Chapter

Application of Fiber Optics in Bio-Sensing

Lokendra Singh, Niteshkumar Agarwal, Himnashu Barthwal, Bhupal Arya and Taresh Singh

Abstract

The unique properties of optical fibers such as small size, immunity to electromagnetic radiation, high sensitivity with simpler sensing systems have found their applications from structural monitoring to biomedical sensing. The inclusion of optical transducers, integrated electronics and new immobilization methods, the optical fibers have been used in industrial process, environmental monitoring, food processing and clinical applications. Further, the optical fiber sensing research has also been extended to the area of detection of micro-organisms such as bacteria, viruses, fungi and protozoa. The validation of optical fibers in bio-sensing applications can be observed from the growing number of publications. This chapter provides a brief picture of optical fiber biosensors, their geometries including the necessary procedure for their development. This chapter could be a milestone for the young researchers to establish their laboratory.

Keywords: optical fiber, biosensors, biomedical sensing, environmental monitoring, micro-organisms detection

1. Introduction

The inclusion of optical fibers in bio-sensing applications was started by two different, but interrelated discoveries, such as the laser light and optical fibers. The theoretical work of C. H. Townes and A. L. Schawlow was used by T. H. Maiman to develop the first laser. A optical signal obtained through laser is highly collimated, inherently coherent, and quasi monochromatic with the data transfer capability. The optical signal propagates in optical fiber by obeying the principle of total internal reflection (TIR) with very low losses and the first working model of optical fiber was proposed in 1965 [1]. The working model of optical fiber was put forwarded 100 years after the demonstration of concept of light. Since, then the main focus was to improve the transmission of optical signal through fibers. Nowadays, the key focus is on long distance high speed communication with low transmission losses such as 2 dB/km [2]. The unique properties of optical fibers such as immunity to electromagnetic (EM) interference and miniature footprints, the optical fiber has found niche application in sensing [3].

A schematic of conventional single mode fiber (SMF) used in the field of telecommunication is shown in **Figure 1**, consisting of three layers such as a silica core having diameter of in order of several microns (∼ 2–9 μm) and doped with germanium to boost up its refractive index (RI), a silica cladding of diameter of 125 μm

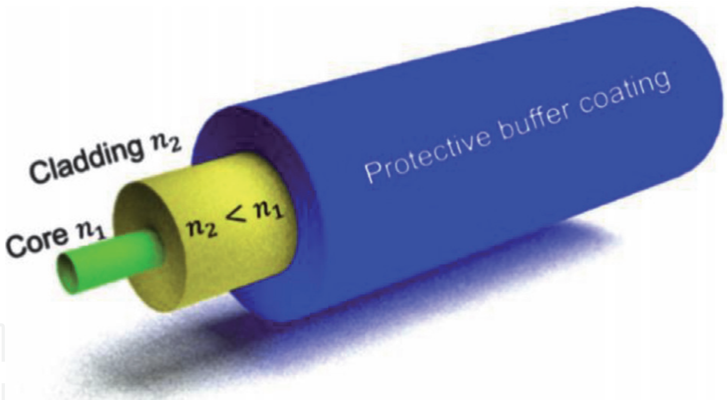

Figure 1.
Schematic of single mode optical fiber [1].

and a coating of plastic jacket. Although, the plastic coating does not play any role in light propagation but provides the mechanical strength to the fiber. The optical fibers can be fabricated by using some other materials such as chalcogenide [4], plastic [5], and composites, with different composite materials in core and cladding. Based on the core size, operating wavelength, and RI difference of core and cladding, an optical fiber can work in the regime of single or multimode. In single mode fibers, the distribution of optical signal profile in core is Gaussian, while in multimode signal profile is more complex [2].

The optical sensors detect the variation in optical properties of propagating signal, that occurs due to the physiochemical change in targeted environment. The optical fiber based sensors classified into two categories on the basis of sensing region such as extrinsic or intrinsic sensors. The sensors directing or collecting optical signal to and from external environment are termed as extrinsic sensors [6]. The sensors in which the properties of optical signal vary within the fiber are known as intrinsic sensors [7]. In general, extrinsic sensors being used for the detection of external stimuli such as physical or biochemical parameters. The optical fiber based measurement techniques have received a great attention especially in the field of structural monitoring, railway and aerospace, chemical and biological sensing, medical diagnosis and environmental monitoring.

Since, the key application of SMF were in the field of telecommunication, and hence, fabricated in such a way that the influence of external field can be minimized on propagating signal. However, for the efficient operation of optical fiber sensors, the interaction of optical signal with external environment should need to be maximized. This can be attained by adopting different optical fiber processing schemes which frequently utilizes the interaction of leaking fields with external environment. The commonly used geometry of optical fiber in sensing applications are discussed in following subsections.

1.1 Cladding less evanescent based optical fiber sensors

The easiest way to increase the interaction of evanescent waves (EW) with external medium is removal of cladding, and a schematic of cladding less optical fiber sensor is illustrated in **Figure 2**. The changes in propagation of optical signals due to variation in external environment facilitates the EW spectroscopy [8]. The facilitation of EW spectroscopy is highly sensitive and powerful technique to quantitatively and qualitatively investigate the environment present in the vicinity of sensing region of sensor. The EW leaks from core to cladding and the distance

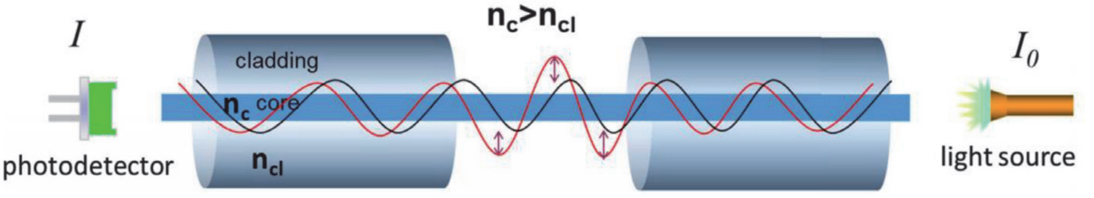

Figure 2.
Schematic of cladding less optical fiber sensor structure [3].

is termed as penetration depth. The penetration depth of EW can be evaluated as [9]:

$$d_p = \frac{\lambda}{2\pi\left(n_{eff}^2 - n_s^2\right)^{1/2}} \tag{1}$$

where, λ is the propagating wavelength, n_s is the RI of surrounding environment and n_{eff} is the RI of guided mode propagating in the core.

