

Conference Report

Biotech 2011 Conference

Zurich University of Applied Sciences

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Abstract: More than 160 experts from industry and academia came together this September for the Biotech 2011 at the Zurich University of Applied Sciences (ZHAW) in Wädenswil. As one of the main topics, the conference addressed innovations in sensor technology, where new measurement principles and methods have helped to enhance robustness and user friendliness. Another main emphasis of Biotech 2011 was the application of sensors and related analytical techniques in bioprocesses. In this area, the sensor industry needs to meet the challenges introduced by the increasing use of single-use bioreactors. With its strong focus on sensor applications, Biotech 2011 successfully promoted interaction between professionals in academic and industrial research as well as with experts who apply sensors in biopharmaceutical production.

Keywords: Bioprocess analytics · Sensors for single-use bioreactors · Sensor technology

Biotech 2011 – Chemical Sensors Forum

In September 2008, the ZHAW and the Division of Analytical Chemistry of the Swiss Chemical Society organized the Chemical Sensors Forum on the Uetliberg, near Zurich. The conference's strong focus on applications of sensors was especially appreciated by the high number of participants from industry, which encouraged the organizing committee to plan a similar conference at a later date.

For many years the ZHAW has successfully organized the Biotech conference series, which focus on various topics in biotechnology. Last year's conference, Biotech 2010, emphasized the use of single-use devices in biopharmaceutical production. One of the most prominent issues discussed were the challenges of online analytics applied to single-use systems. As a result, the organizers decided to return to this theme in an application-oriented way in the Biotech 2011 conference/Chemical Sensors Forum.

Visions and Trends in Sensor Research

Sensors have been employed in on-line process control for many years, and reliable measurement of pH and oxygen is still absolutely crucial to bioprocess control. Although well-established methods have been in use for decades, new technologies for reliable measurement of these parameters are still being sought after. As an example, the currently available non-glass pH sensors are still limited in terms of their measuring range or robustness in harsh process environments.



Discussions in the foyer of the Grüental Campus, ZHAW Wädenswil.

Biotech 2011 opened with a plenary lecture by **Govind Rao**, the Head of the Center for Advanced Sensor Technology at the University of Maryland, Baltimore County USA, and co-founder of Fluorometrix. In his talk, he gave an impressive overview of his group's research and applications of sensors in bioprocesses. He pointed out that non-contact sensing devices that allow measurements in single-use systems have already been established. However, he also mentioned the current challenges in applying these sensors, such as the need for standardization. This will be a crucial issue in the design of sensors and interfaces to guarantee comparability of data and to reduce the validation burden for end users.

Volker Cimalla (Fraunhofer-Institut für Angewandte Festkörperphysik, Freiburg, D) and **Michael J. Schöning** (Aachen University of Applied Sciences, D) presented recent developments in the field of semiconductor-based sensors. Devices based on AlGaIn/GaN seem to be promising, as they exhibit low drift and light sensitivity, withstanding more than 50 cleaning in place (CIP) cycles without performance change.

Silvia Generelli (CSEM, Landquart, CH) presented applications of ion-sensitive sensors in cell cultures, where cell necrosis can be monitored online by measuring potassium ions released by cells. An interesting approach to overcoming some limitations of classical polymeric membrane-based ion-selective electrodes is the use of thin-layer coulometry, allowing measurement without reference electrodes.

Industry Perspectives

Various sensor manufacturers have recently introduced new sensor technologies for 'classical' biotech parameters. These include novel optical or electrochemical sensing principles as well as intelligent sensing systems. In their talks, **Jörg Pochert** (Hamilton, Bonaduz, CH) and **Martin Freudenberger** (Endress+Hauser Conducta, Gerlingen, D) demonstrated the customer benefits of sensors with integrated transmitter signal conversion and data storage capabilities. These products, supplied by major sensor manufacturers, are able to directly deliver robust



A strong focus on applications: a display of new products at the exhibition.

measurement signals to the process control system. Furthermore, they guarantee user-friendly, traceable calibration and sensor diagnostics. **Holger Müller** (Bluesens, Herten, D) summarized the use of gas sensors for bioprocess control: if sensors for oxygen and carbon dioxide are combined, substrate limitations may be detected and the metabolism of microorganisms or cells may be directly followed by measuring respiratory quotients.

