RECENT ADVANCES IN BIOSENSOR TECHNOLOGY

Editors:
Vivek K. Chaturvedi
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Recent Advances in Biosensor Technology

(Volume 1)

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FOREWORD

Recently, there has been a tremendous surge in the research and development of nanoscience and nanotechnology, especially in precisely engineering the size, shape, and composition. A plethora of novel nanomaterials have been developed that possess excellent intrinsic properties of absorbance, fluorescence, chemiluminescence and catalysis. These properties are being harnessed to realize the actual potential of nanotechnology for several applications, such as electronics, optical, nanomedicine, drug delivery, catalysis and biosensing. The use of nanomaterials in developing biosensors holds special promise due to their indispensable role in clinical diagnosis, biomolecule engineering, cancer detection, and sensing of bacteria, viruses, pathogens, and toxic metabolites. Additionally, incorporating suitable nanoparticles has also led to the construction of new biosensors with improved detection ability and ease of handling. Signal transduction-based biosensing technologies incorporating nanoparticles have shown their utility for the multiplexed detection of samples available in extremely low concentrations. Although nanotechnology-based biosensing employs several methodologies, several of these could be merged into the form of a portable “lab-on-a-chip” device that would be capable of running multiple analyses. The readout of such devices could be integrated with cell phones and thus shared with doctors and clinicians. Personalized medicine is another emerging area where nanotechnology could be of tremendous application. Nanotechnology-enabled wearable devices are another such kind that could provide the analysis of essential ions, biomarkers, glucose, and other biomolecules in the blood. The obtained database would be recorded on a microchip, which could be shared as and when required. Such innovations are expected to be an integral part of the future biosensing technologies that would better predict an individual's health state. Considering the above discussion on biosensing, this book is very timely and includes relevant background and the most recent advancements in the field. Graphene and carbon-based nanomaterials produce excellent biosensing platforms; therefore, a comprehensive analysis of their applications has been covered in this book. Other areas, such as heavy metal detection from contaminated wastewater and COVID-19 detection using nanotechnologies, have also been given significant attention. Nutrition, food contamination, and food packaging are other growing areas; producing nanotechnology-based innovations has also found a place in this book. A chapter is also dedicated to the role of biosensing technology in tissue engineering. This book is a must-read for researchers engaged in basic and clinical research related to biosensing technologies. The editors of this book are learned academicians and have produced this book very thoughtfully to provide readers with comprehensive information on biosensor technologies.

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PREFACE

A biosensor is a potential device that covers medical, agricultural, economical, industrial, and medical applications. Over the past few decades, glucose biosensors have emerged as the most acceptable and reliable biosensors; they are inexpensive, fast, and reliable. Biosensors also play a very promising role in detecting and managing COVID-19 cases worldwide. It is notable that modernization, industrialization, and environmental damage have greatly impacted human lives over the past few decades and led to major health concerns. Nowadays, even after exhausting several resources to prevent and treat chronic diseases, the human world bears the never-ending global burden of diseases. In recent years, the development of biosensors has significantly influenced the healthcare sector due to the promising role of biosensors in healthcare management. Biosensors work on the principle of converting a biochemical signal to optical or electrical signals. Signal transduction and its performance depend upon the selection of materials and interaction in biosensors. The application of biosensors is not restricted to detecting, diagnosing, and treating a myriad of chronic diseases; it extends toward monitoring and managing patient health. Therefore, biosensor-based therapies have emerged as possible and crucial approaches to delivering point-of-care diagnostics that match and surpass conventional standards regarding specificity, sensitivity, time, response, accuracy, and cost. In this book, considering the growing number of cancer cases and fatalities due to late illness detection worldwide, we have covered several biosensors and biomarkers as possible tools for early cancer detection. In addition, this book focuses on many types of nanomaterials, such as gold nanoparticles, quantum dots, polymeric nanoparticles, carbon nanotubes, nanodiamonds, and graphene nanostructured materials, which are currently being utilized in biosensors for clean and healthy environments. The study includes the fundamental as well as modern biosensors and their sensitivity and specificity; it also sheds light on their significant applications with attractive prospects in different interdisciplinary fields. This book comprises several new efficient techniques for developing biomaterials to accelerate wound healing and bone tissue engineering. It would interest readers in the areas of health, agriculture, food, industries, and biomedical sciences-related research. Due to its quality content, this book will cater to the academic needs of a long range of readers.

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CHAPTER 1

Nanomaterials for Biosensing Applications

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Abstract: A biosensor is a device that detects the presence of analytes with its biological receptor entity, having unique specificities corresponding to their analytes. Most of these analytes are usually physical in nature, such as DNA, proteins, antibodies, and antigens, but they may also be simple compounds, including glucose, H_2O_2, toxins, and so on. Biosensors' significance rises in providing real-time quantitative and qualitative information on analyte composition. The sensing mechanism involves the transduction of target binding interactions into optical, electrochemical signals, *etc*., which can be amplified and detected.

Nanomaterials (NMs) have shown significant potential in biological sensing—these allow close interactions with target biomolecules due to their extremely small size and suitable surface modifications. Nanomaterials appear to be potential possibilities because of their capacity to immobilize a greater number of bioreceptor units in confined devices and even act as a transduction element, allowing for enhanced sensitivity and reduced detection limits down to specific molecules. Nanomaterials have been widely used for *in vitro* detection of disease-related molecular biomarkers and imaging, contrasts to map out the distribution of biomarkers *in vivo*. This chapter summarizes nanomaterials such as gold nanoparticles, quantum dots, polymeric nanoparticles, carbon nanotubes, nanodiamonds, and graphene nanostructured materials that are currently being researched or utilized as biosensors.

Keywords: Biosensors, Carbon nanostructures, Graphene nanostructure, Nanodiamonds, Nanomaterials, Quantum dots.

INTRODUCTION

Nanomaterials (NMs) have piqued the interest of many people because of the increasing preference to regulate highly favoured molecular systems not only in

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the human body but also in the environment. The interface of nanomaterials with bioactive molecules such as proteins, enzymes, and nucleic acid has arisen as a multidisciplinary area described as “nanotechnology” which refers to the scientific ways by which nanoparticles or nanomaterials are integrated to generate instruments for investigating biological mechanisms [1].

According to the European Commission's 2011 suggestion, nanomaterials (NMs) “are a natural, incidental, or manufactured material containing particles, in an unbound state, as an aggregate, or as an agglomerate, and where, for 50% or more of the particles in the number size distribution, one or more external dimensions are in the size range 1 nm-100 nm” [2]. NMs have distinctive characteristics, including a high specific surface/volume ratio, high sensitivity, excellent electrical properties, and outstanding magnetic and catalytic capabilities, among several others [3]. Adsorption and catalytic activity are very efficient due to active binding sites and an abundant supply of reactive surface functional groups of NMs. As a result, NMs may be employed in a variety of industries, including biosensors, medicines, cosmetics, agriculture, and energy, among others [4]. The increased total surface area of all nanomaterials allows for the immobilization of a more significant number of bio-recognition units. Nano-biochip materials, nanoscale biocompatible materials, nanomotors, nanocomposites, interface biomaterials, nano biosensors, and nano-drug-delivery platforms offer immense potential for industrial, security, food, forensic analysis, and therapeutic applications.

NMs are classified into three types depending on the materials used in their production, including (i) carbon-based nanostructures (*e.g*., Carbon nanotubes or CNTs, Graphene, Nanodiamonds, Fullerenes, *etc*.), (ii) organic (*e.g*., Quantum dots, Nanofilms, Nanogels, Dendrimers, *etc*.) or (iii) inorganic (*e.g*., Magnetic nanoparticles, Ag/Au nanoparticles, Nanoshells, Nanowires, *etc*.). Carbon-based nanostructures (such as carbon nanotubes or graphene) seem to be the most often employed NMs in biological investigations due to their diverse surface properties, and electrical and optical properties [5]. Among metallic NPs, Gold NPs are promising candidates because of their excellent oxidative stability and low toxic effects as contrasted to others, such as Ag, which oxidize and demonstrate cytotoxicity *in vivo* [6]. The large specific surface area of all NMs allows for the immobilization of an increased number of biorecognition units. Nevertheless, one of several ongoing hurdles is the immobilization technique employed to bind the specific analyte intimately onto such nanostructured materials. As a consequence, one of the most important elements in constructing a *via* ble biosensing system is the approach utilized to encapsulate the enzymes. The elements of NMs appropriateness in better transducer circuits are the size and shape-based energy of system distributions. For example, nanorods (NRs), nanotubes (NTs) or cylindrical architectures facilitate many contacts simultaneously at the same time, decreasing the overall reaction time and even expense. In this manner, even little changes in the typical reaction might be efficiently noticed.

