Monolayer Detection of Biochemical Agents Using Etched-Core Fiber Bragg Grating Sensors

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Abstract—It is demonstrated that the etched-core fiber Bragg grating sensor can be used to detect down to a monolayer of biological and chemical agents immobilized on the surface of the fiber. Theoretical models based on calculating the effective index of the surrounding medium in the presence of immobilized layer(s) were developed and confirmed experimentally by immobilizing a monolayer of 3-aminopropyl-monoethoxydimethyl-silane (APMDS) and polymers of 3-aminopropyl-triethoxysilane (APTES) on the surface of the fiber. The immobilization of APMDS and APTES is confirmed by carrying out hybridization of DNA. We also demonstrate that the sensor can be used to understand and optimize biological and chemical processes.

Index Terms—Biological sensor, chemical sensor, evanescent field, fiber Bragg grating (FBG), monolayer detection.

I. INTRODUCTION

Fiber Bragg grating (FBG) sensors have attracted considerable attention in medical and environmental diagnostics due to their small size, high sensitivity, multiplexing ability, and the possibility of distributed measurements [1]. FBG sensors based on evanescent wave interactions with the external environment are attractive because they transduce the change of index in the surrounding medium to a change of reflected wavelength that can be measured easily. In order to make an effective sensor that can detect small changes in the environment, it is important to increase their sensitivity. In our previous work, we have demonstrated a highly sensitive biological and chemical sensor by etching the core of an FBG and using the evanescent field to probe the index of the surrounding medium while measuring the change of the Bragg wavelength in situ [2]–[4]. The sensor had a maximum sensitivity of 1394 nm/RIU providing an index resolution of $7 \times 10^{-6}$ to changes of the index of refraction of the surrounding liquid medium [2]. The sensor surface was further used to detect the hybridization of DNA [3]. Single stranded DNA oligonucleotide probes of 20 bases were immobilized on the surface of the FBG using the glutaraldehyde chemistry, and the hybridization of complimentary target single stranded DNA oligonucleotide was monitored in situ and successfully detected. In other work, we demonstrated that the sensitivity of higher order modes that exist in an etched-core FBG sensors were larger than that of the fundamental mode for the same index of the surrounding medium [4]. It was also shown that the change in wavelength for the higher order mode was equal to that of the fundamental mode when: 1) the period of the grating was altered by physically stretching the fiber or by thermal expansion or 2) with a change of the core index. This property was used to differentiate between the change in wavelength from temperature and stress from the change in wavelength due to the change in refractive index of the surrounding medium.

In this letter, we report that the sensor is sufficiently sensitive to detect and differentiate the number of chemical or biological layers that are deposited on the surface of the fiber. A theoretical model is developed and verified experimentally using the immobilization of 3-aminopropyl-triethoxysilane (APTES) and 3-aminopropyl-monoethoxydimethyl-silane (APMDS) on the surface of the fiber and the in situ monitoring of the Bragg wavelength shift following different chemical steps. The immobilization of APMDS and APTES was further confirmed by carrying out complete DNA hybridization experiments.

II. THEORETICAL MODEL

Previously we have reported on a graphical method to calculate the Bragg wavelength for a given fiber diameter and surrounding medium index condition [2], [3]. Using this approach, the sensitivity of the fiber to change in the index of the surrounding medium can be calculated. However, this method calculates only the change of the surrounding liquid index. In the case where mono- or multi-layers are immobilized on the fiber (as in the case of the hybridization of DNA), the graphical method was extended by calculating the effective index of the surrounding medium in presence of an immobilized layer on the surface of the fiber. The calculation was done directly using the finite-difference method as is shown in Fig. 1. The optical mode of the fiber was calculated for the fiber with the biological/chemical layer added and using a very fine grid (at least ten points in the immobilized layer). The modal index was extracted. In order to calculate the effective index of the surrounding medium, the biological/chemical layer was removed and the mode was calculated again by adding a small perturbation to the index of the surrounding medium until the modal index calculated matched with the previously calculated modal index. The change in Bragg wavelength was calculated using the change in effective index in the presence of the biological or chemical layer(s) on the fiber and multiplying...
Fig. 1. Schematic of the calculation for the effective index of the surrounding medium in the presence of thin layers of chemical or biological agents on the surface of the fiber.

