# **Chapter 59 Pervasive Review of Optic Biosensors-Based on Surface Plasmon Resonance and Its Development**



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# **1 Introduction**

The development of biosensor is motivated by continuous requirement in the field of agriculture, bioprocessing, medical science, food technology, environmental engineering, military applications, etc., for easy, fast, and continuous in-situ monitoring. The biosensor is an integrated device that combines biological structures such as antibodies, tissues, enzymes, microorganisms, and nucleic acids . to detect an analyte and a physico-chemical transducer to produce a measurable signal. Nowadays, optical fibers have played a key role in sensor technology due to their splendid light delivery, low cost, long transmission length, ability to thrill the target molecules, and capture the light from the target.

Generally, optical fiber-based biosensors are divided into two classes: intrinsic and extrinsic sensors based on analyte interaction. In the first case, interaction occurs within fiber with the analyte, whereas in the second situation, fiber is applied to couple the light in the scope where the analyte influenced light beam. Various kinds of spectroscopic techniques like absorption, reflection, phosphorescence, fluorescence, surface plasmon resonance (SPR), etc., are used in optical biosensors. Because of easy handling and accuracy with minimal sample treatment, biosensor based on fiberoptic are useful in surgery, routine tests, intensive care, patient home care, as well as emergencies [\[1\]](#page-7-0). This review article has five sections. A brief idea about biosensor and their application in various field, need for optical fiber in the biosensor is given

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© The Author(s), under exclusive license to Springer Nature Singapore Pte Ltd. 2023 D. Goyal et al. (eds.), *Proceedings of the Third International Conference on Information Management and Machine Intelligence*, Algorithms for Intelligent Systems, [https://doi.org/10.1007/978-981-19-2065-3\\_59](https://doi.org/10.1007/978-981-19-2065-3_59)

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in the first section. Different measurement techniques used in optical fiber-based biosensors are discussed along with few research papers in the second section, SPR mechanism in detail in the third section, conventional optical fiber and photonic crystal fiber (PCF)-based SPR biosensors along with recently published research papers are discussed in the fourth section. In the last section, a summary and future scope of fiber-optic biosensors are provided.

#### **2 Measurement Techniques**

In fiber-optic biosensors, different types of measurement techniques like absorbance, reflectance, fluorescence, chemiluminescence, bioluminescence, etc., are used.

## *2.1 Absorbance Measurements*

In this technique, the biological compound is put at the distal end of the optical fiber, then the light is passed to the sample through the fiber. At the detector end, using same fiber or another fiber, the change in concentration of analyte is measured which is proportional to the light absorbed by the analyte.

For medical applications, an optical fiber-based pH sensor [\[2\]](#page-7-1) and oxygen sensor [\[3\]](#page-7-2) have been developed. In the proposed pH sensor, an absorptive indicator was used with an absorption peak near 625 nm. It shows absorption change is reasonably linear over the pH range of 6.8–7.8, and it is examined by a red pulsed LED and reverts light is split using dichroic mirror into long and short wavelength signals which are detected using photodiodes. It exhibits a response time of 30–40 s and a resolution of 0.01 pH. In the oxygen sensor, after brief UV stimulation, its viologen indicator becomes strongly absorbent, then it reverts to the transparent state. The concentration of local oxygen is proportional to the indicator's rate returns to a transparency state. Indicator absorbance is observed using a red LED. It may be used in vivo and in vitro oxygen measurements.

In the urine samples, the levels of inorganic phosphate are important for the clinical test of hypoparathyroidism, hyperparathyroidism, and Vitamin D deficiency. An enzyme-based fiber-optic biosensor fabrication to estimate the inorganic phosphate in the urine sample is presented by Kulkarni et al. [\[4\]](#page-7-3). The conversion of p-nitrophenyl phosphate into a colored p-nitrophenol by acid phosphatase was detected at 405 nm. It has a response time of 20 min, linearity of  $20-100 \mu M$  and shelf life more than 80 days.

#### *2.2 Reflectance Measurements*

Reflectance is defined by the amount of light reflected from the sample to the light being transmitted to the sample along with the fiber. A new concept to detect molecular interactions using colorimetric diffractive grating has been developed by Cunningham et al. [\[5\]](#page-7-4). Here, diffractive grating is used as a surface binding element and designed to reflect the light of a single wavelength when it is illuminated with white light.

To perform real-time monitoring of the immunoassay, a high-sensitivity optical fiber-based biosensor has been evolved by Yang et al. [\[6\]](#page-7-5) applying the multiplereflection principle. For human consumption, monitoring of fish freshness as the storage conditions and handling process of fish may affect their spoilage patterns. For this, the bienzymatic creatine biosensor has been fabricated by Fazial et al. [\[7\]](#page-7-6).

#### *2.3 Fluorescence Measurements*

This technique is used for the detection of biomolecules (e.g., live cells, nucleotides, antigens, etc.) with remarkable selectivity and sensitivity. The fluorescence measurement system consists of four components: a light source, wavelength filters, fluorophore molecule, and a detector.

