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Biosensors and their biomedical applications: Invited Review

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ABSTRACT

A biosensor is commonly defined as a self-contained analytical device that combine biological recognition system and a physiochemical transducer forthe detection of target molecules by converting recognition signal into detectable output signal. Majority of biosensing platforms generate measurable signal when a sensing element or probe in the detector interacts accurately with ananalyte of biological interest(DNA, biomarkers, cells, tissues, drugs or toxins etc).The probe: analyte interaction can be detected by various types of biosensor platforms, including electrochemical (amperometric and potentiometric), optical and calorimetric. Biosensor technology is constantly evolving to develop novel biosensors for point of care diagnostics. The emergence of nano-bioelectronic technologies has a great potential to lead to the development of next generation biosensors with improved sensitivity, specificity, portability and cost effectiveness. This mini review discusses about biosensors, their classifications, mechanisms involved in their function and their biomedical applications.

Keywords: *Biosensor; classification, mechanism, biomedical application.*

INTRODUCTION

Biosensor technology is an evolving interdisciplinary research field encompassing biological science, chemistry, material science, physics, electronics, engineering and medicine. A biosensor is actually an analytical tool or a system comprising a biological recognition element with a physical or chemical transducer component that converts biochemical signal into measureable signal (electrical, optical etc.) proportional to an analyte. A typical biosensor consist of three main components: the biological recognition element that detect the stimulus, the transducer that convert the stimulus to output signal, and the signal processing system that process the output signal and portray it in an appropriate format.

The first oxygen biosensor was developed by Lel and Clark in 1962 [1]. Since then biosensing research have gained a tremendous attention in recent years in biomedicine and bionano technology. Several research groups in diverse fields from across the globe are actively engaged in biosensor research and have developed numerous biosensors for various applications. Biosensors are gradually becoming an integral

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part of cancer, neurobiology,pathophysiology, nano biotechnology, tissue engineering and regenerative medicine research areas because biosensors usually show the capability to monitor specifi probe- analyte interaction within complex biological system in real-time, at very low concentration levels, through ultra sensitive optical or electrochemical sensing systems[2-7]. Broadly speaking, biosensors research is a rapidly expanding research area in which tens of thousands of reports have already been published over the years, and the industry is now worth billions of dollars. The most frequent use of biosensor so far has been in blood glucose monitoring [8].

The main advantage of applying biosensor for biodetection compared to other conventional approaches including biochemical assays, immunoassays and PCR based assays is that the sample can be used without labeling and washing steps prior to the readout, reusability and rapid response along with high specificity. For example,cancer can be conventionally detected by observing the presence of certain amount of antigens in the bloodstream or other biological fluids, or through histochemistry. Similarly, diabetes is widely detected by assessing the glucose concentrations in the blood. Despite of the wide spread clinical applications of the conventional assays, most of these existing techniques are expensive, require sophisticated instruments to maintain and run, and the procedures for preparation of samples are rather time consuming and have several other shortcomings. Furthermore, these approaches are expensive and cost the health care industry billions of dollars every year. Development of fast and label-free biosensing strategies for the early observation and diagnosis are obviously of much importance and these strategies can be applied to greatly reduce the cost of patient care associated with advanced stages of several debilitating diseases. Thus, there is a need to develop more rapid, facile, efficient and inexpensive analytical tools with the capability to detect pathogenic and physiologically relevant biomolecules in the complex biological samples offers a powerful opportunity in routine analysis, precise clinical diagnosis and treatment of diseases.

CLASSIFICATION OF BIOSENSORS

Broad classification for biosensors includes the following criteria:(i) based on their sensing components, and (ii) based on the methods of signal transduction

Bioreceptor Components

The bioreceptor components of biosensors can be classified either by the type of biological signaling pathway they utilize or by the type of signal transduction they employ. Typically, bioreceptor components use one of following materials: Microbes, enzymes, nucleic acids, organelles, receptors,whole cell, biological tissues, biomimetic materials etc.

Methods of Signal transduction

Biosensors can also be grouped into different types according to their mode of signal transduction. The transducer component of biosensors can be grouped into different types such a electrochemical (amperometric and potentiometric), optical (absorbance, fluorescence, phosphorescence, Raman, SERS, SPR/SPRI, DHM and dispersion spectrometry), piezoelectric (acoustic and ultrasonic) and calorimetric.

