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Sensitive protein detection using an optical fibre long period grating sensor anchored with silica core gold shell nanoparticles

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ABSTRACT

An optical fibre long period grating (LPG), modified with a coating of silica gold (SiO_2:Au) core/shell nanoparticles (NPs) deposited using the layer-by-layer (LbL) method, was employed for the development of a bio-sensor. The SiO_2:Au NPs were electrostatically assembled onto the LPG with the aid of a poly(hydrochloride ammonium) (PAH) polycation layer. The LPG sensor operates at the phase matching turning point to provide the highest sensitivity. The SiO_2:Au NPs were modified with biotin, which was used as a ligand for streptavidin (SV) detection. The sensing mechanism is based on the measurement of the refractive index change induced by the binding of the SV to the biotin. The lowest detected concentration of SV was 19 nM using an LPG modified with a 3 layer (PAH/SiO_2:Au) thin film.

Keywords: long period grating, bio-sensor, antigen-antibody, silica-gold core/shell nanoparticles, layer-by-layer

1. INTRODUCTION

Fast, reliable and highly sensitive detection of proteins and antigen-antibody reaction kinetics is highly desired in biology and medicine because it can facilitate prompt disease diagnosis. The presence of various proteins, or changes in their concentration, can be linked with alternations in physiological conditions and act as an indicator of problems in the organism[1]. The quantitative detection of such proteins is conducted mainly using surface plasmon resonance (SPR) and various immunoassays, providing sensitivity down to pg/mL[2]. In spite of its high sensitivity, the main disadvantage of the SPR sensor is its price. Optical fibre long period grating (LPG) based devices modified with thin functional coatings have attracted a lot of research attention because of their high sensitivity, selectivity and fast response/recovery times[3].

The transmission spectrum of an LPG contains a number of resonance bands, each corresponding to coupling to a different cladding mode and each showing a different sensitivity to environmental perturbation. This has been noted to offer the potential for multi-parameter sensing[4]. The wavelengths at which light is coupled from the core to the cladding modes is governed by the phase matching equation

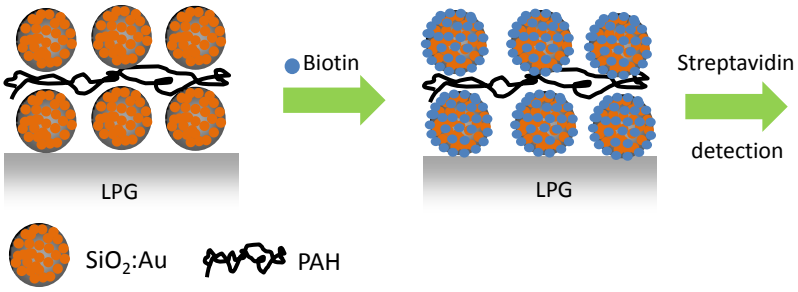
$$\lambda_x = \left(n_{core} - n_{clad(x)}\right)\Lambda \quad (1)$$

where λ_x represents the wavelength at which light is coupled to the LP_{0x} cladding mode, n_{core} is the effective refractive index of the mode propagating in the core of the fibre, $n_{clad(x)}$ is the effective index of the LP_{0x} cladding mode and Λ is the period of the LPG. The phase matching condition described by equation 1 contains a turning point at which it has been shown that the sensitivity of the transmission spectrum to perturbation of the surrounding environment is at its maximum. For subsequent environmentally induced decreases in (n_{core}-$n_{clad(x)}$), the LPGs transmission spectrum is characterised by the formation of a broad resonance band that subsequently splits into two[5]. LPGs of appropriate period, coated with functional materials and operating at the phase matching turning point, have been used to demonstrate sensors for chemical analytes in gaseous[6] or liquid media[7].

