Angular spectrum detection instrument for label-free photonic crystal sensors

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An angular spectrum analysis system was demonstrated to monitor the optical resonant mode of a photonic crystal (PC) sensor comprised of a one-dimensional grating structure. Exposed to solutions with different refractive indices or adsorbed with biomaterials, the PC sensor exhibited changes of the optical resonant modes. The developed detection system utilized a focused laser beam to detect shifts of the resonant angle, and thereby allowed a kinetic analysis of chemical absorption. Such a detection apparatus offers an adjustable angular resolution and a tunable detection range for a wide variety of refractometric sensing applications. A limit of detection of 6.57×10^{-5} refractive index unit has been observed. The instrument also offers an imaging capability of rapidly characterizing low-contrast samples deposited on the PC surface with a spatial resolution of 10 μm.

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Label-free biosensors are an emerging class of analytic methods that are capable of quantifying biomolecular interactions, including binding affinity, specificity, and kinetics [1,2]. Optical label-free sensors are designed as refractometric transducers that are sensitive to refractive index changes caused by the binding of target molecules. A wide variety of optical cavity-based biosensors have been utilized for analyzing biomolecule and chemical compounds and have shown promising results toward rapid, high-throughput, and accurate analysis [3–6]. Among them, photonic crystal (PC) sensors have been successfully applied in life science research, pharmaceutical drug discovery, and environmental monitoring [7,8]. They exploit leaky resonant modes, also known as guided-mode resonance (GMR), to probe refractometric variations. Each GMR mode is associated with a unique resonant wavelength (λ_r) and resonant angle (θ_r) [9,10]. In previous works, PC biosensors were illuminated by a white light source from a fixed angle of incidence and the reflection spectra were captured by a spectrometer to determine λ_r [11].

This Letter reports the design of a low-cost detection instrument that utilized a line-focused laser beam to interrogate shifts in θ_r associated with a GMR, thereby enabling the rapid analysis of chemical and biomolecular absorption on a PC sensor. The performance of the developed system was characterized by monitoring the angular spectral shift in response to the refractive index change. The results showed a sensitivity of nearly 15.2° per refractive index unit (RIU), leading to a detection limit of refractive index on an order of 10^{-5} RIU. By scanning the line-focused laser beam across a region of interest and generating a spatial map of the resonant angle, this system also has the capability to quantitatively image dielectric materials a few nanometer thick on the PC sensor. The primary advantages of this technology include low cost, adjustable detection resolution, and tunable dynamic range.

The PC sensor adopted for this study is shown schematically in Fig. 1(a). The low refractive index subwavelength grating structure was used as a cladding and light-coupling layer upon which the high reflective index dielectric layer provides a vertical light confinement. The subwavelength grating was fabricated using a low-cost nano-replica molding technique that has been described previously [1]. The grating pattern was molded using a silicon master stamp (SNS-C24, LightSmyth Technologies, Inc.) with a period of $\Lambda = 416.6$ nm, a duty cycle of 50%, and a grating depth of $d = 110$ nm. After the replication using a photocurable polymer material (NOA 85, Norland Product Inc.), the surface relief grating was coated with a 100 nm thick TiO_2 dielectric film (refractive index, $n = 2.0$) by electron beam evaporation. The liquid flow chamber was fabricated by trimming a plastic paraffin film into the desired dimensions, sandwiching it between the PC substrate and a glass cover slip, and subsequently baking on a hotplate at 60°C. Two holes with 1-mm diameters drilled in the glass cover slip served as inlet and outlet ports for flexible tubing, as shown in Fig. 1(b).