A biological or biomimetic receiver element with distinct specificities toward related bioanalytics defines a biosensor system. Over the past ten years, substantial work has been spent on pioneering and continuing to develop biosensors with better specificity, responsiveness, affordability, simplicity, and detection time accuracy. In summary, a biosensing system is composed of a selective bioreceptor element (DNA, peptides, cells, aptamers, *etc*.) for analyte acquisition, a physical transducer (*e.g*., optical, electrochemical, thermal, acoustic, *etc*.), and signal processing unit for the electronic assessment of the accompanying interactions. Among the most essential difficulties in biosensing systems is achieving excellent sensitivity while maintaining an incredibly simple format to use, and the selection of an appropriate biological recognition interface is vital to this goal. Nanomaterials, like most other technical segments, have proved their inherent suitability for biological sensing applications. The main purpose of incorporating NMs into a biosensing operation is to optimize and improve responsiveness with the lowest detection limit in the shortest period. Due to their fast reaction times, nano biosensors are becoming more desirable for fast and real-time analyte monitoring and identification. Minimal LOD biosensors are applied to detect bioanalytics at trace amounts or volumes. The LOD is the lowest analyte concentration that a biosensing unit can recognize but not quantify, meanwhile, the LOQ is the lowest analyte concentration that a biosensor can quantify with therapeutic high precision and specificity. The appropriate employment of such nanostructured devices resulted in demonstrably improved performances, higher efficacy with improved sensitivities, and a lower sample amount requirement. Approaches towards engineering the NMs for a predictable output by manipulation of their interacting coordinates are presently being rapidly optimized for biosensing applications. The final attribute of NMs' usage in biosensing is unquestionably their large surface area, which confers stronger surface functionalization capacities, allowing for the tracking of any stimulus of the reactions in biological and environmental settings. The following surface modification methods are significant for attaching bio-physiological constituents to NM surfaces, including thiol-based NM, streptavidin-biotin association, π-π interactions, and EDC-NHS reactions.

The foremost objective of this chapter is to discuss an assessment of developments in the fields of innovative NM-based biosensor systems. We explain the production of carbon-based nanostructured materials, metals/metal oxides, and nanoparticle-based sensor systems, as well as their current and future applications for accurate and consistent monitoring of bioanalytics with higher

CHAPTER 2

Carbon-Based Nanomaterials for Sensing Applications

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Abstract: Recently, carbon-based nanomaterials (CBNM) have been widely used for chemical and biosensing applications due to their outstanding physicochemical properties, such as mechanical, thermal, optical, electrical and structural diversity. Such materials include carbon nanotubes, graphene oxide, graphene quantum dots and fullerene. As a consequence of inimitable features, these give superior strength, electrical conductivity, and flexibility toward numerous chemical and biological objects, which is valuable for chemical sensing and biosensing purposes. However, the specific intrinsic property makes graphene and carbon nanotubes (CNTs) most attractive among the various allotropes of carbon. Since the environmental contaminants in ppm level affect the people, therefore the use of CBNM for environmental sensing provides an accessible cache of data for modelling, which makes it easy to monitor environmental challenges. Thus, the biological, chemical, thermal, stress, optical, strain and flow sensors deliver a larger surface area, excellent electrical conductivity with chemical constancy, as well as mechanical difficulty with straightforward functionalization pathways of CNTs to improve old-style carbon electrode sensor platforms. Therefore, in this chapter, the CBNM for sensing purposes are focused in detail on their mechanism.

Keywords: Carbon electrode, CNT, Optical property, Physicochemical property, Sensors.

INTRODUCTION

Nowadays, due to the great demand for goods for a so-called better life, the production of such materials is being increased day by day, due to which global challenges have emerged, such as massive energy production and environmental pollution. To overcome this, new technologies or advanced materials are needed to improve the processes' efficiencies with an increase in productivity and reduce the generation of pollutants [1 - 8]. In this regard, the sensing technologies are co-

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nsiderable. Recently, there has been a wide range of sensors for sensing heavy/toxic metal ions, humidity, gas and biomolecules, physicochemical parameters and others [9, 10]. Though, these have their own limits in detection, slow responses, little sensitivity/selectivity, and require pre-treatment and expansiveness.

In this context, the nanomaterials offer a solution to overcome such limits of conventional sensors [10], improve parameters such as sensibility/ reliability, and shorten the response/ recovery times. These nanomaterials also make it a possibility to perform *in situ* analysis at a low cost. All these mentioned features are essential for producing effective sensor devices.

Recently, nanotechnology, especially based on carbon, has had rapid development sympathetic to nanoscale phenomena. CBNMs, like CNT, fullerenes, graphene and others, are recently gaining considerable attention from scientific communities because of their specific physicochemical properties. The CBNMs have a wide range of applications, such as detecting or sensing heavy metal ions, food additives, gas molecules, toxic pesticides, antibodies, and bioimaging. Moreover, biomedical applications, energy production, information technology, environmental protection, agriculture, food, *etc*. Thus, much more scientific efforts are being devoted to the mass production of CBNMs with controlled surfaces. Therefore, CBNMs are being utilized in many fields as sensors, such as in the environmental field for water treatment, separation processes [11 - 14] and remediation [15 - 17]; in the electronics field for excellent electrical utility and optical properties [18 - 22]. With electrical/thermal conductivity having high mechanical strength [23 - 26], the CBNMs are reinforcing elements, and protective materials to prepare conductive polymers [27 - 34]. CBNMs also have been used in the biomedical field due to their sensing ability in controlled or targeted drug release [35 - 39]. (Fig. **1**) summarises all the fields where CBNMs are used as sensors.

CBNMs, especially CNT, graphene, fullerene, carbon dots, and nano-diamonds, have several applications as sensor, which are tabulated in Table **1**.

Table 1. CBNMs Applications.

CBNMs	Applications/ Sensor
Graphene	Chemiresister, Optical, Strain, Mechanical, Electrochemical
	Electrical and piezoresistive, Biomolecule, DNA
	Immunosensor, Hemoglobin/ Myoglobin
Gfullerenes	Biochemical reactions, Electrochemical, Biomolecule
	X-ray and MRI contrast agent

(Table 1) cont.....

CBNMs	Applications/ Sensor
	Pharmaceuticals, Tumor cell, redox reaction, Immunosensing
CNT	Photoluminescence imaging, photoacoustic imaging
	Raman Shift imaging and detection
	Resonance frequency shift gas sensing
	Sorption, capacitance and ionization gas sensing
	Electrochemical sensors, detection of specific molecules
	pH sensor, Food quality sensor, Toxic molecule sensor
Nanodiamonds	MRI and fluorescence imaging, Photoacoustic imaging
	Multiphoton excitation imaging, Paramagnetic molecule sensing
	Temperature sensing, Electrochemical biomolecule sensing
	Gas sensing, Gene sensing
Carbon dots	Photoluminescence sensing, Chemosensing
	Electroluminescence, Electrochemical sensing, Bioimaging
	Immunosensing, Temperature sensing, Microfluidic marker

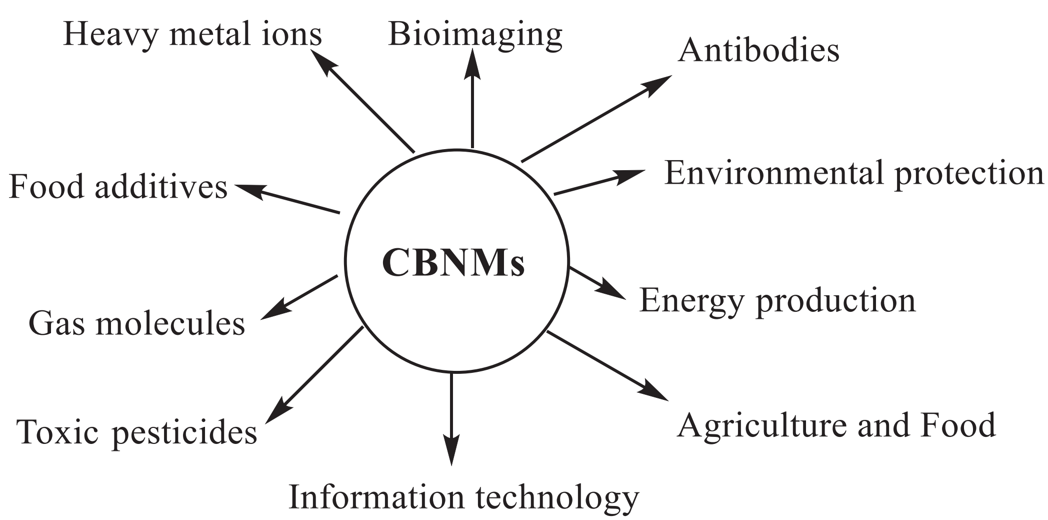

Fig. (1). CBNMs used as a sensor in various fields.

Due to more expansion of technology and automation, there is a need for advanced sensors having potential applications in various industries like electronics and automotive, biomedical, agricultural/ food, environmental monitoring, and defence.

