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All about Biosensors- A Review

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Abstract— Sensors are one of the most important inventions in engineering history, and biosensors are one of them. Biosensors have been under development for over 35 years, becoming more prominent in the last 15 years. Silicon Nanowires, for example, has paved the way for a flood of new signal transduction methods in biosensors, illustrating the field's advancement. Recently, NASA has been developing better physiologic sensor and biotelemetry system technologies, to continuously assess basic physiological indicators in unrestrained space beings, such as heart rate, blood pH, and body temperature, which is a challenging problem to solve.

Approximately 20 to 25 years ago, biosensors were one of the mysterious topics in engineering as they connected two different fields (electronic and biology). But now, from the detection of Covid-19 in medical science to the detection of microorganisms in space technology, biosensors are used on a large scale and have become the most popular choice for manufacturers. In this review, we will encounter every prospect, application, and type of biosensor.

***Key words*: Biosensors, Types of Biosensors, Application of Biosensor**

1. Introduction

Leland C. Clark, Jr, also known as "Father of Biosensors", discovered biosensors in 1954. Leland C. Clark created the first biosensor for the detection of oxygen. "CLARK ELECTRODE" is the name of the oxygen electrode that was invented by him. This electrode was later named as a biosensor. As time passed, biosensors have become popular and in today's era, it is used everywhere in the industry. Various fields like very large integrated circuits (VSLI), electronics, physics, biotechnology, mechanical, etc. are working together to make this sensor more and more viable [1][2][3].

- **What are Biosensors?**

You will find various definitions based on the field of application. But in simple words, we can say that "Biosensors are devices that are used to measure the concentration of the analyte (analyte can be any biological element depending on the application. Examples of analytes for glucometer are Blood and sugar). These devices can convert biological responses (analyte response) into an electronic signal" [1]. A biosensor uses a unique biological recognition element whose characteristic can change when it binds to that particular element. This helps in monitoring its environmental and physical compounds. Biosensors are simple, quick, low-cost, sensitive, and highly selective. Surface chemistry advancements have provided a variety of new ways for developing detector recognition systems. The combination of intelligence by various fields will help to speed up the development of biosensors and help to transform biological disciplines [3][5]. The performance of the biosensor is affected by the optimization of its static and dynamic characteristics.

The attribute or parameters to consider are:

1. Selectivity: When biosensors are constructed, the selection of the correct bioreactor plays an important role. A bioreceptor's selectivity refers to its capacity to identify a single element in the presence of various fillers and pollutants in a sample.

2. Life of a sensor: The average life of a biosensor is three months (90 days).

3. Stability: Stability is the accuracy maintained by the device in the presence of environmental disturbance. More stability causes a small error and precise results.

4. Accuracy: Sensor's accuracy matters the most. As for biosensors, the accuracy rate is almost 92% to 95%.

5. Detection limit: The limit of an instrument that fails to recognize the minimum concentration of an analyte. Mostly estimated from the mean and standard deviation of the solution or sample present.

Biosensors are manufactured by considering these parameters.[5]

I. Working

If you observe a device, you will notice that a biosensor are composed of three main parts :

- Recognition of analyte.
- Converting collected data to signal.
- Reading the signal.

In simple words, a biosensor consists of a biological component that helps the device recognize or communicate with the analyte. This communication produces a physical or chemical response which is further collected by a transducer. These changes can be magnetic, electrochemical, optical, thermal, etc. With this data, the transducer converts it into an electrical signal. These signals are then passed on to the electronic (amplifier, processor) to convert it into a readable form. Finally, after all these processes the output is displayed. [2][5][6]

II. Types of Biosensors

Modern multidisciplinary bioscience techniques involving bioengineering, electrical and electronics engineering, mechanical engineering, biomedical engineering, etc have opened the way for the development of biosensors for a variety of detection methods with a broad array of applications in the field of medical and environmental research. There are many biosensors invented to date based on the transducer and the type of biological material (Bioreceptors) used. We will discuss the types in detail.[6][7][8]

A. Electrochemical Biosensors:

Many electrochemical biosensors have been created and presented in recent years for the identification of multiple medical conditions based on specific indicators, utilizing their properties which were discussed in the previous section. Electrochemical Biosensors are further divided based on the electrochemical parameter measured. [9][10][2]

