Review Article

OPTICAL BIOSENSORS: FUNDAMENTALS & TRENDS

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ABSTRACT

Because of the need in medical diagnostics and more recently, the worldwide concern of the threat of chemical and bioterrorism great demand of bio-intelligence arises. Here, the review of biosensors technology with specific concentration on optical biosensors is provided. Remarkable developments have been reported in the last few years in the field of optical biosensors. Optical biosensors utilize optical techniques to detect and identify chemical or biological species. Due to tremendous advantages, the field of optical biosensors has been emerged as a topic of great interest. In this review article the basic principle, classification, biorecognization systems and immobilization techniques are explained. Finally, some examples of current applications and opportunities for future developments including nanomaterial and nanotechnology are explored.

KEY WORDS: Biosensors, Optical biosensors, Biorecognization, Immobilization, Bio-optrode, Surface plasmon resonance, Applications.

INTRODUCTION

Biosensors represent the end product of a rapidly growing field, which combines fundamental biological, chemical, and physical sciences with engineering and computer science to satisfy needs in a broad range of application areas. Therefore, the term '*biosensor'* has different connotations depending on what field the user comes from [1, 2]. For the purpose of this review**,** we may define a biosensor as "an analytical device, which detects and converts the concentration of the target substance, the analyte (i.e. chemical or biological species or a microorganism), into an electrical signal through a combination of a biological or biologically derived recognition system either integrated within or intimately associated with a suitable physiochemical transducer". The field of biosensors has been active over many decades.

BIOSENSOR SYSTEM

A biosensor in general utilizes a biological recognition element that senses the presence of an analyte (the specie to be detected) and creates a physical or chemical response that is converted by a transducer to a signal [3-6]. The general block diagram [2] of a biosensor system is described in Fig. 1.

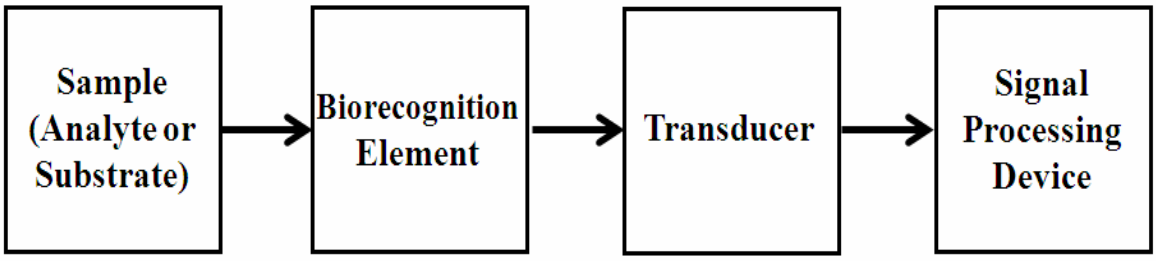

Fig. 1 General scheme Of Biosensing [2]

The sampling unit introduces an analyte into the detector. The recognition element binds or reacts with a specific analyte, providing biodetection specificity [2, 6]. Enzymes, antibodies, receptors, DNA or even cells such as yeast or bacteria have been used as biorecognition elements [7-10]. Stimulation, in general, can be provided by optical, electric, or other kinds of force fields that extract a response as a result of biorecognition. The transduction process transforms the physical or chemical response of biorecognition, in the presence of an external stimulation, into an optical, electrical or any other form of signal that is then detected by the detection unit. The detection unit may include pattern recognition for identification of the analyte.

Professor Leland C. Clark Jr. in 1956, published his definitive paper on the oxygen electrode. Since then, research communities from various fields like, physics, chemistry, biology, material science have come together to develop more sophisticated, reliable, and mature biosensing devices. Biosensors find a wide range of real world applications [11-12]. Potential applications are basically clinical and nonclinical [13, 14]. More recent interest is the use of biosensors to detect toxins [15], microorganisms [16, 17], bacteria, viruses [18] and chemical and biological defence [19] against terrorism. It is also popular in agriculture [20] and environmental [21] applications. Now a days nanotechnology based applications [22] are also in development.

CLASSIFICATION OF BIOSENSORS

Basically, biosensors are classified based on two parameters. Based on the transduction mechanism and second based on the biorecognization elements [2,6,23].

The classification is shown in the following Fig. 2.

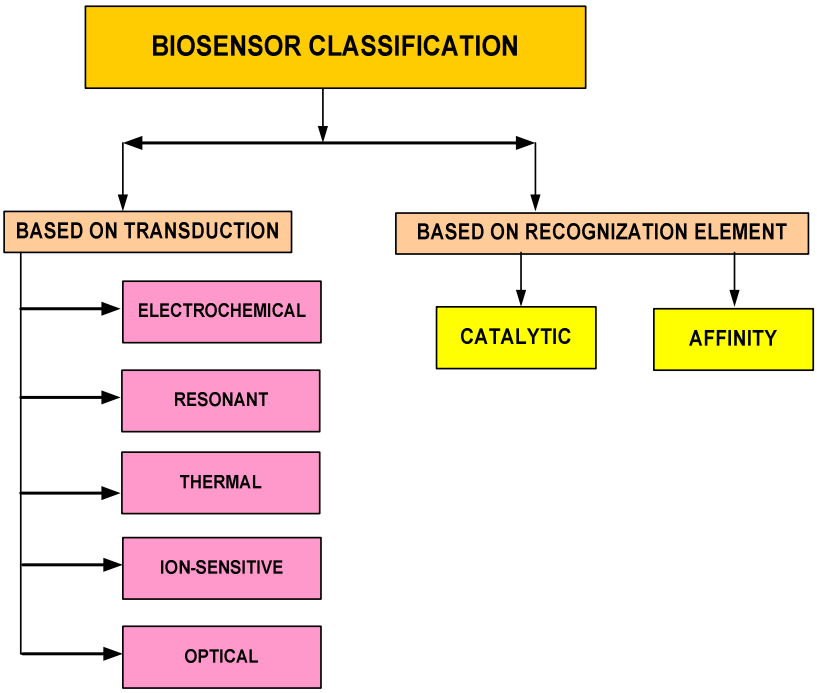

Fig. 2 Biosensor Classification

Electrochemical biosensors [24-26] are mainly used for the detection of glucose concentration, DNA-binding drugs, hybridized DNA, etc. The underlying principle for this class of biosensors is that many chemical reactions produce or consume ions or electrons which in turn cause some change in the electrical properties of the solution which can be sensed and used as measuring parameter.