Various fiber-optic biosensors have been analyzed based on this technology over the past several decades. An optical fiber-based biosensor that integrates an array of electrical and optical elements with silica fibers and proteins to detect an analyte in the given solution is proposed by Anderson et al. [\[8\]](#page-7-7). For DNA hybridization analysis, a biosensor using an optical fiber has been reported by Piunno et al. [\[9\]](#page-7-8). A fiber-optic biosensor based on fluorescence measurement for in-situ and real-time measurement of free Cu(II) metal ion in seawater at picomolar levels is reported by Zeng et al.  $[10]$ .

#### *2.4 Chemiluminescence Measurements*

Chemiluminescence is a process in which light is emitted by exciting biomolecules due to chemical reaction (oxidation of  $O_2$  or  $H_2O_2$ ). For chemiluminescence, external light source is not needed to start the chemical reaction. Chemiluminescence generates with following steps:

$$
P \xrightarrow{r_1} Q
$$
, excitation

 $Q \stackrel{r_2}{\longrightarrow} h\nu$ , emission

where  $r_1$  and  $r_2$  are the rates of excitation and decay, respectively. The chemiluminescence in a living organism is known as bioluminescence. Various organisms like jellyfish, sea stars, worms, fungi, crustaceans, sharks, etc., can generate bioluminescence for mating, self-protection, signaling, and food hunting.

A fiber-optic biosensor to analyze the injection flow of glucose and lactate has been proposed by Marquette et al. [\[11,](#page-7-10) [12\]](#page-7-11). For antioxidants, a chemiluminescence biosensing system using hematin and luminol co-immobilized on a cellulose membrane disc has been developed by Palaoran et al. [\[13\]](#page-8-0).

## **3 Surface Plasmon Resonance**

This technique is used to supervise the real-time binding interaction of biomolecules like antibodies, proteins, DNA, RNA, etc., in a label-free manner. In general setup of SPR, biomolecules (ligand) are immobilized on a metal surface (Au, Al, Ag, or Cu) and mobile molecule (analyte) flow across the metal surface constantly as shown in Fig. [1.](#page-3-0)

When single-wavelength, polarized light is incident at the lower side of a metal surface through a prism. The free electrons (surface plasmons) in the metal absorb some light at a certain angle (resonance angle or SPR-dip) cause minimum intensity (X) at the detector. These electrons are highly sensitive to the environment. Any changes at the metal surface resulting in the resonance angle shift (Y) as depicted in Fig. [2.](#page-4-0) The resonance angle is dependent on the variation in refractive index at the surface of the metal. When an analyte binds with the ligand at the surface, the refractive index at the metal surface will change. Thus, a shift in resonance angle

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occurs that allows measurement of molecules interaction without labels. To make binding sites available for further reactions, metal surface can be wiped to abolish the bound analyte [\[14\]](#page-8-1).

When SPR-dip is measured in real time, then a plot is generated between an angle at which SPR-dip is observed and time. This is called a sensorgram as depicted in Fig. [3.](#page-4-1) Initially, no binding interaction occurs at the metal surface and an SPR-dip is measured at resonance angle (X) which is indicated by baseline in the sensorgram. After injection of an analyte, the ligand will bind with the analyte at the surface, cause the refractive index change at the metal surface and resonance angle shift to position Y (association) at which SPR-dip is observed. This process of adsorption–desorption can be monitored live to measure the amount of adsorbed species. When the sample containing the analyte is swapped with the system buffer then dissociation of the analyte with ligand takes place. Finally, the metal surface can be wiped and reused for subsequent reactions (regeneration) [\[15\]](#page-8-2).

<span id="page-4-1"></span>

#### **4 Fiber-Optic SPR Biosensor**

In 1983, the first SPR-based sensor for biomolecular interaction monitoring was proposed by Liedberg et al. [\[16\]](#page-8-3). However, a prism sensor-based on SPR is used for point-to-point detection due to bulky sensing device. In the SPR biosensor, the use of optical fibers is based on the light guidance in optical fibers using the total internal reflection (TIR). To create TIR in SPR-based sensing system; prism can be replaced by the optical fiber core to make a fiber-optic SPR biosensor. Optical fiber-based sensors also have other advantages such as lightweight, less bulky, long-distance transmission, anti-electromagnetic interference, and so on [\[17\]](#page-8-4). In 1993, the first fiber-optic investigation was carried out based on the SPR proposed by Jorgensen et al. [\[18\]](#page-8-5).

Generally, in a fiber-optic SPR sensor, from a small middle portion of the core of an optical fiber cladding is removed and covered with a metal layer and then covered by a sensing layer as depicted in Fig. [4.](#page-5-0) If the spectral interrogation method is applied then the light is launched into the core of the fiber at one end from a polychromatic source. The TIR occurs for the rays propagating in the core of the fiber with an angle equal to or greater than the critical angle. As a result, the surface electrons (plasmons) are excited by the generated evanescent field at the interface. The merging of this generated field with plasmons depends on the metal properties, wavelength of light, fiber geometry, and parameters. Finally, after passing by the SPR sensing region, the spectrum of the transmitted light is detected by the detector at the distal end of the fiber [\[19\]](#page-8-6).

