provides an alternative approach to this problem by using information theory to identify correlation based purely on dihedral angles or intra-structural distances in a bundle of protein conformers.[1]

In conclusion, NMR spectroscopy is an ideal method for the experimental investigation of protein allostery at atomic resolution due to its dynamic nature and the development of specifically tailored methods.

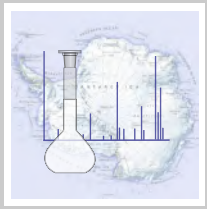
Received: August 8, 2024

Reference

[1] O. Gampp, H. Kadavath, R. Riek, *Curr. Opin. Struct. Biol.* **2024**, *86*, 102792, https://doi.org/10.1016/j.sbi.2024.102792.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2024.782 Chimia 78 (2024) 782



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Greenhouse Gas Measurements in Ice Cores: A Novel Instrument Shifts Borders in Analytical Precision and Resolution

Florian Krauss*[a], Daniel Baggenstos[a,b], Lars Mächler[a], Jochen Schmitt[a], Béla Tuzson[c], Lukas Emmenegger[c], and Hubertus Fischer[a]

*Correspondence: Dr. F. Krauss, E-mail: florian.krauss@unibe.ch
[a]Climate and Environmental Physics, Physics Institute and Oeschger Centre for Climate Research, University of Bern, CH-3012 Bern; [b]Australian Antarctic Division, Kingston TAS 7050, Australia; [c]Laboratory for Air Pollution / Environmental Technology, Empa - Swiss Federal Laboratory for Materials Science and Technology, CH-8600 Dübendorf

Keywords: Beyond EPICA · Greenhouse gases · Ice cores · Laser spectroscopy · Mid-Pleistocene transition · Sublimation extraction

Polar ice sheets serve as the sole direct archive providing information on past fluctuations in atmospheric greenhouse gas concentration by preserving ancient air in bubbles. This unique climate archive extends our understanding of Earth's climate and atmosphere far into the past, with the longest existing, continuous records dating back 800 ka (*kilo annum*).

A new European Commission-funded deep-drilling project in Antarctica, called Beyond EPICA (European Project for Ice Coring in Antarctica) – Oldest Ice Core (BE-OIC), is underway to retrieve a continuous ice core that covers the Mid-Pleistocene Transition (MPT) period from ~1,200 to 800 ka ago. Marine sediment records reveal that the MPT marks a transition in the length and ice volume of ice ages, from glacial cycles with a cyclicity of 40 ka before, to 100 ka after the MPT. The mechanisms driving the transition are not clear and present a major unsolved problem in the field of paleoclimatology. Changing greenhouse gas forcing is at the heart of most hypotheses put forward to explain the MPT and, thus, precise and accurate ice core gas records are essential to resolve this riddle. However, the MPT ice core record will be contained in highly thinned ice at the bottom of the ice sheet, asking for new measurement techniques with higher resolution and precision, and requiring minimal sample volume.

To address this need, a coupled Laser Induced Sublimation Extraction – Quantum Cascade Laser Absorption Spectrometer (LISE-QCLAS) was developed by our laboratories. This allows us to extract and analyse the greenhouse gas composition on ice core air samples of only 1–2 mL, corresponding to 10–15 g of ice or *ca.* 1.5 cm in vertical resolution. The small sample size accounts for a temporal resolution of only a few hundred years in 1.5 Ma old ice. The air is liberated by sublimating the ice under vacuum through irradiation with a near-infrared laser, while avoiding melting by controlled water vapor trapping within the extraction vessel.[1] The QCLAS instrument is based on mid-infrared direct absorption spectroscopy. The dual-laser concept allows us to simultaneously quantify the CO_2 concentration and its stable carbon isotopic ratio ($\delta^{13}C\text{-}CO_2$) as well as CH_4 and N_2O concentrations with precisions of 0.4 ppm in CO_2, 3 ppb in CH_4, 1 ppb in N_2O and 0.04‰ in $\delta^{13}C\text{-}CO_2$.[2]

With the development of the LISE-QCLAS system, we can now perform continuous multispecies greenhouse gas reconstructions from smallest ice core samples with very high precision.

Received: August 31, 2024

[1] L. Mächler, D. Baggenstos, F. Krauss, J. Schmitt, B. Bereiter, R. Walther, C. Reinhard, B. Tuzson, L. Emmenegger, H. Fischer, *Atmos. Meas. Tech.* **2023**, *16*, 355, https://doi.org/10.5194/amt-16-355-2023.
[2] B. Bereiter, B. Tuzson, P. Scheidegger, A. Kupferschmid, H. Looser, L. Mächler, D. Baggenstos, J. Schmitt, H. Fischer, L. Emmenegger, *Atmos. Meas. Tech.* **2020**, *13*, 6391, https://doi.org/10.5194/amt-13-6391-2020.

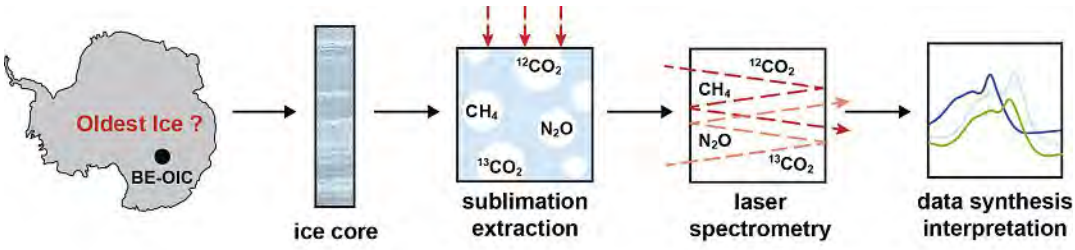


Fig. 1. Schematic illustration, how to decipher past climate and greenhouse gas variations. The air bubbles captured in ice core samples from Antarctica are released through the sublimation extraction step using Laser Induced Sublimation Extraction (LISE). The quantification of greenhouse gases of the air follows, using a dual-Quantum Cascade Laser Absorption Spectrometer (QCLAS). The obtained data are used for synthesis and interpretation.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2025.95 Chimia 79 (2025) 95–96

Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Modular Development of Plasma-Source Ultra-High-Resolution Mass Spectrometry with Constitutional Isotopic Information

Vasily Grebennikov[a,b], Adrian Wichser[b], Jana Wolf[b,c], and Davide Bleiner[b,d]*

*Correspondence: PD Dr. habil. D. Bleiner, E-Mail: davide.bleiner@uzh.ch
[a]ETH Zürich, Department of Chemistry and Applied Life Sciences, Vladimir-Prelog-Weg 1-5/10, CH-8093 Zürich, Switzerland; [b]Swiss Federal Laboratories for Materials Science and Technology (Empa), Überlandstrasse 129, CH-8600 Dübendorf, Switzerland; [c]ETH Zürich, Department of Materials, Vladimir-Prelog-Weg 5, CH-8093 Zürich, Switzerland; [d]University of Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland.

