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A MEMS Based Fabry-Perot Protein Sensor with Reference Sensor

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Abstract:
We have developed a label-free protein sensor based on a MEMS Fabry-Perot interferometer assembled with a reference protein sensor, which simultaneously measures a surface stress and transmittance change caused by immobilization of proteins. The MEMS protein sensor is composed by a silicon photodiode and a free-standing thin film with a nano cavity. A deflection of the thin film caused by an antigen-antibody reaction is detected by a photocurrent change. The MEMS protein sensor utilizes nonlinear transmittance change by using the Fabry-Perot interference to enhance the sensitivity of surface stress. Theoretical minimum detectable surface stress of the proposed sensor is predicted -1μN/m which is two orders of magnitude smaller than piezoresistive type. On the other hand, a reference sensor without the nano cavity measures a transmittance change caused by proteins and liquids. We fabricated the MEMS sensor and the reference sensor in a same chip by semiconductor planer process. A photocurrent from the MEMS protein sensor was demonstrated to shift by 23.7 nA at 3 V bias voltage with immobilized antibodies without any transmittance change on the reference sensor.

Key words: Label-free protein sensor, MEMS, Surface-stress, Fabry-Perot interferometer, reference sensor

Introduction

A label-free protein sensor is an enabling technology for rapid diagnosis. 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.

We have previously developed a Fabry-Perot interferometric protein sensor with on-chip electronics [7]. The electrical read-out signal as photocurrent is obtained using nonlinear transmittance change with the Fabry-Perot interference to enhance the sensitivity of surface stress. However the Fabry-Perot interferometric protein sensor could not be used for opaque liquids such as blood. To overcome this problem, we newly added a reference sensor to measure a transmittance change caused by proteins and liquids. In this paper, we report design, fabrication and experimental results of the MEMS Fabry-Perot interferometric protein sensor assembled with the reference protein sensor.

Design

Fig. 1 schematically illustrates an operational principle of the MEMS Fabry-Perot interferometric protein sensor assembled with the reference sensor. The MEMS protein sensor is composed by a silicon photodiode and a free-standing thin film with a nano cavity. An antibody is pre-immobilized on the flexible film. The deformable thin membrane moves due to a surface stress caused by antigen-antibody reaction, which results in changing the Fabry-Perot interference wavelength. When a single wavelength light is utilized to the sensor, an intensity of the incident light to the photodiode is drastically changed. Therefore, the MEMS Fabry-Perot sensor can detect molecular interaction forces as a photocurrent. On the other hand, a reference sensor without nano cavity only measures a transmittance change

caused by proteins and liquids. Both sensors are exactly same structure except for the nano cavity.

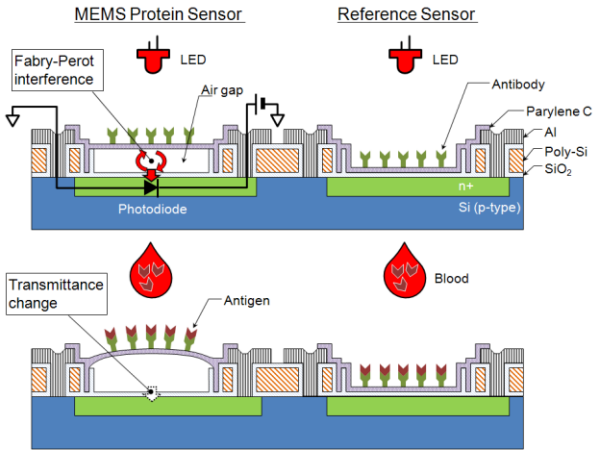

Fig. 1. Operational principle of a MEMS Fabry-Perot interferometric protein sensor assembled with a reference sensor. Photocurrent in the MEMS sensor is changed due to a deflection by an antigen-antibody reaction. The reference sensor only measures turbidity of proteins and liquids.

A key component of the protein sensor is upper membrane which requires transparency, flexibility, and CMOS-compatibility. We choose parylene-C as the deformable membrane because of the high optical transmittance and low Young's modulus of 2.8 GPa, which is two orders of magnitude smaller than that of silicon. Such soft material is quite sensitive to the surface stress.

For quantitative comparison with the conventional cantilever sensor, we calculate output photocurrent when the surface stress was applied to the flexible membrane. Firstly, deformation of the parylene-C membrane with surface stress is calculated by finite element method using ANSYS. Optical multilayer films are designed to be 350 nm thick parylene-C, 200 nm thick air gap, and 270 nm thick silicon dioxide. The output deformation value is applied to an optical simulation. The transmittance of the Fabry-Perot interferometer at 780 nm wavelength is simulated as shown in Fig 2 (a). The wavelength peak of the transmitted light is drastically increased by 60 % with 200 nm displacement of the parylene-C membrane. The sensitivity of the proposed sensor could be increased using the nonlinear transmittance change. A photocurrent is described using the optical intensity ϕ as follows

$$I = -\frac{\phi q \eta \lambda}{h c} \qquad (1)$$

where 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. Fig. 2 (b) shows the output photocurrent as a function of the surface stress. Signal-to-noise ratio of the proposed sensor with the surface stress of -0.01 N/m with 200 μm diameter using a light source of 1 mW is calculated 1.0 x 10^4 with the experimental dark current noise of 10 nA in the photodiode. Therefore, minimum detectable surface stress is less than -1μN/m, which is two orders of magnitude smaller than piezoresistive type.

