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Long-period gratings in photonic crystal fiber as an optofluidic label-free biosensor

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ABSTRACT

Using long-period gratings (LPG) inscribed in photonic crystal fiber (PCF) and coupling this structure with an optically aligned flow cell, we have developed an optofluidic refractive index transduction platform for label-free biosensing. The LPG–PCF scheme possesses extremely high sensitivity to the change in refractive index induced by localized binding event in different solution media. A model immunoassay experiment was carried out inside the air channels of PCF by a series of surface modification steps in sequence that include adsorption of poly(allylamine hydrochloride) monolayer, immobilization of anti-rat bone sialoprotein monoclonal primary antibody, and binding interactions with non-specific goat anti-rabbit IgG (H + L) and specific secondary goat anti-mouse IgG (H + L) antibodies. These adsorption and binding events were monitored in situ using the LPG–PCF by measuring the shift of the core-to-cladding mode coupling resonance wavelength. Steady and significant resonance changes, about 0.75 nm per nanometer-thick adsorbed/bound bio-molecules, have been observed following the sequence of the surface events with monolayer sensitivity, suggesting the promising potential of LPG–PCF for biological sensing and evaluation.

1. Introduction

Photonic crystal fiber (PCF), also termed microstructured or holy fiber, consists of periodically arrayed and axially aligned cladding air channels along the entire fiber length (Knight, 2003; Russell, 2003). The endless flexibility in designing and fabricating PCF of any prescribed cladding microstructure offers a high degree of freedom to tailor the optical properties with dopant-free silica. The open air channels of micrometers in diameter also allow controlled liquid transmission through the PCF waveguide. The light can be manipulated by incorporating fluids in the PCF structure as well (Kerbage et al., 2002; Mach et al., 2002). The synergistic integration of microfluidics with optics thus enables PCF-based fiber optofluidics numerous distinct features compared to its well explored planar counterpart. PCF optofluidics has the advantages of being free-standing (no host substrate), long optical path (limited only by fiber length), high fabrication throughput (via large-scale fiber drawing technique), and easy light input/output coupling and system integration. These features, plus the accessibility of the channels for chemical or biological surface modification, render PCF optofluidics an exciting platform to conduct chem/bio sensing and detection in situ with minimal sampling volume as well as to monitor adsorption or binding events where heat transfer/mass transport is greatly enhanced. Indeed PCF has been increasingly explored for laser interrogation of chemical and biological systems using absorption spectroscopy (Rindorf et al., 2006a), fluorescence spectroscopy (Emiliyanov et al., 2007; Jensen et al., 2004; Konorov et al., 2005), and Raman (including surface-enhanced Raman scattering) spectroscopy (Khaing Oo et al., 2010; Yan et al., 2008).

Long-period grating (LPG) structure with a period of typically hundreds of micrometers is known to couple the fundamental core mode to co-propagating cladding modes in both conventional optical fiber (Vengsarkar et al., 1996) and PCF (Eggleton et al., 1999), resulting in significant attenuation at some resonance wavelengths in the transmission spectrum. The phase-matching condition for LPG is expressed by $\lambda_i = (n^{\mathrm{eff}}_{\mathrm{core}} - n^{\mathrm{eff}}_{\mathrm{clad}(i)})\Lambda$ (Erdogan, 1997), where λ_i is the resonance wavelength of the ith cladding mode coupled by the fundamental core mode, and $n^{\mathrm{eff}}_{\mathrm{core}}$ and $n^{\mathrm{eff}}_{\mathrm{clad}(i)}$ are the effective refractive indices of the fundamental core mode and the ith cladding mode, respectively. The strong dependence of λ_i on $n^{\mathrm{eff}}_{\mathrm{clad}(i)}$ makes LPG inscribed in PCF (LPG–PCF) an refractive index transduction optofluidic platform that is highly sensitive to the changes in $n^{\mathrm{eff}}_{\mathrm{clad}(i)}$ induced by any physical, chemical, or biological perturbations in the cladding structure. The ability to bring a measurant solution inside of the cladding air channels to directly

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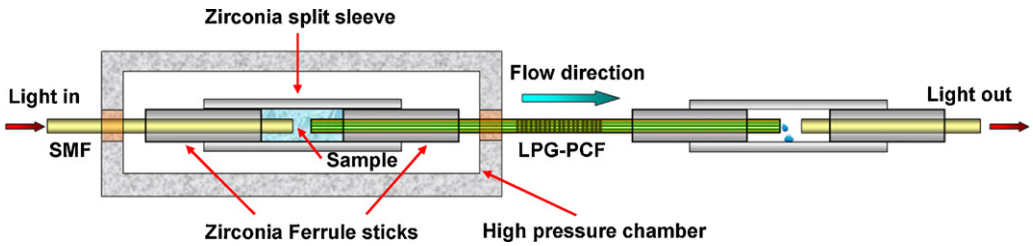

Fig. 1. Schematic of a microfluidic assembly that enables both liquid flow and light transmission measurements through LPG–PCF structure optically coupled with single mode fiber (SMF).