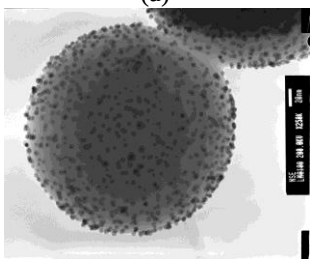
In this work, a novel biosensor based on an LPG coated with SiO2:Au core/shell NPs is demonstrated. The biotin-streptavidin interaction was used for the initial sensing measurements. The biotin is attached directly to the Au shell of the SiO_2 NPs, providing the sensor with high selectivity for protein detection. The selectivity of the sensor towards particular protein of interest can be tailored simply by changing the nature of the ligand, making LPGs modified with SiO_2:Au NPs a generic sensing platform for biosensor development.

2. EXPERIMENT

An LPG of length 40 mm and with a grating period of 110.7 μm was fabricated in boron–germanium co-doped optical fibre (Fibercore PS750, cut-off wavelength 670 nm) in a point-by-point fashion, side-illuminating the optical fibre by the output from a frequency-quadrupled Nd:YAG laser, operating at 266 nm. The transmission spectrum of the optical fibre was recorded by coupling the output from a tungsten-halogen lamp (Ocean Optics HL-2000) into the fibre, analyzing the transmitted light using a fibre coupled CCD spectrometer (Ocean Optics HR4000). The grating period was selected such that the LPG operated at or near the phase matching turning point, which, for coupling to a particular cladding mode (in this case LP_{019}), ensured optimised sensitivity[5].



(a)



(b)

Figure 1. (a) Schematic illustration of the layer-by-layer deposition of $(PAH/SiO_2:Au)_3$ film onto an optical fibre LPG. (b) TEM images of the SiO_2:Au core/shell nanoparticles.

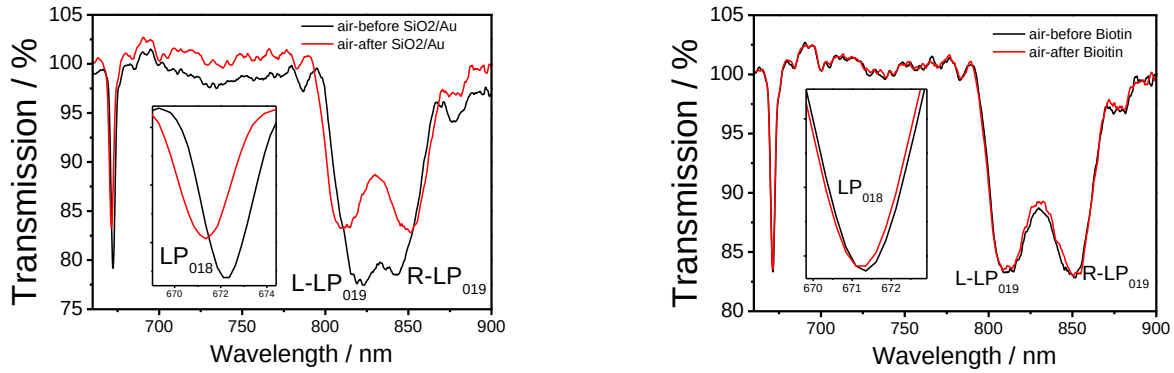
SiO_2:Au core/shell nanoparticles were made by first synthesising silica nanoparticles and then adding Au NPs using the Stober method[8]. A solution of 7 ml of ethanol (99,8% Sigma) and 80 μl of tetraethylorthosilicate (TEOS, Sigma) were mixed with 3 ml of ammonium hydroxide (NH_4OH 28%, Sigma-Aldrich) for 15 min in a sonicator bath. The functionalization of the silica nanoparticles was carried out by adding to the reaction 25 μl of 3-aminopropyltrimethoxysilane (APTES, Sigma-Aldrich) and leaving it to sonicate for an extra 15 min. The silica nanoparticles were purified by centrifugation.

The aqueous gold nanoparticles (2-5 nm in diameter) solution was prepared using the methodology described by Bonnard et al[9]. The solution of APTES-functionalized silica nanoparticles was added dropwise to the solution of gold nanoparticles in a volumetric ratio of 1:3 (SiO_2-NH_2:Au NPs) and stirred overnight. SiO_2:Au NPs were deposited onto the surface of the fibre using the LbL process and functionalised with biotin, as illustrated schematically in Figure 1a.

