Photonic Crystal Biosensor

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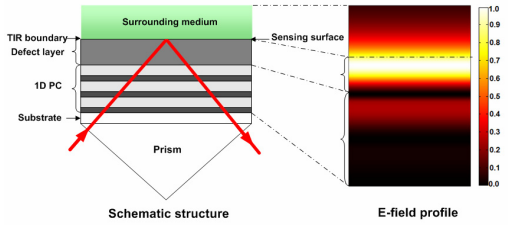
Motivation

- We would like to develop a label-free optical biosensor capable of performing real-time analysis. This biosensor will be significantly more sensitive than the state-of-the-art surface-plasmon-resonance (SPR) based instruments, and will allow us to perform binding studies that are currently out of reach of those systems already on the market.

Principles

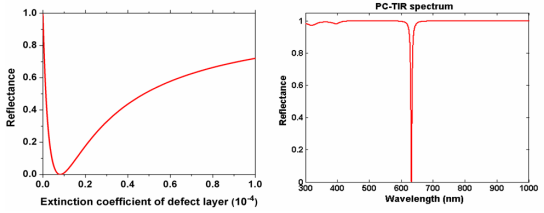


Concept behind the PC-TIR sensor

- A narrow resonance mode ($\Delta\lambda$ ~ 1nm) is achieved by a high finesse Fabry-Perot microcavity formed with a photonic crystal (PC) structure and total-internal-reflection (TIR) boundary in the defect layer;
- Large enhancement in the evanescent field provides high sensitivity to small changes on the sensing surface (>10^3 nm/RIU);
- Open sensing surface enables label-free, real-time measurement.

Operating principle

- Suitable absorption in defect layer used to characterize resonance mode;



- Resonance mode shifts when refractive index of the surrounding medium varies or the analyte is adsorbed on the sensing surface, by changing resonance condition of the Fabry-Perot microcavity:

$$2\cdot\frac{2\pi}{\lambda_R}n_x d_x\cos\theta_x+\alpha=(2m+1)\pi \qquad (m=0,1,2,\ldots)$$

α represents the Goos-Hänchen phase shift between defect layer and bulk solvent

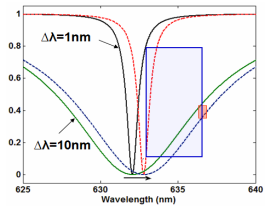
By monitoring the resonance mode, we can get the information on the solvent index change, the analyte's index, thickness, mass density or affinity constants, etc.

- Ways to achieve high sensitivity:

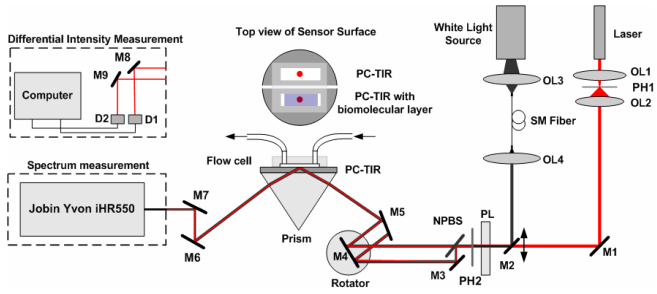
a) Narrow resonance mode for higher resolution;

b) Intensity modulation for larger signal change;

c) Reference channel to eliminate fluctuations of laser intensity and temperature, etc.



Experiment setup



- Two detection methods to measure the shift of the resonance mode:

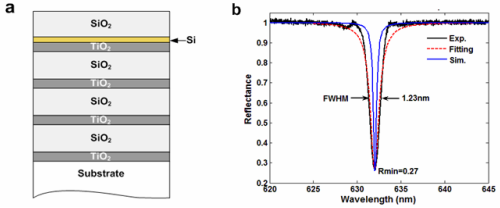
a) Spectrum measurement is to measure the shift of the resonance wavelength that provides large detection range (~ μm) with a reasonable resolution (~$10^{-2}nm$);

b) Differential intensity measurement is used to measure the intensity ratio change of the resonant mode at a single wavelength. This yields a high detection resolution (~10^{-5});

