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ISFET Glucose Sensor with Palladium Hydrogen Selective Membrane

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Abstract

This paper describes the development of a glucose biosensor based on ion sensitive field effect transistor(ISFET) with a palladium(Pd) modified ion sensing membrane. By adopting Pd as a hydrogen sensitive layer and integrating a screen-printed reference electrode, the sensitivity and stability were considerably improved due to the high permeability and selectivity of the Pd hydrogen selective membrane. This paper suggests a new approach for realizing portable and highly sensitive glucose sensors for diagnosing and treating diabetes mellitus.

Keywords : Glucose sensor, ISFET, Palladium, Semiconductor Biosensor

1. INTRODUCTION

The need to diagnose diabetes is on a constant increase as it has become one of the leading causes for death and disability around the world[1, 2]. For the treatment of diabetes mellitus, maintaining a normal glucose level by monitoring and controlling the blood glucose concentration is of primary importance. This in turn can delay or prevent the occurrence of complications. Accordingly, Glucose biosensors have been extensively developed and they occupy the largest portion of the biosensor market[3]. For the purpose of glucose sensing, electrochemical type biosensors account for a large majority. They can be classified into amperometric, conductometric, potentiometric, and semiconductor biosensors.

In the recent decades, as the semiconductor market and related technologies have undergone dramatic development, semiconductor based biosensors have attracted considerable attention over other types of sensors. This is due to their advantages of small size, mass production, short response time, and facile integration with periphery processing units [4, 5]. Ion sensitive field effect transistors(ISFETs) have been the most widely studied among the semiconductor based biosensors after Bergveld reported the first concept[6-8]. However, the use of ISFETs for diabetes has limitations such as low sensitivity(a few mV/decade)[9], insufficient selectivity[10], and strong dependence on the buffer capacity[11, 12]. Palladium has been utilized as a core material for hydrogen gas sensors due to its high sensitivity and selectivity of hydrogen[13]. Hydrogen gas molecules are spontaneously dissociated on the surface and they are dissolved in palladium at room temperature. Diffused hydrogen leads to changes in the surface potential of the device. Although palladium has been used as a catalyst for the oxidation of glucose [14, 15], its high permeability to hydrogen has not been exploited until now for the detection of glucose.

This paper describes a new design for the improvement in the performance of ISFETs by adopting palladium as a hydrogen selective membrane on the sensing channel. Due to high permeability and selectivity of hydrogen in the Pd layer incorporated in the active sensing region[13, 16], the sensitivity and selectivity as well as the buffer capacity dependence of the glucose sensor can be enhanced. Moreover, Ag/AgCl reference electrodes are integrated with the devices. This is achieved by using a one-step screen-printing method for miniaturization

2. EXPERIMENT

2.1 Fabrication of ISFET

Fabrication of the ISFET begins with definition of source/drain regions of p-type silicon on insulator wafer.

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Heavily n-doped source/drain regions were formed on a p-type Si layer(10 Ω · cm) with a spin-on-dopant at 950 °C in a rapid thermal annealing system. A photolithographically defined layer of SiO_2, deposited by plasma enhanced chemical vapor deposition and it was used as a diffusion mask. After doping process, the active regions of the transistors were isolated by SF_6 plasma etching. Ion sensitive layers of silicon oxide(SiO_2, 90 nm) and silicon nitride (Si_3N_4, 110 nm) were deposited by plasma enhanced chemical vapor deposition, respectively. Palladium was deposited on top of the Si_3N_4 layer by RF sputtering. The deposited Pd of 50 nm thickness was patterned by using a lift-off process. After patterning the source and drain electrodes of Cr/Au(10 nm/200 nm) by using standard lithography, the device was passivated by spin-cast SU-8 thin layers except for the channel region and metal pads.

