

Advances in Electrochemical Sensors and Biosensors

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The dynamic development of technology, consumer expectations, legal requirements, quality assurance and health safety systems create the need to develop new, highly selective and, at the same time, simple analytical tools. These are sensors, which constantly constitute a huge research area.

According to the nomenclature of the International Union of Pure and Applied Chemistry (IUPAC), a chemical sensor is a device that converts a chemical information into an analytically useful signal. The chemical information mentioned above may come from a chemical reaction: receptor—analyte recognition or the physical properties of the tested system. The sensor consists of two basic functional elements: the analytically active layer and the transducer element. In the analytically active layer, the process of intermolecular recognition (receptor—analyte) takes place. During this process, a chemical or physico-chemical signal is generated. The transducer is the part of the sensor where this signal is converted into an analytical signal. The used biological element selectively reacts with the tested substance, giving—by means of a transducer—a measurable signal [1].

Biological sensors containing biological receptors in the analytically active layer are called biosensors. In the receptor layer of the biosensor, biological molecules such as enzymes, nucleic acids, antibodies, lipids, tissues, microorganisms, etc. are employed as specific coatings molecules for detection of various analytes. They monitor the progress of biomolecular processes, such as: nucleic acid hybridization or cellular communication processes, enzymatic interactions, antibody—antigen interactions or nucleic acids—proteins interactions [2,3].

Several types of transducers were used in the development of (bio)sensors. One of the most popular is the electrochemical one. Its working principles are based on the electrochemical properties of the converter and the analyte. In this type of (bio)sensor, an electrochemical reaction takes place on the surface of the transducer between the bioreceptor and the analyte, generating registerable electrochemical signals of impedance, capacity, current or voltage. A lot of different substrates can act as a transducer, e.g., conductive electrodes (e.g., made of noble metals and carbon), glass, hydrogels, polymers or paper [3,4].

The interest in electrochemical (bio)sensors is still growing. They represent the highest percentage of all chemical sensors. Currently, they dominate the market, because the production of such sensors is cheaper. They constitute an inherent part of our daily lives. These devices are widely used due to their user-friendliness, ease of miniaturization, high sensitivity and selectivity, simplicity, speed of analysis, low cost, capability to multianalyte determination, compatibility with advanced microfabrication technology and portability and straightforward instrumentation. The most commonly used electrochemical techniques in (bio)sensing are cyclic voltammetry, square wave voltammetry and differential pulse voltammetry or electrochemical impedance spectroscopy.

The development of the (bio)sensor comprises both the immobilization of the receptor itself and the general chemical preparation of the surface of the transducer. Therefore, the sensitivity and specificity of such devices are directly related to the type, availability and activity of the attached molecules. The working principle of the (bio)sensors is based on the specific recognition of the material in contact with the modified transducer.



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The ability of the (bio)sensor to selectively capture analytes is highly dependent on the quality of the analytically active layer and its functionality.

The construction of a (bio)sensor requires the selection of an appropriate receptor element and compatible with an electrochemical converter. An important design stage is also the selection of the appropriate process of immobilization of molecules on the transducer. The measurement parameters of the system should be verified and adapted to the intended function of the device. (Bio)sensors are used in research analyses due to the wide possibilities of modification, high sensitivity, mobility and often the possibility of conducting continuous measurements with their participation in real time [4,5].

The (bio)sensor can be coated with virtually any material, if it can be deployed as a thin (nm range), homogeneous layer stably deposited on the substrate.

Each (bio)sensor should have specific characteristics such as calibration, drift, high resolution, linearity, sensitivity, selectivity, stability, range, repeatability, reproducibility, and response time.

The main challenges related to the development of electrochemical (bio)sensors concern:

- Efficiently converting signals recorded in receptor-analyte intermolecular recognition processes into electrochemical signals;
- Improving the performance of the transducer by increasing the sensitivity, selectivity and reproducibility;
- Shortening the response time, and lowering the limits of detection (determination of an ultra-low concentrations of analytes);
- Miniaturization of the devices using micro- and nano-production technologies. [6]

These challenges can be overcome by using signal amplification strategies. One of them can be the usage of nanomaterials, which increases effective surface of the modified transducer. The integration of (bio)sensor technology with nanomaterials that have a high surface to volume ratio, good conductivity and shock resistance is fundamental task in the design of a variety of high-performance (bio)sensors, especially for the detection of single molecules. Nanomaterials display unique features e.g., high conductivity, compatibility, high surface-to-volume ratio, chemical steadiness, or high mechanical strength, and for these causes they have a use for broad purpose in the (bio)sensing field. Based on these properties, The application of nanomaterials has had a huge impact on the development of electrochemical (bio)sensors. They can act as electrode materials, carriers, markers, separators, or catalysts etc., resulting in significant signal amplification. In addition, multiple amplification strategies that employ two or more types of nanomaterials and amplification methods can further improve the analytical performance of the device [7]. They are used in the construction of (bio)sensors in various forms including core-shell, mesoporous, nanosheets, nanofibers, nanotubes, nanoparticles, nanorods, nanowires and quantum dots [8]. In recent decades, significant advances have been made in the synthesis of nanomaterials with controlled morphology, dimensions, physicochemical properties and surface charges. With the advent of cheaper and cheaper signal amplification technologies, the development of (bio)sensors using nanomaterials has become very attractive [9]. To improve and enhance the performance of the (bio)sensor, the following nanomaterials have been applied to modify the (bio)sensing platforms: noble metal, carbon (graphene, graphene oxide, carbon nanotubes, fullerenes, etc.), carbon-metal nanocomposites, TiO₂-supported nanomaterials, ionic liquids nanocomposites or conductive polymers [10]. From a long-term perspective, nanomaterials, will play a key role in the construction of high-performance electrochemical (bio)sensing [11].