Keywords: Booster · CAMS · FAIMS · Mass spectrometry · Orbitrap

High-field asymmetric-waveform ion mobility spectrometry (FAIMS) allows for the separation of molecules based on their ion mobility in an electrical field with an asymmetric waveform.[1] FAIMS allows for the differentiation of constitutional isotopes, often linear and cyclic compounds, which would usually be non-differentiable with just a mass spectrometer. FAIMS is typically coupled to electrospray ionisation (ESI) sources. A drawback of ESI is its limited range of ionisable molecules, often needing a functional group to allow for the ion detection in the mass analyser. This leaves a plethora of molecules such as apolar molecules or those without a functional group to be invisible during analysis. The coupling of a liquid sampling atmospheric pressure glow discharge (LS-APGD) would allow for such molecules to be analysed.[2] Coupling APGD with FAIMS could unlock new analytical possibilities which are not yet available. By integrating this instrument further with an absorption-mode FT 'booster system', which includes an FPGA module for real-time data display and processing, the analysis achieves ultra-high resolution. The spectrum is then generated by the Spectroswiss software peak by peak (Fig. 1).[4–5]

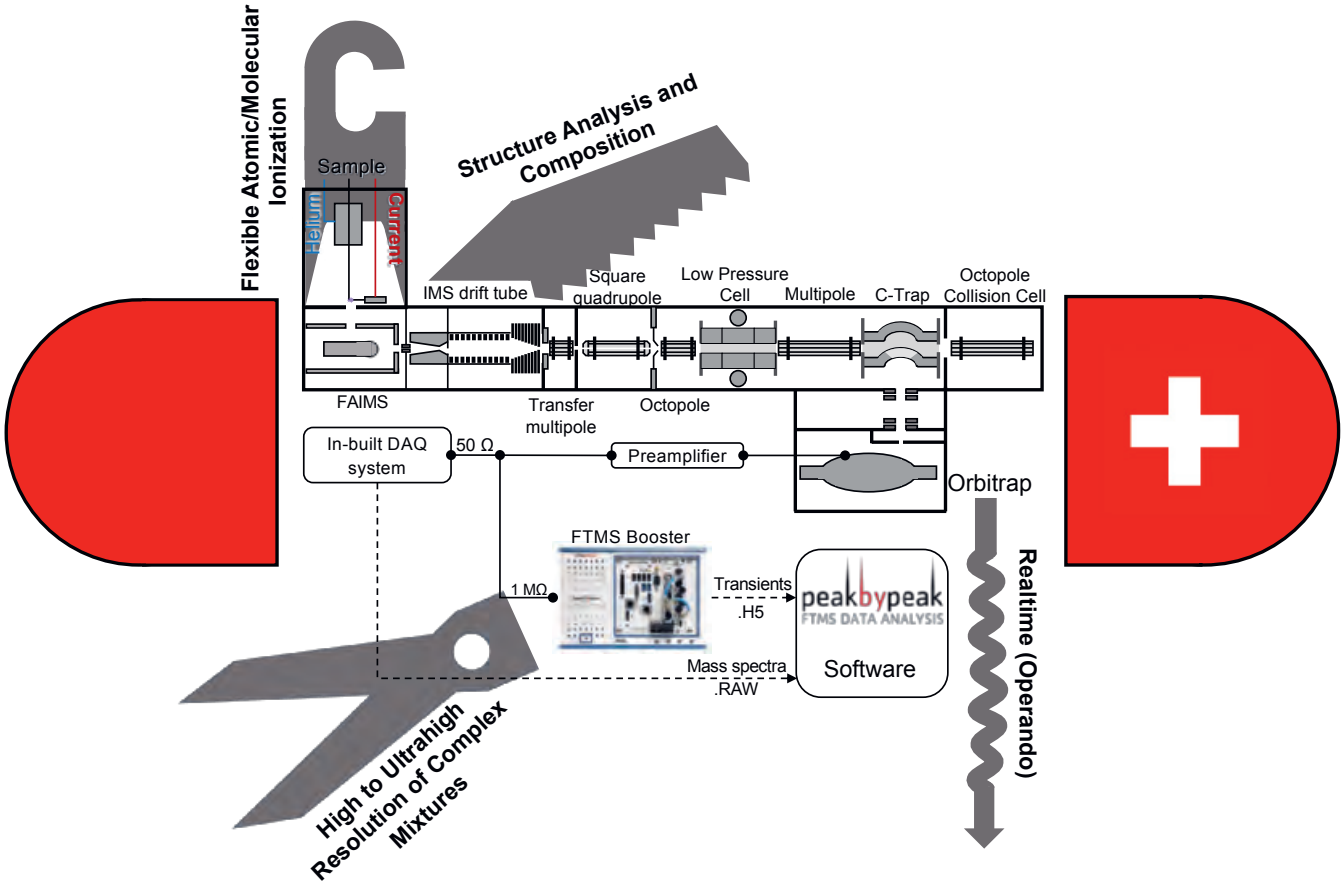


Fig. 1. The desired experimental setup described in this paper. The experiments were conducted with ESI and CAMS without the FAIMS coupled to the system. Each tool represents an important component of the mass spectrometer. The instrument would consist of an APGD, FAIMS, orbitrap and FTMS booster system. Some parts of the figure have been adapted from D. Bleiner *et al.* and A. A. Shvartsburg *et al.* refs. [3,4].

