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Review Article

Biosensors: Functions and Applications

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Abstract

The development of biosensors has been the center of scientist's attention for recent decades. Biosensors can essentially serve as low-cost and highly efficient devices for this purpose in addition to being used in other day to day applications. Biosensor is a device that consists of two main parts: A bioreceptor and a transducer. Bioreceptor is a biological component that recognizes the target analyte and transducer is a physicochemical detector component that converts the recognition event into a measurable signal. Biomolecules such as enzymes, antibodies, receptors, organelles and microorganisms as well as animal and plant cells or tissues have been used as biological sensing elements. In this paper, we review recent development in use of biosensors as a diagnostic tool, as well as some future applications of biosensor technology.

Keywords: Biosensors, Microbial biosensor, Transducer, Pathogen detection

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1. Introduction

The history of biosensors started in the year 1962 with the development of enzyme electrodes by the scientist Leland C. Clark. Since then, research communities from various fields such as VLSI, Physics, Chemistry, and Material Science have come together to develop more sophisticated, reliable and mature biosensing devices for applications in the fields of medicine, agriculture, biotechnology, as well as the military and bioterrorism detection and prevention [1]. Biosensor is a device that consists of two main parts: A bioreceptor and a transducer. Bioreceptor is a biological component (tissue, microorganisms, organelles, cell receptors, enzymes, antibodies, nucleic acids, etc) that recognizes the target analyte. Other part is transducer, a physicochemical detector component that converts the recognition event into a measurable signal [2 and 3]. The function of a biosensor depends on the biochemical specificity of the biologically active material. The choice of the biological material will depend on a number of factors via the specificity, storage, operational and environmental stability [2 and 4]. Biosensors can have a variety of biomedical, industry, and military applications. The major application so far is in blood glucose sensing because of its abundant market potential [1 and 5]. Biomolecules such as enzymes, antibodies, receptors, organelles and microorganisms as well as animal and plant cells or tissues have been used as biological sensing elements [2]. Microorganisms have been integrated with a variety of transducers such as amperometric, potentiometric, calorimetric, conductimetric, colorimetric, luminescence and fluorescence to construct biosensor devices [3, 6 and 7]. In this paper, we review recent development in use of biosensors as a diagnostic tool, as well as some future applications of biosensor technology.

2. Types of Biosensors

2.1. Resonant Biosensor

In this type of biosensor, an acoustic wave transducer is coupled with an antibody (bio-element). When the analyte molecule (or antigen) gets attached to the membrane, the mass of the membrane changes. The resulting change in the mass subsequently changes the resonant frequency of the transducer. This frequency change is then measured [8].

2.2. 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 electrochemiluminescence. Optical transducers are particularly attractive for application to direct (label-free) detection of bacteria. These sensors are able to detect minute changes in the refractive index or thickness which occur when cells bind to receptors immobilized on the transducer surface. They correlate changes in concentration, mass or number of molecules to direct changes in characteristics of light. Several optical techniques have been reported for detection of bacterial pathogens including: monomode dielectric waveguides, surface plasmon resonance (SPR), ellipsometry, the resonant mirror and the interferometer etc [9-11].

2.2.1. Surface plasmon resonance (SPR) biosensor

This is an evanescent field based optical sensors using thin gold film for sensing applications. The interaction between analyte flowing over immobilized interactant on gold surface is probed through the detection of reflection minima on photo-detector array sensors. SPR has successfully been applied to the detection of pathogen bacteria by means of immunoreactions [11 and 12].

2.2.2. Piezoelectric biosensors

Piezoelectric (PZ) biosensor offers a real-time output, simplicity of use and cost effectiveness. The general idea is based on coating the surface of the PZ sensor with a selectively binding substance, for example, antibodies to bacteria, and then placing it in a solution containing bacteria. The bacteria will bind to the antibodies and the mass of the crystal will increase while the resonance frequency of oscillation will decrease proportionally [9 and 11].

2.3. Thermal Biosensors

This type of biosensor is exploiting one of the fundamental properties of biological reactions, namely absorption or production of heat, which in turn changes the temperature of the medium in which the reaction takes place. They are constructed by combining immobilized enzyme molecules with temperature sensors. When the analyte comes in contact with the enzyme, the heat reaction of the enzyme is measured and is calibrated against the analyte concentration. Common applications of this type of biosensor include the detection of pesticides and pathogenic bacteria [11].

2.4. Electrochemical Biosensors

Electrochemical biosensors are mainly used for the detection of hybridized DNA, DNA-binding drugs, glucose concentration, etc. Electrochemical biosensors can be classified based on the measuring electrical parameters as: (i) conductimetric, (ii) amperometric and (iii) potentiometric. Compared to optical methods, electrochemistry allows the analyst to work with turbid samples, and the capital cost of equipment is much lower. On the other hand, electrochemical methods present slightly more limited selectivity and sensitivity than their optical counterparts [9 and 13].

