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Simple immunoglobulin G sensor based on thin core single-mode fiber

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ABSTRACT

In this paper, a simple fiber biosensor (FOB) for immunoglobulin G (IgG) detection is designed and experimentally verified. The FOB is constructed by a 20 mm long thin core single-mode fiber (TCSMF) sandwiched between two single-mode optical fibers (SMFs). First, the refractive index (RI) sensitivity of the fiber structures is calculated by the beam propagation method. The refractive index sensing experiment is performed using different concentrations of glycerol solutions, and the experimental results are mostly consistent with the simulation predictions. The experimental RI sensitivity increases with the surrounding RI and reaches 82.7 nm/RIU. Then the surface of the FOB is functionalized by APTES for covalent bonding. The human IgG and goat anti-human IgG are chosen as a bioconjugated pair to examine the bio-sensing effectiveness of this FOB. The sensitivity of IgG detection is determined to be 10.4 nm/(mg/ml). And the serum IgG concentration in normal adults lies within the range of 6–16 mg/ml (Worsfold et al., 1985), so the sensor is applicable to human IgG monitoring. The specificity of the FOB is also verified by a contrast experiment conducted using rabbit immunoglobulin G. The proposed FOB is simple, low loss, cost-effective, and can be used for various biological and chemical applications.

1. Introduction

Optical fibers play an important role in various sensing technologies. It has been widely used in environmental monitoring, biomedicine, food engineering and other fields. Optical fiber sensors have many advantages, such as immune to electromagnetic interference, cost-effective, high sensitivity, and so on. Optical fiber sensors can also work in high pressure, large noise, high temperature, strong corrosion and other special environments. The most commonly used principle of the fiber sensors is the interference technique. The change of the external parameters is transferred into the phase change of the light transmitted in the optical fiber, which causes the variation of transmitted light intensity. By the interrogation of the transmitted light signal, external physical quantities are measured. The commonly used fiber interferometers include: Michelson interferometer (MI) [2], Fabry-Perot Interferometer (FPI) [3–5], Sagnac interferometer [6], and Mach-Zehnder interferometer (MZI) [7–9], and so on. The comparison of these fiber sensors are shown in Table 1.

With the rapid development of optical fiber sensors, how to apply optical fiber sensing to biological, agricultural, chemical and other fields has also become a research hotspot. Optical fiber biosensor can be based on many fiber constructions, such as D-shaped polymer fiber [10], long period grating [11], photonic crystal fiber [12], multimode fiber [13] and so on. For example, Xin Xin et al. presented a four-layer structure in the sensing region for a D-shaped step-index fiber-optic evanescent wave (FOEW) sensor, which reached $-0.077\,(\mu g/l)^{-1}$ in the detection of the goat anti-mouse IgG. Chen Liu et al. explored graphene oxide (GO) nanosheets functionalized dual-peak long period grating (dLPG) based biosensor for immunosensing detection, and the limit of detection (LOD) is 7 ng/ml. It must be acknowledged that the sensitivity and LOD in the above literatures are excellent, but it is undeniable that they usually require complex or time-consuming fabrication steps. In addition, localized SPR using gold nanoparticles (GNP) [14] or surface plasmon resonance (SPR) using gold films [15]with ultra high sensitivities are also utilized in bio-sensing. However, the realization of the SPR sensor with noble materials is expensive and requires extra processing. In this paper, a simple, cheap Immunoglobulin G (IgG) sensor based on thin core single-mode fiber (TCSMF) sandwiched between two SMFs is proposed. The construction of this fiber sensor is easy with only the common optical fiber fusion splicer required. Furthermore, this fiber sensor has low loss due to the good mode matching between the TCSMF and SMFs.

Another important factor that affects the stability and sensitivity of fiber optic biosensors is the sensitive materials. At present, there are many kinds of biomaterials for the surface functionalization of optical fibers, including: (1) silane coupling agent – the covalent bonding method; (2) polyelectrolyte the physical adsorption method; (3) the sol gel method; and (4) the lipid bilayer membrane method. Among them,

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Table 1
Comparison of experimental refractive index sensitivities of various fiber structures.

Structural configuration	RI range	RI sensitivity nm/RIU	Ref.
MI	1.380–1.435	−48.858	[1]
FPI (air cavity)	1.30–1.38	92.5	[2]
FPI (tapered hollow tube)	1.3333–1.4069	610.47	[3]
PCF-FPI	1.331–1.347	53	[4]
Sagnac interferometer (PMF-LPG)	1.33–1.43	−21.07	[5]
PCF-MZI (HTCR)	1.3333–1.3574	181.96	[6]
PCF m-MZI (multibeam)	1.33–1.37	20.53	[7]
PCF-MZI	1.3411–1.3737	51.902	[8]
TCSMF MZI	1.3345–1.3527	82.7	Present study

*The full name of the above abbreviations are: photonic crystal fiber (PCF), polarization maintaining fiber (PMF), long-period grating (LPG), half-taper collapse region (HTCR), thin core single-mode fiber (TCSMF).

covalent bonding has many advantages, such as secure combination, excellent stability, repeatability, and stability.

In this paper, a simple fiber optical biosensor (FOB) based on a thin core single-mode fiber sandwiched between two single-mode fibers (SMF–TCSMF–SMF) is proposed. The RI sensitivity of the fiber sensor is validated through both simulation and experiment. Then the covalent bonding technique is used to fix silane coupling agent on the surface of the sensing fiber. And human IgG and goat anti-human IgG are chosen as a bioconjugated pair to validate the bio-sensing function of the FOB. The proposed FOB is simple, low loss, cost-effective, and can be utilized in many other related biological or chemical application fields.

