STUDIENBRIEF

Biochemical Sensors

Modul 4.4

Im Studiengang Biopharmazeutisch-Medizintechnische Wissenschaften (Master of Science)

Dott. Alberto Pasquarelli
Institut für Elektronische Bauelemente und Schaltungen
Fakultät für Ingenieurwissenschaften, Informatik und Psychologie
Universität Ulm

Modulinhalte

Modulnummer	4.4
Modultitel	**Biochemical Sensors / Biochemische Sensoren**
Modulkürzel	BioS
Studiengang	Biopharmazeutisch-Medizintechnische Wissenschaften (M.Sc.)
Ort der Veranstaltung	Universität Ulm
Modulverantwortlichkeit	**Dott. Alberto Pasquarelli**
Lehrende	Dott. Alberto Pasquarelli
Voraussetzungen	Grundlagenkenntnisse in Chemie und Biochemie sind erwünscht
Verwertbarkeit	Das Modul komplettiert die in Modul 4.3 "Bioanalytical Methods" und in Modul 3.2a "Methoden der Molekularbiologie: Anwendungsbeispiele" zu erwerbenden Kenntnisse mit speziellem Blick auf die Sensorik. Es werden Grundlagen, Wirkweisen und Anwendungsbereiche von Biosensoren und die Befähigung, eigenständig Sensorkonzepte zu entwerfen, vermittelt.
Semester (empfohlen)	Wintersemester (1 o. 2)
Max. Teilnehmerzahl	25
Art der Veranstaltung	☐Präsenzveranstaltung(en) ☒Präsenzveranstaltung(en) mit E-Learning-Elementen ☐Präsenzveranstaltung(en) im Labor mit E-Learning-Elementen ☐reine E-Learning-Veranstaltung(en)
Veranstaltungssprache	☐Deutsch, ☒Englisch, ☐Weitere, nämlich:
ECTS-Credits	6 Credits
Prüfungsform und –umfang	☒Klausur, ☐Referat, ☐Kolloquium, ☐Posterpräsentation, ☐Podiumsdiskussion, ☐Mündliche Einzel-/ Gruppenprüfungen, ☐Essay, ☐Forumsbeitrag, ☐Übungen, ☐Wissenschaftspraktische Tätigkeit, ☐Bachelor- und Masterarbeit ☒Haus-/ Seminararbeit, ☒Einzel-/Gruppenpräsentation, ☐Portfolio, ☐Protokoll, ☐Projektarbeit, ☐Lerntagebuch/ Lernjournale <u>Umfang der Prüfung:</u> 120 min Klausur. Um an der Prüfung teilzunehmen, müssen folgende Prüfungsvorleistungen erbracht werden: 1) Ein vorlesungsbegleitender Vortrag von 15 min 2) Auswertung der Daten aus den Laborversuchen (Hausaufgabe)
Lernziele	**Fachkompetenz**

	Students can describe basic principles, mechanisms of action and applications of biosensors in different scenarios. After taking this module, participants are able to explain the chemical and physical fundamentals of biosensing. Students asses the clinical and industrial applications, differentiate biosensor market sectors regarding technical and economical properties, e.g. commodities for everyday consumer needs or professional equipment for research. **Methodenkompetenz** Students are further able to analyze biosensors, break-down complex sensors in their elementary components and identify and evaluate every individual function in the information flow, from recognition to transduction and transmission. Students are capable of predicting the effects of elementary components in an integrated biosensor application. **Selbst- und Sozialkompetenz** Furthermore, students are able to reflect and critically analyze research in the field of biosensors. Finally, students are capable of developing appropriate concepts and designs for given biosensing problems in industry and academia. They are further able to independently derive original solutions for new problems.
Lehrinhalte	- Introduction to biosensors - Review of the basics of chemistry and molecular biology - Biological detection methods: catalytic, immunologic, etc. - Physical transduction methods: electrochemical, optical, gravimetric, etc. - Immobilization techniques: adsorption, entrapment, cross-linking, covalent bonds - Biochip technologies: DNA and protein chips, Ion-channel devices, MEA and MTA, Implants - Student seminars - Laboratory practice with experimental demonstrations and quantitative determinations of analytes
Literatur	- Marks R.S. et al., Handbook of Biosensors and Biochips, Wiley, 2007 - Alberts B., Molecular Biology of the Cell 5th ed., Garland Science, 2008 - Gizeli E. and Lowe C.R., Biomolecular Sensors, Taylor & Francis, 2002 - Renneberg R. et al., Biosensing for the 21st Century, Springer 2007 - Orellana G and Cruz Moreno-Bondi M., Frontiers in Chemical Sensors, Springer, 2006

