Analysis, Designing and Working Principal of Optical Fiber (OF) Biosensors

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ABSTRACT: *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 .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, antibodies), 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". Due to tremendous advantages, the field of optical biosensors has been emerged as a topic of great interest. Biosensors are very useful for biological intelligence system, medical and biological examination, biological monitoring/scanning/tracing and processing of biosignals through computer and electronics system, and bioelectronics data acquisition and signal processing and measurement through embedded electronics gadgets and instruments. Hence this paper intended to give fundamental idea about this emerging field, its types, application advantages and modeling review.*

Keywords: *optical biosensor, biomedical instrumentation, bio intelligence systems.*

Review:

Molecular recognition is central to biosensing. Since the first biosensor was developed by Updike and Hicks (1967) many biosensors have been studied and developed. As shown in Fig. , a biosensor can be defined as a "compact analytical device or unit incorporating a biological or biologically derived sensitive 'recognition' element integrated or associated with a physio chemical transducer" (Turner, 2000). Initially, biosensor recognition elements were isolated from living systems. However, many biosensor recognition elements now available are not naturally occurring but have been synthesized in the laboratory. The sensing of targets, i.e. analytes of interest, is already being influenced by the emergence of engineered binding proteins (Feltus and Daunert, 2002). Employing the techniques of modern biotechnology, it is now possible to construct DNA polynucleotides at will, thus opening new paths for generation of biosensor recognition elements arising from paths not taken by nature. The following review is restricted to a selective overview of molecular recognition elements, including receptors, enzymes, antibodies, nucleic acids, molecular imprints and lectins currently impacting biosensor development (Fig.). With the advent of nanostructures and new interface materials, these recognition elements will be major players in future biosensor development. "Transduction" of the biorecognition event constitutes a separate and obviously important area of biosensor development beyond the scope of the present review.

Receptors

For purposes of biosensing, receptors are alluring because of their generic "receiving" as well as "sending" functions. In addition to their being mediators of physiological processes, receptors are natural targets for a variety of toxins as well as drugs. Receptors are transmembrane (plasma and intracellular membranes) and soluble proteins that bind to specific molecules called ligands, the binding event initiating a specific cellular response. Ligand-induced receptor conformational changes give rise to subsequent events such as channel opening, adenyl/guanyl cyclase mediated second messenger generation, and reaction cascades involving a multitude of other proteins, including G proteins, tyrosine kinases, phosphatases, phosphorylases, transcription factors, and antigen processing cell receptor responses all constituting "transduction" in response to the initial ligands binding event. The whole concept as shown in below figure
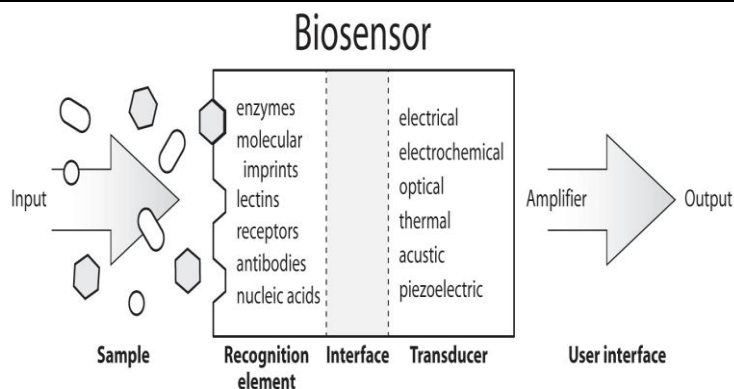
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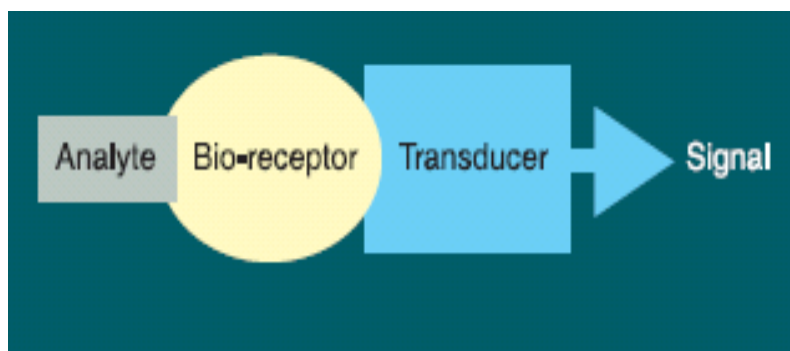
Transducers used in Biosensor development

Biosensors can be grouped according to their biological element or their transduction element. Biological elements include enzymes, antibodies, micro-organisms, biological tissue, and organelles. Antibody-based biosensors are also called immune sensors. When the binding of the sensing element and the analyte is the detected event, the instrument is described as an affinity sensor. When the interaction between the biological element and the analyte is accompanied or followed by a chemical change in which the concentration of one of the substrates or products is measured the instrument is described as a metabolism sensor. Finally, when the signal is produced after binding the analyte without chemically changing it but by converting an auxiliary substrate, the biosensor is called a catalytic sensor. The method of transduction depends on the type of physicochemical change resulting from the sensing event. Often, an important ancillary part of a biosensor is a membrane that covers the biological sensing element and has the main functions of selective permeation and diffusion control of analyte, protection against mechanical stresses, and support for the biological element. The most commonly used sensing elements and transducers are discussed below.