The absorption spectrum of surrounding medium attenuates the EW which hindered the propagating mode. This can be understood from Lambert–Beer Law which is given as:

$$\frac{I}{I_0} = c^* \alpha^* L \tag{2}$$

where, c is the concentration of absorption substance, $\boldsymbol{\alpha}$ is the attenuation constant of EW, and L is the path length in which optical signal interacts with the surrounding medium. I_0 and I are the intensities of the optical signal before or after the interaction to the external environment, respectively. The optical fiber sensor structure presented in **Figure 2** can be attained by removing the cladding part by using conventional approach such as treating the fiber with hydrofluoric (HF) acid [10]. To remove the cladding, fiber structure should need to be immersed in HF acid at constant stirring at 50 rpm. In cladding less optical fiber sensors the interaction of optical signal with surrounding can be enhanced by bending it in U-shape [11]. The U-shape bend is also useful for monitoring because source and detector will be on same side. Although, the cladding less fiber can also be attained by using other techniques such as plasma etching, but it will turn into expensive systems.

1.2 Tapered optical fiber sensor

An access to EW can also be obtained by tapering the optical fiber structure. The tapering of optical fiber usually done within the dimensions varying from

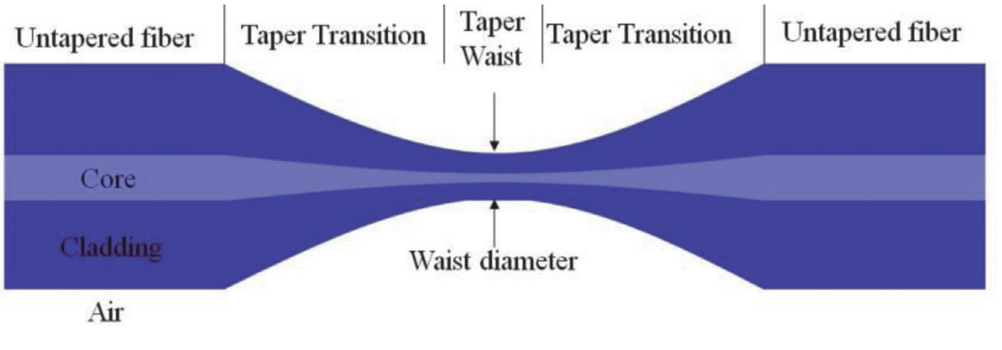

Figure 3.
Schematic of tapered optical fiber structure [12].

submillimeter to several millimeters. The tapered region of the optical fiber maintains the uniform diameter with conical ends to merge it with unaltered part of optical fiber as illustrated in **Figure 3**. The tapering of fiber is done by heating the fiber structure by using flame or CO_2 laser beam. The properties of tapered optical fiber sensor is based on the diameter of conical ends, diameter of tapered region, and RI of surroundings. The proportion of EW power in tapered fiber structure, increases with decrease in diameter of tapered region and with decreasing RI difference of external environment and of fiber [13]. The tapered optical fiber provides numerous advantages to the sensors such as compactness, higher sensitivity and flexibility. The tapered optical fiber classified into categories such as adiabatic and non-adiabatic. When the tapered transition region is small in such a way that maximum optical power confines within the core, then such structure are termed as adiabatic tapered fibers [13]. However, in non-adiabatic one the diameter of tapered region is less than 10 μm and the propagating modes couples into higher order modes [14]. The tapered optical fibers have been utilized in various sensing applications [15–17]. In case of tapered fiber structures, the interaction of EW with surrounding medium can be analyzed by two different.

approaches. In first approach, the attenuation of signal is to be measured which is propagating through tapered region and depends on the RI of surrounding medium [18]. In second one, the variation in surrounding medium affects the RI of modes propagating in the tapered section of fiber and works interferometrically, by using mode theory [19].

1.3 Interferometers

The optical fiber interferometers provide very high sensitivity because of their unique operational mechanism and usually known as modal interferometers (MI). In MI basically, the propagating modes splits into two modes at sensing region which are traveled in different RI regime that causes a difference in their phase and wavelength. The different properties of propagating modes lead to the interference in fundamental and higher order modes and results into a transmission spectrum with fringes. The phase of the fringes ca be given as:

$$\varphi = \frac{2\pi}{\lambda}(\delta n_{eff})L \quad (3)$$

where, L is the center to center distance between two modes and λ is the operating wavelength [20]. A SMF and thin core fiber (TCF) based Mach-Zehnder interferometer (MZI) is presented in **Figure 4**. The first strand of SMF carries a single mode which splits into two parts at TCF due to variation in core diameter. In second strand of SMF the modes from TCF gets recombined at SMF. The difference in phase of recombined modes leads to the addition or cancelation of phase at output of MZI [20].

The optical fiber based Michelson interferometers were also proposed and a schematic is illustrated in **Figure 5**. In Michelson interferometer, the core modes

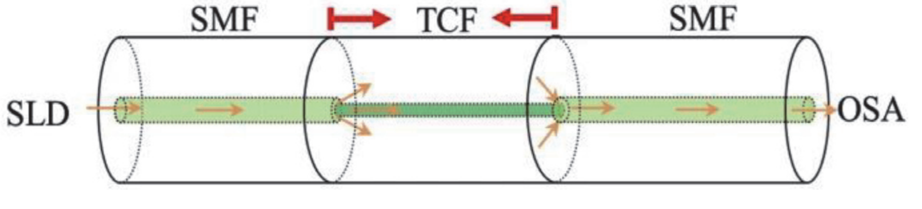

Figure 4.
Schematic of SMF and TCF fiber based Mach-Zehnder interferometer [21].

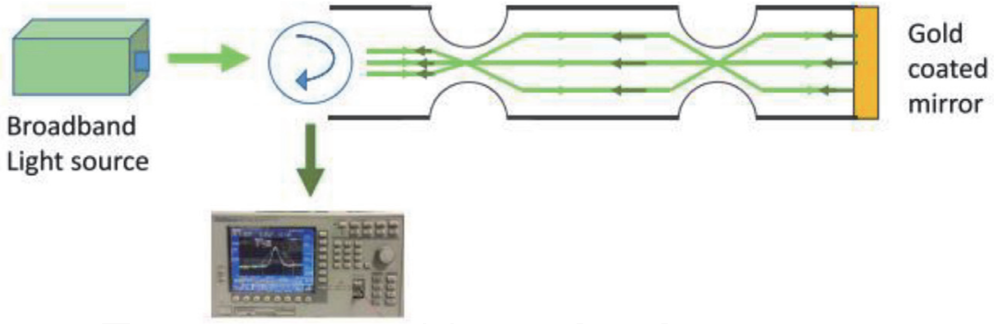

Figure 5.
Schematic of optical fiber based Michelson interferometer [3].