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

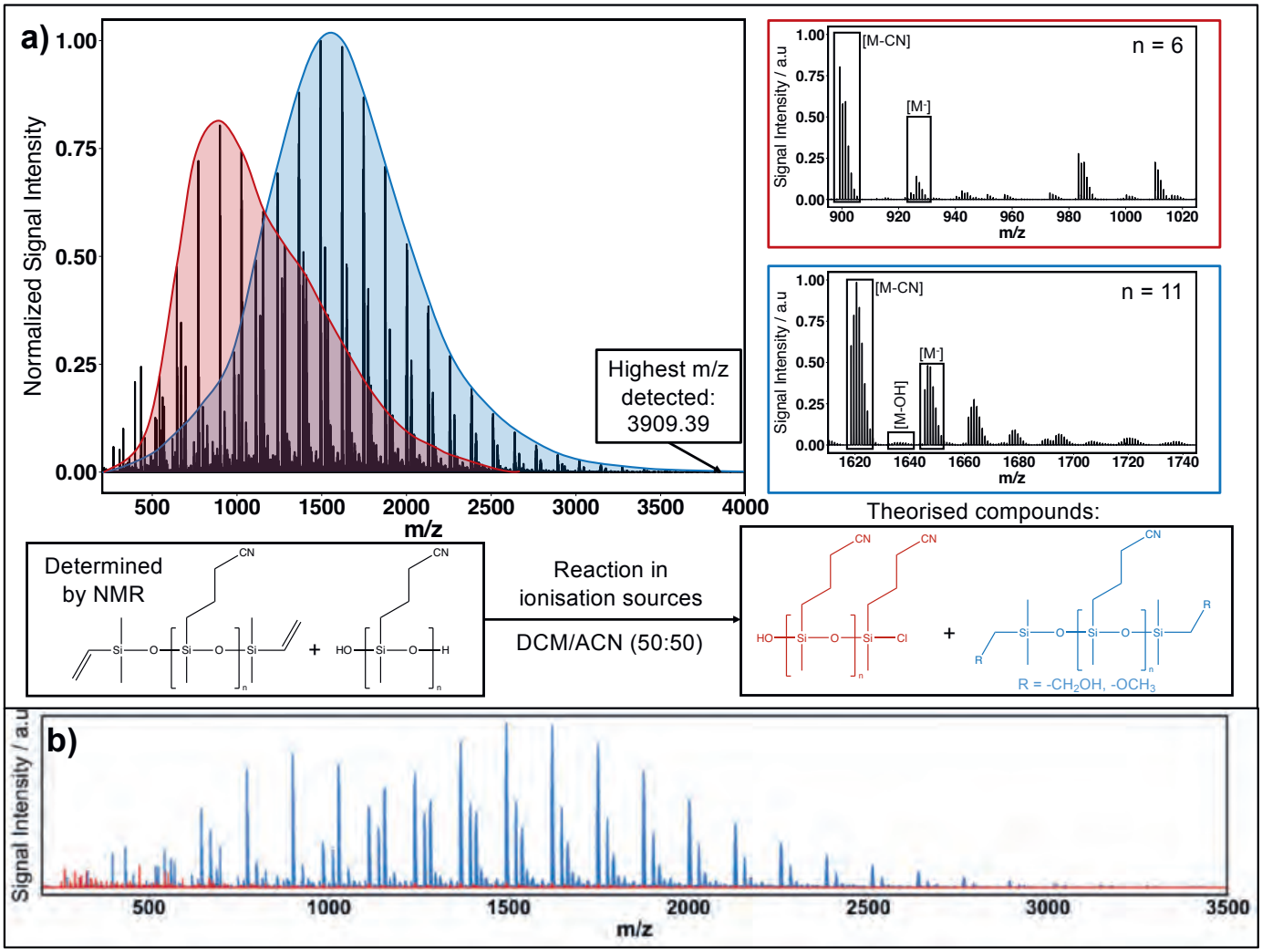


Fig. 2. a) The obtained mass spectrum of the polymer depicted on the bottom left with the theorised compounds that are created during ionisation. The colours correspond to the spectra created by these products. The two spectra on the top right correspond to the highest intensity of the blue and red mass distribution with the corresponding fragments. The red product could either be a reaction from the starting polymer with the hydroxyl end groups or could be a product of a ring opening reaction of the cyclic byproducts of the polymerisation; b) A comparison of the signal intensity between LS-APGD (blue) and ESI (red) as an ionisation source.

To demonstrate the system's applicability, a polymer with two potential end groups was chosen for its complex analysis and ability to form linear and cyclic compounds during polymerisation (Fig. 2).

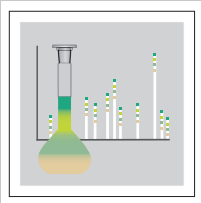
APGD offers a much more complex and detailed mass spectrum due to more species being ionised and detected compared to ESI. ESI furthermore also shows more background due to the lower intensity of the detected species. By coupling FAIMS with APGD the differentiation between cyclic and linear polymers would be simplified and the product created by the ionisation source would be allowed to be analysed more easily. The booster could enhance the contrast for poorly resolved peaks and allow for isotope pattern analysis.

By achieving such high flexibility and utility in the fashion of a 'Swiss army knife', each module synergises with the other to compensate for what it is lacking, making the analysis of complex mixtures possible.

Received: December 18, 2024

[1] A. A. Shvartsburg, 'Differential Ion Mobility Spectrometry: Nonlinear Ion Transport and Fundamentals of FAIMS', **2008**, (1st ed.). CRC Press.
[2] R. Kenneth Marcus, E. D. Hoegg, K. A. Hall, T. J. Williams, D. W. Koppenaal, *Mass Spectrom. Rev.* **2021**, *42*, 652, https://doi.org/10.1002/mas.21720.
[3] K. Tang, F. Li, A. A. Shvartsburg, E. F. Strittmatter, R. D. Smith, *Anal. Chem.* **2005**, *77*, 6381, https://doi.org/10.1021/ac050871x.
[4] C. Masucci, K. O. Nagornov, A. N. Kozhinov, K. Kraft, Y. O. Tsybin, D. Bleiner, *Anal. Bioanal. Chem.* **2024**, *416*, 5133, https://doi.org/10.1007/s00216-024-05450-2.
[5] K. O. Nagornov, M. Zennegg, A. N. Kozhinov, Y. O. Tsybin, D. Bleiner, *JASMS*, **2020**, *31*, 257, https://doi.org/10.1021/jasms.9b00032.

doi:10.2533/chimia.2025.271 Chimia 79 (2025) 271–271



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Inkjet Printing: The Future of Disposable Electrochemical Sensors?

Fabian Weyand[a,b], Andreas Lesch[c], and Jing Wang*[a,b]

*Correspondence: Prof. Dr. J. Wang, E-mail: jing.wang@ifu.baug.ethz.ch
[a]ETH Zürich, Institute of Environmental Engineering, CH-8093 Zürich; [b]Empa, Laboratory for Nano Particles, CH-8600 Dübendorf; [c]University of Bologna, Department of Industrial Chemistry, 40129 Bologna, Italy.

