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# Needle-type Multi-electrode Array Fabricated by MEMS Technology for the Hypodermic Continuous Glucose Monitoring System

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*Abstract*—**A needle-type multi-electrode array for the hypodermic continuous glucose monitoring sensor was fabricated using MEMS technology. The developed multi-electrode sensor has 4 electrodes of two working(Pt) electrodes, one counter(Pt) electrode, and one reference(Ag/AgCl) electrode. Two working electrodes are for the enzyme and non-enzyme electrodes which measure glucose concentration and the background current($I_0$), respectively. The developed integrated sensor system is adequate to accomplish our pre-reported new two-point calibration method using only one-point sample measurement. Results of *in vitro* performance test are also provided.**

*Keywords*—**multi-electrode array, continuous glucose monitoring sensor, MEMS technology**

## I. Introduction

Over 100 million people in the world are afflicted by diabetes. Regular and frequent glucose monitoring is the most essential in treatment of diabetic patients. The study showed that when participants observed data from the implanted continuous glucose monitor, they experienced more reduced glucose fluctuations. There are several technologies under consideration for developing a continuous glucose monitoring system. Most successful implantable glucose sensor so far is based on a hypodermic needle-type amperometric enzyme electrodes[1]. A crucial issue in this type of implantable glucose sensor is the *in vivo* calibration of the system. In our laboratory, a new calibration method for the subcutaneous amperometric continuous glucose sensor based on direct measurement of the background current ($I_0$) using an additional non-enzyme electrode was reported, through which two-point calibration could be performed with a single blood glucose measurement by reference method[2]. In this study we implanted two separate needle-type sensors, one for enzyme electrode and the other for non-enzyme electrode.

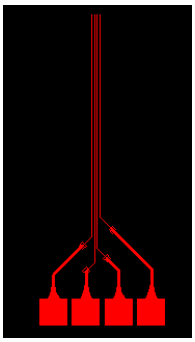
In this paper, we fabricated a micromachined needle-type multi-electrode array as one integrated sensor unit for our unique *in vivo* calibration method. The objective of this study was to demonstrate *in vitro* feasibility of the new sensor fabricated by microelectromechanical systems (MEMS) technology.

## II. Methodology

Since a standard amperometric glucose sensor requires three-electrode configuration (*W*:working, *C*:counter, and *R*:reference electrodes) we provided total four electrode (two *W*'s, one *C*, and one *R*). On two working electrodes, we fabricated one enzyme electrode for glucose sensitive output and one non-enzyme electrode for background current($I_0$) measurement.

### *A.. Electrode Patterning using MEMS Technology*

Substrate material for electrode patterning was a polyimide film(60μm) and an backing layer of transparency film (PET, 85μm) was added to provide rigidity of the substrate. Fig. 1 shows the mask pattern used to fabricate the developed multi-electrode array. All four electrodes were identically designed as a simple rectangular shape.



Fig, 1. Configuration of the developed multi-electrode array (mask pattern)

In the photolithographic procedure, we used the image reversal technique. For patterning of a photoresistive(PR) layer, the polyimide substrate was spin-coated at 4000 rpm for 30 sec with HMDS and at 4000 rpm for 30 sec with AZ5214E and baked on a hot plate at 110ºC for 50 sec. And then it was exposed to UV radiation through the mask film at 20mJ/cm$^2$ for 5.5 sec and baked at 125ºC for 2 min again. Removing the mask film, it was exposed at 20mJ/cm$^2$ for 12.5 sec. After developing for 65 sec, it was finally hard baked at 110ºC for 1 min.

Thin layers of chrome(0.2μm) and gold(1μm) were then evaporated on to the surface of the PR patterned substrate. After gold layer deposition, an additional polyimide film

was attached onto the patterned substrate in order to insulate the connecting wire part between the active electrode and the interfacing pad.

### *B. Fabrication of Platinum and Ag/AgCl electrodes.*

Two working and a counter electrodes were plated with platinum(Pt) and a Ag/AgCl electrode was used for the reference electrode.

1) Pt plating: With separate Pt wire and Ag/AgCl electrode as counter and reference electrode, respectively, the gold-layer pattern was immersed in hydrogen hexachloroplatinate(IV) hydrate(10%, in water) as working electrode. A Pt layer was electroplated onto the gold pattern with potential of 0.1V for 100sec.

2) Ag/AgCl electrode : This process is divided into two steps. Firstly, a Pt wire and the gold-layer pattern as counter/reference and working electrode, respectively, were immersed in 0.1M $HClO_4$ with 1mM $AgNO_3$. Electroplating by potential at -1.6V for 2500 sec gave Ag layer on the gold electrode. Secondly, a Pt wire, a Ag/AgCl electrode, and the previously fabricated Ag electrode were together put in KCl solution as counter, reference, and working electrodes, respectively. AgCl layer was coated by electrochemical reaction with a constant current of 0.5mA for 900 sec.

### *C. Fabrication of Enzyme Electrode*

Out of three Pt electrodes, one selected as an enzyme electrode was immersed in a phosphate buffer saline (PBS) solution containing glucose oxidase(GOD, 8mg), glutaraldehyde(0.025%, 0.8mL), poly-L-lysine(0.005M, 0.5mL), and 1,3-diaminobenzene(1,3-PD). For another Pt electrode for the non-enzyme electrode which will measure the background current($I_0$), the previous process was repeated with exactly same materials except GOD. Electropolymerization by potential cycling between 0.2 and 10V gave a thin enzyme and non-enzyme layer whose thickness is self-controlled[3].

