A LABEL-FREE PROTEIN SENSOR BASED ON MEMS FABRY-PEROT INTERFEROMETER INTEGRATED WITH SILICON PHOTODIODE

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ABSTRACT

We have newly developed a label-free protein sensor based on MEMS Fabry-Perot interferometer integrated with a photodiode, which utilizes nonlinear optical effect of the Fabry-Perot resonance to enhance the sensitivity of surface stress. A parylene was used for a deformable membrane of the protein sensor because of the high optical transmittance and low Young's modulus. Theoretical signal-to-noise ratio of the proposed sensor with the surface stress of -0.1 N/m with 200 μm diameter using a light source of 10 mW is calculated 1.55 x 10^5 with the experimental dark current noise of 10 nA in the photodiode which is two orders of magnitude larger than piezoresistive type. A photocurrent was demonstrated to shift by 23.7 nA at 3 V bias voltage with immobilized antibodies.

KEYWORDS: Label-free, Protein sensor, MEMS, Fabry-Perot interferometer, Photodiode, Surface stress

INTRODUCTION

Surface stress sensors are expected to have many advantages such as label-free and real-time detection. In particular, surface stress sensors based on a semiconductor technology including capacitive type [1,2] and piezoresistive type [3,4] are an enabling technology to develop chemical and biological smart chip with compact and large multidimensional arrays. However, their sensitivity was less than that of optical read-out type [5,6] due to the low conversion efficiency from mechanical deformation into electrical read-out signal. In this paper, we newly developed a Fabry-Perot interferometric protein sensor with on-chip electronics. The electrical read-out signal as photocurrent is obtained using nonlinear transmittance change with the Fabry-Perot resonance.

THEORY

Figure 1 schematically illustrates an operational principle of the Fabry-Perot interferometric protein sensor. A thin flexible film is suspended over a silicon photodiode with an air gap. A Fabry-Perot cavity consisting of the air gap and a silicon dioxide layer is changed due to a surface stress caused by antigen-antibody reaction, which results in changing an intensity of an incident light to the photodiode. We choose parylene-N as the deformable membrane because of the high optical transmittance and low Young's modulus of 2.4 GPa, which is two orders of magnitude smaller than that of silicon. Such soft material is quite sensitive to the surface stress.

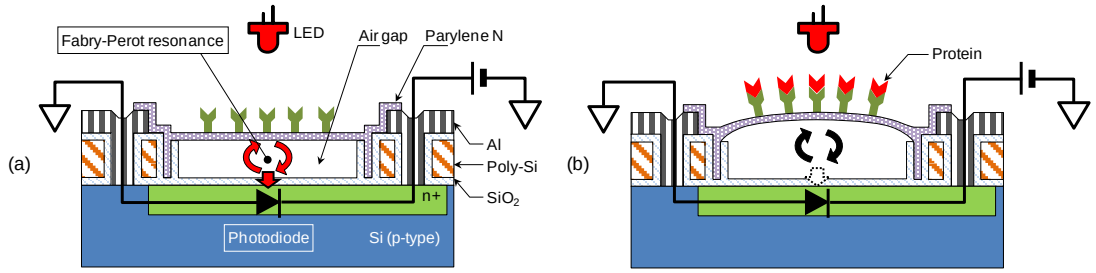

Figure 1: *Operational principle of a Fabry-Perot interferometric protein sensor integrated with photodiode. Photocurrent is changed due to a deflection by an antigen-antibody reaction.*

The transmittance of the Fabry-Perot interferometer at 600 nm wavelength is simulated, as shown in Figure 2. Optical multilayer films are designed to be 800 nm thick parylene-N, 320 nm thick air gap, and 200 nm thick silicon dioxide. The wavelength peak of the transmitted light is drastically decreased by 60 % at 600 nm wavelength with 100 nm displacement of the parylene-N membrane. The sensitivity of the proposed sensor could be increased using the nonlinear transmittance change while a dynamic range is restricted by area of monotone decreasing within 100 nm displacement. For quantitative comparison with the conventional cantilever sensor, we calculated output photocurrent when the surface stress was applied to the flexible membrane. Deformation of the membrane with surface stress can be calculated by finite element method using ANSYS, and photocurrent is described as follows

$$I = -\frac{\phi q \eta \lambda}{h c} \tag{1}$$

where ϕ is the optical intensity, λ is the wavelength, η is the quantum efficiency, q is the elementary charge, c is the speed of light in vacuum and h is the Plank's constant. Figure 2 (b) shows photocurrent as a function of the surface stress. Signal-to-noise ratio of the proposed sensor with the surface stress of -0.1 N/m with 200 μm diameter using a light source of 10 mW is calculated 1.55 x 10^5 with the experimental dark current noise of 10 nA in the photodiode, which is two orders of magnitude larger than piezoresistive type. Therefore, minimum detectable surface stress is less than -1μN/m.