Keywords: Biomolecules · Disposable sensors · Electrochemical detection · Graphene · Inkjet printing · Sensitivity modulation

The global demand for disposable, portable, and miniaturized electrochemical sensors has driven printing-based manufacturing techniques for decades. The potential for low unit costs on a large-scale has been a key driver behind some of the most successful innovations in point-of-care sensor technology, such as the electrochemical sensing of blood glucose. However, other potential fields, such as in-field bacterial detection or roadside drug testing, are still underexplored. While screen printing has been the standard technique for years, modern analytical challenges require high-performance, scarce, and expensive sensing materials (*e.g.* Au, Pt, graphene). This makes screen printing less sustainable due to high material consumption and limited flexibility in pattern design and material choice.

Therefore, digital and mask-less deposition techniques, such as drop-on-demand inkjet printing (IJP), are increasingly replacing traditional mask-based methods. Picolitre-sized droplets (*e.g.* of graphene-based inks) are jetted on-demand at kHz frequencies by piezoelectric actuation of individually addressable nozzles. Combined with precise positioners, high accuracy is achieved, with optimally zero material waste in a reasonably short time. Subsequent thermal processing removes ink solvents and stabilizers, creating conductive electrodes. However, establishing defined printing and heating protocols is challenging to ensure consistent sensor performance and low sensor-to-sensor variation.

Careful optimization of our printing parameters and post-print heating protocols enabled the large-scale fabrication of graphene-based electrodes with controllable and switchable analyte sensitivity. Analytical performance was tested for key antioxidants (*e.g.* uric acid), bacterial infection markers (*e.g.* resazurin) and cannabinol-sensitive redox indicators. By applying defined heating protocols in vacuum and air the same sensor can reversibly switch between a quantitative global signal and qualitative compound identification using the same measurement technique. Combined with superior sensitivity and selectivity over leading-edge carbon-based electrodes, such as glassy carbon, IJP sensors are likely to dominate future single-use applications in electroanalysis.

The optimization of inkjet printing and post-processing enables cost-effective production of high-performance electrochemical sensors with seamless scalability from prototypes to industrial manufacturing.

Received: February 13, 2025

F. Weyand, S. Gianvittorio, F. Longo, J. Wang, A. Lesch, *Electrochim. Acta* **2025**, submitted.

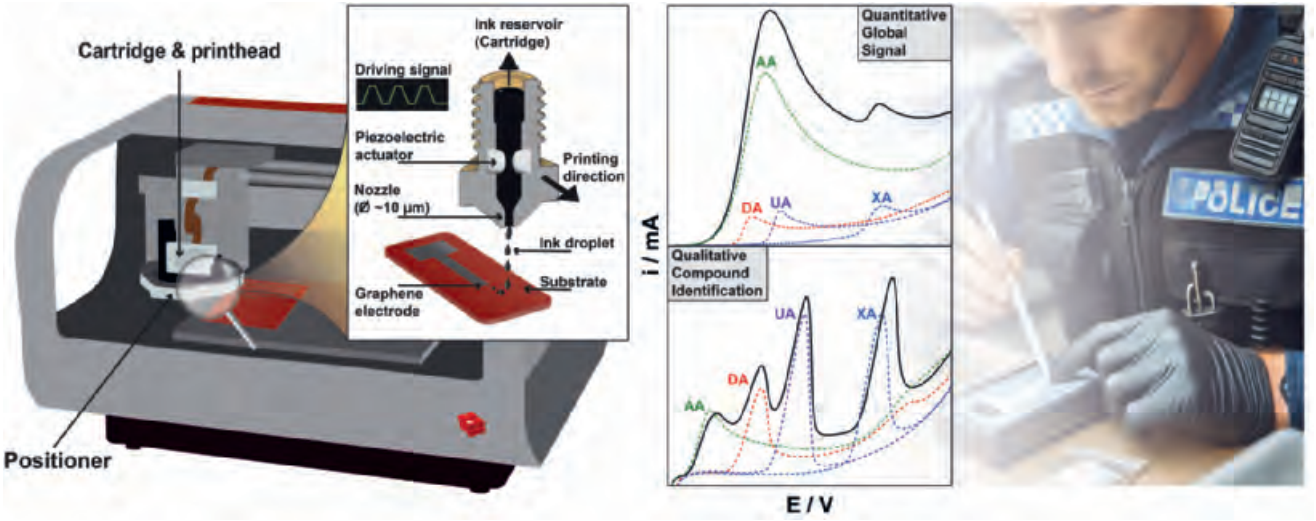
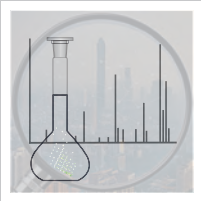


Fig. 1. Schematic illustration of a lab-based inkjet printer showing cartridge, printhead and positioner (left). The magnified inset illustrates the printing process to fabricate high-performance and low-cost graphene electrodes. Defined post-print heating protocols allow reversible switching between a quantitative global signal (*e.g.* for antioxidant potential) and qualitative compound identification using linear sweep voltammetry (center). This provides a versatile tool to advance the use of IJP electrodes in new electroanalytic fields, such as roadside drug testing (right). (UA: uric acid, AA: ascorbic acid, DA: dopamine, XA: xanthine).

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2025.363 Chimia 79 (2025) 363



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Tracing Aerosol Sources *via* Measurements and Data Mining

Kaspar R. Daellenbach* and Lubna Dada

*Correspondence: Dr. K. R. Daellenbach, E-mail: kaspar.daellenbach@psi.ch
PSI Center for Energy and Environmental Sciences, Paul Scherrer Institute, CH-5232 Villigen

Keywords: Air pollution · Air quality · Mass spectrometry · Megacity · Source apportionment

Every breath we take contains countless aerosol particles – some more harmful than others, depending on their origin and processing through the atmosphere. To support efforts in mitigating pollution, particles are traced back to their emission sources, a process akin to searching for the invisible within a sea of invisibles.

But how is this done? One approach involves collecting particles and analyzing their chemical and molecular composition using advanced mass spectrometers (Fig. 1). These instruments generate spectra – unique 'fingerprints' that reveal particles' molecular information. Due to atmospheric complexity, air samples contain diverse particles that evolve chemically over time. Data mining techniques are used to identify patterns in their temporal behaviour and spectral composition, refining the separation of the different sources. By further comparing atmospheric measurements to controlled laboratory experiments, specific emission sources within a collected air sample are determined.

Fig. 1. Combining detailed molecular and chemical composition measurements with data mining techniques allows for source and process identification of air pollutants. (Image generated from https://firefly.adobe.com/, last access 10.02.2025).

