Real-time measurement with fiber optical surface plasmon resonance sensor for biochemical interaction analysis

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ABSTRACT

In this paper we report a fiber optical sensor system based on surface plasmon resonance (SPR) with real-time response for biochemical interaction analysis. The fiber sensor is produce from a multi-mode fiber with plastic cladding. To facilitate the measurement, a software program is developed which integrates the data acquisition and processing for real-time feedback. Polynomial fitting is implemented to smooth out the noise in transmission ratio and a spectral resolution of 0.2 nm is achieved. Ethyl alcohol and water mixtures of different concentration are measured to demonstrate the system real-time ability. This work is essential for the development of a compact, real-time fiber SPR biosensor.

Keywords: Surface plasmon resonance; fiber sensor; Real-time response; integrated measurement system

1. INTRODUCTION

Fiber optical surface plasmon resonance (SPR) sensor was invented by R.C. Jorgenson and S.S. Yee in 1983 as a novel chemical sensor. Currently, with the need for minimization and automation of detection in bio-medical applications, fiber optical SPR sensors have attracted much interest for its compactness and the flexibility. Fiber optical SPR sensor has many features, including label-free detection, high selectivity, low cost and immunity to electromagnetic interference. Since fiber SPR sensor can conduct the measurement in situ and process data remotely, it may be useful in many potential applications, such as environmental monitoring and medical detection. To achieve this, real-time response is necessary for a measurement that feedback the mass change on the surface instantly in a biochemical interaction. In this paper, we describe our work toward a compact, real-time response fiber SPR measure system.

2. PRINCIPLE

Surface plasmon resonance measurement utilizes an evanescent field to sense the change of the environmental refractive index. Meanwhile, an optical fiber confines light by the total internal reflection, and the evanescent field is along the interface of the fiber core and cladding. Apparently, integrating the surface plasmon resonance region along the fiber cylinder surface will make a compact probe which is useful in medical and biological research. The principle of multi-mode fiber optical SPR sensor is shown in Fig. the real and dashed lines depict the track of light ray of different incident angle. Incident light with angle greater than critical angle will be confined inside the cylinder. Since the noble metal film is coating on the cylindrical surface, the free electron will be driven by the evanescent field in the plane and conduct a collective oscillation which is a plasmonic wave. Whenever the wave vector of the incident light matches that of the surface plasmon, energy will transport from input light to the plasmonic wave. An absorption dip will show in the calculated transmission ratio. This dip is sensitive to the change of refractive index that may associate with the mass change on the fiber surface. This mass change may be a result of affinity reaction.

Fiber SPR sensor may operate in three modes: angle interrogation, amplitude interrogation, and wavelength interrogation. Angle interrogation is derived from prism configuration by change the incident angle of laser light. However, it is hard to keep the fiber straight and confine the light at desired angle. Particularly, this will fail under a remote measurement setting. Amplitude interrogation will measure the fiber loss with light of single
Figure 1: The principle of multi-mode fiber SPR sensor. The real and dashed lines depict the track of light ray of different incident angle.

wavelength. Whenever the environmental refractive index changes, the loss will decrease or increase which is easy to measure. However, it will lose much information about the resonance, such as whether the loss change is from a surface plasmon resonance. We preferred the wavelength interrogation which will precisely measure the resonance wavelength with a fiber spectrometer. The theoretical model of the fiber optical SPR sensor has been studied in detail. Here we narrate the calculation shortly.

\[
P_{\text{trans}} = \frac{\int_{\frac{\pi}{2}}^{\theta_c} (R_N(\theta) + R_s(\theta))P(\theta)d\theta}{2 \int_{\frac{\pi}{2}}^{\theta_c} P(\theta)d\theta}
\]

where \( N(\theta) = D/tan\theta, \theta_c = \sin^{-1}(n_c/n_1), P(\theta) = n_2^2 \sin \theta \cos \theta/(1 - n_2^2 \cos^2 \theta)^2, \) \( N(\theta) \) is the number of reflections performed by the ray with incident angle \( \theta \), while \( L \) and \( D \) represent the length of the sensing region and the diameter of fiber core; \( \theta_c \) is the critical angle of the fiber whereas \( n_c \) and \( n_1 \) are the refractive index of the fiber cladding and core. \( P_\theta \) presents the modal power as a function of the incident angle \( \theta \). \( R_p \) and \( R_s \) are the reflection ratio of p- or s- polarized ray.

