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Chemo/Biosensing with Optical Fibres

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Summary:

Chemo/biosensing with optical fibres has played an important role since the 1980s mainly thanks to their invasive capabilities and unique performance that have allowed measurements inside the human body otherwise impracticable. Optical fibre-based platforms for biosensing have been also proposed, by exploiting the refractive index (RI) changes induced on chemical/biochemical recognition layers deposited on fibre surface. Long period gratings (LPGs) and lossy mode resonance (LMR) are among the two most interesting approaches, being characterized by high sensitivity to external RI changes.

Keywords: Optical fibre sensor, bile, pH, long period gratings, lossy mode resonance

Introduction

One of the first invasive optical fibre chemical sensor was a sensor for blood pH developed by Peterson in 1980 [1]. Since then many examples of invasive optical fibre sensors have been described for the measurement of chemical and biochemical parameters. But optical fibres are also being proposed in the last years as essential elements for label-free biosensing by exploiting the changes of refractive index (RI) induced by chemical interaction within a recognition layer deposited on the optical fibres, obtaining comparable performances if not higher than those based on surface plasmon resonance.

Invasive optical fibre sensors

In gastroesophageal apparatus optical fibres have been used to monitor refluxes by measuring bile and pH [2].

The bile presence is measured by measuring the absorption of bilirubin, the main biliary pigment, which is characterized by a strong absorption spectrum in the blue region. The sensor utilizes two light emitting diodes, as sources (λ=465 nm and λ =570 nm for the signal and the reference, respectively) and an optical fibre bundle of 250 µm plastic fibres to transport the light from the sources to the probe and back to the photodetector; the probe is a miniaturised spectrophotometric cell of 3 mm external diameter (Fig.1).

Fig. 1. The optical fibre probe for the bile detection.

Bilitec2000 is the industrialised version of the bile sensor available on the market, produced by Cecchi srl and distributed by Medtronic up to 2007 and now by EBNeuro.

As for detection of gastroesophageal pH, the main hindrance to the development of an optical sensor has been the wide pH range of clinical interest (1.0-8.0 pH units). The first attempts involved the simultaneous use of two pH indicators, being each of them generally able to cover 2-3 pH units. Methyl red was shown to be able to cover the whole range after its covalent immobilization on controlled pore glasses [2]. On this basis an optical fibre probe was developed immobilizing the CPGs with methyl red at the distal end of 500 µm plastic fibres (Fig.2).

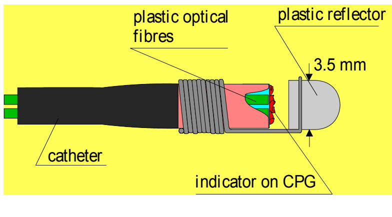

Fig. 2. The optical fibre probe for the pH detection.

The possibility of combining pH and bile measurement using a single fibre catheter is actually under study by reducing the dimension of the fibres for pH detection to 250 µm and integrating them in the same tubing containing the fibres for bile detection. A clinical study is starting with the first measurements on patients.

Besides bile and pH, pressure is the other essential parameter to perform exhaustive diagnosis in gastroesophageal reflux pathologies. An all-optical device was developed for their simultaneous measurement within the European project OPTIMO (http://www.optimo-project.eu) and makes use of a catheter where plastic optical fibres (POFs) for bile and pH measurement and a glass fibre for pressure measurement are integrated [3]. The catheter is formed by an elastomer capable to transfer the radial esophageal pressure in longitudinal strain, extruded on a glass fibre with 10 fiber Bragg gratings. POFs are located on the external surface of the elastomer and a polymeric tubing covers the whole structure which has a diameter of 4 mm. Lateral windows allows the entrance of esophageal content for the measurement of bile and pH.

Gastric carbon dioxide (CO_2) is another important parameter in the gastro-esophageal apparatus. Its monitoring can provide essential information on tissue perfusion, since the stomach is the first organ in the body affected in cases of shock and the last to be restored. An optical fibre sensor using a single 600 µm glass fibre terminating with a probe was developed. The sensor is based on the measurement of the pH change induced by the CO_2 diffusion inside the probe, constituted by a plastic head containing the CO_2-sensitive layer (Fig.3). The sensor was tested on critically ill patients demonstrating the superiority of the optical fibre approach with respect to the traditional one based on gastric tonometry [2].

Fig.3. The pCO_2 probe (left) with the disassembled 500 µm optical fibre (right).

Label-free optical fibre biosensors

Measurements of refractive index in biological fluids are being used since many years for the quantitative measurements of analytes, by means of the use of chemical/biochemical recognition layers deposited on suitable substrates. LPGs [4] and the generation of LMRs allows measuring precisely and accurately surface RI changes [5].

LPGs are characterized by a periodic modulation of a single-mode optical fiber core and they are highly sensitive to the RI changes of the medium surrounding the fiber due to the coupling occurring between the fundamental core mode and different cladding modes. Any interaction occurring along the sensing region modifies the transmission spectrum and this can be evaluated in real-time by recording the shift of the LPG resonance wavelengths (Fig.4). Deposition of nanometric layers of high RI materials along the fibre allows to achieve limit of detection of the order of ng/mL^{-1} in the IgG/anti-IgG immunoassays [6, 7].

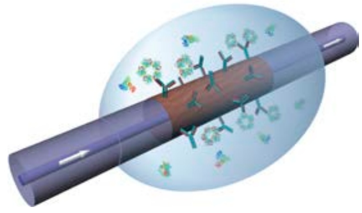

Fig.4. Schematic illustration of the surface sensing of biomolecules by an LPG. (from ref 4).

LMR is an optical phenomenon which takes place when an optical fiber is coated with nm-thick films with a complex refractive index; under specific conditions, coupling between fiber guided modes and guided modes of the thin film (the so-called lossy modes) occurs, leading to the formation of attenuation bands in the transmission spectrum. RI changes in the environment surrounding gives rise to changes in the coupling condition which caused shifts of the attenuation bands, which can be detected. As it occurs in LPGs, biosensing is achieved by means of the deposition of a molecular recognition layer on the fiber surface, with the shift of the resonance taking place following the interaction of the investigated analyte with the sensing layer. With this approach, limit of detections of 100 ng/mL for D-dimer in diluted serum [8] and of 110 pg/ml for tau protein in cerebrospinal fluid [9] were achieved.

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