In our study, we measured aerosol molecular composition in central Beijing using a mass spectrometer over several months including the COVID lockdown period, capturing seasonal variability and periods of reduced urban activity. Results show that in winter, organic aerosols from solid-fuel emissions dominate, both from local sources and long-range transport from the Beijing-Tianjin-Hebei Plain and mountainous areas west of the city. In summer, atmospherically formed so-called 'secondary' organic aerosols from aromatic emissions – likely originating from the Xi'an-Shanghai-Beijing corridor – become the main contributors. While biogenic secondary organic aerosols appear in small amounts, our methods can still detect them. We confirmed source identification by comparing spectra with chamber experiments, revealing interactions between biogenic and anthropogenic emissions (Fig. 2). Beijing is one example of many where severe pollution affects a large population. Our transferable approaches have been, and currently are being applied there to support efforts in improving air quality. **A comprehensive identification and quantification of aerosol particle sources requires the integration of long-term measurements, chamber experiments, and data mining techniques.**

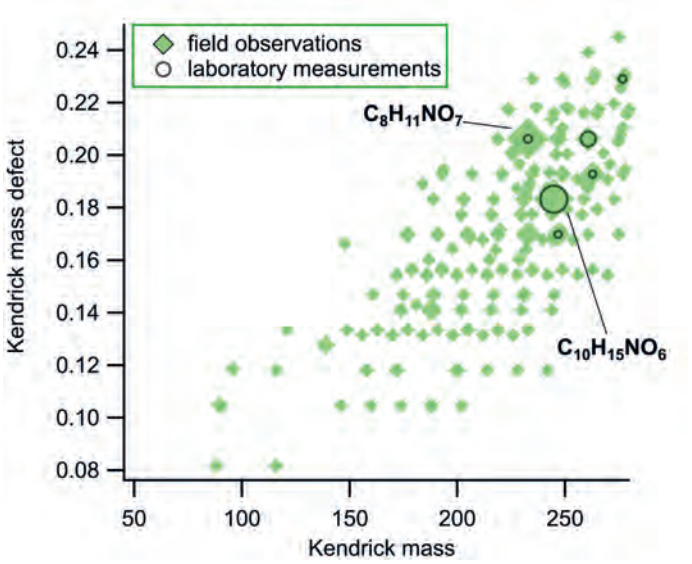
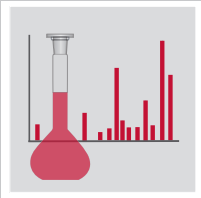


Fig. 2. Comparison of the nighttime biogenic secondary aerosol mass spectrum from Beijing measurements with those from chamber experiments simulating biogenic-anthropogenic interactions (limonene and nitrogen oxides). Marker sizes represent the relative abundance of each molecule. Figure adapted from ref. [1].

[1] K. R. Daellenbach, J. Cai, S. Hakala, L. Dada, C. Yan, W. Du, L. Yao, F. Zheng, J. Ma, F. Ungeheuer, A. L. Vogel, D. Stolzenburg, Y. Hao, Y. Liu, F. Bianchi, G. Uzu, J.-L. Jaffrezo, D. R. Worsnop, N. M. Donahue, M. Kulmala, *Nat. Geosci.* **2024**, *17*, 747, https://doi.org/10.1038/s41561-024-01493-3.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2025.454 Chimia 79 (2025) 454



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

The Quest for Novel Cancer Biomarkers and Drug Targets in the Alternative Splicing Landscape

Abdullah Kahraman*[a,b]

*Correspondence: Prof. A. Kahraman, E-mail: abdullah.kahraman@fhnw.ch
[a]FHNW, School of Life Sciences, Institute of Chemistry and Bioanalytics, Hofackerstrasse 30, CH-4132 Muttenz; [b]Swiss Institute of Bioinformatics, CH-1015 Lausanne

Keywords: Bio/Chemoinformatics · Complex diseases · Isoforms · Machine learning · mRNA · Omics

Alternative splicing is a fundamental cellular process that enhances the functional diversity of genes. Under normal conditions, most genes predominantly express a canonical mRNA molecule upon activation. However, in complex diseases such as cancer and Alzheimer's, disruptions in the splicing machinery can lead to the overproduction of alternative isoforms with distinct biological functions. Understanding and mapping these changes provides critical insights into disease mechanisms and serves as a valuable resource for identifying novel biomarkers and therapeutic targets (Fig. 1).

Despite its significance, the role of alternative splicing in complex diseases remains understudied. To comprehensively identify and functionally assess disease-associated splicing alterations, a multidisciplinary approach is required. In our lab, we integrate bioinformatics, machine learning, sequencing, structural and systems biology with molecular pathology to unravel the full complexity of isoform changes in cancer and other diseases.

As an example, in our latest study, we leveraged a cutting-edge single-cell long-read sequencing technology to analyze the alternative splicing landscape in clear-cell renal cell carcinoma (ccRCC), the most prevalent subtype of kidney cancer. Our analysis identified over 30,000 previously uncharacterized mRNA transcripts, many of which were cell-type specific and associated with genes that drive ccRCC progression. More than half of these novel transcripts had the potential to encode functional proteins.

An interesting discovery was a previously unknown transcript of the NNMT gene. The NNMT gene is known to be part of ccRCC-related pathways. Our newly discovered isoform lacks the substrate-binding site, suggesting a loss of enzymatic activity. We were able to validate the novel mRNA sequence of NNMT using PCR. This finding underscores the importance of looking beyond DNA mutations in current standards of molecular diagnostics, as our samples revealed no functional loss at the DNA level. Functional disruptions of NNMT were only observed at the alternative splicing level. **Our research highlights the transformative potential of splicing-based diagnostics and therapeutics, which will pave the way for new strategies to combat cancer and other complex diseases at their molecular basis.**

Received: March 21, 2025

[1] T. Karakulak, H. A. Bolck, N. Zajac, A. Bratus-Neuenschwander, Q. Zhang, W. Qi, T. Carrasco Oltra, H. Rehrauer, C. von Mering, H. Moch, A. Kahraman, *Genome Res.* **2025**, *35*, 698, https://doi.org/10.1101/gr.279345.124.
[2] T. Karakulak, H. Moch, C. von Mering, A. Kahraman, *Frontiers Mol. Biosci.* **2021**, 8, 726902, https://doi.org/10.3389/fmolb.2021.726902.