In our configuration we don’t distinguish the light in p- or s- polarization. Therefore the light of s- polarization is included in the spectra which will pad the curves. According to Eq. 1, the curve of the reflection ratio is not a valley with symmetric shape, but a result of mixed system with broadband light ray in various incident angles. This theoretical model establishes a basement for the data fitting scheme in our software development.

3. SYSTEM IMPLEMENTATION AND INTEGRATION

Here we show our experimental configuration and the measurement system which is dedicated for the fiber optical SPR sensor. Then we discuss the data fitting scheme and the real-time performance of the fiber sensor system.

3.1 Experimental configuration and measurement

The experimental configuration is shown in Fig. 2a. The fiber optical SPR system comprise of a fiber SPR sensor and a measurement system. The fiber sensor is fabricated from a multi-mode fiber with numerical aperture 0.39 produced by Polymicro Inc. The diameter is 600 \( \mu \)m coated with plastic cladding. This plastic coating can be easy strip down and cleaned with acetone solution. The metal film is deposited with an ion sputtering vapor system. This device is a common one for plane target and the chamber vacuum is below 8.5 \( \times \) \( 10^{-3} \)Pa. We designed a gear commutator which rotates the fiber above the sputtering disk. Therefore, we achieve a uniform coating on the fiber cylindrical surface. The thickness of the deposit film is controlled by the exposed time. Since it is a round fiber, we cannot have an accuracy thickness measurement directly. The thickness of silver film is estimated about 45 nm. Later a thick film is deposited at the fiber end which acts as a reflection mirror. The red circle if Fig 2a present a model of affinity interaction for future development.

The light source is an Oceanoptics DH-2000-BAL with high luminescent tungsten halogen bulb. The spectrum is from 450 nm to 1100 nm, shown in Fig. 4a below. The light is delivered to the sensing region by a 600 \( \mu \)m combiner and the transmission spectrum is measured by a spectrometer. The spectrometer is a portable model.
USB4000 from Ocean optics. This spectrometer has 3648 pixels with measurement range from 345 nm to 1043 nm, cover the surface plasmon resonance region of interesting. Spectral data are collected to the computer through USB port and the transmission time can be ignored.

Fig. 3 shows a group of experimental results with water and ethanol mixture of different concentration. The transmission ratio is similar and greater than 50%. While the ratio of alcohol increases, the refractive index of solution increase and the resonance wavelength move toward the long wavelengths.
3.2 Integrated measurement environment

Based on the system hardware above we can perform a basic fiber SPR measurement with the Spectrasuite software developed by Oceanoptics Inc. Since Spectrasuite is developed for general-purpose usage, and not dedicate for SPR measurement with real-time response, the measurement process is cumbersome. Thus we developed an integrated measurement environment with real-time spectrum display and result show. We prefer java as the development language. The primary reason is that the spectrometer has a native java driver and there are many mature libraries which may help the software development. Java is also well known for its cross platform ability. This may help in the software mitigation for the potential industrial application.

The software interface is shown in Fig. 4a. The main panel is divided into six zones, including a control panel and five spectrum displays. There are a dark spectrum, a source spectrum, a transmission spectrum, a reflection ratio display and the evolution of the resonance wavelength. The dark spectrum and the source spectrum are in the bottom row. The dark spectrum is the background electronic noise from the liner CCD of spectrometer and environmental light. Whenever the fiber optical SPR sensor is immersed in the analyte solution, the transmission spectrum is measured repeatedly, shown in the upper left corner. The upper center display is the transmission ratio with definition.

\[
R = \frac{I_{\text{trans}} - I_{\text{dark}}}{I_{\text{source}} - I_{\text{dark}}}
\]  

(2)

The original spectra are truncated to eliminate the numerical instability caused by the small light intensity in Eq. 2. The reflection ratio chart (upper center panel) is a typical fiber SPR curve with a broad FWHM diagram, and the reflection ratios are greater than 0.5. The blue line is the data fitting results and we will discuss below. The chart in the upper right corner is the time-evolution of the sensing interaction. The red points represent the resonance wavelength after the data fitting procedure. In this chart the resonance wavelength changed in step shape as we add alcohol to the purified water. The control panel is in the bottom right which contains the control buttons and the output information.

Figure 4: (a) Snapshot of the integrated measurement environment. The upper right panel presents the evolution of the resonance wavelength for biochemical affinity analysis. (b) Resonance wavelength before and after data fitting process.

