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Electrochemical biosensors-A Review

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Abstract

A biosensor typically consists of a bio-recognition component, biotransducer component, and electronic system which include a signal amplifier, processor, and display. Over the past decades several sensing concepts and related devices have been developed. In this review, the most common traditional techniques, such as cyclic voltammetry, chronoamperometry, chronopotentiometry, impedance spectroscopy, and various field-effect transistor based methods are presented along with selected promising novel approaches, such as nanowire or magnetic nanoparticle-based biosensing. In particular, this review highlights the importance of the precise control over the delicate interplay between surface nano-architectures, surface functionalization and the chosen sensor transducer principle, as well as the usefulness of complementary characterization tools to interpret and to optimize the sensor response.

Keywords: cyclic voltammetry, chronoamperometry, chronopotentiometry, biosensors, bioelectronics.

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1.0 Introduction

Biosensor-related research has experienced explosive growth over the last two decades. A biosensor is generally defined as an analytical device which converts a biological response into a quantifiable and processable signal [1]. Figure 1 shows schematically the parts comprising a typical biosensor: a) bioreceptors that specifically bind to the analyte; b) an interface architecture where a specific biological event takes place and gives rise to a signal picked up by c) the transducer element; the transducer signal (which could be anything from the in-coupling angle of a laser beam to the current produced at an electrode) is converted to an electronic signal and amplified by a detector circuit using the appropriate reference and sent for processing by, e.g., d) computer software to be converted to a meaningful physical parameter describing the process being investigated; finally, the resulting quantity has to be presented through e) an interface to the human operator. Biosensors can be applied to a large variety of samples including body fluids, food samples, cell cultures and be used to analyze environmental samples.

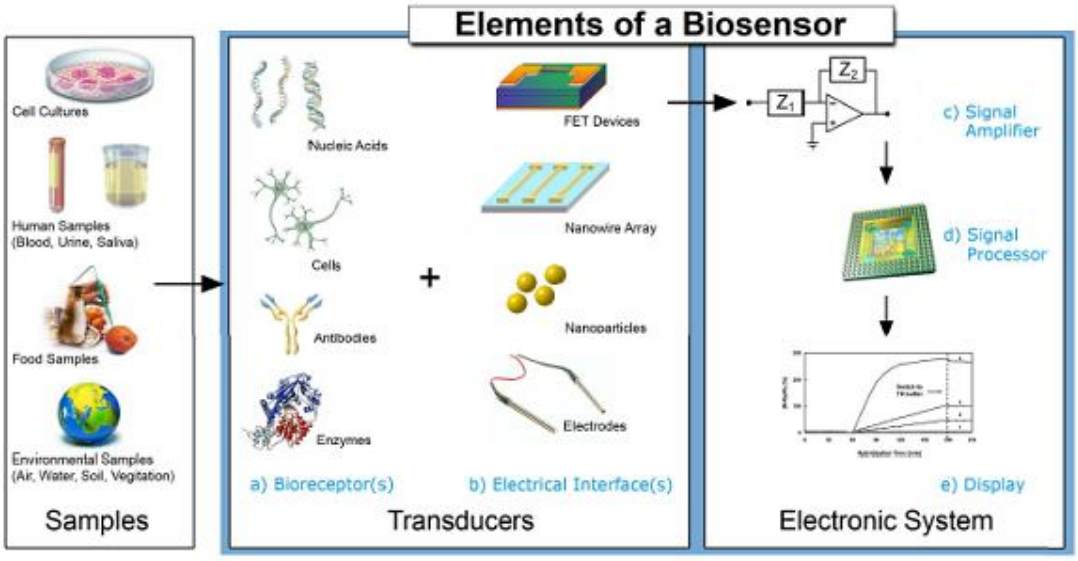

Figure-1: Elements and selected components of biosensor [1-3]

In order to construct a successful biosensor for the non-specialist market a number of conditions must be met:

1. The biocatalyst must be highly specific for the purpose of the analysis, be stable under normal storage conditions and show a low variation between assays.
2. The reaction should be as independent as manageable of such physical parameters as stirring, pH and temperature. This will allow analysis of samples with minimal pre-treatment. If the reaction involves cofactors or coenzymes these should, preferably, also be co-immobilized with the enzyme.
3. The response should be accurate, precise, reproducible and linear over the concentration range of interest, without dilution or concentration. It should also be free from electrical or other transducer induced noise.
4. If the biosensor is to be used for invasive monitoring in clinical situations, the probe must be tiny and biocompatible, having no toxic or antigenic effects. Furthermore, the biosensor should not be prone to inactivation or proteolysis.
5. For rapid measurements of analytes from human samples it is desirable that the biosensor can provide real-time analysis.

