Biosensors and Research on Their Applications

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Abstract. Biosensors are detection devices widely used in fields such as medicine, food safety, and environmental monitoring, integrating biological and chemical principles to efficiently identify and quantify biologically relevant target molecules. Their core structure includes a biorecognition element, a transducer, and a signal processor, all of which work closely together to convert and process biological and chemical signals from target molecules into measurable signals. Biosensors can be categorized in various ways due to differing standards. This review focuses on categorization based on the type of biorecognition element and introduces three primary types of biosensors under this classification. Enzyme sensors excel in detecting biological samples due to the specificity and catalytic abilities of enzymes. Immunosensors employ antigen-antibody reactions for high-sensitivity detection. Nucleic acid sensors, relying on base complementarity, are useful for pathogen detection and genomic analysis. The transducers in these biosensors utilize methods such as electrochemical and optical techniques for signal conversion and amplification, improving detection precision and response speed. This paper provides application examples of different types of biosensors. At last, the paper addresses current challenges in biosensor development and discusses potential optimization directions to provide theoretical guidance for the design and practical applications of biosensors.

Keywords: Biosensor; basic structure; category; application; development.

1. Introduction

Biosensors are an increasingly prominent sensor technology that integrates principles from biology, chemistry, and physics. Using biorecognition elements such as enzymes, antibodies, and nucleic acids, these sensors identify specific biological or chemical substances and convert them into measurable physical signals. Capable of detecting and analyzing target biochemical substances in biological samples with high sensitivity and specificity, biosensors are now widely used in fields such as medical diagnostics, food safety, and environmental monitoring. However, current biosensor research still faces numerous challenges, such as achieving accurate detection in complex samples, enhancing sensor stability and reusability, and controlling production costs.

The significance of biosensor research is substantial, as they hold immense application potential in precision medicine, food safety assurance, environmental pollution monitoring and so forth. Today, thanks to biosensor's sensitivity and stability and advanced detection capabilities, biosensors can better meet the growing demands for medical diagnostics, food quality, and environmental protection. The wide use of biosensors contributes to enhance overall social safety and quality of life.

The goal of this study is to examine the structure and working principles of existing biosensors, analyze their applications across various fields, propose potential strategies for performance improvement, and predict future development directions. This review aims to provide a theoretical foundation for future design and development of biosensors.

2. Overview of Biosensors

2.1. Concept of Biosensors

Biosensors are a type of sensor technology that typically combines biological and chemical principles. They detect biochemical signals related to biological target molecules, chemical substances, cells, and microorganisms. These signals are transformed—often multiple times—into more stable, manageable signals, typically physical signals.

2.2. Main Structure

The primary structure of a biosensor consists of three parts: the biorecognition element, the transducer, and the signal processor.

The biorecognition element identifies the target biological molecules or chemical substances. This target component, which may include biomolecules like enzymes, antigens and antibodies, hormones, specific organic or inorganic compounds, DNA or RNA, cells, or pathogens, serves as the initial signal. It typically interacts directly or indirectly with the target substance.

The transducer converts the biological or chemical signal identified by the biorecognition element into a more detectable, amplifiable, and processable signal. This is often a physical signal such as an electrical, optical, thermal, or mechanical signal, but may also include biological or chemical signals. The goal is to facilitate quantitative and qualitative analysis of the target substance. Additionally, for detecting trace biochemical signals, the transducer will often amplify them effectively, which can enhance detection sensitivity and accuracy.

The signal processor amplifies, converts, and analyzes the signal converted by the transducer. It may include amplifiers, filters, and signal processing systems, either in part or in full. The signal processor is commonly connected to a terminal, either via wired or wireless connections.

3. Classification of Biosensors

3.1. Enzyme Sensors

3.1.1 Principle of enzyme sensors

During the biorecognition phase, enzymes act as biorecognition elements and chemically react with specific substrates that the sensor is designed to detect. For example, glucose oxidase is commonly used in enzyme sensors to detect glucose. It oxidizes glucose into gluconic acid, producing hydrogen peroxide as a byproduct. The resulting product serves as the foundational biochemical signal, which the transducer then converts into an easily measurable physical signal. This physical signal can be further amplified and processed.

3.1.2 Advantages and disadvantages of enzyme sensors

The high specificity of enzymes enables enzyme-based sensors to accurately detect target substances. Their catalytic action allows most detections to be conducted quickly and efficiently, as the catalytic process speeds up the chemical reactions. Enzyme sensors are also highly sensitive, capable of detecting trace amounts of substrates. This advantage makes them particularly useful in fields like medical diagnostics that require precise quantitative analysis. Furthermore, enzyme sensors offer wide application potential, miniaturization, portability, and suitability for non-invasive testing. However, enzymes are highly sensitive to environmental factors like temperature, pH, and humidity, which can easily cause deactivation, potentially impacting the stability of enzyme sensors.

