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On the Gas-Phase Structure of Biomolecular Ions Produced by Native Electrospray Ionization

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Electrospray ionization (ESI) is capable of producing intact gas-phase ions from complex biomolecules, and using “native ESI”, even noncovalently bound complexes survive, which could mean that biomolecular ions produced by native ESI are still in their native form in the gas phase. However, structural information of biomolecular ions in the gas phase is difficult to obtain: many methods give either only global information (e.g., ion mobility spectroscopy), or have serious limitations in terms of molecular size (e.g., cryogenic ion spectroscopy). The question whether biomolecular ions produced by native ESI really assume a native-like structure in the gas phase thus has not yet been answered conclusively.

In this lecture, a new, synergistic approach will be presented, which utilizes ion mobility-mass spectrometry, Förster resonance energy transfer (FRET) of trapped gas-phase ions, and differential ion mobility spectrometry that employs microsolvation by an auxiliary gas, to provide multiple constraints for molecular modeling of gas-phase ion structures. We also developed a novel transition metal FRET method [1] for measuring relatively short distances, 10-40 Å, between a donor dye and a noncovalently bound Cu²⁺ ion serving as a quencher, by measuring fluorescence lifetimes.

Multiple systems are being studied in our laboratory with some or all of the methods mentioned above, including Ala-rich α -helical polypeptides [1, 2], amyloidogenic peptides [3], peptides containing β hairpins, and so-called “stapled” peptides [4], cyclic peptides with -S-S- bonds; both of the latter fix the gas-phase conformation to some degree. The influence of the length of the molecular linker between the peptide scaffold and the dye moiety is also subject of ongoing investigations. In some cases, seemingly contradictory results were obtained that highlight the problem of relying on only a single method for deriving gas-phase structures. These apparent contradictions could be rationalized by an extensive search of the conformational space of the simulated structural ensemble [2], which identified those that satisfied all the experimentally determined constraints as the most probable structures.

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Development, Characterization and Field Assessment of a Submersible Dual-Readout Electrochemical pH Sensor for In Situ Environmental Monitoring

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Up to one-third of the anthropogenic atmospheric carbon dioxide dissolves into the oceans, disrupting the chemical equilibria in seawater [1]. This process is often referred to as ocean acidification (-0.002 pH y^{-1}) and is particularly pronounced in estuarine areas due to elevated organic matter concentration [1]. As pH controls many biogeochemical processes in aquatic environments, accurate monitoring is crucial for a better comprehension of environmental systems [1]. Routine pH measurements are typically performed using zero-current potentiometry with glass electrodes. Their phase-boundary potential, measured against a reference electrode, relates to the sample pH following the Nernst equation. This intrinsic property results in a limited sensitivity that is insufficient for precise environmental pH monitoring. Additionally, changes in ionic strength can introduce significant accuracy errors due to residual liquid-junction potential at the reference electrode.

Our group tackled the sensitivity limitation by developing an alternative readout named *constant potential coulometry* [2]. During this protocol, a high impedance input voltage follower and capacitor are implemented in the electronic readout and the cell potential is kept constant. Thus, any potential change at the glass electrode induces an opposite one on the capacitor and a transient current arises. The latter is then integrated to obtain the charge, resulting in an increased sensitivity compared to potentiometry. This method is successfully applied for pH sensing with benchtop instruments in narrow pH ranges comparable to environmental samples with a precision up to 64 μpH . Notably, the system retains the ability to perform conventional potentiometric measurements, allowing direct comparison between the two readouts. The inaccuracies caused by liquid-junction potential variations can be minimized using open-junction designs as previously reported [3].

This work presents the integration of the coulometric readout and open-junction principle into a submersible probe developed for *in situ* measurements in natural waters, along with the results from the first field deployment in April 2025 in the Krka estuary, Croatia. This stratified environment was selected for its stable pH in the bottom seawater layer for signal stability and precision evaluation, while its pronounced vertical salinity gradient enables evaluation of measurement accuracy under large ionic strength variations through comparison with a commercial multi-parameter probe. For all experiments, the performance of potentiometric and coulometric readouts are compared.

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Structure elucidation of the siderophore phymabactin and characterization of siderophore-metal complexes produced by *Paraburkholderia* spp.

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Symbiotic interaction between rhizobia and host plants takes place inside root nodules. Besides reducing atmospheric nitrogen into ammonium that is used by the plant to grow in nitrogen deficient soils, rhizobia produce siderophores enabling iron uptake.[1,2] Siderophores are strong iron chelators due to their hydroxamate, catecholate or carboxylate functional groups.[3] In this work, the siderophores of the beta-rhizobial genus *Paraburkholderia* were analyzed by ultra-high-performance liquid chromatography high-resolution tandem mass spectrometry (UHPLC-HR-MS/MS). In particular, the production of the novel siderophore phymabactin by *Paraburkholderia phymatum* was confirmed and the structures of eleven derivatives were elucidated by MS/MS and nuclear magnetic resonance (NMR) spectroscopy. Sharing a linear tetrapeptide backbone with hydroxamate and hydroxy-carboxylate groups, phymabactins are structurally closely related to another family of siderophores called ornibactins. Interestingly, spontaneous metal complexation of phymabactin derivatives with aluminum was observed.[4] To explore this in more detail, the collision cross sections (CCS) of phymabactins, ornibactins and corresponding metal complexes were determined by trapped ion mobility spectrometry. The CCS values of aluminum-phymabactin complexes were smaller than those of iron-phymabactin complexes, while an inverse relationship was observed for ornibactin complexes (see Figure). These findings on the chemical nature of phymabactins and their metal complexes disclose many potential application fields, including chelation therapy, crop protection and bioremediation.

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Quantification of azides on the surface of nanoparticles: towards precision bioconjugation

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The precise design of bioconjugated nanoparticles is crucial for cell targeting and cellular uptake.[1] Therefore, an accurate approach to creating and quantifying the organic ligand shell with an ideal number of bioconjugated targeting ligands for efficient and cost-effective bioapplication is needed. In this respect, click-chemistry has emerged as one of the most reliable options for bioconjugation.[2] However, a precise determination of the number of reactive functional groups, typically azides, available for bioconjugation on the surface of NPs has been rarely reported.

In this work, we synthesized catechol-stabilized hafnium oxide nanoparticles with different amount of azide functional groups (0-10 N₃/NP) on the surface as a model system to use in azide-alkyne cycloaddition reactions. We demonstrated that the NMR quantification of azide-carrying ligands, either in the bound state or stripped from the NP surface, comes with several unsolved challenges. To overcome them, we developed two convenient alternatives based on fluorescence or UV-Vis spectroscopy, both having similar accuracy and precision. The first quantification method is based on fluorescence quenching of a conjugated fluorophore by photoinduced charge transfer to nitrocatechol ligands. The second method is more general since it is based on the disappearance of the UV-Vis absorption band of the alkyne. Furthermore, we demonstrate the broader applicability of the second method on hafnium oxide nanocrystals capped with polyphosphonate ligands.