2.4.1. Conductimetric Biosensors

The measured parameter is the electrical conductance/resistance of the solution. When electrochemical reactions produce ions or electrons, the overall conductivity or resistivity of the solution changes. This change is measured and calibrated to a proper scale. Conductance measurements have relatively low sensitivity [9].

2.4.2. Amperometric Biosensors

This is perhaps the most common electrochemical detection method used in biosensors. This high sensitivity biosensor can detect electroactive species present in biological test samples. Amperometric biosensors produce a current proportional to the concentration of the substance to be detected. The most common amperometric biosensors use the Clark Oxygen electrode [9 and 11].

2.4.3. Potentiometric Biosensors

These are the least common of all biosensors, but different strategies may be found nonetheless in this type of sensor the measured parameter is oxidation or reduction potential of an electrochemical reaction. The working principle relies on the fact that when a voltage is applied to an electrode in solution, a current flow occurs because of electrochemical reactions. The voltage at which these reactions occur indicates a particular reaction and particular species [2 and 11].

2.5. Bioluminescence sensors

Recent advances in bioanalytical sensors have led to the utilization of the ability of certain enzymes to emit photons as a byproduct of their reactions. This phenomenon is known as bioluminescence. The potential applications of bioluminescence for bacterial detection were initiated by the development of luciferase reporter phages. The bacterial luminescence *lux* gene has been widely applied as a reporter either in an inducible or constitutive manner. In the inducible manner, the reporter *lux* gene is fused to a promoter regulated by the concentration of a compound of interest. As a result, the concentration of the compound can be quantitatively analyzed by detecting the bioluminescence intensity. Bioluminescence systems have been used for detection of a wide range of microorganisms [2 and 11].

2.6. Nucleic Acid-based Biosensors

A nucleic acid biosensor is an analytical device that integrates an oligonucleotide with a signal transducer. The nucleic acid probe is immobilized on the transducer and acts as the bio-recognition molecule to detect DNA/RNA fragments [11].

2.7. Nanobiosensors

Nanosensors can be defined as sensors based on nanotechnology. Development of nanobiosensor is one of the most recent advancement in the field of Nanotechnology. The silver and certain other noble metal nanoparticles have many important applications in the field of biolabelling, drug delivery system, filters and also antimicrobial drugs, sensors [14].

3. Microbial Biosensors

Microbes have a number of advantages as biological sensing materials in the fabrication of biosensors. They are present ubiquitously and are able to metabolize a wide range of chemical compounds. Microorganisms have a great capacity to adapt to adverse conditions and to develop the ability to degrade new molecules with time. Microbes are also amenable for genetic modifications through mutation or through recombinant DNA technology and serve as an economical source of intracellular enzymes. Purified enzymes have been most commonly used in the construction of biosensors due to their high specific activities as well as high analytical specificity. Over 90% of the enzymes known to date are intracellular. In this respect, the utilization of whole cells as a source of intracellular enzymes has been shown to be a better alternative to purified enzymes in various industrial processes. Whole cells have been used either in a viable or non-viable form. Viable cells are gaining considerable importance in the fabrication of biosensors. Viable microbes metabolize various organic compounds either anaerobically or aerobically resulting in various end products like ammonia, carbon dioxide, acids etc that can be monitored using a variety of transducers. Viable cells are mainly used when the overall substrate assimilation capacity of microorganisms is taken as an index of respiratory metabolic activity, as in the case of estimation of biological oxygen demand (BOD) or utilization of other growth or metabolically related nutrients like vitamins, sugars, organic acids and nitrogenous compounds. Another mechanism used for the viable microbial biosensor involves the inhibition of microbial respiration by the analyte of interest, like environmental pollutants.

The major application of microbial biosensors is in the environmental field [4 and 15]. Environmental applications of biosensors include the detection of harmful bacteria or pesticides in air, water, or food. A microbial biosensor consisting of an oxygen microelectrode with microbial cells immobilized in polyvinyl alcohol has been fabricated for the measurement of bioavailable organic carbon in toxic sediments. Microbial biosensors have been developed for assaying BOD, a value related to total content of organic materials in wastewater. BOD sensors take advantage of the high reaction rates of microorganisms interfaced to electrodes to measure the oxygen depletion rates [2, 16 and 17].

