Photosensitive Biosensor Array Chips not having the Addressing Circuit

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ABSTRACT

This paper presents photosensitive biosensor array chips with the simple photodiode array having the optical input signal and the electrical output signal, which detects the photocurrent change caused by a reaction between probe molecules and target molecules. Using the properties having the optical input, the addressing circuit on the array chips is removed for the low cost application and the real cell addressing is achieved by the LED array module outside of the chips. After PSA antigen capturing in the serum, the anti-PSA conjugated Au nanoparticles is immobilized and subsequently grown by Ag staining process to enhance the sensitivity of the biosensor. The photocurrent of the biosensor tested on the PC-controllable 5X5 LED array module monotonically decreases with increasing the PSA concentration, showing roughly 1 ng/mL resolution in the PSA detection.

Keywords: photosensitive biosensor, array chip, addressing, prostate specific antigen, nanoparticle, Ag staining

1 INTRODUCTION

Biosensors using the electrical detection have begun to be proposed and can be mass-produced through a semiconductor process [1-8]. Up to date, though many research results on an ion-sensitive field effect transistor (ISFET) sensor or a silicon nanowire FET sensor that is fabricated using the CMOS process, have been reported, it still has many problem to overcome for the commercial application. One of them is that pH concentration and salinity of human blood directly affecting the amount of charge of target molecules vary according to persons. Therefore, it is very hard to quantify the target molecules in the serum by detecting a changed amount of charge caused by a reaction between probe molecules and target molecules. To remove dependence on conditions of serum, the serum must be diluted with reference buffer solution, meaning that these kinds of sensors are still in tough demands of dramatic improvement on the lower detection limit and the higher sensitivity. The best candidate sensor to overcome this problem can be a photosensitive biosensor having the optical input signal and the electrical output signal, which detects the photocurrent change caused by a reaction between probe molecules and target molecules. Especially, using the optical source as input signal causes a remarkable property for the implementation of the biosensor array chip that the optical addressing instead of the electrical addressing can be adapted for each cell driving. The optical addressing has many advantages such as a cheap biosensor array chip implementation, a very simple biosensor structure, the low number of input and output node, and easy expansion of the sensor cell number, when compared with the electrical addressing.

In this work, we propose photosensitive biosensor array chips not having the addressing circuit, in which the optical addressing instead of the electrical addressing is adapted in each cell for the implementation of the biosensor array chip. For the optical addressing, the module including the LED array is fabricated. Finally, the detection of a various concentration of prostate specific antigen (PSA), which is well known as the bio-marker for the prostate cancer, is performed on the fabricated array chip.

2 EXPERIMENT

The schematics explaining the sensing principle are shown in Fig.1. Using the properties having the optical input, the addressing circuit for the control of each cell was removed on the array chips for the low cost application and the real cell addressing was achieved by the LED array module outside of the chips. The real measurement module having the optical input and the electrical output consists of three parts; the LED array for the optical input and optical addressing, cell array chip immobilized with the various bio-molecules on the glass surface, and a photosensitive detection array of the solar cell stack structure.

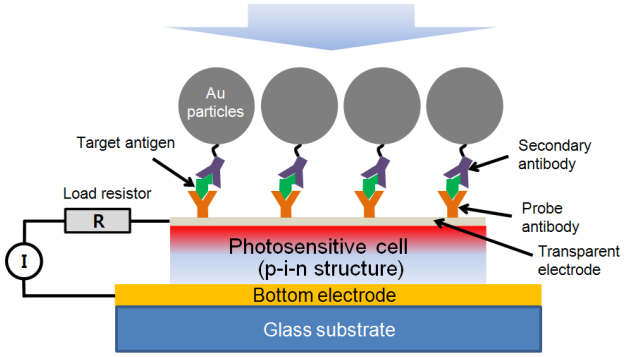

Figure 1: Schematic structure explaining the sensing principle of a photosensitive biosensor

A photosensitive detection array was fabricated on the glass substrate. Fabrication process is very simple. First, transparent electrode, SnO_2 was deposited on glass. Then, amorphous silicon layers were deposited to form the PIN structure using the high vacuum photo-CVD system. Process condition is on the table 1. Finally, Al metel electrode was formed and subsequently used as the etch mask for the array pattern formation.

