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# Label Free Detection of Prostate Specific Antigen Using Photonic Crystal Nanocavity Resonator

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**Abstract**

**A label-free optical biosensor based on two-dimensional Si photonic crystal nanocavity-type resonator is demonstrated. To functionalize the resonator surface with the antibody-antigen, a special method called Si-tag is used. We successfully detected prostate specific antigen at a lower concentration of 0.01 ng/mL (312.5 pM).**

## 1. Introduction

Optical label free biosensors have drawn a great research interest for real time, portable, cost effective, highly sensitive medical diagnosis [1, 2]. Biosensors using silicon-on-insulator (SOI) platform have advantages of strong light-matter interaction between resonant mode and target biomaterials, and compatibility with CMOS fabrication technology. Various types of studies have been devoted to the developed the fast, accurate, and label-free biosensors to enhance medical diagnostics, biomolecules, and organic chemical detection [3,4]. Photonic crystal (PhC) based micro/nano cavities are getting lots of research interest for medical diagnosis purpose due to their strong light confinement nature, high quality factors, and small modal volumes. When the local refractive index of the sensor surface is changed then resonant peak shifts. These shifts are mainly detected to know device performance.

## 2. Device fabrication

The fabrication process is shown in Fig. 2. A 110 nm thick oxide layer was thermally grown as an intermediate layer of pattern transfer on SOI wafer. An electron beam (EB) sensitive photoresist, ZEP-520A was spin coated onto the oxide layer. An Elionix (ELS-G100) electron beam lithography system was used to define high resolution patterns on the resist. The patterns were then developed by xylene and isopropyl alcohol. In order to transfer this pattern into the Si layer we used reactive-ion etching (RIE) and inductively coupled plasma (ICP) using $CF_4$ and $Cl_2$ gas respectively. In a final step, wet etching by diluted hydrofluoric acid was used to remove $SiO_2$ mask. Scanning electron microscope images of the fabricated device is shown in Fig. 3 [5].

## 3. Procedure of antigen-antibody reaction

The uniqueness of this work is the silicon binding protein that binds with $SiO_2$ and Si surface and immobilizes the biomolecules on the PhC cavity surface. The things that we used are the protein G which makes strong bonds with many kinds of mammalian antibodies. The antigen-antibody reaction procedure is shown in Fig. 4. In Fig. 4(a), the receptors are randomly oriented. In this method antigen-antibody immobilization on sensor surface is difficult. In Fig (b), Si-tag was used to immobilize the antigen-antibody on the sensor surface and Fig. (c) shows the full schematic of the antigen-antibody reactions. The optical measurement setup is shown in Fig. 5.

## 4. Results and Discussion

The experimental process is explained in Fig. 6. Firstly Si-tag+Protein G+antibody (IgG2a) solutions are poured on the sensor surface respectively and measured the resonant peak. Next, PSA antigens were added to the solution, and measured the spectral shift of resonance peak. Figure 7 shows the resonance spectra of Si-tag+protein G+IgG2a and various of PSA concentrations and it also shows that at each concentration, the resonance spectra has shifted and at higher concentration the shift has saturated. In Fig. 8, the resonance wavelength shift ($\Delta\lambda$) is plotted as a function of the concentration of the PSA solution. The result fits to the following Langmuir equation [6],

$$\Delta\lambda = \frac{\Delta\lambda_{\max} CK}{1 + CK} \qquad (1)$$

where $\Delta\lambda_{max}$ is the maximum resonance wavelength shift, $C$ is the concentration of PSA biomarkers and $K$ indicates the equilibrium constant of adsorption-desorption reaction. The best fitting is shown in Fig. 8 by adjusting the $K$ values. The performance of the devices is compared in Table I.

## 5. Conclusion

We succeeded in sensing the antibody–antigen reaction using photonic crystal double nanocavity resonator sensor employing PSA marker as an example target. By immobilization of the antigen-antibody on the sensor, we detected the PSA concentration as low as 0.01 ng/mL (312.5 pM).

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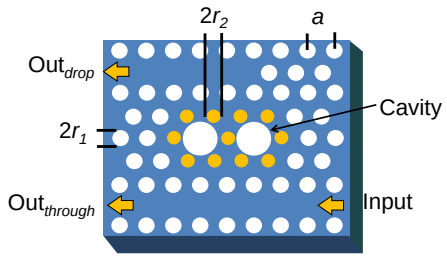


Fig. 1. Schematic of proposed double nanocavity resonator [5].

