A reflection-based localized surface plasmon resonance fiber-optic probe for biochemical sensing

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Abstract: We report the fabrication and characterization of an optical fiber biochemical sensing probe based on localized surface plasmon resonance (LSPR) and spectra reflection. Ordered array of gold nanodots was fabricated on the optical fiber end facet using electron-beam lithography (EBL). We experimentally demonstrated for the first time the blue shift of the LSPR scattering spectrum with respected to the LSPR extinction spectrum, which had been predicted theoretically. High sensitivity [195.72 nm/refractive index unit (RIU)] of this sensor for detecting changes in the bulk refractive indices has been demonstrated. The label-free affinity bio-molecules sensing capability has also been demonstrated using biotin and streptavidin as the receptor and the analyte.

OCIS codes: (060.2370) Fiber optics sensors; (280.1415) Biological sensing and sensors; (220.4241) Nanostructure fabrication.

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1. Introduction

Recently there is widespread interest in the development of chemical and biochemical sensors based on plasmonic resonance of metallic nanostructures. The surface plasmon resonance (SPR) for thin metallic film has been widely studied for label free and high sensitivity biosensing devices [1,2]. The popular SPR sensor setup is based on Kretschmann configuration, which comprises a light source, a prism and a thin metallic film on one side of the prism. SPR biosensing in Kretschmann geometry is now commercially available from several companies.

In the localized surface plasmon resonance (LSPR) for nanometer-sized metallic structures, a resonant oscillation of the conduction electrons within the metallic nanostructures gives rise to an enhanced scattering and absorption of light. The LSPR sensing requires simpler instrumentation than SPR. Nanodots are popular nanostructures used in LSPR researches. Their spectra position is dependent on the size and shape of the nanodots, the composition of nanodots, the interaction of nanodots and the dielectric environment surrounding the nanodots. Controlling the size and the periodicity of an array of gold nanodots, one can engineer the structure to operate at the desired wavelength window. The property of spectra position of metallic nanostructure depended on the dielectric environment is widely used as the working principle for the label-free chemical and biological sensing applications [3–9]. These investigations have been on planar substrates such as glass or sapphire substrates.

In addition to the benefits of LSPR of metallic nanostructures on planar substrates discussed above, using optical fiber as platform has been investigated [10–16] for more advantages including compact and high portability and immunity to electromagnetic interference. Sensors based on ordered arrays of nanoholes fabricated on the gold-coated optical fiber tip using focused ion beam (FIB) have been reported [13,14]. In our previous publication [15], we have reported high sensitive LSPR biochemical sensing based on transmission spectra of ordered array of metallic nanodots fabricated on the optical fiber tip using electron beam lithography (EBL).

Previous attempt for reflection setup for LSPR fiber-optic sensor [16] has utilized random gold nanoparticles produced by annealing thin gold film deposited on the end face of a multimode optical fiber, which has poor uniformity and reproducibility. In this work we report high sensitive LSPR biochemical sensing based on reflection spectra of ordered arrays of metallic nanodots fabricated on the optical fiber tip using EBL. Compared to the transmission setup, which requires optical alignment from free space to fiber, the reflection spectra measurement has additional advantages such as: (1)Very easy to use, no optical alignment is needed, (2) remote sensing capability as optical fiber probe can go into human body or placed in harsh environments, and (3) in vivo detection of antigens and biomolecules. Moreover, optical fiber tip probe could be mass produced cheaply by nanofabrication technology (like molding) and made disposable. Gold was chosen as the metal for forming the nanodots array for the fiber tip sensors as it demonstrates high surface plasmon excitation and bio-compatibility, and is resistant to oxidation degradation.

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2. Experimental

2.1. Preparation of gold nanodots array on optical fiber tip

The fiber-optic based gold nanodots array LSPR sensors were fabricated by patterning of subwavelength gold nanodot arrays on the cleaved tips of optical fiber using EBL and reactive ion etching (RIE) with Ar^{2+} ion. The preparation of the optical fibers used in this experiment involved stripping the polymer buffer with a fiber stripper and cleaving the stripped fiber with a fiber cleaver to obtain a smooth mirror-like surface which is perpendicular to the fiber axis. The single-mode fiber employed in this work has a core diameter of 9 μm, and a cladding diameter of 125 μm. A Denton sputter system was used to coat the fiber tips with 55nm of gold.

