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Biosensor: Concept, Classification and Applications

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Introduction

A biosensor is a device in which a biological element is used to sense chemicals in a system. The goal of the biosensor device is to produce an electric signal that is proportional to the amount of a chemical or a set of chemicals being sensed. Biosensors thus have an interdisciplinary design, combining the sensitivity and specificity of biological systems with the computational abilities of microprocessors. Biosensors are utilized in many fields such as medicine where they may be useful in diagnosing medical conditions and detecting genetic disorders, environmental monitoring of pollution and detection of hazardous chemicals, and in food analysis.

Working of Biosesnsor

Figure 1 shows the sensing process in terms of energy conversion. The form of the output signal will often be a voltage analogous to the input signal, though sometimes it may be a wave form whose frequency is proportional to the input or a pulse train containing the information in some other form.

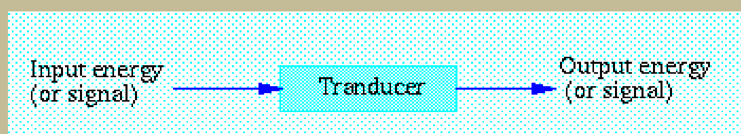

Figure 1 The sensing process

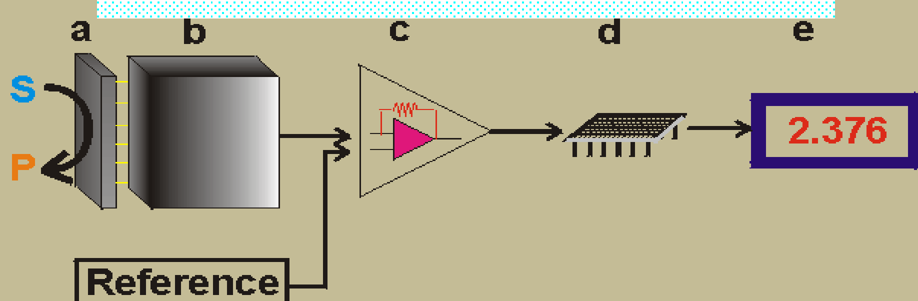

Figure 2. Schematic diagram showing the main components of a biosensor. The biocatalyst (a) converts the substrate to product. This reaction is determined by the transducer (b) which converts it to an electrical signal. The output from the transducer is amplified (c), processed (d) and displayed (e).

The key part of a biosensor is the transducer (shown as the 'black box' in Figure) which makes use of a physical change accompanying the reaction. This may be

1. The heat output (or absorbed) by the reaction (calorimetric biosensors),
2. Changes in the distribution of charges causing an electrical potential to be produced (potentiometric biosensors),
3. Movement of electrons produced in a redox reaction (amperometric biosensors),
4. Light output during the reaction or a light absorbance difference between the reactants and products (optical biosensors), or
5. Effects due to the mass of the reactants or products (piezo-electric biosensors).

History of Biosensor:

The concept of biosensor was come up by Professor Leland C Clark in 1956, who was identified as the father of the biosensor concept.

Year	Invention
1956	oxygen electrode
1962	the idea of more intelligent electrochemical sensors by adding enzyme transducers
1974	thermal transducers such as thermal enzyme probes and enzyme thermistors were proposed
In 1975	the idea of oxygen electrode Clark came to reality
In 1975	idea of utilizing bacteria as the biological element in microbial electrodes for the measurement of alcohol
1975	Lubbers and Opitz coined the term optode, the concept of an optical biosensor for alcohol was mentioned.
In 1976	Clemens incorporated Biostator an electrochemical glucose biosensor.
In 1976,	La Roche introduced the Lactate Analyser LA 640
In 1982,	Shichiri et al. reported in vivo application of glucose biosensors
In 1984,	A cited paper on the use of ferrocene and its derivatives as an immobilised mediator for use with oxidoreductases was published.
In 1987	a pen-sized meter for home blood glucose monitoring was launched by MediSense.
In 1996,	the sale of this home blood glucose monitoring reached 175 million dollars