We believe that this quantitative analysis of surface functional groups will play an important role in precise bioconjugation, which is crucial for biomedical applications of NPs.

Figure 1. a) Schematic process behind the quantification method 1: DBCO-functionalized dye emits green light in the free form, but the fluorescence is quenched upon click reaction with surface azide groups due to PCT to acceptor nitrodopamine groups of the ligands; b) Chemical reaction behind the method 2: UV-tracking of azide-carrying nanoparticles with alkyne; c) Comparison of the quantification results by two developed methods.

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Visualizing Chemical Dynamics of On-surface Boronic Acid Condensation using Tip-Enhanced Raman Spectroscopy

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Boronic acids have been extensively applied as versatile building blocks in constructing supramolecular architectures and other advanced materials. The on-surface boronic acid condensation reaction, particularly for forming boroxine-based two-dimensional (2D) networks or nanostructures, is a topic of great scientific interest.^[1,2] Despite its significance, elucidating the chemical dynamics of the on-surface boronic acid condensation reaction remains challenging for conventional analytical tools. In this presentation I will introduce a powerful label-free and non-destructive nanoanalytical technique called tip-enhanced Raman spectroscopy (TERS) and demonstrate its application to directly observe the formation of boroxine-based nanostructures in the 4-mercaptophenylboronic acid (4-MPBA) self-assembled monolayer (SAM) on a Au (111) surface, a study that was recently published in ACS Nano.^[3]

The 4-MPBA SAM forms through robust S-Au bonding between the molecules and the Au (111) substrate. A dehydration coupling reaction within the 4-MPBA adlayer, induced by thermal treatment, leads to molecular rearrangement and unique intermolecular binding on the surface. We systematically examine this dynamic process using hyperspectral TERS imaging, capturing the interplay of molecular dehydration and the reversible nature of the condensation process with remarkable sensitivity (See in **Fig. 1**). The a few nanometers spatial resolution of each pixel, enables the precise acquisition of chemical information from a localized area, facilitating the accurate monitoring of the reversible reaction and the assessment of its homogeneity.

Our experimental insights are complemented by density functional theory (DFT) modeling, which verifies the progression to boroxine ring formation and rules out alternative open-ring configurations, providing molecular-level understanding of the reaction mechanism. This study not only offers the first direct chemical imaging of boroxine nanostructures but also underscores the indispensable role of TERS in elucidating on-surface coupling reactions with exceptional sensitivity and resolution. Our findings demonstrate that label-free, non-destructive nanoanalysis via hyperspectral TERS imaging can facilitate a rational approach to on-surface architectural synthesis, thereby advancing the frontiers of surface science.

Fig. 1. Average spectra from hyperspectral TERS images illustrating the chemical evolution of the 4-MPBA adlayer on Au (111) through stages of dehydration and hydrolysis. TERS image step size: 50 nm.

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Analytical Characterization of Stoichiometric Ho₂O₃ Thin Films Grown by Pulsed Laser Deposition

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The precise analytical evaluation of thin film materials is essential for their integration into high-performance photonic devices. Holmium oxide (Ho₂O₃), a rare-earth sesquioxide with potential in integrated X-ray laser technologies [1], was deposited on yttria-stabilized zirconia (YSZ) substrates using pulsed laser deposition (PLD) with both KrF (248 nm) and Nd:YAG (532 nm) laser sources.

Structural analysis through high-resolution X-ray diffraction (XRD) confirmed oriented, crystalline growth. Reciprocal space mapping (RSM) was employed to determine both in-plane and out-of-plane lattice constants, yielding values of approximately 10.61 Å, consistent with bulk Ho₂O₃ [2] and indicating strain-free, relaxed films without lattice tilt. Stoichiometry and compositional uniformity were investigated using ¹⁶O resonance-enhanced Rutherford backscattering spectrometry (RBS), confirming stoichiometric film growth and high elemental accuracy.

These findings underscore the importance of integrating structural and ion beam analysis techniques to verify the crystalline quality and compositional accuracy of thin films intended for advanced photonic applications.

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Detecting and Differentiating Aggregates in the Production of GLP-Analogous Peptides

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Aggregation presents a significant challenge in the production and purification of active pharmaceutical ingredients (APIs) – particularly GLP-analogous peptides.^{1,2} Uncontrolled aggregation can lead to batch failures and substantial economic losses.³ Additionally, the presence of aggregates in the final drug product can reduce its biological activity⁴ and – in the worst case – pose a potential risk of immunogenicity⁵. With the growing global demand for these peptides, regulatory agencies and contract development and manufacturing organizations (CDMOs) have intensified their focus on controlling aggregation. In response, quality control departments have developed and adapted a diverse array of analytical techniques to detect, monitor, and mitigate aggregation.

Here, we will provide an overview of key methodologies used in the industry, with a particular emphasis on distinguishing between two critical aggregate types: reversible, soluble aggregates and irreversible, insoluble aggregates. We will illustrate these approaches through stylized case studies, highlighting practical applications and insights gained from real-world scenarios.

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Gaseous Species Formation in LA-ICP-MS: Influence of Sample Matrix, Laser Pulse Width, and Ablation Conditions

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Accuracy in quantitative analysis using laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) depends on the availability of matrix-matched external calibration standards. While several certified reference materials have been developed, suitable standards for carbon-rich matrices, such as polymers and biological tissues, remain scarce. Consequently, many laboratories rely on in-house standards and carbon as an internal standard.[1]

However, earlier studies on the analysis of polymers by Todolí et al. (1998) and Frick et al. (2012) demonstrated that up to 80% of ablated carbon is transported in the gaseous phase[2], and that gaseous carbon species formation critically depends on the oxygen content of the sample matrix and the ablation environment.[3] Therefore, both studies were raising concerns about the reliability and suitability of carbon as an internal standard.

More recently, Van Helden et al. (2024) reported the formation of gaseous species for various elements upon laser ablation on a spiked gelatine sample.[4] They showed that gaseous species formation during LA is both element- and matrix-dependent and further modulated by instrumental parameters such as laser wavelength and fluence.

In this study, we extend these investigations by analyzing gaseous species formation across different sample matrices and instrumental conditions, with particular emphasis on the effect of laser pulse width. Both nanosecond (ns) and femtosecond (fs) lasers were employed. Gaseous and particulate fractions were separated using a Gas Exchange Device (GED), 0.2 µm Milipore filter and an elongated aerosol transport tube between the ablation cell and the ICP-MS. The temporal separation of gas and particle phases was investigated under different ablation cell designs and ablation gas compositions.