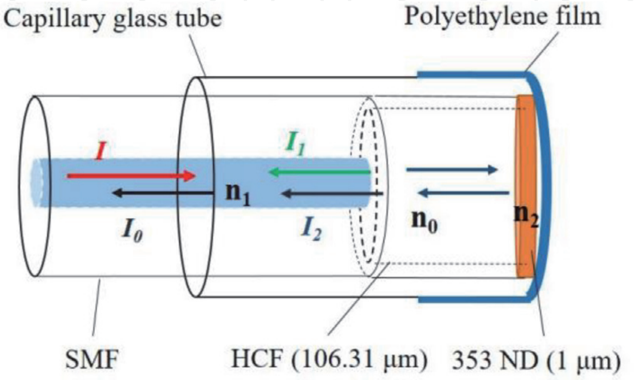

Figure 6.
Schematic of optical fiber based FPI sensor [22].

distributed into higher order modes at tapered section and after striking to gold film reflects back and recombined at the tapered section. Therefore, an interference between the modes occurs at the tapered region that causes the generation of fringes. The presence of external medium in the region separating the taper and gold films introduces the interfering features in the received signal. In similar physical length, Michelson interferometer provides higher sensitivity because the twice interaction of optical signal with sensing region. These interferometers works on the basis of measurement of wavelength or amplitude of the spectrum.

received at the output. An another type of optical fiber based interferometer is Fabry-Perot interferometer (FPI). The FPI is consisting of a cavity between two reflectors and illustrated in **Figure 6**. Alternatively, a FPI can be developed by coating a thin metallic layer at the tip of the fiber which acts as a mirror and the distance between metallic layer and surrounding medium as an another mirror. A change in the RI of cavity or its length can modulate the signal. The modulated signal will be further used to measure the targeted measurand that modulates the signal.

1.4 Grating based optical fiber sensor

An optical fiber grating is consisting of slots placed periodically with an equal proportion. The slots in optical fiber structure leads to the modulation of the propagating optical signal. The grating can be incorporated by exposing the fiber structure to the ultra-violent or femtosecond laser with desired geometry [23]. The optical fiber based grating structure were also found to be a good candidate for the sensing applications [23]. A schematic of FBG sensor with its measurement setup is illustrated in **Figure 7**. The grating structure couples the forward and backward propagating modes of the core at the particular wavelength that satisfies the Bragg condition. A Bragg grating is considered as reflector which reflects a specific wavelength band

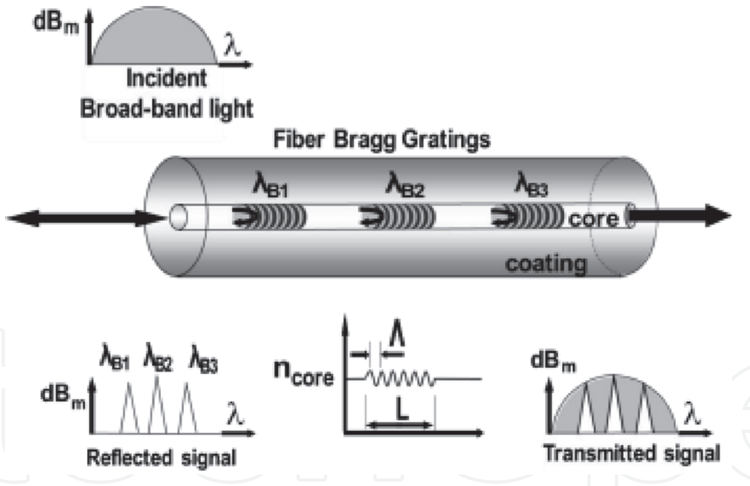

Figure 7.
Schematic of measurement setup of FBG sensor [24].

along the optical fiber and transmitted all others. The reflected Bragg wavelength is governed by a mathematical expression which can be given as [23]:

$$\lambda_{\text{Bragg}} = 2\eta_{\text{eff}} \tag{4}$$

In Bragg grating based sensors, the interaction of EW with surroundings can be maintained or enhanced by modifying the fiber geometry such as tapering, etching of cladding of sensing region. Therefore, to overcome this limitation, tilted Bragg grating can be utilized in which the gratings are designed at a specific angle with respect to the axis of the core. The interaction of cladding modes with EW changes the wavelength of propagating cladding modes [25]. The interaction of EW with surrounding medium leads to the induction of inherent sensitivity to the external RI and to the nano-coatings placed over the cladding layers. While considering the fact long periodic (LPG) grating structures were come into origin. The LPG are generally created with in the length of 100 microns to 1 mm as illustrated in **Figure 8**. LPG usually couples the light form the core modes to the co-propagating modes of the structure [27]. The cladding mode suffers higher attenuation, therefore, the transmission spectrum of LPG can be analyzed by using the series of resonance bands.

From the above discussion, it can be concluded that optical fiber based sensors have wide applications in bio-sensing applications. A short summary of above discussed different geometries of optical fiber sensor structures is tabulated in **Table 1**. The tabulated form is easy enough to get a brief introduction to the required geometry of sensor.

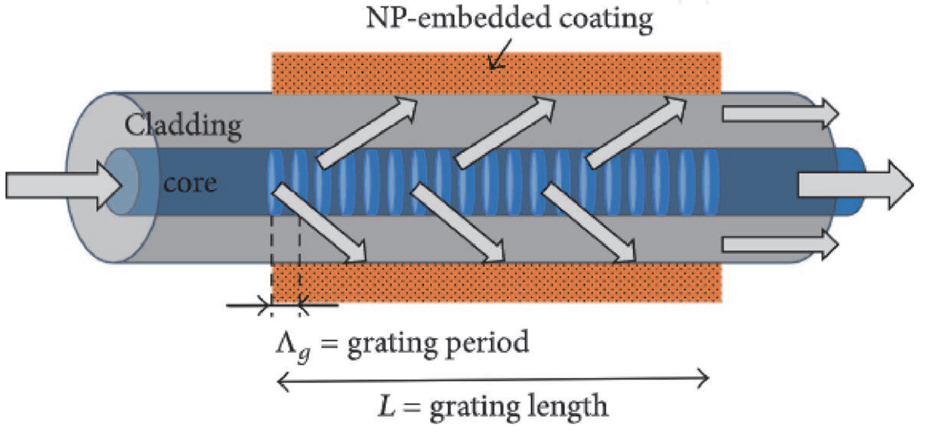

Figure 8.
Schematic of NP coated LPG sensor structure [26].

