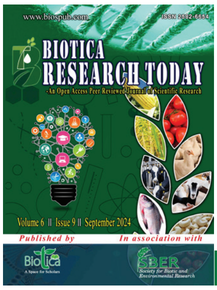

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Biosensors: A Living Analytic

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Abstract

The diverse applications of biosensors highlight their critical importance across various fields such as biotechnology, medicine, agriculture and fisheries. This page delves into the different models and functionalities of these versatile devices, illustrating how their operational profiles enable a broad spectrum of uses. Each component is examined in detail, contributing to the overall understanding of their working principles. Biosensors, which can be composed of microorganisms, polymers or nanomaterials, offer numerous potential applications. To develop biosensors with an inclusive range of uses, it is crucial to employ diverse design methodologies. By exploring this article, readers will gain a comprehensive understanding of living sensors and be equipped to think critically about their applications.

Keywords: Applications, Bio-receptor, Biosensor, Transducer

Introduction

A "biosensor," or "biological sensor," is a device that utilizes living organisms or biological elements to detect and measure various substances. According to Ziegler and Göpel (1998), biosensors represent a critical intersection of biology and technology, offering innovative possibilities for real-time analysis and monitoring across a wide array of fields, encompassing medical diagnostics and environmental evaluation. The device integrates a biotic component, like an enzyme, antibody or nucleic acid, with a transducer to achieve the detection. The transducer converts the biological interface with the analyte being tested into an electrically modified signal. Biosensors are referred to different names based on their specific applications, including immunosensors, chemical canaries, optrodes, resonant mirrors, biochips, biocomputers and glucometers. A widely recognized description of a biological sensor or biosensor is "a chemical sensing device that enables the quantitative measurement of a complicated biochemical parameter by connecting a transducer to a biologically derived recognition element." A biosensor, also known as a bio-detector or biological sensor, is an analytical instrument that combines itself with a biological element, like enzymes, antibodies or microorganisms, with a physical or chemical sensor to sense or detect and measure specific substances. The biological or biomimetic component, known as the delicate yet sensitive biological element, engages with, binds to or distinguishes the intended analyte. The transducer or detecting element then transforms this interaction into a measurable signal through various physicochemical methods, including optical, piezoelectric, electrochemical or electrochemiluminescence processes. This conversion facilitates the measurement and quantification of the interface of analyte with the biotic element. The electronics or signal processors manage the data collected by the biosensor, ensuring it is displayed in a user-friendly manner. Although the electronic component can be the costliest part of the sensor system, an intuitive display can be designed to integrate both the transducer

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and the sensitive element, as seen in holographic sensors. The readers for biosensors are often custom-built to accommodate the diverse operating principles of different sensors.

Parts of Biosensor

Biosensors find applications in numerous fields, including monitoring illnesses, discovering drugs and detecting contaminants, pathogenic microorganisms and disease markers or biomarkers in biological fluids like blood, urine, saliva and sweat. Figure 1 illustrates a typical biosensor, consisting of the components as follows.

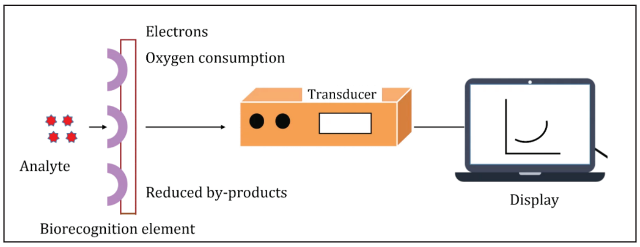

Figure 1: Working of a biosensor (Source: Anonymous, 2022)

• *Analyte:* A target material that seeks detection. For example, in a biological sensor or biosensor designed to measure glucose levels then glucose would be considered the analyte.

• *Biological receptor or Bioreceptor*: A bioreceptor is a type of molecule that can specifically detect the analyte. The interface between the biological receptor and the analyte initiates a bio-recognition process, resulting in an indicator such as light emission, heat generation, pH change, charge variation or mass shift.

• *Transducer*: A transducer is an instrument that transforms energy from one form into another. In biosensors, transducers are essential for converting bio-recognition events into measurable signals. This process, known as "signalization," is critical for the operation of biosensors. The interface between an analyte and a biotic receptor is typically directly related to the optical/photonic or electrical signals shaped by the transducer.