Sensing Elements

Enzymes are proteins with high catalytic activity and selectivity towards substrates they have been used for decades to assay the concentration of diverse analytes. Their commercial availability at high purity levels makes them very attractive for mass production of enzyme sensors. Their main limitations are that pH, ionic strength, chemical inhibitors, and temperature affect their activity. Most enzymes lose their activity when exposed to temperatures above 608C. Most of the enzymes used in biosensor fabrication are oxidizes that consume dissolved oxygen and produce hydrogen peroxide. Enzymes have been immobilized at the surface of the transducer by adsorption, covalent attachment, and entrapment in a gel or an electrochemically generated polymer, in bilipid membranes or in solution behind a selective membrane.

Antibodies

Antibodies are proteins that show outstanding selectivity. They are produced by b-lymphocytes in response to antigenic structures, that is, substances foreign to the organism. Molecules larger than about 10 kDa can stimulate an immune response. Smaller molecules like vitamins or steroids can be antigenic (also called haptens) but they do not cause an immune response unless they are conjugated to larger ones like bovine serum albumin. Many antibodies are commercially available and commonly used in immunoassays. Antibodies are usually immobilized on the surface of the transducer by covalent attachment by conjugation of amino, carboxyl,

aldehyde, or sulfhydryl groups. The surface of the transducer must be previously functionalized with an amino, carboxyl, hydroxyl, or other group. Antibodies share similar limitations with enzymes. Furthermore, binding may not be reversible and regeneration of the surface may require drastic changes in conditions like low pH, high ionic strength, detergents, etc. Therefore, efforts are being made to produce low cost, single use sensors. Probably the main potential advantage of immunosensors over traditional immunoassays is that they could allow faster and in-field measurements. Immunosensors usually employ optical or acoustic transducers.

Microbes

The use micro-organisms as biological elements in biosensors is based on the measurement of their metabolism, in many cases accompanied by the consumption of oxygen or carbon dioxide, and is, in most cases, measured electrochemically. Microbial cells have the advantage of being cheaper than enzymes or antibodies, Micro-organisms have been immobilized, for example, in nylon nets, cellulose nitrate membranes,] or acetyl cellulose. Other biological elements such as animal of vegetable tissue and membranes as well as organelles and nucleic acids have been researched but are out of the scope of this article. A summary of some biological elements and transducers used in the fabrication of biosensors is presented in Table.

Category	Principle	Examples
Electrochemical	(a) potentiometric: depends on changes in potential of a system at a constant current (I=0) (b) amperometric: detects changes in current as a function of concentration of electroactive species	Ion-selective electrodes, ion-selective field effect transistors, LAPS Solid electrolyte gas sensors, electronic noses
Optical	Link changes in light intensity to changes in mass or concentration, therefore, fluorescent or colorimetric molecules must be present	Optical fibres, surface plasmon resonance, absorbance luminescence
Piezoelectric	Sensitive to changes in mass, density, viscosity and acoustic coupling phenomena	Surface acoustic wave sensors
Thermal	Detect changes in temperature	Calorimetric sensors

Introduction

Optical techniques have always been used for a large number of metrological and sensing applications. The conventional methods based on free-space interferometer and spectroscopy, for example, are outstanding examples of optics capabilities. This kind of free-space monitoring, however, is effective only for line of sight and suffers from undesired misalignments and external perturbations. Guided-wave sensing adds to intrinsic advantages of optical techniques the possibility of guiding the light beam in a confined and inaccessible medium, thus allowing more versatile and less perturbed measurements. Fiber- and integrated- optics technologies were primarily developed for telecommunication applications. However, the advances in the development of high quality and competitive price optoelectronic components and fibers have largely contributed to the expansion of guided wave technology for sensing as well. The main reasons which make guided wave optics attractive for sensing can be abstracted as below.

➢ Non-electrical method of operation, which is explosion-proof and offers intrinsic immunity to radio frequency and, more generally, to any kind of electromagnetic interference;
➢ Small size/weight and great flexibility, that allow access to otherwise restricted areas;
➢ Capability of resisting to chemically aggressive and ionizing environments;
➢ Easy interface with optical data communication systems and secure data transmission.

