Biochemical

INNOVATIVE SENSOR TECHNOLOGY

Focus on Biosensors

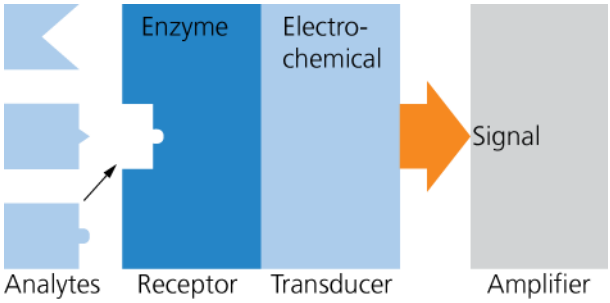
Biosensors – a new Sensor Type from IST AG

What are Biosensors?

A biosensor is a device capable of detecting a certain substance or analyte with high specificity. Examples of such analytes are glucose, lactate, glutamine and glutamate. Most biosensors measure the concentration of an analyte in an aqueous solution, usually producing an electrical signal, which is proportional to the analyte's concentration in its measuring range.

An enzymatic biosensor comprises an enzyme, which recognizes and reacts with the target analyte generating a chemical signal, a transducer, which produces a physical signal out of that chemical one, and an electronic amplifier, which conditions and amplifies the signal.

Biosensors allow the analysis in complex biological media. The detection of a large number of compounds is of great relevance not only for scientific research but also for process control in the chemical and food industry. It is also indispensable in the health care field for the diagnosis and treatment of diseases and monitoring of illnesses. The pharmaceutical and biotechnology industries greatly desire frequent to continuous analysis of biological media.



General structure of a biosensor. Sensors by IST AG use enzymes to detect glucose, lactate, glutamine and glutamate. The transducer principle is electrochemical, producing a current as output signal (amperometric).

Such analyses are conducted with the aid of analytical instruments like HPLC systems, which, although robust and reliable, are expensive and have a limited suitability for online operation. For this reason, the acquisition of Jobst Technologies GmbH positions IST AG as a key provider of high-performance and reliable online biosensors.

Enzymatic Biosensors for Metabolic Parameters

Back in the early 1960's Clark and Lyons introduced the first glucose sensor using an enzyme (glucose oxidase, GOx) as receptor, this enzyme being specific for glucose. Enzymes enable the highly specific measurement of their corresponding analyte even in complex mixtures like fermentation broth and blood; it is like finding a needle in a haystack.

Analytes such as glucose, lactate, glutamine and glutamate play an important role in the metabolism of living organisms. Glucose and glutamine support the cell function and growth; lactate is produced by cells and allows judging the efficiency of the cells metabolism; and glutamate is an amino acid consumed by cells. Each of these analytes requires a specific set of enzymes for its detection.

The continuous (on-line) monitoring of the concentration of such parameters enables among numerous others

- the generation, optimization and control of feeding strategies in cell cultures
- the minimization of patients' risks during surgery and intensive care
- on-site analysis of food processes

Presentations at the Biotechnica by Gerhard Jobst:

- Miniaturized analytical systems for bio/medical monitoring (Tuesday, 6th October / 3:30 - 4:00 pm / Hall 9 Booth C55)
- Biosensors for reliable monitoring (Wednesday, 7th October / 3:45 - 4:05 pm / Hall 9 Booth F51)

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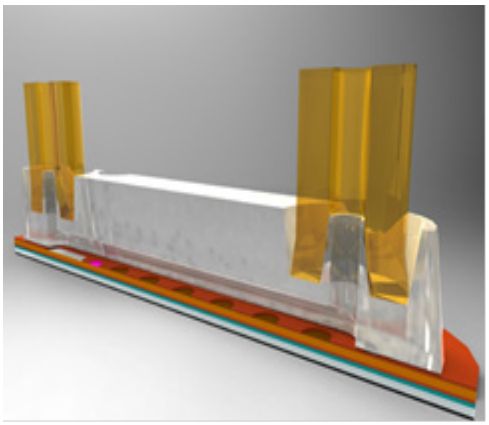
Versatile Sensors

Jobst Technologies GmbH has decades of experience in enzymatic biosensors. Enzymes are immobilized in a stack of four permeable polymeric membranes on top of platinum micro-electrodes, which pick up an electrical current originating from the enzymatic reaction. The superior membrane technology by Jobst Technologies allows for easy tuning of performance parameters like sensitivity, measurement range and response time. Moreover, this technology is compatible with sterilization by irradiation (gamma, beta). All this makes our biosensors suitable for a large variety of applications.