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From Solution to Spectrometer: Tracking Gold-Diazenyl Intermediates and the Impact of Gas-Phase Events

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The use of mass spectrometry in mechanistic studies allows for detection, characterisation and investigation of short-lived intermediates. However, the gap between solution-phase environment and gas-phase observations inherent to mass spectrometry adds a layer of complexity to the interpretation of the results.

Our work[1] presents a multifaceted investigation, exploring a ligand-based divergent selectivity in the reaction of [(NHC)Au-aryl] complexes with aryldiazenyl radicals to form either biaryl- or azoarene products. While electrospray ionization mass spectrometry (ESI-MS) serves as a powerful tool for detecting the putative gold-diazenyl intermediates, we reveal a critical challenge: the propensity for these species to undergo significant structural rearrangements during their transfer into the gas phase. Through the synergistic application of ion mobility spectrometry (IMS) and infrared photodissociation (IRPD) spectroscopy, we demonstrate that the detected ions correspond to isobaric gold(I)-azoarene product complexes, formed *in situ* during the ESI-MS process, rather than the true solution-phase intermediates.

Despite these gas-phase transformations, kinetic studies utilizing isotopic labeling provide compelling evidence for the transient nature of genuine solution-phase intermediates, indicating sub-second lifetimes. Furthermore, our findings highlight the role of gold-chloride complexes in facilitating the oxidative addition of aryldiazonium ions, leading to distinct gold(III) intermediates detectable in the gas phase.

Our efforts to bridge the gap “from solution to spectrometer” reveal lessons about the necessity of rigorous analytical validation in mechanistic studies and offer new avenues for rational ligand design to control selectivity in gold catalysis.

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Tracking protein misfolding and oligomerization in ALS: A temperature-controlled mass spectrometry approach

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Neurodegenerative diseases share complex molecular mechanisms, including protein misfolding, oligomerization, and aggregation.[1] A prominent example is Amyotrophic Lateral Sclerosis (ALS), a fatal neuromuscular disorder characterized by the accumulation of both soluble oligomers and insoluble aggregates of Cu/Zn Superoxide Dismutase (SOD1) bearing non-native conformations, resulting from over 120 distinct gene mutations.[2] Despite the central role of early aggregation in ALS pathology, the underlying mechanisms remain poorly understood, primarily due to the lack of analytical techniques capable of capturing the dynamic processes of SOD1 misfolding and oligomerization. In this study, bovine SOD1 was used to establish an assay that combines temperature-controlled nano-electrospray ionization (TC-nESI) with ion mobility-mass spectrometry (IM-MS), enabling real-time structural and conformational analysis of accelerated early aggregation events.

Native bovine SOD1 exists as a homodimer, with each subunit coordinating one Cu(II) and one Zn(II) ion. As metal loss is known to destabilize SOD1 and promote aggregation, the study focused on holo-SOD1 and apo-SOD1 (metal-free) variants. Thermal unfolding experiments were conducted using a custom-built TC-nESI source coupled to cyclic IMS, to examine the effects of metal-dependent structural stability under different solution heating rates (1.0 and 0.3 °C/min). For holo-SOD1, both fast and slow heating led to dimer dissociation into monomers of variable folds; however, only slow heating resulted in sufficient accumulation of misfolded monomers to enable enhanced and fast oligomer formation. Interestingly, slow thermal denaturation of apo-SOD1 revealed trimers and misfolded monomers as intermediates in subsequent apo-oligomer assembly. Compared to holo-SOD1, apo-SOD1 produced more compact and abundant oligomers, following a more gradual assembly process, while collision cross section (CCS) calculations indicated that both variants follow isotropic oligomer growth pathways. Surface-induced dissociation MS/MS (SID-MS/MS) experiments unveiled oligomerization assembly mechanisms, with primarily monomeric and dimeric subunits acting as building blocks in apo-derived oligomers. Additional insights from limited proteolysis and heat-induced fragmentation identified loops V, VI, and VII near the C-terminal region as particularly labile in misfolded apo-SOD1 monomers. Collectively, these findings highlight the power of TC-nESI combined with IM-MS to simultaneously resolve misfolding transitions, identify key intermediates, and characterize the architecture of co-populated oligomeric species, crucial for elucidating protein dynamics in neurodegeneration.

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Automated Structure Elucidation at Human-Level Accuracy via Multitask Multimodal Language Model

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Structure elucidation is crucial for identifying unknown chemical compounds, yet traditional spectroscopic analysis remains labour-intensive and challenging, particularly when applied to large-scale datasets. Although machine learning models have successfully predicted chemical structures from individual spectroscopic modalities, they typically fail to integrate multiple modalities concurrently, as expert chemists usually do. Here, we introduce a multimodal multitasking transformer model capable of accurately predicting molecular structures from integrated spectroscopic data, including Nuclear Magnetic Resonance (NMR) and Infrared (IR) spectroscopy. Trained initially on extensive simulated datasets and subsequently finetuned on experimental spectra, our model achieves top-1 prediction accuracies up to 96%. We demonstrate the model's capability to leverage synergistic information from different spectroscopic techniques and show that it performs on par with expert human chemists, significantly outperforming traditional computational methods. Our model represents a major advancement toward fully automated chemical analysis, offering substantial improvements in efficiency and accuracy for chemical research and discovery.

Perturbatively Corrected Instanton Rate Theory

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Correctly describing quantum effects is necessary for determining the rate of many reactions, e. g. in atmospheric chemistry or catalysis. While transition state theory (TST) is widely used to calculate rate constants, it has limitations, as it fails to account for quantum tunneling and anharmonic effects. One efficient method that goes beyond TST is *instanton theory* [1]. It only requires information from the least-action tunnelling path (called the instanton) and in return it can describe quantum tunnelling. In this contribution, I will explain how to improve upon instanton theory by adding to it *perturbative corrections* which describe the anharmonicity perpendicular to the tunnelling pathway. With this, much greater accuracy is achieved while maintaining computational efficiency and physical insight already present in instanton theory.

Our perturbative corrections to instanton theory were derived using asymptotic theory similarly to our previous research on tunnelling splittings [2]. In addition to the instanton path and Hessians along it (which are required for the leading-order theory), we now also require third and fourth derivatives along the instanton trajectory. Since the higher-order derivatives are readily available by numerically differentiating the PES, our method is efficient and scalable. As a result, both tunnelling and anharmonicity are included and our theory vastly exceeds the accuracy of TST for little effort.

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Exploring Collagen Triple Helices Using Native Mass Spectrometry: Insights into the Dynamics of Strand Exchange

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Collagen, the most abundant protein in mammals, is critical for the strength and stability of connective tissues. Short collagen model peptides (CMPs) serve as effective surrogates of the native protein to study the structural features of the collagen triple helix, and there is great potential for CMPs in biomedical applications, such as in wound healing, drug delivery and tumour tissue targeting.