In resonant biosensors, an acoustic wave or piezo-electric [1, 24] transducer is coupled with a bio-element. When the analyte molecule gets attached to the membrane, the mass of the membrane changes. The resulting change in the mass subsequently changes the resonant frequency of the transducer. This frequency change is then measured.

Thermal biosensors, exploits one of the fundamental properties of biological reactions, namely production of heat, which in turn changes the temperature [1, 24] of the medium in which the reaction takes place. Due to the biological reactions, the temperature of the medium changes. This temperature change is measured. It is constructed by combining enzyme with temperature sensors. When the analyte comes in contact with the enzyme, the heat

reaction of the enzyme is measured. The measurement is done by thermistor known as 'enzyme thermistor'. Used for the detection of pesticides and pathogenic bacteria.

Semiconductor FET having an ion-sensitive surface (ISFET) is used in ion sensitive biosensors. Sensor electrode is covered with a polymer layer. Polymer layer is selectively permeable to the analyte ions. When the ion concentration in solution changes, the ions diffuse through the polymer layer. It causes a change in the FET surface potential. It is known as ENFET (Enzyme Field Effect Transistor) and is primarily used for pH detection.

OPTICAL BIOSENSORS

In the most commonly used form of an optical biosensor [27-30], the transduction process induces a change in the phase, amplitude, polarization, or frequency of the input light in response to the physical or chemical change produced by the biorecognition process [27, 28]. Some of the advantages [11] offered by an optical biosensor are selectivity and specificity, remote sensing, isolation from electromagnetic interference, fast, real-time measurements, multiple channels/multi parameters detection, compact design, minimally invasive for *in vivo* measurements, choice of optical components for biocompatibility, detailed chemical information on analytes, The main components [2] of an optical biosensor are: light source, optical transmission medium (fiber, waveguide, etc.), immobilized biological recognition element (enzymes, antibodies or microbes), optical detection system. Optical biosensors can be broadly classified based on the different parameters [2] as shown in Fig. 3.

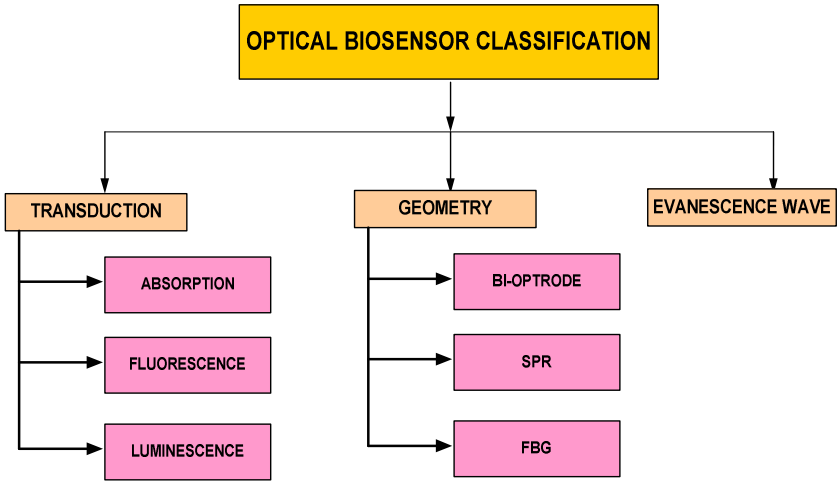

Fig. 3 Classification of Optical Biosensors

BASED ON TRANSDUCTION

Absorption:

The simplest optical biosensors use absorptions phenomenon to determine changes in the concentration of analytes [23]. The sensor works by sending light through an optical fiber to the bio sample. The amount of light absorbed by the analyte is determined by measuring the light coupled out via the same fiber or a second optical fiber. From the physics point of view, absorption is a process in which light energies are absorbed by an atom or a molecule. Based on the Lambert–Beer law (usually referred to as Beer's law), the intensity of transmitted light (I) through a uniform absorption medium can be mathematically described by [23] the following equation (1).

$$I = I_o \exp^{-\varepsilon C \Delta x} \quad \text{.....(1)}$$

Where, I_0 denotes the incident light intensity, ε is the extinction coefficient, C represents the concentration of the absorption of analyte, and Δx is the thickness (or length) of the absorption medium. Since the absorption is usually wavelength dependent and different species may have different absorption spectra, by measuring the absorption spectra via fiber optic sensor, different species and concentration levels can be determined. In Fig. 4, absorption spectrum [24] of phenol red dye in solution at various pH values is shown. If the measurement is conducted in living samples, the light source power will need to be carefully controlled to avoid damaging of the living samples. The major advantages of absorption-based sensors are that they are simple, easy to use, and cost effective.