Cross section of a flow-through LV5 biosensor featuring a flow-through cell for measuring of glucose, lactate, glutamine and glutamate

Thanks to the small size of the electrodes, a single chip can hold several electrodes. The array sensor LV5 from Jobst Technologies features up to 6 sensitive electrodes where glucose, lactate, glutamine and glutamate can be detected simultaneously. Very small liquid samples can be analyzed as they flow through its 1-µL flow cell, thus being suitable for offline analysis as well as for online operation.

Last but not least, each sensor is factory calibrated and marked in an automated process providing full traceability making it ideal for ready-to-use and single-use applications.

Biomedical Application – A new Landmark Product: EIRUS

Optimal treatment of critically ill patients requires the continuous surveillance of their blood values. Recently, a world-leading provider of medical systems for hospitals, Maquet Critical Care, has been setting a new standard by introducing the EIRUS platform specifically developed to provide continuous monitoring of both glucose and lactate in critically ill patients. In addition to optimizing patient care quality, it reduces nurses workload compared to frequent intermittent blood analysis. This system relies on micro-dialysis technology that feeds a flow-through sensor developed and manufactured in Freiburg (Germany) by Jobst Technologies GmbH.

EIRUS system by Maquet for continuous monitoring of glucose and lactate in intensive care patients. Copyright: Maquet Critical Care

During several days of continuous operation, EIRUS reports glucose and lactate blood levels every minute and raises alerts whenever the values fall outside the preset ranges. This enables the rapid assessment of the patient's glycemic condition, which in turn ensures for prompt and swift glucose management with insulin. Tighter glycemic control benefits not only diabetic patients but has been shown to improve outcome also in non-diabetic critical care patients who frequently display a condition called 'stress diabetes'.

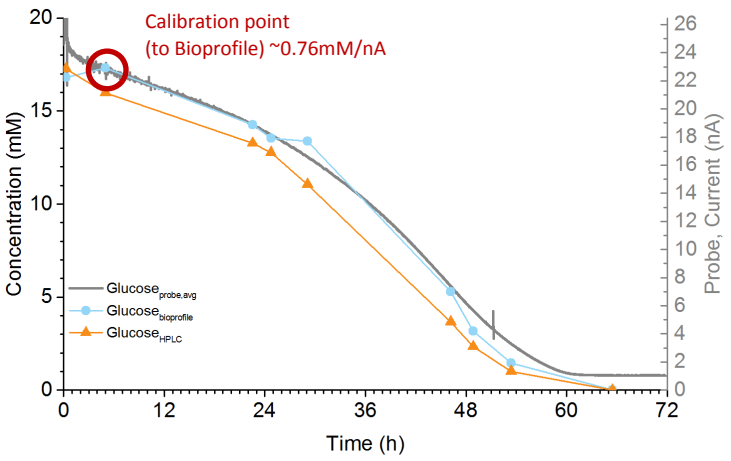
Elevated lactate levels (hyperlactatemia) are an indicator of increased morbidity and mortality. Monitoring of lactate enables an early and continuous risk assessment, diagnosis and therapy minimizing patients' risks.

Focus on Biosensors

Biosensors – Their Application in Biotechnology

Nowadays cell cultures aid in the development of new drug and medication. Animal cells are engineered to express proteins and antibodies used in the treatment of several illness and conditions. In order to maximize yield and product quality, conditions of cell cultures must meet optimal values. Monitoring of nutrients, like glucose, plays a vital role in the feeding strategy of a cell culture. One type of glucose sensors used in biotechnology requires a fluidic-dilution stage that has to be outside the culture vessel. Such systems show problems like large latency due to the transit time through the dilution stage; more footprint since an external analyzer is required; contamination risk because it is necessary to invasively take samples inside the bioreactor and dealing with the dead volume in the tubes. Other sensors cannot survive prolonged shelf storage after sterilization by irradiation. The technology developed by IST AG and Jobst Technologies allows for continuous glucose monitoring either inside the culturing vessel or by means of a probing system.

A Chinese-hamster-ovary (CHO) cell line was used for a batch[1] culture in a conventional glass bioreactor. The glucose concentration was continuously monitored for several days. For the control measurements a Nova Bioprofile Analyzer and a HPLC system were used. Due to their robustness, sensors can be gamma irradiated and stored before utilization. Sensors are precalibrated; however a single calibration at start provides increased accuracy throughout the entire cultivation lasting days. During this time, a measurement point is acquired every second without requiring any manual work as the used reference systems do.



Comparison of glucose values during batch culture

Acknowledgment

Special thanks to Dr. Caspar Demuth, Dr. Iris Poggendorf, Fabienne Seiler and Irène Stutz from the Zurich University of Applied Sciences (Institute for Biotechnology, Wädenswil, Switzerland) for carrying out the cultivation and providing us with the data.

[1] In a batch culture, the nutrient medium has starting glucose concentration and no further nutrient feeding is performed.

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