Sensor type	Measurand	Light parameters	Units
Cladding less	Absorption, concentration	Intensity	dB, %
Tapered	RI, absorption, concentration, pressure, temperature, strain	Wavelength shift, intensity	dB, %, nm
Interferometers	RI, absorption, concentration, pressure, temperature, strain	Intensity, wavelength shift, phase	dB, %, nm, degrees
FBG	pressure, temperature, strain	Intensity, wavelength shift	dB, %, pm
LPG	RI, absorption, concentration, pressure, temperature, strain	Intensity, wavelength shift	dB, %, nm

Table 1.
Summary of measurand and light parameters of different sensor structures.

2. Biochemical measurands in healthcare

The optimum properties of optical fibers such as higher sensitivity and low limit of detection are the crucial parameters, but in addition, the selectivity is also an important concept in biochemical measurement. The selectivity or specificity is important to avoid the interference of other biomolecules or biomarkers presented in targeted analytes. There are two approaches based on which the selectivity of biosensor can be attained. The first approach is to use special material fibers such as chalcogenide glasses, fluoride or silver halide glasses [28]. These fibers are transparent to IR wavelength, and on the contrary, biomolecules pursue the highly absorption features [29, 30]. However, the use of chalcogenide fibers is not useful because of their potential toxicity and still an effort is required to improve their responses towards biomolecules [28]. In second approach, there is indirect sensing of analytes by placing a biochemical layer over the sensing region. The biochemical layer changes the optical properties on the basis of surrounding RI. Such biosensors provide the quantitative and qualitative information of the chemical reagent under examinations. The chemical layer over the sensing region means the wavelength of output optical signal is managed by the properties of biochemical layer instead of absorption spectra. The sensitivity of such biosensors is depends on the length of sensing area, amount of EW and optical properties of the coated biochemical layer [31].

2.1 Chemical optical Fiber sensors

The diagnosis of biomolecules present in human bodies can be detected in two phase such as in gases or in liquid. In gas phase, the analysis can be done by analyzing the gases exhaled from skin or breath. In liquid phase, the analysis of biomolecules can be done by testing the samples such as urine, saliva, blood, sweat and tears.

2.1.1 Diagnosis in gas phase

The biomarkers released from human bodies are useful to develop the non-invasive techniques. The diagnosis of these biomarkers is important to find the presence of disease [32, 33]. The breath sniffing method is useful to analyze the patient suffering from renal failure in rats [34] and lung cancer detection [35]. Oxygen and carbon dioxide are the two gases that are routinely checked in clinical applications. The detection of these two gases was also performed by using optical fiber sensor by using pH indicator separated with well separated with emission bands [36]. Ammonia is one of the major component that affects the body metabolism and can disturb the functioning of kidney and liver [37, 38]. In normal conditions, the ammonia releases from body skin from slight alkaline blood and its detection is used to diagnose the disease related to kidney and liver [39]. The ammonia diagnosis was carried out by using optical fiber sensors. Initially, the detection was done by employing pH detector based on indications [40]. Since then, reflector sensor tips [41], EW based fiber grating [42], and lossy mode resonance (LMR) [43] were reported. The sensitivity and limit of detection of such optical fiber sensor was extremely good in comparison of existing works.

The diagnosis of various organic compound is hardly done at clinical level, but number of studies were reported. Although, the optical fiber sensors for the detection of organic compounds are not very sensitive [44]. An EW based optical fiber sensor was put forwarded for the detection of gas exhaled from human skin [45]. The proposed sensor is also capable of analyzing the physiological changes by applying a pattern recognition technique. The optical fiber sensors have also been utilized for the diagnosis of humidity, which is one of the important factor in case of critical conditions [46]. The increase in humidity in human bodies leads to the dryness in mucosa and cause difficulties in breathing. However, instead of such critical need, the optical fiber based humidity sensors cannot be used in medical applications because of slow response and recovery time.

2.1.2 Diagnosis in liquid phase

The diagnosis of biomarkers present in human bodies can be done by measuring the pH of liquid. The pH of liquid present in stomach is varies from 1.3 to 3.5, and of urine and pancreas is from 8.0 to 8.8 [47]. A tilted FBG based sensor structure was reported to detect the pH of human body fluids [48]. The sensor is working on the basis of coated polymer films whose thickness varies according to the variation of body fluid concentration and leads to the change in optical properties of the signal. Despite of reported articles, the pH sensors have been utilized *in vivo* applications and are commercially provided by the Ocean Optics [49] and PreSens [50] with enough capabilities to be utilized in medical applications.

The pH detection in bio-fluids is also useful to detect the presence of drugs which will be helpful for pharmaceuticals and could be a milestone to develop therapeutic aids for human and animals [51]. The detection of antibiotics in human blood stream can be a useful step to prevent the overdose or to provide the effective dose for specific disorder. A LPG based vancomycin sensor was reported which can be used to treat some severe gram-positive infections [52]. The sensor is capable of detecting the very low concentration of antibiotics present in blood stream which were at the concentration of 10 nM with high specificity towards other biomolecules. Similarly, propofol is an anesthetic usually used in surgery and in regular use in intensive care units. Therefore, the detection of presence of propofol in human body is also an important factor, and a work was put forwarded for its detection while employing the optical fibers [53]. The reported work demonstrated a strong linearity with whole blood samples of human bodies.

3. Characterization and analysis process of optical fiber biosensors

The different geometries of optical fiber sensors should need to be characterized before involving them in sensing of biomolecules. The development of optical fiber biosensors involves four different process such as fiber geometries, used nanoparticles, detection of biomolecules and sensing analysis of developed sensor probes. Therefore, this section presents a brief discussion of about the necessary characterization of optical fiber sensors at all the steps.

3.1 Optical fiber sensor geometry

The validation of drawn fiber sensor geometry such as tapered fiber, MZI etc. can be done by using scanning electron microscopy (SEM). SEM is a kind of electron microscopy which employs a focused beam of the electron to analyze the surface of optical fibers. The SEM image of a tapered optical fiber probe is illustrated in **Figure 9**. In **Figure 9**, there are two SEM images where the first one is representing an image of tapered optical fiber sensor and another image such as **Figure 9(b)** is representing the distribution of nanoparticles coated over the sensing region of fiber structure. In some other cases, the diameter analysis of tapered optical fiber sensor structure was measured directly by using the fabricating machine, but the accuracy of the measured diameter was not up to the mark, and illustrated in **Figure 10** [55].

3.2 Nanoparticles

The optical fiber sensor structures also utilize the immobilization of nanoparticles over the sensing region to enhance the sensitivity by means of introducing the concept of localized surface plasmon resonance (LSPR) phenomenon.