As shown in Fig. 4a, with this software we achieve an online measurement with optical fiber sensor which is remarkable for a biochemical interaction analysis. In the software development, the main issues that may affect our measurement are the real-time response ability and the data fitting process, and we discuss below.

3.3 Real-time response ability

The data acquisition involves a setting of CCD integration time which should adapt to the measurement. The overall integration time should small than that of the timer setting which is determined by the updating frequency.
The real-time response may be slowed by the graphical toolkit and the data fitting procedure if we handle it carelessly. The graphical user interface is based on JFreechart which is a famous free Java chart library released under the terms of the GNU LGPL. It is a rich-featured chart library. Since whenever the chart dataset is updated, the program should repaint these charts completely. This may be limited by the “frames per second” rate that we can achieve with the graphical library. JFreechart can afford a refreshing speed of once per second and updating multiple times per second may results in high CPU load. Actually, the data fitting process is very quick since it is a matured algorithm.

In common a biochemical interaction will last for several minutes to tens minutes. Therefore we may update the resonance wavelength every second. Consequently, this will get over hundreds data points which is enough for the data process. Moreover, JFreechart is on developing which may improve its real-time response ability in the future. So, this graphical library is enough to satisfy the real-time requirement for SPR analysis.

### 3.4 Data fitting for the resonance wavelength

Since the fiber optical SPR sensor based on multi-mode fiber is a mixture system with light in various wavelengths and incident in different angles, the transmission ratio is quite different from a simple Gaussian shape. Therefore, we prefer a general polynomial fitting scheme. The data region is around the valley position with a length of 300 pixels, about 70 nm. Then we recalculate the value at each pixel and get the absorption peak position. The fitting procedure shows quite well result in a 95% confidence and the fitting curve keeps the data shape and smooth out the fluctuation.

![Fig. 4b](image)

Fig. 4b shows the wavelengths before and after the data fitting procedure. The dotted blue line represents the minimum position among the ratio which is from a peak find function provided by Oceanoptics. The red points are the resonance wavelengths fitted with polynomial function. Since data fitting is a key issue in our sensor and it provides the ultimate resonance wavelength for the biochemical interaction analysis, we would like have a detailed discussion about our experience. We have tried the average method. Multi-time average method will decrease the real-time response ability. Meanwhile, the fluctuation in reflection ratio chart cannot be suppressed by average because of the intrinsic properties of the spectrometer. For a common measurement, we can average two results to reduce the systematic error. The data fitting procedure may incorporate an interpolation algorithm to increase to resolution of the sensor. The premise is that the fiber sensor system should have a good dynamic resolution than that of the spectrometer. The resolution can be estimate by the variation of the time series of resonance wavelength which correspond to the minimal RI change that the fiber sensor can measure. The variation of the resonance wavelength may be influenced by many factors, such as film thickness, film pattern, and light source stability et al. Currently, the micro-fluid system is not implemented and the experimental measurement are conduct in simple configuration which increase the experimental variation.

### 3.5 Improvement in the future

Since the intensity of source light may decrease in a long-term monitor and the spectrum changes, we may add another spectrometer to synchronously measure the spectrum of light source. The fluidic system is in our plan. Another issue is to improve the system resolution with interpolation and algorithm improvement.

### 4. APPLICATION FOR CHEMICAL AND BIOCHEMICAL INTERACTION

Fig. 5 shows the processing result of the dynamic measurement. The resonance wavelengths are averaged with data in the middle of step region. The refractive index of mixture is interpolated based on the volume ratio of alcohol. The sensitivity of fiber sensor is 1428 nm/RIU. Therefore, a corresponding resolution in RI is about $1 \times 10^{-4}$ RIU. For a typical biochemical interaction with 0.002 RI changes, the data interval in y-axis is near 20 which are decent for a data processing. In Ref. [10] the authors had made a measure of bio-chemical interaction with the fiber SPR sensor in a similar configuration. Although the resolution of fiber SPR sensor is much low than that of a prism configuration, this gap may be decreased or filled by some special design, such as fiber SPR sensor with photonic crystal fiber. The characteristic of fiber optical SPR sensor with in situ measurement and compactness may meet some special application, for example, a fast detection in vivo.
5. CONCLUSION

We construct a fiber optical SPR system and build an integrated measurement environment to record a real-time response for biochemical interaction analysis. The fiber optical SPR sensor is measured with water and alcohol mixtures of different concentration. The system real-time performance and data processing are discussed in detail. This integrated fiber SPR measure system will help to realize a minimized SPR biosensor with in situ and real-time measurement ability.

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