High Sensitivity Plastic-Substrate Photonic Crystal Biosensor

Ian D. Block, Maria Pineda, Charles J. Choi, and Brian T. Cunningham

***Abstract*—A photonic crystal biosensor incorporating a nanomolded porous dielectric is fabricated for the first time on a flexible polysulfone substrate. The plastic substrate necessitates several changes to the fabrication procedure, including reduced processing temperatures. The resulting structure shows excellent response uniformity across a large area in the steady state as well as for perturbations of the bulk and near-surface dielectric permittivity. Kinetic binding data for a representative biomolecular assay demonstrate robust sensor operation.**

***Index Terms*—Biomedical transducers, flexible structures, optical resonance, plastics.**

I. Introduction

PHOTONIC CRYSTAL (PC) optical biosensors have previously been demonstrated as a highly sensitive label-free detection platform for performing a wide variety of biochemical and cell-based assays [1]. The device structure, shown in Fig. 1, is designed to reflect only a narrow band of wavelengths with 100% efficiency when illuminated with white light at normal incidence; positive shifts of the reflected peak wavelength value (PWV) indicate adsorption of detected material on the sensor surface [2]. Previously, photonic crystal optical biosensors have been fabricated on continuous sheets of plastic film using a process in which the periodic surface structure is replicated directly from a silicon master wafer using a UV-cured polymer material. The continuous rolls of plastic used as a device substrate and the high-throughput replication process enable low-cost mass-production of large surface-area devices for single-use disposable products, capable of incorporation with microplates and microarray slides. Recently, we have demonstrated that substituting a low refractive index porous dielectric for the UV-cured polymer significantly increases the sensitivity of the label-free photonic crystal optical biosensor [3]. However, the high temperatures employed in the new fabrication process necessitated the use of a glass substrate. In this letter, we present a modified fabrication approach and a new substrate to enable plastic-based roll-to-roll processing of the high-sensitivity device, and demonstrate the new sensor's performance with a biomolecular assay and several basic sensitivity tests.

II. Sensor Fabrication

A detailed description of the nanoreplica molding process for the fabrication of glass-substrate porous dielectric PC biosensors can be found in the literature [4]. In summary, a polydimethylsiloxane (PDMS) replica of a periodic structure etched into silicon is used to mold a porous dielectric sol-gel precursor spun onto a glass substrate. This film is baked at a low temperature (110 °C) while in contact with the PDMS mold until it holds its shape (60 s), is subsequently cured at high temperature (250 °C) for 15 min after removal of the mold, and finally it is coated with a high-refractive index TiO_2 film. Two significant changes to the process have been implemented in this work. First, 250 μm thick polysulfone (K-mac Plastics) film, exposed to an oxygen plasma (300 W, 30 s; Texas Instruments) before sol-gel coating to enhance adhesion, is used in place of the glass substrate. Second, the high temperatures employed in the previous fabrication process are limited here to 175 °C in order to maintain processing conditions below the glass transition temperature of the polysulfone ($T_g = 190$ °C). Successful molding of the sol-gel dielectric and its transformation into a low-loss optical film require complete solvent removal. The commercially available sol-gel used in this work (Nanoglass, Honeywell) utilizes a dual solvent system, where one solvent (ethanol) has a low boiling point while the other (monoethylene glycol, MEG) has one significantly higher [5]. Once the initial low-temperature PDMS molding step has been performed and the low boiling point solvent has been eliminated, the de-molded device is placed in a vacuum oven at 175 °C for 1 h to drive out the remaining solvent and form the nanopores of the low-index film. By using a vacuum oven, the high atmospheric-pressure boiling point of the second solvent (197 °C for MEG) can be significantly reduced. To complete the device, a TiO_2 film is deposited onto the patterned dielectric using a plasma sputtering system (AJA International).