• *Electronics*: This particular component of the biological sensor quite responsible for dealing out the altered signal and formulating it for display. Its features elaborate electrical system that grips signal optimization routines, including analogue signal amplification and digital conversion and transformation quantification of processed signals were computed by the display of biological sensors.

• *Display*: The display embraces a user interface system that creates logical numbers or curves for the user, like those shown on the liquid crystal display of the computer or produced by a direct printer. In accordance with the requirements of the end-user, the output on the display can be in the version of visuals, tables, numbers or graphs.

Mechanism of Biosensors

The specific biological material, usually an enzyme, is immobilized using techniques like physical or membrane trapping or through non-covalent or covalent bonds. This powerless material is in straight contact with the transducer. When the analyte interrelates with the biological substance and forms a bound analyte, it produces a detectable electrical signal. In some cases, the interaction may lead to the generation of a product that emits heat, gas (such as oxygen), electrons or hydrogen ions. The transducer then alters these deviations associated with the produce into electrical impulses, which are then augmented and recorded.

History of Biosensors

Clark and Lyons (1962) conducted the pioneering experiment that laid the groundwork for biosensor technology. In their experiment, they used platinum (Pt) electrodes to measure oxygen levels. They employed a dialysis membrane to immobilize the enzyme glucose oxidase (GOD) near the electrodes, bringing it close to the platinum surface. The enzyme activity was influenced by the surrounding oxygen concentration. When GOD interacts with glucose, it produces gluconic acid, which reduces GOD by generating two protons and two electrons. This reduction reaction makes more GOD available for glucose to react with. As reduced GOD, electrons, protons and ambient oxygen interact; hydrogen peroxide and oxidized GOD (the original form) are produced. Higher glucose concentrations result in more oxygen consumption, while lower glucose concentrations lead to greater hydrogen peroxide formation. Therefore, glucose concentration can be determined by measuring either the increase in hydrogen peroxide or the decrease in oxygen.

Types of Biosensors

The types of biosensors as per the biological and transducing element are shown in figure 2.

1. Biological Element

In a biosensor, the biological element is a bioreceptor, a living mechanism or material that provides information that can be converted into electrical signals. This recognition component or bioreceptor interacts with the target analyte using biomolecules derived from animals or receptors engineered to mimic biological systems. The bio-transducer measures this interaction and produces a quantifiable signal that reflects the concentration of the focused analyte in the sample taken. The main objective in designing biosensors is to empower rapid and accessible testing at the location where the sample was collected. The biological element may include the following types of living sensor receptors.

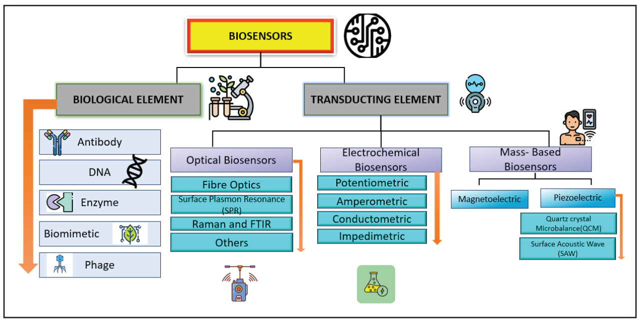

Figure 2: Types of biosensors

Antibody/ Antigen Interactions

An immunosensor leverages the highly explicit binding attraction of antibodies for a certain antigen. The antigen will stick to the antibody only if it is in the accurate conformation, akin to a lock-and-key mechanism. When combined with a tracer like fluorescent molecules, enzymes or radioisotopes, binding events have resulting in a biophysical or physicochemical change that can be detected as a signal. Additionally, serological testing, which involves identifying immune antibodies in reply to a precise disease, utilizes antibody-antigen interactions. This type of testing has become a vital component of the universal effort to manage the COVID-19 pandemic.

Bioengineered Binding Proteins

Using antibodies as the bio-specific interaction component in biological sensors have numerous downsides: they are expensive to produce, have large molecular weights, exhibit low stability and require disulfide bonds. To address these limitations, one approach is to develop antibody domains (VH, VHH) or recombinant antibody fragments (*E.g.*: Fab, Fv or scFv). Another alternative is to form non-natural families of antibodies (immunoglobulins) like AgBP by engineering minor protein platforms with desirable biomolecular properties. These AgBPs can bind to specific target proteins with high precision while retaining the beneficial attributes of their parent molecules.