The surface of the section of the optical fibre containing the LPG was treated with a 1 wt% ethanolic KOH (ethanol/water = 3:2, v/v) solution to terminate it with OH groups. The fibre was then immersed alternately into a 0.17 wt % solution containing a positively charged polymer, PAH (pH=11), and, after washing, into a 1mg/mL solution containing the negatively charged SiO_2:Au NPs, each for 15 min, as illustrated in Figure 1a. This process was repeated until the required coating thickness was achieved, in this case after 3 deposition cycles. The coated fibre was then immersed in a 6.8 μM aqueous solution of biotin ((+)-Biotin N-hydroxysuccinimide ester, Sigma) for 30 min to functionalise the SiO_2:Au NPs coating and to provide the sensor with its specificity to Streptavidin (SV). The fibre was then rinsed in distilled water and dried by flushing with N_2 gas. The biotin remaining in the film was bound to the surface of each NP. This increased effectively the surface area available for the binding of SV compared with a bare fibre. The presence of the functional chemical compounds increased the refractive index (RI) of the porous coating and resulted in a significant change in the LPG's transmission spectrum, consistent with previous observations for increasing the optical

thickness of coatings on LPGs. To avoid the effect of the bulk RI of the solution the data were recorded in air after SV exposure and drying the LPG sensor. All experiments were conducted at 23 ^{o}C and 50% of rH. For protein measurements, the $(PAH/SiO_2:Au)_3$ - coated LPG was exposed to aqueous SV solutions of concentrations ranging from 19 nM to 2.6 μM. The sensor response was recorded at a frequency of 1 Hz. The transmission spectrum of the LPG was recorded in each analyte solution and after washing and drying the LPG sensor.

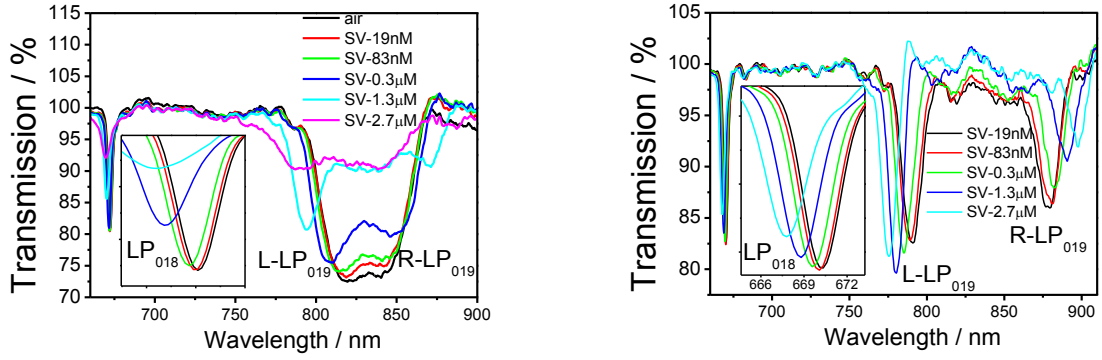
3. RESULTS AND DISCUSSION



(a) (b)

Figure 2. (a) The transmission spectrum of an LPG of period 110.7 μm , measured with the LPG in air, before and after $(PAH/SiO_2:Au)_3$ film deposition; and (b) transmission spectrum of the LPG coated the $(PAH/SiO_2:Au)_3$ film, measured with the LPG in air, before and after biotin deposition.