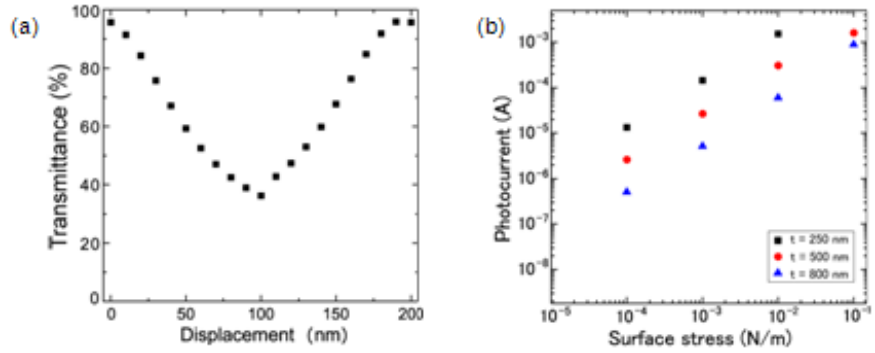

Figure 2: *(a) Calculated transmittance of the Fabry-Perot interferometer as a function of displacement of the sensor membrane. (b) Calculate photocurrent as a function of surface stress.*

EXPERIMENTAL

Process overview is shown in Figure 3; (a) a photodiode was made into a p-type silicon wafer using an ion implantation of phosphorus. (b) A polysilicon was deposited as a sacrificial layer by an LP-CVD. (c) Thermal oxidation was used to make a side wall passivation for sacrificial etching. (d) An aluminum was sputtered for interconnection, and then (e) a parylene-N was vacuum-deposited and etched for deformable membrane. (f) The sacrificial layer was etched by XeF_2. (g) The etching holes were sealed with a dry film resist. (h) Finally, a parylene-AM was coated on the deformable membrane for immobilization of bio molecules.

Figure 4 shows an optical micrograph and an SEM image of the developed Fabry-Perot interferometric protein sensor. The photoresist blocks were used to prevent any liquid contamination into Fabry-Perot cavity at bio molecules interaction. The sensing area was found to be blue color at initial state of the deformable membrane. The deformable thin membrane was 350 nm thick and 150 μm diameter with 300 nm air gap.

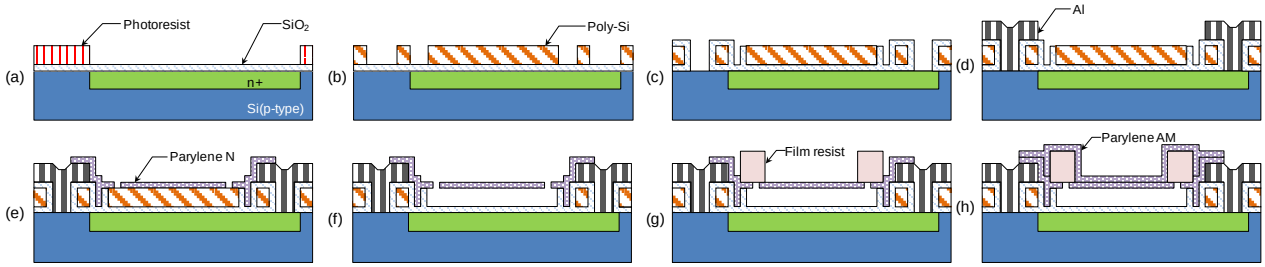

Figure 3: Process overview

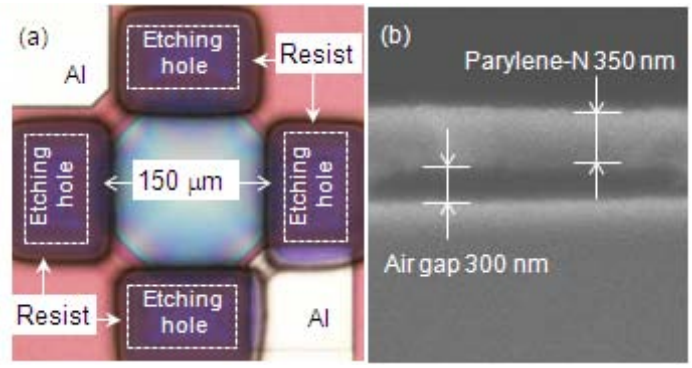

Figure 4: *(a) Optical micrograph and (b) Cross-sectional view of the Fabry-Perot interferometric protein sensor*