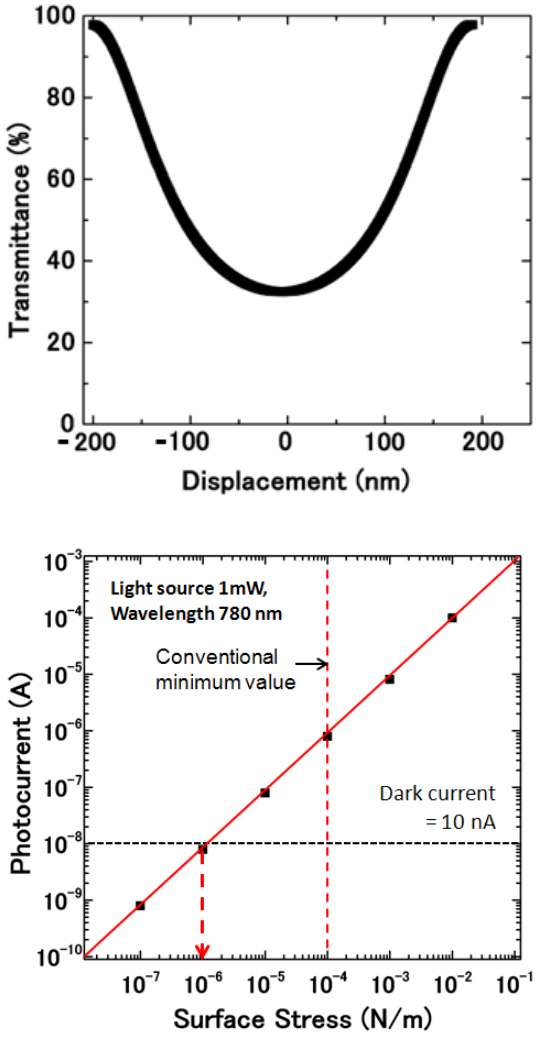

Fig. 2. (a) Calculated transmittance of the Fabry-Perot interferometer as a function of displacement of the sensor membrane. (b) Calculate photocurrent as a function of surface stress.

Fabrication

The MEMS protein sensor was developed using a 4-inch p-type silicon wafer. Process overview is shown in Fig. 3 (a) a photodiode was made into the silicon substrate using an ion implantation of phosphorus. (b) A polysilicon was deposited as a sacrificial layer by an LP-

CVD. The polysilicon layer in a reference sensor area was only removed by RIE. Thermal oxidation was used to make a side wall passivation for sacrificial etching. (c) An aluminum was sputtered for interconnection, and then a parylene-C was vacuum-deposited and etched for deformable membrane. (d) The sacrificial layer was isotropically etched by XeF_2. (e) The etching holes were sealed with a dry film resist to prevent any liquid contamination into Fabry-Perot cavity at bio molecules interaction. (f) Finally, an amino-methyl-functionalized parylene (parylene-AM) was coated on the deformable membrane for immobilization of bio molecules through the electrostatic coupling between proteins and amino-group of parylene-AM.

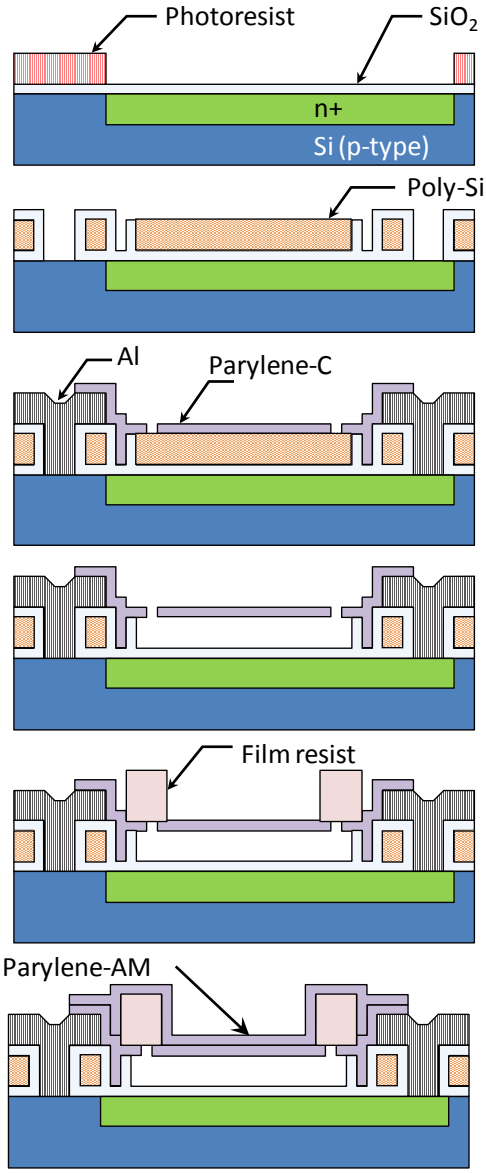

Fig. 3. Fabrication process for Fabry-Perot interferometric MEMS protein sensor.