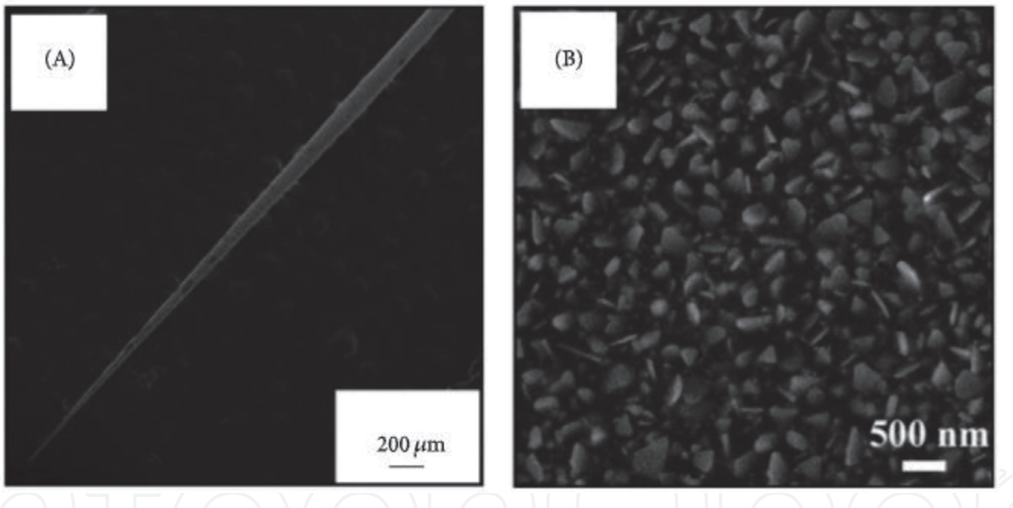

Figure 9.
SEM image of SERS probe of a tapered optical fiber sensor structure: (A) tapered optical fiber, and (B) distribution of nanoparticles over the fiber [54].

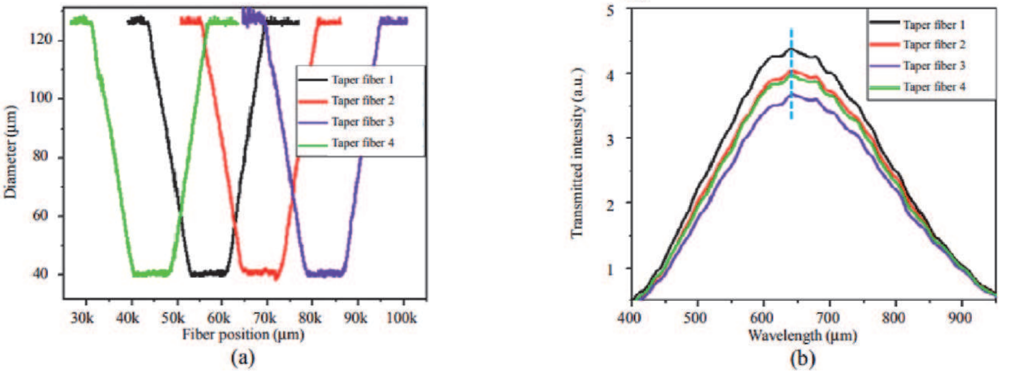

Figure 10.
Analysis of tapered optical fiber sensor structure: (a) diameter analysis, and (b) transmitted spectra [55].

The characterization of nanoparticles can be done by using UV-spectrophotometer and by observing their distribution through transmission electron microscopy (TEM) images. TEM is also a technique that employs a focused beam of electrons to visualize the distribution of particles in nanometer dimensions. The UV-spectrophotometer provides the resonance peak of the nanoparticles through the absorbance spectrum and is useful to confirm their initial synthesis. The resonance peak of all the nanoparticle is different and usually falls in the visible spectrum of white light. The peak resonance wavelength in absorbance spectrum of gold and zinc oxide nanoparticles appears at 519 nm and 370 nm for the particles size of less than 15 nm and 50 nm, respectively, and illustrated in **Figure 11**. The initial confirmation of nanoparticles can be carried forward to analyze their distribution which usually done by using capturing the microscopic image by using TEM. The TEM images of gold and zinc nanoparticles are illustrated in **Figure 12**. From the TEM images it can be concluded that the distribution of nanoparticles is uniform and easily visible. Further, the morphology of the nanoparticles or layered nanomaterials is also an important factor to assure the synthesis of nanoparticles,

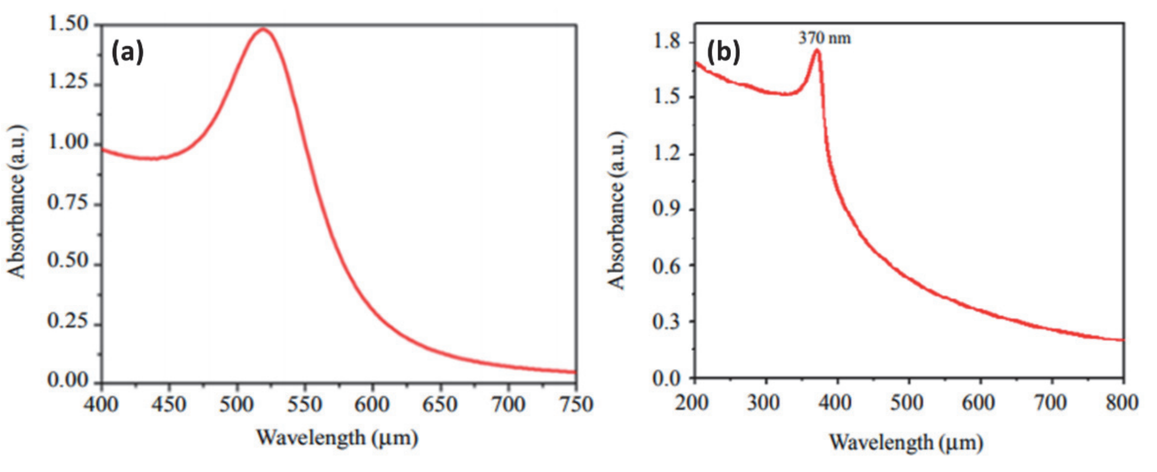

Figure 11.
Absorbance spectrum of nanoparticles: (a) gold, and (b) zinc oxide [55].