To immobilize monoclonal antybodies of PSA (anti-PSA) on the glass chip, the glass surface was modified to chemically active surface through the following chemical process; First, oxygen plasma treatment (42 Pa, 25 W, 5 min) was performed. As a result, hydroxyl group-terminated Si surface was formed. Then, the hydrophilic Si nano-channels were exposed to 1% ethanol solution of 3-aminopropyltriethoxysilane (APTES, Sigma-aldrich) for 30 min, followed by rinsing with ethanol and baking at 120°C for 10 min in nitrogen. To bio-activate the surface for anti-PSA immobilization, the amine-functionalized Si nano-channels were immersed in a 25 wt.% glutaraldehyde aqueous with 160 mM sodium cyanoborohydride for 4 h, followed by rinsing with deionized water. Using this surface functionalization method, immobilization of anti-PSA was achieved by exposing the aldehyde-modified Si nano-channels to 120 μg/ml anti-PSA (clone 6915780, Cortex Biochem) in a 10 mM phosphate buffer solution with pH 8.4 containing 4 mM sodium cyanoborohydride ($NaBH_3CN$) overnight. After the immobilization of anti-PSA, the Si channel surface was washed with 3 steps to remove the unreactive analytes; sequentially 1XPBS solution, 0.05% Tween 20 (Pierce) buffer in 1XPBS solution twice, and then DI water. To block the unreacted aldehyde, the device was immersed in a 0.5 mM ethanolamine solution (10 mM phosphate buffer, pH8.4) with 4 mM $NaBH_3CM$ for 30 min.

	p layer (a-SiC:H)	i layer (a-Si:H)	n layer (a-Si:H)
Method	photo-CVD	RF-PECVD	photo-CVD
Temp.	250℃	250℃	250℃
Pressure	0.5 Torr	0.7 Torr	0.5 Torr
Gas flow (sccm)	SiH_4:C_2H_4: B_2H_6 =5:0.7:1.7	SiH_4:H_2=5: 10	SiH_4:H_2=5:3
Thick.	5 nm	500 nm	80 nm

Table 1: Process conditions to fabricate a photosensitive detection array

3 RESULTS AND DISCUSSION

The real measurement was started by putting a cell array chip, immobilized with the various bio-molecules on the glass surface, on the LED array module, which is for the optical input and optical addressing. Then a photosensitive detection of PSA concentration on each cell was done by the photocurrent change from its reference value.

3.1 LED addressing module

The 5X5 LED array module, which is PC-controllable, was designed, assembled for emitting the light on the individual cell and shown in Fig. 2. The 2012 size LED was used and ATMega128 16AY AVR micro controller is adapted for the addressing control. The module is connected to PC via RC-232 serial port. Buffer part plays a role of the noise reduction and the control of the LED brightness. On time duration and its interval can also be controlled by the control program on PC.

3.2 Surface immobilization of the AuNPs

PSA antigen capturing in the serum was performed by the sandwich-type immunogold assay which was using the anti-PSA conjugated Au nanoparticles. Serum containing the various concentrations of the PSA was exposed to the anti-PSA immoblilized glass surface, followed by the injection of anti-PSA conjugated Au nanoparticles. The SEM images of the immobilized NPs are shown in Fig. 3. The photocurrent is affected by the immobilized Au nanoparticles which block the input light. It is clearly seen in Fig. 3 that as the concentration of PSA in serum decreases, the number of NPs immobilized on the surface decreases. In case of the 1 ng/mL PSA, the number of the immobilized NPs just shows 42, which is considered to be too small to block the light and induce the photocurrent change, when compared to the reference (0 ng/mL PSA).

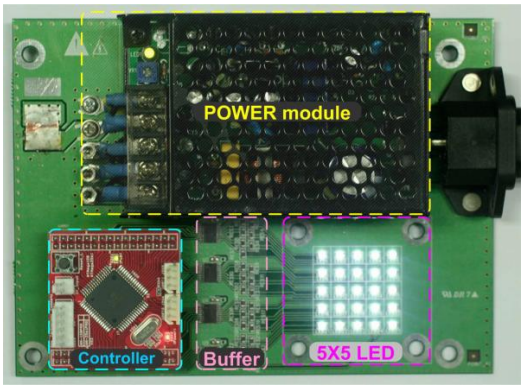

Figure 2: The PC-controllable 5X5 LED array module assembled for emitting the light on the individual cell