CHAPTER 3

Graphene-Based Nanomaterials and Their Sensing Application

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Abstract: Carbon-based materials (CBMs) like graphene, hybrid graphene compounds (HCOGs), graphene nanoplatelets (GNPs), graphene oxide (GO), reduced graphene oxide (RGO), and graphene quantum dots (GQDs), as well as their derivatives like graphane, graphone, graphyne, graphdiyne, and fluorographene, are the direct descendants of graphene-based nanomaterials (GBNs). GBNs are graphene derivatives with single and multilayered graphene products. Their doped versions have marked remarkable significance over the past decade in scientific fields for applications due to their physical as well as their chemical properties. Graphene has emerged as a promising application for sensing, gas separation, water purification, biotechnology, disease diagnosis, bioengineering, and biomedicine. Graphene nanomaterials also play an important role in surface engineering (bioconjugation), improving their performance *in vitro*/*in vivo* stability and elevating the functionality of graphene-based nanomaterials, which can enable single/multimodality image optical imaging, positron emission tomography, magnetic resonance imaging and therapy photothermal therapy, photodynamic therapy, and drug/ gene delivery in cancer. Graphene nanoparticles have the natural fluorescence properties of graphene, which helps to bioimage cancer cells. They are perspective drug carriers appropriate for their target selectivity, easy chemosensitization, functionalization, and excellent drug-loading capacity. Iron-based graphene composites are with other companionable materials of exploration to make novel hybrid complexes with preferred uniqueness for biointerfacing.

Keywords: Bioimaging, Cancer, Diagnosis, Graphene oxide, Nanomaterials.

INTRODUCTION

Graphene nanocrystals are entirely made up of carbon atoms. It is precisely described as a nanoscale, minute-sized, two-dimensional substance with an atom-

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Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

wide linear surface. A hexagonal pattern formed by bonding carbon atoms produces a conjugated material with the pattern of a valuable honeycomb stone [1]. Graphene substances are made up of two concepts: GRAPHITE and -ENE into graphene: It has drawn a lot of emphasis on the form of graphene since Novoselov discovered crystal graphene in 2004 utilizing the scotch tape method (wherein a strip of tape is applied to peel graphene flakes off of a block of graphite) [2].

The density of graphene is represented by 0.335 nanometers as the marginal distance. The thinnest, most prevalent nanomaterial is 100–300 times stronger than steel [3 - 5]. The material was one atom thick, and exhibited 97.7% of optical transmittance and a substantial 3000 $W \cdot m^{-1} \cdot K^{-1}$ (watts-per-metre-kelvin) heat conductivity [6]. The Nobel Prize was awarded in 2010 for their achievements in physics. Currently, they are actively utilised in a variety of applications, including sensors, catalysts, healthcare, electronics, energy, and biology. The synthesis of graphene is usually done in one of two ways: bottom-up or top-down approach. In the bottom-up approach, graphite oxidised in aqueous media under extremely harsh conditions producing well-dispersed graphene oxide, a reduced version of graphene but graphene is not produced by the reduction process that is totally reduced because the chemical procedure produces graphene with certain flaws instead of being called graphene, it is called reduced graphene oxide. Chemical vapors are crystallized on an appropriate substrate to produce an individual layer of graphene on a top-down approach. However, this is incompatible with mass-production methods because of the benefits of manufacturing huge amounts of graphene in a reasonably easy procedure; many different types of exfoliation processes have been created.

In it, the status of science was discussed, and the knowledge gaps for future study were noted. Graphene, graphene oxide (GO), reduced graphene oxide (RGO), graphene nanoplatelets (GNPs), graphene quantum dots (GQDs), and chemically modified graphene, all members of the large family of GBNs covered in this study (Functional groups covalently bonded to the surface of each graphite-like carbon layer). The versatile graphene-based nanomaterials (GBNs) are widely employed in physics, chemistry, biology, and medicine. They are easily created by different surface modifications [7 - 11].

HISTORY OF GRAPHENES

First acknowledged between 1840 and 1958, graphene was the subject of study; in these time periods, Schafhaeutl, Hummers and others shaped graphene oxide.G. Ruess and F. Vogt have been descriptions of few-layer graphite published in 1948 that is reported to the TEM at the first time. In the year 1962, the chemical reduction of GO was observed by Boehm to discover rGO. In the time range of 1968 and 1969, a single layer of graphene stratum in the ground of Pt 100 is discovered by Morgan. A carbon surface and silicon carbide were arranged into monolayer graphite by Blakely and van Bommel, respectively, between 1970 and 1975; Boehm proposed the name “graphene “to describe a monolayer of graphene in 1986. In 1999, theoretically, one layer of graphene was described by Wallace P. R in 1947 and published his discovery in 1999. In 2004, they successfully produced, characterized, and extracted graphene for the first time from the graphite team led by Andre Geim and Konstantin Novoselov. The discovery of graphene has been recognized for its scientific importance and the potential for future innovation with the discovery 2010 Nobel Prize in Physics; when Geim and Novoselov isolated a single sheet of graphene before 2004, nothing was known about the material. Even though they give credit to Hanns Peter Boehm and a colleague for the initial exploratory finding of graphene in 1962 and subsequently, single graphene layers could only be seen using electron microscopy. Before 2004, intercalated graphite compounds were investigated using a transmission electron microscope (TEM). Before 2004, studies used multilayer graphene sheets that Ruoff had made by peeling graphite.

Graphene and its plagiarism have recently emerged since exceptional biomaterials for use in biomedical treatment, drug design, bio-sensing, and cancer therapy due to its adjustable assembled unusual physicochemical properties, and outstanding biocompatibility [11 - 15] and developed a nanocomposite of graphene oxide (GO) for the delivery of drugs [11]. Since then, there has been a boom in the exploration of using graphene nanocomposites to treat illnesses and deliver a variety of medicinal chemicals [12]. For all foreseeable future devices and nanosystems, the explored properties or even uses of such a two-dimensional arrangement of the carbon structure have already offered unique, inventive potential [9].

CHARACTERIZATION OF GRAPHENE

Blends of one and more layer graphemes, in addition to an atomically thin, two-dimension (2D) sheet of sp^2 carbon items synchronized in a bee hive pattern, usually make up the final output. It has been demonstrated to possess several favorable qualities, including strong mechanical strength [3], electrical conductivity [16], molecular barrier abilities [17], and other remarkable properties [18], as explained in the exfoliation and synthesis technique for graphene. Many graphene characterization approaches are aimed at distinguishing between those species because GO is reduced to rGO in the chemical synthesis technique; understanding the differences between the genus and the quantity of diminution is

CHAPTER 4

SPR-Based Biosensors in the Diagnostics and Therapeutics

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Abstract: To analyze the physio-chemical measures of the cellular environment and display them in digital units, transducing methods are applied in biosensors. The label-free biosensors employ biophysical characteristics such as spectroscopic methods, crystallization, and Surface plasmonic resonance (SPR) to determine the availability or concentration of substances. SPR is a method to elucidate interaction among biomolecules exhibiting affinity binding, structural changes, or alteration in pathological conditions. SPR methods are now employed in conjunction with a variety of transducer topologies, including optical fibers, nanoparticle-based SPR, immobilized or localized SPR (LSPR), long-range SPR, image SPR, immune-assay-based SPR, and phase sensing SPR biosensors' versatile configuration allows for the early detection of several illnesses, such as COVID-19, dengue, non-invasive cancer, biomarker-based fetuses identification, therapeutic antibody characterization, drug monitoring, *etc.* SPR system is leading in diagnostics and therapeutics with various advantages, such as their portable size, cost-effectiveness, quick result, and easy-to-handle method, but at extension, this technique needs development to ensure high sensitivity, averting background effect and evolution of label-free direct detector to quantify real sample. This chapter reviews the model's instrumentation and bioassay of clinical samples from SPR and its associated biosensor.

Keywords: Biosensor, Diagnostics, Surface plasmonic resonance (SPR).

INTRODUCTION

Surface plasmon resonance (SPR) was first introduced by Liedberg *et al* ., in 1983; this technique has been utilized widely for the development of label-free and real-time biosensors [1]. SPR-based biosensors have been developed approaching various parameters (Affinity Binding, kinetics, Stoichiometry, Thermodynamics, and Analyte concentration) and interactions (Antibody–antigen, Ligand–receptor, Protein–DNA, Protein–protein, DNA–DNA, Protein–carbohydrate, Cell membrane interactions and Protein/DNA–virus interaction) upon various samples.

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The history of this technology started with the discovery of surface plasmon excitation (Table **1**). Still, this technique continuously upgrades different parameters, such as instrument design, data analysis, and high-quality sensing.

Table 1. History, discovery, and development of Surface Plasmon resonance.