Despite rapidly developing signal amplification strategies with using nanomaterials, there are still many challenges to overcome in (bio)sensing in terms of:

- Gentle methods of producing monodisperse nanomaterials;
- Methods excluding non-specific adsorption of coexisting molecules on nanomaterials in a complex matrix;

- Controlled synthesis of nanomaterials with repetitive structure and physicochemical features in different batches.

Increasing the analytical signal of a given (bio)sensor can be achieved not only with the application of appropriate nanomaterials, but also with the use of mechanisms classified as enzyme-based amplification (catalytic redox cycling), or DNA-based amplification (rolling-cycle, hybridization chain reaction) [12].

The electrochemical (bio)sensing can successfully compete with other analytical methods currently used. It has more benefits compared to them mainly by reason of their low cost, quickness, and portability. In addition, this type of research is conducted in real time. It can be a fully automated method that allows to selective analysis even several substances at the same time. Simultaneous determination of different analytes not only speeds up the analysis, but also generates a reduction in reagents and material consumption. Due to the user-friendliness and the wide variety of electroanalytical (bio)sensors, such devices are anticipated to be the next generation of analytical systems. Important aspect of (bio)sensors fabrication is their miniaturization. Electrochemical methods facilitate these processes thanks to advances in microelectronics, the production of microelectrodes and portability of potentiostat. Therefore, they are the most promising substitute for traditional methods [13]. Miniaturized (bio)sensors afford many advantages over traditional ones. The major benefits concern less reagent consumption, simultaneous measurement of several samples, environmental manipulation, mergence of various separate elements on a common substrate, or the capability to precise control the automatization system. In (bio)sensor technology, the miniaturization of the set-up also roots out some drawbacks, such as electrical distortions, uneven pH layout, non-uniform application of electrical disturbances by controlling spatio-temporal changes. However, the process of miniaturization of (bio)sensors has some drawbacks at the same time: the fabrication technology is quite difficult, requires expensive equipment, optimization is time-consuming, and the preparation of these sensors takes a long time too due to the several steps involved. On the other hand, portability and cost-effectiveness could lead these systems to commercialization and wide use in many areas of everyday human life. Undoubtedly, further research is needed to develop the miniaturization of (bio)sensors and thus design highly efficient portable tools [14]. Some devices have been successfully implemented and are available commercially. However, many of them need to be improved in order to hit the market. It depends on their accuracy, reliability, price, as well as the time-consuming nature of individual analyses, etc. [15].

Electrochemical (bio)sensors are up-and-coming analytical tools applicable in all areas, where prompt and righteous analyses are essential. The field of applications for which electrochemical (bio)sensors are employed and/or under development is perspective.

Overall, with technological advances, electrochemical (bio)sensing has evolved over the years into a broad, transdisciplinary branch, offering great opportunities for practical applications in various areas of life [4].

Advancements in (bio)sensor technology are acquiring importance because of a wide range of applications, as follows: medical purposes, environmental research, applications in the agri-food industry, and defense. (Bio)sensors used in medicine and diagnostics constitute the largest part of this market. They have been employed to detect electrolytes, lactates, glucose, cholesterol, hormones or pathogens including Ebola virus, hepatitis C virus or SARS CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2). These devices also enable the diagnosis of civilization diseases like cancer and cardiovascular diseases based on specific biomarkers e.g., C-reactive protein. They are also finding purpose in environmental research, where they are mainly used in the determination of heavy metals in soil and the levels of plant protection products (herbicides, insecticides, etc.). In the agri-food industry, (bio)sensors detect some pathogens (e.g., for example *Salmonella*, *Listeria monocytogenes* or *E. coli*). They can also be employed to determine the presence of foreign genes in GMOs. Another application of (bio)sensors by military services is the identification and determination of chemical and biological warfare agents including *B. anthracis* (*Bacillus anthracis*) or botulinum toxin [16].

Over the past few years, electrochemical (bio)sensors combined with wearable devices have attracted a great deal of attention due to their unparalleled properties such as instrumental simplicity, low cost, flexibility, and ease of miniaturization. These unique properties match the desired qualities for continuous on-body analysis. Wearable electrochemical (bio)sensors provide insight into a patient's health by non-invasive monitoring of clinically relevant biomarkers in a variety of body fluids (saliva, sweat, tears, and interstitial fluids) without complicated handling, sampling, and treatment. The electrochemical system can be fabricated on a variety of substrates and transferred to the human body or combined with common tools to monitor (bio)chemical species or potentially hazardous compounds surrounding users without disrupting their ordinary activities. It is a really promising future research direction [17].

To sum up, great interest has been attracted to the research and advancement of low-cost tools that swiftly, effectively and credibly fulfil requirements of different sectors of latter-day society. Therefore, the search for unique materials with properties that can be freely modulated in accordance with the intended application is important in the design of complex tools such as (bio)sensors, which are necessary for the development and functioning of the modern world.

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