GSC Biological and Pharmaceutical Sciences

eISSN: 2581-3250 CODEN (USA): GBPSC2

Cross Ref DOI: 10.30574/gscbps

Journal homepage: https://gsconlinepress.com/journals/gscbps/

(REVIEW ARTICLE)

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Biosensor: An easier way of diagnosis

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GSC Biological and Pharmaceutical Sciences, 2024, 28(03), 149–157

Publication history: Received on 04 August 2024; revised on 16 September 2024; accepted on 18 September 2024

Article DOI: https://doi.org/10.30574/gscbps.2024.28.3.0329

Abstract

These days, there is a growing emphasis on the need to analyze and control a wide range of factors in fields like the food business, medical treatment, sanitation, atmospheric safeguarding, drug research, and forensic science. By producing impulses corresponding to the amount of a metabolite in the interaction, a biological sensor is an instrument which analyzes physiological and molecular interactions. The word 'biosensor' can be described as the device that senses or records the concentration or biological response from analyte-receptor interaction in a biological system. Leland Clark Jr. constructed the Clark oxygen electrode, the very initial real biosensor for the monitoring of oxygen levels, in 1956. Clark is referred to as the pioneer of biological sensors. The first biosensors to be efficiently employed and marketed to measure different analytes were electrochemical biosensors. Electrochemical biosensors produce an electric charge in line with the percentage of the materials that need to be analyzed. The vital monitoring of athletes, mental health sufferers, long-term care recipients, and residents of remote areas is displayed by wearable biosensors. Biosensors are portable diagnostic devices used for prediagnosis or to check for any symptoms of the disease. Many innovative technologies for the benefit of humanity will soon be ready to be unveiled to the world.

Keywords: Biosensor; Bioreceptor; Transducer; Analyte

1. Introduction

Nowadays, biosensors are used in drug research, food regulation, ecosystem inspection, scientific study findings, forensics, and biomedical diagnosis. They are also used in therapy and illness monitoring. For decades, experts from all around the world have emphasized the latest advancements in the world of biological sensors. Like that, we examine current advancements in wearable technologies that serve as stress relievers for healthcare professionals and hospital spaces for patient care. In the future, wearable biosensors will prevent road accidents, saving lives. In essence, biological sensors are inexpensive and incredibly effective tools for these common uses. Biological sensing elements comprise biomolecules like tissue, animal mitochondria, bacteria, organelles, enzymatic proteins, immunoglobulins, and receptors. By producing a signal equivalent to the proportion of an analytical agent in the process, it quantifies physiological and molecular interactions. In addition to being utilized for biorecognition of contaminants and diagnostics, biological sensors can also be employed to recognize bacteria and pathogenic antigens in biological secretions like blood, urine, saliva, and sweat[1].

1.1. Biosensor Development Timeline

- M. Cremer demonstrated in 1906 that the electromagnetic impulse that develops between liquid components that are on different ends of a glass barrier determines the proportion of an acid in a solution.
- In 1909, Soren Peder Lauritz Sorenson, a Danish chemist, proposed the notion of pH concentrations around the globe.

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- 1922 saw the establishment of an electrode for pH monitoring by W.S. Hughes.
- Leland Clark Jr. constructed the initial real biosensor for the monitoring of oxygen levels in 1956. Clark is referred to as the pioneer of biological sensors and is named Clark Electrode after an oxygen electrode that he built.
- Leland Clark in 1962 described how an amperometric enzymatic protein-based electrode for glucose detection functions.
- In 1969, Guilbault and Montalvo constructed the original urea-detecting potentiometric biological sensor.
- The inaugural commercialized biological sensor was introduced in 1975 by YSI, or Yellow Spring Instruments.
- 1976 saw the creation of the initial synthetic pancreas by Miles Laboratories in the United States.
- In 1980, Peterson created the very initial optical fiber pH detector for in vivo blood gas analysis.
- The initial glucose biological sensor made from optical fiber was developed in 1982.