3.1.3 Applications of enzyme sensors

In medical diagnostics, enzyme sensors are widely used to detect biochemical substances in patients' bodies. For example, glucose enzyme sensors are widely used for blood glucose monitoring, and lactate sensors are one of the most successful commercial enzyme sensors, available in various forms and applications. Zhou et al. [1] developed a novel enzyme biosensor which can immobilize phenylalanine ammonia-lyase onto an ammonia-sensitive electrode for clinical phenylketonuria testing. Bareket [2] used carbon nanotube-modified screen-printed electrodes (SPE) to detect formaldehyde released by human malignant glioma U251 cells treated with formaldehyde-based anticancer compounds. This biosensor creates a low-cost, sensitive formaldehyde dehydrogenase biosensor

In the food industry, enzyme sensors are used to detect additives in food and to ensure product quality meets regulatory standards. For instance, in research on nitrite enzyme sensors based on electrochemical detection, Silveira et al. [3] immobilized cytochrome c nitrite reductase (ccNiR) from Desulfovibrio desulfuricans onto a glassy carbon electrode surface. The surface forms an enzyme electrode with a porous matrix created using a sol-gel solution. This enzyme electrode achieved maximum current in only five seconds and showed stable performance. However, further research is needed to resolve issues such as low electron transfer efficiency, poor reproducibility, and interference from oxygen.

In environmental monitoring, enzyme sensors can detect specific substances in liquids and gases, allowing for sensitive and rapid pollutant detection. For example, in research on heavy metal detection using enzyme sensors [4], heavy metals interact with specific enzymes. Their interaction causes a fluorescent inhibition gene in the sensor to become inactive, generating fluorescence as a signal. Since enzymes participate in the reaction, the process and fluorescence development are rapid. By assessing fluorescence intensity, heavy metal concentrations can be quantitatively analyzed. These biosensors are palm-sized and can measure heavy metal levels in water within 2–3 minutes. However, tests for lead, cadmium, copper, and zinc showed relative errors between 20-40% which is comparatively high, indicating a need for improved precision.

Additionally, enzyme sensors are applied in industries such as bioprocess monitoring, drug development, and personal health care devices.

3.2. Immunosensors

3.2.1 Principle of immunosensors

In immunosensors, antibodies act as the recognition elements, binding specifically with antigens to form an antigen-antibody complex. This binding event serves as the primary signal, which the transducer converts into an easily measurable optical or electrochemical signal. The transformed signal is often amplified to facilitate detection.

3.2.2 Advantages and disadvantages of immunosensors

Antibodies possess high specificity, providing some level of interference resistance in complex samples like blood (though nonspecific molecular interactions may still introduce errors or false positives). The high sensitivity from the specific binding between antibodies and antigens enables immunosensors to detect low concentrations of analytes. This feature makes them effective for early-stage disease detection. Additionally, antibodies are versatile for detecting a wide range of target substances, such as hormones, proteins, bacteria, and viruses, which broadens the potential applications of immunosensors. Immunosensors are also compact, often portable, suitable for on-site testing.

However, antibodies are natural proteins. Thus, they are prone to instability and deactivation due to sensitivity to environmental factors. Producing high-quality antibodies, especially highly specific and sensitive monoclonal antibodies, can be a complex and costly process. Furthermore, separating antibodies from antigens after binding requires specific techniques, which can impact reusability.

3.2.3 Applications of immunosensors

In medical diagnostics, immunosensors are widely used to detect disease-related biomarkers, such as cancer markers, pathogens, and hormones. For instance, a label-free immunosensor based on gold-cobalt nanoparticles (Au-Co NPs) [5] has been developed to detect two key biomarkers for coronary heart disease. The nanoparticles are synthesized through a simple aqueous phase method, and their excellent conductivity provides an effective platform for the sensor. Antibodies are immobilized on the electrode surface and modified by Au-Co nanoparticles to form the basic structure of the sensor. When the antigen binds to the antibody, the electrochemiluminescence signal of the sensor is significantly suppressed. Experimental results demonstrate that the sensor has a very low detection limit and can sensitively detect LDL and oxidized LDL over a wide concentration range. Its high sensitivity makes the sensor a promising tool for early diagnosis of coronary heart disease, offering a new method for rapid detection with potential clinical applications.