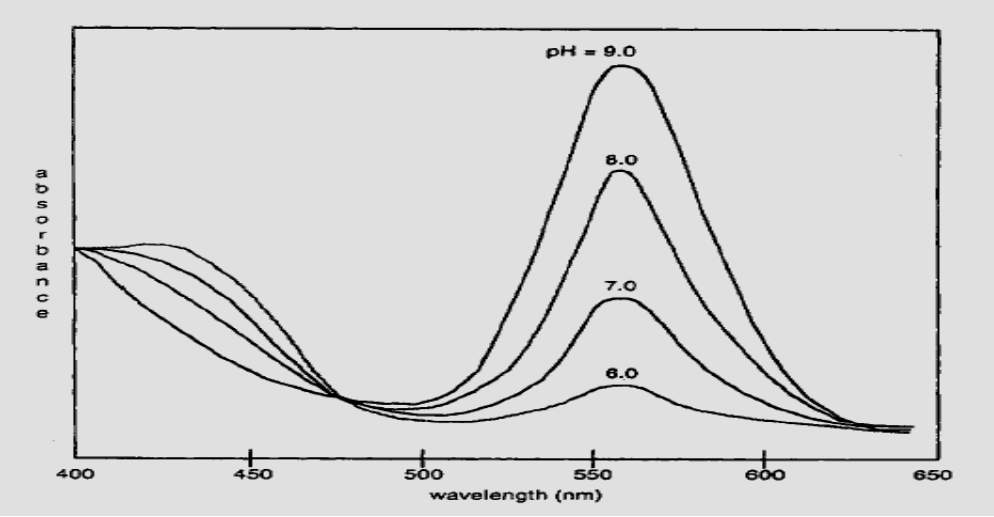

Fig. 4 Absorption Spectra of Phenol Red Dye [24]

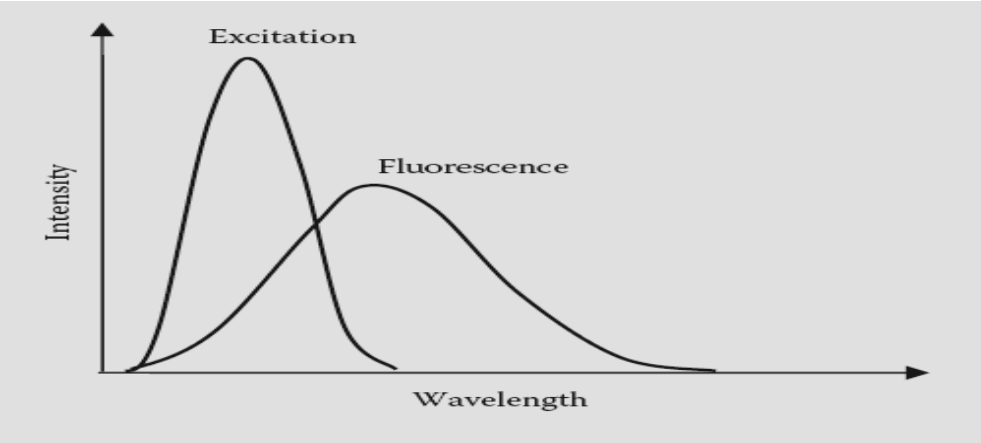

Fig. 5 Fluorescent Light Emission [23]

Fluorescence:

Fluorescence [1, 2] is commonly used in bio-Optrodes. Fluorescence occurs when molecules absorb light at one wavelength and then emit light at a longer wavelength [23, 29], as illustrated in Fig. 5. Since the excitation and emission occurs only at distinct energy levels, each fluorescent molecule has a unique fluorescence spectral fingerprint, which is very important for the optical biosensor application [31].

An example of fluorescence enzyme-catalyzed reactions sensing is NADH. NAD^+ (nicotinamide adenine dinucleotide) is nonfluorescent but NADH is fluorescent. Therefore, dehydrogenase enzyme-catalyzed substrate reaction as can be followed by monitoring the NADH fluorescence [1, 2, 28] as shown in relation (2).

$$\text{Substrate}+NAD^+ \xrightarrow{dehydrogen} \text{Product}+NADH \quad \ldots.(2)$$

NADH can be detected using fiber optics through its fluorescence at λ_{ex} = 350 nm, λ_{em} = 450 nm. Several optical sensors have thus been produced by integrating different dehydrogenase or oxidoreductase enzymes with optical fibers.

Chemiluminescence and Bioluminescence:

Chemiluminescence [23, 28] is similar to fluorescence. The difference is that chemiluminescence occurs by exciting molecules with a chemical reaction (usually occurring by the oxidation of certain substances such as oxygen or hydrogen peroxide), whereas fluorescence occurs by exciting molecules via light. Thus, in the case of chemiluminescence, no external source of light is required to initiate the reaction. Chemiluminescence is usually involved with two steps, as illustrated by relation (3) and (4).

$$A \xrightarrow{k_1} A', \quad \text{exciting step} \qquad \ldots\ldots..(3)$$

A' $\xrightarrow{k_2}$ hv, emission step ……..(4)

Where, k_1 is the excitation rate, and k_2 is the decay rate. A chemiluminescence based sensors commonly use chemical for generating light signal in many bio-Optrodes. The reaction between luminol and HO produces a luminescence signal and this reaction is also catalyzed by certain ions or molecules.

Bioluminescence [23, 28] is simply chemiluminescence occurring in living organisms, which represents a biological chemiluminescent reaction process. Many organisms produce bioluminescence for signaling, mating, prey attracting, food hunting, and self-protection. A very familiar example of high-efficiency bioluminescence is the fire fly. The ratio of the number of photons produced for a given number of molecules is as high as 0.9. Since the bioluminescence is generated via biological reaction processes, the certain biological process can be sensed by detecting the bioluminescence.

BASED ON THE OPTICAL GEOMETRIES

A number of optical geometries [2] have been used in the design of various optical biosensors. The choice of any of these geometries is dependent on the nature of the analyte and the optical probing method used. Here, the major consideration is to enhance the sensitivity and specificity.

Bio-Optrode:

The word "Optrode" is a combination of the words "optical" and "electrode". Optrode-based [3, 28] fiber optic biosensors (bio-Optrodes) are analytical devices incorporating optical fibers and biological recognition molecules. The basic structure of an optrode is composed of a source fiber and a receiver fiber that is connected to a sensing fiber by a special connector as illustrated in Fig. 6.

