01 Jan 1997

Miniaturized ISFET Glucose Sensor Including a New Structure Actuation System

Chang-Soo Kim
Missouri University of Science and Technology, ckim@mst.edu

Hwa-Il Seo

Chae-Hyang Lee

Byung-Ki Sohn

Recommended Citation

C. Kim et al., "Miniaturized ISFET Glucose Sensor Including a New Structure Actuation System," *Proceedings of the 1997 International Conference on Solid State Sensors and Actuators, 1997*, Institute of Electrical and Electronics Engineers (IEEE), Jan 1997.
The definitive version is available at https://doi.org/10.1109/SENSOR.1997.635250

Miniaturized ISFET Glucose Sensor Including a New Structure Actuation System

Chang-Soo Kim*, Hwa-Il Seo**, Chae-Hyang Lee* and Byung-Ki Sohn*
* Sensor Technology Research Center, Kyungpook National University, Taegu 702-701, KOREA
** Dept. of Electronic Eng., Korea University of Technology & Education, Chonan 333-860, KOREA

SUMMARY

A new principle of an amperometric actuation technique was incorporated in the ISFET glucose sensor. The ISFET is fabricated by the CMOS process and the platinum working electrode is deposited by the lift-off process. A sensor with a specially designed ladder type working electrode exhibits improved operation in response time, response magnitude and detection range. An expectation concerning with the reduction of sensor size is also discussed.

Keywords: glucose, ISFET, amperometric actuation

Introduction

The ISFET-based biosensor[1,2] is a very proper configuration for application to *in situ* monitoring of various chemical processes, *in vivo* medical diagnosis and many other fields to which the conventional analytic apparatuses have difficulties to apply. A representative ISFET-based biosensor is the glucose sensor[2,3,4]. In spite of the advantages of small size and the compatibility with on-chip circuit integration, the ISFET glucose sensor has inherent problems: low sensitivity, drift and long response time. Recently, an amperometric actuation technique was proposed to obtain a high sensitivity of the ISFET glucose sensor with a built-in working electrode[5,6]. With this mechanism, two additional hydrogen ions are produced by the electrolysis of the hydrogen peroxide by the working electrode:

$$\beta\text{-D-glucose} + H_2O + O_2 \xrightarrow{GOD} \text{Gluconic acid} + H_2O \quad (1)$$

$$\text{Gluconic acid} \longleftrightarrow \text{Gluconate} + H^+ \quad (2)$$

$$H_2O_2 \longrightarrow 2H^+ + O_2 + 2e^- \quad (3)$$

A conventional ISFET glucose sensor only makes use of the reaction (2). If the hydrogen peroxide can be electrolyzed by using an working electrode near the gate region of the ISFET, the sensitivity would be increased by the addition of two hydrogen ions. It would also be expected that the additional oxygen by reaction (3) would increase the reaction (1), resulting in a wider dynamic range. In this paper, we report improved characteristics of an ISFET glucose sensor by actuation system.

Experimental

The pH-ISFET was fabricated on a p-well in n-substrate by using a CMOS process. The well structure was used to obtain a better electrical isolation between the ISFET and the solution. The gate material consisted of 50nm thick silicon oxide and 50nm thick silicon nitride. The chip size was 1.0mm × 1.8mm and the gate size 20μm × 400μm. The sensitivity of the fabricated ISFET was about 55mV/pH.

To ensure the high sensitivity of the sensor, the distance between the pH-sensing gate and the working electrode should be as close as possible, since the hydrogen ions diffuse from the platinum electrode surface at which these ions are generated. Two kinds of electrodes were designed: a simple rectangular-shaped electrode surrounding the rectangular-shaped pH-sensing gate of the ISFET and a ladder type electrode in which many bridges traversing the pH-sensing gate are included. The distance through which the hydrogen ions should transport can be shortened in the ladder type electrode. The width of a bridge measures 20μm and is the same with the spacing between each bridge. In order to form the platinum electrode, 30nm thick titanium and 200nm platinum were deposited by sputtering and patterned using a lift-off process. The Pt/Ti layer was formed around the gate region of the ISFET. Fig. 1 shows the gate regions of the sensor with the built-in rectangular type electrode and the