Since the creation of the i-STAT biological sensor, extraordinary advancements have been accomplished in the world of biosensors. These days, the discipline is a hub for interdisciplinary study that connects the core concepts of nanotechnology, gadgets, and applied medicines with the physics, chemistry, and biology of the core sciences. From 2005 to 2015, the Web of Science network has categorized more than 84,000 papers on the subject of biosensors [1].

2. Biosensor Elements

2.1. Analyte

A constituent that is used for analysis or to study the reactions. For instance, in a biosensor classified as a glucometer, glucose functions as an analyte.

2.2. Bioreceptor

Bioreceptors are the target sites where the analyte binds and activity is recorded. Bioreceptors also identify the analyte in the system. Among the biological receptors are enzymatic proteins, mitochondria, aptamers, genetic materials, and immunoglobulins. When an analyte binds to the bioreceptor, a certain kind of signal is generated; this phenomenon is known as biosensing.

2.3. Transducer

An electrochemical output is produced when a metabolite and antibodies react biologically, and this process is handled by the transducer in a biological sensor. Thus, a transducer's primary job is to transform a biorecognition action into an electromagnetic output that can be monitored. Signalization is the term for this impulse transformation process. The majority of transmitters generate photonic or electromagnetic impulses that correspond to the degree of the metabolite antibody reaction process.

2.4. Electricals

The biosensor's electronic components simplify the signal analysis and present it in a way that is easy to comprehend. An electronic circuit makes up a biosensor, and it is in charge of amplifying and digitizing analog outputs for editing purposes. The electrochemical impulses that will be shown in digital analog are then evaluated by the biosensor.

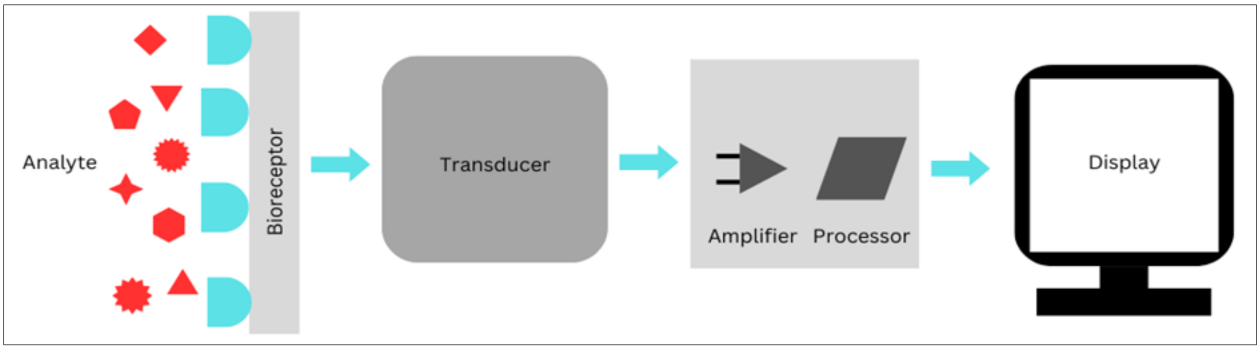

Figure 1 Biosensor Elements

2.5. Display

The main aim of display is to show the data or results of biological responses in a user-friendly way. This can be achieved by combining hardware and software elements in the biosensor. The display might be an in-built projector that generates graphs as well as statistics that the user can read, or it could be a computer's LCD screen. According to the end user's needs, the resulting data on the monitor may be a chart plot, a table, quantitative, or picture[2].

3. Principle

A biosensor is a diagnostic instrument that converts the response of a physiological reaction into an electronic output. The word 'biosensor' can be described as the device that senses or records the concentration or biological response from analyte-receptor interaction in a biological system. The selected enzymatic protein is rendered static through ionic or covalent interactions, membrane trapping, or mechanical means. The transducer, along with that motionless enzyme, is closely connected. Following the transducer's detection of biological reactions, electronic impulses are generated, enhanced, and computed. A biosensor uses a biological sensing parameter that senses the presence of an analyte. In order to create a physiological unit that delivers data to an autonomous monitoring device, a biological sensor structure may be the amalgamation of various devices and instruments, including an extraction device, a biological sensor, a restocking data instrument, and a database interpretation device. The choice of analyte will be based on a number of factors, including concentrations, stability, physiochemical attributes, and the capacity to generate a biological impulse which a transmitter can convert to an electronic signal[2].

