Introduction to fiber optics: Sensors for biomedical applications

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Shah and Agrawal: Fiber Optics for Pharmaceuticals

The paper focuses on the introduction of fiber optics, a fusion of science and engineering and describes the materials generally used for its construction along with the procedure used to design the fibers. It gives an idea of the materials used for the construction along with the pros and cons associated with them and various factors governing the emission of ultraviolet, infrared or visible radiations. The central core revolves around the applications of optical fibers in the medical and biomedical field and extending the use of the same in pharmaceutical industry as probes in quality control and dosage form analysis.

Key words: Optical fibers, optical sensors, pharmaceuticals, total internal reflection

Fiber optics, though used meticulously in the modern world, is a quite simple and old technology. The principle of light guidance by refraction phenomenon, was first established by Colladon and Babinet in Paris in the early 1840s, as a base for fiber optics[1]. Fiber optics is mainly used for transmitting radiation from one component to another with help of fibers[2]. Optical fibers are fine strands of glass or plastic, single or bunch of which is used for transmission of radiation from one compartment to another to several hundreds of feet, not only for observation purpose, but also for illumination of objects. The essential feature for transmission of light in an optical fiber which occurs by total internal reflection is that the transmitting fiber must be coated with the material that has refractive index smaller (Cladding material) than that of fiber material (Core) as shown in the fig. 1. The emission of ultra violet, visible or infrared radiations by the fiber depends on the choice of construction material[3].

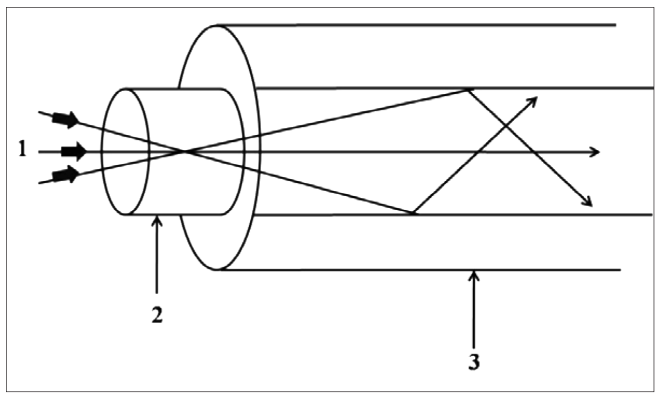

Fig. 1: Optical fiber based total internal reflection
Light transmission (1) in an optical fiber occurs by total internal reflection for which the transmitting fiber is coated with outer cladding material (3) that has lower refractive index than the inner core material (2).

The transmission of light by total internal reflection along the fiber allows only certain modes for propagation which depend on the diameter of the fiber and the wavelength of the light used. Two types of fibers are offered for a given incident wavelength namely, monomode and multimode. Monomode fibers have a narrow glass core of uniform refractive index profile and transmit only a single mode for light of a specific wavelength range and linearly polarized state. Monomode fibers produce a Gaussian spatial intensity distribution at their distal end, whereas multimode fibers have a greater core diameter and can transmit many a hundreds of light modes having either a uniform or parabolically profiled cross sectional refractive index. It is much easier to commence high intensities into multimodal fibers because of their larger core size and higher numerical aperture, than their monomodal equivalents or counterparts. They do however, have disadvantages related to modal noise. Any thermal or mechanical annoyance to the fiber

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affects each transmitted mode in a diverse way. As a result, although the total light intensity at the fiber exit remains constant, the far field radiation pattern formed by intervention of these modes changes with time[4].

Unlike glass or plastic, the varied materials of construction are silica, fluorides, phosphates and chalcogenide. The construction of model optical fiber initiates with the development of large diameter preform of desired refractive index, pulling from which produces a long thin optical fiber. The preform is commonly made by three chemical vapour deposition methods: Inside vapour deposition, outside vapour deposition, and vapour axial deposition[5]. Extensively used phosphate glass can be advantageous over silica glass for optical fibers with a high concentration of doping rare earth ions for the transmission of radiations. A mixture of fluoride glass and phosphate glass is fluorophosphate glass, which is not associated with the disadvantage of modal noise[6,7].

SENSOR SYSTEMS AND SENSOR TYPES

The simplest partition of optical sensors is into so called intrinsic devices, where the interaction occurs actually within an element of the optical fiber itself and extrinsic devices where the optical fiber is used to couple light, usually to and from the region where the light beam is influenced by the substance which is being measured[8].

Luminescent optical fiber sensors:

The use of luminescent phenomena, directed chiefly on fluorescence for optical sensing, has been observed with a range of diverse fiber hosts. Evidently, those rare earths, which have been doped most usually into silica based fibers, or alternatively into fluoride glass or more unusual fiber materials, can evenly be applied to the generation of simple fluorescence as to the creation of laser action. However, unlike the plastic host that has disadvantage of quenching laser action, there are ample varieties of other fluorescent materials which can be used for sensing purpose, where their primary focus is only on the fluorescence. A key distinction between silica and plastic fiber is the extreme elasticity of the latter, which allows it to bent to a greater extent with a smaller radius than silica fiber[9].