2.2 Integration of Screen-Printed Reference Electrode

The Ag/AgCl reference electrode was fabricated by using a screen-printing technique. Initially, a silver paste(DS-0715AT(N) DAEJOO Electronic Materials Co. Ltd.) was printed onto the substrate of the device through a screen of mesh size 250 and dried at 120 °C for 10 min. After the formation of an Ag metal line, Ag/AgCl ink(SC155 Screen-Printable Ag/AgCl paste, KETI) was printed onto the device by using a 250 mesh screen-printing mask(12 μm thickness). The device was then treated at 120 °C for 10 min and cleaned with deionized water.

2.3 Immobilization of Enzyme on the Ion Sensitive Layer

In order to immobilize the glucose oxidase(GOx) (EC.1.1.3.4, Sigma Aldrich) enzyme on the substrate, 5 mg of GOx and 5 mg of bovine serum albumin was dissolved in a phosphate buffer solution(PBS). In order to establish cross linking, a GOx solution and 2.5 % of glutaraldehyde (GA) were mixed at a ratio of 10:1 and dropped on the gate surface. After dropping 5 μL of the mixed enzyme solution, the surface was dried at room temperature for 6 h and washed with deionized(DI) water to remove unattached GOx.

3. RESULTS AND DISCUSSION

Fig. 1 shows the schematic representation of the device structure of the ISFET glucose sensor with an additional Pd hydrogen selective membrane. The upper inset of Fig. 1 shows a cross-sectional scanning electron microscopy (SEM) image of uniform ion selective gate layers. The specific enzyme glucose oxidase was immobilized on the Pd surface for the detection of glucose[11]. The overall reaction of glucose oxidase between glucose and dioxygen can be written in the form of the following equations.

$$\beta\text{ - D - Glucose} + O_2 \longrightarrow \text{D - glucono - }\delta\text{ - lactone (or gluconic acid)} + H_2O_2 \tag{1}$$

$$\text{D - glucono - }\delta\text{ - lactone (or gluconic acid)} \longleftrightarrow \text{D-gluconate} + H^+ \tag{2}$$

Glucose is oxidazed into gluconolactone by glucose oxidase while the reduction of dioxygen by GOx yields hydrogen peroxide. Gluconolactone, or gluconic acid in the hydrolysed form, dissociates and releases H+ ions which is is the target of glucose detection using ISFET.

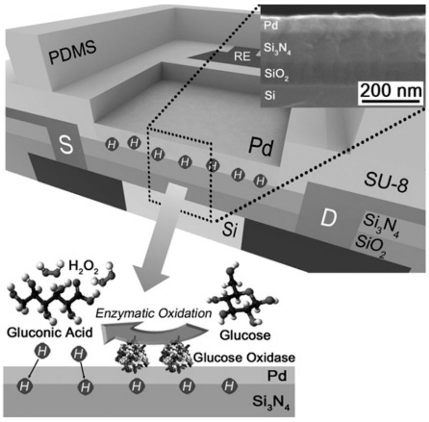

Fig. 1. A schematic of the device structure of the ISFET glucose sensor with an additional Pd hydrogen selective membrane on the sensing channel.

Fig. 2a shows the output performance characteristics of ISFET without a Pd layer immersed in PBS(pH 7) solution. The gate voltage(V_G) was applied through the reference electrode from -2 V to 3 V. The drain current(I_D) was plotted as a function of the drain voltage(V_G) swept from 0 V to 3 V while V_G is applied. This device has a threshold voltage(V_T) of 0.2 V with an on/off ratio of 104 obtained from the I_D-V_G curve(transfer curve) at V_D= 1 V.

This is shown in the inset of Fig. 2a. The transistor device showed stable performance and it worked consistently with the screen-printed Ag/AgCl reference electrode as a gate.

Fig. 2b shows the I_D-V_G characteristics of the ISFET without the Pd layer in different pH solutions at V_D = 1V. Instead of varying V_G, the pH of the standard solutions in which the ISFET was immersed was changed from pH 10 to 4. At a constant V_D, V_T decreased(51.7 mV/pH) as the concentration of H^+ ion increased. These results indicate that the threshold voltage of the transistor is decreased, as an increased amount of positive ions(H^+) attract more electrons in the silicon channel region[11]. This result coincides with the conventional pH sensitivity of Si_3N_4, which is known to have 46 mV/pH ~ 56 mV/pH(Matsuo et al., 1974).