Light Source

A wide selection of light sources is available for optical sensor applications. These include: highly coherent gas and semiconductor diode lasers, broad spectral band incandescent lamps, and narrow-band, solid-state, light-emitting diodes (LEDs). The important requirement of a light source is obviously good stability. In certain applications, for example in portable instrumentation, LEDs have significant advantages over other light

sources because they are small and inexpensive, consume lower power, produce selective wavelengths, and are easy to work with. In contrast, tungsten lamps provide a broader range of wavelengths, higher intensity, and better stability but require a sizable power supply and can cause heating problems inside the apparatus.

Optical Elements

Various optical elements are used routinely to manipulate light in optical instrumentation. These include lenses, mirrors, light choppers, beam splitters, and couplers for directing the light from the light source into the small aperture of a fiber optic sensor or a specific area on a waveguide surface and collecting the light from the sensor before it is processed by the photodetector. For wavelength selection, optical filters, prisms, and diffraction gratings are the most common components used to provide a narrow bandwidth of excitation when a broad width light source is utilized.

Photodetectors

In choosing photodetectors for optical sensors, a number of factors must be considered. These include sensitivity, detectivity, noise, spectral response, and response time. Photomultipliers and semiconductor quantum photodetectors, such as photoconductors and photodiodes, are both suitable. The choice, however, is somewhat dependent on the wavelength region of interest. Generally, both give adequate performance. Photodiodes are usually more attractive because of the compactness and simplicity of the circuitry involved. Typically, two photodetectors are used in optical instrumentation because it is often necessary to include a separate reference detector to track fluctuations in source intensity and temperature. By taking a ratio between the two detector readings, whereby a part of the light that is not affected by the measurement variable is used for correcting any optical variations in the measurement system, a more accurate and stable measurement can be obtained.

Signal Processing

Typically, the signal obtained from a photodetector provides a voltage or a current proportional to the measured light intensity. Therefore, either simple analog computing circuitry (e.g., a current-to-voltage converter) or direct connection to a programmable gain voltage stage is appropriate. Usually, the output from a photodetector is connected directly to a preamplifier before it is applied to sampling and analog- to- digital conversion circuitry residing inside a computer. Quite often two different wavelengths of light are utilized to perform a specific measurement. One wavelength is usually sensitive to changes in the species being measured, and the other wavelength is unaffected by changes in the analyte concentration. In this manner, the unaffected wavelength is used as a reference to compensate for fluctuation in instrumentation over time. In other applications, additional discriminations, such as pulse excitation or electronic background subtraction utilizing synchronized lock-in amplifier detection, are useful, allowing improved selectivity and enhanced signal-to-noise ratio.

Optical Fiber

Several types of biomedical measurements can be made by using either plain optical fiber as a remote device for detecting changes in the spectral properties of tissue and blood or optical fibers tightly coupled to various indicator-mediated transducers. The measurement relies either on direct illumination of a sample through the end face of the fiber or by excitation of a coating on the side wall surface through evanescent wave coupling. In both cases, sensing takes place in a region outside the optical fiber itself. Light emanating from the fiber end is scattered or fluoresced back into the fiber, allowing measurement of the returning light as an indication of the optical absorption or fluorescence of the sample at the fiber optic tip. Optical fibers are based on the principle of total internal reflection. Incident light is transmitted through the fiber if it strikes the cladding at an angle greater than the so-called critical angle, so that it is totally internally reflected at the core/cladding interface. A typical instrument for performing fiber optic sensing consists of a light source, an optical coupling arrangement, the fiber optic light guide with or without the necessary sensing medium incorporated at the distal tip, and a light detector. A variety of high-quality optical fibers are available commercially for biomedical sensor applications, depending on the analytic wavelength desired. These include plastic, glass, and quartz fibers which cover the optical spectrum from the UV through the visible to the near IR region. On one hand, plastic optical fibers have a larger aperture and are strong, inexpensive, flexible, and easy to work with but have poor UV transmission below 400 nm

Optical Fiber Sensors

Advantages cited for fiber sensors include their small size and low cost. In contrast to electrical measurements, where the difference of two absolute potentials must be measured, fiber optics are self-contained and do not require an external reference signal. Because the signal is optical, there is no electrical risk to the

patient, and there is no direct interference from surrounding electric or magnetic fields. Chemical analysis can be performed in real-time with almost an instantaneous response. Furthermore, versatile sensors can be developed that respond to multiple analytes by utilizing multi wavelength measurements. Despite these advantages, optical fiber sensors exhibit several shortcomings. Sensors with immobilized dyes and other indicators have limited long-term stability, and their shelf life degrades over time. Moreover, ambient light can interfere with the optical measurement unless optical shielding or special time synchronous gating is performed.