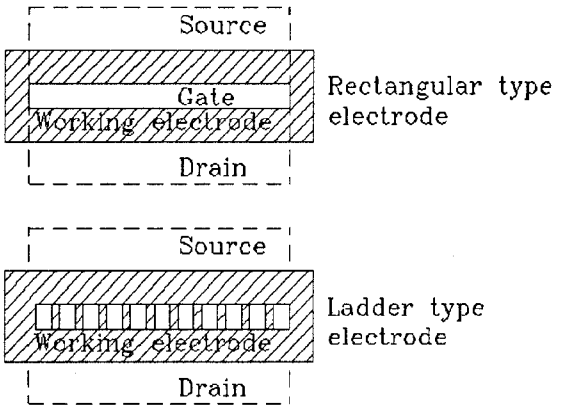

Figure 1: Gate regions of the sensors with the built-in rectangular type electrode and the ladder type electrode.

ladder type electrode.

The glucose sensor was completed by forming a GOD-BSA membrane onto the gate region. Glucose oxidase(GOD, EC 1.1.3.4) from the *Aspergillus niger* and bovine serum albumin(BSA) were both obtained from Sigma while the 25% solution of glutaraldehyde(GA) came from Aldrich. All other reagents employed were of analytical purity grades. The gate surface of the ISFET gate and the electrode were pretreated in a diluted hydrofluoric(HF) acid. The GOD(5mg) and the BSA(5mg) were dissolved in 100μl of 10mM phosphate buffer solution(pH 7.4). The 0.8μl of the solution was cast onto the gate region and then addition of 1.3μl of GA was followed to chemically crosslink the membrane. The GOD membrane was left to dry at room temperature for 4 hours. The sensor was finally wire-bonded and encapsulated with silicone rubber.

The measurement was carried out by the standard addition method of the standard glucose solution. The sensor was immersed in a measuring vessel filled with 10mM phosphate buffer solution(pH 7.4) and then a small amount of glucose solution was added. All measurements were carried out at room temperature. To ensure homogeneity, the solution was magnetically stirred in all measurements.

Fig. 2 shows the conceptual time response of the glucose sensor during the onset of the potential pulse(usually 0.7V vs. Ag/AgCl) applied to the working electrode. The glucose response includes the background response (A) which can be observed in a blank solution in which glucose is not included. The change in the effective gate geometry(aspect ratio) of the ISFET, which is caused by the potential pulse to the working electrode that traverses the gate region, gives rise to the background response. This response does not give any information on the glucose concentration. The response (B) is caused by the reaction (2), the pH variation within the GOD membrane only by the dissociation of the gluconic acids. The amperometric actuation in which the hydrogen peroxide is electrolyzed to the additional hydrogen ions corresponds to the response (C). The glucose response by the amperometric actuation (C) is obtained by subtracting a previously evaluated background response (A) from the total response (A+C).

Results and discussion

The electrochemical behavior of the deposited working electrode was investigated to certify the availability for an electrochemical tool. Fig. 3 shows the voltammogram obtained with the deposited platinum working electrode and the Ag/AgCl reference electrode. The reference electrode in this study was not an integrated one but a commercial single junction reference electrode(ORION 900100). The scan rate was 5mV/sec. A negligible residual current in the glucose-free blank solution was observed. This intefering current comes mainly from the electrolysis of the other redox couples present in the solution or the electrode surface. The current begins to increase as the positive potential is applied to the working electrode and reached the peak at around 0.7V, which indicates that the oxidation of hydrogen peroxide is maximized at that potential. The oxidation potential of the hydrogen peroxide was determined to be 0.7V from the voltammogram.