6. The complete biosensor should be cheap, small, portable and capable of being used by semi-skilled operators.

Designed for the purpose, biosensors are generally highly selective due to the possibility to tailor the specific interaction of compounds by immobilizing biological recognition elements on the sensor substrate that have a specific binding affinity to the desired molecule [4]. Typical recognition elements used in biosensors are: enzymes, nucleic acids, antibodies, whole cells, and receptors. Of these, enzymes are among the most common [3]. To fully exploit the specific interaction through biorecognition, the surface architecture of the sensor also must suppress any non-specific interaction. A tremendous research effort has been invested to find surface modifications with specific interaction capabilities over prolonged periods of time in biological fluids [5]. Today, a multitude of instruments referred to as biosensors can be found in labs around the world and there is a growing number of biosensors being used as diagnostic tools in point-of-care testing, but the realization of cheap handheld devices is almost limited to one well-known example: the glucose sensor [6]. In many cases the main limitation in realizing point-of-care testing/sensing devices is the ability to miniaturize the transduction principle and the lack of a cost-effective production method. Thus, they have to be confined to expert users of high-cost equipment in a lab environment and cannot be used e.g.by patients themselves or doctors in the field. The whole area of biosensors started with the introduction of the first generation glucose oxidase (GOx) biosensor in 1962 [7]. The GOx sensor is still the most widely used, although many improvements (generations) have been added since the 1960's [8]. As exemplified by the glucose sensor, electrochemical biosensors do not suffer the drawback of high sensor setup complexity and cost. This is due to their close link to developments in low-cost production of microelectronic circuits and their easy interface with normal electronic read-out and processing. Other inherent advantages of electrochemical biosensors are their robustness, easy miniaturization, excellent detection limits, also with small analyte volumes, and ability to be used in turbid biofluids with optically absorbing and fluorescing compounds [9, 10]. However, several aspects could be considered to have held back the emergence of additional breakthrough applications built on electrochemical biosensing. Electrochemical biosensors have suffered from a lack of surface architectures allowing high enough sensitivity and unique identification of the response with the desired biochemical event. For example, pH and ionic strength in biofluids can differ significantly, which affects the response of important classes of biosensors such as immunosensors [10]. Thus, there has recently been an increased emphasis on using nanotechnology to shrink the dimensions of electrochemical sensor elements to sizes which can increase the signal-to-noise ratio for processes designed to occur at the interface of the device and to find ways of using, e.g., multiple enzymatic labels to increase the signal per event. The combination of knowledge in bio- and electrochemistry, solid-state and surface physics, bioengineering, integrated circuit silicon technology and data processing offers the possibility of a new generation of highly specific, sensitive, selective and reliable micro (bio-)chemical sensors and sensor arrays addressing these remaining issues [11]. It is thus timely to summarize recent progress in this diverse field and to discuss its future prospects for development. After introducing the many incarnations of electrochemical biosensors this review will discuss how electrochemistry has been and can be combined with complementary sensor techniques to enhance data interpretation. The latter we believe to be very important to optimize given biosensor designs and also for the increased use of electrochemical sensors to characterize biointerfaces. Emerging devices for electrochemical biosensors inspired by advances in microelectronics and

nanotechnology like the biofield effect transistors, nanowires and other ”near-molecular scale devices” will be introduced. The last part of the review will address surface architectures and modifications used in electrochemical biosensors to improve on sensitivity and biospecificity, as well as discuss the emergence of new devices from the multi-disciplinary field where nanotechnology, material science and biology converge.

Devices

Biosensor-related publications were sparse in the early 20th century. The early era of biosensing research and development was first sparked with the defining paper by Clark [12, 13] and his invention of the oxygen electrode in 1955/56. The subsequent modification of the oxygen electrode led up to another publication in 1962 [7], which reported the development of the first glucose sensor and the enhancement of electrochemical sensors (e.g. polarographic, potentiometric and conductometric) with enzyme-based transducers. Clark’s work and the subsequent transfer of his technology to Yellow Spring Instrument Company led to the successful commercial launch of the first dedicated glucose biosensor in 1975 [14]. Since then, various forms of glucose biosensors have been developed, as well as many other sensing technologies and biosensing devices. This section attempts to describe operating principles of electrochemically-based biosensors by reviewing representative devices and their techniques from the aforementioned categories. Although the general topic of this review is electrochemical biosensing devices, a detailed overview is given in this section of various combinations of electrochemical sensing with other well-established sensing techniques and biosensor devices. Therefore, special attention is given to aspects of complementarity techniques and their advantage of independent, simultaneous measurements with (bio-) electrochemistry.

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