A schematic of the angular dispersed detection instrument is shown in Fig. 1(b). The system consisted of a laser source, a beam expander, two cylindrical lenses (CL1 and CL2), two mirrors (M1 and M2), a sample holder, and a CCD camera. As the light source, a 0.8 mW He–Ne laser outputted a linearly polarized beam at $\lambda = 632.8$ nm. The beam was expanded using a pair of convex lenses ($f_{L1} = 10$ mm and $f_{L2} = 50$ mm) to a diameter of 5 mm and was subsequently focused into a line by a cylindrical lens ($f_{CL1} = 35$ mm). At the focal plane, the laser line aligns along the y-direction, which was parallel to the direction of the PC grating [as shown in Fig. 1(a)]. In the x–z plane, the beam was focused and contained incoming rays within a range of $-8.31° < \theta < 8.31°$, which was limited by the numerical aperture (NA) of CL1. The focal plane of the cylindrical lens resides at the surface of the PC sensor, which was placed on a motorized translation stage (MS-2000, Applied Scientific Instrumentation). Transmitted through the PC sensor, the laser beam diverged in the x–z plane and the intensity profile was

analyzed using a CCD imaging sensor (2048×2048 pixels, 7.4 μm × 7.4 μm pixel size, CoolSNAP K4, Photometrics) as illustrated in Fig. 1(b). Adjusting the distance between the PC sensor and the CCD offers a convenient way to tune the detection range and the sensing resolution. The second cylindrical lens (CL2, $f_{CL1} = 35$ mm) oriented orthogonally to the first cylindrical lens (CL1) and was used to project the image of the laser line onto the CCD sensor and maintain the beam path of the angularly dispersed light. This lens was optional for most experiments demonstrated in this Letter but required for the spatially resolved measurement.

By expanding and focusing the laser beam toward a PC substrate, we ensured that the angle of marginal rays was larger than θ_r of the target resonant mode. When the laser light passed through the PC sensor, the strong resonant reflection at $\pm\theta_r$ caused transmission minimums corresponding to the two resonant angles. As illustrated in the inset of Fig. 1(b), two symmetrical dark lines were observed on the image captured by the CCD, as a result of resonant reflection at $+\theta_r$ and $-\theta_r$, respectively. It is possible to utilize one of the lines or both to quantify the change of the resonant mode. With this intensity image, the resonant angle is determined by $\theta_r = \text{acrtan}(\Delta d/L)$, w here Δd is the offset from the point of intensity minimum to the center of the optical axis, and L represents the distance between the sensor and the CCD chip. A computer program was developed to acquire intensity data from the CCD, display the angular transmission spectrum, and mathematically determine the resonant angle by fitting the transmission curve with a Lorentzian profile. The amount of resonant angle shift is proportional to the refractive index change, which is usually caused by the deposition of biomaterials on the sensor surface.