Year	Events
1902	Thin dark bands were observed by Wood through a diffraction grating [2]
1957	Ritchie predicted the elementary surface excitation value of SPP as a surface plasmon [2]
1968	The coupling of light with the surface plasmon by Otto which leads to the formulation of surface plasmon polariton (SPP) using attenuated total reflection (ATR) [3]
1971	Proposal of Kretschmann configuration of ATR coupling by Kretschmann, whose excitation method is followed in SPR biosensor [3]
1975	Term 'Biosensor' coined for the direct detection of biomolecules present at the surface using the transducer principle [4]
1983	SPR-based biosensor was first demonstrated by Liedberg *et al* . [4]
1988	Introduction of Surface plasmon microscopy by Rothenhäuslar and Knoll, which enables in imaging of interfacial structure through microscope [2]
1990	First SPR biosensor instrument was commercialized by Biacore [4]
1990	The carboxymethylated dextran labeled surface has been introduced for SPR application [4]
1996	Technique for phase interrogation was introduced by Nelson *et al* ., based on SPR sensing [2]
1998	First phase-resolved SPR imaging (SPRi) sensor was proposed by Nikitin *et al* . [2]
2012	Brian Kobilka and his coworkers win the Nobel prize in chemistry for application of Kretschmann configuration [2]

The basic principle of the SPR technique is based on the signal detection of altered refractive index developing at the surface of the sensor when the analyte flows around the channel (Fig. **1**) and interacts with the immobilized ligands. As per the current estimate, a report has been published in 'Future Insight Market' that SPR global market will reach up to US$ 910.4 million in 2022 and US$ 1.5 billion by 2029 [5].

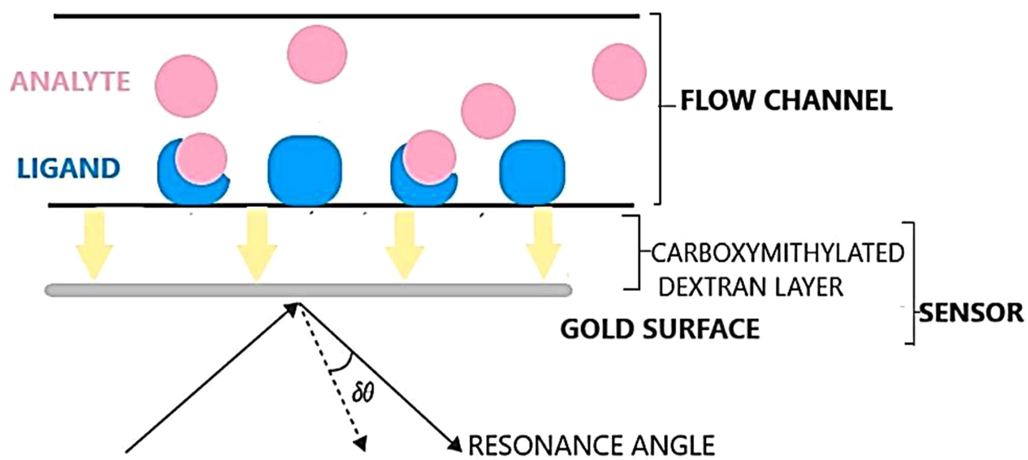

Fig. (1). Representation of SPR sensor surface showing flow channel, metallic nanomaterial, and refraction.

Many new SPR technologies are revolutionized by collaborating with microscopy and spectroscopic methods to integrate their value. Some recent applications of SPR are surface plasmon resonance imaging (SPRI), SPR-Biolayer Interferometry (SPR-BLI) [6], and SPR-enhanced electro-chemical-luminescent (ECL) [7] (Fig. **2**). In such a technique, a metallic surface consists of densely packed nanoparticles, where plasmonic interaction with metals such as silver and gold nanoparticles is utilized for medical sensing and the determination of biological and chemical analytes from a sample. Here, analyte separation and the refractive index at the surrounding medium are very sensitive aspects for their application. The change in the dielectric environment occurs due to the binding of a molecule, and altered refractive angle.

Consequently, causing resonance shift that allows the determination of analytes such as biomolecules and chemicals. The fundamental aspect on which analyte separation and the refractive index at the surrounding medium depends is the characteristic of metal and the immobilized surface.

Investigated chemicals are allowed over the surface of chips, and specific binding of analyte present in the sample, to the nanoparticles, will change local dielectric properties resulting in a noticeable shift in localized surface plasmonic resonance (LSPR) [8]. However, by using basic principles of functionalized nanoparticles, resonance angle, enhancement of interfacial means, and biomolecular interactions, continuous advances are used in SPR biosensors, which provide broad significance in diagnosis and therapeutics.

CHAPTER 5

Implication of Biosensors For Cancer Diagnosis And Therapeutics

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Abstract: "Caution is the parent of Safety". Early-stage diagnosis of Cancer can provide better medicinal therapeutic responses. Currently, a majority of cancer is diagnosed after having metastasized throughout the body. This led to the urgent requirement for potent and precise cancer detection methods for clinical diagnosis. Over the last several decades, the majority of researchers have concentrated their efforts on developing a potential rapid detection technique based on Biosensor technology for a variety of frightening human health-related disorders, such as cardiovascular disease, cancer, diabetes, and others. Significant advances were made in a wide range of fields attributed to the designed techniques having enhanced sensitivity, specificity, and repeatability. The development of diagnostic treatments in medicine was aided by noteworthy advancements in other scientific fields, including genetics, chemistry, micro-electrical engineering, and computational biology. As a result, efficient, accurate, rapid, and steady sensing platforms have been successfully developed for specific and ultrasensitive biomarker-based disease diagnostics. Biosensors are analytical devices designed to detect biological analytes by converting biological entities' responses (DNA, RNA, Protein) into potent electrical signals. The biosensor device combines a biological component with a physiochemical detector for sensing an analyte (biological samples). The discovery of the Biosensor boosted the potential clinical diagnosis of cancer at a large scale. Biosensors can be designed to detect emerging cancer biomarkers and determine drug efficacy at various target sites.

Biosensor technology has the potential to be used as a diagnostic tool for accurate and impressive cancer cell imaging, tracking cancer cell angiogenesis and metastasis, and evaluating the efficacy of treatment for the disease. This chapter will provide a quick overview of the challenges facing the early diagnosis of cancer, get through the depth of how biosensor technology may be used as a reliable diagnostic tool, and highlight potential uses for biosensor technology in the future.

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Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

Keywords: Biosensors, Cancer detection, Early-stage diagnosis, Nanotechnology, Oncogene.

INTRODUCTION

Cancer is a significant health problem affecting people worldwide; additionally, it is one of India's leading causes of death. In 2018, 18.1 million new cancer cases (17.0 million excluding non-melanoma skin cancer) and 9.6 million cancer deaths (9.5 million excluding non-melanoma skin cancer) were predicted by Globacon. As per ICMR data published in May 2016, the new instances of cancer in India had increased to 14.5 lacs per year, with the number expected to rise to 17 lacs by 2020 (http://icmr.nic.in/ncrp/pbcr2012-14/index.htm), owing in part to lifestyle changes and economic advancements in the country. Lung, prostate, breast, ovarian, hematologic, skin, and colon cancers, as well as leukemia, can take over 200 different forms, and both environmental comprising tobacco smoke, alcohol, radiation, and chemicals and genetic factors, *i.e.,* inherited mutations and autoimmune dysfunction linked to a higher chance of getting cancer. Additionally, there is a strong correlation between the development of several cancers involving bacterial and viral diseases comprising stomach cancers and cervical cancer, respectively. Even though cancer is more usually identified in older age (The majority of instances 77%, are found in adults 55 and over), Children ages 0 to 14 will receive diagnoses for 11,000 instances. According to the American Cancer Society (ACS), the worldwide cancer survival rate estimated for 5 years increased to 67 percent between 2010 and 2016, up from 50 percent between 1975 and 1977. This rise in survival can be ascribed to the biomedical advancements that have resulted in better treatment and earlier detection. The application of developing biosensor technology could help with the early-stage diagnosis of cancer and thus more effective therapies, increasing the likelihood of overall survival and improving patient quality of life. Cancer is a group of specific genetic and epigenetic abnormalities, which can be either environmental or inherited and result in uncontrolled cell development. Uncontrolled cell proliferation creates cancer cells that develop immunity to regular checking and balancing within the homeostasis over time. Tumors develop immunity to apoptosis and other anti-growth mechanisms in the body [1]. As cancer spreads to other body organ systems, the tumor keeps expanding past its original location, at which time it is essentially incurable. The two primary routes for carcinogenesis are oncogene activation and tumor suppressor gene (TSG) inactivation [2 - 5]. When a typical gene (a proto-oncogene) involved in cell formation, multiplication, and/or diversification is altered or duplicated, oncogenes are activated. This usually leads to excessive production of a typical gene product or unregulated stimulation, which causes cell growth to be disrupted, cell division to rise, and tumor formation to occur. As potential cancer indicators, growth factor receptors have been studied, more than any other type of oncogene. In 33 percent of all breast tumors, for example, the human epidermal growth factor receptor Her-2 is amplified, and tumors having amplified Her-2 develop and spread more aggressively. As a result, knowing of Her-2 condition is crucially important for developing the best therapeutic approach. Trastuzumab, a transgenic humanized monoclonal antibody aimed towards Her-2, is now the mainstay palliative therapy for individuals with this level of elevated transcriptional [6, 7]. By slowing or preventing mitosis, TSGs help control unregulated cell cycle progression by delaying or inhibiting mitosis. Retinoblastoma protein (Rb), BRCA1/2, and p53 were indeed a few of such TSGs in cancer that have undergone the most investigations [3]. Rb is said to be a master regulator of cell division, and Rb mutations are linked to a variety of malignancies. The far more typical reasons for Rb1 gene silencing are point mutations and deletions [8 - 10]. BRCA1 is the DNA repair enzyme that checks to validate the newly replicated DNA for fidelity and mutations. Normally, DNA repair enzymes eliminate replication defects before a cell multiplies. About 50% of hereditary breast cancers and 80%-90% of hereditary breast and ovarian cancers are caused by BCRA1 gene abnormalities [11, 12]. Eventually, the p53 protein controls apoptosis or programmed cell death. Brain, breast, colon, lung, hepatocellular carcinomas, and leukemia have all been shown to have p53 mutations. The potential for p53 dysfunction to serve as a mechanism for chemotherapy chemoresistance is another significant danger [4, 5, 13]. The creation of biosensors that are capable of spotting p53 mutations, Rb, and BRCA1 genes is critical for better-determining cancer risk and developing more effective cancer treatments.