Evanescent wave fluorescent sensor:

A negative or non-guiding fiber is a permeable fiber in which the power loss depends on the length of the fiber and can be optimised for fluorescence collection efficiency into the positive or guiding fiber attached to the output end of the negative fiber. This is in contrast to the positive fibre for which the collection efficiency is independent of fibre length and depends only on the difference in refractive index between core and cladding material of the fiber. The sensor described is based on a fiber having two different fibres, one guiding and other non-guiding. The combination of a guiding fibre and a non-guiding fibre can detect fluorescence emitted from molecules attached to the surface of the negative fibre as shown in fig. 2[10,11].

Thin film sensors:

The presence of immobilizing enzyme layers of glucose oxidase on chalcogenide fibers lead to the novel concept of IR fiber optical chemical sensors to analyse glucose in complex aqueous matrices. The sensing design is based on following the catalyzed reaction of glucose to gluconic acid and hydrogen peroxide. Monitoring the concentration of reaction products in the surrounding aqueous solution by evanescent wave spectroscopy believe an enzyme layer thinner than the penetration depth of the irradiation but with maximum reactivity of the catalytically active surface to offer a fast sensor response. Hence a careful treatment of the fiber surface with 3 aminopropyltriethoxysilane (APTS)/ glutaraldehyde before immobilizing the enzyme is apparent[12,13]. A newer approach by Taga *et al.*

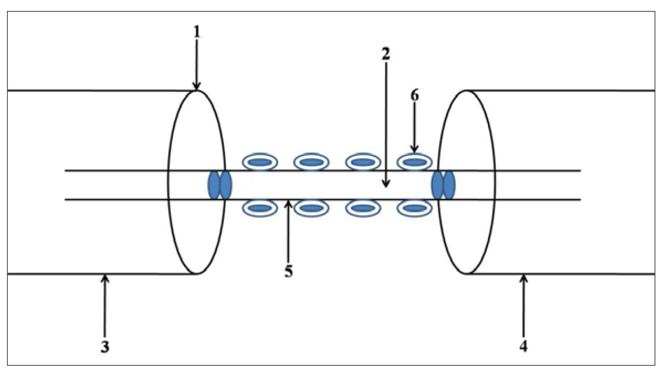

Fig. 2: Fiber based evanescent fluorescent sensor
The combination of a guiding fibre (1) and a non-guiding fibre (2) can detect fluorescence emitted from molecules attached to the surface of the core of the negative fibre with the help of sensing element (5) and index matching liquid containing laser sensitive dye (6). This fluorescence is channeled by transmission fibers (3) and gathered by collecting fibers (4). Adopted from ref 11.

improves the enzyme density on the fiber surface was developed by immobilizing glucose oxidase via bacterial S-layer protein[14].

Fluorescent plastic optical fiber sensors:
Fibers in this category are characteristically doped with organic dyes which are used extensively in the printing industry and for display purposes. They are frequently used for decorative purposes, but clad (dressed) and coated fibers with a fluorescent core are often used in sensing and measurement as a result of their ability to capture light, which excites them over their whole length. The kind of fluorescent sensors are used to measure ambient light[15], monitor faults in circuits and switches[16], humidity measurement[17], environment sensing and detection of gaseous pollutants[18].

APPLICATIONS

Fibre optic sensors have numerous applications in diverse branches of science and engineering, as is evident from a vast range of properties which has been sensed optically, ranging from light intensity, vibration, temperature, pressure, calibration of accelerometers, strain, liquid level, pH, chemical analysis, concentration, density, refractive index of liquids etc[19,20]. Refractometer are frequently used for the study of molecular structure and identification of organic compounds[21,22]. The overall general applications of optical fibers are described in Table 1.

TABLE 1: GENERAL APPLICATIONS OF OPTICAL FIBERS

Application of optical fibers in various industries
Communications
Pharmaceuticals
Spectroscopy
Biological and biomedical sciences
Petrochemicals
Food and beverage industry
Plastic industry
Study of soil samples
Understanding the basic chemical reactions
Energy and military services

Glucose sensor:
Earlier times, ultra violet radiation and immobilized probes were used for sensing purpose[23,24], but nowadays a fiber based pH meter has been developed in which the cladding material is replaced with polyaniline polymer, a polymer with broad sensitivity to pH[25]. Since only a single broad band is to be measured, the system adapts itself to an IR laser diode system which offers a potential for miniaturization and greater portability. Brown *et al.* modified the sensor by using glucose oxidase immobilised on the polyaniline polymer surface (an enzyme which converts glucose to glucuronic add, resulting in a pH change) to predict glucose concentration[26].

Laminate cure analysis:
Monitoring reactions in hostile environment becomes much easy with these probes having smaller dimensions and enough durability. Fiber optic probes can be introduced into an autoclave (via the usually standard thermocouple calibration port) and thus can continuously monitor the progress of reactions (e.g. degradation) as a function of the operating conditions. Druy *et al.* utilized this approach to monitor ongoing processes in industries, notably to monitor heal rates of polymer laminates at higher temperature and pressures[27,28].