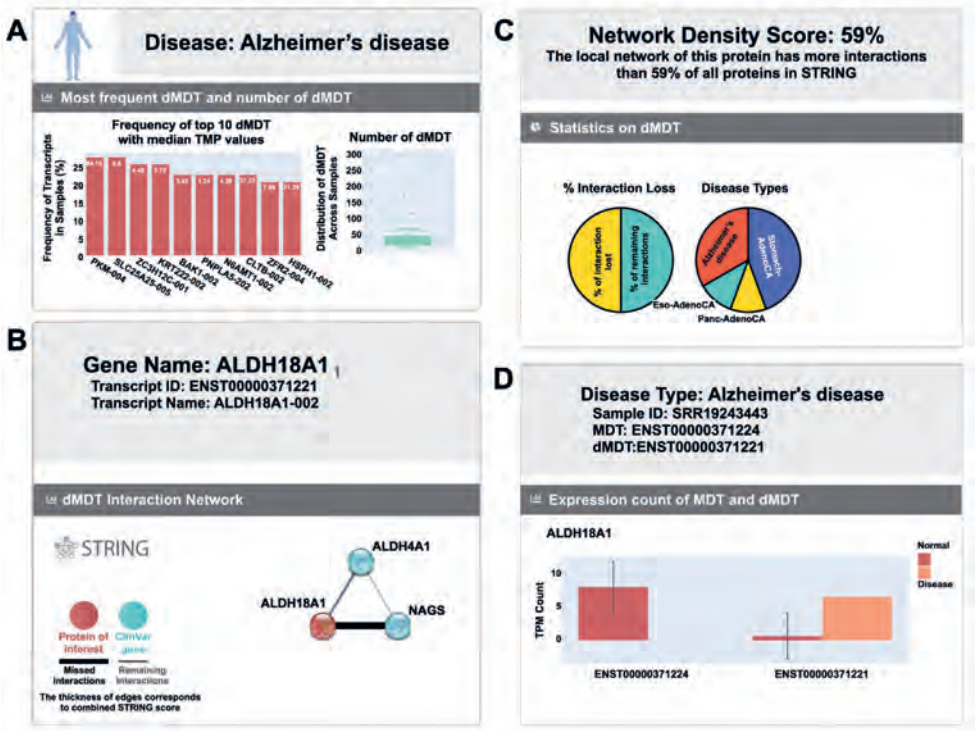
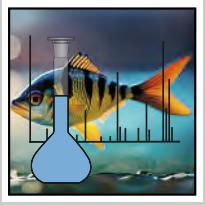


Fig. 1. Overview of functionalities of our disease-specific isoform database www.caniso.net. The database provides users with various statistics to support the functional interpretation of disease-specific mRNA transcripts (dMDT). (A) *Disease page*: frequency of top 10 dMDT, most frequently observed in Alzheimer's Disease. (B) *Isoform page*: visualization of interaction losses due to the disease-specific protein isoform of the gene ALDH18A1, which is known to be mutated in neurodegenerative diseases. (C) *Network density score* and the percentage of interaction loss of the ALDH18A1 isoform. (D) *Sample page*: Median and sample-specific expression level of normal and disease-specific mRNA molecules.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2025.573 Chimia 79 (2025) 573



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Per- and Polyfluoroalkyl Substances in Swiss Fish – a Health Problem?

Fiorella Lucarini[a]* and Davide Staedler[b,c]

*Correspondence: Prof. Dr. F. Lucarini, E-mail: Fiorella.lucarini@hefr.ch
[a]School of Engineering and Architecture of Fribourg, Institute of Chemical Technology, HES-SO University of Applied Sciences and Arts of Western Switzerland, Boulevard de Pérolles 80, CH-1700 Fribourg; [b]TIBIO Suisse romande, Chemin de Bérée 4C, CH-1010 Lausanne; [c]Department of Biomedical Sciences, University of Lausanne, Rue du Bugnon 27, CH-1011 Lausanne

Keywords: Environmental pollutants · Fish fillet · LC-MS/MS · PFAS · QuEChERS

Per- and polyfluoroalkyl substances (PFAS) are anthropogenic chemicals widely utilized in various industrial and consumer products due to their exceptional water and oil repellent properties. Their persistence and bioaccumulation in the environment, particularly in aquatic ecosystems, have made PFAS global contaminants. Fish, due to their position in the food chain and direct exposure to aquatic contaminants, are vulnerable to PFAS accumulation, making them effective bioindicators of environmental contamination and potential sources of human exposure.

We recently investigated the presence and levels of PFAS in freshwater fish from Swiss lakes, addressing concerns about widespread environmental contamination and potential health risks associated with fish consumption (Fig. 1).

Fig. 1. PFAS analysed in 218 fish samples. Fish species analysed: *Coregonus wartmanni* (whitefish) (N = 20), *Cyprinus carpio* (common carp) (N = 11), *Oncorhynchus mykiss* (rainbow trout) (N = 11), *Perca fluviatilis* (perch) (N = 38), *Salmo trutta* (brown trout) (N = 131), and *Squalius cephalus* (common chub) (N = 7).

We analyzed 15 PFAS in 218 fish fillet samples from six species commonly found in Switzerland. An optimized QuEChERs (Quick, Easy, Cheap, Effective, Rugged, and Safe) extraction method was employed, followed by LC-MS/MS analysis. The results were compared to EU regulations (Commission Regulation (EU) 2022/2388) and EFSA guidelines for tolerable weekly intake (TWI) to evaluate potential risks to human health. The optimized QuEChERS method offered a simplified and cost-effective approach for extracting PFAS from complex matrices like fish tissues, reducing interferences and improving analyte recovery.

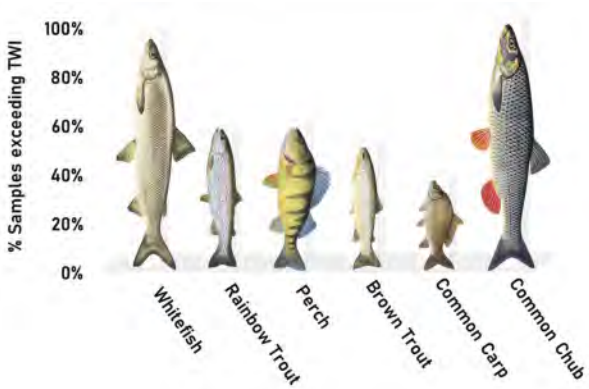


Fig. 2. Percentage of fish exceeding the TWI set by EFSA here calculated for a person of 70 kg body weight and an intake of 200 g of fish fillets.

The analysis revealed significant PFAS contamination across all species. Perch exhibited the highest levels of PFOS and PFHxS, with concentrations frequently exceeding EU safety limits. TWI calculations, based on a 70 kg person consuming 200 g of fish fillet per week, were exceeded in a significant percentage of fish (Fig. 2).

