Lossy Mode Resonances biosensor for the detection of C-reactive protein

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Abstract: The fabrication and characterization of optical fiber biosensor based on Lossy Mode Resonances (LMR) to detect C-reactive protein (CRP) are presented. Indium tin oxide (ITO) coatings deposited on side-polished D-shaped optical fibers are used as LMR supporting coatings. The aptamer was immobilized on the ITO film using the Layer-by-Layer (LbL) nano-assembly process. The optical fiber sensor presented shows a high selectivity and low limit detection.
OCIS codes: (060.2370) Fiber optics sensors; (280.1415) Biological sensing and sensors; (310.6870) Thin films, other properties;

1. Introduction

The liver produces C - reactive protein (CRP) and it is used mainly as a marker of inflammation. C-reactive protein concentration levelincreases when there's inflammation in your body and can be measured in urine, saliva and blood. A high level of CRP is a marker of any condition that causes inflammation, from an upper respiratory infection to cancer [1][2]. High CRP levels can indicate that there is inflammation in the arteries of the heart, which can mean a higher risk for heart attack. Therefore, rigorous measure and control of this protein is very important in our lives. As an example, the risk of developing cardiovascular disease is low below 1 mg/L, average between 1.0 and 3.0 mg/L and high above 3.0 mg/L.

Different methods are used to detect CRP protein such as ELISA, immunoturbidimetry, nephelometry, rapid immunodiffusion, and visual agglutination. In respect of optical fiber sensor different techniques to detect CRP have been developed, such as those based on interferometry [3], fiber gratings [4], surface plasmon resonance (SPR) [5] and LMRs [6]. The latter, permits to obtain highly sensitive devices to refractive index variations in the surrounding medium, which enables their application in different fields [7]. These devices are used here to measure the interaction of the C-reactive protein with an aptamer layer that acts as receptor.

In this communication, we report the characterization of the response of the optical fiber aptasensor based on Lossy Mode Resonance for different C-reactive protein, urea and creatinine solutions.

2. Experimental Procedure

2.1 LMR coating

The optical fiber used to fabricate the biosensor is a D-shaped optical fiber obtained from Phoenix Photonics LTD. The sensor developed in this work consists of a standard single mode fiber (Corning® SMF-28) with a cladding/core diameter of 125/7 μm and a polished length of 1.7 cm coated with an LMR supporting film made of ITO (see detail in Figure 1). Indium tin oxide (ITO) films have been fabricated on the polished side of the optical fibers using a DC sputtering fabrication technique described in previous works [8].

2.2 Aptamer layer

The CRP selectitivity of the fabricated device can be obtained by means of a highly selective aptamer chain (5′-GGCAGGAAGACAAACATATAATTGAGATCGTTTGATGACTTTGTAAGAGTGTGGAATGGTCTGTGGTG CTGT-3′) immobilized onto the ITO coated sensitive region (LMR) using the layer-by-layer nano-assembly (LbL) [9]. The LbL polymer-aptamer layer consisted of a structure formed by four Poly(allylamine hydrochloride) (PAH) and Poly(sodium 4-styrenesulfonate) (PSS) bilayers followed by the CRP-aptamer layer.

2.3 Experimental setup

CRP concentration measurement has been performed using a typical transmission setup as it is represented in Figure 1. This setup consisted of a multi-LED light (HP83437A) connected to depolarizer. The polarization controller (Agilent 8169A) connected between the light source and the sensitive region (D-shaped). Finally, the output of the sensor is attached to an OSA (HP- 86142A) in order to monitor the response of the device. The utilization of this setup

enables to monitor the interactions between the aptamer and the protein in real-time and collect the spectral information every minute.

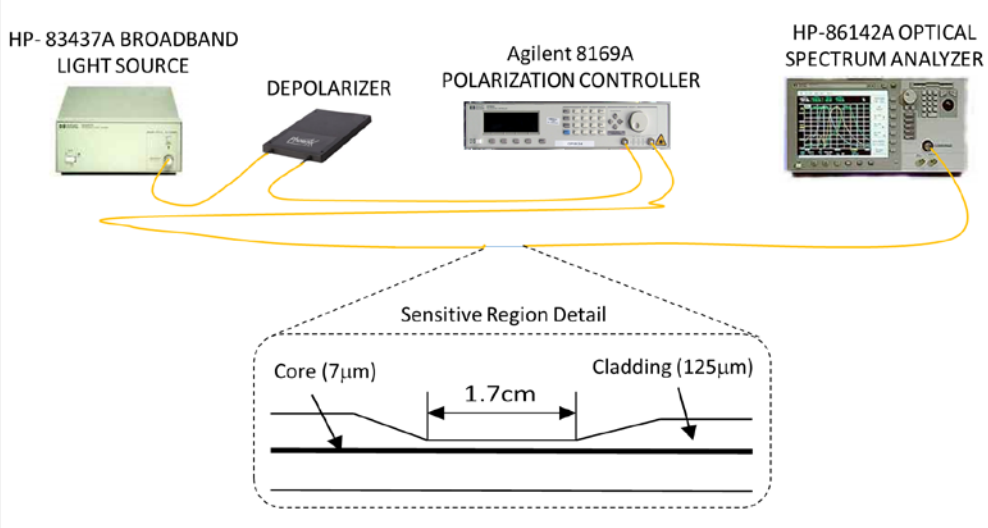

Fig. 1. Experimental setup to measure the C-reactive protein and detail of the sensitive region.