- Amperometric Biosensor: As we have previously discussed the invention of "CLARK ELECTRODE'', in 1962 (nearly ten years later) he used the same glucose oxidized enzyme and reversed its polarity of the electrode to create the first Amperometric Biosensor. Amperometric biosensors work on the moment of electrons produced in a redox reaction. The glucometer is probably the most well-known amperometric biosensor. This is one of the most popular devices that is used to check glucose levels in the blood. At the bottom of the biosensor, the glucose oxidase enzyme is immobilized. Oxygen is released when glucose combines with the glucose oxidase enzyme and passes through an oxygen-permeable membrane. It then reacts with the platinum electrode, resulting in electron flow and current flow. A voltage will be created from this current. With the assistance of an amplifier, the voltage will be amplified, and the glucose level in the sample will be displayed.

- Potentiometric Biosensor: Potentiometric biosensor in simple terms converts mechanical displacement into voltage difference. These biosensors play a major role in Clinical chemistry. The core principle of this biosensor is that while the length of a variable is varied at a constant distance, the corresponding resistance will be experiencing some changes. It must have a steady current running through it as a requirement. Potentiometric biosensor makes use of ion electrodes to transduce biological response in electrical form.

- Conductive Biosensor: When a constant potential is supplied between a reference electrode and a polymer-modified electrode, a change in electrical conductivity or resistivity is detected against the analyte concentration in conductometric conducting polymer-based biosensors. To boost the sensor's sensitivity, the conducting polymer must be electrically efficient when charged (doped) and lowly conductive when neutral, resulting in a significant conductivity shift when the conducting polymer reacts with the analyte.

B. Thermometric Biosensors:

Thermal sensors and calorimetric biosensors are other names for these biosensors. The colorimetric biosensor is based on the fact that various biological processes are linked to the creation of heat. A calorimetric biosensor measures the amount of heat produced during an enzyme process. Thermistors are used in most of these sensors to convert heat created or lost during the reaction into an electrical signal. There are several drawbacks to using a calorimetry sensor, including the need for an insulated jacket to minimize heat loss by radiation, which makes the device large. Also, the sensitivity of the calorimetric sensor is low. To quantify or estimate serum cholesterol, a thermometric biosensor is utilized. When cholesterol is oxidized using the enzyme cholesterol oxidize, heat is generated, which may be estimated. These biosensors may also be used to test for glucose, urea, uric acid, and penicillin G.

C. Optical Biosensor

The optical biosensor works on the premise of light output during a reaction or light absorbed by the difference in reactant and product concentration. Let's have a look at an optical biosensor as an example. Consider a biosensor used in the food industries to determine whether a food product is polluted at the time of consumption. A small biosensor strip will be inserted inside the food packet, and if it is contaminated with bacteria, it will be lighted [10]. This is done with the help of an enzyme called luciferase. Luciferase enzyme is obtained from fireflies. When the luciferase enzyme interacts with the bacterial cell, it is lysed and the ATP content is released. The biosensor will be lighted and luminance will be created when ATP reacts with the luciferin included in it. By doing so, we can determine whether or not food is polluted. Optical biosensors are the most widely used biosensors in healthcare, environmental science, and the biotechnology industry.

D. Piezoelectric sensors

Because they function with the idea of sound, piezoelectric biosensors are also known as acoustic sensors. Positive and negative charge crystals have a certain frequency of vibration. Electronic equipment can detect the resonance frequency. There are certain disadvantages to using a piezoelectric sensor. For example, it is difficult to use a biosensor to determine the material in a solution since the crystal may stop oscillating entirely in a viscous liquid. Piezoelectric ceramics may adapt to a variety of shapes while maintaining their fundamental characteristics because of their great elasticity, Piezoelectric biosensors offer a wide range of applications. For example, in a microphone, the sound signal is turned into an electrical signal, which is then amplified to provide a louder sound. In medical science, piezoelectric is used in ultrasonic equipment, disposable monitoring, and fetal heart monitors.