3.1. Background

Leland C. Clark Jr. (1918–2005) was an American biochemist born in Rochester, New York, also known as the pioneer of biosensor technology. The Clark Electrode, a gadget created by Leland C. Clark Jr., measures the amount of oxygen in blood, water, and other liquids. The glucose sensor used by millions of diabetics today was also developed from the Clark electrode and the research of Leland C. Clark Jr.

Hydrogen peroxide and gluconic acid are produced when glucose reacts with oxygen and water in the presence of glucose oxidase. The platinum cathode was exposed to a negative potential in order to detect oxygen absorption reductively.

A conclusive paper on the oxygen electrode was published in 1956 by Leland C. Clark Jr. Originally, the idea of a glucose enzyme-based electrode was constructed on the idea of a thin surface of glucose oxidase masked by a semipermeable membrane used for dialysis on an oxygen-based electrode. In the framework of estimating the oxygen taken by the enzyme-initiated interactions, calculations were built[2].

A study where glucose oxidase was hidden underneath a Clark oxygen electrode by a membrane used for dialysis helped to understand the mechanism. A fine film of glucose oxidase above an oxygen-based electrode was used to create this biosensor. The total quantity of glucose was estimated through calculating the reduction in the absorbed oxygen content. In 1975, Yellow Springs Instruments Company successfully relaunched the glucose analyzer, making biosensors a commercial reality. The amperometric analysis of hydrogen peroxide provided evidence of its operation. After urease enzyme hydrolysis, Katz presented what was among the earliest publications in the world of biosensors using a simple potentiometric method for estimating urea[3].

4. Biosensor Attributes

4.1. Selectivity

One of biosensors primary aspects is selectivity. Selectivity is one of the most important functions of a biosensor. Selectivity is the ability of a receptor to recognize a particular analyte within a material that contains adjuvants and contaminants. The association of an antigen and an antibody serves as the ideal illustration of selectivity[4].

4.2. Consistency

The ability that allows the biosensor to yield comparable results in a research setting is known as reproducibility. The transmitter and circuitry in a biosensor's sensitivity and repeatability are what make it reproducible. Sensitivity is defined as the transducer's capacity to produce an average value that is near the actual amount when a specimen is analyzed several times, whereas specificity is the transducer's capability to produce comparable outcomes every single time a specimen is tested[2].

4.3. Uniformity

The degree of susceptibility of the biorecognition mechanism to ambient influence within and surrounding it is known as stability. The generated output of a biosensor may fluctuate as a result of certain interferences. This may result in an inaccurate quantity being detected and have an impact on the biosensor's sensitivity and specificity[5].

4.4. Accuracy

The lowest concentration of metabolite that a biosensor can find indicates its responsiveness or threshold of recognition. To detect antigen concentrations as small as ng/ml or as high as fg/ml and verify the presence of antigen residue in the specimen, a biosensor is required in numerous atmospheric and healthcare monitoring systems. When an individual's blood level of PSA, or prostate-specific antigen, is 4ng/ml, doctors may recommend biopsy examinations for a tumor in the prostate. Accuracy is therefore among a biosensor's most crucial characteristics.

4.5. Linearity

The metric known as linearity is the capability to measure two variable responses with accuracy, or the number of measurements that are proportionate to each other. The linearity formula is $y = mx + c$, where m is the biosensor's sensitivity, c is the analyte's concentration, and y is the generated signal. The accuracy and spectrum of the analyte quantities during examination can be evaluated with the regression of the biosensor[4].