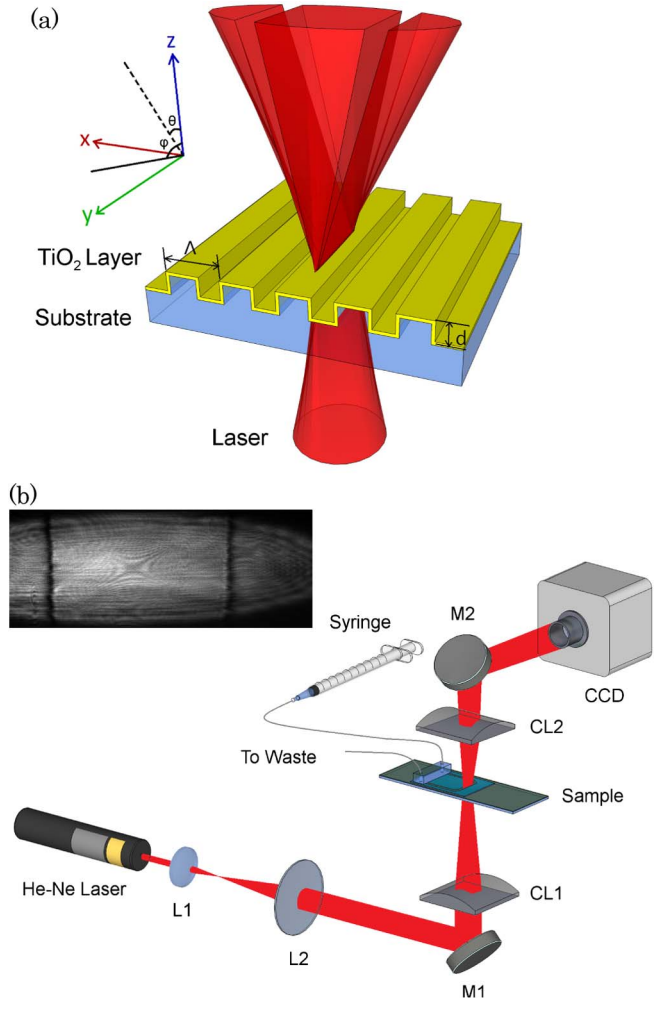

Fig. 1. (a) A schematic of PC structure (not to scale). The grating structure was fabricated using replica-molding. (b) The complete layout of the experimental setup. The PC sensor is illuminated with an expanded He–Ne laser beam. The incoming laser light was focused along the θ-direction in the x–z plane while being collimated in the y–z plane. The transmitted light was collected by a cylindrical lens and quantified by a CCD camera. Inset: the intensity image captured by the camera showing two minimums of transmission intensity as "dark lines."

To characterize the sensitivity of the system, different concentrations of dimethyl sulfoxide (DMSO) were loaded into the flow cell and the angular spectra from the PC sensor were measured. The DMSO was diluted in deionized (DI) water at a range of volume ratios from 1% to 10%. Figure 2 compares the angular transmission spectra recorded for the DSMO solution and DI water. According to the inset of Fig. 2, the bulk refractometric sensitivity, $S_b \equiv \Delta\theta_r/\Delta n$, was found to be 15.2 °/RIU. By monitoring the angular transmission output of the PC senor over time, the developed instrument can also be used to study dynamic characteristics. Figure 3 illustrates the kinetic progression of the PC resonant angle when eight different solutions flowed through the channel sequencing. The channel was rinsed with DI water ($n = 1.333$) for 5 min, and then isopropyl alcohol (IPA, $n = 1.377$) was introduced, causing an increase of angle shift of 0.61°. When six different DMSO solutions (10%, 5%, 4%, 3%, 2%, and 1%) passed through the PC sensor, the corresponding decreasing angle shifts were recorded as shown in

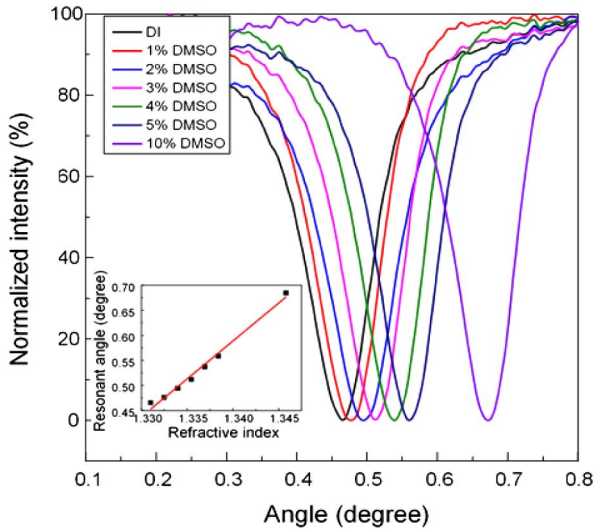

Fig. 2. Angular transmission spectra with the PC sensor immersed in DMSO–water mixture solutions with concentrations of DMSO varying from 1% to 10%. Inset: the measured resonant angles versus the index of refraction of DMSO solutions [12]. The measured resonant angles were fitted with a linear function shown by the red line.

Fig. 3. In order to determine the detection limit, the resonant angle was measured every two seconds with DI water flowing in the flow cell for 12 min (Fig. 4). The resonant angle varied by 1.6×10^{-3} degrees with a standard deviation (σ) of 3.33×10^{-4} degrees. With a minimum detectable resonant angle shift of $3\sigma = 9.99 \times 10^{-4}$ degrees, the refractive index resolution was calculated as $3\sigma/S_b = 6.57 \times 10^{-5}$ RIU.