E. Whole-Cell Biosensors:

Microbial Biosensor is another name for whole-cell biosensor. The complete cell is immobilized on the surface of the transducer in a whole-cell biosensor. It doesn't matter if the cell is alive or dead. In a multistep process or a process that requires a cofactor, these sensors are useful. Whole-cell biosensors are less expensive and have a longer lifespan. When compared to an isolated enzyme, they are less susceptible to changes in pH and temperature.

F. Immuno-Biosensor:

Immuno-biosensors work by combining immunological distinctiveness with measurements taken by an amperometric or potentiometric biosensor. The relative concentrations of labeled and unlabelled antigens affect the activity of enzymes linked to immunosensor. The enzyme activity can be used to determine the concentration of the enabled antigen.

III. APPLICATIONS

A. Environmental Science:

Our environment has acquired different pollutants as a result of recent industrialization and modernization. Heavy metals, herbicides, complex hydrocarbons, and several other substances are among them. However, numerous biosensors have been developed solely to address environmental issues.[11]

- Heavy metal Detection: As we all know the environment contains both vital and hazardous metals. Toxic heavy metal accumulation in humans may cause a range of major health problems, including damage to the liver, kidneys, brain system, and even our reproductive system. An enzyme can respond to a variety of heavy metals, but it won't be able to respond to all of the heavy metals in the environment [3]. As a result, they are only suitable for the development of specialized heavy metals. However, if we want to construct a biosensor for toxicity and analysis, we can use a variety of enzymes. This is where enzyme-based products come in handy. Biosensors based on enzymes can be used in this situation.

- Pesticide Detection: We all know the disadvantages of using pesticides as they can be dangerous to human health. If farmers are exposed to pesticides without using any suitable protective equipment, they may develop major long-term health problems such as cancer. It can also cause our healthy environments to go out of balance. Pesticide detection is carried out using an amperometric biosensor that is a type of electrochemical biosensor.[13][15]

- BOD (Biochemical oxygen demand) biosensors: BOD is the quantity of oxygen required by aerobic living organisms in water to break down organic molecules present in a particular water sample during a specific time and at a certain temperature. The elements utilized to determine BOD are primarily pure cultures of a combination of known microorganisms. Because yeast is resistant to unfavorable environmental variables, it is the best biological agent for BOD biosensors. In comparison to pure cultures, microbial consortia are employed to broaden the range of oxidized substrates. To increase substrate specificity and ensure the long-term functioning of the biosensor, *Trichosporon Cuteneum* and *Bacillus licheniformis* are commonly utilized combined. The use of a biochemical oxygen demand (BOD) biosensor is to improve biological molecule detection that contaminates water bodies and cause dangerous diseases that can lead to death.

B. Medical Science:

- Cancer detection: Cancer is the biggest cause of mortality in the world, and its incidence has increased. Each year, 12.7 million people are diagnosed with cancer, and 7.6 million die from it. However, data suggests that 30 to 40% of these deaths can be avoided, and one-third can be cured if diagnosed and treated early [6]. For breast cancer, the survival rate is 98% if discovered early [10]. The biosensor, which operates on the idea of surface plasmon resonance, or SPR, is a device that aids in the early detection of cancer. Biosensors can transform biological reactions into electrical signals, as we know [14]. Tumor cells, in the case of cancer detection, serve as analytes. In biosensors, cancer cells can be identified by detecting the amount of a specific protein released or expressed by tumor cells. We can determine if a tumor cell is malignant or non-cancerous by collecting data from it.[15][16][11][12][13]

● Wearable Biosensors: In the old days, patients used to have to go to the doctor to discuss their sugar levels, their weight if they had heart failure, or their breathing if they had COPD or asthma. However, today's patients have access to a wearable sensor that can be utilized at home to deliver all of their body's information with accuracy. During dangerous operations or even in a busy emergency department, patients can be monitored using wireless technology, and wearable Biosensors play a big part.[17]