5. Biosensor Functioning

Typically, the transducer's electronic response is moderate and overlaid with an erratic, slightly elevated baseline. This can be explained by having a frequency signal element that appears strange and is produced by electromagnetic interference and the transducer's electrical component. The analysis of signals usually involves deducing the test signal from a standard baseline output that is derived from a parallel transmitter that does not include a biological catalyst barrier. Then, the electrical signal gap is enhanced, and the extraneous output distortion is technologically tuned. The issue of electromagnetic interference filtering is significantly resolved by the biosensor signal's relatively moderate speed. A microchip computer processes the information, analyzes it, maneuvers it to the necessary measurements, and transmits it to a digital analog or digital cache. The digitized response detected at this phase is sometimes transmitted right away, but it is typically converted into an analog response.

The organic material becomes bound by covalent or ionic interactions, physiological entanglement, or bilayer entanglement. A link is established between the transmitter and the organic material. When a substance binds with a physiological receptor, it forms an attached analyte that may be detected by an electrical signal. Sometimes the substance is converted to an intermediate that may be associated with air, temperature, electron, and H^+ ion loss. The digital display can then be employed to calculate, exhibit, and magnify the electronic output that the transmitter creates from the outcome-related modifications[5].

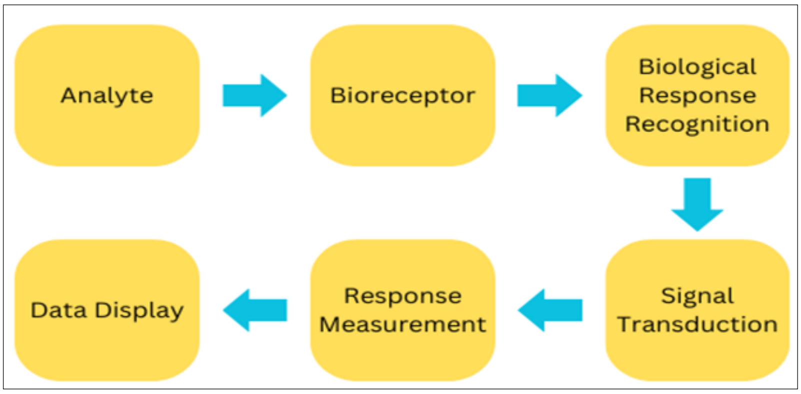

Figure 2 Working of Biosensors

6. Biosensor Types

- Electrochemical
- Amperometric
- Potentiometric
- Conductometric
- Thermometric
- Optical
- Piezoelectric
- Microbial
- Enzyme

6.1. Electrochemical Biosensor

Electrode configurations are a frequent provision for electrochemical biosensors. Typically, they are segregated among three main categories based upon their primary measurement characteristic. Amperometric, potentiometric, and conductometric biosensors are the three categories; the latter two are grouped together into a single category. Numerous compounds found within the body of an individual, including urea, lactic acid, glucose, genetic material, hemoglobin, cholesterol, and others, can be detected by electrochemical biosensor[4].

6.1.1. Amperometric Biosensor

The widely employed technique for biosensors is electrochemical detection. Physiological examination specimens can contain conductive species, which can be found using highly sensitive equipment called amperometric biosensors. These biosensors produce an electric charge in line with the percentage of the materials that need to be analyzed. The Clark oxygen electrode is the amperometric biosensor that is frequently utilized[3].

Example: Glucose Meter

6.1.2. Potentiometric Biosensor

Although potentiometric biosensors are the rarest kind of biosensors, other methods can still be discovered. The oxidative or reductive state in an electrochemical response serves as a recognition parameter for this type of detection device. The voltage variations among the sample and standard electrodes at different analyte concentrations are commonly calculated using potentiometric biosensors in order to determine the analyte concentrations. ISFET falls under the category of potentiometric biosensors[6].

Example: pH Meter and Ion-Selective Field Effective Transistor

6.1.3. Conductometric Biosensor

The resistance to the electrical response of the substance serves as the conductometric biosensor's evaluation parameter. An electrochemical reaction that produces electrons and ions disrupts the entire resistivity of the sample. The change in resistance is detected and calculated on a suitable scale. Conductivity detectors have relatively low sensitivity[5].