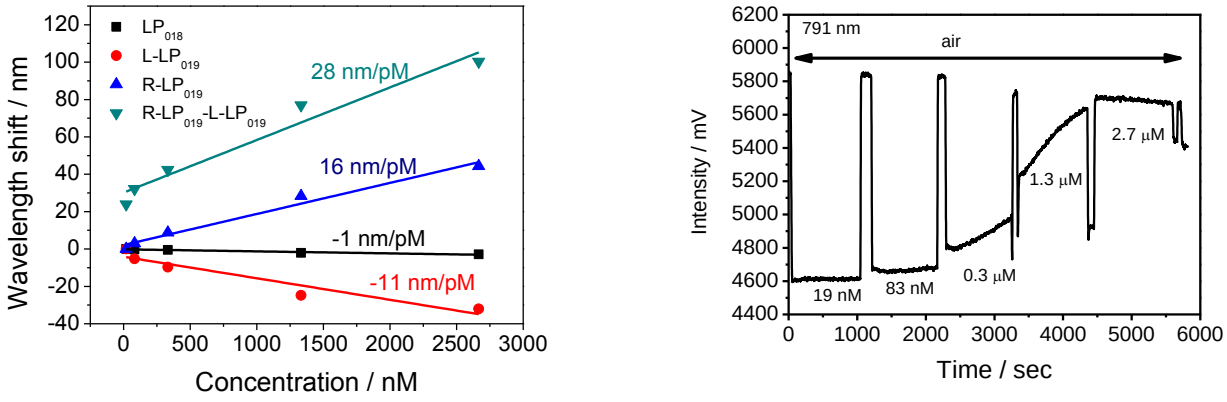
Figures 2a and 2b show the transmission spectrum of the LPG measured in air after the deposition of the $(PAH/SiO_2:Au\ NPs)_3$ film and after the binding of biotin, respectively. Similarly to observation of other LPG based chemical sensors[7], the first resonance band (@ ca. 670 nm), corresponding to coupling to the LP_{018} cladding mode, exhibited blue wavelength shifts of ca. 1 nm and ca. 0.11 nm for $(PAH/SiO_2:Au\ NPs)_3$ film and biotin deposition, respectively. The second resonance band (@ ca. 830 nm), corresponding to coupling to the LP_{019} cladding mode at the phase matching turning point, exhibited wavelength shifts of 14 nm and 10 nm for L-LP_{019} and R-LP_{019}, after PAH/SiO_2:Au NPs film deposition as shown in Figure 2a. The small wavelength shift observed after biotin adsorption, visible in figure 2b, most likely relates to the small RI change induced by the biotin molecule. After deposition of the $(PAH/SiO_2:Au\ NPs)_3$ film and functionalisation with biotin, the LPG sensor was exposed to the SV solutions of different concentrations.



(a) (b)

Figure 3. Transmission spectrum of the $(PAH/SiO_2:Au)_3$ coated LPG modified on exposure to SV of different concentrations in: (a) air and (b) aqueous solution.

Figures 3a and 3b show the changes in the transmission spectrum of the LPG sensor upon exposure to aqueous solutions of SV of different concentrations, by removing washing and drying LPG after each exposure, measured in air and in solution, respectively. Figure 4 (a) shows that the wavelength shift of the resonance bands was observed to exhibit a linear dependence on the concentration of SV. The sensitivity was 28 nm/pM when the difference between the centre wavelengths of the R-LP_{019} and L-LP_{019} resonance bands (Figure 3a) was considered. The response time for lower SV concentrations (up to 83 nm) was of the order of several seconds, suggesting the completion of SV binding to biotin (Figure 4b). For higher concentrations, however, the response time was much slower and was not complete within 15 min for SV concentration ranging from 0.3 to 2.7 μM possibly owing to the physical adsorption of the SV to SiO2 NPs. This phenomenon needs further experimental investigation and will be explored in future work



(a) (b)

Figure 4. (a) Concentration dependence of the wavelength shift derived from the data shown in figures 3a and 3b. (b) The change in transmission of the device measured at a wavelength of 791 nm on immersion into solutions of different SV concentration.

4. CONCLUSIONS

An LPG coated with a $(PAH/SiO_2:Au\ NPs)_3$ film and functionalised with biotin was used as a sensor for streptavidin protein. The response of the device to SV concentration was linear with a sensitivity of 28 nm/pM. Future work will study the effect of the film thickness and the size of the SiO_2 NPs on sensor performance. In addition, different ligands will be used to target different clinically relevant protein compounds.

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