

Sensitivity Alterable Biosensor Based on Gated Lateral BJT for CRP Detection

Heng Yuan, Byoung-Ho Kang, Jae-Sung Lee, Hyun-Min Jeong, Se-Hyuk Yeom, Kyu-Jin Kim, Dae-Hyuk Kwon, and Shin-Won Kang

Abstract—In this paper, a biosensor based on a gated lateral bipolar junction transistor (BJT) is proposed. The gated lateral BJT can function as both a metal-oxide-semiconductor field-effect transistor (MOSFET) and a BJT. By using the self-assembled monolayer (SAM) method, the C-reactive protein antibodies were immobilized on the floating gate of the device as the sensing membrane. Through the experiments, the characteristics of the biosensor were analyzed in this study. According to the results, it is indicated that the gated lateral BJT device can be successfully applied as a biosensor. Additionally, we found that the sensitivity of the gated lateral BJT can be varied by adjusting the emitter (source) bias.

Index Terms—Gated lateral BJT, MOSFET-BJT hybrid, biosensor, C-reactive protein, self-assembled monolayer (SAM)

I. INTRODUCTION

Human C-reactive protein (CRP) is one of the proteins

produced by the liver, and a high or increasing amount of CRP in the blood suggests that there is an acute or chronic inflammation occurring [1]. In recent years, because of the increasing perception that CRP has a strong relationship with colon cancer and cardiovascular diseases [2, 3], many researchers have laid their focus on CRP detection. An optical-type CRP biosensor, which is based on the wavelength shift of the output light according to the antibody-antigen reaction in the sensing membrane, is highly sensitive but has a large size and high cost and requires a light source and a detector [4]. These problems can be overcome by electrical sensors, such as electrical CRP biosensors that are based on a metal-oxide-semiconductor field-effect transistor (MOSFET) [5, 6]. However, the abovementioned biosensors have a weak point in that their sensitivities are determined by the sensing membrane.

In this study, we propose a new type of semiconductor CRP biosensor based on a gated lateral bipolar junction transistor (BJT) whose sensitivity can be changed by adjusting the emitter (source) bias supply. The device was fabricated using a standard CMOS process, with the advantages of having a small size and being easy to manufacture. This device combines the properties of both a MOSFET and a BJT by emitter and source coupling and collector and drain coupling, respectively, and can be operated in a MOSFET-BJT hybrid mode, which enables the device to display a favorable capability for noise resistance, owing to the low-noise characteristic of a BJT [7]. Meanwhile, the gated lateral BJT with a MOSFET-BJT hybrid mode was reported to have a transconductance approximately 1.5 times higher than a MOSFET [8, 9]. Therefore, gated lateral BJT sensor development has

Manuscript received Apr. 23, 2012; revised Nov. 20, 2012.

Heng Yuan, Jae-Sung Lee, Hyun-Min Jeong, and Kyu-Jin Kim are with School of Electrical Engineering and Computer Science, Kyungpook National University, Daegu, Republic of Korea.

Byoung-Ho Kang and Se-Hyuk Yeom are with Center for Functional Devices Fusion Platform, Kyungpook National University, Daegu, Republic of Korea.

Dae-Hyuk Kwon is with Department of Electronic Engineering, Kyungil University, Gyeongsan-si, Republic of Korea.

Shin-Won Kang is with School of Electronics Engineering, College of IT Engineering, Kyungpook National University, Daegu, Republic of Korea. (Corresponding author)

E-mail : swkang@knu.ac.kr

great significance for the nano-scale sensor technology. The proposed device can also be operated in the MOSFET mode and has the same properties as other sensors based on a MOSFET structure. By fabricating a floating gate on the lateral BJT, the gated lateral BJT was formed; it can be used as a sensor for ion detection and gas sensing [10, 11]. According to the experiment, the proposed gated lateral BJT operated in the MOSFET-BJT hybrid mode can be used as a biosensor and the sensitivity can be controlled by input biases.