Fundamentals of Waveguiding:
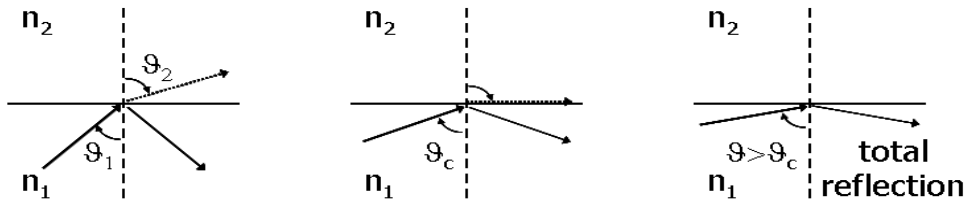
With the ray theory of light propagation, when light impinges at the interface between two transparent media, it is partially reflected and partially refracted. The Snell's law describes the refraction phenomena as

$$n_1 \sin \theta_1 = n_2 \sin \theta_2$$

When $n2 < n1$, any ray impinging at the interface with an incident angle greater than θc is totally reflected inside the first medium.

$$\theta_c = \sin^{-1} \frac{n_2}{n_1}$$

An optical fiber consists of layered cylinders of glass or plastic, as shown in Fig. Inner and outer cylinders, namely 'core' and 'cladding', have refractive indices *n1* and *n2*, respectively. Any ray impinging at the core-cladding interface with an incident angle greater than θc is undergoing multiple reflections within the core, in which it results trapped and propagates.
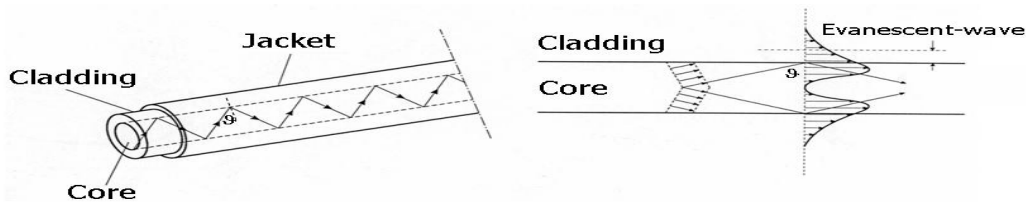

Fig: Propagation in optical fiber

An integrated optical waveguide, on the other hand, consists of a thin film structure supported by a substrate. The simplest structure is shown in Fig. Where the guiding layer (the core, with refractive index *n1*) is deposited on a transparent substrate (having refractive index *n0*) and is covered by another layer (the cladding, with refractive index *n2*). If *n2=n0* we have a symmetrical structure, analogous to an optical fiber; in fact, while the x-y cross sections of the fiber and the slab waveguide are different from each other, their x-z cross sections are identical and one can expect that their waveguiding properties are fundamentally the same ones. In most cases, however, the cladding is air (*n2=1*), and we speak about a planar asymmetric waveguide. In this case light is confined only along the x direction, while the light energy can diffract in the y-z plane. The confinement of light also along the y direction is obtained by a strip waveguide, as shown in Fig. 3b, where reflections of light rays total occur also at side walls. For both fiber and slab waveguide the dependence of the refractive index on the x coordinate *n(x)* is called the refractive index profile. In the simplest case, i.e. *n(x) = n1* = constant, we refer to step-index waveguides; otherwise, we speak about gradient-index waveguides, and sophisticated profiles may be produced as well, either by a multi-layer deposition technique or by a diffusion process.

Slab waveguide (a), and strip waveguide (b).
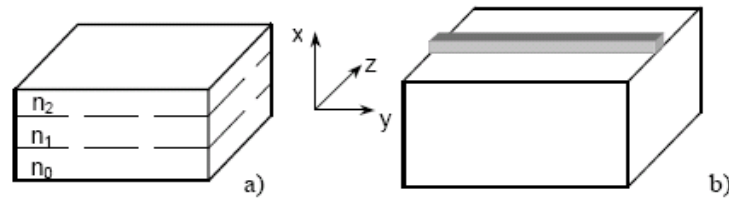
Taking into account that light is an electromagnetic wave phenomenon; a more accurate description of light propagation within a waveguide is obtained by means of Maxwell's equations. When the geometric boundary conditions at media interfaces are introduced, only discrete solutions of the wave equations are permitted. This means that only discrete waves can propagate, namely 'modes', characterized by discrete amplitudes and discrete velocities.5,6 Waveguides can be single-mode or multimode according to whether a single or a multiplicity of modes can propagate. Once the materials constituting the waveguide are set for a given wavelength, the number of supported modes depends on waveguide dimension, namely on the fiber core radius or the planar waveguide thickness. A characteristic of a guided mode which is particularly important for sensing devices is its spatial amplitude distribution. Often, in fact, the interaction between the propagating mode and the quantity to be measured (the measured) occurs through the evanescent field of the mode itself, namely its exponentially-decreasing tail.

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