Fig. 4 shows the typical time response (response (C) shown in Fig. 2) by the reaction (3). The output reached a

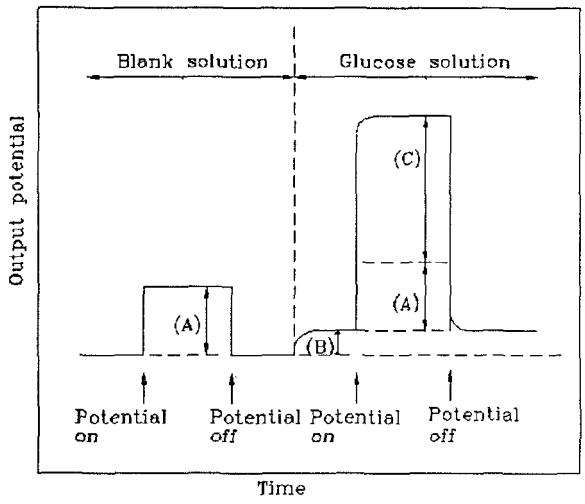

Figure 2: A conceptual time response of the glucose sensor incorporating the amperometric actuation technique.

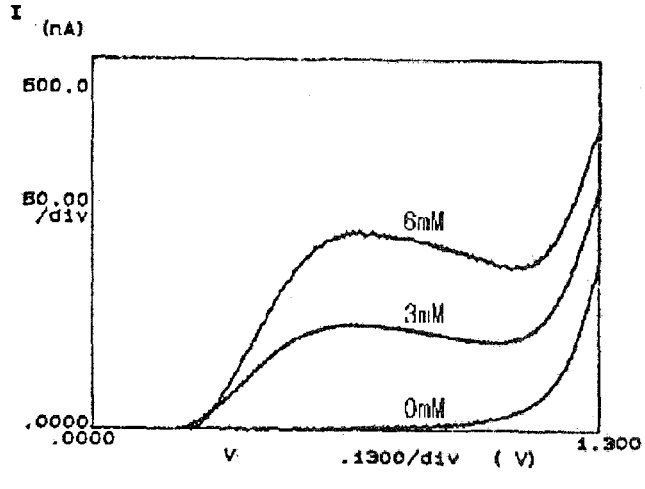

Figure 3: Voltammograms of the platinum working electrode in glucose solutions.

steady state after a step wise potential pulse was applied to the working electrode, and then returned to the baseline as the pulse was removed. The baseline represents the sensor output which was set by the reaction (2). Knowing the ISFET has a considerable drift rate, it is very important to monitor the baseline. For conventional ISFET glucose sensors, this is normally obtained using a blank solution before the addition of the glucose solution. By the amperometric actuation technique, however, the baseline monitoring is simply achieved by taking the response (B) for the baseline before and after the potential pulse application, regardless of the ISFET drift rate. This is considered to be highly advantageous for the continuous monitoring. The glucose response (c) only by the amperometric actuation took typically one minute to reach the 95%, while more than three minutes had been required in the previous sensor[5] without the ladder structure in its electrode. It is obvious that the response time is influenced by the geometry of the working electrode because the generated hydrogen ions would be able to reach the gate region faster having a shorter distance to travel.

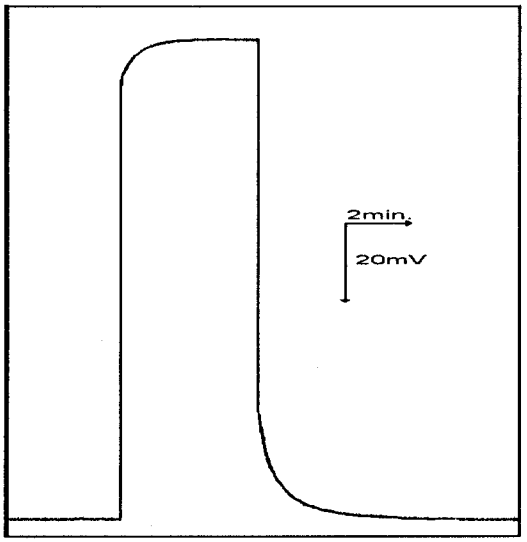

Figure 4: Time response of the sensor operated with the amperometric actuation technique.