Example: Urea Biosensor

6.2. Thermal Biosensor

The principles behind calorimetry, which call for the determination of heat variations, are the foundation of thermo transduction. The detection device used in thermo biosensors is often a heat sensitive regulator called a thermistor. The first ever thermal biosensor used was an enzyme thermistor. Thermal biosensors take advantage of particular primary characteristics of biological processes, such as how heat is absorbed and released, altering the temperature of the reaction environment. Heat detection devices and dormant protein enzymes are put together to create thermal biosensors[3].

Example: Isothermal Calorimeter

6.3. Optical Biosensor

The framework for such kinds of biosensors involves optical monitoring. Optical biosensors employ an optode, a compound word derived from the terms optic and electrode, as well as fiber optics. The transforming elements, like antibodies and proteins, are present in the optical biosensors. An important component of optical biosensors is optical fibers. The measurement of various sensory constituents using different light properties such as absorption, fluorescence, and scattering is made possible by the optical fibers[6].

Example: Fluorescence Immunoanalyzer

6.4. Piezoelectric Biosensor

Piezoelectricity is a phenomenon in which crystals are used to transform mechanical energy into electric energy. By converting changes in power, temperature, velocity, and stress into a voltage response, these biosensors take advantage of the piezoelectric phenomenon. In Greek, the word piezo means to press or squeeze[5].

Example: Accelerometer

6.5. Microbial Biosensor

A microbial biosensor's primary goal is to combine microbes with a transmitter to enable the quick, accurate, and specific identification of particular compounds in a variety of industries, including safety, food manufacturing, atmospheric evaluation, and healthcare. The pulmonary and digestive traits of the microbes were employed by the earlier microbiological biosensors to identify a compound which might be either a bioreceptor or an impediment to the procedure[3].

6.6. Enzyme Biosensor

Biosensors that use enzymes operate on the basis of biological responses. The enzymes need to remain robust in the biosensor's surrounding atmosphere and accessible to initiate a certain biological process necessary for the biosensor to work as intended. The responsive membrane, dormant enzyme, and electrode amplifier unit that combine electrode and enzyme make up the enzyme biosensor1.

7. Applications of Biosensor

7.1. Food Sector

Biosensors can be utilized for identifying foodborne infections. The fecal contamination of food products or food can be confirmed by the collection of evidence of Escherichia coli present in vegetables. A potentiometric biosensor was developed and utilized to measure the pH change brought due to ammonia in order to analyze E. coli[7].

7.2. Agricultural Industry

Enzyme biosensors that rely on the cholinesterase inhibitory effect can be used to identify the traces of pesticides' carbamates and organophosphates. Studies have been conducted on specific and sensitive microbiological sensors in order to identify methane and ammonia. The BOD biological oxygen demand biosensor, which functions on bacteria such as Rhodococcus erythropolis, is necessary for the treatment of wastewater[4].

7.3. Health Sector

Glucose biosensors are the most often utilized biosensors in clinical settings to diagnose diabetes mellitus. The most recent biosensor, which analyzes human interleukin at the first step, is determined by hafnium oxide. Cardiovascular disease research also utilizes biosensors[1].

7.4. Bacterial Monitoring

E. coli, Listeria monocytogenes, Campylobacter, and Salmonella are bacteria causing food poisoning, which can turn into a health hazard. If the food transported by the company is degraded, then the biological components are responsible for food poisoning. This is a big problem in the food sector since it lowers customer demand, which has a significant impact on industries. The most common reason for food poisoning is a rod-shaped bacteria called Salmonella, which causes the body to lose salt and water uncontrollably[2].

7.5. Biosensors in Drug Discovery and Drug Analysis

Biosensors are used for monitoring parameters in the productionprocess of the pharmaceutical industry. Affinity biosensors are used for more output in antibody and drug screening processes. To study the interaction between surface-linked DNA and a target drug, oligonucleotide biosensors are used.

7.6. Epigenetic

To trace a tumor cell in a urine sample closely, the most commonly used biosensor is a photonic biosensor. Epigenetic changes are measured after the utilization of homogeneous optical resonators[1].