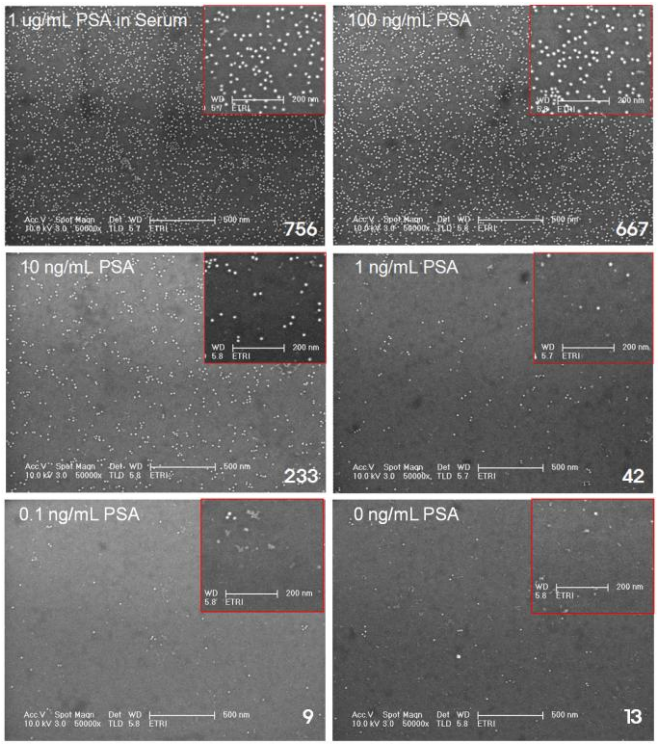

Figure 3: SEM images of the Au nanoparticles immobilized by the sandwich-type immunogold assay

3.3 Signal enhancement

To enhance the sensitivity of the photosensitive biosensor from growing the nanoparticles immobilized on the surface, Ag staining process was adapted, resulting in covering most of the area with Ag from just 9 min dipping in case of 10 ng/ml PSA concentration, as shown in Fig. 4.

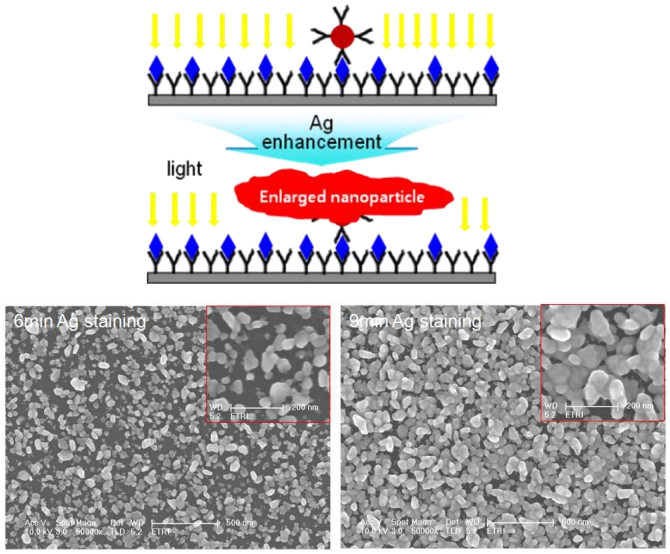

Figure 4: SEM images of the NPs after Ag staining in case of 10 ng/ml PSA concentration sample

3.4 PSA detection

Though it is not shown here, size dependence of the photosensitive biosensors was first checked, showing the little dependence up to the 500umX500um pattern. Then, the optical properties of the fabricated biosensor array chips were tested on the 5X5 LED array module. Figure 5 shows the photocurrent dependence on the PSA concentration with the applied voltage. The PSA concentration in serum ranged from the 1 ng/mL to 100 ng/mL. Ag enhancement was performed on the NPs immobilized surface. It is clearly seen in Fig. 5 that the photocurrent on the biosensor is depending on the PSA concentration, showing the monotonic decreasing with increasing the PSA concentration. Figure 6 shows the dependence of the photocurrent changes on the light intensity, resulting in little change of photocurrent with the light intensity. When the PSA detection in the detailed range of 1 ng/mL to 10 ng/mL was performed, the PSA concentration could be clearly clarified as shown in Fig. 7. In case of 10 ng/mL PSA, the photocurrent was reduced up to 45%, when compared to the reference of 0 ng/mL PSA. When the same experiment was repeated 3 times, the photocurrent variation was not big, as shown in Fig. 8. It is worthwhile to notice that the photocurrent results indicate roughly 1 ng/mL resolution in the PSA detection.