Biosensors -combines multiple disciplines

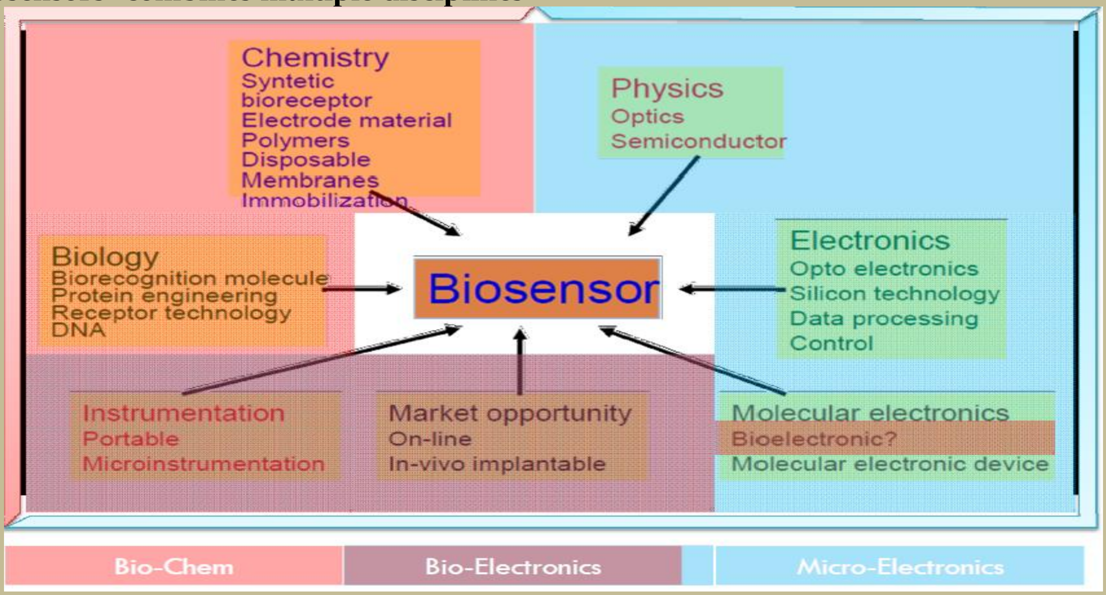

Figure 3. Biosensors in multiple disciplines

Components and mechanism of a biosensor:

A biosensor mainly consists of two parts(i) a biological part: this constitutes of enzymes antibodies etc., which mainly interacts with the analyte particles and induce a physical change in these particles (ii) a transducer part: which collects information from the biological part, converts, amplifies and display them. In order to form a biosensor, the biological particles are immobilized on the transducer surface which acts as a point of contact between the transducer and analyte. When a biosensor is used to analyse a sample, the biological part specific to the analyte molecules, interacts specifically and efficiently. This produces a physicochemical change of the transducer surface. This change is picked up by the transducer and gets converted into electric signals. These then undergo amplification, interpretation and finally display of these electric units accounting to the amount of analyte present in the sample.

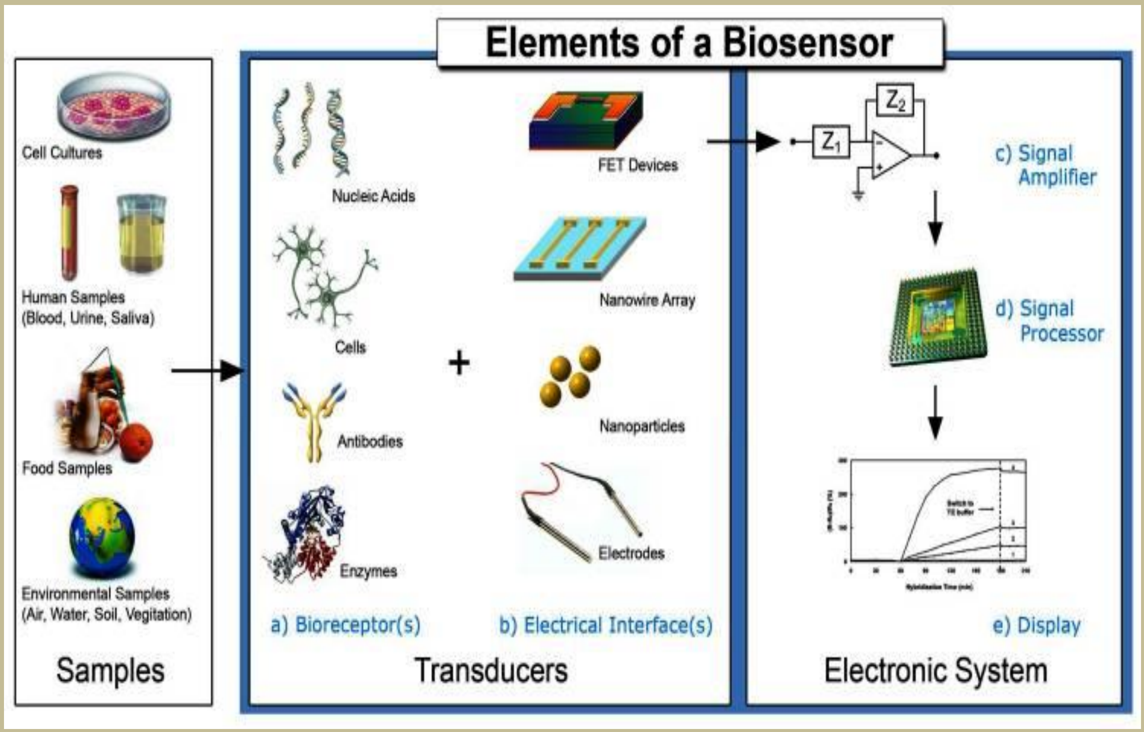

Figure 4.Elements and selected components of a typical biosensor.