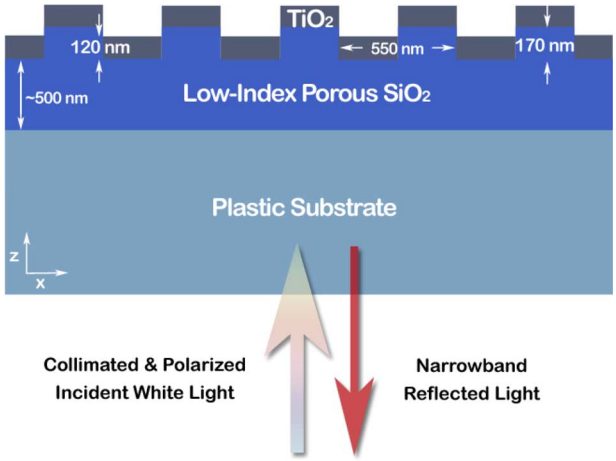

Fig. 1. Photonic crystal biosensor schematic.

III. Results

The plastic-substrate devices were bonded to bottomless 96-well microplates and were characterized using instrumenta-

Manuscript received January 30, 2008; revised February 15, 2008; accepted February 18, 2008. This work was supported by SRU Biosystems and by the National Science Foundation under Grant BES 04-27657. The associate editor coordinating the review of this paper and approving it for publication was Dr. Andreas Hierlemann.

The authors are with the University of Illinois at Urbana-Champaign, Urbana, IL 61801 USA (e-mail: bcunning@uiuc.edu).

Color versions of one or more of the figures in this paper are available online at http://ieeexplore.ieee.org.

Digital Object Identifier 10.1109/JSEN.2008.924377

tion described previously [1]. The size of the devices fabricated for this study permitted the use of 36 ∼6 mm diameter test wells. Each well was filled with deionized (DI) water and allowed to stabilize for 6 h. PWV measurements following stabilization yielded a mean and standard deviation of 872.69 ± 2.61 nm. The response of the sensor to changes in refractive index was tested via a bulk solution exchange of isopropyl alcohol (IPA) for DI water. The PWV shift due to the differing refractive indices of these two solvents was measured to be 13.80 ± 0.12 nm, corresponding to a sensitivity of 306.7 ± 2.6 nm/RIU, where RIU is a refractive index unit. While bulk solution refractive index discrimination is a common metric for optical biosensors, a more practical test involves probing the device response to a polymeric thin film since detection of surface-based biomolecular binding is the primary application for such sensors. The near-surface sensitivity was characterized by the detection of a self-limiting monolayer of Poly (Lys, Phe; Sigma Aldrich), the deposition protocol for which has been described previously [3]. We observed a PWV shift of 1.65 ± 0.10 nm for the polymeric monolayer.

Optical biosensors employing surface-binding detection are most often used to quantify the affinity of an analyte for its ligand. To provide such a realistic display of sensor operation, we investigate sensor response to the binding of lactoferrin, a soluble protein with antimicrobial and anti-inflammatory activity, to biotinylated heparin, a sulfated polysaccharide that comprises much of the extracellular matrix in humans. Biotinylated heparin binds to a layer of streptavidin attached to the sensor surface through a thin-polymer coating and bifunctional linker, the immobilization procedure for which has been described by our group [6]. 100 $\mu g/mL$ heparin (Sigma-Aldrich) is incubated with the streptavidin coated surface at 5 °C for 20 h. The surface is blocked with Starting Block (Pierce Biotechnology) to minimize nonspecific binding. Fourfold dilutions of lactoferrin (Sigma-Aldrich) are tested on two types surfaces: test wells with a blocked heparin layer and those with just blocked streptavidin. Active wells, those with the heparin layer, are referenced to blocked streptavidin wells to account for nonspecific binding of the protein to the blocked surface. Kinetic data given in Fig. 2 demonstrate the high resolution and robust nature of the plastic-based photonic crystal biosensor.