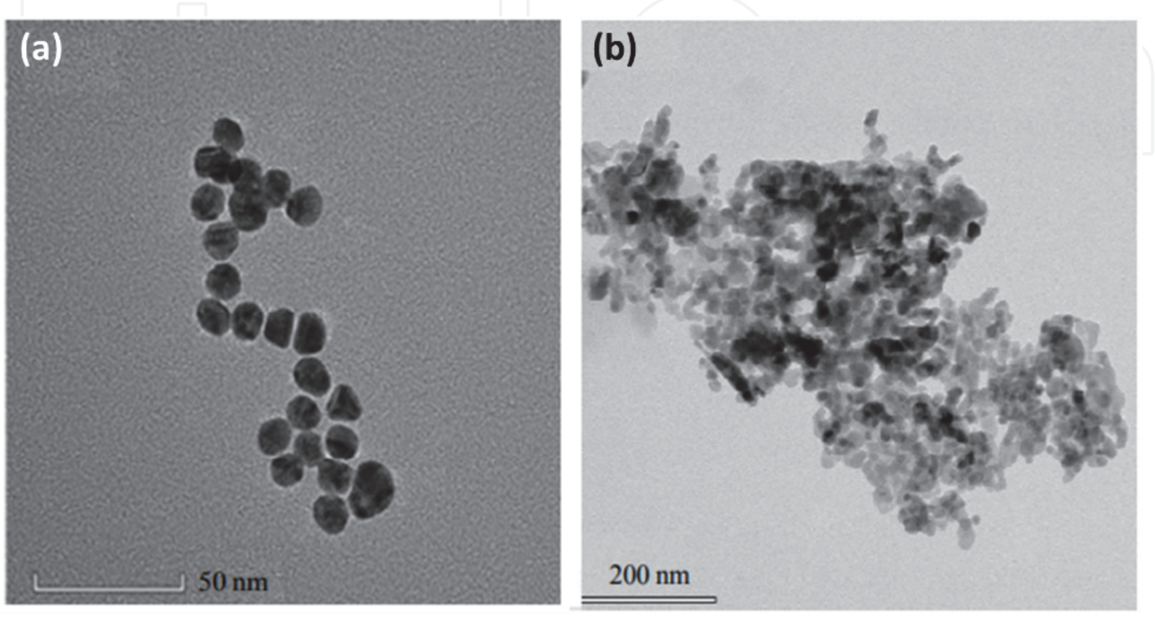

Figure 12.
TEM images of nanoparticles: (a) gold, and (b) zinc oxide [55].

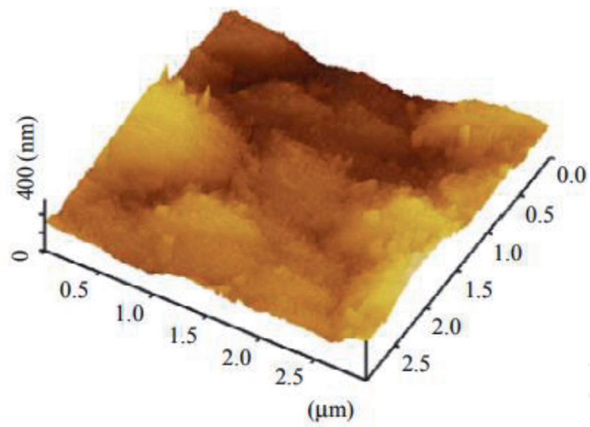

Figure 13.
AFM image of zinc oxide nanoparticles [55].

and can be done by taking the images by using atomic force microscopy (AFM). An AFM image of zinc oxide nanoparticles is illustrated in **Figure 13**.

3.3 Biomolecules

The preparation of samples of targeted biomolecules is also an important factor which helps in increase the performance of sensor probe. The analysis of samples of the targeted biomolecules can be done by preparing them in different pH base solutions. The similar kind of approach has been used to analyze the validity of ascorbic acid (AA) samples and illustrated in **Figure 14**. The performed test was basically done to check the solubility of artificial samples of AA [55]. The analysis was done by dissolving the artificial sample of AA in different pH solutions and the samples of lowest and highest concentration were prepared. Then, the peak resonance wavelength was measured for the highest and lowest sample concentration and their difference is plotted with respect to each pH solution. For the reported work, it was concluded that the AA samples are highly soluble in phosphate buffer solution (PBS) whose pH is about 7.4.

3.4 Sensing analysis

The sensing analysis of the sensor probe can be done in several steps. The first step is to sense all the samples through the sensor probe. For each measurement

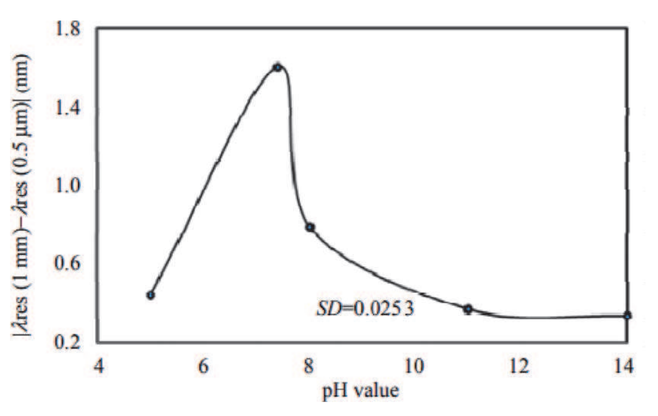

Figure 14.
Solubility test of ascorbic acid samples in different pH solutions [55].

respective peak resonance wavelength can be recorded which is useful to plot the autocorrelation coefficient of the sensor probe. The autocorrelation curve is used to evaluate the linearity, regression coefficient, sensitivity and resolution of the sensor. Then, the analysis of sensor can be done in terms of stability, reusability, reproducibility and selectivity.

The stability of any optical fiber biosensor can be evaluated by measuring the base solution through a sensor probe more than 10 times. The results can be plotted in terms of number of measurements and peak resonance wavelength. Then, the standard deviation (SD) can be evaluated to observe the stability and for a good sensor SD is usually less than 0.1.

The reusability is an another important parameter to analyze the performance of optical fiber sensor. Reusability can be evaluated by measuring two different concentration of bio-molecules through the same sensor probe. The measurement of any concentration should need to be performed three times to attain higher accuracy. The sensor head must need to be rinsed properly after all the measurements by using base solution. Then, the results can be plotted in terms of recorded spectra or in terms of peak absorbance wavelength. The resonance wavelength for similar concentration should be same for each measurement to attain the higher reusability.

The reproducibility is also an another important factor to analyze the performance of any optical fiber sensor. The reproducibility test can be done by measuring the similar concentration of bio-samples through one sensor probe. The measurement must need to be done at least 5 times to attain the higher accuracy. The outcome of the measurements can be plotted in terms of recorded spectra and in terms of peak resonance wavelengths. The higher reproducibility of the probe can be claimed if the peak resonance wavelength for all the measurements is similar.