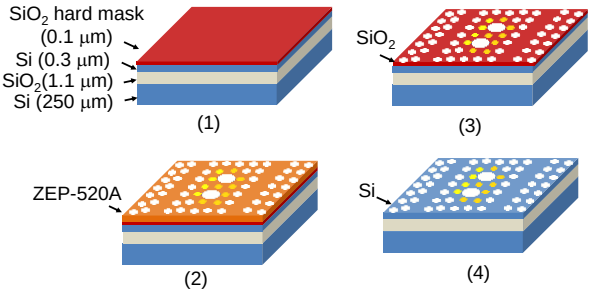


Fig. 2. Fabrication process for Si PhC resonators [5].

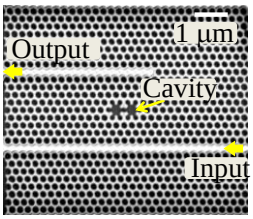


Fig. 3. SEM image of double nanocavity resonator [5].

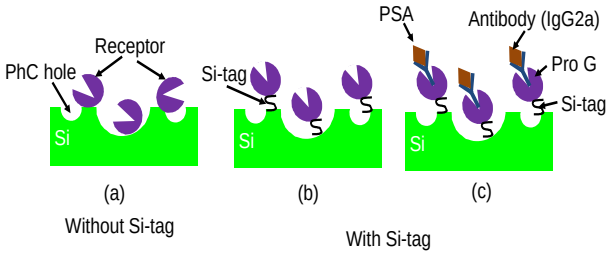


Fig. 4. Antigen-antibody reaction mechanism [6].

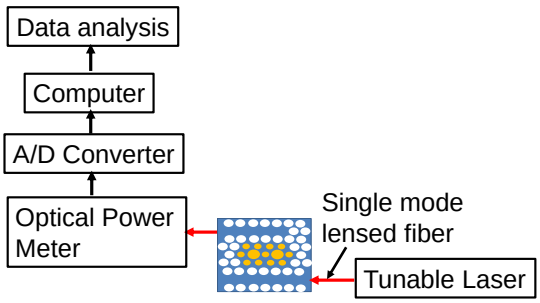


Fig. 5. Optical measurement setup [5].

1. SH ($H_2S0_4$+$H_2O_2$) clean for 10min.
2. Device surface wash by Tris-HCl (pour Tris-HCl and wait 10 min).
3. Pour 20μL of Si-tag + Protein G and wait for 10min.
4. Wash by Tris-HCl.
5. Measure the resonant peak.
6. Pour 20μL of IgG2a and wait for 10min.
7. Wash by Tris-HCl.
8. Measure the resonant peak.
9. Pour 20μL of PSA antigen and wait for 10min.
10. Wash by Tris-HCl.
11. Measure the resonant peak.

steps 9-11 be repeated from lower to higher concentration.

Fig. 6. Experimental procedure to detect prostate specifi antigen [6].

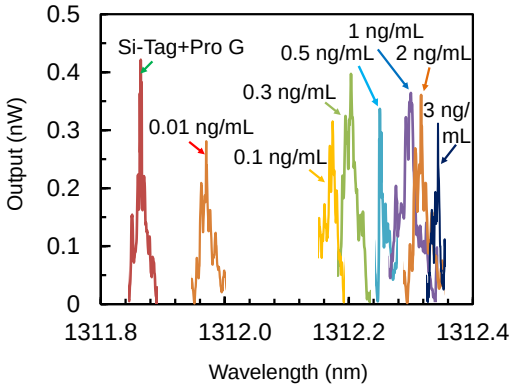


Fig. 8. Langmuir's fitting with experimental results.

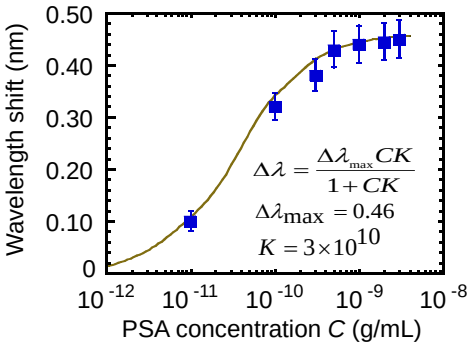


Fig. 7. Experimental results of various concentration of PSA.

Table I. Performance comparison with other works.

| Ref. | Sensor type | Concentration of biomaterials | Sensing materials | Q value |
|---|---|---|---|---|
| This work | PhC double cavity | 312.5 pM | PSA | $2\times10^5$ |
| [7] | PhC waveguide | 0.15 μM | BSA proteins | - |
| [8] | PhC cavity | 233 pM | Anti-biotin | - |