Fig. 4 shows an optical micrograph of the developed Fabry-Perot interferometric protein sensor with the reference sensor. The sacrificial polysilicon layer was laterally etched using etching holes for thin parylene-C film release. The sensing area in the MEMS sensor was found to be red color at initial state of the released parylene-C membrane. The deformable perylene-C membrane was 360 nm thick and 200 μm diameter with 300 nm air gap. The same parylene-C film was fixed on the photodiode with 100 μm diameter. The fixed parylene-C film was found to be different color of dark blue due to the different optical multilayer.

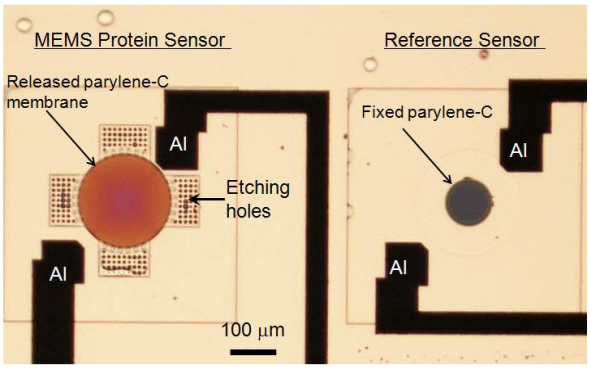

Fig. 4. Optical micrograph of the Fabry-Perot interferometric protein sensor with the reference sensor.

Experimental

We used anti-bovine serum albumin antibodies (anti-BSA) to estimate the protein detection and the transmittance change caused by the immobilization of a protein on the proposed sensors. Fig. 5 plots a diode current as a function of bias voltage. After immobilization of 1 mM anti-BSA, we measured to shift by 23.7 nA at 3 V bias voltage using a light source of 10 $\mu W/cm^2$ at 600 nm wavelength. We also measured turbidity of the anti-BSA using a light source of 400 $\mu W/cm^2$ at 780 nm wavelength, as shown in Fig. 6. The photocurrent and dark current noise were measured 3.26 μA and 1.8 nA, respectively. The photocurrent change was not visibly observed before and after immobilization of anti-BSA.

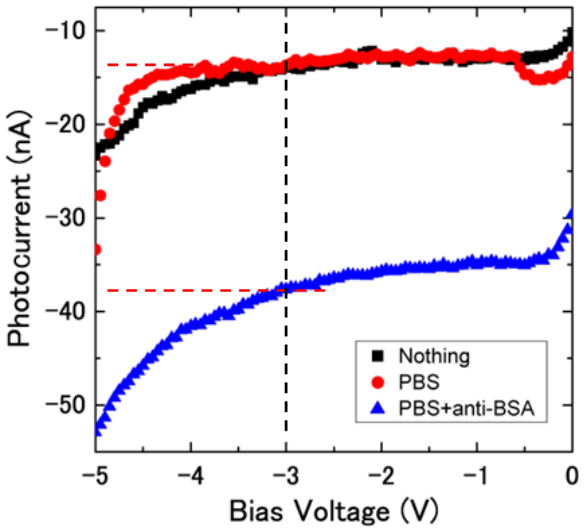

Fig. 5. Measured photocurrent of the MEMS protein sensor immobilized anti-BSA.

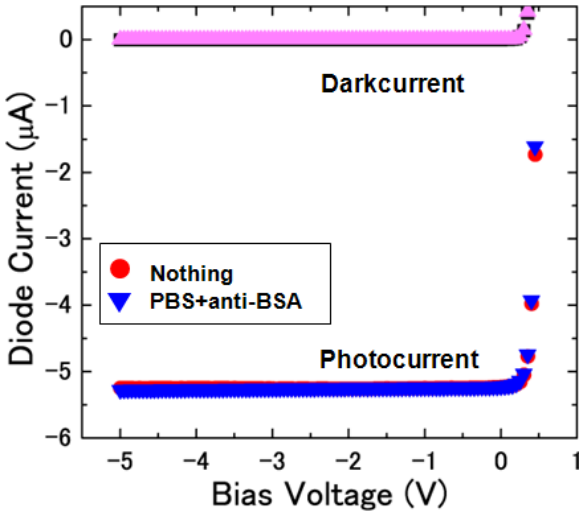

Fig. 6. Measured photocurrent of the reference sensor immobilized anti-BSA.

Conclusion

We have developed a label-free protein sensor based on MEMS Fabry-Perot interferometer assembled with a reference sensor for transmittance mesurement. The MEMS sensor and the reference sensor was simply fabricated using semiconductor planer process at the same time because both sensors are exactly same structure except for the nano cavity. The photocurrent from the prototype sensor was demonstrated to shift by 23.7 nA at 3 V bias voltage with immobilized antibodies without any transmittance change on the reference sensor. The proposed protein sensor could be used for opaque liquids such as blood.

Acknowledgement

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