Fig. 2. shows the cross sectional structure of the multi-electrode array. All electrodes have same Au/Cr layer on the polyimide film substrate. Electrodes #1 and #4 are two working electrodes which correspond to enzyme and non-enzyme electrode, respectively. Electrode #2 is the counter electrode plated with platinum and #3 reference electrode was coated with Ag/AgCl.

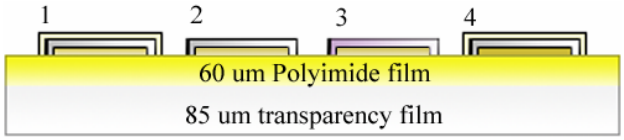



Fig. 2. Cross sectional diagram of the developed multi-electrode array. #1 : working enzyme electrode, #2: counter Pt electrode, #3: reference Ag/AgCl electrode, and #4: working non-enzyme electrode

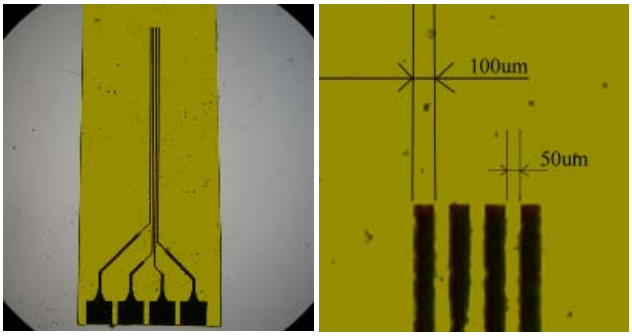
Finally, for enhanced biocompatibility, an outer layer was added onto the enzyme and non-enzyme electrodes by dipping the electrode in Kel-F-oil(20%), 15% perfluorinated tetrafluoroethylene(PTFE), and 1.5% Nafion. After each dipping, it was dried in a vacuum chamber for 30 min.

### *D. In vitro Performance Evaluation of the Sensor*

*In vitro* performance tests were performed in a cell containing 21mL of PBS(pH 7.4, 37ºC) with a water-jacket. With thermostatic bath (Ultra-Thermostat NB5, Colora), we measured outputs of two working electrodes in the PBS solution with no glucose injection. After stabilization, we sequentially introduced glucose into the PBS solution to make four different glucose concentration levels of 5, 10, 15, and 20 mM and measured the sensor' outputs. At the end of experiment, in order to investigate the effect of typical interfering agent, we measured the current output of the glucose sensor with the injection of physiologically maximal amount of ascorbic acid(AA).

## III. RESULTS

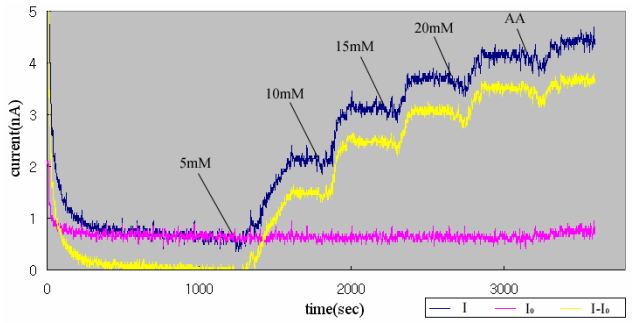
Fig. 3. shows the pictures of the fabricated multi-electrode array. The width of each electrode is 100μm, and the gap between the adjacent electrodes is 50μm.



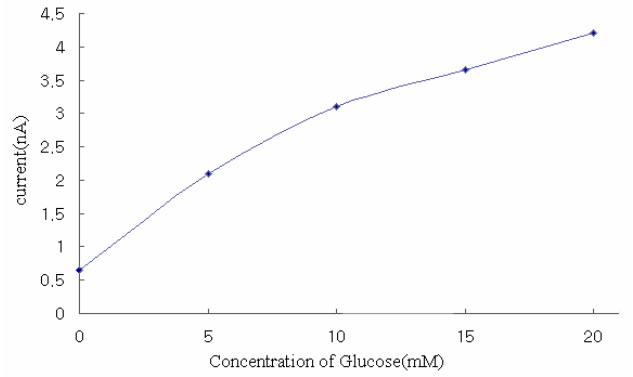

(a) (b)

Fig. 3. Pictures of the fabricated multi-electrode array; (a) overall view and (b) active electrode part.

The current outputs of the enzyme and non-enzyme electrodes is shown in Fig. 4.(a). In Fig. 4.(a), we can see a direct response of the enzyme electrode's output to the glucose injection. As shown in the graph, we can easily remove the background current by subtracting the non-enzyme electrode's output from the enzyme electrode's output. Since the last two step-responses are of the same level, we can say that the developed sensor is insensitive to AA..




(a)




(b)

Fig. 4. Results of in vitro performance tests; (a) current waveforms from the enzyme and non-enzyme electrodes and (b) calibration curve of the developed sensor. Overshooting in (a) between each concentration is due to stirring for mixing the glucose well in the PBS solution.

## IV. Discussion & Conclusion

We fabricated a MEMS technology-based multi-electrode array for the hypodermic amperometric glucose sensor as an integrated sensor unit including both enzyme and non-enzyme electrodes. According to the *in vitro* experiment results, the feasibility of the new sensor system and the subsequent simplified calibration method was demonstrated. The developed sensor system is expected to provide both simplicity and easiness to subcutaneously implanted glucose monitoring system. For future research, we will find the optimal area of each electrode to provide maximum signal-to-noise ratio as well as implantable needle size and in vivo performance evaluation using appropriate animal models.

## Acknowledgment

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