4. Biosensors and cancer

Cancer diagnosis and treatment are of great interest due to the widespread occurrence of the diseases, high death rate, and recurrence after treatment. According to the National Vital Statistics Reports, from 2002 to 2006 the rate of incidence (per 100,000 persons) of cancer in White people was 470.6, in Black people 493.6, in Asians 311.1, indicating that cancer is wide- spread among all races. Cancer can take over 200 distinct forms, including lung, prostate, breast, ovarian, hematologic, skin, and colon cancer, and leukemia, and both environmental factors, and genetic factors are associated with an increased risk of developing cancer. Bacterial and viral infections are also strongly associated with some types of cancer [18 and 19]. In medicine, biosensors can be used to monitor blood glucose levels in diabetics, detect pathogens, and diagnose and monitor cancer [20]. The use of emerging biosensor technology could be instrumental in early cancer detection and more effective treatments, particularly for those cancers that are typically diagnosed at late stages and respond poorly to treatment, resulting in improvements in patient quality of life and overall chance of survival [19]. By measuring levels of certain proteins expressed and/or secreted by tumor cells, biosensors can detect whether a tumor is present, whether it is benign or cancerous, and whether treatment has been effective in reducing or eliminating cancerous cells [19 and 20].

5. Biosensors and Pathogen detection

Bacteria, viruses and other microorganisms are found widely in nature and environment. Microbial diseases constitute the major cause of deaths in developing countries [11]. Pathogen detection is of the utmost importance primarily for health and safety reasons. Polymerase chain reaction (PCR), culture and colony counting methods as well as immunology-based methods are the most common tools used for pathogen detection. They involve DNA analysis, counting of bacteria and antigen–antibody interactions, respectively. In spite of disadvantages such as the time required for the analysis or the complexity of their use, they still represent a field where progress is possible. Biosensors have recently been defined as analytical devices incorporating a biological material intimately associated with or integrated within a physicochemical transducer or transducing microsystem, which may be optical, electrochemical, thermometric, piezoelectric, magnetic or micromechanical [9 and 21]. There are three main classes of biological recognition elements which are used in biosensor applications. These are enzymes, antibodies and, nucleic acids. In the detection of pathogenic bacteria, however, enzymes tend to function as labels rather than actual bacterial recognition elements. Enzymes can be used to label either antibodies or DNA probes much in the same fashion as in an ELISA assay. In the case of amperometric biosensors enzymatic labels are critical. More advanced techniques may operate without labelling the recognition element, such as the case of surface plasmon resonance (SPR), piezoelectric or impedimetric biosensors. The use of antibodies in biosensors is currently more spread than that of DNA probes, the following sections deal mainly with antibody-based biosensors. Fig.1 shows the three most frequent antibody immobilisation routes, which are:

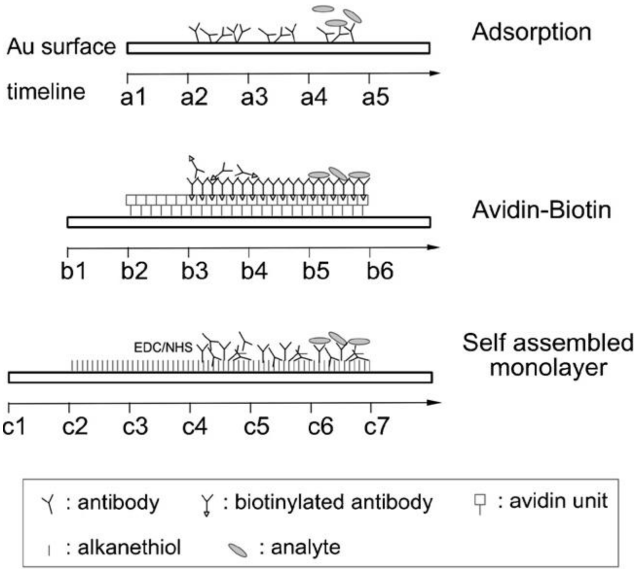

Figure 1. Main immobilization strategies

Different types of biosensor are being employed for detection of pathogenic microbes. Piezoelectric immunosensors were developed for *Listeria monocytogenes* and members of the Enterobacteriaceae family etc [22]. In the immunogravimetric microbial assay, a PZ crystal coated with anti-*C. albicans* antibody was used for the detection of *C. albicans* concentrations in the range of 106–108 cells/ml [22]. In study pyle *et al*, Indirect detection of *Escherichia coli* O157:H7 by flourescent labeled antibody method [23]. Amperometric biosensors have been developed for indirect detection of *E. coli* by Nakamura *et al*. Brooks *et al*, developed amperometric biosensor for Salmonella detection [24 and 25]. Light addressable potentiometric sensor array have been developed for *Neisseria meningitidis*, *Brucella melitensis* by Lee *et al*. [26]. Nucleic acid hybridization based biosensor schemes are being developed for pathogens such as *E. coli* and *Mycobacterium tuberculosis.* Bioluminescence systems have been used for detection of a wide range of microorganisms [11].

6. Conclusion

Biosensors have been miniaturised extensively in the recent years. Keeping in line with such developments, microbial cells with high enzyme activities may be required. This is essential especially when microbial cells are used as substitutes to enzyme based sensors. Microorganisms, due to their low cost, long lifetime and wide range of suitable pH and temperature, have been widely employed as the biosensing element in the construction of biosensors.

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