Sensors in the PAT Framework

With rising quality requirements, spurred by regulatory guidelines (such as the FDA's PAT initiative) and a growing need to achieve an even deeper understanding of processes, the need for robust and accurate tools for online measurement in biomanufacturing is obvious. **Andreas Schneider** (Roche Diagnostics, Rotkreuz, CH) presented the role of PAT and Quality by Design in the pharmaceutical industry, explaining that manufacturers should aim to implement quality within the process rather than focus on controlling quality. If process variability can be explained, product quality can be guaranteed and reliably predicted. In their contributions **Christoph Herwig** (Vienna University of Technology, Austria) and **Wolfgang Budach** (Novartis Pharma, Basel, CH) emphasized that scientifically based bioprocess development is the key to efficient scale-up to production. 'Soft sensors', which provide online estimates of non-accessible process variables from available sensors, are expected to play an important role in bioprocess control.



Sensors for Single-use Bioreactors

Single-use bioreactors have become widespread in biomanufacturing, not only in R&D, but also in pilot and production plants. Therefore, new sensing principles needed to be developed for these devices. Compared to traditional process sensors, some of the requirements for sensors in single-use bioreactors are less demanding (*e.g.* lifetime, steam sterilizability). Hence, new opportunities arise for sensors and measuring principles if applied to disposable bioreactors.

Barbara Paldus (Finesse Solutions, San Jose, USA) summarized Finesse's contributions to improving the performance of optical sensors for single-use systems. Whereas sensors for dissolved oxygen are now widely accepted as reliable and robust, the optical measurement of pH remains a challenge. Even so, traditional (electrochemical) sensors need to be compared carefully with newly developed optical methods, as absolute reference standards are not always available. The issue of comparability was again raised by **Stefan Spichiger** (C-Cit AG, Wädenswil, CH), who presented results obtained with disposable inline sensors for nutrients and metabolites such as glucose, glutamate and lactate. Although it is highly necessary to compare inline and offline methods, the users' awareness and understanding of this issue is not always well established.

Several talks confirmed that the use of sensors in disposable systems is becoming widely accepted. This was underscored by contributions from academic researchers (**Peter Neubauer**, TU Berlin, D), manufacturers of disposable systems and sensors (**Henry Weichert**, Sartorius Stedim, Göttingen, D, and **Gernot T. John**, PreSens, Regensburg, D) and users of single-use devices in



Peter Neubauer, presenting his research on consistent bioprocess development at the Technical University of Berlin.



Frieder W. Scheller, speaking about biomimetic sensors based on molecularly imprinted polymers and aptamers.

process development and biopharma manufacturing (**Wolfgang Paul**, Roche Diagnostics, Penzberg, D). The relevance of single-use sensors is also illustrated by the fact that suppliers of classical reusable sensors are now entering the market. **Kurt Hiltbrunner** (Mettler Toledo, Urdorf, CH) presented a new single-use pH electrode with high potential stability and a wide measuring range.

Again, many experts pointed out that the field of single-use sensors is still highly fragmented. They agreed that standardization of sensor and port dimensions as well as physical and software interfaces and protocols is a prerequisite for customer acceptance of this technology.

The conference concluded with a contribution from **Frieder W. Scheller** (University of Potsdam, D), a leading expert in the field of biosensors for many decades. He presented sensors that could be applied to disposable bioreactors within the next few years. Biomimetic sensors, based on molecularly imprinted polymers, are especially promising as they allow reversible interaction with demanding analytes and can be operated under difficult conditions. New recognition schemes have become feasible using aptamers, based on highly efficient ways of selecting oligonucleotides binding to target analytes. Over the past few years, these methods have evolved from experimental status to prototypes successfully applied to assays, sensors and separation problems.

Conclusion

Biotech 2011 brought together experts from different areas to share their views about applications of and research on sensor technology. The high proportion of participants from industry confirmed that this topic is not just of academic interest. In this respect, the conference contributed to intensifying the interaction between research and application.

Further information on Biotech 2011 can be found on the conference website (www.biotech2011.ch). The next Biotech conference is scheduled for June 2013, with a special emphasis on single-use devices in biopharma production.

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