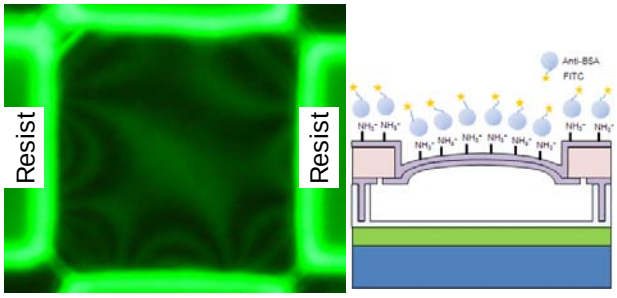

Figure 5: Fluorescence micrograph of the immobilized anti-BSA with FITC on the deformable thin membrane.

RESULTS AND DISCUSSION

We used FITC-conjugated anti-bovine serum albumin antibodies (anti-BSA) to confirm the immobilization of a protein, and found fluorescence on the deformable membrane, as shown in Figure 5. We observed the reflected light from the sensing area. Figure 6 (a) shows the theoretically predicted reflection spectrum and a red shift with the deflection of the membrane. Figure 6 (b) and (c) show blue and red color with the deformable membrane after washing with PBS and immobilized anti-BSA, respectively. Therefore, the membrane deformation due to the immobilized anti-BSA was demonstrated by the color change. Figure 7 plots a diode current as a function of bias voltage. After immobilization of anti-BSA, we measured to shift by 23.7 nA at 3 V bias voltage using a light source of 1 nW at 600 nm wavelength. Electrical characteristics can be improved by tuning the process condition and using a high power laser.

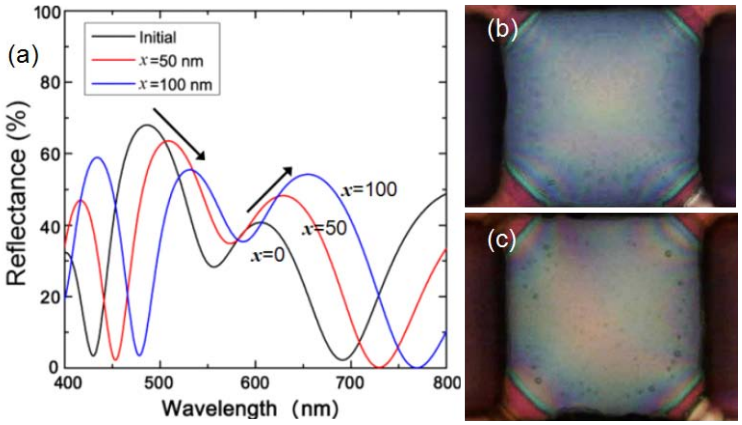

Figure 6: (a) Calculated reflectance as a function of displacement. (b) Blue and (c) red color with the deformable membrane after washing with PBS and immobilized anti-BSA, respectively.

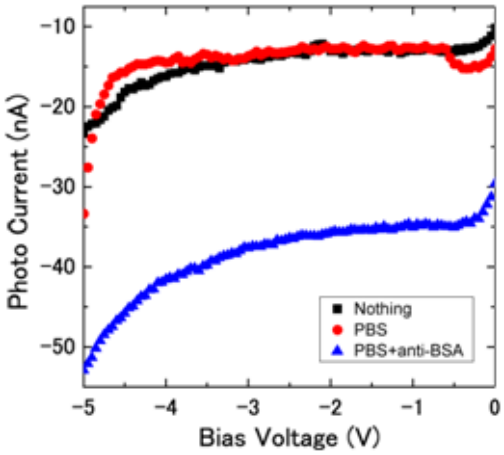

Figure 7: Measured photocurrent of the protein sensor immobilized anti-BSA.

CONCLUSION

We have newly developed a label-free protein sensor based on MEMS Fabry-Perot interferometer integrated with a photodiode, which utilizes nonlinear optical effect of the Fabry-Perot resonance to enhance the sensitivity. The photocurrent from the prototype sensor was demonstrated to shift by 23.7 nA at 3 V bias voltage with immobilized antibodies. The sensitivity can be improved by tuning the process condition and using a high power laser.

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