In food safety, immunosensors are commonly used to detect pesticide residues, toxins, and pathogenic microorganisms in food. For example, a new method combining immunochromatographic test strips with laser-induced breakdown spectroscopy (LIBS) has been developed for detecting trace pesticide residues in food [6]. Researchers captured pesticides with metallic nanoparticles on the test strip and used LIBS for spectral analysis, successfully expanding the detection range of traditional immunochromatographic test strips. Taking chlorpyrifos as an example, the spectral signal intensifies with increasing chlorpyrifos concentration. The calibration curve based on ΔLIBS intensity shows good linearity, with a detection limit as low as 0.39 ng/mL. This study demonstrates that the combination of immunochromatographic test strips and LIBS can remarkably enhance the detection capabilities for trace pesticide residues in food, expanding the application scope of immunosensors in food safety.

In addition to medical and food safety applications for detecting biological and chemical markers, immunosensors are also applied in environmental monitoring, where they can detect pollutants in water, air, or soil, such as heavy metals and organic pollutants.

3.3. Nucleic Acid (DNA/RNA) Sensors

3.3.1 Principle of nucleic acid sensors

The core of a nucleic acid sensor is the probe nucleic acid, usually a single-stranded DNA or RNA sequence that is complementary to the target nucleic acid sequence. The probe nucleic acid pairs with the target nucleic acid in the sample to form a double-stranded structure. Once binding occurs, the transducer converts this binding signal into detectable signals such as optical, electrochemical, or mass spectrometric signals, which can then be amplified further.

3.3.2 Advantages and disadvantages of nucleic acid sensors

Nucleic acid molecules exhibit high specificity due to complementary base pairing, ensuring precise binding. These sensors are capable of detecting extremely low concentrations of target nucleic acids, offering high sensitivity. Additionally, they can be designed with multiple probes to detect various targets simultaneously, increasing efficiency. Nucleic acid sensors also provide rapid responses, beneficial for emergency scenarios like epidemic control and pathogen identification.

However, nucleic acid probes may degrade or denature in varying temperatures, pH levels, and enzymatic environments. Especially, RNA is prone to degradation due to the ubiquitous presence of RNase enzymes in nature. Thus, they require specific environmental conditions. Non-specific binding in complex samples can still interfere, causing errors or false positives. Operating nucleic acid sensors often requires specialized knowledge, posing a technical barrier for users.

3.3.3 Applications of nucleic acid sensors

In medical diagnostics, nucleic acid sensors can detect and screen for pathogens, cancer markers, and genetic disorders. For instance, a nucleic acid sensor based on surface-enhanced Raman scattering (SERS) technology is used for early cancer biomarker detection [7]. Using high-sensitivity materials such as silver nanorod arrays and tetrahedral DNA probes, this sensor can effectively detect microRNA biomarkers associated with lung cancer (e.g., miRNA-21, miRNA-486, and miRNA-375) in serum. Compared to traditional methods, this SERS sensor provides high sensitivity, excellent specificity, and reusability, showing potential for early tumor detection.

In food safety, nucleic acid sensors can detect pathogens and genetic components in food products. For example, a study developed a nucleic acid sensor based on CRISPR/Lb Cas12a technology to detect meat adulteration, specifically identifying pork content [8]. By combining PCR and LAMP techniques with an electrochemical sensor, it achieved high sensitivity in detecting pork content in various samples. The sensor accurately detected pork in beef at an adulteration ratio as low as 0.05%. With a detection limit down to 0.008%, the sensitivity demonstrates a new approach for meat adulteration detection in food safety. Combined with CRISPR technology, this sensor not only enhances sensitivity but also enables rapid, intuitive on-site testing, highlighting its huge potential in the food safety field.

Nucleic acid sensors also have applications in biological research, analyzing gene expression and gene sequences in molecular biology and genomics, and in environmental monitoring and other fields.

4. Development Directions of Biosensors

4.1. Challenges and Issues in Biosensor Development

The development of biosensors faces several primary challenges, beginning with sensitivity and specificity. Although many biosensors demonstrate high sensitivity, such as the immunosensor for coronary heart disease detection [5] and the nucleic acid sensor for early cancer detection [7], background signals in complex biological samples may interfere with their results. Additionally, biosensors may lack specificity when distinguishing between structurally similar biomarkers, leading to false positives or negatives. Stability and reusability are also concerns because many biosensors lose activity over prolonged use or in unstable environments. These problems affect their reusability and necessitating frequent replacement or recalibration.