II. EXPERIMENTS

1. Sensing Device Structure and Fabrication

The schematic diagram of the gated lateral BJT device is shown in Fig. 1. It can be seen from this figure that the sensor has a two-layer sensing architecture which includes a gated lateral BJT (layer 1) and a sensing membrane (layer 2). In terms of the first layer, a gated lateral BJT with a p-channel transistor was fabricated by Magnachip-Hynix Co. Ltd. via the Integrated Circuit Design Education Center Multi-Project Wafer (IDEC-MPW) project using a standard 0.35- μm logic process. Fig. 1 assumes that the device has a bilaterally symmetrical structure. Therefore, the equivalent circuit is illustrated on the left-hand side, and the electrodes are explained on the right-hand side. In this figure, E is the emitter (source), C is the collector (drain), B is the base, and S is the p-substrate. The widths of the n and p regions were designed to be 1.5 μm , the width of the gate was designed to be 0.5 μm , and the thickness of the gate oxide was approximately 7.3 nm. A lateral and a vertical BJT were embedded in the n-well and the p-substrate region. With an electron beam evaporator, a gold layer (approximately 30-nm thick) was deposited on the floating gate of the device. As the gated lateral BJT was fabricated by a conventional CMOS process without any modification, it has the advantages of easy fabrication, mechanical flexibility, and low-cost.

Unlike common MOSFETs, the gated lateral BJT can be operated in multiple modes, including a typical MOSFET mode, a typical BJT mode, and a MOSFET-BJT hybrid mode. For this study, the lateral collector (drain) and p-substrate of the device were connected to the ground, and a positive bias was applied to the emitter

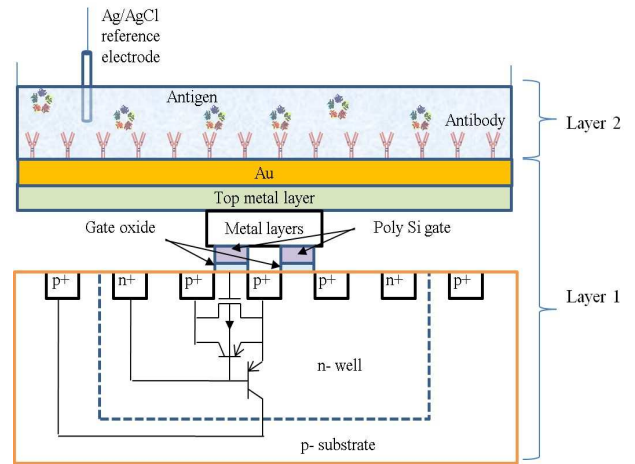


Fig. 1. Schematic diagram of the gated lateral BJT.

(source). The operational modes can be switched using the gate bias and base current supply, i.e., by applying a gate bias smaller than the threshold voltage for a p-type MOSFET, the MOSFET component will be enabled, whereas applying a negative base current induces BJT component operation.

In the second layer, the sensing membrane (CRP antibodies) was immobilized on the gold surface of the gated lateral BJT using the self-assembled monolayer (SAM) method at room temperature.

2. Sensing Membrane Fabrication

In this experiment, we fabricated the sensing membrane by using the SAM method that has been used by a large number of researchers [12, 13]. The following is the detailed processes that had been carried out in order to fabricate the sensing membrane on the floating gate of the gated lateral BJT device. To start with, we putted the 11-mercaptoundecanoic acid (99%, Sigma-Aldrich) solution (1 mmol/L in ethanol solution) on the surface of the floating gate of the gated lateral BJT device for approximately 24 hours, thereby forming the SAM layer. The second process is the activation of the SAM. To be more Specifically, N-Hydroxysuccinimide (NHS, Sigma-Aldrich) (50 mmol/L) was used in combination with N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDC, Sigma-Aldrich) (50 mmol/L) to create a stable amine-reactive product. Next, the monoclonal anti-CRP antibody produced in mice (Sigma-Aldrich) (50 $\mu\text{g}/\text{ml}$ in 1X phosphate-

buffered saline (PBS) (Sigma-Aldrich)) was applied on the surface of the device for approximately 1 hour to immobilize the CRP antibodies. After completing the above processes, making the device rinsed with PBS and dried with N₂ gas.