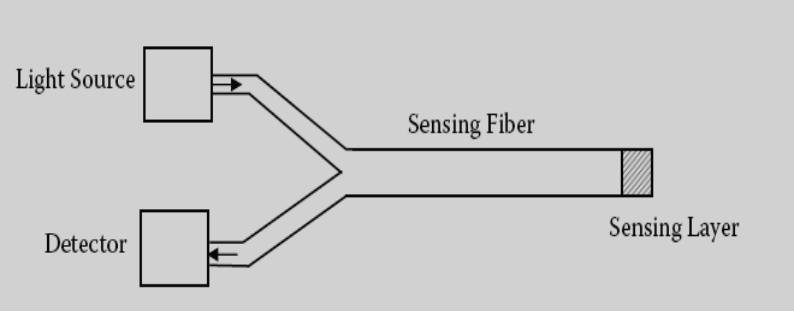

Fig. 6 Configuration of Bio-Optrode [23]

To achieve sensing capability, the tip of the sensing fiber is usually coated with a sensing material by the dip coating procedure. The analyte to be sensed may interact with the sensing tip by changing one or several of the parameters like, its refractive index, absorption, reflection, scattering properties; or polarization behaviors. The fiber in this case acts as a light pipe transmitting light to and from the sensing region.

Surface Plasmon Resonance:

Surface plasmon resonance (SPR) [34-36] is a unique optical transduction method, which has been commercially employed for optical biosensors. SPR biosensors exploit special electromagnetic waves - surface plasmon to probe changes in the refractive index at surfaces of metals.

Surface plasmon resonance biosensors can therefore be used to monitor the interaction between an analyte and its biospecific partner immobilized on the metal surface without the use of labels. A major application area includes detection of low levels of biological analytes and study of biomolecular interactions. In the past 15 years, SPR biosensor technology has been commercialized, and SPR biosensors have become a central tool for characterizing and quantifying biomolecular interactions both in life science and pharmaceutical research. To effectively generate SPR, proper exciting wavelength is needed. The basic SPR apparatus is referred to as the Kretschman prism arrangement [1, 23], as illustrated in Fig. 7.

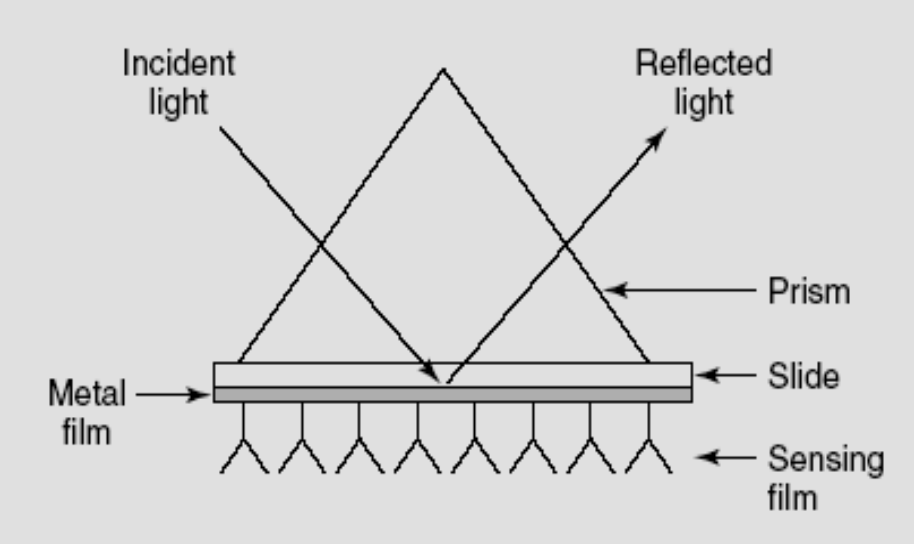

Fig. 7 Kretschmann prism-based SPR Sensor [1]

In the device, first, a thin film of metal (usually a 400–500 Å thick gold or silver film) is coated on the prism, and a biosensing layer containing an immobilized biorecognition element is also coated on the metal surface. When the light of an appropriate wavelength interacts with the dielectric-metal interface at the proper angle, it can induce the electron plasmatic resonance at the metal surface. Under this situation, the photon energy is largely transferred to the resonant energy of SPR, so that the reflection light from the metal film will greatly be attenuated. Thus, one can observe a sharp minimum of light reflectance when the angle of incidence is at this proper resonant angle. Since the resonance angle depends on several factors (e.g.; the wavelength of the incident light, the metal, and the nature of the media in contact with the surface) the nature of the media can be sensed by measuring this resonance angle. Furthermore, in addition to the prism coupling, SPR sensors can also be based on optical fibers or integrated optical waveguides.

In biosensor applications, SPR has been successfully used to detect DNA or proteins by measuring the changes in the local index of refraction upon adsorption of the target molecule to the metal surface. The major advantages of SPR sensors includes, high sensitivity, label-free, enabled analysis for a wide range of bio systems requiring only small amounts of samples.

Fiber Grating Based Sensors:

Fiber gratings [23, 37] are effective elements not only for enhancing the sensitivity and selectivity but also for enabling the multi parameter, multifunctional and distributed sensing capability. In general, gratings can be photo induced into a silica fiber. For the Bragg grating, the Bragg resonance condition can be mathematically expressed as equation (5).

$$\lambda_B = 2n_{eff}\Lambda \qquad \text{……..(5)}$$

Where, n_{eff} is the effective refractive index of the fiber, Λ is the grating pitch, and λ is the resonant reflected Bragg wavelength. However, in general, the effective refractive index of the fundamental mode of a standard fiber is practically independent of the refractive index of the surrounding medium. In order to enable the ambient sensing capability, it is important to make optical modes penetrate evanescently into the surrounding media. So, there is an interaction between the guided light field and the bio agents to be sensed. Many methods have been proposed to optimize this interaction, such as using blazed gratings or long period gratings [23, 37], etching the fiber close to the core diameter to increase the sensitivity, or side polishing the fiber. In Fig. 8, different types of fiber gratings are shown.