2. Methods and simulations

2.1. Sensor structure and principle

Fig. 1 provides a schematic illustration of the proposed MZI based fiber optic biosensor. The fiber structure of this sensor consists of two single mode fibers and one thin core single mode fiber. The functionalization of the fiber surface and the IgG detection process are also shown in this figure, which will be explained later. The cladding diameter of both the TCSMF and the SMF is 125 μm, while the core diameters of them are 8.3 μm and 2.1 μm, respectively. Due to the unmatched core diameter, when the broadband light incidents from the SMF into the TCSMF's cladding at the first interface, some of the light propagates in the cladding part of the TCSMF, hence the cladding modes are motivated consequently. When the light spreads to the second interface, the core mode and the cladding modes will bring into an interference signal due to the optical path difference. That is the Mach-Zehnder interference principle. Finally, the sensor is connected to a spectrometer. The transmission spectrum is recorded on the

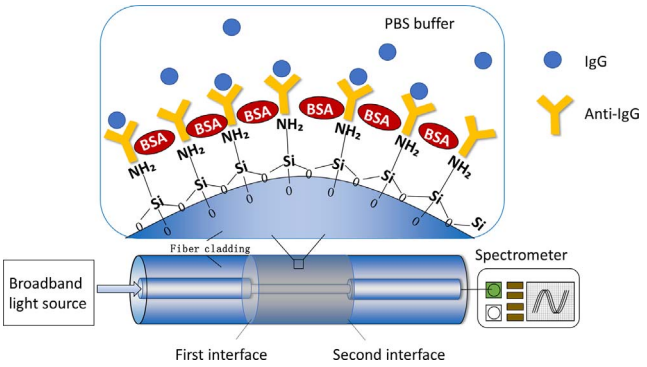

Fig. 1. Schematic diagram of the fiber optic biosensor with a TCSMF sandwiched between two SMFs.

spectrometer. The peaks and dips of the spectrum correspond to the constructive and destructive interferences. In analysis of the transmission spectrum according to the interferometric phase matching condition is defined as [16]:

$$2\pi\left[n_{eff}^{co}(\lambda)-n_{eff}^{cl,j}(\lambda,n_{ext})\right]\times\frac{L}{\lambda_D}=(2k+1)\pi \tag{1}$$

where L is the length of the TCSMF, λ_D is the peak wavelength of the interference signal, k is a positive integer, $n_{eff}^{co}(\lambda)$ and $n_{eff}^{cl,j}(\lambda,n_{ext})$ are the effective RI of the core mode and the jth order cladding mode, respectively. And the change of the refractive index of the ambient media n_{ext} only affects $n_{eff}^{cl,j}(\lambda,n_{ext})$ which corresponding to the change of the peak wavelength. From Eq. (1) we can deduce the relationship between the wavelength of the characteristic peak and the ambient media as:

$$\frac{d\lambda_D}{dn_{ext}}=\frac{-2L}{2k+1}\times\frac{\partial n_{eff}^{cl,j}}{\partial n_{ext}}\div\left[1-\frac{2L}{2k+1}\left(\frac{\partial n_{eff}^{co}}{\partial\lambda}-\frac{\partial n_{eff}^{cl,j}}{\partial\lambda}\right)\right] \tag{2}$$

Based on Eq. (2), when the refractive index of the surrounding media changes, the characteristic peak wavelength λ_D will shift consequently. Therefore, by observing the characteristic peak wavelength or its offset, the refractive index of external solutions can be determined. Since the reference arm and sensing arm of this MZI are from the similar fiber core and cladding, this FOB structure has low loss, and can also effectively weaken the influence of external environment (such as temperature [17]). Moreover, this sensor possesses the temperature-insensitive characteristic on account of the similar thermo-optic coefficient among three cores. Thus, the structure has a higher accuracy.

2.2. Simulations

First, the theoretical calculations of the refractive index sensitivity of this FOB are performed. The simulation is performed using the beam propagation method with the boundary condition of perfect match layers (PML). The simulation results of this FOB immersed in different refractive index media are presented in Fig. 2. As shown in Fig. 2(a), the transmission spectrum red shifts with the increase of the RI. Clear interference spectra can be observed, which confirms the above MZI theory. Since the refractive indices of the reagents prepared for our experiments are in the low refractive index range, RI lower than 1.355 are considered. After a fitting of the relationship between the dip wavelength and the refractive index, the calculation results are shown in Fig. 2(b). The relationship equation is $y = 1378.274 + 147.075x$, and the fitting parameter of R^2 equals to 0.995. The RI sensitivity in this RI range is 147.075 nm/RIU.

2.3. Materials

Both TCSMFs (S405-HP) and SMFs (SMF-28) were purchased from Nufern which is agented by Shanghai hanyu optical fiber communication technology co. Ltd. Human immunoglobulin G and goat anti-human immunoglobulin G were purchased from Dingguo Biotechnology Co., Ltd. (Hangzhou, China), Glycerol, ethanol, 30% hydro-gen peroxide (H_2O_2), 98% concentrated sulfuric acid (H_2SO_4) and phosphate buffer saline (PBS) were purchased from Jiachen Chemical Industry, Inc. (Hangzhou, China), Bovine serum albumin (BSA) were purchased from Dingguo Changsheng Biotechnology, Inc. (Beijing, China), APTES, Glutaraldehyde and silane coupling agent were purchased from Sigma Aldrich Trading Co., Ltd. (Shanghai, China).

2.4. Biosensor construction

Firstly, the fiber structure of this FOB is manufactured. The external protection layer and the coating of the fibers are stripped with strippers. The surface residue and dirt on the surface of the fibers are washed with