3. CRP Detection Experiment

The schematic diagram of the sensing system is shown in Fig. 2. It consists of a semiconductor test & analyzer (STA), a gated lateral BJT device (embedded on a printed circuit board), a test fixture, and a PC. The gated lateral BJT device was connected to the STA by the test fixture that can decrease the circuit noise. Through the program control of the PC, the STA was used to supply the necessary bias of the sensor, obtain the experimental results, and send the data to the PC.

In order to evaluate the characteristics of the device, we conducted the following experiment.

At first, the terminals of the gated lateral BJT that have been immobilized with sensing membrane (CRP antibodies) had to be configured properly, thereby operating the device in MOSFET-BJT hybrid mode. Therefore, the emitter was biased positively (0.5 V), the gate was biased negatively (-0.8 V), which was conducted by the STA through the program control of the PC. Next, CRP from human plasma (Sigma-Aldrich) was used as the detection target whose concentration varied from 0 mol/L to 1 μmol/L with PBS solution as the standard reference solution and a commercial Ag/AgCl electrode as a reference electrode (MF-2052, BASi, U.S.A). Last, through the test fixture and STA, receiving the detection data from the emitter terminal of the gated lateral BJT device, and sending the data to PC.

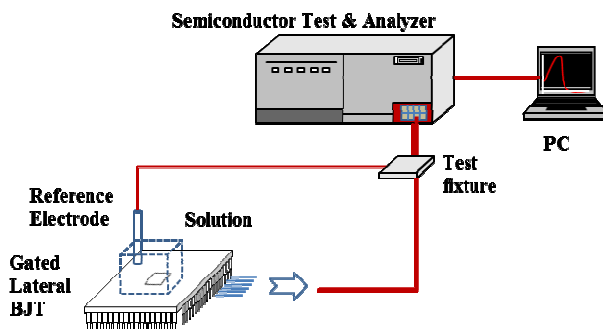


Fig. 2. Schematic diagram of sensing system.

III. RESULTS AND DISCUSSION

In this experiment, in order to confirm the effectiveness of molecular immobilization on gold surface, we conducted the atomic force microscope (AFM) and surface plasmon resonance (SPR) measurement that have been carried out by many researchers [14, 15].

The AFM images of the device surface after Au deposition using the e-beam evaporator, before and after SAM formation, after CRP antibodies immobilization, and after antigen-antibody reaction are shown in Fig. 3. According to the thickness of the SAM should be approximately 3 nm; the CRP antibody layer, approximately 6 nm; and the CRP antigen layer, approximately 10 nm [13], it was concluded that the SAM was formed on the Au thin film, CRP antibody was immobilized using SAM, and antigen-antibody specific

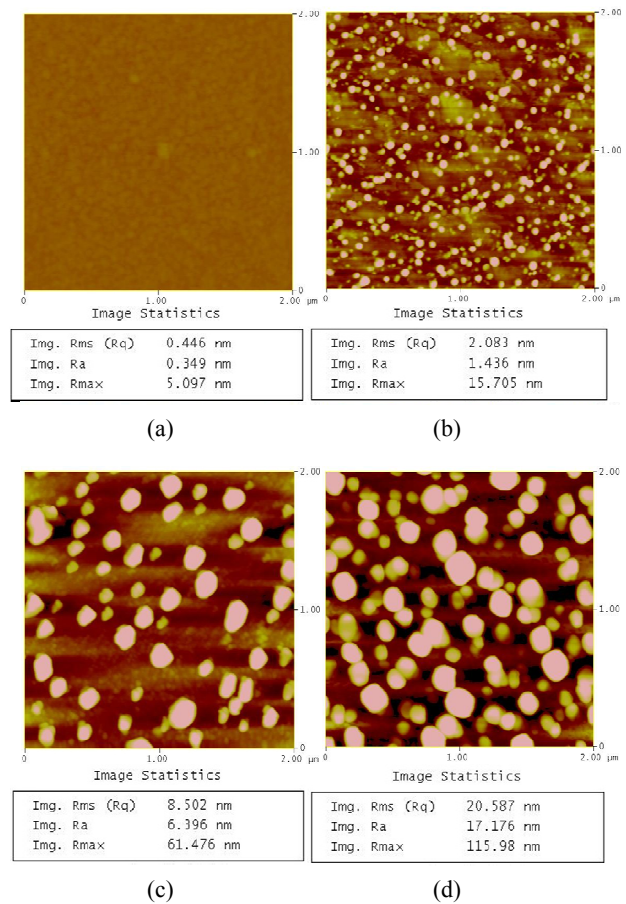


Fig. 3. AFM image of the device surface after Au deposition by e-beam evaporation (a), after SAM formation (b), after CRP antibody immobilization (c), after CRP immobilization (d).