Biomarkers of Cancer

“A biological molecule present in the blood, other body fluids, or tissues that is a symptom of a normal or aberrant process, or of a condition or disease; a biomarker can be used to determine how effectively the body reacts to an illness or condition's therapy.” according to the National Cancer Institute (NCI) [14]. DNA (particular mutation, translocation, amplification, and loss of heterozygosity), RNA, and protein can all be used as biomarkers (*i.e.,* hormone, antibody, oncogene, or tumor suppressor). Cancer biomarkers have the potential to be the most beneficial tools for detecting cancer initially, accurately staging it before surgery, figuring out how it responds to chemotherapy, and monitoring the course of the disease [15, 16]. Biomarkers are commonly found in physiological fluids, including blood, serum, urine, and CSF; however, they are also present in or on tumor cells [17]. Table **1** contains a fragmented list of tumor biomarkers. On the other hand, the bulk of these biomarkers hasn’t yet demonstrated enough sensitivity and specificity for regular clinical use or suitable treatment. Biosensor technology may be useful in this particular situation.

CHAPTER 6

Recent Advances in the Application of Nano-Biosensor in Tissue Engineering

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Abstract: Nanotechnology has a profound influence on environmental research, infrastructure, energy, food standards, information technology, and medicine. In biomedicine, nanotechnology primarily aims to provide solutions for preventive care, diagnosis, and therapy. Biosensors have significantly revolutionized the medical sector by offering on-site diagnostic capabilities. Since 1962, the combination of biosensors with nanotechnology has made a significant contribution to therapeutics and tissue engineering. Biosensors are diagnostic devices that monitor biochemical interactions and translate them into measurable electrical, optical, or mechanical signals. The tissue-engineered technology has gained popularity in the postmodern era to confront the shortcomings of biomedical applications, graft rejection, challenges in the recuperation of functional tissue, and specificities in the tissue regeneration site. The multitude of techniques for evaluating cell counts, growth, metabolic activity, and viability across the scaffolding of regenerated organs is reportedly labor-intensive and time-consuming. Biosensors have been rapidly advancing and influencing the field of tissue engineering in the last several decades. Recent developments in nanomedicine and biomaterial science have enabled them to overcome long-standing challenges. Biosensors used in tissue engineering and regenerative medicine (TERM), unlike the other biological systems, must comply with the requirements mentioned above: (i) biocompatible, causing no or little response to foreign materials; (ii) non-invasive while probing the whole three-dimensional structure for targeted biomarkers; and (iii) should offer long-term monitoring (days to weeks). This chapter offers a comprehensive set of biosensors as well as their implementations in the field of tissue engineering and regenerative medicine (TERM). This chapter reviews current breakthroughs in nanobiosensors, their implementations in tissue engineering, and their promise for diagnostic purposes.

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Keywords: Biosensors, Nanotechnology, Tissue engineering and regenerative medicine (TERM).

INTRODUCTION

The damage or malfunction of organs and tissues as a consequence of an accident and other such sorts of trauma is a serious health and safety concern. The conventional approach for treating these individuals is tissue or organ transplantation; however, donor availability is highly curtailed. Alternative treatments, such as surgical treatments, therapeutic interventions, artificially synthesized prostheses, and biomedical gadgets, are not supply-limited; however, they have drawbacks. The emergence of novel nanomaterials and potential alternative therapies has resulted from efforts to solve these issues and limits. Tissue engineering has been identified as a potential alternative to conventional therapy for managing tissue, organ loss, or dysfunction. The fundamental goal of this fast-emerging emerging field of study and technology is to use tissue engineering to replace dysfunctional internal organs with the ability to heal and regenerate [1]. In the last decade, advances in nanotechnology and nano-therapeutic devices have given tissue engineers' conventional methodologies a new perspective on life [2]. Ongoing advancements in the discipline of tissue engineering and regeneration need the deployment of authentic, non-invasive, and non-destructive diagnostic technologies for evaluating the validity and properties of the interaction of cultured cells with biocompatible scaffolds and tissue regeneration.

Since the emergence of the very first biosensor by researcher Leland C. Clark in 1962, investigation on bioanalytical chemistry and biosensors has achieved tremendous progress and drawn significant prominence [3]. The sensors are systems that generate measurable signals in response to various physical and chemical inputs. Generally, the biosensor's key purpose is to analyze and examine instant, efficient, and specific real-time biological reactions of analytes. Most such sophisticated biosensors potentially trace particular molecules in minimal amounts and are thought to be a valuable tool for detecting disorders at a preliminary phase and initiating therapy. However, only low amounts of biomolecules are needed, but still, their purity may be critical to accuracy. Conventionally, a biosensor is a diagnostic technique that combines a biological or biologically derived specific element and a particular analyte with a transducer to identify and transform a biological input into an electrical output and the detector that shows the signal values. The basic schematic representation of a biosensor is shown in Fig. (**1**).

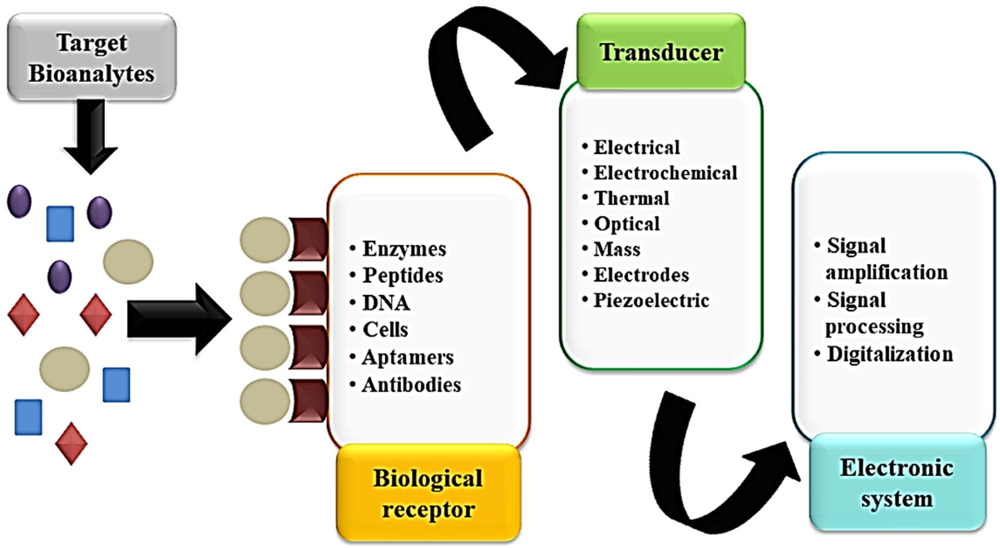

Fig. (1). Schematic representation of the working principle of biosensors.

A biosensor typically consists of four major components:

Bioanalytes

A substance of concern whose components are indeed being characterized or recognized (such as glucose, DNA, proteins, lipids, *etc*.)

Bioanalyte receptor system

This system functions as a receptor for a specific analyte (material to be recognized or quantified) and aids in determining the amount, interaction, and existence of these target analytes in a sample. Commonly used biomolecules as sensing elements involve enzymes, aptamers, cells (animal or plant), peptides, antibodies, and so on. The accessibility and accessibility of a huge range of biological receptors capable of detecting multiple kinds of analytes make biosensors a desirable device that could be employed in a wide range of study fields.