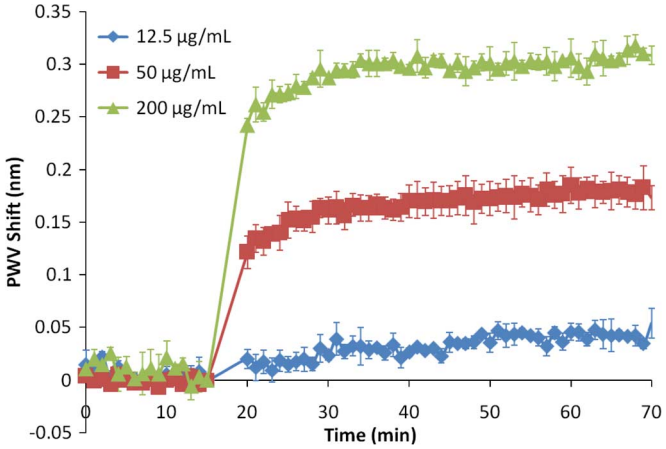

Fig. 2. Binding kinetics at varying lactoferrin concentrations to a heparin saturated PC biosensor surface. Data acquisition was paused (at 15 min) while solutions were pipetted into wells. Data represented as mean ±SD, n = 3.

IV. Discussion

Plastic-based processing is complicated by thermal expansion and low glass-transition temperatures. The polysulfone substrate for the PC biosensor fabricated here has a low coefficient of thermal expansion $(5.6\times10^{-5}\,;^{\circ}\,C^{-1})$ and we observed no significant delamination or bowing during processing. The unusually high T_g of polysulfone enabled patterning of a thermally cured sol-gel. When the T_g was approached during processing, we observed a rapid rolling-up of the device as the inter-chain bonds of the polymeric substrate weakened and allowed the thermal expansion differential between materials to dominate the force balance. Reducing the solvent boiling point below the substrate T_g by lowering the pressure from ambient was therefore crucial to the success of this process.

The completed devices are flexible and can maintain a ∼15 cm radius of curvature before any damage to or delamination of the sol-gel or sputtered layers occurs. Sensor performance is not affected by the substrate composition, as the resonant energy responsible for label-free detection is strongly confined to the device surface. Large rolls of thin polysulfone films are commercially available and would enable a stamp-and-step fabrication procedure with higher throughput and lower cost than would be possible with the use of a glass-substrate. Furthermore, the ability to pattern sol-gel-derived dielectrics on plastic substrates will enable roll-to-roll fabrication of a wide variety of integrated optical components requiring low refractive-index materials.

References

[1] B. T. Cunningham, P. Li, S. Schulz, B. Lin, C. Baird, J. Gerstenmaier, C. Genick, F. Wang, E. Fine, and L. Laing, "Label-free assays on the BIND system," *J. Biomol. Screen.*, vol. 9, pp. 481–490, 2004.

[2] D. Rosenblatt, A. Sharon, and A. A. Friesem, "Resonant grating waveguide structures," *IEEE J. Quantum Electron.*, vol. 33, no. 11, pp. 2038–2059, Nov. 1997.

[3] I. D. Block, L. L. Chan, and B. T. Cunningham, "Photonic crystal optical biosensor incorporating structured low-index porous dielectric," *Sens. Actuators B*, vol. 120, pp. 187–193, 2006.

[4] I. D. Block, L. L. Chan, and B. T. Cunningham, "Large-area submicron replica molding of porous low-k dielectric films and application to photonic crystal biosensor fabrication," *Microelectron. Eng.*, vol. 84, pp. 603–608, 2007.

[5] D. M. Smith *et al., Low Volatility Solvent-Based Method for Forming Thin Film Nanoporous Aerogels on Semiconductor Substrates*. Dallas, TX: Texas Instruments, 1999, p. 34.

[6] W. Zhang, N. Ganesh, I. D. Block, and B. T. Cunningham, "High sensitivity photonic crystal biosensor incorporating nanorod structures for increased surface area," *Sens. Act. B*, to be published.