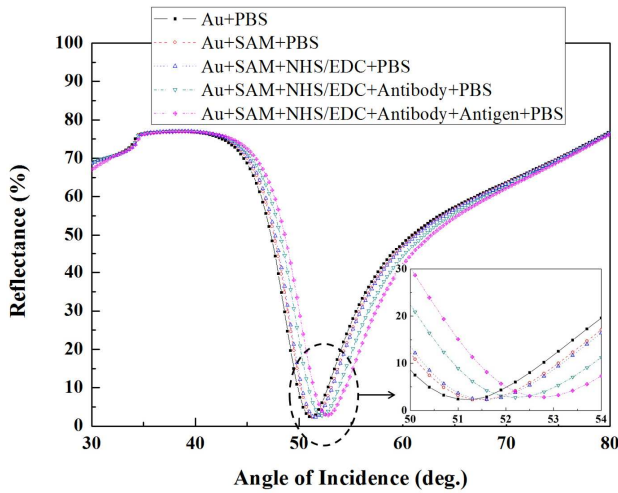


Fig. 4. Results of SPR measurement of CRP antigen immobilization on surface of gated lateral BJT.

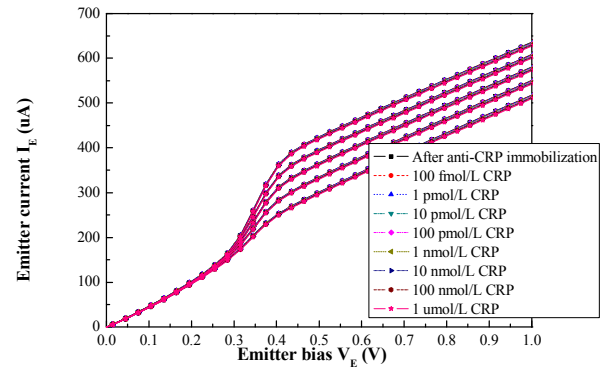
binding occurred.

The results of SPR measurement are shown in Fig. 4. As can be seen from the results, the resonance angle shift before and after SAM formation, after NHS/EDC process, after CRP antibodies immobilization, and after antigen-antibody reaction were 0.3° , 0.4° , 0.9° , and 1.5° , respectively.

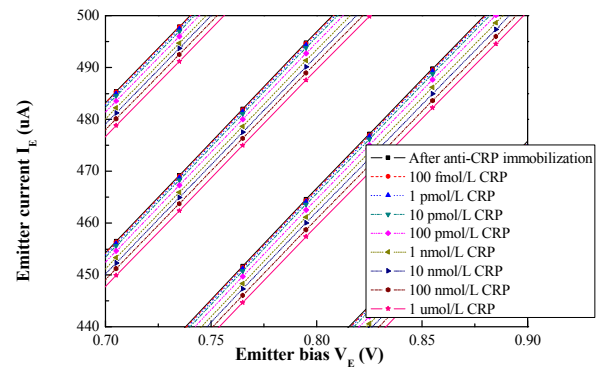
According to the principle of the SPR measurement, the refractive index of gold layer can determine the resonance angle, and refractive index depends on the depth of molecular immobilization on gold surface; therefore, the SPR resonance angle shift can reflect the molecular immobilization on gold surface.

Both the AFM and SPR measurements can confirm that the above biomaterial immobilization processes and the antigen-antibody reaction were completed.

