Sensitivity Improvement of Biosensors Using Si Ring Optical Resonators

Masataka Fukuyama¹, Yoshiteru Amemiya¹, Yosuke Abe, ¹ Yuto Onishi¹, Anna Hirowatari¹, Kei Terao¹, Takeshi Ikeda¹, Akio Kuroda², and Shin Yokoyama¹

¹Research Institute for Nanodevice and Bio Systems, Hiroshima University

²Department of Molecular Biotechnology, Graduate School of Advanced Sciences of Matter, Hiroshima University

1-4-2 Kagamiyama, Higashihiroshima, Hiroshima 739-8527, Japan

Phone: +81-82-424-6265 Fax: +81-82-424-3499 E-mail: fukuyama-m@hiroshima-u.ac.jp

1. Introduction

Si microring optical resonator is one of the candidates for the high-sensitive compact biosensor [1]. We have demonstrated a variety of antigen-antibody reactions using Si ring resonator [2, 3]. However, the detection sensitivity is in the order of 10^{-6} g/ml as shown in Fig. 1. The practical biosensor requires the sensitivity of 10^{-9} g/ml.

In this paper, we show that the sensitivity of 10^{-9} g/ml will be possible by (1) slot-type waveguide [4] at wavelength of 1.3 µm, (2) improving quality factor Q of the resonator, (3) specific adsorption of the analyte to the detector surface, and (4) maintaining temperature within \pm 0.005°C. We found that the electron-beam (EB) positive-type resist exhibits a good specific adsorption (no adsorption) of green fluorescent protein (GFP) at NaCl concentration of 0.5 M. The practical temperature compensation method without control of the real sample temperature is proposed.

2. Experimental

The sensitivity of the ring-resonator using the slot-waveguide (shown in Fig. 2) was simulated at the wavelength of 1.3 μ m where the light absorptions by the water and Si are both small [2]. The refractive-index change is much higher than the normal waveguide because the light intensity takes maximum in the slot where the biomaterials are present. The sensitivity of the resonator depends on the *Q* factor when the input light wavelength is fixed, and is drastically changed with the surface roughness. The *Q* factor was simulated using the equation given by Payne *et al.* [5]. The specific adsorption of the analyte on the ring surface was investigated using the GFP for various materials at different NaCl concentration. The temperature dependence of the resonance wavelength was measured and a compensation method is proposed.

3. **Results and Discussion**

3.1 Slot-waveguide

Figure 2 compares the sensitivity of the slot-waveguide with normal waveguide. The adsorbing biomaterial is simulated as a thin layer with refractive index of 1.45 [4]. The sensitivity is defined as the change in the effective refractive index when the adsorbing layer is added. The obtained value is almost constant for the adsorbing-layer thickness ranging 1 to 10 nm. The thickness of the one monolayer of biomaterial is usually < 10 nm. Wavelength of 1.3 µm results in better results (7) while it is 5 for 1.5 µm. The better result may be attributed to the higher light energy density for 1.3 µm in the slot than 1.5 µm because the light is more efficiently confined at short wavelength.

3.2. Effect of roughness to Q factor

Figure 3 shows the effect of roughness to Q which is approximated by $2\pi n_{\text{eff}}/\alpha \lambda_{\text{res}}$ [6] where n_{eff} , α and λ_{res} respectively indicate effective refractive index, absorption coefficient and resonance wavelength. The world record of

the *Q* factor is 2.5×10^5 while our top value is 1.5×10^5 , the roughness ~1.7 nm. We have found that the surface roughness is improved to 40% by the isotropic chemical dry etching using CF₄+O₂ plasma with high O₂ content and small etch rate (O₂/ CF₄=3, not shown).

3.3 Specific adsorption of analyte

Fluorescence intensity of GFP on variety of materials is examined. Example results are shown in Fig. 4, comparing with SiO₂ and EB positive resist (ZEP 520A) at different NaCl concentration. The results are summarized in Fig. 5. It is found that the intensity is minimum for EB positive resist at NaCl concentration of 0.5M. The effect of this specific adsorption to the sensitivity of the biosensor was calculated using the model shown in Fig. 6, where the analyte solution is dropped on the sensor. The result is shown in Fig. 7. The sensitivity for the specific adsorption case is much higher than the non-specific adsorption case. In the case of 5 mm x 5 mm sample with the thickness of the solution of 0.5 mm, the volume is 5 μ L then the sensitivity ratio is 4.5.