Monitoring the resonant angle shift over time enables dynamic quantification of mass adsorption upon a PC sensor. As an example, the deposition process of a polyelectrolyte stack that contained positively and negatively charged monolayers was measured using the PC sensing system. Before building up the stacked layers, a 0.9 M sodium chloride (NaCl) buffer was used to establish a baseline and was subsequently replaced by a cationic poly(ethylenimine) (PEI) solution. After being incubated for 10 min, the flow cell was washed with a NaCl buffer and three alternating layers of anionic poly(sodium 4-styrenesulfonate) (PSS) and cationic poly(allylamine hydrochloride) (PAH) were pumped into the flow cell. All polyelectrolytes were dissolved in the NaCl buffer at a concentration of 5 mg/mL and formed monolayers on the PC surface with a refractive index of 1.49 and ~5 nm-thickness [13]. Figure 5 shows the time-resolved resonant angle shift (θ_r~1.2°) caused by the PEI and the three PSS-PAH layers, with the measurement interval set to 2 s.

Quantifying low-contrast samples is always challenging for conventional optical imaging approaches [14]. Because of its high sensitivity and the spatially confined optical resonance, a PC sensor is capable of determining the density of biomaterial attachments with subtle spatial variations. Label-free detection of live cell behaviors upon a PC sensor has been successfully demonstrated in the recent work [15]. The readout system shown in Fig. 1 offers a cost-effective apparatus for label-free imaging applications compared to the established method that involves expensive imaging spectrometers. To illustrate this imaging scheme, we used photolithography and

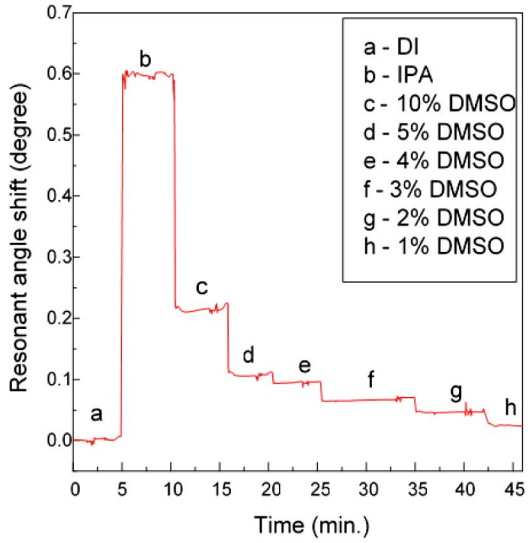

Fig. 3. Dynamic detection of resonant angle shifts for solutions with different refractive indexes pumped through the channel.

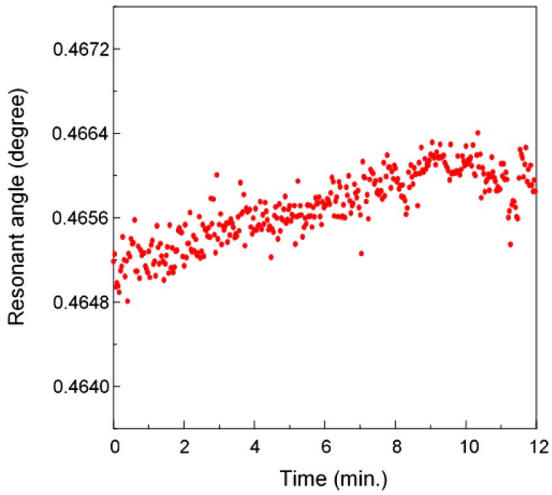

Fig. 4. Time-dependent resonant angle variation when the PC sensor was immersed in DI water.

lift-off process to create a low-contrast pattern (USAF1951 resolving pattern) upon the PC surface using a 5 nm TiO_2 layer deposited only in the transparent regions of the resolving pattern. The additional TiO_2 coating increased the local resonant angle by a small amount relative to the uncoated regions. By measuring the resonant angles on a pixel-by-pixel basis over an area of interest, a map of surface absorbed mass can be generated. In order to assemble the map, a series of lines were recorded by translating the sample linearly across the laser line with a step size of 1.5 μm and an acquisition rate of 20 lines per second. Each intensity image from the CCD contained the angular spectra from 2048 pixels along the sampling line. The pseudocolor plot shown in Fig. 6(a) consists of 1024 × 2048 sensing pixels and covers an area of 1536 μm × 3368 μm on the PC sample. With a magnification of 4.5, each pixel in the θ_r distribution image represented an area of 1.50 μm × 1.64 μm on the PC surface. A line profiled taken through the three line pairs marked in Fig. 6(a) is shown in Fig. 6(b). The cross-section plot showed the resonant angle contrast of ~0.04° and the