The emitter (source) current I_E was detected to evaluate the characteristics of the proposed device. The V_E-I_E curve results as the base current was varied from $-50 \mu\text{A}$ to $-10 \mu\text{A}$ are shown in Fig. 5. Fig. 5(b) shows the enlarged views of certain portions of Fig. 5(a). More specifically, as the common MOSFET-based biosensor, a bias was supplied to the reference electrode. Then, the bias is conveyed to the floating gate of the device with the potential decreased by electrode, electrolyte solution, and biomaterial layer. After the CRP antigens react with the antibodies, the potential decrement between the liquid and the floating gate (biomaterial layer) increases. Therefore, the potential of the floating gate decreases, which diminishes the areas of the inversion region and



(a)



(b)

Fig. 5. (a) V_E-I_E curve of CRP detection using gated lateral BJT, (b) enlarged view of (a).

the depletion region between the emitter (source) and collector (drain); this decreases the MOSFET channel current. However, the lateral bipolar current does not change with a decrease in the potential of the sensing layer. As we know, when the gated lateral BJT device was operated in the MOSFET-BJT mode, I_E consisted of two parts: the MOSFET channel current and the bipolar current. Thus, the sum of the currents of the MOSFET channel and bipolar current (I_E) decreased.

Furthermore, according to Fig. 5, Fig. 6 can be clarified with a base current of $-10 \mu\text{A}$. Fig. 6 indicates that the sensitivity can be varied by adjusting the emitter (source) bias supply. The reason for this can be explained as follows. The forward bias between the emitter (source) and base increased with an increase in the emitter (source) bias. Subsequently, the transconductance of the gated lateral BJT increased. However, the transconductance of the gated lateral BJT can be defined as how the emitter (source) current varies with the gated potential, which is the same as the sensitivity of the gated lateral BJT. Therefore, a higher transconductance can cause a higher

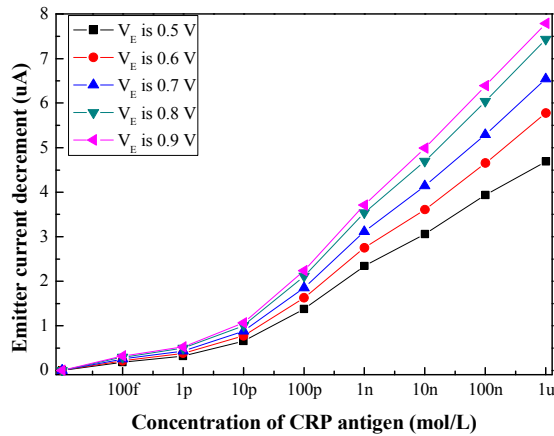


Fig. 6. Results of CRP detection according to different V_E .

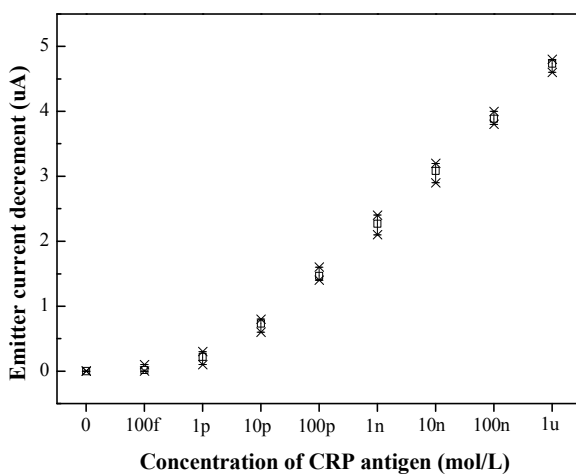


Fig. 7. Results of CRP detection using gated lateral BJT.

sensitivity. According to the results, when V_E was equal to 0.5 V, 0.6 V, 0.7 V, 0.8 V, and 0.9 V, the sensitivity of the gated lateral BJT device for CRP detection was approximately 0.80, 1.00, 1.13, 1.29, and 1.35 $\mu\text{A}/\text{decade}$, respectively.

According to this characteristic, the sensitivity of the gated lateral BJT can be controlled by the emitter (source) bias. This has a significant impact on biomaterial detection.

Finally, because of the results shown in Fig. 7, the reproducibility of the gated lateral BJT was confirmed when V_E was equal to 0.5 V. According to the results, when the concentration of the CRP is 100 fmol/L, there is only a small change in the emitter (source) current being observed. Moreover, for a CRP concentration greater than 1 pmol/L, an obvious change in the emitter current occurred, and there was a strong correlation between the CRP concentration and the decrease in the

emitter (source) current.