3.4 *Temperature compensation*

The temperature dependence of Si is relatively large and the resonance wavelength shifts toward longer wavelength at high temperatures. Figure 8 shows temperature dependence of the resonance wavelength. In order to overcome this problem we propose temperature compensation method using two ring resonators. The input light is the LED light in which the wavelength is expanding ~10 nm. First-stage ring resonator acts as the filter with the same temperature dependence as the detector ring. The intensity change with the temperature is stored in the computer memory and the deviation from this intensity is attributed to the adsorbed analyte on the detector ring. The temperature uniformity for two adjacent Si ring can be maintained within $\pm 0.005^{\circ}$ C.

4. Conclusion

Employing the variety of proposed approach it is suggested that the sensitivity of the biosensor will be improved by factor of >100. Then the practical Si ring biosensor will be realized.

Acknowledgments

This work was partly supported by "Interdisciplinary Research on Integration of Semiconductor and Biotechnology at Hiroshima University" from the Ministry of Education, Culture, Sports, Science, and Technology of Japan and New Energy and Industrial Technology Development Organization (NEDO) of Japan. **References**

[1] K.D. Vos *et al.*: Opt. Express **15**(2007)7610. [2] S. Yamatogi *et al.*: Jpn. J. Appl. Phys. **48**(2009) 04C188. [3] M. Fukuyama *et al.*: ibid. **49**(2010)04DL09. [4] T. Claes *et al.*: IEEE Photonics Journal **1**(2009)197. [5] F.P. Payne *et al.*: Opt. Quant. Electronics **26**(1994)977. [6] Y. Amemiya *et al.*: Jpn. J. Appl. Phys. **49**(2010) 04DG18.

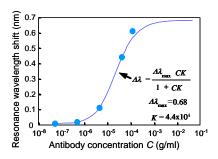
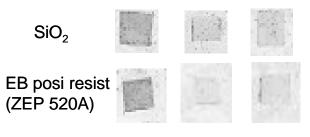


Fig. 1. Concentration of mouse antibody versus resonance wavelength shift and Langmuir's fitting curve.



0M 0.5M 2M

Sensitivity ratio (Slot/Normal)

8

7

6

5

4

3

2

1

0

1.3 μm

better results.

Slot water (n=1.333) 0.1μ m 0.2μ m n=1.45 (0-10 nm)

0.3u m

1.55 μm

Si Si 0.3µ m

Normal

0.4µ m

Si

Wavelength

Fig. 2. Effect of slot waveguide.

Wavelength of 1.3 µm results in

0.1<u>µ</u> m

Fig. 4. GFP fluorescence intensity for SiO₂ and EB posi resist (ZEP 520A) at different NaCl concentration. Dark region indicates high fluorescence intensity region.

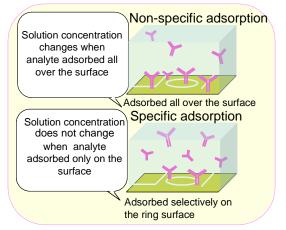


Fig. 6. Model for non-specific and specific adsorption of analyte. Non-specific adsorption results in the deteriorated sensitivity especially for the small-volume of analyte solution.

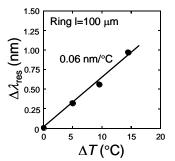


Fig. 8. Temperature dependence of the resonance wavelength shift. The circumference of the ring is 100 µm.

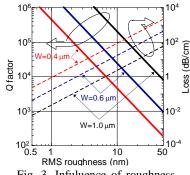


Fig. 3. Infuluence of roughness to Q factor.

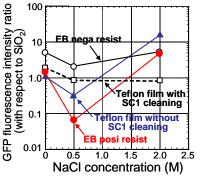


Fig. 5. Effect of NaCl concentration to GFP adsorption on variety of materials at different NaCl concentration. GFP adsorption on EB posi resist at 0.5 M is minimum.

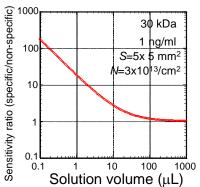


Fig. 7. Analyte solution volume versus sensitivity. Sensitivity improvement of x 4.5 is obtained in the realistic case of 5 µL (5 mm x 5 mm x 0.2 mm).

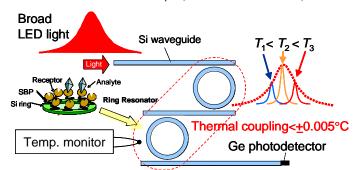


Fig.9. Proposed temperature compensation method using two ring resonators. First-stage ring resonator acts as the filter with the same temperature dependence as the detector ring. The intensity change with the temperature is stored in the computer memory and the deviation from this intensity is attributed to the adsorbed analyte on the detector ring.