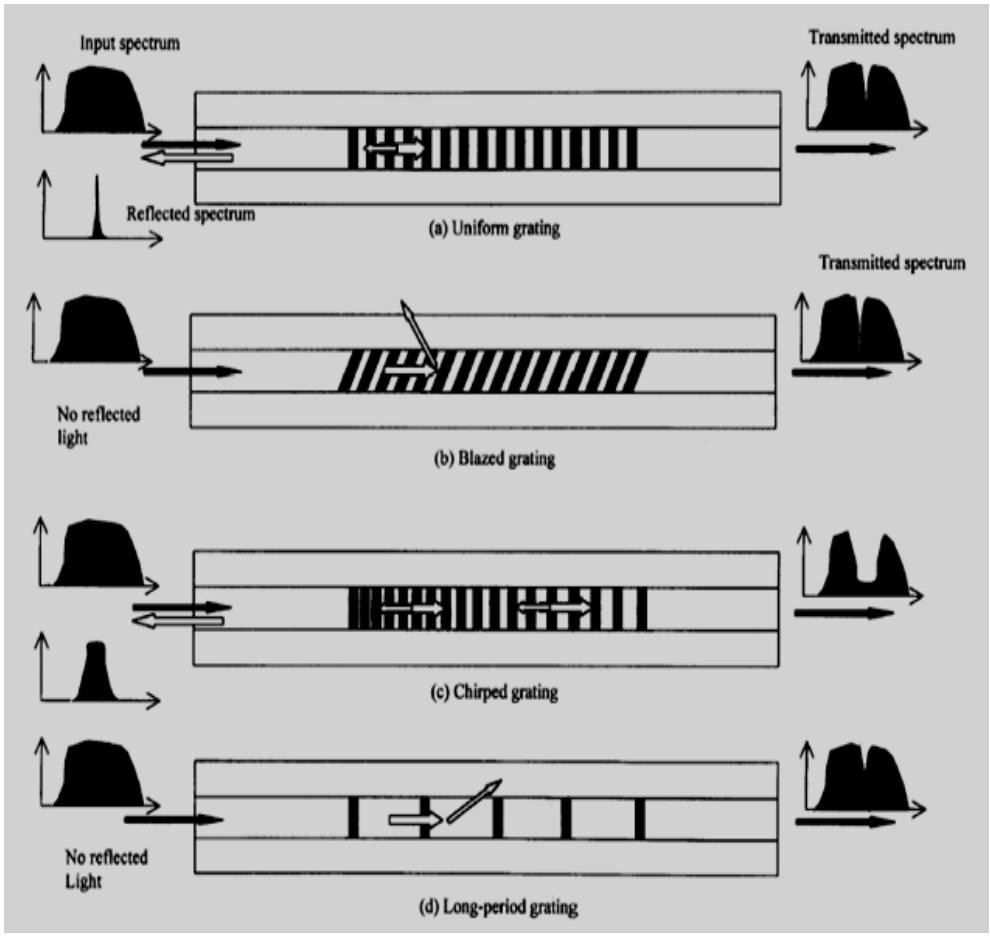

Fig. 8 Different Types of Fiber Gratings [37]

When there is a change in refractive index or grating period (e.g., induced by the measurand), the resonant wavelength will be shifted. Thus, by measuring the resonant wavelength shift, the measurand can be measured. Furthermore, by employing a set of gratings with different resonant wavelengths, multiple agents or distributed sensing can be realized because these sensing data can be distinguished by the different resonant wavelength regimes.

Evanescent Wave Fiber Optic Biosensors:

When the incident light is reflected from an interface at an angle greater than the critical angle, the total internal reflection occurs. However, its intensity does not abruptly decay to zero at the interface and a small portion of light penetrates into the reflecting medium. This penetrated electromagnetic field is called the evanescent wave [1, 2, 23]. Evanescent wave sensors utilize the electromagnetic component of the reflected light at the side surface between the fiber

core and the fiber cladding as shown in Fig. 9. The evanescent wave can interact with analytes within the penetration depth; thus, by immobilizing biological material within this region, the absorption of propagating light or generation of fluorescence during the binding of analytes can be detected.

The major advantage of using evanescent wave is the ability to couple light out of the fiber into the surrounding medium, which offers a large interaction surface. Therefore, higher sensitivity can be achieved.

BIORECOGNIZATION ELEMENTS

Other way to classify the biosensors is based on the biorecognization elements [6]. The biorecognition elements are biologics such as enzymes, antibodies, DNA, receptors and even biological cells and microorganisms that selectively recognize an analyte. They are often immobilized to increase their local concentration near the sensing element and to allow them to be reused. Some of the molecular bioreceptors used for biorecognition in biosensitizing are described here. In Fig.10, different types of biorecognition elements are shown.

The nature of interaction between the analyte and the biological material used in the biosensor are basically of two types. Based on the biorecognization mechanism, the biosensors may be classified into the following categories: (1) Catalytic biosensors and (2) Affinity biosensors.