Analysis of 121 brown trout specimens revealed positive correlations between fish size and PFBS, PFDA, and PFHxS levels, suggesting bioaccumulation increases with age and size. In contrast, PFPeA – a short chain C5 PFAS – showed a negative correlation, likely reflecting the lower bioaccumulation potential and short half-life typical of short-chain PFAS in animals.

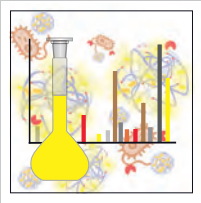
These findings highlight the need for ongoing monitoring, further research into PFAS sources and pathways, and stronger regulations to protect aquatic ecosystems and human health from PFAS exposure *via* fish consumption.

Received: May 23, 2025

[1] M. Soudani, L. Hegg, C. Rime, C. Coquoz, D. B. Grosjean, F. Danza, N. Solcà, F. Lucarini, D. Staedler, *Anal. Bioanal. Chem.* **2024**, *416*, 6377, https://doi.org/10.1007/s00216-024-05524-1.

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, Unterstrasse 58, CH-9000 St. Gallen
Tel.: +41 71 222 16 81, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2025.657 Chimia 79 (2025) 657



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Optical Point-of-Care Diagnostics Against Superbugs

Luciano F. Boesel[a]* and Giorgia Giovannini[a,b]*

*Correspondence: L. F. Boesel, E-mail: luciano.boesel@empa.ch; G. Giovannini, E-mail: giorgia.giovannini@marionegri.it
[a]Empa, Swiss Federal Laboratories for Materials Science and Technology, Laboratory for Biomimetic Membranes and Textiles, Lerchenfeldstrasse 5, CH-9014 St. Gallen; [b]Department of Biochemistry and Molecular Biology, Mario Negri Institute for Pharmacological Research IRCCS, Via Mario Negri 2, I-20156 Milano

Keywords: AMR · Bacterial infections · Diagnostic · Nanotechnology · Optical biosensors · Point-of-care devices

Antimicrobial resistance (AMR) is one of the most concerning health threats worldwide, with 4.95 million deaths reported in 2019. The spread of AMR is so rapid and challenging to handle that it is considered a 'silent pandemic'. Current diagnostic methods are based on time-consuming or expensive techniques. As a result, clinicians often prescribe broad-spectrum antibiotics, a practice that helps bacteria develop resistance mechanisms and is one of the main causes of AMR.

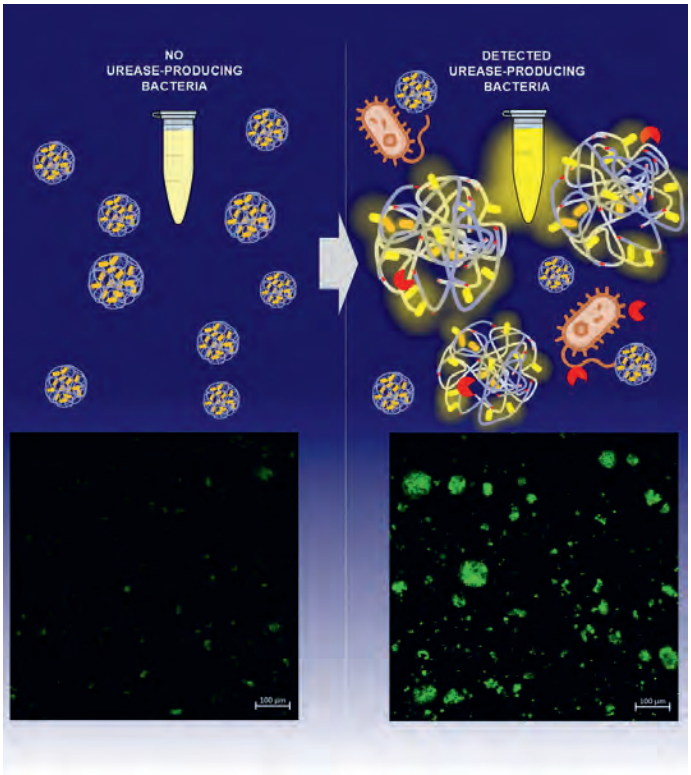


Fig. 1. Fluorescent particles enabling the selective detection of urease-producing bacteria. Confocal microscopy analysis confirmed the mechanism of detection: In the presence of urease-producing bacteria, the particle's matrix expanded, leading to an increase in the fluorescent signal, enabling the quantification of the bacteria in the sample.

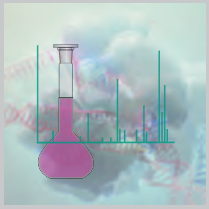
Our research focuses on developing optical sensors based on bioresponsive nanomaterials suitable for the rapid and sensitive diagnosis of bacterial infections. Our strategy is to synthesize nanomaterials that react selectively with specific biomarkers released by the bacteria, leading to a variation of optical signals easily detectable without the need for sophisticated instrumentations. Such systems are also designed to be cost-efficient, easy-to-use, and equipment-free, meeting the ASSURED criteria (*i.e.* Affordable, Sensitive and Selective, User-friendly, Rapid, Equipment-free, and Delivered). For example, in collaboration with Prof. Dr. W. Albrich and PD Dr. med. C. Kahlert from the Cantonal Hospital St. Gallen KSSG, we recently developed fluorescent particles for the selective detection of urease-producing bacteria such as *K. pneumoniae*, which is relevant for respiratory tract infections and ranked with high priority in the WHO's 2024 Bacterial Priority Pathogens List. To note, the particles enable the detection of 10^3 bacteria/mL in 5 hours, which were not detectable using a standard pH-based method. We are also developing wearable devices enabling self-monitoring by patients based on fluorescent or color changes, supporting rapid and accessible care.[1] These are intended to detect bacteria causing urinary tract infections (*i.e. E. faecalis*) and wound infections (*i.e. S. aureus*), among others. By reducing the delay in the diagnosis, these approaches will enable the prompt administration of the appropriate treatment, limiting the misuse of antibiotics, but also significantly improving patient outcomes. Furthermore, thanks to the cost-efficacy and portability, these methods will be suitable for the ambitious but necessary goal of globally tackling AMR, also in countries where access to medical care is limited. **Such responsive materials will pave the way for the next generation of diagnostics, combining sensitivity, specificity, and cost-efficacy.**

Received: July 4, 2025

[1] W. C. Albrich, C. R. Kahlert, S. Nigg, L. F. Boesel, G. Giovannini, *Anal. Chem.* **2024,** *96*, 20578, https://doi.org/10.1021/acs.analchem.4c05182.