The calibration curve of the sensor is plotted in Fig. 5. The sensor with the ladder type electrode exhibits a higher response magnitude and a wider dynamic range than those of the sensor without the ladder type electrode. It is believed that these improved characteristics are caused by the small gaps between each bridges, so that the generated hydrogen ions can be captured by the pH-sensing sites of the ISFET gate much easily before a carrier-mediated transport occurs by the mobile buffer species[7].

Furthermore, from a standpoint of the compatibility with miniaturization and smart sensor, the proposed sensor is a recommendable configuration. In the amperometric glucose sensor, the output current is directly related to the surface area of the working electrode. Consequently, a large electrode is required for the ease of signal processing. The decrease in sensor dimension results in a low signal-to-noise ratio[8] at the expense of a large current signal. In contrast, a potentiometric sensor has less dependence of such factors on its size. Even if the dimension of the proposed ISFET glucose sensor becomes much smaller, that is, the simultaneous reduction of the gate and the working electrode proportionally, it is suggested that the sensitivity of the sensor will less dependent on its size than that of the 'pure amperometric sensor'. The improvement in the dynamic range as well as the sensitivity of the proposed sensor incorporating the amperometric actuation technique can be expected by adjusting the geometry of the gate and the working electrode.

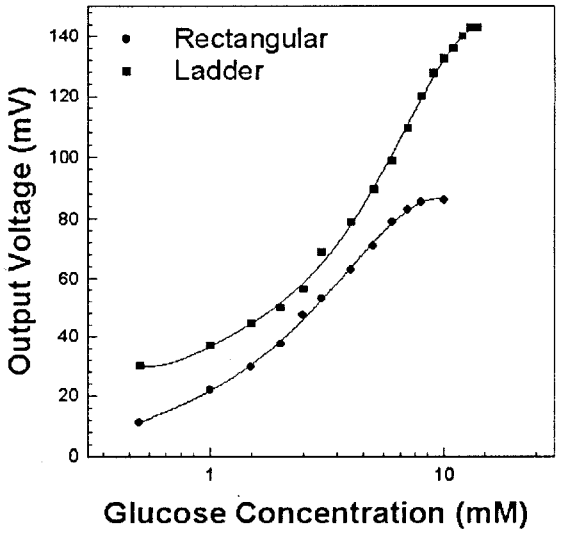

Figure 5: Calibration curves of the sensors with a rectangular type electrode and a ladder type electrode.

Conclusion

A new principle of an amperometric actuation technique was incorporated in the ISFET glucose sensor. With this method, the glucose response caused by the electrolysis of hydrogen peroxide is only detected. The sensor with a specially designed ladder type electrode showed a fast response time, high response magnitude and a wide dynamic range. This method is also expected to allow the ISFET glucose sensor for the continuous monitoring without being suffered from the ISFET drift problem.

Acknowledgment

This research was financially supported by Korea Science & Engineering Foundation(KOSEF) and Sensor Technology Research Center(STRC).

References

[1] S. Caras, J. Janata, Anal. Chem.,52(1980)1935-1937.
[2] B. H. van der Schoot, P. Bergveld, Biosensors, 3(1987/88) 161-186.
[3] A. Saito, N. Ito, J. Kimura, T. Kuriyama, Sensors and Actuators B, 20(1994) 125-129.
[4] A. A. Shul'ga, M. Koudelka-Hep, N. F. de Rooij, Anal. Chem., 66(1994) 205-210.
[5] H.-I. Seo, C.-S. Kim, B.-K. Sohn, T. Yeow, M.-T. Son, M. Haskard, Sensors and Actuators, accepted.
[6] B.-K. Sohn, B.-W. Cho, C.-S. Kim, D.-H. Kwon, Sensors and Actuators, accepted.
[7] A. P. Soldatkin, A. V. El'skaya, A. A. Shul'ga, L. I. Netchiporouk, A. M. Nyamsi Hendji, N. Jaffrezic-Renault, C. Martelet, Anal. Chim. Acta., 283(1993) 695-701.
[8] D. Morgan, S. Weber, Anal. Chem., 56(1984) 2560-2567.