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Highly sensitive optical fibre long period grating biosensor 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 core gold shell (SiO_2:Au) nanoparticles (NPs) deposited using the layer-by-layer method, was employed for the development of a biosensor. The SiO_2:Au NPs were electrostatically assembled onto the LPG with the aid of a poly(allylamine hydrochloride) (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 effect on sensitivity of increasing the surface area by virtue of the SiO_2:Au nanoparticles' diameter and film thickness was studied. The lowest measured concentration of SV was 2.5 nM, achieved using an LPG modified with a 3 layer (PAH/SiO_2:Au) thin film composed of SiO_2 NPs of 300 nm diameter with a binding constant of $k = 1.7\ (\mathrm{pM})^{-1}$, sensitivity of 6. 9 nm/$\left(\mathrm{ng/mm^2}\right)$ and limit of detection of 19 pg/mm^2.

1. Introduction

Fast, reliable and highly sensitive detection of proteins and antigen–antibody reaction kinetics are 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 alterations in physiology and act as an indicator of problems in the organism (Wulfkuhle et al., 2003). The quantitative detection of such proteins is conducted mainly using surface plasmon resonance (SPR), planar waveguides (Orgovan et al., 2014) and various immunoassays, providing sensitivity typically down to pg/mL (Homola, 2008). In spite of its high sensitivity, the main disadvantage of the SPR sensor is its price and real life applicability. A recent fabrication breakthrough in planar waveguides allows the use of grating coupled interferometry to achieve extremely high sensitivities to refractive index (RI) change in the order of 10^{-7} and a protein surface coverage sensitivity of 0.1 pg/mm^2 (Patko et al., 2012). In spite of the high sensitivity, their practicability for in vivo measurements remains limited. In this regard, optical fibre sensors modified with thin functional coatings offer a promising alternative to facilitate highly sensitive, selective and fast measurement in real time with the reported resolution of RI change of 10^{-6} (Korposh et al., 2012b).

Among various optical fibre sensors designs and measurements schemes, refractometers and chemical sensors based on optical fibre gratings have been employed extensively, in part because they offer wavelength-encoded information, which overcomes the referencing issues associated with intensity based approaches. A long period grating (LPG) is a core-cladding mode coupling device, where the in-fibre grating has a period of order 100–500 μm, Fig. 1a and b. The high attenuation of the cladding modes results in the transmission spectrum of the optical fibre containing a series of resonance bands centred at discrete wavelengths, with each attenuation band corresponding to the coupling to a different cladding mode, Fig. 1c. Fibre gratings facilitate the controlled coupling of light between modes of the optical fibre structure at specific resonant wavelengths, with the resonant wavelength showing sensitivity to perturbation of the fibre. Such devices have been used extensively as sensors (Grattan and Meggitt, 1999; James and Tatam, 2003, 2006).

Similar to SPR and planar waveguide devices, LPG sensors can provide highly precise analytical information about adsorption and desorption processes associated with the RI and thickness of the sensing layer. For instance, the sensitivity of LPG sensors (ca. 1 nM for antigen–antibody reactions) has been demonstrated to be of the same order of magnitude as SPR sensors (Homola, 2008; DeLisa et al., 2000). The high sensitivity of LPG based optical fibre

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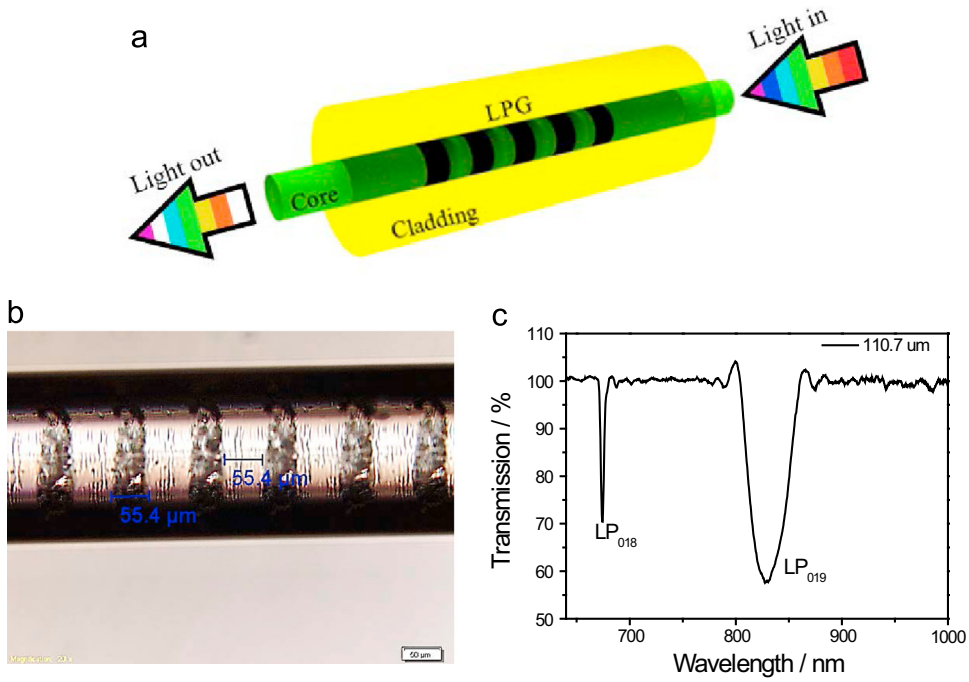