The defined self-assembly of collagen triple helices is fundamental for their functioning but is difficult to control. Various designs for selective formation have been proposed, yet only very little is known about the dynamic changes occurring in CMP triple helices.

From an analytical point of view, distinguishing between different coexisting collagen triple-helical species is very challenging using conventional analytical techniques such as nuclear magnetic resonance or circular dichroism spectroscopy. Native mass spectrometry (MS), which preserves the native structures of the analytes, allows the analysis of macromolecules and the differentiation of non-covalent complexes of different composition, including those of CMPs.

Building on our previous work [1, 2], we optimized a nano electrospray high-resolution MS approach to identify and monitor coexisting CMP triple-helical species under native conditions. Ion mobility separation allowed us to distinguish isobaric signals from singly charged monomers and triply charged triple helices.

We used well-characterized homotrimeric CMPs composed of monomers built from seven repeating units of the amino acids proline (P), hydroxyproline (O) and glycine (G). These monomers differ in the frame ([POG]₇, [OGP]₇ and [GPO]₇) and the acetyl capping group (C₁-C₄) at the N-terminus. [3] By mixing two different homotrimeric CMP solutions in a 1:1 ratio, we observed the formation of heterotrimeric species over time and gained insight into the kinetics of strand exchange and the molecular characteristics that govern it.

The results reveal key mechanisms underlying triple helix dynamics and highlight the power of native MS for CMP analysis. Our work examines collagen from a new perspective, as a dynamic system rather than a static scaffold. As such, the findings provide an important tool for understanding the dynamic changes in native collagen and the residence times of collagen-based probes.

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Integrated Three-Electrode Flow Cell for Time-Resolved IR Pump–Probe SpectroscopyS. Aranda-Ruiz¹, E. Service^{1*}, P. Hamm^{1*}¹University of Zurich

Behind the reduction mechanism of CO₂ lies an ongoing debate surrounding the potential pathways that lead to distinct product distributions, which are often highly dependent on the nature of the metal surface [1]. To gain deeper insights into these mechanistic complexities, we have developed a novel cell that integrates a traditional three-electrode electrochemical setup with a flow-through design—an approach commonly employed in time-resolved spectroscopic measurements to ensure continuous sample refreshment and maintain experimental reproducibility [2].

This new cell design is optimized for ultrafast infrared pump–probe spectroscopy, enabling the detection of short-lived intermediates formed during photoreduction. A key innovation lies in the careful selection and doping of semiconductor materials, tailored to achieve both an accurate and tunable band gap suitable for photoactivation, while also retaining high IR transparency. This dual functionality allows for simultaneous optical excitation and spectroscopic probing of chemical species transiently adsorbed or formed at the catalyst surface under operational conditions.

By integrating optical accessibility, controlled electrochemical potential, and continuous flow, this hybrid cell rebrands the classical spectro-electrochemistry (see Fig.1). It allows for in situ tracking of reaction intermediates with high temporal and spectral resolution, offering a powerful platform to disentangle complex reaction pathways and surface dynamics in catalytic CO₂ reduction and related processes.

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Quantification of Peroxides in Organic Aerosols using HPLC In-Column Derivatisation with Chemiluminescent Detection

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Secondary organic aerosols (SOA) are formed by the oxidation of volatile organic compounds in the atmosphere and have been the subject of numerous studies due to their impact on human health and the Earth's climate. A significant fraction of SOA can be attributed to organic peroxides, which are considered to have a major impact due to their high reactivity and oxidation potential. The majority of quantification methods described in literature are employed for the determination of the total peroxide concentration of samples and are based on UV-vis spectroscopic detection. However, these techniques lack the ability to differentiate between individual organic peroxides and usually requires a reaction time of several hours.

In order to overcome these drawbacks, we developed a high-performance liquid chromatography (HPLC) in-column derivatisation method to separate and quantify individual organic peroxides. We adapted a detection method from Calandra et al. [1], in which the cytochrome c-catalysed luminol reaction was used for derivatisation after chromatographic separation. A novel in-column derivatisation (ICD) fitting [2] was utilised in order to minimize the dead volume and optimize the mixing to increase the chromatographic separation performance.

First, we optimised different HPLC parameters including the eluent flow rate, the column temperature, the mixing ratio of the HPLC and derivatisation reagent, and pH of the buffer solution. Subsequently, different commercially available peroxide standards were used for the calibration of the system. Complex samples containing mixtures of peroxides using liquid-phase ozonolysis [3] of α -pinene and 3-carene were synthesized. Furthermore, laboratory generated SOA, using an oxidation flow reactor (OCU [4]), from α -pinene, 3-carene, naphthalene were generated and analyzed.

We identified significant differences in chromatograms for different types of SOA samples, including the overall peroxide content. Comparisons between the total peak area obtained through HPLC chemiluminescent detection (HPLC-CL) and the peroxide concentration obtained through iodometric titration revealed a linear correlation, which confirms the quantitative capability of the novel HPLC chemiluminescent detection method developed here.

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Investigating Enzymatic Phosphoryl Transfer Reactions by ESI-Orbitrap-MS Analysis of Oxygen Isotopes in (Organo-)Phosphates

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The analysis of variations of natural abundance $^{18}\text{O}/^{16}\text{O}$ ratios in phosphate and organophosphates allows to track phosphoryl transfer reactions catalysed by various enzymes in fundamental biological processes and thus to infer changes in metabolic activity in natural and anthropogenically perturbed environments. However, current methods for O isotope analysis in (organo)phosphates limit the elucidation of phosphoryl transfer reactions to the quantification of leaving group isotope effects with the remote labelling approach (i.e., ignoring isotope effects associated with attack of O-containing nucleophiles) or enable only phenomenological interpretation of the observable O isotope fractionation. In this work, we explore novel analytical ESI-Orbitrap-high resolution mass spectrometry (HRMS) approaches to quantify $^{18}\text{O}/^{16}\text{O}$ ratios in phosphate and organophosphates through systematic application of low-energy in-source and high-energy collision cell-based fragmentation, and evaluation of O isotopologues of PO_3^- ions. Using alkaline phosphatase as model enzyme, we explore how to combine measurements of reactant and product O isotope fractionation can lead to the quantification of ^{18}O kinetic isotope effect from both nucleophilic attack and leaving group departures in phosphoryl transfer reactions.