Electrochemical Biosensors

Electrochemical biosensorsare generally applied for the monitoring of DNA hybridization, DNA-binding drugs, blood glucose concentration, and antigen antibody binding reactions, cancer cell detection and so on. The underlying mechanism for this category of biosensors is that several chemical interactions consume or produce ions/ electrons which in turn lead to alteration in the electrical properties of the solution which can be recorded and used as measuring parameter. Electrochemical biosensors can be generally categorized based on the measuring electrical parameters such as: (i) amperometric, and (iii)potentiometric types. The electrochemical sensor platform is usually constructed using three electrode system: a reference electrode, a working electrode, and a counter electrode. The reaction for target analyte takes place on the active working electrode surface [9-12].

Amperometric Biosensor

Ultrasensitive amperometric biosensor can detect electro active substances present in test sample. The potential between two electrodes can be adjusted and current generated by the oxidation or reduction of electro active species can be recorded and correlated to the concentration of the analyte of interest. Since the biological test samples may not be intrinsically electro-active, enzymes are needed to catalyze the production of radio-active species. Alternatively, various conducting nanohybrids structures or conducting polymer incorporated nanomaterials can be used to modify the electrode surface. The application of amperometric biosensors in signal transduction has proved to be the most reliable and easy approach for point of care diagnostics [13-14].

Potentiometric Biosensor

Potentiometric biosensors are based on observing the potential of a system at a working electrode, with respect to an accurate reference electrode, under conditions of essentially zero current flow. In this system, the measuring parameter is oxidation or reduction potential of an electrochemical reaction. In this case ion selective sensor probes can be used to record changes in the concentration of chosen ions. The underlying working principle relies on the fact that when a ramp voltage is applied to sensor placed in the measuring solution, a current flow takes place due to electrochemical reactions. The voltage at which the sereactions happen indicates a particular reaction for a given species[15-17].

Optical Biosensors

Optical biosensors are the most diverse class of biosensors which are based on signal responses due to light illumination, light emission or optical diffraction. Optical sensors can monitor microscopic alterations during cells-receptors binding maintained on the transducer surface. They use the changes in mass, concentration, or number of molecules to direct changes in characteristics of light. Optical biosensors can use a variety of techniques including surface plasmon resonance (SPR), surface plasmon resonance imaging (SPRi), fluorescence,chemiluminescence, light absorbance, phosphoresence, light polarization and rotation, total internal reflectance and photothermal techniques[18-29].

Calorimetric Biosensor

In calorimetric transducers, most of the biochemical reactions are accompanied by either heat production or absorption. These sensors are constructed in such a way that they can quickly detect changes in the temperature generated or consumed during biochemical reactions. Various enzymes catalyzed reaction are exothermic in nature and generating heat which is used as a basis for measurement of rate of reaction and analyte concentration[30-31].

Biomedical and Diagnostic Applications (detection of glucose)

Development of the novel bio-micro and nano-biosensors with the capability to monitor pathogenic and physiologically relevant biomolecules, such as pathogens, neurotransmitter, nucleic acids, proteins, disease-specific metabolites, and cells such as circulating tumor, is very essential not only for disease diagnosis and treatment in the routine clinical analysis but also for biomedical research approaches involving drug development and discovery[2,3,32-40].

Several biomolecules relevant to pathophysiology are greatly useful to assess normal or pathophysiological state of health disorder. Thus, real time observation of health condition for early detection of disease disorders in human beings is very essential for maintaining a normal and healthy life. For example, diabetes mellitus is a serious metabolic health disorder, and the number of diabetic patients has largely increased despite advances in modern biomedical research and technology. Thus, in order to prevent and reduce complications from diseases associated with diabetes mellitus, accurate and reliable observation of blood glucose levels is of paramount significance in clinical diagnostics as a diabetic marker[41].

Over the last decade, a tremendous progress has been made in the research area of diagnostics along many fronts, in particular in the area of biosensing, both for single analyte detection methods or multi-array based technology. In the last few years, numerous studies regarding glucose sensors have been reported, and millions of diabetes patient test their blood glucose levels daily, making glucose the most commonly tested analyte. The biodetection strategies that have demonstrated promising successes for analysis of glucose levels with high accuracy include electrochemical methods [42-43], colorimetry, fluorescent spectroscopy, polarimetry [44-45], absorption/transmission spectroscopy [46-47], diffuse reflection spectroscopy [48-49], thermal emission spectroscopy [50-51], near-infrared spectroscopy (NIRS) [52-54] and photo acoustic spectroscopy [55].

The recent advances in application of micro and nanoscale biosensor strategies have become a major diagnostic tools to accurately trace glucose concentration, and these biosensors are primarily targeted toward the measurement of blood glucose level in diabetic patients. Glucose biosensing techniques can also be useful to detect intracellular metabolism given that consumption of glucose by the cells is the best indication of cell metabolism and developed techniques can be further applied to detect glucose consumption in cell proliferation, differentiation and engineered tissue constructs.