V. CONCLUSIONS

In this study, we proposed a new type of CRP biosensor based on a gated lateral BJT. The fabrication of the sensor utilized the common semiconductor manufacturing technology (0.35- μm CMOS process). The gated lateral BJT shares the properties of both a MOSFET and a BJT and can be operated in the MOSFET mode, BJT mode, and MOSFET-BJT hybrid mode by configuring the emitter (source) bias, gate bias, and base current properly. By using the SAM method, the sensing membrane (CRP antibodies) was immobilized on the floating gate of the gated lateral BJT device. The CRP antigens solutions, the concentration of which varied from 100 fmol/L to 1 $\mu\text{mol/L}$ were used as the detection target to evaluate the characteristics of the biosensor in the MOSFET-BJT mode. Through the experiment, we found that the sensitivity of the gated lateral BJT can be varied by adjusting the emitter (source) bias with a concentration greater than 1 pmol/L, and the proposed device presented good reproducibility for bio-sensing effectively. In future studies, we intend to detect other biomaterials and design a multi-sensing system.

ACKNOWLEDGMENTS

This work was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (No. 2012-0000632). And this work was supported by Samsung Electronics Co., Ltd. And this work was supported by IDEC.

REFERENCES

- [1] D. M. Steel and A. S. Whitehead, "The major acute phase reactants: C-reactive protein, serum amyloid P component and serum amyloid A protein," *Immunology Today*, Vol.15, No.2, pp.81-88, Feb., 1994.
- [2] T. P. Erlinger, et al, "C-reactive protein and the risk of incident colorectal cancer," *Journal of the American Medical Association*, Vol. 291, No.5, pp.

- 585-590, Feb., 2004.
- [3] R. Ross, "Atherosclerosis - An inflammatory disease," *The New England Journal of Medicine*, Vol.340, pp.115-126, Jan., 1999.
- [4] S. H. Yeom, et al, "Highly sensitive nano-porous lattice biosensor based on localized surface plasmon resonance and interference," *Optics Express*, Vol.19, No.23, pp.22882-22891, Nov., 2011.
- [5] Y. S. Sohn, et al, "Detection of C-reactive protein using BioFET and extended gate," *Sensor Letters*, Vol.5, No.2, pp.421-424, Jun., 2007.
- [6] Y. S. Sohn and Y. T. Kim, "Field-effect-transistor type C-reactive protein sensor using cysteine-tagged protein G," *Electronics Letters*, Vol.44, No.16, pp.955-956, Jul., 2008.
- [7] S. A. Parke, et al, "Bipolar-FET hybrid-mode operation of quarter-micrometer SOI MOSFET's," *IEEE Electron Device Letters*, Vol.14, No.5, pp.234-236, May, 1993.
- [8] S. R. Chang and H. Chen, "A CMOS-compatible, low-noise ISFET based on high efficiency ion-modulated lateral-bipolar conduction," *Sensors*, Vol.9, No.10, pp.8336-8348, Oct., 2009.
- [9] S. V. Vandebroek, et al, "High-gain lateral bipolar action in a MOSFET structure," *IEEE Transactions on Electron Device*, Vol.38, No.11, pp. 2487-2496, Nov. 1991.
- [10] H. C. Kwon, et al, "The characteristics of H⁺ ion-sensitive driving with MOS hybrid mode operation," *IEEE Electron Device Letters*, Vol.29, No.10, pp.1138-1141, Oct., 1999.
- [11] H. Yuan, et al, "Volatile organic compound gas sensor using a gated lateral bipolar junction transistor," *Journal of the Korean Physical Society*, Vol.59, No.2, pp.478-481, Aug., 2011.
- [12] Y. Sato and F. Mizutani, "Electrochemical responses of cytochrome c on a gold electrode modified with mixed monolayers of 3-mercaptopropionic acid and n-alkanethiol," *Journal of Electroanalytical Chemistry*, Vol.438, No.1, pp.99-104, Nov., 1997.
- [13] W. Limbut, et al, "A comparative study of capacitive immunosensors based on self-assembled monolayers formed from thiourea, thioctic acid, and 3-mercaptopropionic acid," *Biosensors and Bioelectronics*, Vol.22, pp.233-240, Aug., 2006.
- [14] S. K. Lee, et al, "Binding behavior of CRP and anti-CRP antibody analyzed with SPR and AFM Measurement," *Ultramicroscopy*, Vol.108, No.10, pp.1374-1378, Sep., 2008.
- [15] M. H. F. Meyer, et al, "CRP determination based on a novel magnetic biosensor," *Biosensors and Bioelectronics*, Vol.22, pp.973-979, Jan., 2007.