Protein analysis:
FTIR with fiber optic probe is useful for protein analysis since high quality spectra can be obtained from low concentrations of analyte in a variety of environments without any interference. Globular proteins usually exhibit regions of secondary structure including alpha helices, P-sheets, turns and non-ordered regions. Each of these conformational entities contributes to the IR spectrum in the amide I contour region. In addition to the study of protein in its dried state, FTIR coupled with fiber optic probes has been particularly useful for the study of soluble proteins, whose structures had not previously been elucidated using X-ray diffraction or NMR spectroscopy[29,30].

Dosage form analysis:
Dreassi and co workers have reported the application of an optical fiber probe for quality control in the pharmaceutical industry[31]. The system was used to quantitatively determine the content of a number of pharmaceutical solid dosage forms containing ibuprofen, and powders containing benzydamine an analogue of cetrimide. A team from Burroughs-Wellcome have taken this one step ahead and have performed identification tests on tablets through the plastic wall of the blister packaging[32] to distinguish between film coated and uncoated tablets and

between active and placebo forms. The technique satisfied the requirements of a confirmation of identity test prior to use in a clinical trial[33].

Fiber optical scanning in TLC for drug identification:
Ahrens *et al.* proposed an organized toxicological analysis procedure using high-performance thin layer chromatography in combination with fibre optical scanning densitometry for recognition of drugs in biological samples. The technique allowed parallel recording of chromatograms by identifying the drugs and comparing their ultra violet spectra with the data obtained from library as a reference spectra[34].

Determination of DNA oligomers:
Kleinjung and group demonstrated the binding of DNA oligonucleotides to immobilized DNA targets using a fiber optic fluorescence sensor. 13 mer oligonucleotides were attached to the core of a multimode fiber and the complementary sequence was identified by using a fluorescent double stranded specific DNA ligand. The evanescent field was used to differentiate between bound and unbound species. The template DNA oligomer was immobilized either by direct coupling to the activated sensor surface or using the avidin biotin bridge to detect the single base mismatches in the target sequence[35].

Pesticide detection:
Rajan and group, fabricated and characterized surface plasmon resonance (SPR) based fiber-optic sensor for the detection of organophosphate pesticide. Over the silver coated core of plastic cladded silica (PCS) fiber, the acetylcholine esterase (AChE) enzyme was immobilized to prepare the probe, the detection of which is based on the principle of competitive binding of the pesticide (acting as inhibitor) for the substrate (acetyl thiocholine iodide) to the enzyme AChE. For the fixed concentration of substrate, the SPR wavelength decreases with increase in the concentration of the pesticide, this increase in pesticide amount causes an overall decrease in the sensitivity[36].

Effluent monitoring:
Krska *et al.* reported the environmental hazard associated with the use of chlorinated hydrocarbons by pharmaceutical manufacturers[37,38]. Chlorohydrocarbons have their strongest absorption bands and therefore polycrystalline silver halide fibers are of value as light guides. For quantitative measurements, the 10 cm fiber collectors were coupled to the FTIR and samples were monitored. Further study revealed the comparative analysis of tetrachlorethylene and waste water samples showing a good concord with standard gas chromatographic techniques[39].

Other applications:
Fiber optic probe is not only used for the determination of water by near infrared reflectance spectroscopy[40] but also for determination of penicillamine in pharmaceuticals and human plasma by capillary electrophoresis with in column fiber optics light emitting diode induced fluorescence detection[41]. Fiber lasers are also used for the military applications, biological and biomedical applications and highly sensitive airborne trace gas detection[42,43].

Applications that are made possible by the use of filtered fiber optic Raman probes include such things as measuring high levels of organic solvent contaminants in soils and aquifers, chemical process monitoring of petrochemicals and distillation products, monitoring polymer cure reactions in situ and many others[44-46].

In spectroscopy, in order to analyse the composition of substance that cannot be placed into the spectrometer itself can be measured by optical bundles by transmitting the light from a spectrometer to a substance. A spectrometer analyzes substances by bouncing light off of and through them. By using fibers, a spectrometer can be used to study objects that are too large to fit inside, or gases, or reactions which occur in pressure vessels[47].

FUTURE PERSPECTIVES

With such an ongoing demand of optical fibers in the science world, novel techniques like such fiber optic probes in Raman and Attenuated Total Reflectance can be used for communications, military and defense, sensing and biomedical imaging. These probes can also help in the authentication of the drug product, and thus preventing the drug counterfeit.

CONCLUSIONS

An optical fiber made up of a core carries the light pulses which are not only used for sensing but also for the illumination purpose. Fiber optic probes undergo total internal reflection and aid in possible future biomedical applications to carry out the simultaneous collection and analysis of samples for drug safety evaluation. It also helps in the sensing of biomolecules, identification of drug molecules, effluent monitoring and overall pharmaceutical quality control of the product. Probes aid in the development of kinetics profile and are associated with short sample times, allowing the identification and measurement more accurate and reliable.

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Accepted 18 January 2011
Revised 12 January 2011
Received 7 July 2010
Indian J. Pharm. Sci., 2011, 73 (1): 17-22