Electron beam (e-beam) resist (ZEP 520A, Zeon Chemicals) was coated on the fiber tip by dipping in the diluted ZEP solution, followed by mechanically vibrating the fiber tip to shack off extra liquid resist. The resulted thickness of electron beam resist on the optical fiber tip is highly depended on the ZEP dilution ratio. The resist was hardened by baking in a 120°C oven for 30 minutes. An EBL system, which was converted from a field emission scanning electron microscope (FE-SEM), was used to create the nanodot arrays in the e-beam resist. The voltage used was 30 kV and the dose was 70 $\mu C/cm^2$. After e-beam exposure, the fiber tip was developed by dipping in the e-beam resist developer (ZEP N50) for 1 minute, followed by DI water rinse for 1 minute. The sample was dried by a pure nitrogen stream and baked in the oven at 120°C for 30 minutes for dehydration and hardening. Then we flood exposed the e-beam resist on the fiber tip using 5kV electron beam to harden the resist. The nanodots array pattern in the e-beam resist was transferred to Au layer by RIE with argon ions. The etch time was 3.5 minutes with 200 W platen power and Ar gas flow rate of 20 standard cubic centimeters per minute (sccm). The etch time was set to over etch the gold film to make sure the gold between the nanodots was clearly removed. The remaining ZEP film was striped by dipping in the ZEP remover for overnight.

The SEM image of the gold nanodots array on optical fiber tip is shown in Fig. 1(a). The fabricated area of gold nanodot array is a 40 μm by 40 μm square. The periodicity of the array is 400 nm; the size of the Au nanodots is 190 nm in diameter, and 55 nm in height. The circle in the fiber tip is attributed to the e-beam resist film thickness variation due to edge bead. The ZEP film thickness inside of the circle is uniform. The diameter of the uniform thickness area is found to be around 60-80 μm, which is large enough to cover the optical fiber mode, which has a diameter of ~10μm. Figure 1(b) shows the zoom-in image of Au nanodot array on the optical fiber tip.

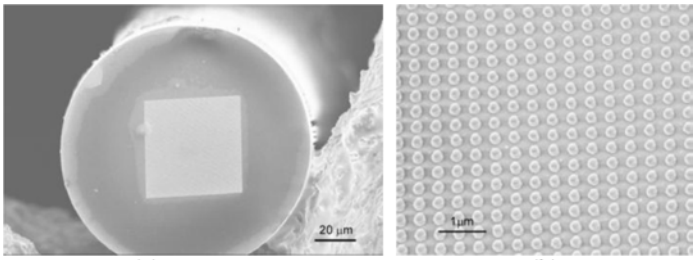

Fig. 1. Scanning electron micrographs of a gold nanodot array on an optical fiber tip. (a) Overview of the optical fiber end facet, and (b) the gold nanodot array on the optical fiber facet.

2.2 Measurements setup

Figure 2 illustrates the setup for characterizing the optical fiber tip LSPR sensors based on spectra reflection. The light source used is a tungsten halogen white light source LS-1 (Ocean Optics Inc., USA.). The light was coupled into a 2X1 50/50 singlemode fiber coupler (F-CPL-

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S12635, Newport Corp., USA). The fiber probe was spliced to the single arm of the fiber coupler by a fusion splicer. The return light was detected by a USB-2000 spectrometer (Ocean Optics Inc., USA).