The selectivity or specificity of the optical fiber sensor is a crucial factor of an optical fiber biosensor which helps in to remove the interference of other biomolecules present in real liquid samples of human bodies. The higher specificity of any optical fiber sensor can be attained by functionalizing the sensor head with appropriate enzyme which oxidize only in the presence of targeted bio-samples. For instance, the AA oxidized only in the presence of ascorbate oxidase.

4. Conclusions

This book chapter presents a brief discussion about the different optical fiber geometries which have been utilized for the development of different optical fiber sensors and biosensors. The mostly common used geometry of optical fibers is cladding less, tapered, interferometers, and gratings. The second section of the chapter presents the brief discussion about the presence of biochemical markers usually used in bio-sensing applications. The detection of biochemical markers is generally done in two phases such as in gas phase and in liquid phase. The third section of the chapter presents a brief discussion of the characterization and sensing process of the optical fiber based biosensors. The characterization of optical fiber sensor is done by capturing the images through TEM, SEM and AFM. The analysis of nanoparticles can be done by recording the absorbance spectrum by using UV-spectrophotometer. The sensing analysis of the optical fiber sensor can be done by performing the stability, reusability, reproducibility and selectivity test of the sensor probe. The optical fiber based biosensors are emerging in current era and can be employed in various health care applications.

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References

[1] Hecht J, City of Light, The Story of Fiber Optics (New York: Oxford University Press) 1999, p 114.

[2] Parries M C, Optical fiber Contemp. Phys. 1989; 30: 303–304. DOI: 10.1080/00107518908225520.

[3] Correia R, James S, Lee S-W, Morgan S P and Korposh4 S. Biomedical application of optical fiber sensors. J. Opt., 2018; 20: 073003.

[4] https://thorlabs.com/newgrouppage9.cfm?objectgroup. (Accessed July 29, 2021)

[5] https://thorlabs.com/catalogPages/1100.pdf. (Accessed July 29, 2021).

[6] Grattan K and Meggitt B. Chemical and Environmental Sensing. 1999; Boston, MA: Kluwer Academic.

[7] Mehvar M, BIS C, Scharer C M, Young M M and Luong J H. Fiber-optic biosensors-trends and advances. Anal. Sci., 2000: 16, 677–672.

[8] Korposh S, Kodaira S, Lee S-W, Batty W J and James S W. Nano-assembled thin film gas sensor: II. An intrinsic high sensitive fibre optic sensor for ammonia detection. Sensor Mater., 2009: 21, 179–189.

[9] Grattan K and Meggitt B. Chemical and Environmental Sensing, Boston, MA: Kluwer Academic, 1999.

[10] Singh L, Singh R, Zhang B, Kaushik B K, Kumar S. Localized Surface Plasmon Resonance Based Hetero-Core Optical Fiber Sensor Structure for the Detection of L-Cysteine. IEEE Transactions on Nanotechnology, 2020: 19, 201-208. 10.1109/TNANO.2020.2975297.

[11] Fang Y-L, Wang C-T and Chiang C-C. A small U-shaped bending-induced interference optical fiber sensor for the measurement of glucose solutions. Sensors, 2016: 16 1460. DOI: 10.3390/s16091460.

[12] Tian Y, Wang W, Wu N, Zou X, Wang X. Tapered optical fiber sensor for label-free detection of biomolecules. Sensors (Basel). 2011: 11 (4), 3780-3790. DOI: 10.3390/s110403780.

[13] Jarzebinska R, Korposh S, James S, Batty W, Tatam R and Lee S-W. Optical gas sensor fabrication based on porphyrin-anchored electrostatic self-assembly onto tapered optical fibres. Anal. Lett. 2012: 45, 1297–309. DOI: /10.1080/00032719.2012.673097.

[14] Vahala K J. Optical microcavities. Nature, 2003: 424, 839–846. DOI: 10.1038/nature01939.

[15] Edwards P S, Janisch C T, He L, Zhu J, Yang L and Liu Z. Fibre taper based Raman spectroscopic sensing. Photonics Conf. (IPC) (IEEE), 2012, 501–2.

[16] Brambilla G. Optical fibre nanotaper sensors. Opt. Fibre Technol. 2010: 16 331–42. DOI: org/10.1016/j.yofte.2010.08.009

[17] Brambilla G. Optical fibre nanowires and microwires: a review. J. Opt., 2010: 12, 043001

[18] Lucas P, Coleman G J, Jiang S, Luo T and Yang Z. Chalcogenide glass fibers: optical window tailoring and suitability for bio-chemical sensing. Opt. Mater., 2015: 47, 530–536. DOI.10.1016/j.optmat.2015.06.034.

[19] Farnesi D et al. Quasi-distributed and wavelength selective addressing of optical micro-resonators based on long period fiber gratings. Opt. Express, 2015: 23, 21175–80. DOI.org/10.1364/OE.23.021175

[20] Lee B H, Kim Y H, Park K S, Eom J B, Kim M J, Rho B S and Choi H Y. Interferometric fiber optic sensors. Sensors, 2012: 12, 2467–2486.

[21] Huang, X., Li, X., Yang, J. et al. An in-line Mach-Zehnder interferometer using thin-core fiber for ammonia gas sensing with high sensitivity. Sci Rep., 2017: 7, 44994. DOI .org/10.1038/srep44994.

[22] Zhang W, Wang R, Rong Q, Qiao X, Guo T, Shao Z, Li J, Ma W. An optical fiber Fabry-Perot interferometric sensor based on functionalized diaphragm for ultrasound detection and imaging. IEEE Photonics, 2017: 9, DOI: 10.1109/JPHOT.2017.2694480.

[23] Kashyap R. Fiber Bragg Gratings, 2010. (San Diego, CA: Academic).

[24] Venkatesan, V. N., Ramalingam, R. Numerical and experimental investigation of FBG strain response at cryogenic temperatures. IOP Conf. Series: Materials Science and Engineering, 2017: 171, 012133. DOI: 10.1088/1757-899X/171/1/012133.

[25] Maguis S. et al. Biofunctionalized tilted fiber Bragg gratings for label free immune-sensing. Opt. Express, 2008: 16, 19049–62. DOI: .org/10.1364/OE.16.019049.

[26] Urrutia A., Goicoechea J., and Arregui, F. J. Optical Fiber Sensors Based on Nanoparticle-Embedded Coatings. Journal of Sensors, 2015: 2015, 805053. DOI: 10.1155/2015/805053.

