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Wavelength-based localized surface plasmon resonance optical fiber biosensor

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ABSTRACT

Two types of localized surface plasmon resonance (LSPR)-based optical fiber biosensors using gold nanospheres (GNSs) and gold nanorods (GNRs) have been developed and their performance characteristics evaluated and cross-compared successfully in this work. Based on the results obtained from the optimization of each of these types of biosensor and reported by the authors elsewhere, GNSs with a diameter of 60 nm and GNRs with an aspect ratio of 4.1 were specifically chosen in this work for the fabrication of two representative sensor probes, with an aim to create a highly sensitive and wavelength-based LSPR sensor to overcome the limitations arising from other intensity-based sensors. In order to develop effective LSPR biosensors, both GNSs and GRNs respectively were immobilized on an unclad surface of an optical fiber, prior to the functionalization with human IgG in order to create a device for the detection of anti-human IgG, at different concentrations. The experimental results obtained from tests carried out show that the sensitivities of GNSs and GNRs-based LSPR sensors to refractive index variation are 914 and 601 nm/RIU respectively; however as biosensors they have demonstrated the same detection limit of 1.6 nM for the detection of anti-human IgG.

1. Introduction

The development of label-free biochemical sensors based on the localized surface plasmon resonance (LSPR) technique has attracted increasing attention, due to the advantages seen such as high sensitivity to refractive index change and ease of fabrication, modification and control. The approach is similar to the well-known surface plasmon resonance (SPR) phenomenon, where the frequency of the evanescent electromagnetic wave propagating at the metal-dielectric interface is resonant with the oscillation of the surface conduction electrons in the metal [1]. LSPR is also a resonance phenomenon which normally occurs when the frequency of the incident photon is resonant with the collective oscillation of conduction electrons in the metallic nanoparticles [2]. Compared to SPR sensors, LSPR sensors not only retain the advantages of SPR sensors, such as the high sensitivity to the surrounding refractive index change, fast and real time detection and label-free technology, but also their fabrication processes are much simpler and easier to implement. In addition, despite the fact that SPR sensors provide much higher sensitivity to the change in the bulk refractive index [3,4], LSPR sensors can offer a comparable sensitivity when measuring a short range change in refractive index caused by the molecular adsorption for instance [2,4]. Moreover, as the properties of the metallic nanoparticles are highly dependent on their material, size and shape [5], controlling these three parameters allowing an optimum performance of a LSPR sensor for detecting a particular target to be realized.

LSPR sensors based on various structures have been developed and reported, such as solution-phase-based [6–9], chip-based [10–12] and optical fiber-based [13–15] LSPR sensors. Compared to other LSPR sensors, optical fiber-based LSPR sensors have shown many advantages including small sample requirement, simplified optical design, remote sensing capability and resistance to electromagnetic interference. In addition, being relatively inexpensive to fabricate, such sensors can be disposable after use avoiding problems of cross-contamination and potential loss of calibration after cleaning. In light of such advantages, extensive research has been undertaken to develop a number of interesting and promising optical fiber-based LSPR sensors [15–18], demonstrating the strength of label-free bio-sensing capabilities. Compared to the other metallic nanoparticles reported, gold nanoparticles are preferable for the preparation of label-free biosensors as gold demonstrates better affinity with biomolecules and resistance to oxidization [19]. Most of these previously reported optical fiber LSPR sensors have shown good sensitivities to the surrounding refractive index change with their resonance peak wavelength shifts being observed when the sensors were subjected to the testing solutions with different refractive index. However, when these sensors were used as

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biosensors, absorbance or intensity measurement is widely considered rather than the peak wavelength shift [17,20–24]. This is because that the resonance wavelength of these sensors has not demonstrated sufficient sensitivity to detect the small refractive index change caused by the biomolecule interaction, although this wavelength-based technique is preferable due to its insensitivity to the interference arising from the surrounding environment, compared to absorbance and intensity-based techniques.

In previous research by the authors, the effects of size and shape of gold nanoparticles (GNPs) on the sensitivity of GNPs-based optical fiber sensors were studied [25,26]. This work builds on the experimental results obtained, where it was concluded that gold nanospheres (GNSs) of larger size and gold nanorods (GNRs) with a higher aspect ratio demonstrate higher sensitivities to the refractive index change. The results obtained indicate a strong possibility that by employing GNPs with high refractive index sensitivity, a wavelength-based measurement could be applied in the case of LSPR based optical fiber biosensor and thus the more problematic intensity-based approach could be avoided. Therefore, in order to verify this possibility and building on the previous findings, in this paper two representative LSPR-based optical fiber biosensors are fabricated using both GNSs and GNRs, with their sizes being chosen particularly to enhance the sensitivities of the biosensors created.

Thus the detailed fabrication processes for both LSPR biosensors are introduced in this work, with their refractive index sensitivities being examined and compared. This is followed by an evaluation of their performance as label-free biosensors by studying the interaction between the human IgG immobilized on the GNPs and anti-human IgG in a PBS buffer using a wavelength-based interrogation method rather than the conventional absorbance or intensity-based technique to improve the quality of the measurement.