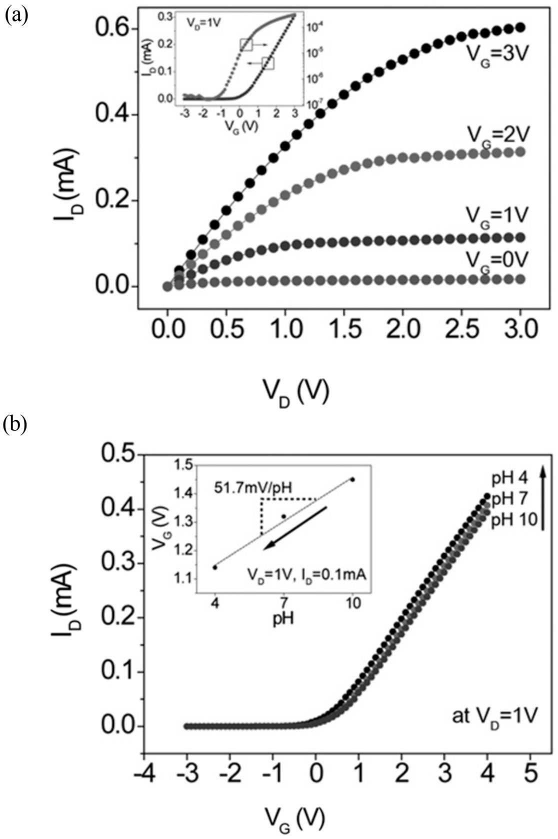

Fig. 2. (a) Output characteristics of the ISFET without a Pd layer immersed in PBS (pH7) solution. (b) I_D-V_G characteristics of the ISFET without the Pd layer in different pH solutions at V_D = 1 V.

Fig. 3a shows the schematic illustration of the hydrogen ion detection mechanism of the ISFET with a Pd hydrogen selective membrane. Hydrogen is known to be adsorbed at the outer surface of Pd, and then diffuses through the Pd layer[13, 17]. The produced hydrogen ions are converted to a hydrogen atom by accepting an electron from Pd. These hydrogen ions diffuse through the Pd layer and they combine with the binding sites on the surface of Si_3N_4. At the Pd-insulator interface, the bounded hydrogen changes the work function of the interface by forming a dipole[17]. Thus, the threshold voltage of the transistor changes as follows:

$$\Delta V_T = -\mu N\theta / \square_0 \qquad (3)$$

where, μ is the dipole moment of hydrogen, N is the density of adsorption sites, θ is the fractional coverage of adsorbed hydrogen atoms, and $\square_0$ is the dielectric permittivity in the free space. In this case, the fractional coverage depends on the H^+ ion concentration.

$$\theta / (1 - \theta) = \text{const}\,[H^+] \qquad (4)$$

More hydrogen atoms are located at the Pd/Si_3N_4 interface compared to the solution-nitride interface without Pd. As a result, more reactions between hydrogen ions and $SiNH_2$ can occur. Therefore, potential changes become greater when the Pd layer exists due to the increased fractional coverage.

Comparison of the glucose response of the ISFET glucose sensor without and with an additional Pd layer is shown in Fig. 3b. The drain current of the ISFET with the Pd layer increased sharply compared to the current of the ISFET without the Pd layer. At 9 mM glucose concentration, ΔI_D increased from 11 μA to 32 μA with the adoption of the Pd layer. As depicted in Figure 3a, the hydrogen adsorption property and the permeability of Pd can improve the selectivity and lessen the interference effects of other ions in the electrolyte solution[18]. Fig. 3c presents the comparison between the gate voltage changes of the ISFET without and with the Pd layer. At high glucose concentration, the rate of increase of the drain current decreased. This is due to the limited dynamic range of the ISFET which is caused by the oxygen limitation via biocatalytic glucose oxidation[19]. The ISFET with the Pd layer showed glucose sensitivity of roughly 16.48 mV/mM with a 0.96 % r^2 while the ISFET without the Pd layer presented 7.98 mV/mM glucose sensitivity. As seen from the results, the glucose sensitivity increased twofold by applying an additional Pd layer and this causes an increase in the amount of hydrogen ions which are transported to the Si_3N_4 surface. The methods described in this work may offer a solution for the realization of a highly sensitive glucose biosensor.