3. Results

In order to check the response of the device to the C-reactive protein, the sensitive region of the device is dipped into different solutions in presence of CRP, urea and creatinine. Figure 2 shows the transmittance response of the sensor when it is subjected to buffer, urea and CRP. Figure 3 presents the dynamical response of the sensor.

A negligible change in the sensor can be observed when the device is immersed in urea and creatinine solutions, which confirms that the aptamer layer is highly selective to C-reactive protein. It can be seen that the spectral response of the sensor changes with the concentration of CRP protein and the resonance shifts towards higher wavelengths as the concentration of CRP increases. In particular, a variation of 10 nm can be observed when the device is immersed in 0.125 mg/L of CRP.

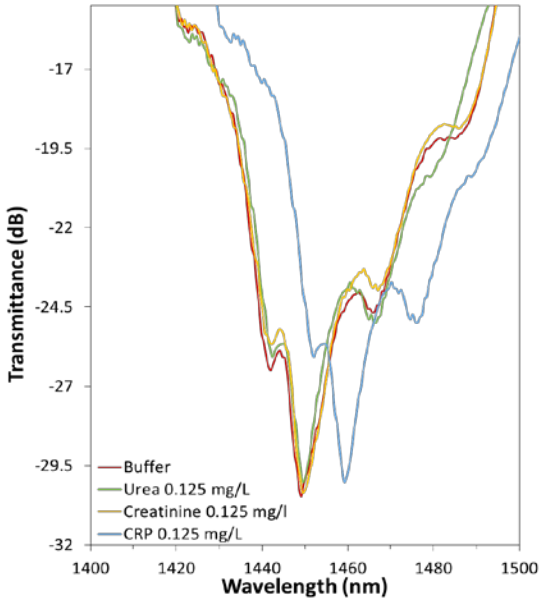

Fig. 2. Spectral response of the sensor when the sensitive region is exposed to buffer, urea and C-reactive protein.

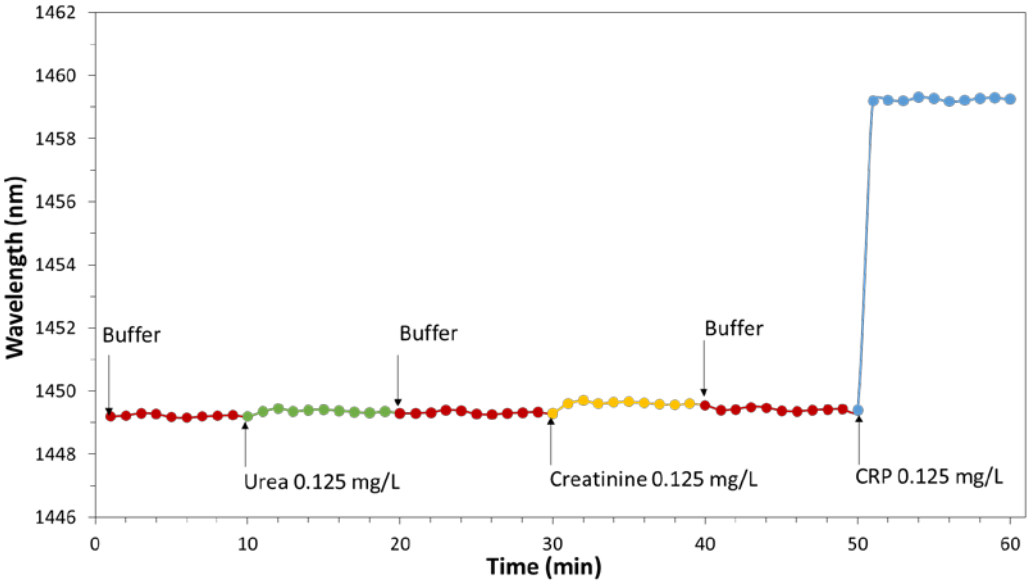

Fig. 3. Dynamical response of the sensor when the sensitive region is exposed to buffer, creatinine and C-reactive protein.

4. Conclusions

Fiber optic biosensor based on Lossy Mode Resonance (LMR) is developed for detection of C-reactive protein. The sensor is based on the LMR wavelength shift associated to the interaction of C-reactive protein with the aptamer layer. Fabricated devices show high selectivity to CRP, low detection limit (0.125 mg/L) and fast response time. Therefore, this sensor is candidate to be used as a diagnostic test to rapidly detect C-reactive protein.

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