III. EXPERIMENT

The capability of detecting single layer versus multiple layers and the verification of the theoretical model were carried out by immobilizing APTES and APMDS on the surface of the fiber. Previously we had used APTES immobilization to attach glutaraldehyde to the fiber surface in our DNA hybridization experiments. It has also been shown that while APTES produces polymers with 3–8 chains on the surface of glass, APMDS led to a monolayer deposition approximately 10 Å thick [5], [6]. The measurement methodology is described in [3] and consists of an erbium-doped fiber amplifier as a broadband light source, a 3-dB coupler, the etched core FBG sensor as the device under test, and a high-resolution optical spectrum analyzer to detect the change in wavelength of the reflected light. A measurement accuracy of 1 pm in wavelength change was obtained by using an optical spectrum analyzer with 7-pm resolution and by curve fitting the reflected spectra.

The sensors used for this experiment were etched to a core diameter of 5 μm leading to a sensitivity of 28 nm/RIU at the index of ethanol. The sensitivity was measured using ethanol and water as the surrounding mediums. The core diameter was precisely controlled by measuring the Bragg wavelength as the sensor was etched [2] in buffered oxide etch. Ethanol was used as the surrounding medium for the experiment. Silanization of the fiber grating surface was performed by immersion in fresh 1% APTES and 1% APMDS in ethanol for 30 min at room temperature. The temperature was monitored during the experiment and the Bragg wavelength corrected for temperature change.

Fig. 2 shows the wavelength change at individual steps of the experiment with the data baselined to ethanol and APTES and APMDS both diluted in ethanol. The theoretical results are also plotted on the chart assuming that only a single monolayer of 1-nm thickness is attached on the fiber. The index of refraction of both APTES and APMDS in ethanol was 1.346 [0.1]. When either APTES or APMDS are diluted in ethanol, the resulting index of refraction for the compound solution is assumed to be the average of the index of refraction of each component in the solution weighted by its percentage volume. No fitting parameter was used for calculating the theoretical results. It was observed that there was a shift in Bragg wavelength of 28 pm in ethanol before and after silanization of the fiber in APTES as opposed to a shift of only 5 pm in ethanol before and after silanization of the fiber in APMDS. It is also seen that the theoretical results match very well with the APMDS silanization showing that only a monolayer of APMDS is immobilized on the fiber. However, for APTES about seven-chained polymer seems to have been immobilized. This also agrees very well with what had been observed by other groups [5], [6].

In order to verify that the immobilization of APMDS and APTES took place, complete DNA hybridization experiments were conducted. Single stranded DNA oligonucleotide probes of 20 bases were immobilized on the surface of the fiber grating using glutaraldehyde chemistry. Hybridization of a complimentary target single strand DNA oligonucleotide was monitored in situ. Measurements of change in the Bragg wavelength were recorded with time at every step of the process. Details of the experimental steps can be seen in [3]. It was expected that for both the APMDS and the APTES immobilized fiber, the number of amine terminated sites on the surface should be the same as can be seen in Fig. 3. Hence, there should be a similarity in the hybridization of DNA processes. After immobilization of either
APMDS or APTES on the fiber surface, glutaraldehyde is attached using the amino termination. The sensor is then cleaned and stabilized in saline sodium citrate buffer with magnesium chloride (SMB) and then (probe DNA) is attached by overnight immersion. The sensor is then cleaned and sensitized in Sigma PerfectHyb hybridization buffer (HB buffer) and the hybridization of complimentary target DNA (TDNA) is performed. The sensor is again cleaned by SMB and the reference signal measured.

The measurements are baselined to the initial SMB after the glutaraldehyde attachment on the APMDS or APTES immobilized fiber. The various steps of the hybridization process are shown in Fig. 3. It is seen that the wavelength shifts for the fibers with APMDS and APTES immobilized are nearly the same showing that both APMDS and APTES have a similar number of sites on the surface for the DNA to immobilize. It also confirms that there was an attachment of APMDS on the surface of the fiber and the shift of wavelength is due to this attachment and not an experimental error.

These experiments demonstrate an advantage of the etched-core sensor in that in situ measurements can be taken and the various steps in a chemical reaction can be observed. This not only makes for an efficient sensor, but also allows optimizing and understanding the chemistry. For example, it was observed during the above experiments that the silanization process occurred in the first 15 min of immersion.

IV. CONCLUSION

We have demonstrated that the etched-core FBG sensor can be used to detect down to a monolayer of deposition on the fiber surface. A theory was developed for calculating the wavelength change as thin films of biological and chemical layers are immobilized on the surface of the fiber in the presence of a surrounding medium. The theory was confirmed by demonstrating a monolayer attachment of APMDS as opposed to a polymer attachment of several layers for APTES. Excellent agreement of the experimental results with theoretical values was observed without any fitting parameters. The sensor can be used to detect biological and chemical changes on the surface of the fiber. We have already demonstrated that this sensor can be used for detecting the hybridization of DNA. By using the in situ properties, the sensor can be used to understand and optimize biological and chemical processes.

REFERENCES