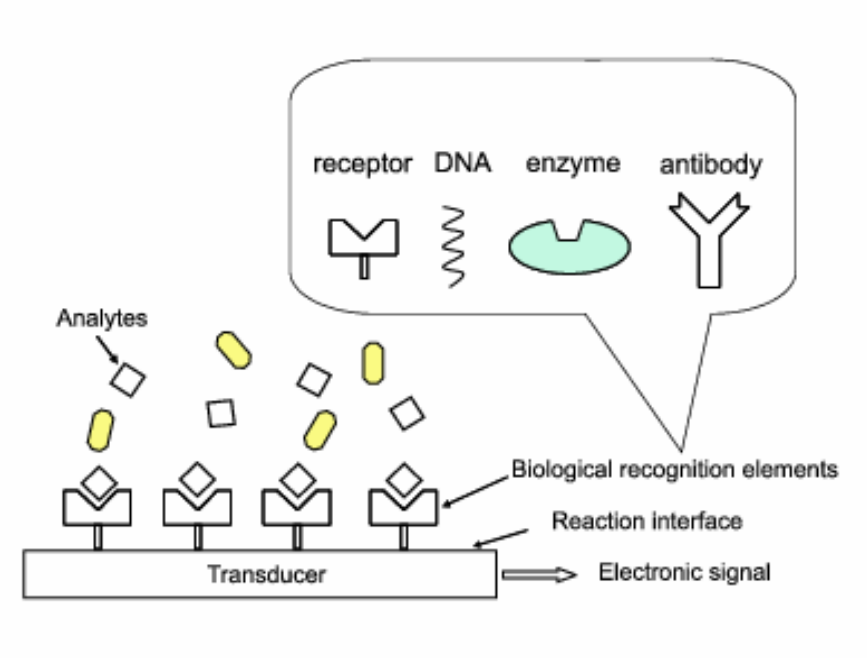

Fig. 10 Biorecognition Elements [1]

Catalytic Biosensors:

In this type of biosensors, the analyte may be converted into a new chemical molecule by enzymes; such type of biosensor is called *'catalytic biosensors'*. The function of catalytic biosensors is realized by recognizing and binding of an analyte followed by a catalyzed chemical conversion [3, 5] of the analyte from a non detectible form to a detectible form. The reaction progress of the biocatalysis can be monitored by detecting the rate of formation of a product, the disappearance of a reactant, or the inhibition of the reaction.

Enzymes:

Any of several complex proteins that are produced by cells and act as catalysts in specific biochemical reactions are known as enzymes [1]. Ureases, glucose oxide, calmodine, are known enzymes. The use of an enzyme as a biorecognition element utilizes its selectivity to bind with a specific reactant (substrate) and catalyze its conversion to a product. This enzyme–substrate-catalyzed reaction [3, 11] is often represented in equation (6).

$$E + S \rightleftharpoons ES \rightarrow P \qquad \text{.....(6)}$$

In addition to providing selectivity, the reaction of certain analytes/substrates with enzymes can also provide optical transduction by producing a product that absorbs at a different wavelength (change in absorption), or is fluorescent (fluorescence sensor). The advantages [2] of enzyme based optical biosensors are, easily bind to the substrate, highly selectivity, catalytic activity, which improves sensitivity, fairly fast acting. The disadvantages are, expensive, loss of activity when they are immobilized on a transducer, tend to lose activity after a relatively short period of time.

Affinity Biosensors:

In this type of biosensors, the analyte may simply bind to the biological material present on the biosensor e.g., antibodies, receptors and nucleic acids. These types of biosensors are known as *'affinity biosensors'*. Hence, bioaffinity biosensors are based on affinity interactions by separating an individual or selected range of components from complex mixtures of biomolecules.

Antibodies:

Antibodies are proteins that selectively bind with an antigen or analyte because of their geometric (site) compatibility. Very often, an antibody-antigen pair's selective association in terms of their conformational compatibility is represented as a lock (antibody) and key (antigen) combination, as shown in Fig. 11.

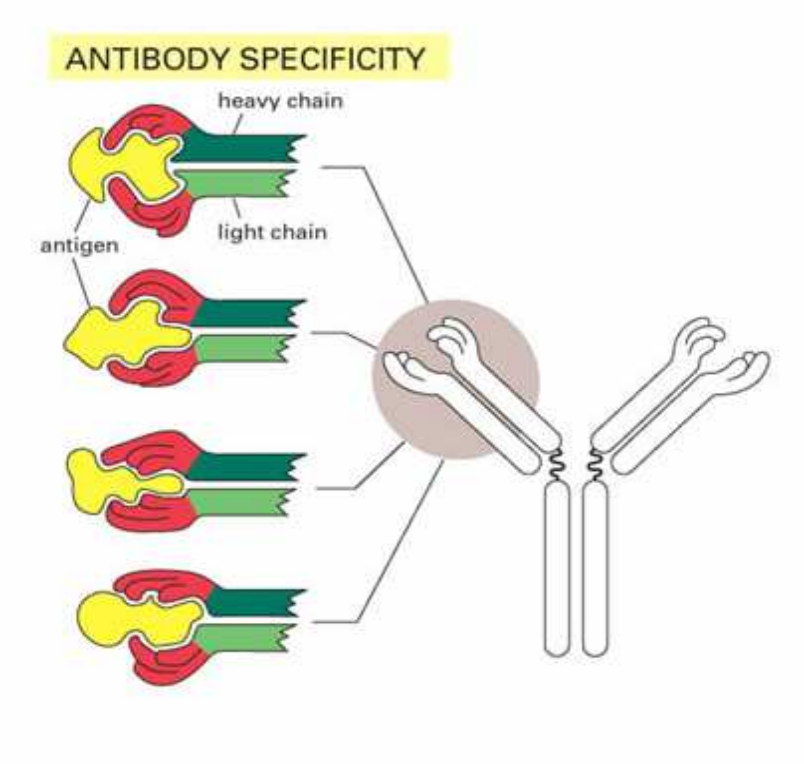

Fig. 11 Antibody-Antigen Lock & Key Combination [2]

An individual animal can make billions of different antibody molecules, each with a distinct antigen-binding site. Each antibody recognizes its antigen with great specificity. This specific physical association can also produce an optical response that can be intrinsic such as a change in the optical property of the antibody or the antigen as a result of association. Alternatively, an optical transducer (such as a fluorescent marker) can be used to tag the antibody or the antigen. Advantages of antibodies based affinity biosensors are highly selective, ultra-sensitivity, bind powerfully. The disadvantages are no catalytic effect.