	- Homola J., Surface Plasmon Resonance Based Sensors, Springer, 2006 - Hierlemann A., Integrated Chemical Microsensor Systems in CMOS Technology, Springer, 2006 - Steinem C. and Janshoff A., Piezoelectric Sensors, Springer, 2007 - Jay J. M. et al., Modern Food Microbiology, Springer, 2008 - Morrison D. et al., Defense against Bioterror, Springer, 2007 - Willner I. and Katz E., Bioelectronics, Wiley, 2005

Inhaltsverzeichnis

1

Introduction

In this chapter, you will gain an overview over the functions of biosensors and the history behind their development, as well as various types and their properties. Furthermore, you will learn about the meaning and potential of these sensors alongside their most important usages. You will then be able to explain the advantages upon usage of biosensors, name various application fields, and make statements about the development of biosensors.

1.1 Biosensors

A biosensor is an analytical device which converts a biological response into an electrical signal. Nevertheless, the term 'biosensor' is also often used when a sensor device is used to measure biological parameters, even if it does not itself contain biological receptors.

Bioreceptors are generally very specific and tailored to a particular application.

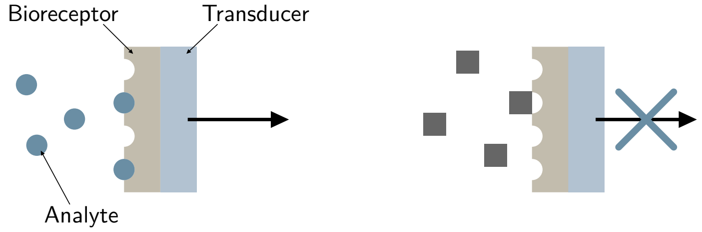

Fig. 1.1: Signal with selective bioreceptor: If the analyte matches the bioreceptor, a signal is generated (left). On the other hand, a non-matching analyte does not produce a signal at the output (right).

A biosensor system generally consists of

a) Bioreceptor
b) Transducer, delivers an electrical current (e. g. electrodes)
c) Signal conditioning (amplifier, filter etc.)
d) Computer unit for data acquisition
e) Display and storage system

1

The Development of Biosensors

1

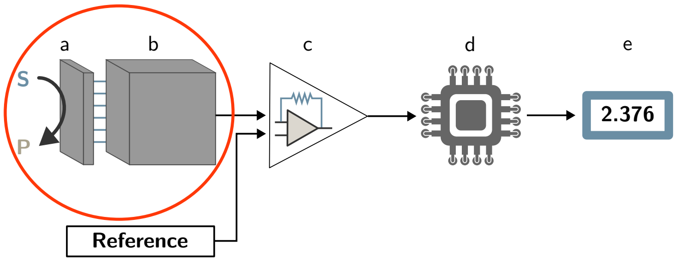

Fig. 1.2: The biosensor system: This lecture focuses primarily on components (a), the bioreceptor system, and (b), the physical transducer, (circled in red)

What is a biosensor? What components typically make up a biosensor system?

1.2 The Development of Biosensors

Advantages and applications of biosensors

Biosensors combine the selectivity of biology with the processing power of modern microelectronics, providing us with powerful diagnostic tools. Ideally, biosensors should enable better measurements and analysis compared to traditional analytical methods.

Advantages of Biosensors:
- Require smaller sample sizes
- Sensitive, selective, and specific
- Easier to use
- Faster procedures
- Cost effective
- Allow online monitoring

Areas of application:
- Medicine (e. g. clinical diagnostic)
- Pharmaceutical drug analysis
- Industrial processes
- Food quality control
- Environmental monitoring
- Monitoring of biological and chemical threats (terror attacks or warfare agents)

Milestones in the development of biosensors
- 1956 – L.D. Clark developed the oxygen electrode. 6 years later, he proposed the enzyme electrode by entrapping the enzyme glucose oxidase at an oxygen electrode using dialysis membrane.
- 1969 – Guilbault and Montalvo reported the first potentiometric biosensor, a urea sensor based on urease.