interact with the cladding mode further boosts the refractive index sensitivity of LPG–PCF to bulk solution by 2–3 orders of magnitude (up to $\sim 10^{-7}$ RIU) compared to LPG inscribed in conventional all-solid fiber (He et al., 2008). The LPG–PCF exhibits comparable sensitivity with the PCF sensor achieved by coupling the core mode to a mode in the adjacent fluid-filled waveguide (Wu et al., 2009) yet it is more suited for the refractive index range of aqueous solutions. The LPG–PCF is also comparable with the most-sensitive surface plasmon resonance technique achieved to date (Gopinath, 2010). LPGs have been explored as candidate for evanescent-field sensor to detect the bio-molecules interaction using the all-solid conventional optical fiber, which does not lend it for optofluidics integration. Besides, extra steps were needed to improve the sensitivity, such as forming gratings on side-polished fiber (Jang et al., 2009), etching fiber cladding to dispersion turning points (Chen et al., 2007; Wang et al., 2005) or depositing thicker multilayer coatings on the LPG to excite the transition mode (Pilla et al., 2011). The LPG–PCF platform has excellent prospects of robust sensitivity to surface binding events at the monolayer scale due to the high surface-to-volume ratio and strong evanescent field interaction at the interface of silica and immobilized layers. However, few attempts have been made to effectively couple liquid flow with LPG–PCF so as to achieve a truly integrated optofluidic device (Monat et al., 2007). While the potential of LPG–PCF for biological sensing has been demonstrated in the immobilization of double-stranded DNA on the surface of the cladding air channels (Rindorf et al., 2006b), related studies have been limited to the measurement of single surface event with a sensitivity of $\sim 10^{-4}$ RIU and a broadened resonance.

We report in this paper the first attempt, to the best of our knowledge, to modify the cladding air channels of PCF for biomolecular binding and to use LPG–PCF to monitor each and every step of the multiple modification and binding sequences. Further unique in this study is that we designed and integrated a microfluidic cell that can optically couple light into and out of PCF while enabling continuous liquid flow through the air channels as part of an integral surface modification/binding and in situ measurement scheme. We have demonstrated that the LPG–PCF optofluidics refractive index transduction platform is sensitive to monolayer adsorption/binding event.

2. Materials and methods

2.1. Materials

Poly(allylamine hydrochloride) (PAH), MW~15,000 g/mol, Phosphate Buffered Saline (PBS) 0.01 M, Albumin from human serum (HSA) ≥97% were purchased from Sigma–Aldrich. Anti-rat bone sialoprotein (BSP) (WVID1-9C5) monoclonal primary antibody was obtained from Developmental Studies Hybridoma Bank, Iowa City, IA. Goat anti-rabbit IgG (H + L) (AP307P) was received from Chemicon. FITC-goat anti-mouse IgG (H + L) was obtained from Invitrogen. All chemicals were used as received without further purification.

2.2. Optical and flow-through coupling with PCF optofluidics

The prevailing approach utilized in the experiments with liquid-containing PCF has been to fill the air channels with the solution of interest, followed by separate optical measurements of the solution retained in the PCF via capillary force under static conditions (Rindorf et al., 2006b). This approach suits the purpose of most laboratory research while avoiding the challenge in integrating optically coupled flow cells for continuous transport of solution through the cladding air channels. The ability to inscribe LPG in PCF and to chemically and biologically modify the surface of the air channels under continuous liquid flow while optically accessible for process monitoring is critically important for better process control, enhanced experimental efficiency and consistency, and for system integration. First, it ensures reproducibility in LPG fabrication of solution-filled PCF as solution loss at the open ends of the PCF will otherwise take place under static conditions due to rapid heating and expansion of the solution upon CO_2 laser irradiation, significantly altering the absorption condition in the subsequent laser inscription step. Second, continuous supply of fresh reagent makes surface modification and subsequent rinsing of cladding air channels more efficient. Third, the optical coupling enables in situ measurements of light transmission, hence constantly monitoring the evolution of resonance band during LPG fabrication and the shift of the resonance wavelength as adsorption or binding events take place.

Depicted in Fig. 1 is the schematic of the optically coupled flow cell system constructed for the investigation. It consists of two main parts. One part is in essence a compressed air pressure chamber (~200 psi) that houses the flow entrance end of the PCF and an optically aligned (within ±1 μm) single mode light-source fiber in a zirconia microfluidic reservoir of 50 μl capacity. The other part is the same type of zirconia microfluidic reservoir that houses the exit end of the PCF and a single mode light-collection fiber optically aligned to the same precision as above but under ambient pressure. The pressure difference between the two reservoirs forces continued liquid flow through the PCF air channels during LPG fabrication or surface modification. Liquid addition to or extraction from the reservoirs is done via a syringe. The flow system can be easily disassembled and cleaned to ensure a contamination-free environment.

2.3. LPG–PCF fabrication

The PCF used in this work is ESM-12-2 from NKT Photonics. The cross-section scanning electron microscope (SEM) image of the fiber is shown in Fig. 2. Its microstructure is featured by a hexagonal array of ~3.2 μm cladding air channels with an inter-channel distance of ~8 μm. The ESM-12-2 is endlessly single mode with a large mode area. A CO_2 laser (Synrad, water-cooled 48-1 10W)