Neuro Receptors:

These are neurologically active compounds [2] such as insulin, other hormones and neuro transmitters that act as messengers via ligand interaction. They are also labeled with a fluorescent tag to produce an optical response through chemical transduction.

DNA:

The specificity or complementary base pairing (that provides the basis for the DNA double-helical structure) can be exploited for recognition of base sequence in DNA and RNA. An example is a DNA microarray that consists of micro patterns of single-stranded DNA or finite-size oligonucleotides

immobilized on a plate. They act as biorecognition elements by forming hydrogen bonds with a specific single-stranded DNA or RNA having a complementary base sequence. This process of base-pairing to form a double-stranded DNA is called *hybridization*.

IMMOBILIZATION TECHNIQUES

To make a biosensor, the biological component has to be properly attached to the transducer. This process is called immobilization. The biorecognition elements are normally immobilized on a solid support [1, 2, 26]. The solid supports are usually a membrane, polymer, copolymer, or semiconductor material. A biorecognition element is immobilized on the solid support, either by a physical method (such as adsorption) or by chemical attachment. In some approaches, a biorecognition element is entrapped in the volume of a matrix (solid support) with controlled porosity, in which case the solid support also provides selectivity toward an analyte of certain size compatible with its pore dimension. Following five methods of immobilization [24] are popular.

Adsorption:

It is association of the active component with a film or coating through hydrophobic, hydrophilic, and/or ionic interactions. Many substances adsorb enzymes on their surfaces. The adsorption approach itself includes using physical adsorption and chemical adsorption. Physical adsorption is usually weak and involves the formation of van-der waals bonds. Chemical adsorption is much stronger due to the formation of covalent bonds. Advantages are simplicity, absence of a clean-up step, and highly reproducible. Drawbacks are susceptible to changes in pH, temperature, ionic strength of the substrate. Physical adsorption is shown in Fig. 12.

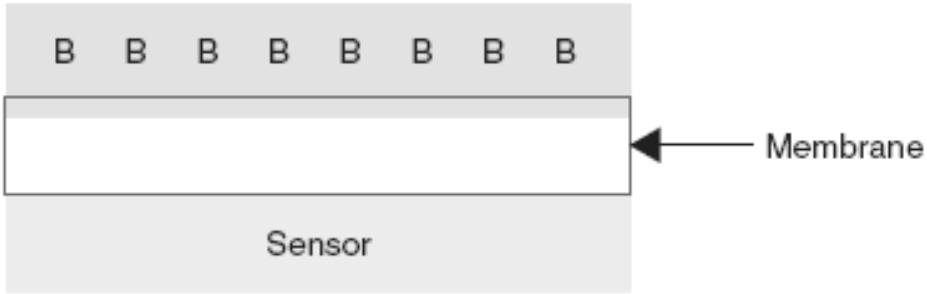

Fig. 12 Physical Adsorption [6]

Microencapsulation:

A semi permeable membrane is used to trap the biomaterial on the transducer. This keeps close contact between the biomaterial and the transducer. Membrane materials include cellulose acetate, polycarbonate or Teflon. It is stable towards changes in temperature, pH, ionic strength and chemical composition. Microencapsulation is shown in Fig. 13.

Entrapment:

Entrapment immobilization involves the physical trapping of the active biomolecules into a film or coating.

In the operation, biomolecules are mixed with a monomer solution. e.g., polymer gel. It is strong, but has a slow diffusion rate of analytes. Membrane entrapment is shown in Fig. 14.

Covalent Bonding:

Attachment of the active component to the transducer surface using a chemical reaction. Covalent bonding agent is employed in the biomaterial to support the matrix. e.g., thiol, epoxy, amino, carboxylic. Advantages are stability, avoid problems of leaching. Drawbacks are covalent linkage. Covalent bonding immobilization is shown in Fig. 15.

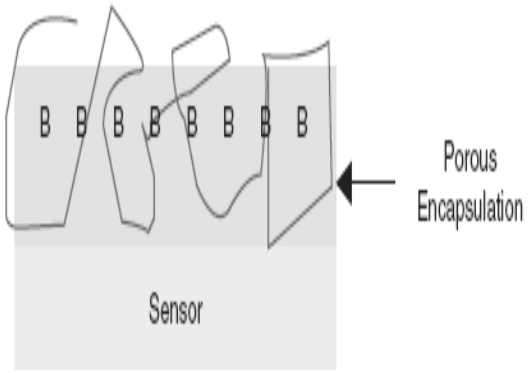

Fig. 13 Microencapsulation [6]

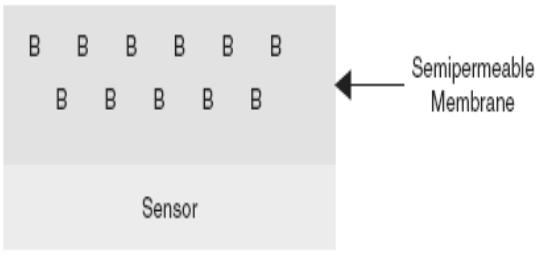

Fig. 14 Membrane Entrapment [6]

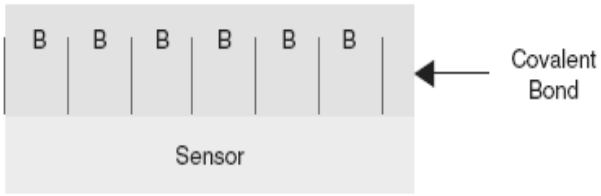

Fig. 15 Covalent Bonding Immobilization [6]

Cross-Linking:

It is similar to entrapment, only a polymerization agent (such as glutaraldehyde) is used to provide additional chemical linkages between the active, entrapped component and the film or coating. The biomaterial is chemically bonded to solid supports or to another supporting material such as a gel. It is useful to stabilize adsorbed biomaterials. However, it causes damage to the enzyme, limits the diffusion of the substrate, and there is poor mechanical strength.