Enzymatic Interactions

Enzymes are the proteins undergo catalytic activity or specific chemical reactions. These can be used in a decontaminated form or be existing in a microorganism or in a slice of undamaged tissue. The mechanisms of operation of these biological receptors can involve: (i) conversion of the analyte into a maker or a sensor-detectable merchandise, (ii) recognition of an analyte that performs as an enzyme inhibitor or activator, or (iii) estimation of the amendment of enzyme properties upon interface with the analyte.

Ligand-Binding Receptors

Antibodies demonstrate a high binding kinship, generally having association constant exceeding 10^8 L mol^{-1} that signifies that the association between the antigen and antibody is almost irreversible after binding. Specific analyte molecules, like glucose, have affinity binding proteins receptors that interact with their ligands with high accuracy, similar to antibodies, but with a considerably lower binding constant, ranging from 10^2 to 10^4 L mol^{-1}. The interaction between the analyte and the receptor is flexible and free molecules are present in measurable concentrations. For example, concanavalin is used in the case of glucose. The concept of using target-specific receptors for biosensing was first proposed by Schultz and Sims (1979).

Nucleic Acid Associations

Biosensors utilizing nucleic acid-built receptors can be categorized into apt sensors and Geno-sensors. Apt sensors are based on unique nucleic acid-based analogues of antibodies, while Geno-sensors rely on complementary base pairing interactions. Apt sensors use the perception of complementary base pairing, for instance adenine binds to thymine and cytosine to guanine in DNA, for their recognition process.

Epigenetics

It has been proposed that physiological secretions from patients with cancer or added conditions could be used to detect epigenetic changes, like DNA methylation and histone post-translational alterations or modifications, using specially tuned integrated optical resonators. At the research level, ultra-sensitive photonic biosensors are being developed to rapidly identify malignant cells in a patient's urine. Several research projects are focused on creating innovative portable devices that use affordable, disposable, eco-friendly cartridges which are easy to handle and do not require supplementary processing, cleaning or manipulation by skilled specialists.

Cells

Cells are recurrently utilized in bioreceptors due to their sensitivity to the environment and their ability to react to various stimuli. They have a propensity to adhere to surfaces, facilitating their immobilization. When compared to organelles, cells maintain their activity over a more extended period and their ability to be reproduced allows for their reuse. They are typically employed to identify broad parameters such as stress conditions, toxicity and the presence of organic compounds. Additionally, they serve to assess the efficacy of drug treatments. One specific use of cells is in the detection of herbicides, which are a primary contaminant in water bodies. Microalgae are collected on a small filter and their response to herbicides can be measured by analyzing the light emitted at the end of a specialized fiber optic bundle, which is then transmitted to a fluorimeter.

Tissue

Tissues are employed in biological sensors to assess the levels of present enzymes. The usage of tissues offers several advantages: they are easier to immobilize equated to cells and organelles, provide greater activity and constancy and are more accessible and cost-effective. This method avoids the need for enzyme extraction, centrifugation and purification. Additionally, tissues contain the necessary cofactors for enzyme activity and offer a broad range of options for various objectives.

Microbial Biosensors

Microbial biosensors take use of how microorganisms react to a particular material. For instance, the Ars operon, which is present in several bacterial taxa, may be used to detect arsenic.

2. Transducing Element/ Bio-Transducer

The recognition-transduction component of a biosensor system is known as a bio-transducer. It consists of two closely related parts: a physicochemical transducer and a bio-recognition layer. These mechanisms work together to convert a biotic signal into an electric or optical/ophthalmic signal. Typically, the biological recognition layer includes an enzyme or any other type of binding protein, like an antibody. It provides specificity and selectivity to the biosensor. Usually, the physicochemical transducer and the recognition layer are in close, regulated contact. The presence and biochemical activity of the target of interest or analyte, cause a physio-chemical change inside the biorecognition layer. This change is recorded by the physicochemical transducer. According to the type of bio-transducer, biosensors can be categorized as shown in figure 3. Some examples are listed below.

Optical Biosensors

An essential component of optical biosensors is optical fibre. Based on the various characteristics of light, such as absorption, scattering and fluorescence, the optical fibres enable the sensor elements to be detected. Due to the change in the interacting surface index of refraction, the reaction affects any of the attributes. The liquid that comes into touch with this layer will have a different refractive index, for instance, if the biotic elements are the antibodies fused to a metal layer, one of the main advantages of optical biosensors is their non-electrical nature.