Transducer

These components recognize the signal produced by the analyte's engagement with the biological recognition component and convert it into measurable output. In most advanced biosensors, many types of transducers, such as electrical, optic-

CHAPTER 7

DNA Biosensors: Effective Tool in Biotechnology

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Abstract: A biosensor is a device that converts a biological response into a detectable electrical signal. In recent years, biosensors have gained significant interest due to a plethora of applications in the field of disease diagnosis, detection of various environmental pollutants, food quality analysis, and pharmaceutical drug research. Among various types of biosensors, (such as enzyme-based, immunosensors, DNA biosensors, thermal and piezoelectric biosensors) DNA biosensors are being widely employed because of superior biocompatibility, thermal stability and alternative functionalization. DNA biosensors introduced in recent years include an aptamer-based sensor, molecular beacon-based biosensors, fluorescence-based sensors, hybridizationbased sensors and electrochemical-based DNA biosensors. This chapter highlights the fundamental knowledge and recent advances in the field of DNA-based biosensors. This chapter also focuses on the significance and wide application of DNA-based biosensors in the diverse areas of biotechnology and allied fields.

Keywords: Aptamers, Biosensor, Diagnosis, DNA-based, Environment, Fluorescence-based.

INTRODUCTION

Biosensors are devices that employ biological reaction to detect target analytes [1 - 3]. It entails the combination of biological receptors with a physical transducer that converts biorecognition into usable electrical impulses [4]. The signal generated is proportional to the analyte concentration [5 - 10]. The bioreceptor, transducer and the detection system are the three essential components of a biosensor (Fig. **1**) [11]. Bioreceptors *viz* enzymes, cells, aptamers, deoxyribonucleic acid (DNA or RNA), and antibodies recognizes the analyte to produce detectable signals during the interaction. The transducer associated with the sensor converts the biorecognition event into a measurable signal to be displayed. Based on the receptors involved, biosensors can be catego-

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rised into immuno biosensors, DNA biosensors, enzyme biosensors, whole-cell biosensors, and phage biosensors [12].

Transducers may be amperometric (current measurement at constant potential) [13], potentiometric (potential measurement at constant current) [14], piezoelectric (measurement of changes in mass [15], thermal (measurement of changes in temperature) [16] or optical (detect changes in transmission of light) [17]. Among these several biosensors DNA biosensors, utilizing DNA as a probe, hold great potential in the field of biosensing. The present review throws light on recent applications of DNA-based biosensors.

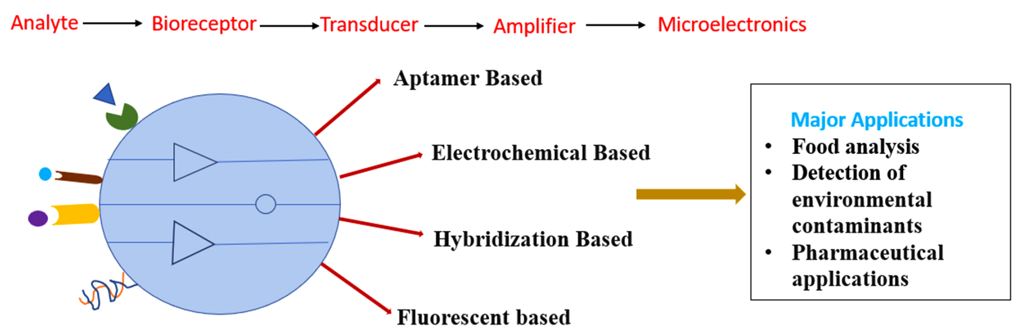

Fig. (1). Biosensors, types and applications.

Types of DNA-Based Biosensors

Aptamer Based

Aptamers are synthetic single-stranded DNA or RNA with 15–80 nucleotides capable of binding to the target. It can be chemically synthesized and are structurally and functionally stable over a wide range of temperatures and storage conditions. The first aptamer was acquired in 1990 by Ellington *et al*. [4, 18]. Aptamers can be isolated from oligonucleotide libraries by an *In vitro* selection mechanism, SELEX (Systematic Evolution of Ligands by Exponential enrichment) [19, 20]. It can bind to a large number of targets (*e.g*., proteins, drugs, cell, amino acids, natural and inorganic particles) by folding into three-layered structures with high fondness and particularity [12, 21 - 24]. These molecules can be amplified by polymerase chain reaction (PCR), which increases the sensitivity of aptasensors [5, 25], LAMP [26], and RCA [27 - 29]. Aptamers possess several advantages over traditional bio probes and are thus regarded as promising alternatives for antibodies in bioassay areas. They are stable even in drastic environmental conditions and does not require special transport or storage conditions. DNA aptamers are steady to incredibly high temperatures, pH values, and high ionic fixations. Beside this, modifications of functional groups can be done without losing the biological activity. It can be prepared on a large scale by simple chemical synthesis with inexpensive nucleotides [30]. When it detects and captures a target, the aptamers roll into a three-dimensional alignment. Since the essential atomic design of aptamers is poor in strength and stability, some unbound nucleobase interacts to form basic themes to choose from. The interaction of these themes leads to more complex designs for higher education such as coaxial stacking and G-quadruplexes.

Approaches involving nanoparticles (NPs) in electrochemical aptamer sensors, eno sensors, and immunosensors have been developed [31]. The construction of nanoscale electrical biosensors using aptamers as molecular recognition elements are reported [32]. A sensitive ratiometric fluorescence aptasensor for the determination of ochratoxin A (OTA), a small molecular mycotoxin produced by Aspergillus and Penicillium strains, has been successfully constructed. Leng *et al*., 2016 studied the framework for the development of aptamer-based biosensors and bioassay techniques [33]. Sefah and the participants discussed the use of aptamers in biosensor development by classifying them into three standard levels: structural exchanges, chemical based, and aptazyme-based biosensors. The most commonly used method of DNA aptamer detection is to make the DNA aptamer work with report particles, such as ferrocene or methylene blue and static particles, such as alkane thiol, alkane amino, streptavidin or hydrazoate at the end of the 5 'and 3' DNA strand, respectively. An electrochemical sensor in the light of 34-mer IFN-γ-retricing aptamer interferon-gamma (IFN-γ) was developed by Liu *et al*. [13]. In their review, the proposed DNA aptamer was concentrated in the outer layer of the cathode using a combined reaction of gold and alkyl mercaptan. Without any specific purpose, the DNA aptamer was shown to fold down to form a circle, making the particles that are exposed affect the end of the sensor. Limiting the target and the DNA aptamer alters the adaptation to the aptamer, extending the distance between the detailed particles and the storage area. This results in differences in the technology of electronic exchange between the declining atoms and the storage areas. The detection limit (LOD) reached 0.06 nM, and the direct detection range was found to be 10 nM. The DNA aptamer can also be activated by synthetic polymers, which are commonly used as report labels in fluorescent and colored biosensors due to their excellent optical properties [34]. The DNA aptamer can penetrate polymers formed by electrostatic forces [35]. While limiting biotarget, modification of the aptamer DNA sequence will trigger the modification of the polymer structure, which will affect the simulation and output frequency of the formed polymers [36]. This strategy has been effectively used to distinguish human α-thrombin, with a LOD of 2×10^{-15} M [37]. Although biosensors for active DNA aptamers show many benefits, the ineffectiveness of aptamers against the nervous system is a challenge. Graphene

CHAPTER 8

Biosensors for the Diagnosis and Therapeutics of Cardiovascular Diseases

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Abstract: Biomedical diagnostic research is becoming increasingly important in the modern medical profession. Infectious disease inspection, initial detection, chronic disease treatment, clinical services and well-being hunt down are the various applications of biosensors. Advanced biosensor technology permits the identification of the disease and the examination of the patient's responses to medication. Sensor technology is crucial for a broad range of low-cost and practicable developed medical appliances. Biosensors offer many possibilities because they are unambiguous, ascendable and capable of synthesizing procedures. Cardiovascular disease(CVD) is now recognized as the leading cause of death. It is estimated that the number of people dying from heart disease and stroke will approach 20 million by 2015. The risk event of unexpected death associated with it can be minimized by recognizing the challenges involved in its beginning, symptoms, and early detection. Therefore, this chapter aims to provide an idea for the diagnosis and therapeutics of CVD. Biosensors, created to be utilized as quick screening instruments to detect disease biomarkers early on and classify the condition, are revolutionizing CVD diagnosis and prognosis. Biosensors have become faster, more accurate, portable, and environmentally friendly diagnostic equipment as a result of advances in interdisciplinary study domains.