Nanoscale Structural Insights into Thermochromic VO₂ Thin Films using Tip Enhanced Raman Spectroscopy

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Vanadium dioxide (VO₂) thin films exhibit a well-known reversible metal-insulator transition (MIT) near 68 °C, positioning them as attractive materials for thermochromic smart coatings and energy-efficient device applications.^[1] However, optimizing their performance requires a deeper understanding of their nanoscale structural and interfacial properties, which are often beyond the reach of conventional analytical methods. In this study, we utilize hyperspectral tip-enhanced Raman spectroscopy (TERS) imaging to investigate the local structure and strain distribution in VO₂ and VO₂/TiO₂ thin films fabricated via pulsed layer deposition.^[2]

TERS imaging of pristine VO₂ films reveals a homogeneously distributed M1 phase, alongside nanoscale regions of lattice deformation and different orientated nanocrystals. These features result in a high density of grain boundaries, which are likely responsible for shifting the MIT to higher temperatures, thus affecting thermochromic efficiency. In VO₂/TiO₂ heterostructures, TERS surprisingly reveals the coexistence of brookite alongside the dominant anatase phase within the TiO₂ layer, as shown in Figure 1. The brookite phase exhibits tensile strain, evidenced by shifts in specific Raman bands, as well as reduced crystallinity. Additionally, the interface displays pronounced roughness and nanoscale intermixing.

These findings demonstrate the unique capability of TERS to deliver nanoscale-resolved chemical and structural information, surpassing the limitations of traditional techniques. By offering valuable insights into how local structural features may influence macroscopic behavior, this study contributes to a better understanding that could support the future design and optimization of VO₂-based smart coatings.

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Stepwise Exploration of Human Choriotropic Gonadotropin Deglycosylation and Structural Stability by Native MS and Ion Mobility Spectrometry

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Human chorionic gonadotropin (hCG) is an essential glycoprotein hormone, involved in the regulation of pregnancy and used as a biomarker in clinical practice.^{1,2} Its structure, as a heterodimer composed of two subunits, is strongly influenced by glycosylation, which plays a key role in its stability and biological activity. However, detailed characterization of its glycoforms remains a challenge.

Understanding the glycosylation profiles of glycoproteins has been identified as a key objective in proteomic research, according to previous studies. Such analyses are often performed after proteolytic digestion, leading to the loss of information on the combination of different glycopeptides in the intact protein. However, mass spectrometric analysis of intact molecules has proved to be a powerful tool for characterizing glycosylation profiles. A large number of glycosylation sites have been identified on hCG, highlighting a diversity of glycoforms influencing its biological properties.^{3,4}

In this study, we explore the impact of glycosylation on the structure of hCG by combining native mass spectrometry (Native MS), ion mobility spectrometry (IM-MS) and a temperature-controlled ESI source. The aim is to assess how glycans and glycosylated modifications influence the mass, conformation and thermal stability of the hormone in the gas and liquid phases, as well as to analyze structural modifications induced by the removal of glycans.

This approach could provide new insights into the relationship between glycosylation and glycoprotein conformation, with implications for hormone biology and the development of more precise biomarkers.

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LC-Inspector: a free and open-source tool for targeted mass spectrometry analysis

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Mass spectrometry has revolutionized the life sciences, offering unprecedented accuracy and sensitivity, particularly when paired with chromatography techniques. Its widespread adoption across various disciplines, from pharmacology to metabolomics, has driven many laboratories around the world to invest in mass spectrometry.¹ However, analyzing data from diverse vendors and instruments with varying technologies, remains a significant challenge, especially for non-mass spectrometrists.²

To address this, LC-Inspector has been developed as a free, open-source, and cross-platform tool for viewing and analysis of hyphenated mass spectrometry data, regardless of the vendor or instrument used. With support for liquid chromatography, gas chromatography, ion mobility, and various tandem mass spectrometry fragmentation techniques, LC-Inspector provides a comprehensive alternative to vendor software. Notably, the application runs entirely locally on the user's system, ensuring complete data ownership, privacy, and security. The source code is openly available on GitHub and Zenodo, with user-friendly binaries distributed for both Windows and macOS.³

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Palladium-107 as a new forensic tracer in uranium material

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In a nuclear forensic investigation, it is of high interest to trace an investigated material back to its origin and/or to match evidence found at a crime scene. Hence, unique signatures are needed to provide a high level of information. When focusing on uranium (U), the supply chain in the nuclear fuel cycle can be divided into two parts, namely (1) the supply of fresh material, and (2) reprocessed material which was previously irradiated¹. To date, most of the analytes studied in the context of nuclear forensics are isotopes of actinide elements and γ -emitting fission products. However, barely detectable, purely β^- -emitting radionuclides are rarely investigated. Therefore, the case of palladium (Pd) has been targeted and is presented here.

Pd is a noble metal with six natural isotopes in the mass range 102 - 110 amu. This mass range overlaps with the mass range of most ²³⁵U fission products from the lighter mass peak (90 - 105 amu)². In addition to the natural isotopic composition of Pd, nuclear fission leads to an additional input of a non-natural Pd isotope, i.e., ¹⁰⁷Pd. With a half-life of approximately 6.5 million years, ¹⁰⁷Pd is an ideal analyte to indicate prior irradiation of the material in question. Together with a low-energy β^- -decay (emission of 33 keV electrons), radiation damage is considered negligible³. Furthermore, the concentration of Pd in reprocessed U is expected to depict the degree of ageing of the organic phase used for U extraction during reprocessing, something only few publications have addressed so far. However, there is evidence that radiolysis may produce a variety of organic impurities that can affect the selectivity of the extraction process and thus, lead to an increased content of Pd isotopes in the reprocessed fuel⁴ (Fig. 1).

Figure 1: Co-precipitation of Pd via a bis(dimethyl-glyoximate)nickel(II) complex formation (left side) and isolated yield of the co-precipitation with different reaction times (right side).

The newly developed chemical separation method presented here provides reasonable yields above 90%. Currently, its suitability in combination with sector field inductively coupled plasma mass spectrometry is explored for the future screening of U materials for Pd traces.

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Structural mass spectrometry resolves the complexities of early-state semaglutide oligomerization

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Soluble oligomers of peptide and protein are believed to be the key neurotoxic species in neurodegeneration and promising targets for drug development.^{1,2} However, transient, heterogeneous peptide and protein oligomers evade conventional structural characterization. To overcome these challenges, we developed a mass spectrometry (MS) platform that integrates native MS (nMS) with orthogonal gas- and solution-phase probes—ion mobility MS (IM-MS), hydrogen–deuterium exchange MS (HDX-MS), cross-linking MS (XL-MS), collision-induced unfolding (CIU), temperature-controlled nano-electrospray ionization MS (TC-nESI-MS), collision-induced dissociation (CID) and transition metal ion Förster resonance energy transfer (tmFRET)—into a unified workflow. By merging high-sensitivity mass-based separation with complementary distance and dynamics measurements, this approach delivers molecular-level insights into oligomer assembly pathways beyond the reach of any single method.