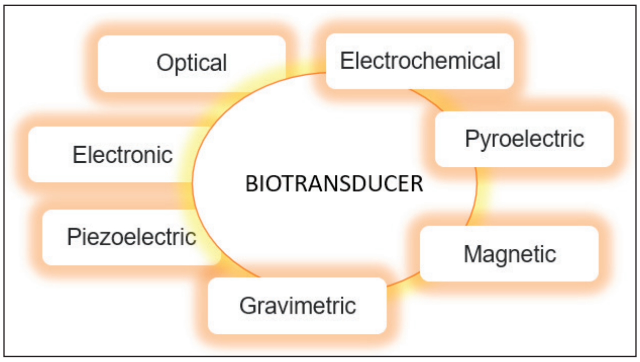

Figure 3: Types of bio-transducer used in biosensors

Bioanalytical Sensors

Biotic biosensors, also referred to as optogenetic probes or sensors, often utilize genetically improved versions of natural enzymes or proteins. These proteins generate a signal that is detected by a device, such as a luminometer or fluorometer, which is calibrated to identify a specific analyte. A recent example of this type of biosensor measures the levels of cAMP (a molecule involved in cell communication) within a cell, activated by ligands interacting with receptors on the cell membrane.

Piezoelectric Biosensors

These biosensors are categorized under the mass-based subclass. Piezoelectric biosensors, sometimes called acoustic biosensors because they rely on acoustic (or sound vibration) principles, produce an electric signal in riposte to mechanical stress. The biotic components are attached to the surface of the piezo element sensor. Essentially, a piezoelectric biosensor operates as a piezoelectric mass sensor, translating the mechanical fluctuations of the detected molecules into corresponding electric impulses.

Applications of Biosensors

Biosensors offer transformative applications that significantly enhance human health and well-being. They play crucial roles in food safety, disease detection, medication development and environmental monitoring as shown in figure 4. Often designed as "single-use" analytical tools, these biosensors are affordable and disposable, making them ideal for rapid and efficient testing. Conversely, biosensors for pollution monitoring are engineered for extended operation, ranging from hours to days and are known as "long-term monitoring" instruments. Vigneshvar *et al*. (2016) discuss various applications of biosensors, starting from the medical diagnostics to environmental monitoring as well as food safety. The advancements in biosensor technology have expanded their use across different sectors, highlighting their versatility. These advanced devices are versatile, finding vital applications in both resource-constrained environments and cutting-edge medical settings.

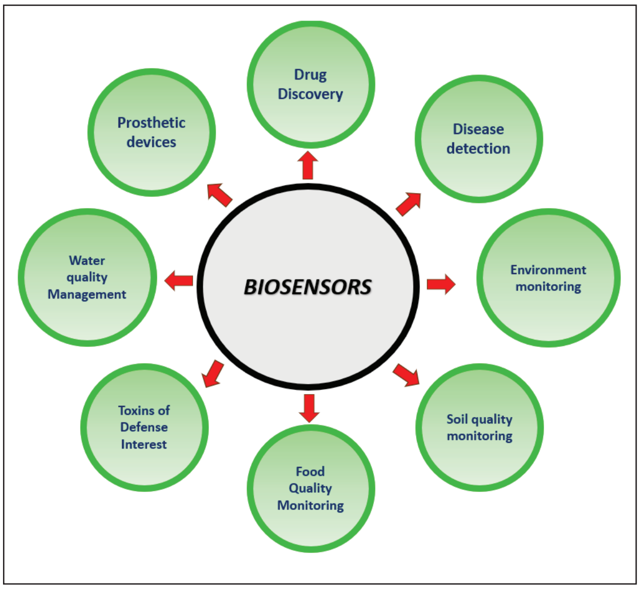

Figure 4: Application of biosensor

Conclusion

When creating biosensors, it's important to focus on making them very sensitive, specific, safe, able to detect small amounts of substances and cost-effective. Paying attention to these things will help to overcome the main issues with biosensor technology. The biosensor technology could able to act as a prime gadget for the advancement in the field of science. Singing a pivotal role in the role of agriculture and allied sectors, including medicine for monitoring, analysis and testing, it can be a great replacement for labour-intensive farming.

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