Can you show us your analytical highlight?
Please contact: Dr. Bodo Hattendorf, ETH Zürich, E-mail: analytical_highlights@chimia.ch

doi:10.2533/chimia.2025.726 Chimia 79 (2025) 726



Highlights of Analytical Sciences in Switzerland

Division of Analytical Sciences

A Division of the Swiss Chemical Society

Beyond 3D Structures: New Ways to Study Biomolecular Gymnastics

Sonja Schmid*

*Correspondence: Prof. Dr. S. Schmid, E-mail: sonja.schmid@unibas.ch
Biomolecular Nano-Dynamics Lab, Department of Chemistry, University of Basel, Mattenstrasse 22, CH-4058 Basel; Swiss Nanoscience Institute, University of Basel, Klingelbergstrasse 82, CH-4056 Basel.

Keywords: Biomolecular dynamics · Conformational change · Energy landscape · Ensemble averaging · FRET · Nanopores · Single-molecule techniques

Traditionally, analytical chemistry has relied on measuring billions of molecules at once, to obtain one characteristic ensemble average. While this approach has underpinned the success of chemistry for centuries, it is naturally limited in its ability to resolve differences between individual molecules. Such differences exist in mixtures as well as in pure samples, *e.g.* if molecules undergo conformational changes or transient interactions (like those essential for biomolecular function). Just as the average posture of all players in the Euro 2025 football tournament fails to capture their individual movements, an ensemble average is similarly insufficient to fully characterize intrinsic molecular heterogeneity.

Therefore, in biophysical chemistry, a range of techniques were established that now enable the investigation of single molecules. For example, mixtures can be studied with the ultimate resolution of one single molecule, as in our work using label-free electrical nanopore recordings.[1] And fluorescence-based experiments can observe single proteins at work: how they undergo intra- and inter-molecular rearrangements to perform their biomolecular function.[2] The resulting single-molecule trajectories uniquely reveal the timing and sequence of distinct functional events (*e.g.* a conformational change), which is usually 'averaged out' and lost in ensemble experiments. This is because the latter rely on observing averaged equilibrium relaxation kinetics, while single-molecule trajectories can provide direct observations under all thermodynamic conditions, including the out-of-equilibrium steady-state of the biological cell, and also thermal equilibrium. Ultimately, these studies offer combined kinetic and thermodynamic descriptions of biomolecular mechanisms, including quantitative kinetic rate constants and free-energy landscapes (Fig. 1).

Recently, our group described a new Förster Resonance Energy Transfer (FRET) approach offering up to 100-fold more information per single molecule.[3,4] We achieved this advance with a trick we term *DyeCycling*, where we continuously replace the fluorescent markers to prevent them from bleaching, which would end the experiment. In this way, we can record the gymnastics of a single biomolecule for over an hour, offering unprecedented kinetic insight and data credibility.

While 3D structural models of biomolecules are readily available today, they lack temporal information to link protein structure and function. **Time-resolved single-molecule techniques, such as DyeCycling, bridge this gap by providing a better mechanistic understanding of biomolecular function, to stimulate progress in biomedicine and biotechnology.**

Received: September 2, 2025

[1] D. Fuentenebro Navas, J. A. Steens, C. de Lannoy, B. Noordijk, M. Pfeffer, D. de Ridder, R. H. J. Staals, S. Schmid, *ACS Nano* **2024,** *18*, 16505, https://doi.org/10.1021/acsnano.3c11769.
[2] T. Ha, J. Fei, S. Schmid, N. K. Lee, R. L. Gonzalez Jr., S. Paul, S. Yeou, *Nat. Rev. Methods Primers* **2024,** *4*, 21, https://doi.org/10.1038/s43586-024-00298-3.
[3] B. Vermeer, S. Schmid, *Nano Research* **2022,** *15*, 9818, https://doi.org/10.1007/s12274-022-4420-5.
[4] S. Ghosh, S. Schmid, *QRB Discovery* **2024,** *5*, e8, https://doi.org/10.1017/qrd.2024.11.

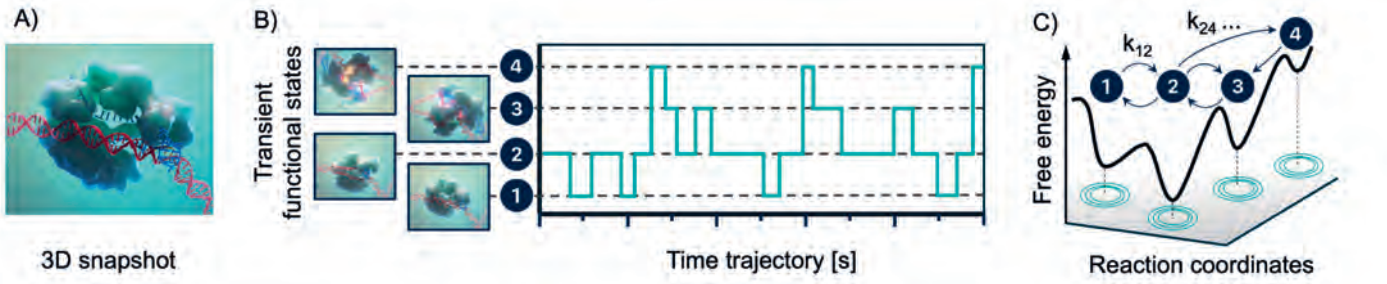


Fig. 1. Bio-macromolecules, such as proteins, DNA, RNA, are dynamic systems. (A) A three-dimensional (3D) structural snapshot represents one out of many functional states, *e.g.* conformational or interaction states adopted by the molecule in solution. (B) Time-resolved single-molecule techniques zoom in on one individual molecule and track these excursions into transient functional states in real time (here schematic states 1 to 4), revealing the timing and order of events. These data offer direct access to kinetics and thermodynamics that would be lost by ensemble averaging: (C) Schematic kinetic model (here 4 states, 6 rate constants k_{ij}) and the resulting free energy landscape. Structures in A and B) adapted from *BioInteractive*, HHMI, 4000 Jones Bridge Road, Chevy Chase, MD 20815.

Can you show us your analytical highlight?
Please contact: Dr. Bodo Hattendorf, ETH Zürich, HCI G105, Vladimir-Prelog-Weg 1, CH-8093 Zürich, Tel.: +41 44 632 44 72
E-mail: analytical_highlights@chimia.ch