MR4 (Contributed Oral)
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External Cavity Laser Biosensor

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Abstract: We have demonstrated a novel single-mode continuous-wave narrow bandwidth emission and widely tunable external cavity laser biosensor that simultaneously achieves high resolution, high sensitivity and large dynamic range.

I. INTRODUCTION

Since the first demonstration of surface plasmon resonance (SPR) as a label-free optical biosensor [1], there has always been a desire to pursue high sensitivity, high resolution, robust, and inexpensive detection approaches based upon the properties of optical resonators to extend the limits of detection of label-free assays to lower concentrations and to increase the signal-to-noise ratio for observation of lower concentrations or smaller molecules.

Here, utilizing a tunable photonic crystal (PC) resonant reflector as a mirror of an external cavity laser (ECL) cavity, we demonstrate a new type of label-free optical biosensor that achieves a high quality-factor through the process of stimulated emission, while at the same time providing high sensitivity and large dynamic range. The PC is fabricated inexpensively from plastic materials using nanoreplica molding, and its resonant wavelength is tuned by adsorption of biomolecules on its surface. Gain for the lasing process is provided by a semiconductor optical amplifier (SOA), resulting in a robust and simple detection instrument that operates by normally noncontact illumination of the PC and direct back-reflection into the amplifier. We demonstrate single-mode, mode-hop-free, biomolecule-induced tuning of the continuous-wave laser wavelength with the ability to generate wavelength shifts as large as 13 nm, and the ability to discriminate wavelength shifts as small as <1 pm. Because the approach includes a mechanism for optical gain, the device represents a departure from previous optical biosensors using passive resonators. It enables simple optical coupling and a sensor format that is amenable to high-throughput multiplexed analysis for a broad array of applications in life science research, pharmaceutical screening, diagnostics, and environmental monitoring.

II. ECL BIOSENSOR: DESIGN

As shown in Fig. 1, an optical fiber-coupled SOA (SAL-372, Superlum Inc., λ_0= 850; 3-dB bandwidth $\Delta\lambda$ = 40 nm) is used as the gain medium. The SOA has both edge facets coated with antireflective layers (R < 10^{-3}) with a tilted waveguide design to obtain a gain ripple as low as 0.2 dB [2]. Each end facet of the SOA is coupled to a single mode polarization maintaining fiber with a length of 1 m. The output of one side of the SOA is reflected against a mirror, while the other end directs light through a collimating lens against the PC at normal incidence. The PC reflects a narrow band of wavelengths back into the SOA to establish a laser cavity whose emission wavelength is tuned by the adsorption of biomaterial on the PC surface. A portion of the lasing emission is directed by a 98:2 beam splitter to a spectrometer. The smooth gain spectrum of the SOA and the length of the external cavity result in continuous tuning of the lasing wavelength without abrupt hops between modes. The 1-D PC incorporates a low refractive index (RI) polymer periodic grating (Λ = 550 nm, $t_{grating}$ = 170 nm) coated with a high RI film of TiO_2 (n = 2.35, t_{TiO2} = 120 nm, a design which is intended to provide a resonant reflection near λ = 855 nm in water. Importantly, the PC is inexpensively fabricated over large surface areas based on a nanoreplica molding technique [3] to produce biosensors in a standard microplate format, for compatibility with automated liquid handling formats used for applications that require high throughput.

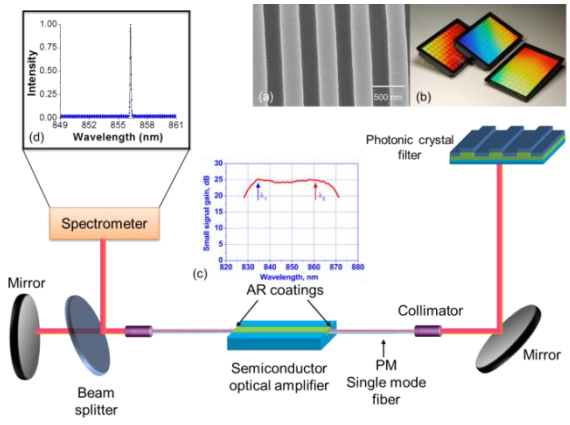

Fig.1.Schematic of the ECL biosensor system. Inset a: Cross-section scanning electron micrograph (SEM) image of the PC structure. Inset b: PC resonator in standard microplate-based formats. Inset c: The small signal gain spectrum of the SOA. Inset d: A typical lasing spectrum of the PC based ECL.

III. ECL BIOSENSOR: CHARACTERIZATION

The reflection spectrum of the PC, the spontaneous emission spectrum of the SOA, and the laser emission spectrum of the ECL-PC are shown together in Fig. 2(a). Using a spectrometer (IHR550, Horiba Jobin Yvon), the lasing peak is measured to be as narrow as $\Delta\lambda$ = 30 pm, as limited by the resolution of the spectrometer. To more accurately measure the quality factor (*Q-factor,* $\lambda_0/\Delta\lambda$), a scanning Fabry-Perot cavity interferometer with a resolution of 7.5 MHz was used, as shown in Fig. 2(b-c). The *Q*-factor of 2.8×10^7 is determined. The light vs. current (L.I.) curve is shown in Fig. 2(d), demonstrating a threshold current of 48 mA and a slope efficiency of 39 mW/A at 20 °C.