[27] Seitz W R. Chemical sensors based on fibre optics. Anal. Chem., 1984: 56, 16–34. DOI: org/10.1021/ac00265a711.

[28] Wilhelm A, Lucas P, DeRosa D and Riley M. Biocompatibility of Te–As–Se glass fibers for cell-based bio-optic infrared sensors. J. Mater. Res., 2007: 22, 1098–1104. DOI: 10.1557/jmr.2007.0127.

[29] Anne M-L et al. Chalcogenide glass optical waveguides for infrared bio-sensing. Sensors, 2009: 9, 7398. DOI: 10.3390/s90907398

[30] Wiercigroch E. et al. Raman and infrared spectroscopy of carbohydrates: a review. Spectrochim. Acta A, 2017: 185, 317–335. DOI: 10.1016/j.saa.2017.05.045

[31] Korposh S, James S, Tatam R and Lee S-W. Fibre-optic chemical sensor approaches based on nanoassembled thin films: a challenge to future sensor technology. Optical Fiber, 2013 ed S W Harun (Rijeka: InTech) ch 9. DOI: 10.5772/53399.

[32] Turner A P F and Magan N. Electronic noses and disease diagnostics. Nat. Rev. Microbiol., 2004: 2, 160–166. DOI: 10.1038/nrmicro823

[33] Pavlou A K, Magan N, Jones J M, Brown J, Klatser P and Turner A P F. Detection of Mycobacterium tuberculosis (TB) in vitro and in situ using an electronic nose in combination with a neural network system. Biosens. Bioelectron., 2004: 20, 538–544. DOI: 10.1016/j.bios.2004.03.002.

[34] Haick H, Hakim M, Patrascua M, Levenberg C, Shehada N, Nakhoul F and Abassi Z. Sniffing chronic renal failure in rat models via an array of random network of singlewalled carbon nanotubes. ACS Nano, 2009: 3, 1258–1266. DOI: 10.1021/nn9001775

[35] Peng G et al. Diagnosing lung cancer in exhaled breath using gold nanoparticles. Nat. Nanotechnol., 2009: 4, 669–673. DOI: 10.1038/nnano.2009.235.

[36] Wolfbeis O S, Weis L J, Leiner M J P and Ziegler W E. Fiber-optic fluorosensor for oxygen and carbon dioxide. Anal. Chem., 1988: 60, 2028–2030. DOI: 10.1021/ac00170a009.

[37] Weiner I D, Mitch W E and Sands J M. Urea and ammonia metabolism and the control of renal nitrogen excretion. Clin. J. Am. Soc. Nephrol., 2014: 10, 1444–1458. DOI: 10.2215/CJN.10311013.

[38] Schmidt F M, Vaittinen O, Metsälä M, Lehto M, Forsblom C, Groop P H and Halonen L. Ammonia in breath and emitted from skin. J. Breath Res., 2013: 7, 017109. DOI: 10.1088/1752-7155/7/1/017109.

[39] Turner C, Španěl P and Smith D. A longitudinal study of ammonia, acetone and propanol in the exhaled breath of 30 subjects using selected ion flow tube mass spectrometry. SIFT-MS Physiol. Meas., 2006: 27, 321–337. DOI: 10.1088/0967-3334/27/4/001.

[40] Wolfbeis O S and Posch H E. Fibre-optic fluorescing sensor for ammonia. Anal. Chim. Acta, 1986: 185, 321–7. DOI: .org/10.1016/0003-2670(86)80060-5.

[41] Wang T, Yasukochi W, Korposh S, James S W, Tatam R P and Lee S-W. A long period grating optical fiber sensor with nano-assembled porphyrin layers for detecting ammonia gas. Sensors Actuators B, 2016: 228, 573–580. DOI: 10.1016/j.snb.2016.01.058.

[42] Rodríguez A J et al. A fiber optic ammonia sensor using a universal pH indicator. Sensors, 2014: 143, 4060–73. DOI: .org/10.3390/s140304060.

[43] Tiwari D, Mullaney K, Korposh S, James S W, Lee S-W and Tatam R P. An ammonia sensor based on Lossy mode esonances on a tapered optical fibre coated with porphyrinincorporated titanium dioxide. Sensors Actuators B, 2017: 242, 645–652. DOI: 10.1016/j.snb.2016.11.092.

[44] Shirasu M and Touhara K. The scent of disease: volatile organic compounds of the human body related to disease and disorder. J. Biochem., 2011: 150, 257–266. DOI: 10.1093/jb/mvr090

[45] Elosua C, Matias I R, Bariain C and Arregui F J. Volatile organic compound optical fiber sensors: a review, Sensors, 2006: 6,1440–1465.

[46] Hernandez F U et al. Optical fibre sensing during critical care. Proc. SPIE, 2017: 10340, 1034012.

[47] Schwalfenberg G K. The alkaline diet: Is there evidence that an alkaline pH die benefits health. J. Environ. Public Health, 2012: 2012, 727630. DOI: 10.1155/2012/727630

[48] Shao L-Y, Yin M-J, Tam H-Y and Albert J. Fiber optic pH sensor with self-assembled polymer multilayer nanocoatings. Sensors, 2013: 13, 1425–1434. DOI:10.3390/s130201425

[49] https://oceanopticscom/measurementtechnique/ph-sensing.

[50] https://presensde/products/ph/sensorshtml.

[51] Tiwari G et al. Drug delivery systems: an updated review. Int. J. Pharm. Invest., 2012: 2, 2–11. DOI: 10.4103/2230-973X.96920

[52] Korposh S, Chianella I, Guerreiro A, Caygill S, Piletsky S A, James S W and Tatam R P. Selective vancomycin detection using optical fibre long period gratings functionalised with molecularly imprinted polymer nanoparticles. Analyst, 2014: 139 2229–36. DOI: 10.1039/c3an02126b

[53] Li L, Ding H, Lia B D W and Chen J. Rapid detection of propofol in whole blood using an automated on-line molecularly imprinted pretreatment coupled with optical fibre detection. Analyst, 2012: 137, 5632. DOI: 10.1039/c2an35523j

[54] Zhu, G., Singh, L., Wang, Y. et al. Tapered Optical Fiber-Based LSPR Biosensor for Ascorbic Acid Detection.

Photonic Sens.: 2020). DOI: 10.1007/s13320-020-0605-2.

[55] Urrutia A., Goicoechea J., and Arregui, F. J., Optical Fiber Sensors Based on Nanoparticle-Embedded Coatings. Journal of Sensors, 2015: 2015, 805053. DOI: 10.1155/2015/805053.