Finally, we would like to point out that no matter which immobilization method is used, to achieve best performance, the immobilization procedure should be optimized in terms of signal intensity, selectivity, and sensitivity by choosing proper materials (e.g., fluorophore) and methods depending on the application.

CURRENT AND EMERGING TRENDS

There is a greater demand for biological intelligence on the planet now than there has ever been in the history. Such demand stems from the desire to gain a better understanding of the major issues like, the impact of infectious diseases, bioterrorism, bio-energy, global warming & climate change and so many new things [1]. Optical biosensors have been applied extensively in many fields, for biotechnology quality control, in clinical analysis, environmental control, fermentation monitoring, product control in the food and beverage industry etc. Here some current and emerging area of optical biosensors are explored in brief.

Life Science Applications:

Optical biosensors are highly sensitive. These high sensitivity results are impressive considering that no labeling of the biomolecules is required. In life sciences [12], this technique has been applied in biomolecular engineering, clinical analysis, new drug design, and virus-protein interaction among others interesting problems. Several optical biosensors are designed and commercially available for the human beings. e.g. glucose sensors, billirubin sensors, blood gas sensors,

cholesterol sensors, endoscopy surgery fiber optic sensors and many more.

Environmental Applications:

The application of optical immunosensors for environmental monitoring [21] started some years ago. Strict limits have been placed on the release of certain pollutants into the environment. The enforcement of this legislation necessitates reliable monitoring of the environment for the presence of compounds which may adversely affect human health, and local ecosystems. Some applications are bioprocess sensors, ozone sensors, pesticide sensors, chlorinated contaminants sensor, waste monitoring sensor, etc...

Chemical and Biological Warfare and Defence:

This is a new area of application for the optical biosensing techniques and is due to the current world situation. The best defence against these agents is the early detection and/or identification [19]. A wide variety of synthetic chemicals, toxins of plant or animal origin and biological materials including various disease micro-organisms as well as some bacterial exotoxins have either been used as warfare agents or are perceived as having the potential to be used for that purpose. A critical need exists for a field deployable biosensor to detect biological and chemical warfare agents in air and water samples, both rapidly and with a high sensitivity and sensitivity approaching standard laboratory procedures. For this field several portable optical biosensors are developed like, TNT sensors, RDX sensors, and many more sensors are developed.

Genetic Applications:

DNA biosensors and gene chips [1] are of considerable interest due to their potential for obtaining sequence-specific information in a faster, simpler and cheaper manner compared to traditional hybridization assays. DNA optical biosensors, based on nucleic acid recognition processes, are rapidly being developed towards the goal of simple, rapid and low cost testing of genetic and infectious diseases and for detection of DNA damage and interactions. SPR sensors have been used to monitor in real time the binding of low molecular weight ligands to DNA fragment that were irreversibly bound to the sensor surface. Binding rates and equilibrium coverage were determined for various ligands by changing the ligand concentration.

Multianalyte Detection:

Multianalyte detection will continue to be a major focus of future development. Different methods of patterning efficient and mutually compatible biorecognition

elements, as well as coupling them separately to an array of light sources and an array of detectors are opportunities for chemists, biomedical researchers and engineers. Various imprint technologies will be of value in patterning. An important consideration will also be the capabilities of these sensors for real time continuous monitoring. Here the long-term stability of the pattern of immobilized biorecognition elements and fluidic consideration will play an important role.

Optical Sensor Array and Integrated Light Source:

A new multianalyte detection scheme that utilizes an optical sensor array and integrated light source (OSAILS) has recently been introduced [2]. They utilized microwells of dimensions approximately 250 mm machined directly into the light-emitting diode (LED) face. The individual microwells are filled with a sol–gel precursor solution containing an oxygen-sensitive emitter. The xerogel (porous gel) forms within individual microwells. The OSAILS is then placed within a flow cell holder and can be powered by a low-voltage dc power supply or a battery. The LED light output is used directly to excite the emitter immobilized within the microwell-entrapped xerogel. The fluorescence output from the array of microwells is collected by a charge coupled device (CCD).

Optical Nano Biosensors:

Nanotechnology [39] is playing an increasingly important role in the development of biosensors. The sensitivity and performance of biosensors is being improved by using nano materials for their construction. The use of nano materials has allowed the introduction of many new signal transduction technologies in biosensors. Because of their submicron dimensions, nano sensors, nano probes and other nano systems have allowed simple and rapid analyses. Portable instruments capable of analyzing multiple components are becoming possible. Using micro- and nanotechnologies [22, 38], optical biosensors could be integrated in "lab-on-a-chip" microsystems which could be used in real applications in many different scenarios (home, patient office, work, etc.) for real-time and on-line monitoring.

SUMMARY

Optical biosensors are studied and discussed qualitatively. Working principles, constructions, advantages, and applications of optical biosensors are presented. We found that, optic biosensors play a significant role in the field of biosensors because they can be easily miniaturized and

integrated for the determination of different target compounds. These biosensor types have been the objective of a large number of investigations in the last years and they provide numerous ways of performing the rapid, remote, in-line and on-line determination of a lot types of analytes in a wide range of application fields. There are various technical solutions exist with current methodology, but still more research efforts are needed to find better alternatives. There is still a lot of ground to cover in the optical biosensing field. We can develop new applications or enhance the performance of conventional biosensors with nanotechnology. A nanotechnology is attractive for the research in this field.

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