Heng Yuan was born in Shandong province, China, in 1981. He received the B.S. degree in College of Information and Electrical Engineering from Shandong University of Science and Technology, China in 2003. He

completed his M.S. degree with semiconductor and display major in School of Electrical Engineering and Computer Science for Kyungpook National University, Korea, in 2007. He is currently pursuing the Ph.D. degree in School of Electrical Engineering and Computer Science for Kyungpook National University, Korea. His interests include semiconductor sensors, optical sensors, and nano devices development. He is a student number of IEEE.



Byoung-Ho Kang received the B.S. degree in the Department of Physics and Semiconductor from Daegu Catholic University and M.S., Ph.D. degrees in the School of Electrical Engineering and Computer Science from Kyungpook National University,

Daegu, Korea, in 2005, 2007, and 2012, respectively. In 2012, he joined at Center for Functional Devices Fusion Platform, where he has been working in the area of OLED and nano-crystal application.



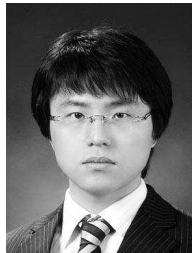
Jae-Sung Lee received the B.S. degree in the Department Electrical Engineering from Kyung-Il University of Kyungsan, Korea, in 2012. He is currently pursuing the M.S. degree in School of Electrical Engineering and Computer Science for Kyungpook National University, Korea. His interests include semiconductor sensors, and optical fiber sensors. He is a student number of IEEE.



Hyun-Min Jeong received the B.S. degree in the Department Electrical Engineering form Catholic University of Daegu, Korea, in 2012. Recent, He He is currently pursuing the M.S. degree in School of Electrical Engineering and Computer Science for Kyungpook National University, Korea. His interests include semiconductor sensors. He is a student number of IEEE.



Se-Hyuk Yeom received the B.S. degree in the Department Physics form Keimyung University, Korea, in 2004. He completed his M.S. and Ph.D. degrees in Department of Sensor and Display Engineering and the School of Electrical Engineering and Computer Science, respectively, from Kyungpook National University, Korea, in 2006, and 2012, respectively. In 2012, he joined at Center for Functional Devices Fusion Platform, where he has been working in the area of optical sensors and nano devices development.



Kyu-Jin Kim received the B.S, M.S, Ph.D. degrees in School of Electrical Engineering and Computer Science from Kyungpook National University, Korea, in 2005, 2007, and 2012, respectively. In 2012, he has been working in the area of organic solar cell, displays, optical devices, and sensors.



Dae-Hyuk Kwon received the B.S, M.S, Ph.D. degrees in Department of Electrical Engineering from Kyungpook National University, Korea, in 1984, 1986, and 1992, respectively. Then, he works in Department of Electronic Engineering, Kyungil University, Korea. His research interests include semiconductor manufacturing process, semiconductor sensors, and display (TFT-LCD). Prof. Kwon is a member of IEEE.



Shin-Won Kang received his B.S degree in Department of Electrical Engineering from Kyungpook National University, Daegu, South Korea in 1978. He completed his Ph.D degree with biomedical engineering in Graduate School of Biomedical Engineering from Keio University, Tokyo, Japan in 1993. He works in Kyungpook National University from 1994. He is the chief of the Center of Function Devices Fusion Platform, South Korea, and the chief of the Display Technology Education Center, Kyungpook National University, Korea. His research interests include SPR sensor, optical taste sensor and odor sensor, semiconductor chemical and biological sensors, organic-inorganic LED manufacture and encapsulation formation using Quantum dot, and organic solar cell. Prof. Kang is a member of IEEE.