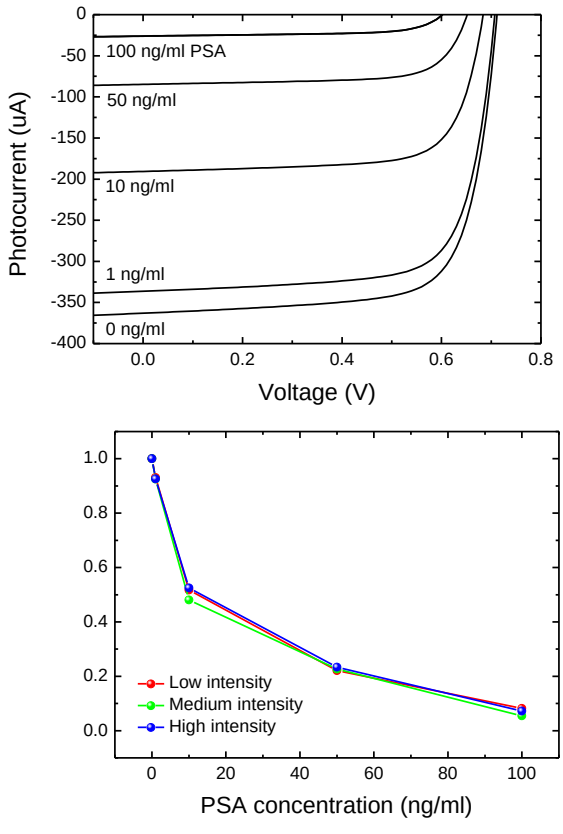

Figure 5: Photocurrent dependency on the PSA concentration and the light intensity

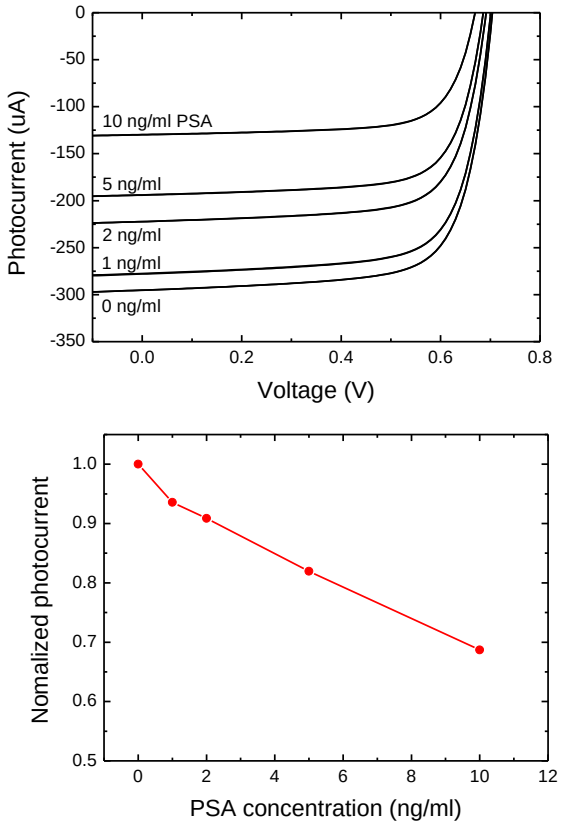

Figure 6: Photocurrent dependency on the PSA concentration (detailed view)

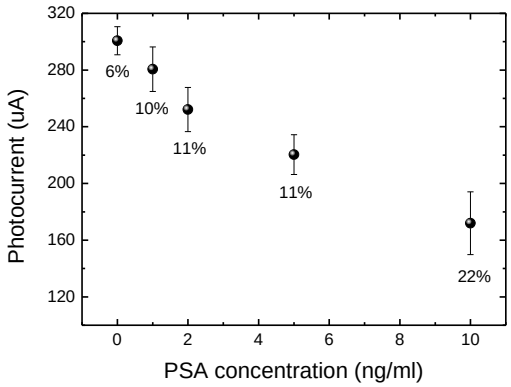

Figure 7: Photocurrent variation with 3 times repetition on the PSA concentration

4 CONCLUSION

We have proposed photosensitive biosensor array chips with the simple photodiode array having the optical input signal and the electrical output signal, which detects the photocurrent change caused by a reaction between probe molecules and target molecules. The real cell addressing was achieved by the LED array module outside of the chips. After PSA antigen capturing in the serum, the anti-PSA conjugated Au nanoparticles was immobilized and subsequently grown by Ag staining process to enhance the sensitivity of the biosensor. The photocurrent of the biosensor tested on the PC-controllable 5X5 LED array module monotonically decreases with increasing the PSA concentration, showing roughly 1 ng/mL resolution in the PSA detection.

5 ACKNOWLEDGEMENTS

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