Keywords: Bio-element, Biosensors, Biomarker, Cardiovascular disease, Healthcare service, Immunosensor.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in the globe, causing the deaths of nearly 17 million people each year [1]. It was estimated that 17.7 million people died from cardiovascular disease till 2015, reporting for 31% of all deaths planetary; also, coronary heart disease and stroke took away the lives of 7.4 million and 6.7 million people [2]. A person with CVD needs early identifica-

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tion and care, both medically and psychologically. The current method for detecting CVD is based on a traditional procedure that involves tests that might take many hours or even days to complete, including either costly imaging techniques like the ultrafast computerized tomography (CT) or magnetic resonance imaging (MRI) or hazardous invasive techniques like cerebrovascular or coronary angiography. Such invasive diagnostic procedures are risky and not good for mass screening [3]. The patients must meet up the following conditions to undergo CVD therapy, conditions like alterations in electrocardiogram (ECG), biochemical markers rising in blood tests and distinguishable pain in chest. An indispensable tool to regulate CVD treatment embodied ECG, although it is a poor diagnostic tool for CVD since 50% of CVD patients have a normal cardiogram, making it more difficult to detect CVD [4]. Biosensors with biomarkers are playing a critical role in the diagnostic revolution of cardiovascular illnesses. For the precise diagnosis of cardiac disorders, the design and development of highly sensitive and specific biosensors using practical surface chemistries and non-materials is imperative. Biosensors are made up of a biocatalyst that can detect a biological element and a transducer that can turn the biocatalyst and biological element's combined event into a detectable parameter. Biomolecules such as metabolites, enzymes, cells, DNA, RNA, and oligonucleotides can act as biocatalysts, and transducers can be acoustic, electrochemical, piezoelectric, optical, or calorimetric. Biosensors based on immobilised cells, enzymes, and nucleic acids have recently entered the field of disease diagnosis. Nano biosensors have also been employed to develop disease-diagnostic biosensors, because of their ultrasmall size and unique features. With the use of a multidisciplinary combination of chemistry, medical science, and nanotechnology, biosensors can quickly assess health state, illness start, and progression, and can help plan therapy for various diseases. The gadgets are low-cost, extremely sensitive, quick, and user-friendly, and they may be mass-produced for human usage. Biosensors may help with rapid diagnosis, good health care, and reducing the time it takes for findings to be distributed, which is extremely stressful for patients. This article examines biosensors for the diagnosis and therapeutics of cardiovascular disease.

Biosensor's Distinct Characteristics in Healthcare Services

Biosensors have found their most useful uses in various industries, the most prominent of which are medical, healthcare, and clinical services. Disease detection, retinal prosthesis, contrast imaging during MRIs, cardiac diagnostics, medical mycology, health monitoring, and other broad categories of biosensor applications are effectively serviced (Fig. **1**). With great social services, these wide capacities raise healthcare to a new level [5, 6]. COVID-19 is a highly contagious pandemic caused by a newly discovered coronavirus that has spread over the world. Various infectious diseases, including SARS, nipah, hendra, and avian influenza, have drawn interest. Biosensors technology possesses massive capabilities and offer enormous probabilities and capability for examining viral and/or disease outburst. Another important feature of the biosensor is its capacity to diagnose cardiac problems. Cardiovascular illnesses are the leading cause of mortality globally. The use of biomarkers in biosensors is critical in the diagnostic revolution of cardiovascular illnesses. For the exact detection of cardiac disorders, the design and development of highly sensitive and selective biosensors employing practical surface chemistries and non-materials are critical. Diabetes prevalence and diabetic patients' use of bio-sensors are significant factors in corporate earnings globally. The demand for rapid and preventative diabetes diagnosis is growing. Advancements in biosensors monitored blood glucose levels on a large scale in the presence of varied temperature gradation. The accuracy and sensitivity of biosensors to detect samples within a minute are developing in the area of diabetics and also have huge market demand, with a great capacity for treatment, monitoring, diagnosis, fitness, and well-being. Portable electronic devices are an integral element of the total healthcare system. They will work together to increase preventative activities and a better understanding of their well-being, using a combination of therapy tools available in hospitals and emergency rooms. It has been seen that acute kidney injury and chronic kidney disease were correctly identified in living mice by photoacoustic imaging using synthetic black phosphorous quantum dots (BPQDs) with an ultra-small size (1.74 0.23 nm after surface modification), with improved detection sensitivity than the clinical serum indices examination method [7]. Moreover, drug hepatotoxicity has been successfully assessed using a polydopamine polyethyleneimine/quantum dot sensor at the cellular level [8]. The market is being driven by technological advancements and the rising usage of biosensors in a variety of applications. Wearable biosensors have improved the quality of life [9, 10]. In addition, the deployment of wearable devices reduces the financial burden of health-care costs. As a result, growing senior populations and rising wearable technology preferences among young people may open up new market segments. Biosensors are an effective approach to diagnosing diseases, detecting microorganisms, and detecting dangerous substances in humans and the environment. A study-developed fluorescent sensor shows tremendous potential for the speedy and precise identification of diseases brought on by bacterial infection. It may be utilised to differentiate between pathogenic bacteria that are found in the urinary system [11]. Research suggests that kidney damage progression can be monitored by determining the dimensions and polarity of urine protein. In order to expand the sensor array's potential medical uses, the researchers further boosted the sensor array's high resolution by including more sensor components [12].

CHAPTER 9

Biosensors for Food Analysis, Food Additives, Contaminants and Packaging

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Abstract: It is essential to manage the food requirement for the growing population. Food safety is important for health, but maintaining nutrients and food quality is also necessary for better health. Food storage and packing should be done carefully in order to avoid food contamination and ensure long-term food storage. There are various types of food hazards (biological, chemical, and others) that may contaminate food and cause food poisoning, foodborne diseases, allergies, and other health issues. For food quality examination, traditional procedures, such as chromatographic methods, are used, but these are time-consuming, labour-intensive and require an expert in instrumentation. It is critical to inspect the quality of food on a regular basis and as quickly as feasible. The greatest approach for overcoming these issues is the use of biosensor. As food additives and pollutants, the biosensor is extremely quick, sensitive, and selective. Biosensors are equipped with a transducer and a biological identification element, allowing them to evaluate food quality. Pesticides, poisons, microbial growth, protein, metals, fatty acids, antibiotics, vitamins, and other compounds can all be detected in food using biosensors. Biosensors have a wide range of applications in the food industries but there is also the demand for novel, inexpensive, simple, small-sized, portable, and multifunctional biosensors for food analysis. Biosensor can also detect food additives and pollutants throughout the packaging process.

Keywords: Food analysis, Food contaminants, Food packaging, Types of Biosensor.

INTRODUCTION

Food is a major source of energy that also shows antioxidant, antimicrobial, anti-

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viral, anti-inflammatory, anti-mutagenic and other health-making activities. Food contamination and foodborne disease are the major problems during food storage and processing. There are different food contaminants, such as physical, chemical and biological contaminants. Microorganisms and toxins are the major food contaminants and health hazards.

Food contaminants cause different types of diseases, such as infectious and life-threatening diseases. A much part of the budget in the growing country is spent to control food contamination and foodborne disease. Different molecular techniques such as Fluorescence microscopy, PCR and Hybridization, and ribosomal DNA sequencing are used in microbial detection. However, good hygienic practices and food regulation (FDA) are being used to reduce food contamination and foodborne disease [1]. But, a new reliable, stable and real-time method is needed for better assessment of food quality. Food quality maintenance and food safety measures are important features in food storage and preservation for a long time. Food quality monitoring is also an essential part of food safety. Analytical methods are used for the food quality measurements, but it is time-consuming, laborious, and requires an experienced person. Therefore, there is a need for special techniques which should be fast, reliable, time-saving and sensitive for food quality measurement.

A biosensor is a device that is being used in food industries due to its rapid and specific food quality measurement. In the food sector, it is used in many different ways. It is predicated on the idea that a physical amount can be measured and transformed into a signal that an observer can sense. It is a small bio-electronic device which is consisting of a sensing element with a signal transducer [2]. It consists of a receptor biomolecule that measures the amount of analyte while a transducer detects the amount of analyte. The receptor biomolecules may be the enzymes, proteins, organelles, antibodies, nucleic acid (DNA), tissues, receptors and microorganisms. Different types of biosensors are available, which are based on different working principles. Based on the different transducers, different biosensors are available such as Optical biosensors (based on fluorescent or luminescent/ chemiluminescent reactions), Potentiometric biosensors (change in voltage), Amperometric biosensors (current generated between electrodes), Piezoelectric biosensors (changes in the oscillating frequency of a piezoelectric crystal) and Thermal or Calorimetric biosensors (change in thermal energy). Whereas based on the biological receptor element there are enzyme-based, the whole cell-based (Microbial) and affinity-based biosensors (antibody, nucleic acid and receptor) [2, 3].

Food packaging is an important procedure to protect food from chemical, biological and physical changes. The main contaminants are heat, moisture and microorganisms. Food packaging material is also an important factor to avoid the contamination of food during packing. Plastic packaging is being used at present, but there is a need to make a biodegradable packing material that can protect food quality. Food processing causes change in the food structure, taste, texture and function [4]. In food packaging, a food sentinel system (having antibodies) has been designed to detect pathogens in food packages [3]. But, smart food packaging is being used at present that senses and conveys information about the state of a product. It also provides information about food quality during transport and distribution [11, 41].

