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Immobilized optical fiber microprobe for selective and high sensitive glucose detection

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ABSTRACT

Optical fiber microprobe functionalized with Glucose oxidase (GOD) has been proposed for bio-selective and high-sensitive glucose detection. Taking advantages of the free amine groups of 3-aminopropyltriethoxysilane (APTES), the enzymes (GOD) are immobilized on the multimode microfiber through covalent interaction. Surface characterization offered by optical microscopy, scanning electron microscope and multiphoton laser scanning microscopy provide detailed evidences about the effect of the bio-functionalization. The fabricated microfiber sensor is immersed into glucose solutions at different concentrations to record and analyze the transmission spectrums from an optical sensing interrogator. The experimental results demonstrate that the resonant wavelength shift is linearly correlated with the glucose concentration in the range of 0–3.0 mg/ml with a response coefficient of 1.74 nm/mg^{-1} ml^{-1}. Meanwhile, the reported sensor is also proved to be of practical utility by accurately detecting glucose content in animal serum samples. Due to the small size, label-free sensing capacity and excellent practicality, the proposed device has great potential to be applied in the fields like disease diagnosis, clinical analysis and food safety.

1. Introduction

The precise and rapid detection of glucose concentration is crucial in many fields such as disease diagnosis, clinical analysis and quality monitor in food industry. In particular, the abnormal body blood glucose level monitoring is critically important for human health. According to World Health Organization (WHO), diabetes caused 1.55 million deaths in 2012 and higher-than-optimal blood glucose caused an additional 2.2 million deaths by increasing the risk of cardiovascular and other diseases [1]. Diabetes describes a group of metabolic diseases in which the person has high blood glucose, either because insulin production is inadequate, or because the body's cells do not respond properly to insulin. Symptoms of high blood sugar include frequent urination, increased thirst and hunger. If left untreated, diabetes can cause many complications such as cardiovascular disease, stroke and chronic kidney failure that do great damage to health [2]. Precise monitoring and careful control of the glucose level in the blood are essential for proper diagnosis and diabetes treatment, therefore, routine testing of physiological glucose levels is critical to avoid diabetic emergencies as well as to prevent long-term complications from arising. The enormous signification of glucose detection and potential commercial value have always attracted continually effort on researching novel glucose sensor.

Most of the traditional methods for glucose monitoring employ electrochemical system, which can be prone to certain electrode-sensitive compounds, meanwhile, the high cost and time-consuming preparation processes limit their applications as well. Compared to electrochemical method, the optical fiber devices have offered a good platform for biochemical sensing due to their small size, passivity, electromagnetic immunity, low cost and easy fabrication [3]. Coating by special biomolecules like antibody or enzyme, fiber-based sensors have performed selectivity and high sensitivity for corresponding biologic substance measurement even in low concentration, which makes it more accurate and effective. Actually, standard optical fiber is not sensitive to the surrounding medium and cannot be utilized to detect biological parameters directly owing that its optical filed is mostly confined in the core of fiber. Many techniques so far have been developed to enhance the interaction between the optical field and surrounding. According to the working principle, the fiber-based biochemical sensors can be simply classified into two categories. One is based on the surface plasmon resonance (SPR) [4] and the other is based on the mode coupling of fiber [5–9]. Sarika Singh et al. demonstrated

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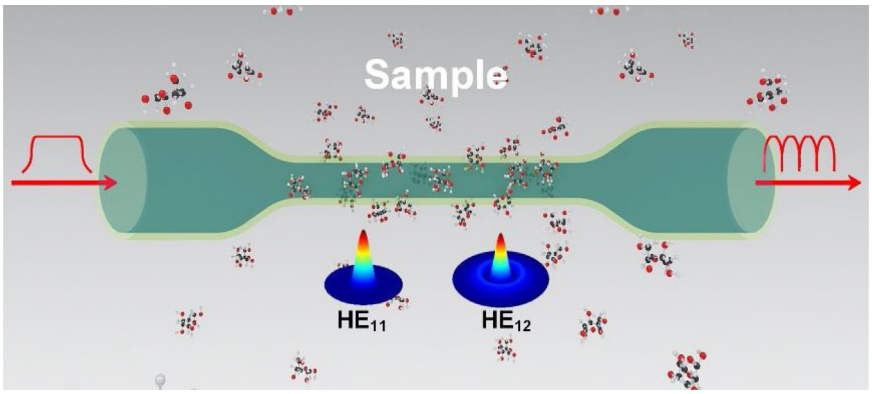

Fig. 1. Schematic diagram of multimode microfiber probe.