In Fig.3, the sensor's bulk RI sensitivity and dynamic range are obtained by exposing the PC surfaces to dimethyl sulfoxide (DMSO) solutions at varying concentrations in water. A linear bulk RI shift coefficient of S_b = 212 nm/RIU over a dynamic range of 13 nm is found. The widely adopted metric for the intrinsic resolving power of resonator sensors is the figure of merit (FOM), defined as FOM = $S_b\times Q$. Our obtained FOM is 5.9×10^9, representing the state-of-the-art resolving capability.

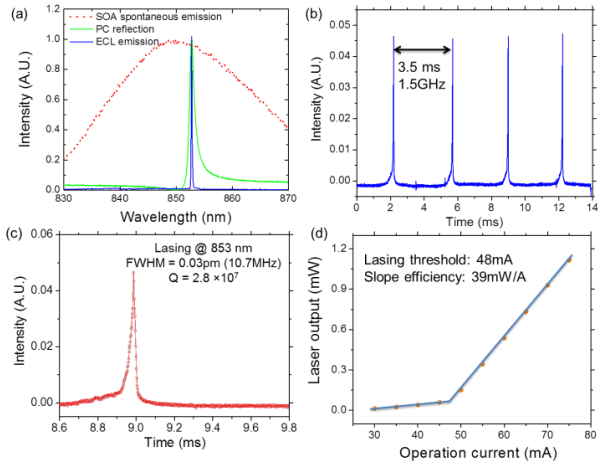

Fig.2. Lasing characterization. (a) Overlaid SOA spontaneous emission spectrum, PC resonant reflection spectrum, and ECL single mode emission spectrum. (b)(c) Interferogram of the ECL emission. (d) The I-L curve associated with the ECL.

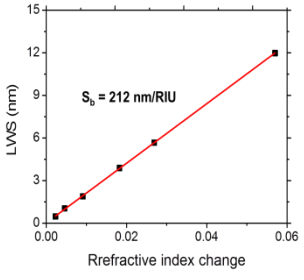

Fig.3

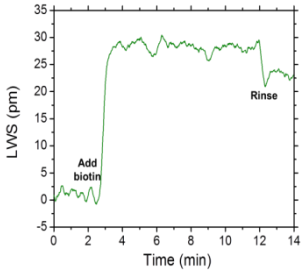

Fig.4

Fig.3. Bulk sensitivity characterization. Fig.4. Dynamic binding of biotin to SA.

A conventional demonstration for characterizing the ability of a sensor to observe small molecule adsorption is the detection of biotin (MW = 244 Da) by an immobilized capture layer of streptavidin (SA, MW = 60,000 Da). The dynamic binding of the biotin (250 ng /mL) to the immobilized SA is shown in Fig. 4. Biotin binding produces a lasing wavelength shift of ~23 pm. For kinetic measurement of an individual sensor without referencing or temperature control, small fluctuations in the ECL wavelength are observed with a magnitude of ~4 pm.

To demonstrate detection of biomolecular interactions with binding affinities more representative of biological systems, sensors were functionalized with synthetic 20-mer single-strand DNA oligonucleotide probes subsequently exposed to complementary DNA targets to kinetically monitor the hybridization process. The sensor was monitored continuously during the entire sequence of capture probe immobilization, washing, blocker blocking and hybridization as shown in Fig. 5(a). To prevent the non-specific binding of the target DNA to the sensor surface, a blocking step using ethanolamine (EA, 200 mM) was performed. Six separate microplate wells were prepared to separately evaluate six target DNA concentrations. A plot of the target DNA binding phase of the process is shown for all the analyte concentrations in Fig. 5(b).

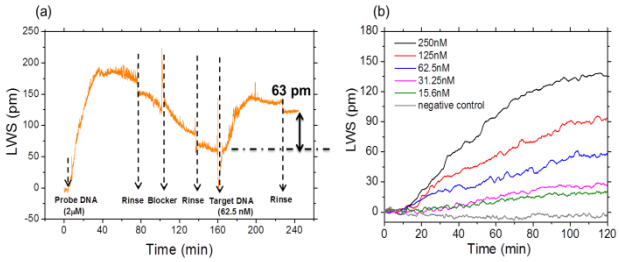

Fig.5. Dynamic measurement results of the specific hybridization of complement probe DNA and target DNA molecules. (a). Lasing wavelength shiftsthrough the probe DNA immobilization, blocker blocking, and target DNA hybridization and buffer rinsing process. (b) Selection of binding curves with varying target DNA concentrations.

IV. CONCLUSION

In conclusion, we have demonstrated a novel ECL label-free biosensor that simultaneously achieves high resolution (narrow resonant linewidth), high sensitivity and large dynamic range, offering opportunities in extending the limits of detection of label-free assays for observation of lower concentration targets or smaller molecules.

REFERENCES

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