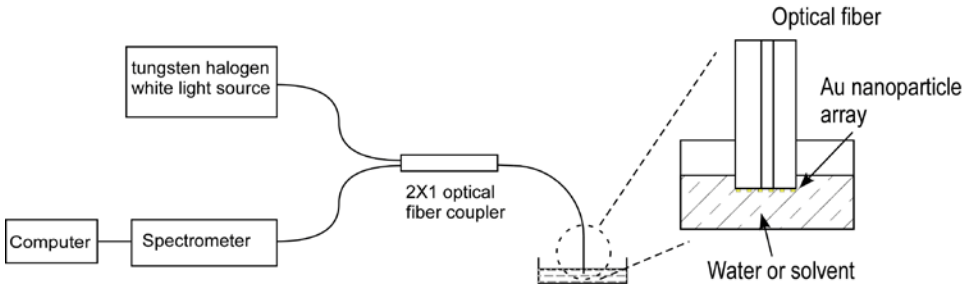

Fig. 2. Optical setup for the fiber tip LSPR sensor based on reflection spectra measurement.

To get a reference reflection spectra, we fusion-spliced a piece of optical fiber with both ends freshly cleaved to the single arm of the singlemode optical coupler. The reflection light spectra was measured and saved as a reference. The dark spectrum was obtained by turning off the tungsten halogen light source and room light. The measured reflection spectra (M_λ) of the fiber tip sensor probe was obtained by the following equation [Eq. (1)],

$$M_\lambda = \frac{S_\lambda - D_\lambda}{R_\lambda - D_\lambda} \times 100\% \quad (1)$$

where S_λ is the sample intensity at wavelength λ, D_λ is the dark intensity at wavelength λ, R_λ is the reference intensity at wavelength λ.

2.3 Reagents and materials

Singlemode silica optical fiber (SMF-28) was obtained from Corning Incorporated, USA. Acetone, isopropyl alcohol (IPA), methanol, and ethanol were purchased from Fisher Scientific, USA. All of the chemicals used here were of analytical reagent grade. Biotinylated PEG alkane thiol was purchased from Nanoscience Instruments, USA. Affinity purified streptavidin was purchased from Thermo Scientific, USA. All the biological reagents were kept at 4 °C. All aqueous solutions were prepared with purified water with a specific resistance of 18 MΩ-cm. Piranha solution (30% H_2O_2 / 70% H_2SO_4) was used in chemical cleaning process. Piranha solution is highly hazardous and reactive and may explode on coming into contact with organic solvents. Extreme precaution should be taken at all time.

3. Results and discussion

The strongly enhanced localized surface plasmon resonance in gold nanostructures excited by direct light illumination makes them excellent light scatter and attenuator at wavelength of visible and near infrared light. Two different mechanisms contribute to extinction: absorption and scattering. In the transmission measurement, both scattering and absorption of gold nanostructures contributes to the total transmission spectra loss in the LSPR condition. However, for the spectra reflection measurement, only scattering light can be collected and detected. Therefore, high scattering cross-section is the criteria for the design of gold nanostructures for reflection spectra based LSPR sensing devices. As discussed theoretically in the reference [17], the gold nanostructure optical properties, such as LSPR resonance wavelength, the extinction cross-section, the scattering cross-section, the absorption cross-section, and the ratio of scattering efficiency to the absorption efficiency depend on the gold nanostructure dimensions. For small nanoparticles (diameter smaller than ~20nm), the optical absorption is dominated, while for larger nanoparticles, the scattering become dominated. For example, as the diameter of the gold nanospheres increases from 20 nm to 80 nm, the magnitude of extinction as well as the relative contribution of scattering to the extinction

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rapidly increases [17]. The variation in the plasmon resonance wavelength maximum of gold nanospheres also depended on their dimensions, which can be useful in engineering of the LSPR sensors to operate in a desired wavelength window.