Cost and manufacturing complexity are other factors to consider. Some advanced biosensors require expensive materials or complex production processes, resulting in higher production costs and limiting large-scale applications. Finally, a critical issue is sample processing for real applications. If a sensor cannot effectively handle real samples, it cannot be reliably used for diagnostics. Real samples typically include saliva, blood, urine, sweat, body fluids, and tears [9]. Effectively processing these samples to remove interfering substances but not losing target molecules remains a technical challenge.

4.2. Prospects for Biosensor Development

4.2.1 Integration with nanomaterials and new detection techniques

The rapid development of nanotechnology presents new opportunities for biosensors. Nanomaterials, such as gold nanoparticles, have low toxicity and high biocompatibility, making them suitable for medical biosensor applications [10]. Additionally, the unique electrical and optical properties of nanomaterials can significantly enhance sensor sensitivity, contributing to more accurate and reliable detection.

4.2.2 Portability and wearability

Future biosensors will become increasingly miniaturized and portable, evolving into convenient or wearable devices capable of complex detection and analysis anytime and anywhere. For example, wearable biosensors integrated with microfluidics enable non-invasive, continuous monitoring [11]. Such sensors will be widely used in home health monitoring, on-site food safety testing, and environmental monitoring. Users will be able to obtain results quickly through smartphones or portable reading devices.

4.2.3 Integration with intelligent systems

With advancements in artificial intelligence and big data, biosensors will be closely integrated with intelligent systems. Biological information collected by sensors can be transmitted in real time to the cloud for analysis. AI can interpret data rapidly, providing diagnostic insights through machine learning (ML) methods, such as image analysis and deep learning for pattern recognition [12]. Combining biosensors with ML will significantly enhance their detection, analysis, and diagnostic capabilities, paving the way for smarter, more accurate health assessments.

5. Conclusion

This study provides an overview of the fundamental principles and structure of biosensors, highlighting their crucial role in advancing scientific research, improving public health, and protecting the environment. With the growing demand for early disease detection and monitoring of target analytes in food and environmental samples, the potential applications of biosensors are expected to expand further. In the future, biosensors will integrate with advanced technologies and new materials to enhance detection accuracy and range. Coupled with data analysis capabilities, biosensors will broaden their applications, significantly improving both the convenience and efficiency of detection processes.

Reference

[1] Wang, Z., Zhou, Z., Guo, Z., et al. Research on enzyme biosensors for detecting phenylketonuria. Journal of Harbin University of Science and Technology, 2002,7(2): 54-56.

[2] Lilach Bareket, Ada Rephaeli, Gili Berkovitch, et al. Carbonnanotubes-based electrochemical biosensor for detection of formaldehyde released from a cancer cell line treated with formaldehyde-releasing anticancer prodrugs. Bioelectrochemistry, 2010,77(2):94-99.

[3] Silveira C M, Gomes S P, Araujo A N, et al. An efficient -mediated amperometric biosensor for nitrite determination. Biosens Bioelectron, 2010,25:2026-2032.

[4] Bai, R., Yin, H., & Huang, F. A new method for measuring heavy metal elements—biological enzyme sensor method. Proceedings of the 17th Annual Meeting of the Chinese Society of Mineralogy and Petrology,2019.

[5] Lian, X. Research on electrochemical luminescent immunosensor for early prevention of coronary heart disease using dual biomarkers, Soochow University,2020.

[6] Cui, Y., Zheng, P., Wang, X., et al. Trace pesticide measurement method based on immunosensor and laser-induced breakdown spectroscopy. Spectroscopy and Spectral Analysis, 2021, 41(07): 2275-2278.

[7] Yang, Y. Construction and application of a highly sensitive SERS sensor for tumor nucleic acid markers, Nanjing University of Posts and Telecommunications,2017.

[8] He, J. Development of a detection method for pork-derived components in food based on CRISPR nucleic acid sensors.2023.

[9] Singh, Anoop, et al. "Recent advances in electrochemical biosensors: Applications, challenges, and future scope." Biosensors,2021,6: 33.

[10] Hammami, Inès, and Nadiyah M. Alabdallah. Gold nanoparticles: Synthesis properties and applications. Journal of King Saud University Science, 2021,33(7): 101560.

[11] Ye, Shun, et al. Recent progress in wearable biosensors: From healthcare monitoring to sports analytics. Biosensors,2020, 10 (12): 205.

[12] Cui, Feiyun, et al. Advancing biosensors with machine learning. ACS sensors, 2020,5: 3346-3364.