Central to this platform, nMS resolves coexisting oligomeric states by mass-to-charge ratio, facilitating further structural interrogation. Applied to semaglutide, a well-known GLP-1 receptor agonist approved for diabetes and obesity and under investigation for neurodegenerative diseases, nMS first showed that Cu²⁺ dramatically shifts its oligomer distribution toward higher-order species. TC-nESI-MS and CIU then revealed that this shift reflects Cu²⁺-mediated stabilization of semaglutide dimers—information inaccessible to bulk aggregation assays. Next, we localized the Cu²⁺ binding site through convergent tmFRET, IM-MS, and CID data, demonstrating that the ion bridges the fatty-acid moiety and peptide backbone via coordination with carboxylate and aromatic residues (Tyr₁₉, Phe₂₈, Trp₃₀). This precise mapping highlights the platform's ability to dissect transient metal-cofactor interactions within noncovalent assemblies. To define the quaternary geometry of the minimal assembly unit, we integrated XL-MS and HDX-MS with tmFRET distance constraints, revealing that semaglutide dimers adopt a parallel, head-to-head orientation across residues 19–37. The agreement between gas-phase and solution-phase measurements confirms the robustness of the platform in mapping the spatial arrangement and interface of labile oligomeric species. Finally, we extended the platform to a physiologically relevant interaction by measuring the binding of semaglutide oligomers to native and glycosylated HSA using nMS. The workflow revealed enhanced affinity for glycosylated HSA while cyclic IM-MS confirmed preservation of the albumin acyl-binding pocket, establishing a direct link between oligomer structure and physiological function in complex biological contexts.

In summary, our integrated structural MS platform offers an unprecedented level of mechanistic detail for transient peptide oligomers. By enhancing mass-based oligomer separation with orthogonal distance and stability measurements, it delivers a comprehensive toolkit for probing cofactor-driven assembly, interface architecture, and functional binding events. Although validated on semaglutide, this approach is broadly applicable to diverse aggregation-prone peptides and proteins, advancing mechanistic insight across the proteome.

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Towards quantification of drugs in exhaled breath aerosol.

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Human breath contains not only inorganic gases and water vapor, but also a variety of organic compounds. Some of these compounds are transferred from the blood to the breath in the alveoli, providing valuable information about the body's health. Sensitive analytical techniques such as proton transfer reaction mass spectrometry, selected ion flow tube mass spectrometry, and secondary electrospray ionization mass spectrometry can measure these compounds online at concentrations as low as parts per billion (ppb).

In addition to volatile organics, non-volatile compounds are also present in breath at even lower concentrations and are believed to be exhaled in aerosol form. Measuring these compounds, therefore, requires preconcentration combined with the most sensitive techniques available to detect them in the part per trillion (ppt) range in breath. Different sampling devices, e.g., impactors, have been successfully used for the sampling and detection of drugs and phospholipids in breath [1,2]. However, quantification remains challenging due to the variation in the number and size of exhaled aerosol particles among individuals. As a result, new approaches are necessary to standardize these measurements.

As part of a randomized controlled trial at the Institute of Forensic Medicine in Zürich to determine the driving performance under the influence of attention-deficit/hyperactivity disorder (ADHD) drugs, we are measuring a variety of drugs to treat ADHD in breath, and correlate these measurements with blood concentrations. We will present preliminary results from the optimization of our analytical protocols and the quantification of ADHD-related compounds in breath samples, including comparative data that correlate breath with matched blood concentration levels.

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Sources of Fractionation and their Impact on LA-ICPMS Applications

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Elemental analysis by Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICPMS) has been widely accepted and successfully applied over the years for a broad range of applications in geology, forensics, material sciences and biomedicine.[1] However, non-stoichiometric effects have been shown to limit the accuracy of geochronological measurement using Pb/U dating.[2] In this context, the stoichiometry of the sample was not reproduced by analysis of deposited material given that a Pb-enrichment was measured in comparison to more refractory elements. This observation demonstrated that LA sampling causes laser-induced fractionation effects, while incomplete vaporization, atomization and ionization of larger particle sizes or agglomerates within the ICP were also shown to result in non-stoichiometric effects.[3]

The re-ablation of the deposits following crater generation recently confirmed these previous observations, while allowing the distinction of laser- and ICP- induced fractionation effects and the introduction of the Laser Induced Fractionation Indices.[4] Optimizing the operating conditions for the recommended U/Th sensitivity ratio of 1 proved to minimize the ICP-induced fractionation to a level that is masking the occurrence of laser-induced fractionation of a 193 nm excimer laser.[1,4] These general findings and their order of magnitude are now quantitatively investigated for samples with different ablation properties and for analysis with various operating parameters. In addition, elemental fractionation effects observed in nitrogen will be compared to those obtained in helium, based on the recent figures of merits obtained with these carrier gases[5]. The consequences of the elemental fractionation observed for the different operating parameters on the quantification accuracy will be reported.

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Assessment of Infrared Atomic Force Microscopy (AFM-IR) to detect Nanoplastic ParticlesN. Kummer¹, C. Hüglin^{2*}, R. Kägi^{1*}¹Eawag, ²Empa

Nanoplastics (NPs) pose environmental and health risks due to their persistence and potential for cellular uptake. Traditional correlative imaging and spectroscopy methods fail to provide chemical information at the nanoscale. Atomic force microscopy coupled with infrared spectroscopy (AFM-IR) combines the nanoscale resolution of AFM with chemical identification through infrared spectroscopy.

To assess the potential of AFM-IR to selectively detect individual NPs particles, aqueous suspensions of polystyrene (PS)-NPs covering the size range from 20nm – 200nm were drop casted on silicon wafers. Although the NPs formed large aggregates upon drying, individual PS-NPs were detected on the silicon wafers. Whereas PS-NPs of all sizes were successfully detected based on their morphology using the AFM, characteristic spectra of individual PS-NPs were only obtained for particle sizes larger than 50nm. Experiments with silica spheres of the same sizes revealed lower size detection limits of around 20nm. The irradiation of the particles with the laser during the AFM-IR analysis most likely degraded the PS-NPs whereas the (inorganic) silica spheres remained unaffected by the laser beam. In mixtures of PS-NPs and silica spheres, the two particle types were unambiguously distinguished by their characteristic IR spectra. The specificity of the method will further be evaluated by including other polymer types such as polyethylene, polymethyl methacrylate and polyvinyl chloride.