7.7. The Role of Biosensors in Environmental Monitoring

Biosensors are usually used to measure and decrease air, water, and soil pollutants. Pesticide analysis is done by a potentiometric biosensor. Water contaminants are measured by an amperometric biosensor. Microbial biosensors help to determine the concentration of ammonia[5].

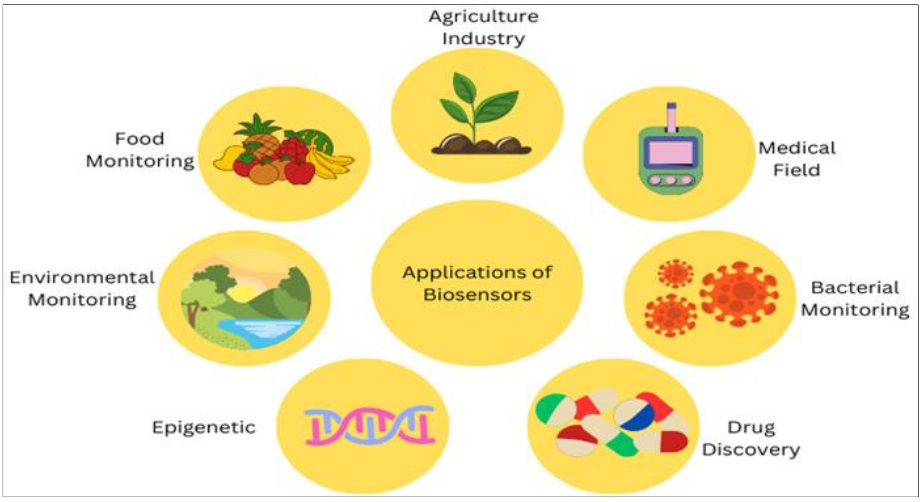

Figure 3 Applications Of Biosensors

7.8. Nanobiosensor

The primary purpose of a nanobiosensor is the detection of the physical and chemical reactions that occur within a cell. To accelerate molecular diagnosis, biosensors can be merged with suitable instruments or software, like lab-on-chip. Nanobiosensors are used for measuring microorganisms in several samples, monitoring metabolites in body fluids, and identifying tissue pathologies like cancer[3].

8. Smart Activewear Biosensor

Smart gadgets used as an adjunct to activewear are called smart activewear biosensors. Smart gadgets like smart watches, thin bandages, glucose patches, rings, etc. are wearable biosensors. The vital monitoring of athletes, mental health sufferers, long-term care recipients, and residents of remote areas is displayed by wearable biosensors. The primary applications of wearable biosensors involve the detection and treatment of medical disorders.

8.1. Smart Watches

Smart watches are one of the most widely used wearable biosensors globally. A smart watch keeps track of human vitals, so it can be used as a fitness tracking biosensor that helps users record their workout times, heart rate, step counts, and calories burned. With the combination of sensors attached to a lithium-ion battery,smart watches track and transfer vitals to the smartphone.

8.2. Ring Sensor

A ring sensor is a pulse oximetry sensor that measures the heart rate and oxygen saturation in the blood. This biosensor is available in a ring shape and can be used just like any other normal ring. The ring consists of infrared and red LEDs and a photodiode to measure oxygenated and deoxygenated blood hemoglobin. This process is carried out by a single processor.

8.3. Eyeglasses

These eyeglass biosensors consist of a computer with a digital analog. The eyeglasses are combined with a nose pad containing a lactate biosensor, whose job it is to monitor sweat lactate and potassium levels using the gel membrane present on the biosensor.

9. Conclusion

Biosensors are portable diagnostic devices used for prediagnosis or to check for any symptoms of the disease. Biosensors are economical, quick to respond, and accurate. Since the invention of the first biosensor, the Clark electrode, in 1954, biosensors have changed the medical diagnosis field. Now we are using all these smart watches, glucose patches, oximeters, and pregnancy test kits. Additionally, biosensors are utilized to detect pollutants, assess the condition of the water, soil, and air. So, we can conclude that the biosensors have made the diagnosis process easier for everyone.

Compliance with Ethical Standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interests.

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