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Tapered optical fiber biosensor for the detection of anti-gliadin antibodies

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A B S T R A C T

A new biosensor has been developed by coating a tapered optical fiber with an anti-gliadin antibodies (AGAs) sensitive nanofilm using the electrostatic self-assembled (ESA) monolayer technique in order to aid the diagnosis of celiac disease. Optical fibers were tapered and then the specific antigen was deposited using the ESA method which allows the construction of nanometric scale recognition surfaces on the fiber optic and helps to create fast response sensors for real time observation of the binding process. Power changes up to 6 dB have been recorded during the antibodies binding process with concentrations in the range 1–15 ppm. Optimal deposition parameters have been selected using an in situ interferometric characterization technique which allows to state the working point of the sensor accurately. The high sensitivity and continuous monitoring of the proposed scheme can reduce importantly the time and serum volume required for celiac disease tests.

1. Introduction

Fiber-optic biosensors (FOBS) have been widely investigated because of their potential sensitivity, fast detection, biocompatibility and adaptability to a wide variety of assay conditions [1]. Using FOBS it is possible to measure absorbance, scattering, or fluorescence in the analyte of interest using either a reflection [2–4] or transmission scheme. Several sensing structures have been already used, such as long period grating to implement interferometric immuno-sensors [5], biconical tapered fiber sensors [6] and surface plasmon resonance [7], just to mention a few. Among these transmission structures, biconical tapered optical fibers are highly sensitive and have a low fabrication cost. Stretching and waist radius reduction made in the tapering process cause the core/cladding interface to be redefined in such a way that the fiber in the tapered region will act as a multi-mode fiber, leading to mode coupling in the high slope zone and originating an oscillatory optical power output as a function of either the refractive index thickness of the external medium or the thickness of an overlay film.

In this work, the electrostatic self-assembled (ESA) technique is proposed to create a uniform sensitive thin layer of material onto the surface of the tapered optical fiber waist. This method allows monitoring the sensor behavior while the deposition is in process and to stop at the optimal sensitivity layer thickness. This technique involves immobilizing the specific antigen by a coupling matrix yielding to a change in the transmitted output optical power, which is due to the interaction of the evanescent field with the outer medium, proportional to the change in the concentration of antibodies bound on the surface. Owing to its limited range, an evanescent wave can interact selectively with the antibodies at or near the interface without any interference from other molecules in bulk.

One method for the diagnostic of celiac disease (CD) consists of detecting antibodies to some proteins called gliadins in the patient's sera. Using enzyme-linked immunosorbent assay (ELISA) antibodies are detected after several incubations, washing and separation steps. As an early diagnosis in celiac patients may improve their quality of life through a strict avoidance of gluten in the diet, there is an increasing need for simple, rapid and easy-to-use sensors to aid clinical diagnosis for anti-gliadin antibodies (AGAs) [8,9].

The aim of this study is to develop a biosensor to determine the presence of AGA by measuring the interaction with antigen Gliadin. The antigen is deposited using the ESA multilayer technique. Due to the absence of many washing and blocking steps as needed in conventional methods, it is possible to obtain a shorter performance time. The use of the ESA method, which can be carried out under standard temperature and humidity room conditions in the fabrication process, as well as the low cost of the materials and instruments used while the tapering of the fiber, can help to develop low cost sensors.

The paper has been divided as follows: in Section 2 the tapering process and the ESA technique used for the fabrication of AGA

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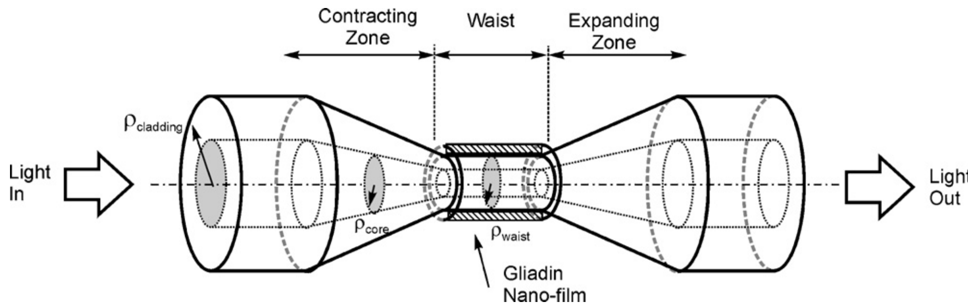

Fig. 1. Tapered optical fiber sensor geometrical parameters.

sensor is described. The experimental set-up is discussed in Section 3. In Section 4, the experimental behavior of the taper during the coating process is shown. The sensitivity of the sensor to the binding of the antibodies is discussed in Section 5. Finally, some concluding remarks will be given in Section 6.