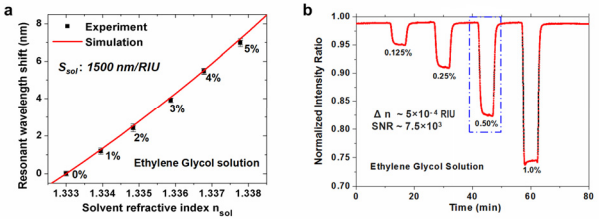
- A microfluidic flow system enables real-time measurement.

Experiment results

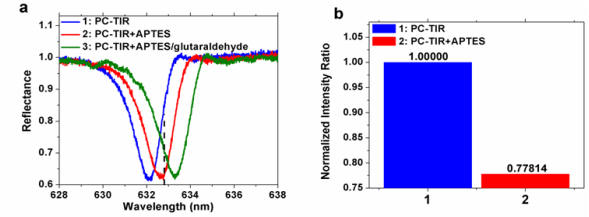
Typical PC-TIR sensor structure & reflectance spectra



Bulk solvent index change (detection limit: 7×10^{-8} RIU)



Thin molecular layer adsorption (detection limit: 6×10^{-5} nm)

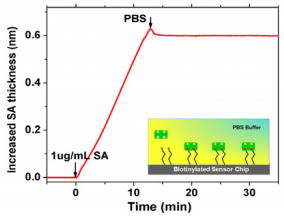


(a) Resonance wavelength shifts with binding of APTES (0.55nm) and APTES/glutaraldehyde (1.33nm)
(b) Intensity ratios at 632.8 nm without treatments (blue) and with APTES monolayer (red).

Developed surface chemistries on sensing surface

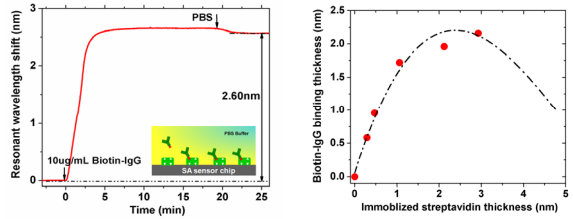
- Biotinlyated chip: used for immobilization of streptavidin (SA)
- Carboxyl chip : used for immobilization via –NH_2 or –COOH groups
- Streptavidin chip: used for immobilization of biotinylated peptides, proteins, nucleic acids, or carbohydates

Real-time protein binding (mass density detection limit: 0.02pg/mm²)

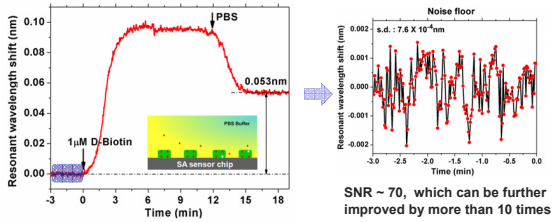


SA layer thickness : 0.60 nm
Detected surface density : 240 pg/mm²
Signal to noise ratio (SNR) : 1.2×10^4
Detection limit : 0.02 pg/mm²

Large molecule-protein interaction (Biotinylated IgG: 150kDa)



Small molecule-protein interaction (D-Biotin: 244Da)



SNR ~ 70, which can be further improved by more than 10 times

Summary

- Developed a novel optical biosensor which can perform label-free, real-time analysis on biomolecular interaction;
- Achieved orders of magnitude higher detection sensitivity than the state-of-the-art SPR-based system.

Sensor	FWHM	Detection limits			
		Solvent RI	Thickness	Mass density	MW
PC-TIR	Δλ ~ 1 nm	7×10^{-8} RIU	6×10^{-5} nm	0.02 pg/mm²	< 244 Da
SPR	Δλ ~ 40 nm	5×10^{-7} RIU	3×10^{-3} nm	> 1 pg/mm²	> 1,000 Da

Acknowledge

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