Classification of biosensors

Biosensors may be classified according to the biological specificity-conferring mechanism , or the mode of signal transduction or, alternatively, a combination of the two. These might also be described as amperometric, potentiometric, field-effect or conductivity sensors. Alternatively, they could be termed, for example, amperometric enzymme sensors [6]. As an example, the former biosensors may be considered as enzyme- or immuno-sensors.

1.Receptor Based

Biocatalytic: In this case, the biosensor is based on a reaction catalysed by macromolecules, which are present in their original biological environment, have been isolated previously or have been manufactured. Thus, a continuous consumption of substrate(s) is achieved by the immobilized biocatalyst incorporated into the sensor: transient or steady-state responses are monitored by the integrated detector. Three types of biocatalyst are commonly used.

(a)Enzyme(mono-or multi-enzyme): the most common and well-developed recognition system.

(b)Whole cells(micro-organisms, such as bacteria, fungi, eukaryotic cells or yeast) or cell organelles or particles(mitochondria, cell walls).

(c)Tissue(plant or animal tissue slice)

Biocomplexing: The biosensor operation is based on the interaction of the analyte with macromolecules or organized molecular assemblies that have either been isolated from their original biological environment or engineered. Thus, equilibrium is usually reached and there is no further net consumption of the analyte by the immobilized biocomplexing agent. These equilibrium responses are monitored by the integrated detector. In some cases, this biocomplexing reaction is itself monitored using a complementary biocatalytic reaction. Steady-state or transient signals are then monitored by the integrated detector.

2. Based on Mode:

a.Electrochemical

Amperometric Biosensors: These electrodes function by the production of a current when potential is applied between two electrodes, the magnitude of current being proportional to the substrate concentration. The simplest amperometric biosensors use the Clark oxygen electrode which determines the reduction of O_2 present in the sample (analyte) solution. These are the first generation biosensors. These biosensors are used to measure redox reactions, a typical example being the determination of glucose using glucose oxidase. A major problem of such biosensors is their dependence on the dissolved O_2 concentration in the analyte solution. This may be overcome by using mediators; these molecules transfer the electrons generated by the reaction directly to the electrode rather than reducing the O_2 dissolved in analyte solution. These are also called second generation biosensors. The present day electrodes, however, remove the electrons directly from the reduced enzymes without the help of mediators, and are coated with electrically conducting organic salts.

Potentiometry (Potentiometric Biosensors): These biosensors use ion-selective electrodes to convert the biological reaction into electronic signal. The electrodes employed are most commonly pH meter glass electrodes (for cations), glass pH electrodes coated with a gas selective membrane (for CO_2, NH, or H_2S) or solid state electrodes. Many reactions generate or use H^+ which is detected and measured by the biosensor; in such cases very weak buffered solutions are used. Gas sensing electrodes detect and measure the amount of gas produced. Biosensors can now be prepared by placing enzyme coated membranes on the ion-selective gates of ion-selective filed effect transistors; these biosensors are extremely small.

Conductometry(Calorimetric Biosensors): Many enzyme catalyzed reactions are exothermic. Calorimetric biosensors measure the temperature change of the solution containing the analyte following enzyme action and interpret it in terms of the analyte concentration in the solution. The analyte solution is passed through a small packed bed column containing immobilized enzyme; the temperature of the solution is determined just before entry of the solution into the column and just as it is leaving the column using separate thermistors. This is the most generally applicable type of biosensor, and it can be used for turbid and strongly coloured solutions. The greatest disadvantage is to maintain the temperature of the sample stream, say ± 0.01° C, temperature. The sensitivity and the range of such biosensors is quite low for most applications. The sensitivity can be increased by using two or more enzymes of the pathway in the biosensor to link several reactions to increase the heat output. Alternatively, multifunctional enzymes may be used. An example is the use of glucose oxidase for determination of glucose.

Voltammetry: This type belongs to a category of electro-analytical methods, through which information about an analyte is obtained by varying a potential and then measuring the resulting current. It is, therefore, an amperometric technique. Since there are many ways to vary a potential, there are also many forms of voltammetry, such as:

polarography (DC Voltage), linear sweep, differential staircase, normal pulse, reverse pulse, differential pulse and more.