Ligand-substituted inorganic-organic hybrid materials for efficient urea-assisted electrocatalytic water splitting

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Strategies for the structural tuning of inorganic-organic hybrid materials are crucial for their technological application. We present a ligand replacement strategy, for NiClOH-Pm_xPz_{1-x} inorganic-organic hybrid nanorods (Pm = pyrimidine, Pz = pyrazine) to improve their performance in urea-assisted water oxidation reaction. Through the partial substitution of pyrimidine ligands with pyrazines, significant oxygen vacancies on the surface of NiClOH-Pm nanorods were introduced, while improving electrocatalytic performance through additional π - π interaction in between ligands. The composite material exhibits excellent performance in electrocatalytic urea oxidation, with a higher electrochemical double layer capacitance (23.8 mF cm⁻²) and a small Tafel slope (41.9 mV dec⁻¹), reaching potentials of 1.37 and 1.53 V at 10 mA cm⁻² and 100 mA cm⁻², respectively. The optimized ligand ratio (Pyrimidine/Pyrazine = 33/1) enhances π - π interactions, which improves electron transferring between ligands and Ni and thereby catalytic efficiency. DFT calculations show that the adsorption of Ni on urea takes precedence over the adsorption of OH⁻ during the electrocatalytic process. This work offers a design strategy to improve the electrochemical performance of hybrid inorganic-organic materials through substitutional ligand design.

Impact of Topical Formulations on Skin Lipids analyzed by HR-MAS NMR Spectroscopy

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Introduction: Developing effective topical drug formulations for the treatment of superficial skin conditions involves overcoming the protective barrier function formed by the structured lipid layers of the stratum corneum, the outermost epidermal layer. Specifically, we explore suitable carriers that are capable to shuttle porphyrinic photosensitizers (PSs) into the epidermal layer for improved topical photodynamic therapy (PDT) [1].

Objective: The main aim is to investigate the molecular interactions between phospholipid-based carriers, chemical penetration enhancers (CPEs), PSs, and skin lipids at a molecular level to gain insights into the mechanisms of action and aid rational design of topical drug delivery.

Methods: High-Resolution Magic Angle Spinning Nuclear Magnetic Resonance (HR-MAS NMR) spectroscopy is directly applied to skin samples to investigate the molecular effects of the formulation components on the structure and dynamics of skin lipids. HR-MAS NMR uniquely generates "liquid-like" spectra from semi-solid samples, enabling non-destructive studies that offer insights into molecular dynamics [2]. Using Franz diffusion cells, porcine skin is treated with different formulations, and the epidermal and dermal layers will be examined separately.

Result: In a first step, different methods for separating epidermis and dermis were employed, including chemical and enzymatic treatment. The tissue samples obtained were analysed histologically. Subsequently, an HR-MAS NMR methods protocol was established. Skin lipid resonances were assigned with the aid of reference and skin extract spectra. First results indicate strong temperature dependence of epidermal lipids, indicating observable phase transitions (see Figure). In our ongoing experiments, we will characterize formulation-induced changes in lipid structure and dynamics by thoroughly comparing HR-MAS NMR spectra from treated and untreated skin samples.

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Hydration in Lipid-Cyclodextrin Interaction

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Biological water refers to the water content existing in and around biological molecules. It is special and different from the usual bulk water since it is confined, H-bonded with lipid headgroups and affected by interfacial molecular arrangements [1]. This limits the rotational and translational dynamics of water molecules, resulting in a non-random orientation. The membrane stability and functions can critically rely not only on lipid interactions but also the interfacial region mainly comprising water and vice versa [2]. Thus, the impact of hydration on lipid membranes is particularly an interfacial phenomenon, which can be probed by surface sensitive techniques like sum-frequency scattering (SFS) [3]. In this work, we exhibit how membrane-sugar interactions can induce extended chiral ordering in water surrounding the membrane. This is achieved by a special class of cyclic oligosaccharides called cyclodextrins (CD) which are capable of forming water-soluble complexes with water-insoluble molecules, making them a popular choice in pharmacology and cosmetics [4]. Despite their widespread utilization, little is known about their molecular interaction with lipid membranes. Here, we utilize the technique of vibrational SFS to investigate lipid-CD interactions between various types of CD (differing size, composition) and lipids (charged/uncharged headgroups, dependence on acyl chains). We examine the interfacial water structure at the nanoscale on the lipid membranes interfaces to find extended CD assemblies surrounded by highly ordered, chiral ice-like water. The CD assembly shows strong headgroup selectivity, highlighting the role of H-bonding in CD-lipid interactions. The extended chiral water hints at the role of water in facilitating chiral-selectivity in relation to origin of life [5].

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Using Forward Linear Scattering for highly material-saving solubility measurements.

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A novel pulsed ultrafast laser-based technology has been developed by an innosuisse project (EASY) that will be commercialized by Oryl Photonics. This patented technology combines Second Harmonic Light Scattering (SHS) with Forward Linear Light Scattering (FLS). SHS leverages the solvent redistribution method [1] to provide structural insights into aggregates present in solution. FLS is distinct from traditional linear and dynamic light scattering techniques and detects light in-line with the laser path through a narrow iris. Preliminary results suggest a high sensitivity and further investigations and benchmarks are being conducted within the *Fast and Accurate Solubility for Sustainability* (FASS) project, a european collaboration funded by a HORIZON grant.

We aim to find applications within the pharmaceutical and chemical industry for this promising technology, more specifically in pre-formulation, where studies rely on limited quantities of compound. In this specific field, there is a lack of early-sceneing methods for the selection of suitable excipients in the development of co-crystals or co-amorphous solids [2] with enhanced properties, such as increased dissolution rate, prolonged shelf life or increased solubility in aqueous media. We aim to demonstrate that, by combining computational predictions and efficient screening tools, the pre-formulation of co-crystal and co-amorphous solids will become more sustainable, fast and thorough.

Computational tools are widely implemented in the pharmaceutical industry as a preliminary screening tool. As an example, a successful use of COSMOquick for co-crystal screening has been reported in the recent literature [3]. The identified promising excipients then undergo further experimental or computational investigations. The miniaturized FLS technology would have a high potential as a first experimental screening method for excipient selection and optimization (see Figure below). This method requires a minimal amount of drug (as little as 2µL of a stock solution per replica) with a library of excipients that can be readily available as stock solutions. This screening could, down the line, be automated with technologies that are compatible with a 96- or 384-well plate format.

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In vitro Fossilization as Novel Sample Preparation for Quantitative Bioimaging of Mammalian Tissue in LA-ICP-MS

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Laser ablation inductively coupled mass spectrometry (LA-ICP-MS) provides rapid generation of spatially resolved elemental data and has found broad applicability in the life-sciences, particularly for the imaging of biomaterials. However, accurate quantification requires both internal and external standardization. Carbon, although uniformly distributed in biological samples, is often considered unsuitable as an internal standard due to its distinct ablation behaviour. Up to 80 % of the total carbon signal can originate from gaseous species formed during ablation [1], whose transport and ionization dynamics differ from those of the particulate phase. In recent years, gelatine has been successfully established as a matrix-matched standard for biological tissue, however, sample thickness is limited due to required total consumption of the sample during ablation. As an alternative to matching the standard to the sample matrix, an inverse strategy involves matching the sample matrix to a well-characterized standard. [2] Townson et al. reported the in vitro fossilization of whole chicken embryos via in situ produced silicic acid [3] offering a promising route to assimilate a silicate matrix. This transformation enables the introduction of internal standards such as silicon and facilitates calibration using widely available reference materials like the NIST SRM 61X glass series.