Fig. 1. (a) Schematic illustration of the LPG optical fibre; (b) optical image of the LPG written in the plastic jacket of the optical fibre; and (c) transmission spectrum (TS) of the LPG optical fibre operating at phase matching turning point (PMTP) with the grating period of 110.7 μm measured in air.

sensors operating at the phase matching turning point (PMTP) to RI change provides a high potential for detection of clinical analytes (Mishra et al., 2011). One of the earliest applications of an LPG to label free immunoglobulin (IgG) detection was demonstrated by DeLisa et al. (2000). The LPG was modified with goat anti-human IgG (antibody) and detection of specific antibody/antigen binding was investigated in the range of the concentrations of 2–100 μg/mL. Pilla et al. (2012) recently demonstrated an LPG immunosensor operating at the PMTP that provided a sensor with high sensitivity of 5 pg/mm^2 to anti-IgG analyte. Wang et al. (2009) used layer-by-layer (LbL) electrostatic self-assembly method for the deposition of polyion materials of poly(allylamine hydrochloride) and poly{1-[4-(3-carboxy-4-hydroxyphenylazo)-benzensulfonamido]-1,2-ethanediyl, sodium salt} onto the surface of the LPG with the aim of developing a biosensor using biotin–streptavidin as a demonstration bioconjugate pair. The lowest detected concentration of streptavidin was 12.5 μg/mL. Bandara et al. (2015) recently reported the detection of methicillin-resistant staphylococci using a biosensor assay consisting of nanoscale films deposited onto an LPG.

The characteristics of optical fibre sensors, such as sensitivity, response/recovery times and especially selectivity, depend strongly on the performance capabilities and the properties of the functional layer. Research in the field of optical fibre sensors (OFS) has focused on the development of new materials that can be used as sensitive elements. In this work, a novel biosensor based on an LPG coated with SiO_2:Au core/shell NPs is demonstrated with sensitivity to streptavidin of an order of magnitude greater than previously reported with LPG sensors (Wang et al., 2009). This paper expands research results presented originally as an extended abstract at OFS 23 (Marques et al., 2014) and provides a more detailed study on the effect of the SiO_2 NPs' diameter and on the presence of Au NPs. Two sets of SiO_2:Au NPs of diameters 80 and 300 nm were used to generate coatings of different layer thickness and surface areas on the LPG sensing platform. The use of a SiO_2:Au NP complex brings several advantages to biosensor development. For example, the diameter and number of Si and Au NPs can be controlled to optimise sensitivity. The Au NPs can be functionalised with different molecules, such as proteins, to provide sensor selectivity. The Au NPs' surface plasmon resonance (SPR) can then be linked to the presence or absence of target molecules. Controlling the size of the Au NPs means that the sensor can operate within a working window of 700–900 nm, which allows for optimum penetration of light across samples such as physiological fluids. A further advantage is that, since the Au NPs are covalently bonded to the Si NP surface, the system is stable and is not affected over time by washing processes.

SiO_2 NPs on the other hand have two important functions: (i) they endow the sensitive layer of the sensor with higher porosity and thus larger surface area and (ii) they optimise the efficiency of the interaction between evanescent wave and sensitive layer via optimisation of the sensitive layer thickness. Both factors are contributing to the increase of the sensitivity of the sensor. For example, it was observed that coating the optical fibre without SiO_2 nanoparticles resulted in a reduction in sensitivity by a factor of 2 (Kodaira et al., 2008).

The biotin–streptavidin interaction was used as a model system to characterise performance. The biotin is attached directly to the Au shell of the SiO_2 NPs, providing a 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. Theory

2.1. LPG operation

The wavelengths at which light is coupled from the core to the cladding modes is governed by the phase matching equation

$$\lambda_i = (n_{\text{core}} - n_{\text{clad}(i)})\Lambda \quad (1)$$

where λ_i represents the wavelength at which light is coupled to the linearly polarised (LP_{0i}) cladding mode (where i =1,2,3…), n_{core} is the effective refractive index of the mode propagating in