After 27 years of development, SPR-based sensing technology using an optical fiber has been very ripe. In this review, the recent development of SPR based fiberoptic biosensors is presented.

A D-shaped plastic optical fiber based SPR sensor using thin Ag film coated with graphene layers is proposed by Arthur A. Melo et al. [\[20\]](#page-8-7). For 16 graphene layers, it exhibits a sensitivity of 5161 nm/RIU. This sensor may be useful for biosensing application for aqueous media. The SPR-based fiber optic biosensor using Tin Selenide (SnSe) allotropes as sensing layer over silver metal for DNA hybridization has been proposed by Rahman et al. [\[21\]](#page-8-8). The SPR sensor with Ag-only has a sensitivity of



<span id="page-5-0"></span>**Fig. 4** Illustration of an optical fiber-based SPR sensor [\[19\]](#page-8-6)

1800 nm/RIU. Tin Selenide allotropes are overlaid on Ag films to increase the sensitivities to 3225 nm/RIU for α-SnSe, 3300 nm/RIU for δ-SnSe, and 3475 nm/RIU for ε-SnSe.

For breast cancer detection, graphene-coated SPR-based fiber-optic biosensor has been reported by Md. Biplob Hossain et al. [\[22\]](#page-8-9). To detect early breast cancer, the attenuated total reflection method is used. Two mutations, 916delTT in the BRCA1 and 6174delT in the BRCA2, have been selected for analysis of breast cancer using DNA hybridization. A fiber optic SPR biosensor has been proposed by Li et al. [\[23\]](#page-8-10) for genetic screening, biomarkers, medical diagnostics, and transcriptional profiling by mean of concentration and time-dependent DNA hybridization. In this design, a D-shaped plastic fiber with a 3D  $Au/Al_2O_3$  multilayer metamaterial structure and graphene film is used. It exhibited high sensitivity of 4461 nm/RIU with good repeatability, linearity, and stability for refractive index detection.

Nowadays, PCF-based SPR sensor is an emerging technology and getting strong acceptance in the biosensing field. However, conventional optical fiber provides high channel capacity and high data rate; it lacks the usage of the full optical spectrum and designing flexibility yet. PCF is a special class of fiber that overcome all the limits of conventional optical fiber. The PCF-SPR sensor technology has a lot of advantages such as smaller size, high sensitivity, high accuracy, larger detection range, and more design flexibilities [\[24–](#page-8-11)[28\]](#page-8-12).

A PCF-SPR biosensor to detect unknown biological analytes using the wavelength interrogation is proposed by Rifat et al. [\[29\]](#page-8-13). It exhibits the maximum sensitivity of 1,000 nm/RIU and sensor resolution  $1 \times 10^{-4}$  RIU. It consists the symmetrical circular air holes with three rings hexagonal PCF structure.

A sensitivity enhanced co-modified PCF-SPR immunosensor by composite graphene oxide and staphylococcal protein A (SPA) has been proposed for human IgG detection by Wang et al. [\[30\]](#page-8-14). In this proposed sensor design, using an optical fiber fusion splicer technique, between two sections of multimode fibers, a PCF spliced and sputtered with the Au film, then it was modified by SPA and graphene oxide for further immunosensing. It exhibits a refractive index sensitivity of 4649.8 nm/RIU. Ultra-low loss SPR-based PCF biosensor for organic molecules, biomolecules, and biological substances sensing application has been reported by Sayed Asaduzzaman et al. [\[31\]](#page-9-0). The gold (Au) is used in this sensor as a plasmonic material. It exhibits maximum sensitivity of 8500 nm/RIU and sensor resolution of  $1.16 \times 10^{-5}$  RIU for the wavelength range of  $0.5-1.20 \mu m$ .

An ultrahigh sensitivity PCF-SPR refractive index biosensor with Au-coated circular nano-film has been reported by Abdullah et al. [\[32\]](#page-9-1). It exhibits maximum sensitivity of 45,003.05 nm/RIU and birefringence of  $1.9 \times 10^2$  for Au film thickness of 50 nm and analyte refractive index range of 1.33–1.40. By changing the gold film thickness to 70 nm, it exhibits the sensitivity of 48,269.50 nm/RIU. A butterfly coreshaped SPR based PCF refractive index sensor for real-time biomolecules detection has been developed by Mashrafi et al. [\[33\]](#page-9-2). In this design, the analyte detection layer and plasmonic material gold are used on the PCF surface to produce the SPR phenomenon. It shows the maximum sensitivity of 56,000 nm/RIU with an analyte refractive index range of 1.33–1.42 for the wavelength range from 450 to 2100 nm.

## **5 Conclusion and Future Prospects**

In summary, in the advancement of biosensors, optical fiber-based biosensor will play an important role because they can be easily integrated and miniaturized to determine target biomolecule in clinical diagnostics, food processing, and environmental monitoring. This article summarizes the different measurement techniques used in fiber optic biosensor and recent research in the highly promising field of SPR-based fiberoptic biosensors. At present, the existing SPR-based fiber optic biosensors are only used in laboratory environments, successful commercial application is a challenge. Response time and reuse of biosensor are also a lack of concern.

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