To get strong spectra reflection, the dimension of the gold nanodot on the optical fiber tip was designed to be in the range of 180 to 200nm in diameter, 400nm in periodicity, and 55nm in height. The transmission and reflection spectra of the optical fiber tip LSPR sensor are shown in Fig. 3(a). It is observed that the peak of the reflection spectra is blue shifted by 2.8nm, compared to the peak of transmission spectra. This can be attributed to the different peak plasmon wavelength of scattering and absorption spectra for the gold nanostructures. To numerically calculate the Au plasmonic scattering and extinction of the Au nanostructure, we conducted the electromagnetic simulations using commercial finite-difference time-domain (FDTD) software (Lumerical Solution Inc., Canada). The spectra were calculated at normal incidence, i.e., the incident plane wave propagated along the z axis, and the x-y plane is parallel to the surface of glass substrate. The incident light is polarized along the x-axis. We use periodic boundary conditions in the x and y directions, and absorbing boundary conditions, perfectly matched layer (PML), in the z direction. Drude-Lorentz model was used for the dispersive properties of gold. As shown in Fig. 3(b), the calculation results indicate that the plasmon scattering peak wavelength is blue shifted by 7.3nm, when compared to the total extinction spectra, which is the sum of the scattering and absorption spectra. We also note that the amount of blue shift is not matched to the experiment result, which can be attributed to the fabrication imperfection.

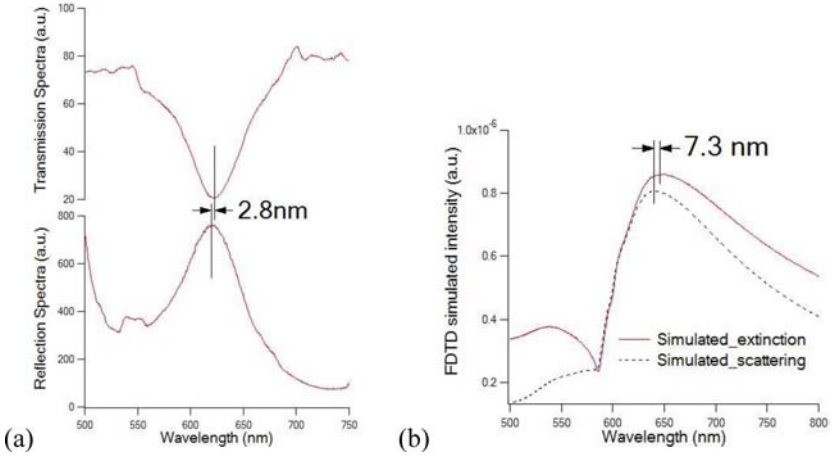

Fig. 3. (a) The transmission spectrum (top) and reflection spectrum of the fiber tip LSPR sensor in the air, and (b) the calculated spectra for extinction (solid line) and scattering (dash line) for the LSPR on the gold nanodot array.

The spectra respond of the reflected light for changing refractive index of the medium surrounding the fiber tip sensor was investigated by taking reflected light spectra of the fiber sensors in air (1.000), methanol (1.329), water (1.333), acetone (1.359), ethanol (1.362), and isopropyl alcohol (1.378). Three of these reflection spectra are shown in Fig. 4(a). One can observe in Fig. 4(a) that there was a large changes (~70nm) in the reflection spectra maximum wavelength as the medium surrounding the optical fiber tip sensor was changed from air to methanol, and there was a relatively small change (~10nm) in the reflection spectra maximum wavelength as the medium changed from methanol to isopropyl alcohol. The amount of the reflection spectra maximum wavelength change is linearly proportional to the refractive index change surrounding the fiber tip sensors. Experimentally measured relative shifts of the reflection spectra peak position of the optical fiber tip sensor as a function of the refractive index of the medium surrounding the fiber tip sensors is shown in Fig. 4(b), in which a linear line can be fitted to the data. This demonstrates high sensitivity (~195.72 nm/RIU) of this sensor for detecting changes in the bulk refractive indices for different chemicals surrounding

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the sensor. The sensitivity of the optical fiber tip LSPR sensor based on spectra reflection is very close to the sensitivity based on the transmission spectra measurement (195.84 nm/RIU) [15].