a fiber-SPR sensor for the detection of glucose [4]. The sensor is fabricated using multimode plastic clad silica (PCS) fiber coated by a film of silver and then immobilized by GOD. Although the optical fiber-SPR based glucose sensor achieves a high sensitivity, the high cost and bad biocompatibility of heavy metal make it hard to be widely applied in clinical analysis. Therefore, the mode coupling based fiber glucose sensor are more popular and many techniques has been researched in recent reports such as U-shaped fiber [5], tapered fiber [6] and special fiber gratings mainly including long-period grating (LPG) [7] and titled fiber grating (TFG) [8,9]. Compared with these methods, microfiber naturally has strong and externally exposed evanescent field due to its subwavelength diameter, and therefore the input light can interact with ambient bio-molecules directly through evanescent field, which makes microfiber more effective and compact in detecting biochemical substance [10–14]. Apart from the recent applications of microfiber in testing abrin [12] and Alpha-fetoprotein [13], our previous work in detecting glucose has also proved this [14]. Although the sensitivity of glucose detection has been improved greatly, the sensing structure is somewhat complicated.

For further simplifying the detecting structure, a more compact glucose sensor using multimode microfiber was fabricated in this study. Schematic diagram of glucose detection was exhibited in Fig. 1. Multimode microfiber was non-adiabatically drawn from single mode optical fiber until the fiber diameter decreasing into several micrometers. With abrupt taper, fundamental and higher order modes were excited (mainly HE_{11} and HE_{12}) [15–19] and form mode interference. For selective glucose analysis, the multimode microfiber was functionalized by GOD at first. The GOD immobilized on multimode microfiber will catalyze glucose and generate glucose acid, which will change the ambient refractive index (RI), and the different modes will interact directly with ambient medium. By tracking the resonant wavelength shift of the mode interference spectrum causing by the variation of ambient RI, a high glucose sensitivity was experimentally achieved. It is noted that the size of the glucose sensor demonstrated in this work is decreased into only several micrometers, which is comparable with a single living biological cell. The small size and relatively higher sensitivity indicate that the techniques utilized in our research work has great potential to be applied in the vivo detection of body fluid element including (but not limited to) blood glucose.

2. Materials and methods

2.1. Materials

The pristine SMF-28e optical fibers were purchased from YOFC. GOD, 3-aminopropyl-triethoxysilane (APTES), Sodium acetate (SA) buffer solution and D-glucose were all purchased from Sigma-Aldrich. Deionized water was derived from a Milli-Q water purifying system. The horse serum and new-born calf serum were purchased from Thermo Fisher Scientific.

2.2. Multimode microfiber fabrication and functionalization

The heat drawing is the most widely used method in manufacturing microfiber due to its advantages of fast fabrication, low surface roughness, easy control of taper profile, and economical efficiency [20]. Typical heat drawing system usually includes a heating source and a set of displacement platform through which the stretching length and velocity could be controlled precisely. For multimode microfiber, it is non-adiabatically drawn from single mode fiber (SMF) until the desired length or diameter of the fiber waist is reached [16].

In order to make the multimode microfiber only selective for glucose detection, it should be bio-functionalized with GOD at first. The key functionalization process was schematically described in Fig. 2. The multimode microfiber was initially immersed in 5% HNO_3 solution for 2.5 h at room temperature and then washed by de-ionized water and ethanol to be completely cleaned. At this moment, the multimode microfiber was prepared to be functionalized. Firstly, as illustrated in Fig. 2(a), to activate the hydroxyl-groups on the microfiber surface, the cleaned microfiber was immersed in H_2SO_4 solution (95% v/v in H_2O_2) for about 1 h, followed by drying for about 20 h at room temperature. After that, the microfiber was left in APTES solution (10% v/v in ethanoic solution) for 30 min and then washed by de-ionized water and ethanol again to remove non-covalently bonded silane compounds. As can be seen from Fig. 2(b), there were many free amine groups contently immobilized onto the APTEs-deposited multimode microfiber. Afterwards, the silanized microfiber was immersed in 10 mg/ml sodium acetate (SA) buffered solution of GOD for 2 h incubation, thus the GOD's-COOH groups would bind with the NH^{3+} on the surface of microfiber which was shown in Fig. 2(c). Finally, the enzyme-immobilized microfiber was washed with SA buffer and de-ionized water and dried in the air.

2.3. Experimental setup

The functionalized multimode microfiber was bended serving as probe and then placed into the U groove serving as sample container (see the inset of Fig. 3). In future, the multimode microfiber probe could be further simplified by laser cutting equipment since the reflection spectrum contained sensing information as well. In this work, the sensing performance of fabricated microfiber probe was examined by the system schematically illustrated in Fig. 3. Microfiber probe was placed in U groove with an outlet and an inlet ports through which the glucose sample could be injected into

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