In this work, a fossilization approach for the in vitro fossilization of bovine kidney and liver sections is presented, building on the method reported by Townson et al. [3] Both acidic and alkaline conditions were compared to account for differences in analyte mobility. Time series were carried out and analyte leaching as well as silicon incorporation was investigated monitoring the average silicon, sodium, phosphorus and iron content in fossilized samples by microwave assisted acid digestion and subsequent ICP-OES analysis. Fossilization behaviour between tissue types, first quantitative LA-ICP-TOFMS imaging results and investigation into possible analyte leaching will be presented.

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Implementation of FT-FEIR Spectroscopy and site-specific application to biomolecules

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Fluorescence-encoded infrared (FEIR) spectroscopy is a technique that uses the sensitivity of fluorescence to investigate vibrational dynamics in solution.^[1–3] Here, we present the development of a versatile experimental setup capable of simultaneously measuring FEIR and 2D infrared (2D-IR) spectra. The setup is designed to operate with sample concentrations below 20 μ M. The combination of a non-collinear optical parametric amplifier (NOPA) in the visible, as well as a OPA in the infrared, enables the measurement of a wide range of different molecular systems. By resolving the vibrations and couplings of the chromophore within a protein LOV domain, we demonstrate the potential of FEIR to isolate local vibrational features in complex biological systems.

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Rapid Intact IgG Glycosylation Profiling by Temperature-Controlled Online Reduction ESI-MSC. Tan¹, Y. Zhou^{1*}, R. Zenobi^{1*}¹Department of Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH), CH-8093 Zürich, Switzerland.

Immunoglobulin G (IgG) glycosylation is important in modulating antibody efficacy and can serve as biomarker for various diseases that include autoimmune disorders, inflammatory conditions, and cancer. The N-linked glycans at Asn297 on the heavy chain govern immune activity through modifications such as galactosylation, fucosylation, and sialylation, while light chain glycosylation affects antibody stability and antigen binding. Traditional mass spectrometry (MS)-based analysis of IgG glycoforms are compromised by lengthy sample preparation steps, that often include enzymatic digestion and purification. Here, we present a rapid, streamlined workflow leveraging temperature-controlled electrospray ionization mass spectrometry (TC-ESI-MS) that includes online dithiothreitol (DTT) reduction, to analyze intact IgG glycosylation within 15 minutes. In this innovative method, online reduction is performed directly within the electrospray capillary, which preserves the glycosylated light and heavy chains, thus allowing simultaneous characterization of glycan location and pattern from only picomole sample quantities. We validated the method using IgG1 and IgG2 subclasses and were able to demonstrate comprehensive glycoform profiling without separate proteolytic digestion or extensive sample cleanup. This method significantly simplifies analysis, reduces cost and time, and maintains structural integrity, making it an attractive tool for therapeutic antibody quality control, biomarker discovery, and clinical diagnostics requiring rapid, high-resolution glycosylation assessment.

Quantitative imaging of Dawsonite using LA-ICP-MS

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Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICP-MS) elemental imaging is a powerful technique for visualizing compositional variations in geological materials. Quantification of elemental maps via 100 wt% normalization¹ is straightforward in homogeneous matrices but becomes challenging in heterogeneous or fine-grained samples, where mixed mineral phases such as oxides and carbonates coexist. Accurate quantification under these conditions requires assigning an appropriate matrix type at the pixel level - a task that is non-trivial in complex geological samples.

To address this, dimensionality reduction techniques can be employed to classify individual pixels based on the multi-element data acquired by LA-ICP-MS. This facilitates matrix-specific normalization and enhances both the accuracy of elemental quantification and the interpretability of mineralogical images.

This approach is demonstrated on the mineral Dawsonite, $\text{NaAl}(\text{CO}_3)(\text{OH})$, and its host-rock matrix from Mt. Amiata (Italy), which exhibits significant compositional heterogeneity. Dawsonite is of particular interest for carbon capture and storage (CCS) due to its capacity to sequester up to 100 kg/m³ of CO_2 through mineral trapping in saline aquifers.² The composition of the surrounding host-rock minerals is assumed to play a crucial role in Dawsonite formation.^{2,3} Despite its importance, the detailed elemental characterization - particularly at the trace element level - of both Dawsonite and its host-rock remains incomplete.

This study aims to improve the accuracy of quantitative imaging using LA-ICP-MS and will provide new insights into the composition of Dawsonite and its host-rock minerals, thereby advancing our understanding of this promising material for carbon storage applications.

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Exhaled Metabolome Analysis using SESI-HRMS Following a Low FODMAP diet

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Diagnosing lactose malabsorption (LM) remains challenging due to variability in symptom presentation and the limited sensitivity and specificity of current methods¹. Additionally, not every lactose malabsorber exhibits symptoms, which complicates the accurate diagnosis of lactose intolerance (LI). The Lactobreath² study utilizes secondary electrospray ionization (SESI) coupled to high-resolution mass spectrometry (HRMS) to detect volatile biomarkers in exhaled breath in a non-invasive way. Since breath profiles can be heavily influenced by the diet³, the participants in the study follow a standardized meal plan for 3 days before the lactose challenge to ensure a comparable baseline between individuals. However, the role of other potential confounding factors, such as gender, age, ethnicity, BMI, and genetics, needs assessment.

Forty participants followed a low-FODMAP diet plan for 3 days, consisting of breakfast, lunch, dinner, and two snacks per day, tailored to each individual's caloric needs based on their BMI, age, and gender. After overnight fasting, online breath analysis was performed at 3 time points (baseline of lactose challenge) with 10-minute intervals in between using a SESI source (*Fossil Ion Tech*, Spain) coupled to a Q-Exactive Plus Orbitrap mass spectrometer (*Thermo Fischer Scientific*, Germany). Additionally, the breath hydrogen and methane concentrations were determined using a QuinTron BreathTracker SC (*Quintron Instrument Company*, USA). Demographic data of the participants were assessed during screening for the Lactobreath study. Participants were grouped into 3 groups based on a genetic test and an at-home lactose tolerance test: non-symptomatic lactase persistent, non-symptomatic lactase non-persistent, and symptomatic lactase non-persistent.

SESI-HRMS online analysis detected features in both positive and negative ion modes. The baseline breath profiles of the 3 phenotypes were compared. Data on intra- and inter-individual variability are presented. Clustering of the data was also performed with regard to ethnicity, gender, age, and BMI of the participants, to investigate possible differences in breath profiles caused by these factors and identify features of interest (e.g., fasting metabolites). Tentative chemical formula annotation was performed using the m/z values obtained and heuristic algorithms.

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