There are various other clinical diagnostic applications that are principally being enabled by applying point of care biosensors in routine analysis. These applications include the observation of bacterial infections in urinary tract [56], detection of HIV-AIDS [57-58], cardiac infarctions and the diagnosis of cancer [59–61]. Indeed, all the aforementioned problems are associated with very critical health disorders affecting the human beings at present throughout the globe. Prior to the application of biosensing approaches, the analysis and diagnosis of these disease disorders were significantly default, labor intensive, time consuming and expensive. The advent of biosensor technology has really improved the clinical diagnosis of all these debilitating diseases and related malfunctions. Furthermore, with the addition of nanoscale interventions and the incorporation of nanostructures in biosensing methodology in combination with various natural and synthetic biomaterials, is creating a deep impact on the design of novel biological machines, bio-production systems, biological circuits, biopolymers, and consequently on the fabrication of diagnostic tools for biomedical, pharmaceutical, agriculture, and environmental monitoring application. Various sophisticated signal responses have been observed for biodetection via nanobiosensors techniques using different ways of their conductive material incorporation in sensing mechanisms [62-66]

CONCLUSION

Over the past few years, biosensors are widely applied in pharmaceuticals, biomedical,

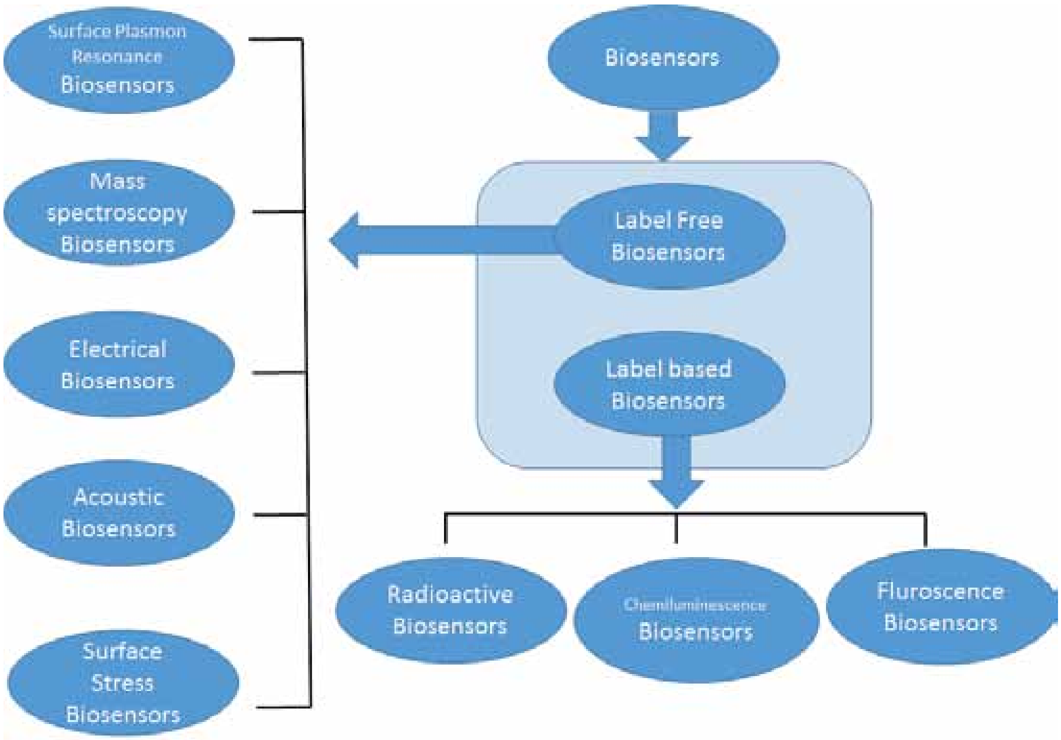

Fig. 1. Classification of the design art of biosensors based on the detection method

health care settings. Advancements in bioanotechnology, with its nanostructures-enhanced sensitivity and miniaturization strategies, will rapidly improve our current bio diagnostic capacity in terms of selectivity, sensitivity, robustness and cost effectiveness. More importantly, miniaturization of the biosensor probeis expected to provide great versatility for integration of sensing platforms into multiplexed, portable wearable, and even implantable point of care devices for in vitro and in vivo analytical applications. Furthermore, the incorporation of micro and nanoscale ultrasensitive biosensing platforms with other conventional medical devices will pave the direction to emerging medical research fields, including ubiquitous healthcare systems and point-of-care diagnostics.

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