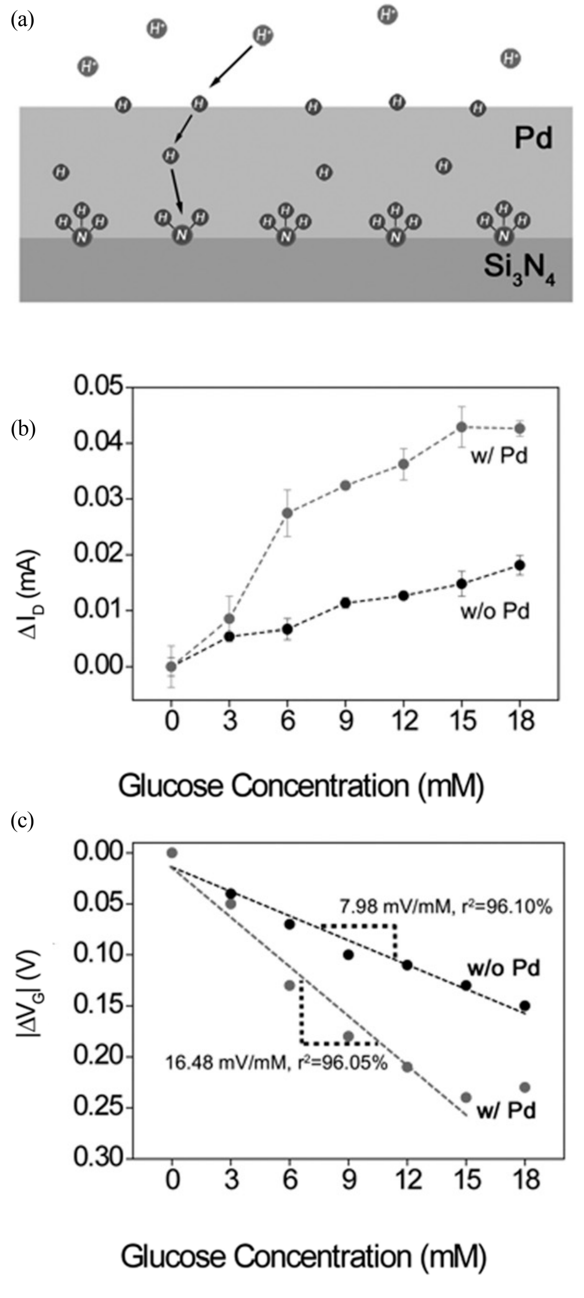

Fig. 3. (a) Schematic illustration of the hydrogen ion detection mechanism of the ISFET with a Pd hydrogen selective layer. (b) Comparison of the glucose response of the ISFET glucose biosensor without and with an additional Pd layer. (c) Comparison between the gate voltage changes of the ISFET without and with the Pd layer.

4. CONCLUSION

We developed an ISFET glucose biosensor with an additional Pd layer. A palladium thin layer was adopted in an ion selective gate membrane in order to increase the hydrogen adsorption property and permeability to the silicon nitride surface. The ISFET glucose sensor with an additional Pd layer showed increased sensitivity and selectivity compared to an ISFET glucose sensor without any additional layer. Moreover, one step fabrication of a screen-printed Ag/AgCl reference electrode can be applied to the compact bio-sensing device. This ISFET with the Pd layer is expected to provide a new opportunity for the practical application of semiconductor based glucose biosensors.

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