2. Experimental setup

2.1. Materials

Gold (III) chloride trihydrate ($HAuCl_4{\cdot}3H_2O$), sodium citrate, ascorbic acid, silver nitrate ($AgNO_3$), cetyltrimethylammonium bromide (CTAB), sodium borohydride ($NaBH_4$), sodium citrate tribasic dehydrate ($Na_3C_6H_5O_7$), 3-aminopropyl trimethoxysilane 97% (APTMS), 3-Mercaptopropyltrimethoxysilane (MPTMS), potassium hydroxide (KOH), tin (II) chloride dehydrate, dextrose, human IgG (purified immunoglobulin, reagent grade), anti-human IgG (whole molecule, produced in goat), 11-Mercaptoundecanoic acid (MUA), bovine serum albumin (BSA), N-(3-Dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (EDC) and *N*-hydroxysulfosuccinimide (Sulfo-NHS) were purchased from Sigma–Aldrich. Ultrapure de-ionized (DI) water (18 MΩ) was used to prepare all solutions. All chemicals and reagents were of analytical grade and used as received. All procedures were conducted at room temperature unless specified otherwise. Multimode optical fibers of diameter 600 μm and NA = 0.37 were purchased from Thorlabs.

2.2. Synthesis of GNPs and characterization

GNSs with a mean diameter of 60 nm and GNRs with a mean aspect ratio about 4.1 were chosen as the basis of this work to enhance the refractive index sensitivity of the LSPR sensors and prepared by the methods reported previously [25,26]. In brief, 60 nm GNSs solution was synthesized by dissolving 5 mg of $HAuCl_4{\cdot}3H_2O$ in 50 mL DI water. After this solution was heated to boiling, 300 mL of 1% sodium citrate tribasic dehydrate solution was rapidly added, resulting in a color change to dark-green after few seconds. The color then slowly changed to red/purple, and the mixture was heated for a further 10 min before the heat source was removed, followed by stirring the solution for a further 15 min.

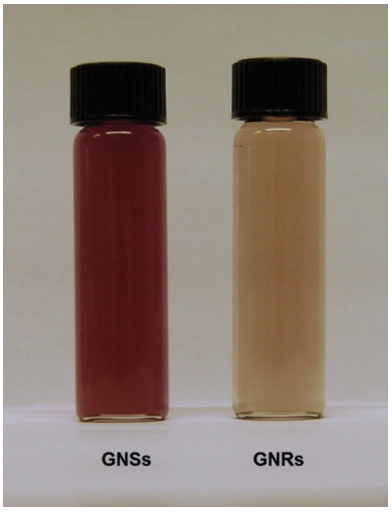

Fig. 1. Illustration of 60 nm GNS solution (left) and GNR solution with an aspect ratio of 4.1 (right).

GNR solution was synthesized by a seed-mediated method reported by Nikoobakht and El-Sayed [27], with slight modification. Seed solution was prepared by adding 600 μL of 0.01 M ice-cold $NaBH_4$ solution into a mixture with 5 mL of 0.2 M CTAB solution with 5 mL of 0.0005 M $HAuCl_4$ solution with vigorous stirring for 2 min. After being aged at room temperature for 3 h, 100 μL of the seed solution was added into the growth solution containing 30 mL of 0.2 M CTAB, 30 mL of 0.001 M $HAuCl_4$, 310 μL of 0.02 M $AgNO_3$ solution and 420 μL of 0.0788 M ascorbic acid. The mixture was kept in an oil bath at 30 °C for 24 h to grow the GNRs. Prior to the immobilization of the GNRs on an optical fiber, the excess CTAB in the GNRs solution was removed by twice centrifugation at 8000 rpm for 20 min each time. Fig. 1 shows the colors of the GNSs and GNRs solutions synthesized using the above methods (from a sample in a small vial).

The absorbance spectra of the gold nanoparticles solutions were measured by using a LAMBDA 35 UV/VIS spectrophotometer (PerkinElmer Inc.), over the wavelength range from 400 nm to 1100 nm. The mean diameter and aspect ratio of the GNSs and GNRs were determined by using a JEOL 1010 transmission electron microscope (TEM). The TEM samples were prepared by placing 2 μL of diluted GNS or GNR solutions on a 3 mm 400-mesh Formvar coated copper grid (purchased from Agar Scientific) and evaporating the solution at room temperature. Fig. 2(a) and (b) shows the TEM images of the as-synthesized GNSs and GNRs respectively.

2.3. Preparation of LSPR sensor probes

Fig. 3(a) and (b) demonstrates the schematic diagrams of the GNSs- and GNRs-based LSPR sensor probes prepared in this work respectively. In essence, a piece of polymer-clad silica multimode optical fiber with a core diameter of 600 μm was cut into several 10 cm long sections to be used as sensor substrates. Subsequently each fiber section was carefully polished at both end surfaces by using polishing films with 5, 3, 1 and 0.3 μm roughness in sequential order, and 2 cm unclad portion at one end of the fiber was used as the sensing area after the cladding having been removed with acetone. The sensing area of the fiber was then cleaned by use of piranha solution (H_2O_2:H_2SO_4; 30%:70%) for 30 min (it should be noted that this solution is extremely aggressive and thus required handling with extreme care). After a thorough rinse with DI water,