Field-Effect Transistor (FET): The FET is a type of transistor that uses an electric field to control the conductivity of a channel (*i.e.* a region depleted of charge carriers) between two electrodes (*i.e.* the *source* and *drain*) in a semiconducting material. Control of the conductivity is achieved by varying the electric field potential, relative to the source and drain electrode, at a third electrode, known as the *gate*. Depending on the configuration and doping of the semiconducting material, the presence of a sufficient positive or negative potential at the gate electrode would either attract charge carriers (*e.g.* electrons) or repel charge carriers in the conduction channel.

b.Optical Biosensors: The output transduced signal that is measured is light for this type of biosensor. The biosensor can be made based on optical diffraction or electro chemiluminescence. In optical diffraction based devices, a silicon wafer is coated with a protein via covalent bonds. The wafer is exposed to UV light through a photo-mask and the antibodies become inactive in the exposed regions. When the diced wafer chips are incubated in an analyte, antigen-antibody bindings are formed in the active regions, thus creating a diffraction grating. This grating produces a diffraction signal when illuminated with a light source such as laser. The resulting signal can be measured or can be further amplified before measuring for improved sensitivity.

c.Piezoelectric

Piezoelectric transducers are the smallest of balances. Crystals, such of those of quartz, have no center of symmetry and produce an electrical signal when stressed mechanically (i.e.by applying some pressure on them).A crystal oscillates at a certain frequency, which can be modulated by its environment. When the crystal is coated with some material, the actual frequency depends on the mass of the crystal and the coating. The resonant frequency can be measured with great accuracy hence making it possible to calculate the mass of analyte adsorbed onto the crystal surface. This means, that with these devices, detection limits are down to the picogram level. Antibodies, enzymes and antigens have been used as biological elements in these devices.

Ultrasonic

It is also known as transceivers when they both send and receive, but more generally called transducers work on a principle similar to radar or sonar, which evaluate attributes of a target by interpreting the echoes from radio or sound waves respectively. Active ultrasonic sensors generate high frequency sound waves and evaluate the echo which is received back by the sensor, measuring the time interval between sending the signal and receiving the echo to determine the distance to an object. Passive ultrasonic sensors are basically microphones that detect ultrasonic noise that is present under certain conditions.

Medicinal Application:

(Some of the Biosensors are mention below)

Glucose Biosensors

The most commercially successful biosensors are amperometric glucose biosensors. These biosensors have been made available in the market in various shapes and forms such as glucose pens, glucose displays, etc.. The amperometric reading of the biosensor (current versus glucose concentration) shows that the relationship is linear up to a specific glucose concentration. In other words current increases linearly with glucose concentration, hence it can be used for detection. The current and future applications of glucose biosensors are very broad due to their immediate use in diabetic self-monitoring of capillary blood glucose. These types of monitoring devices comprise one of the largest markets for biosensors today and their existence has dramatically improved the quality of life of diabetics.

Lactate Biosensor

As the biosensors were on the developing stages, the approach towards the miniaturization was also progressing. National Physical Laboratory, India developed a lactate biosensor based on screen printed electrode

Cholesterol Biosensor

Cholesterol Biosensor was fabricated by immobilizing the enzymes in the sol gel films and then utilized these films on amperometer instrument.

DNA Biosensor

DNA biosensor is of utmost importance in diagnosis of inherited diseases, screening of c-DNA colonies required in molecular biology. The technique here is same as of immobilization of DNA on conducting polypyrrole and these were adopted for response on electrochemical sensor.

Ampicilin electrochemical sensor was developed by Khalilzadeh et al in 2009.It has a linear range of 2.34 – 30 μ mol/L with a detection limit of 0.67 μ mol/L. This sensor had been applied for detection of drugs in urine samples.

Fructosyl Valine

Chun and Chou developed a elctrochemical sensor for estimation of Fructosyl Valine.Its measurement is far better and sensitive than Glucose for diabetes management. The minimum detection limit is <0.05mM.

Conclusion:

In this paper presents various, basic concepts of the biosensor various elements of biosensors were described, and a brief review of bioreceptors and transduction mechanisms were provided. A high level overview of different types of biosensors is also given and applications of many biosensors are presented. In recent years the emerging area of nanotechnology has produced very interesting materials, some of which provide opportunities for new sensing transduction technologies useful for biosensor development. Population growth and the increasing number of people suffering from chronic debilitating illnesses are the main causes for the growing biosensor market in medical diagnostics. I hope that this brief overview has illustrated that biosensors have achieved considerable success both in the commercial and academic arenas.

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