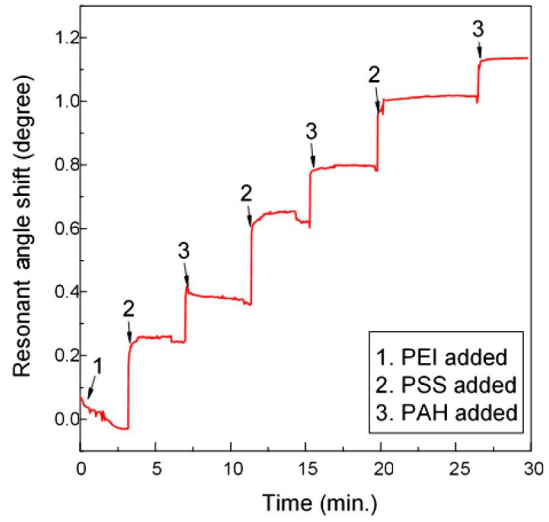

Fig. 5. Time resolved resonant angle shift due to the deposition of the alternating polyelectrolyte multilayers.

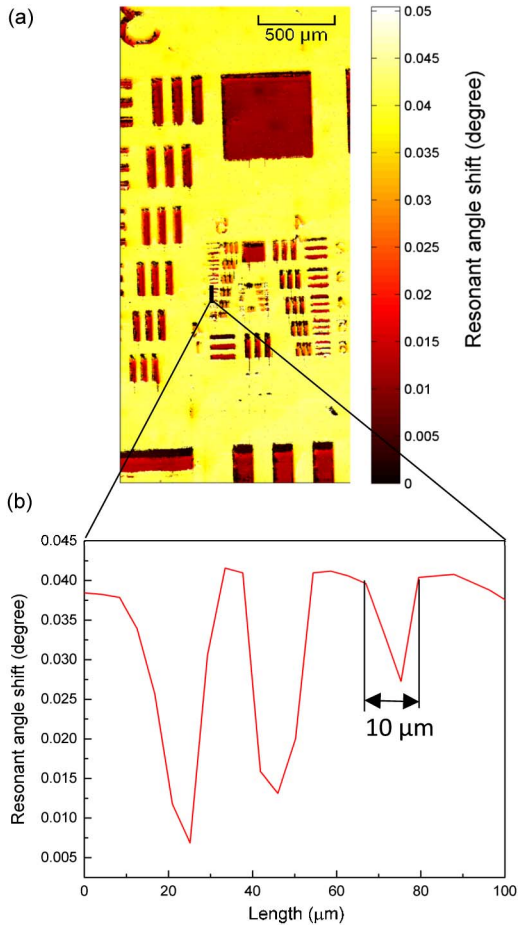

Fig. 6. (a) The reconstructed USAF1951 pattern. The color bar represents the angle shift of the PC sensor. (b) The profile of resonant angle distribution along the three line pairs marked in (a).

minimum resolvable feature of 10 μm, which was close to the diffraction limit of the cylindrical lens (CL2). The map of resonant angle distribution represented the thickness of the TiO_2 pattern, which was analogous to the absorption of biomaterials on the PC substrate.

In conclusion, this Letter reports a low-cost detection instrument for refractometric sensing using PC biosensors. The developed detection system utilizes a focused laser beam to precisely measure changes in the resonant angle of a PC sensor. Such an optical arrangement allows flexible selection of detection range and offers adjustable angular resolution. A detection limit of 6.57×10^{-5} refractive index RIU to bulk index changes and the kinetic characterization of surface-adsorbed monolayers of polymers have been demonstrated. We demonstrated its capability for quantitative mapping of a thin dielectric film patterned upon a PC sensor with a spatial resolution of 10 μm. For future works, the developed technology will be applied to image biomaterials, such as antibodies and DNA microarrays, printed on PC sensors. Due to its simplicity, the developed readout approach can also be utilized to further reduce the size of portable PC sensor systems [16].

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