Fiber-optic coupler based refractive index sensor and its application to biosensing

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A simple and highly sensitive biosensor based on a fiber-optic coupler is developed. The change of refractive index due to biomolecular interaction on the surface of the coupler can be detected as the change of the transmission power. The sensitivity of the sensor is evaluated to be a noise level equivalent to a refractive index variation of $4 \times 10^{-6}$. The binding of streptavidin is detected to be concentration dependent over a range of 0.5–2 µg/ml, by immobilizing biotin on the coupler surface via aminosilan treatment. This sensor allows the construction of a low-cost, portable, and label-free biosensing system. © 2007 American Institute of Physics. [DOI: 10.1063/1.2783278]

Biosensors utilizing biomolecular interactions have been widely used in biomedical diagnosis and environmental monitoring, and the majority of these are based on the measurement of the absorbance or fluorescence of a labeled molecule. Meanwhile, label-free biosensors as typified by surface plasmon resonance (SPR) sensors have been well established as laboratory tools for studying the processes of biological binding or adsorption, but their uses have been limited in field applications such as point of care (POC) diagnosis, environmental monitoring, and food safety testing. For further penetration of use of label-free biosensors in field applications, label-free biosensors are required to have higher sensitivity, lower price, and smaller size and provide faster measurement and easier examination procedures. Label-free sensing is a suitable technology for meeting these requirements in terms of reducing the test reagents consumed and shortening the experimental procedures, and fiber-optic biosensors make it possible to realize a small sensing system. Hence, fiber-optic label-free biosensors based on SPR, long period grating, and Fabry–Pérot interferometer, have been developed. These are basically based on measuring a refractive index change due to the binding of biomolecules.

Fiber-optic couplers are widely used in optical fiber communications to split optical signals between two fibers, or to combine optical signals from two fibers into one fiber. They are fabricated by fusing and tapering two fibers together. It has long been known that the transmission spectrum of a fiber-optic coupler is strongly affected by the refractive index of the surrounding medium because the evanescent field is generated on the fiber surface at the fused region. Thus a fiber-optic coupler can be used as a refractive index sensor. Since coupler sensors do not require fiber treatments such as Au coating, UV exposure, or etching, fiber-optic biosensors can be fabricated at low cost. The application of fiber-optic couplers to biosensing has been proposed and preliminary demonstrated, but the performance of fiber-optic coupler based refractive index sensors has not been fully investigated. This letter describes the experimental evaluation of sensitivity of the specially fabricated coupler sensor and the demonstration of protein detection.

Figure 1 shows the experimental setup and conceptual schematic of coupler sensor. A coupler made by two identical fibers shows sinusoidal transmission spectrum, being used as a wavelength division multiplexing (WDM) coupler. When a ligand is immobilized on the surface of a coupler, the change of refractive index in the evanescent field due to the binding of an analyte to the ligand shifts the transmission spectrum, and thus can be detected as the change of transmission power at a fixed wavelength. In the experiment, a laser (HP 8168) tuned at a 3 dB splitting wavelength in the C or L band was used as the light source to obtain maximum sensitivity. The transmitted light was received by a photodiode (New Focus NF Corp. LI5640), and the signal was collected by a lock-in amplifier (NF Corp. LI5640). As shown in Fig. 2 WDM coupler was specially fabricated to have the transmission spectrum with a peak-to-valley pitch of 35 nm in air. The peak-to-valley pitch is narrower than that of the standard coupler for optical fiber communications, so as to increase the sensitivity of the sensor. A fabricated coupler was made by the standard silica-based single-mode fibers, and mounted it in a case with 60 mm length. The diameter of the coupler at the fused region was 9 µm. In water, the transmission spectrum shifted considerably, but no incidental loss was observed.

The sensitivity of the coupler sensor was evaluated using ethanol-water solutions with different ethanol concentrations.

Figure 1. (Color online) Conceptual schematic of coupler sensor and experimental setup.
The coupler sensor was set in a thermostatic oven, and the sensor responses were obtained when the injected solution was changed from water to ethanol-water solution of 0.1, 1, or 10 wt%. The refractive index of the solutions was checked by the minimum deviation method at a wavelength of 1530 nm. The relationship between the sensor responses and the variation of refractive index is plotted in Fig. 3. The linear response was verified for a refractive index variation up to the order of $10^{-2}$. The noise standard deviation for 5 min corresponded to a refractive index variation of $4 \times 10^{-6}$ for a measurement time of 1 s. The likely noise sources include laser intensity variations due to drive current variations and temperature fluctuations and noises in electronics due to source noises and temperature fluctuations. No effects of the flow of a test solution and laser frequency drifts were observed. This sensitivity is comparable to or better than the published sensitivity values for fiber-optic biosensors, and can be improved by narrowing a peak-to-valley pitch of a coupler sensor. A temperature stabilization system of a test solution or a temperature-drift compensation scheme is essential to measure a refractive index variation less than $10^{-4}$.

To demonstrate protein detection, avidin-biotin coupling was used. First, the coupler was cleaned and then silanized with 3-aminopropyltrimethoxysilane (Shin-Etsu Chemical Co., Ltd.). Next, the silanized coupler was immersed in 2 mM sulfo-NHS-LC-biotin (Pierce) for 90 min at room temperature. Finally, the biotinized coupler was immersed in the buffer solution of pH=7 (Wako Pure Chemical Industries) for 5 min to check the stability, and then the buffer solution was replaced by a solution of streptavidin (Amersham) with a concentration of 0.5, 1, or 2 μg/ml at room temperature. Figure 4 shows the time profile of avidin binding to biotin. The binding response was almost proportional to the avidin concentration although the fluctuation of output due to temperature drift was observed. The sensor output was maintained constant when the coupler was rinsed with the buffer solution after the binding of avidin. Streptavidin used in this experiment was Cy3 labeled to verify the binding response. The fluorescence microscope images of couplers after avidin-binding experiments are shown in Fig. 5. The dependence of fluorescence intensity on avidin concentration is consistent with that of the coupler sensor responses.

In conclusion, we have developed a fiber-optic coupler based refractive index sensor and evaluated the sensitivity of it to be $4 \times 10^{-6}$ in refractive index. The detection of avidin has also been demonstrated by immobilizing biotin on the coupler. This simple and highly sensitive fiber-optic biosensor is suitable for use in POC diagnosis, environmental monitoring, and food safety testing.

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