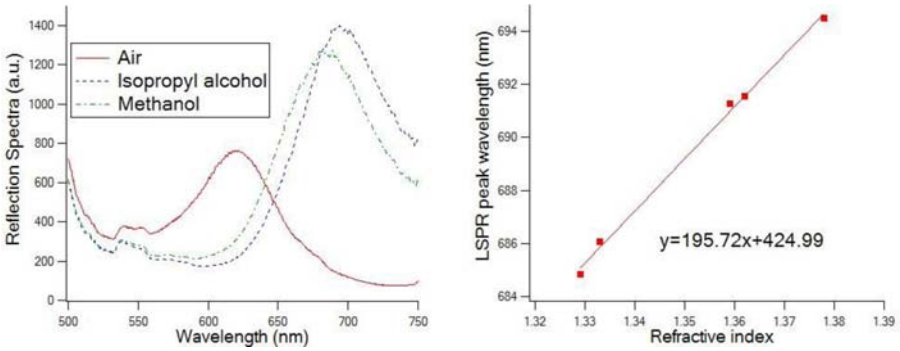

Fig. 4. (a) Measured transmission spectra for the fiber sensor in various solvents. (b) Dependence of the LSPR peak wavelength on the index of refraction of the solvents, methanol (1.329), water (1.333), acetone (1.359), ethanol (1.362), and isopropyl alcohol (1.378).

To demonstrate the bio-affinity sensing capability of this spectra reflection based optical fiber tip LSPR sensor, we applied these sensors to detect the presence of bimolecular such as biotin and streptavidin [18,19]. The fiber tip LSPR sensors were prepared for biosensing in the following way. First, the surface of the Au nanodots was cleaned two times by soaking in piranha solution for one minute and then rinse with DI water for 2 minutes. Then the optical fiber tip LSPR sensors were functionalized with biotinylated PEG alkane thiol (concentration of 1 mM in anhydrous ethanol) for 24 hours in the room temperature. A monolayer of biotin was deposited onto the gold nanodots surface via a covalent bond between biotinylated thiol group and the Au. After that, the sample was rinsed by DI water to remove the unbound molecules and dried by nitrogen stream. The doted curve in Fig. 5 shows reflection spectra of the biotin-functionalized Au nanodots measured at this step. The functionalized optical fiber tip was incubated in 200μl of 10^{-7} M streptavidin in water at room temperature for one hour. Then the fiber tip LSPR sensor was rinsed by DI water and dried by nitrogen. Dash-dot curve in Fig. 5 shows the reflection spectra of the optical fiber tip sensor measured after the binding of the streptavidin.

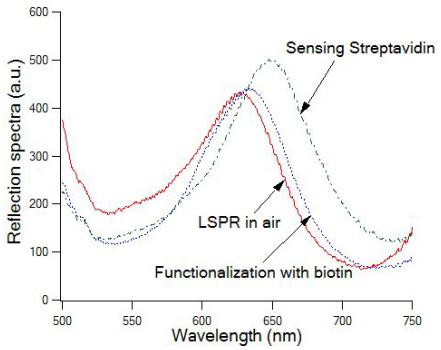

Fig. 5. The reflection spectra of the Au nanodots array on the optical fiber end facet when it is in air (red solid curve), functionalized with biotin (blue doted curve), and bound with streptavidin (green dash-dot curve). Plasmonic peaks shift due to the functionalization of biotin and specific binding of streptavidin can be clearly observed.

One can observe in Fig. 5 that there were substantial shifts in the optical reflection spectra as the fiber tip sensor was reacted with biotin and then with streptavidin. A shift of ~8 nm was observed on the addition of biotin to the gold nanodot surface, and a shift of ~15 nm was observed on the binding of streptavidin to the biotin coated on the fiber tip LSPR sensor.

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These results demonstrate the feasibility of the optical fiber tip LSPR sensor based on gold nanodot array for the detection of biomolecules and the potentiality for in vivo detection of antigens.

4. Conclusions

In summary, we report the fabrication and characterization of the reflection spectra based ordered gold nanodot array LSPR biochemical sensing on optical fiber tip. The fiber tip sensor with reflection setup is very easy to use with no alignment needed, and can be used for in vivo detection as optical fiber can be inserted into human body. In the future research we will investigate this fiber tip probe for surface enhanced Raman spectroscopy (SERS) sensing for chemical and biological applications. High sensitivity (195.72 nm/RIU) of this sensor for detecting changes in the bulk refractive indices has been demonstrated, as well as label-free affinity sensing of bio-molecules using biotin/streptavidin as receptor/ analyte.

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