● Covid-19 Detection: Covid-19 and other respiratory virus interactions are detected using biosensors. To detect the presence of the virus, these biosensors just required a saliva sample. Simply place a sample in the gadget, wait a few minutes, and the gadget will tell you if you are infected or not, as well as the value of your antibody levels in your body [13][14]. While they are extremely accurate in the instance of covid-19, they may take some time to get a result. Biosensors were crucial in the detection of this pathogen as it is safe and easy to handle [18]. Further according to [18], a FET or a field-effect transistor based biosensing device can be a promising way to detect viral or sensitive immunological diseases. This is because of the reason that these FET based biosensors use semiconductor materials like graphene etc and are highly sensitive which results in a very quick detection of even very small amounts of analyte [18]. Graphene based FET biosensors are very responsive and can sense changes in the surroundings or on their surface, which provides a very good sensing environment and serves the purpose very well. Further [22] have developed FET biosensor to detect COVID-19, which has proved very effective as it provides a prompt, accurate and specific response to SARS-CoV2 in the tested samples[22]. With technological and industrial advancement around the world, there is also a sharp rise in the emergence of new viruses such as the coronavirus, which are highly contagious and have the capability to cause a major loss of life. In such situations, biosensors have been of great help due to their quick and accurate responses. Thus they have proved to be a stepping stone for doctors as they can rely on biosensors for diagnosis and thus plan the line of action to cure the disease.

C. Food Technology

● Quality of Food: Food can degrade as a result of digestion in microbial development, and tracking such deviations over time might provide us with an overall estimate of food quality [1][4]. Biosensors enable smart and responsive packing for food product freshness monitoring, which plays a significant role in food science. When the biosensor is near food, it may evaluate readings from signals obtained to determine the quantity and purity of the sample food. The outcome is shown on an LCD, and it is then possible to assess if the food is of high or low quality. Biosensors may be used in a range of situations, including hotels, private residences, and even small enterprises. This technology manages food chain monitoring without the need for human interference. (A buzzer linked to the sensor is used in some small experiments to support the blind and people with vision problems in determining the food quality).

● Detection of allergen: Food allergies are becoming a serious public health and food safety problem worldwide. People who are allergic to certain foods have negative reactions. Because it's incurable, the best course of action is to avoid it. The demand for fast, accurate, and accurate technologies for tracking food allergens has grown throughout the world as the danger of hidden allergies in foodstuff has grown. the microfluidic biosensor can help to detect these allergens present in the food.[15] Further according to [3], E-coli is the most dangerous pathogen which is food borne. It causes extreme symptoms such as bloody diarrhea, hemorrhagic colitis etc. it is so deadly that it is one of the major reasons of food related deaths around the world. Traditional methods to detect this pathogen are very time consuming and inefficient. Since E-coli has the ability to convert into a non-curable disease, it is very important to diagnose it well in time. Hence biosensors such as optical and electrochemical biosensors were developed to diagnose E-coli. In 2017, Zhang et al, developed a biosensor, which is a multichannel SPR based biosensor, which was able to detect the pathogen in very less quantity as well,[3] thus proving to be a life saver.

D. Market Analysis:

From 2021 to 2030, the biosensors market is estimated to increase at a CAGR (Compound annual growth rate) of approximately 8%, from USD 25.5 billion in 2021 to USD 36.7 billion [20]. The development of nanotechnology-based biosensors, considerable technological advances in recent years, growing need for biosensors for monitoring glucose levels in diabetes patients, surging demand for portable and easy to use devices in the COVID-19 pandemic, and increasing social programs toward medical therapies are some of the important primary drivers in the biosensors business (Biosensors based on nanotechnology are created of nanoparticles with diameters size less than 100 nanometers[18]. These biosensors are critical for understanding how the biosensing system works). According to the WHO, approximately 1.7 billion people were suffering from obesity in 2016, with almost 648.8 million of them being overweight. This has boosted industry growth by increasing sales of monitoring and analysis equipment used for the medical sensors in the house and hospital settings. During the projection timeframe, 2017-2024, the international demand for wearable sensors is expected to grow at a rapid rate [17]. Moreover, growing demand and acceptance of healthcare applications, along with rising government expenditure, are some of the primary factors expected to drive the worldwide wearable biosensors market over the forecast period.[21]

Conclusion

Biosensors are becoming increasingly popular as a result of their numerous uses. This technology is progressing at the same rate as demand. According to me, the scientist must concentrate on three major elements to increase the quality of biosensors: specificity, detection limit, and detection time. Biosensors have a bright future ahead of them, with widespread applications in screening tests, food analysis, smart manufacturing, and remote sensing.

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