2

- 1972/1975 – *Yellow Springs* launched the first commercial glucose analyzer based on Clark's ideas.
- 1974 – Mosbach proposed to use of enzymes with thermal transducers for biosensors.
- 1975 – Divis suggested the use of bacteria as biosensitive element for measurement of alcohol. Lubbers and Opitz describde the first optical biosensor, a functionalized fibre-optic sensor with immobilized indicator (optode).
- 1976 – Clemens et al. incorporated a glucose biosensor in a bedside artificial pancreas. *Roche* introduced the Lactate Analyser LA 640, using hexacyanoferrate as mediator for the electrons transfer.
- 1982 – Shichiri et al. described the first needle-type glucose biosensors for subcutaneous implantation.
- 1983 – Liedberg described real-time monitoring of affinity reactions by "surface plasmon resonance" (SPR).
- 1984 – Ferrocene was introduced as an immobilised mediator for use with oxidoreductases in the construction of inexpensive devices, leading to the screen-printed enzyme electrodes launched by *MediSense* in 1987, for home blood-glucose monitoring. *MediSense*'s sales grew exponentially, reaching US$ 175 million by 1996 when *Abbott* purchased them. *Roche Diagnostics* (formerly *Boehringer Mannheim*) and *Bayer* now have similar biosensors and these three companies dominate 85 % of the world market for biosensors home diagnostics.
- 1990 – *Pharmacia* launched the BIAcore, based on SPR (*GE-Healthcare* aquired BIAcore in 2006).

Academic journals now contain descriptions of a myriad of devices which combines a huge variety of bioreceptors and transducer technologies. The present focus is on methods to improve the sensitivity, selectivity, stability, and costs of biosensors.

Name some advantages and fields of application for biosensors.

1.3 Biosensor Components

A biosensor is normally made up of three components:

Components of a biosensor

- Biological component (bioreceptor): enzymes, microorganisms, antibodies, proteins, DNA arrays, chemoreceptors, tissues, or organelles
- Physical component (transducer/converter): amperometric, potentiometric, semiconductor, thermometric, photometric, or piezoelectric
- Interfacial component (polymeric thick- or thin-film, chemically modified surface) as connection between the two other components

Biosensor Components 1

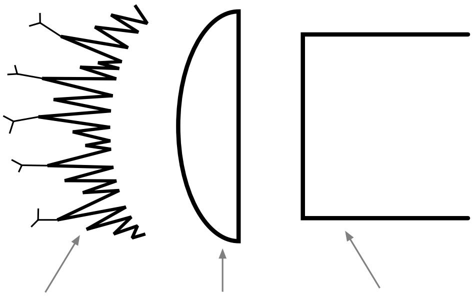

Fig. 1.3: The three fundamental components of a typical biosensor

1.3.1 Biological Component

The biological component reacts or interacts with the specific substances to detect. We divide the biological component into two groups: **catalytic** elements and **non-catalytic** elements. Enzymes, microorganisms, and tissues belong to the first group, whereas antibodies, membrane receptors, nucleic acids, and synthetic receptors belong to the second group.

Enzymes are proteins that recognize a substrate molecule and accelerate its conversion to the product molecule through a chemical reaction (catalysis, acceleration up to 10^{14}) without influencing the reaction equilibrium. The signal is either measured indirectly, for instance via the change of Oxygen pressure, pH, H_2O_2, color, temperature etc., or directly through electron transfer of the redox enzymes (see figure below).

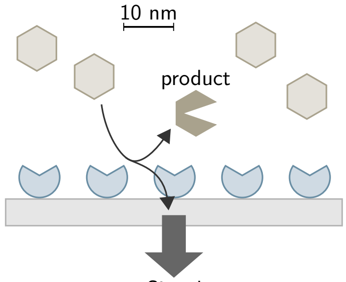

Fig. 1.4: Catalysis through enzymes and delivery of a signal

Antibodies are proteins as well (Immunoassay):

- They are y-shaped immunoglobulin with a specific binding site (Fab).
- They are produced as natural recognition molecules by the immune system of a body.

4

- They are able to bind several antigens (viruses, microbes),
- The signal output is gravimetric, optic, etc.

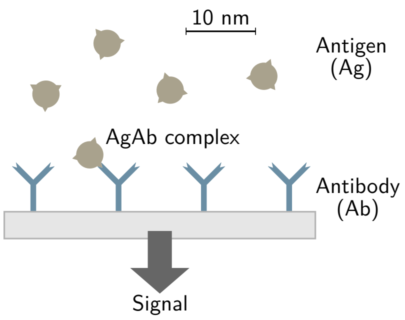

Fig. 1.5: Antibody-antigen bonding

What is the function of the biological component of a biosensor? Which categorization do you know for this component?