BIOSENSOR

The biosensor is an analytical device which consists of a transducer and a receptor that transforms input signals into a continuous output signal. In a biosensor, receptors convert physical or chemical data into an energy form which is converted into a useful analytical signal, like an electrical signal by a transducer. The biosensor was created in the 1960s by Clark and Lyons [5]. It involves a biological sensing component that is either integrated inside or close to a physicochemical transducer as a quantitative or semiquantitative analytical experimental technique [6]. Chemical information is transformed into a signal that may be used for analysis by a chemical sensor. These sensors typically couple a physicochemical transducer with a chemical (molecular) recognition mechanism (receptor). Similar to chemical sensors, biosensors use a biological process to interface with an optoelectronic system *via* the recognition system [6, 7]. It is a tool that recognizes chemical compounds by means of specific biological processes mediated by individual enzymes, immune systems, tissues, organelles or whole cells, typically employing electrical, thermal or optical signals [8]. In order to create a reagent-free sensing system that is selective for the target analyte, the biosensor consists of a biological sensing component and a signal transducer. Highly specialized macromolecules or complex systems with the proper selectivity and sensitivity make up the biological component of a biosensor.

Biosensor Principle

The main element of a biosensor, which exploits a physical change brought on by the reaction, is the transducer (Fig. **1**). It senses the difference in light output or light absorbance between the reactants and products (Optical biosensors) and based on the mass of the reactants or products, are examples of heat output (or absorption) by the reaction (Calorimetric biosensors), changes in electrical or electronic output (Electrochemical biosensors), and redox reaction (Amperometric biosensors) (Piezo-electric biosensors). Despite the relatively modest difference

CHAPTER 10

Biosensors For Monitoring Heavy Metals Contamination In The Wastewater

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Abstract: Several anthropogenic activities, chemical manufacturing, mining, nuclear waste, painting, metal processing, agricultural activities, cosmetic products and industrial activities are associated with heavy metal contamination in the wastewater. Heavy metals, such as arsenic, cadmium, chromium, lead mercury and nickel, are nonbiodegradable and highly toxic. They can directly or indirectly enter the food chain and cause several health issues, such as cancer, liver and kidney, asthma and mental retardation. Analytical methods such as inductively coupled plasma mass spectrometry (ICP-MS), atomic absorption spectroscopy (AAS), ultraviolet-visible spectroscopy and chromatography are widely used for heavy metal monitoring in heavy metal contaminations. These methods provide a sufficient level of sensitivity and selectivity, but these methods are costly, time-consuming and require sample preparation. Currently, biosensors are considered an alternative to conventional heavy metal monitoring methods due to high sensitivity, selectivity, inexpensiveness and simplicity. Herein, the authors report several biosensors and their application in monitoring heavy metal contaminations.

Keywords: Biosensor, Heavy metals, Microorganisms, Wastewater.

INTRODUCTION

With the inception of industrialization, mankind has grown much over the past centuries [1]. However, the dark side of it comes with it, which manifests itself in our ecosystem in various forms. One such impact is visible in our water bodies, such as water pollution [2, 3].

Wastewater can be defined as used water from any combination of domestic, ind-

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ustrial, commercial or agricultural activities, surface runoff/stormwater, and any sewer inflow or sewer infiltration [4, 5]. Effluents from a large number of industries viz., electroplating, leather, tannery, textile, pigment & dyes, paint, wood processing, petroleum refining, photographic film production, and water from Agricultural lands (containing fertilizers, weedicides, herbicides, *etc*.) add a significant amount of heavy metals in the wastewater [6, 7]. Reports of water pollution, aquatic habitat degradation, and decline in aquatic biodiversity are increasing rapidly while on the other hand, freshwater reserves are depleting, and about 71% of the world's population (about 4.3 billion people) is facing some form of water adversity or scarcity during some months of the year [8]. It is a very well-established fact that high levels of heavy metals are highly toxic for all life forms, especially aquatic life forms and humans.

The wastewater is usually substantially loaded with heavy metal pollutants, due to agricultural sullage, industrial effluents, nuclear wastes, metal processing, *etc* [9]. It is well known that biochemical reactions need certain heavy metals such as Co, Cu, Fe, Mn, Mo, Ni, Se, and Zn. However, there are some non-essential Heavy metals present in the wastewater, such as Lead (Pb), Chromium (Cr), Cadmium (Cd), Mercury (Hg), and Arsenic (As), which are non-biodegradable and are highly toxic and carcinogenic even in low dosage. They can bind to the surface of microorganisms and reach humans *via* the food chain (Jaishankar *et al*. 2014).

Biosensors

A biosensor is an analytical device used to detect a chemical substance that combines a biological component with a physicochemical detector. A biosensor consists of two components: A Bioreceptor and a transducer. The Bioreceptor is a biomolecule that recognizes the target analyte, and the transducer converts the recognition event into a measurable signal [10]. The components of the functional biosensor are shown in Fig. (**1**).

There are several characteristics of biosensors are given:

1. Sensitivity: Response of the sensor to per unit change in analyte concentration.
2. Selectivity: Ability of the sensor to respond to the only target analyte.
3. Reproducibility: Accuracy with which the sensor's output can be obtained.
4. Stability: Characterizes the changes in its baseline or sensitivity over a fixed period time.
5. Range (Linearity): is the concentration range over which the sensitivity of the sensor is good.

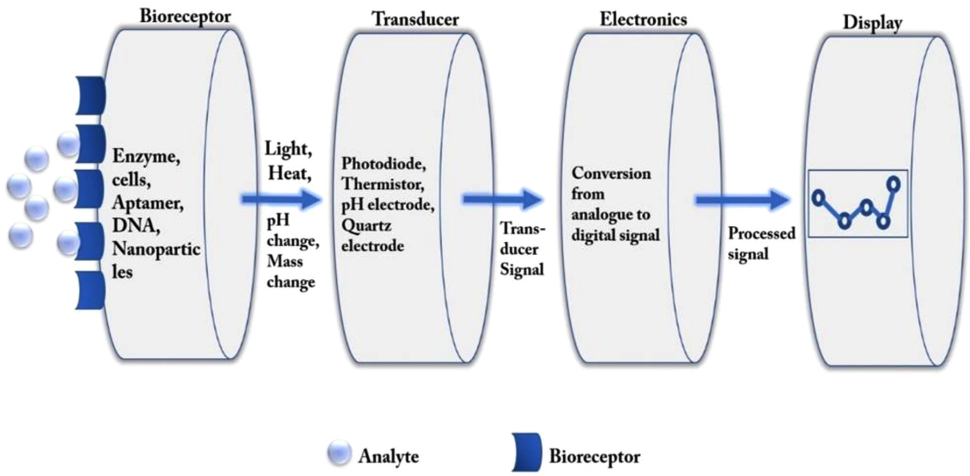

Fig. (1). Biosensor and its components.

Types of Biosensors and Their Applications

There are several types of biosensors, such as Enzyme based, whole-cell-based, piezoelectric, optoelectronic, electrochemical transducer, and thermal sensors. Biosensors are very specific and designed for the specific application. The various type of biosensors and their application is shown in Fig. (**2**).

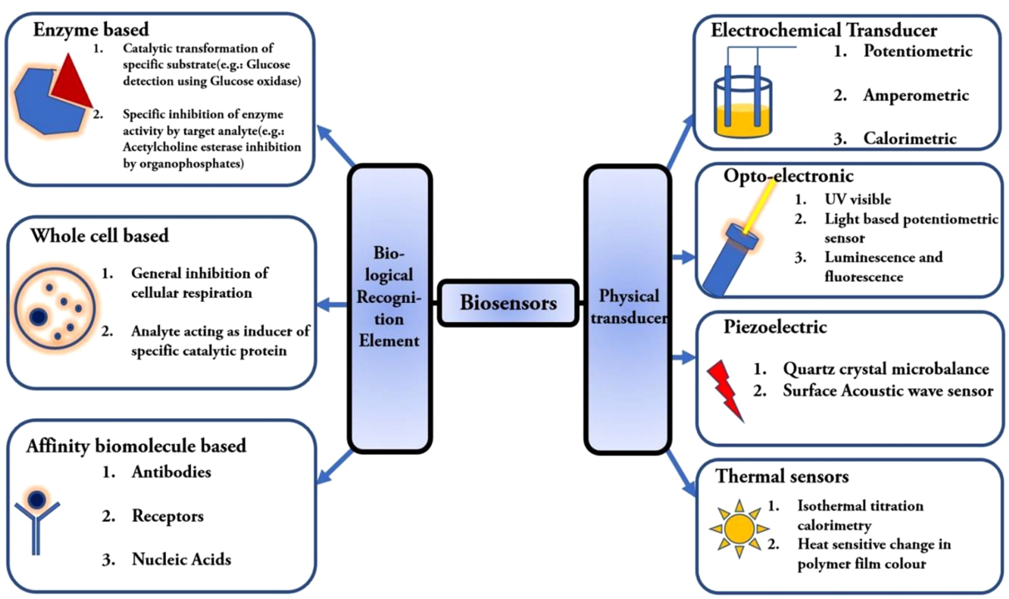

Fig. (2). Schematic illustration of various types of biosensors [11].

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