2. Sensor fabrication

Standard optical fibers have a cladding of enough thickness to make them insensitive to the outside environment. One possibility to make the evanescent component of the guided light interact with the external medium is get the fiber tapered. When an optical fiber is tapered, the core/cladding interface is redefined in such a way that the light propagation inside the core of the waist of the taper spreads to the cladding, which plays the role of the new core, and the external medium is now the new cladding; this fact eases the interaction of the evanescent field with the outer medium so that small changes of the outer medium can modulate the transmitted output optical power.

In Fig. 1, a scheme of a tapered optical fiber profile is shown. The physical parameters of the tapered fiber, which depend on the method employed in its fabrication, has an important effect on the light transmission properties. Heat pulling tapers can be fabricated using laser, flame or electrical arc. In this work, the last two methods have been employed. The parameters of the fusion (electrical current intensity and fusion times) are programmed in the splicing unit in such a way that minimizes the temperature reached by the fiber. By means of several tests, the fusion system is calibrated in order to make the fiber malleable but not degraded by heat and to give enough time to pull the fiber. The fiber was placed in a glass holder to be used in the experiments, making the sensor insensitive to external mechanical forces.

The geometrical dimensions of tapers used in this work, characterized by the waist diameter and taper length, were measured using an optical microscope and are shown in Table 1. Two different structures were employed. Firstly, taper T1 was made using standard step index optical fibers (Thorlabs FT-200-EMT). The tapering method used was gas flame. The 200-μm diameter silica core allows measuring better the behavior of the binding process in the visible part of the spectrum. Also, the long waist length of this taper (23 mm) allows creating a contact surface of enough area to detect absorbance changes.

Taper T2 was designed to detect refractive index changes during the binding process in the infrared part of the spectrum. A standard single-mode optical fiber (SMF Corning 125/8 μm cladding/core diameters) was tapered from 125 to 20 μm with an electric arc. Using this method it is possible to construct high sensitive and short tapers (2 mm length). Also differently from taper T1, the slopes of the contracting and expanding zones are much higher, given non-adiabatic structures. The light source was a 1310 nm laser and a photodetector was used to measure the transmitted power. The experimental set-up required with this type of sensor is simple and allows a high SNR and sampling frequency. The performance is explained by the classical modal domain interferometric structure (single-mode–multi-mode–single-mode) [10]. When the thin film is deposited onto the waist of the tapered optical fiber, the modes effective indexes change. Those physical parameters, which induce variations in the thickness and refractive index of the film, will change the transmitted optical power of the modes.

Table 1
Geometrical parameters

Taper	ρ_{core} (μm)	$\rho_{cladding}$ (μm)	ρ_{waist} (μm)	Waist length (mm)
T1	100	115	10	23
T2	4.15	60	10	2

2.1. ESA deposition

Once the tapered fibers have been fabricated, they are coated using the electrostatic self-assembled process technique. This method is based on the construction of molecular multilayers by the electrostatic attraction between oppositely charged polyelectrolytes in each monolayer deposited, and it involves several steps [11,12]. First, the optical fiber is cleaned and treated to create a negatively charged surface using piranha solution (70% H_2SO_4, 30% H_2O_2). Then, the substrate is exposed to a solution of Gliadin antigen, for a short time (5 min) and by adsorption a monolayer is formed on the surface. The deposition time is selected by observing the evolution of the sensor output while the deposition is realized. As the transmitted power stabilizes after 5 min of immersion in Gliadin solution, this time was used as dipping time. After each monolayer is formed it is necessary to rinse the sample with pure water to remove the excess of molecules that are not bound and that do not contribute to the monolayer structure. Then the substrate is dipped in a solution of poly(sodium 4-styrenesulfonate). This way, the substrate is alternately dipped into solutions of cationic and anionic molecules to create a multilayer thin film, a polyanion–polycation multilayer. This process is repeated increasing, layer by layer, the thickness of the material deposited.

The parameters of the ESA process are critical for the thickness and the refractive index of the film, especially the pH of the solution. In order to obtain uniform and repeatable depositions it has been employed a layer-by-layer deposition device (Riegler & Kirstein GmbH) which always positions the taper in the solutions for the same periods and rinses with ultrapure water in the same way. The pH is controlled periodically (each five layers) and adjusted if necessary using hydrochloric acid or sodium hydroxide. In addition, the thin film construction process was monitored using a method that does not interfere with the deposition process. It is observed that depositions realized with identical temperature, pH and dipping times give different characterizations depending on whether or not the construction get interrupted between layers