1.3.2 Physical Component

The physical component converts the biochemical reaction or interaction into a quantifiable and processable electrical signal. This can be a simple electrochemical device or a complex, multitechnological instrument. The signal conversion can be based on various methods:

- pH-metric
- amperometric
- potentiometric
- calorimetric
- thermal
- optical
- gravimetric
- etc.

1.3.3 Interfacial Component

The interfacial component links the biological component with the transducer. It can be used to immobilize the bioreceptor. Furthermore, it can have a selective or protective function (e. g. a thin film membrane) for the cases of labile, toxic or corrosive substances, or to prevent signal errors. Examples are membranes, conductive polymers, gel matrices, or self-assembled monolayer (SAM) of cross-linkers.

The following figure shows the structure of a glucose biosensor as a classic example of the interaction of the three components in a biosensor.

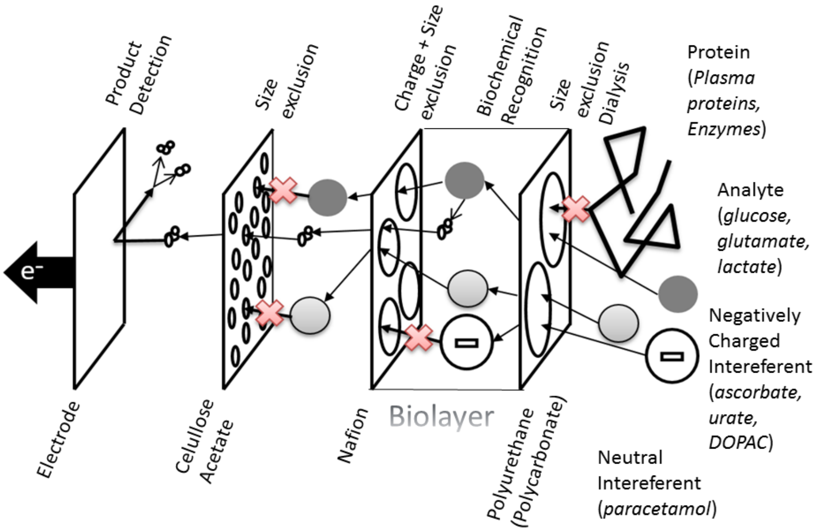

Fig. 1.6: Structure of a glucose biosensor

Which methods do you know for signal conversion of the physical components?

1.4 Biosensors Significance and its Market Potential

Significance and market potential of biosensors

Biosensors have the potential to impact many areas. The main fields of application include medicine, environmental monitoring, food-quality control, and control of industrial processes, but also physical therapy, music, and the video game industry, can all potentially benefit from the introduction of biosensors.

Blood glucose sensing for diabetics plays a central role in supporting biosensor research and successful commercialization. Diabetes market is by far the largest biosensor market, because no other disease or illness combines the two requirements for mass monitoring: affliction of a large population (2 % on world-wide average, but in some countries up to 6 %) coupled with the need for frequent (on average 2 – 4 times per day) recording of clinical data (i. e. blood glucose concentration).

For comparison, one requires only one cholesterol measurement per week or even per month, although a large proportion of the population needs it.

The development of biosensors over the last 40 years begins with the development of the biosensor concept as a simple, specific, robust, cost-effective, portable and easy-to-use technology. Throughout the first generation, the focus has been on integration, sensor

Beratung und Kontakt

Ansprechpartner

School of Advanced Professional Studies
saps@uni-ulm.de
www.uni-ulm.de/saps

Tel +49 731/50-32401
Fax +49 731/50-32409

Geschäftsführende Direktorin: Prof. Dr. Tina Seufert

Studiengangskoordinator

- Studiengang Biopharmazeutisch-Medizintechnische Wissenschaften: Lena Harsch (bm-wiss@hochschule-bc.de)
- Studiengang Sensorsystemtechnik: Steffen Moser

Postanschrift

Universität Ulm
School of Advanced Professional Studies
Lise-Meitner-Straße 16
89081 Ulm

Gefördert vom Ministerium für Soziales und Integration Baden-Württemberg aus Mitteln des Europäischen Sozialfonds sowie vom Ministerium für Wissenschaft, Forschung und Kunst Baden-Württemberg.

ESF
Chancen fördern
EUROPÄISCHER SOZIALFONDS IN BADEN-WÜRTTEMBERG
www.esf-bw.de

Gefördert vom
Baden-Württemberg
MINISTERIUM FÜR WISSENSCHAFT, FORSCHUNG UND KUNST

EUROPÄISCHE UNION