

Patch type glucose sensor for low-invasive glucose monitoring

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It is well known that keeping good control of the blood glucose degree can prevent the onset and progression of serious diabetes complications. Therefore, it is important to accurately recognize the blood glucose degree and provide appropriate treatments, such as insulin therapy. Development of implantable glucose sensors for a continuous glucose monitoring system (CGMS) has provided significant benefit, since it lower physical and mental load of diabetes patient on glucose measurement and present continuous glucose trend, which is useful for treatment evaluation. However, length of 1 cm must be injected in the tissue for the placement of the sensor. Therefore, the development of lower invasive CGMS is longed to improve the quality of life of the diabetic patients.

In this study, a unique fine needle tube type glucose sensor, which has sensing region at the tip inside wall of a fine tube, was proposed. The schematic illustration of the tip of such glucose sensor is shown in Figure 1. Since the sensing region is at the inside of fine needle tube, it has space to immobilize certain amount of enzyme, while it require only the tip of sensor probe to be implanted in the tissue for glucose monitoring. CGMSs in the market are designed to measure glucose concentration in subcutaneous tissue, while the proposed sensor has the possibility to be inserted in dermis and measure its glucose concentration, which is significantly shallow from the skin surface. The potential of the prepared sensor as a minimally invasive glucose sensor probe was investigated.

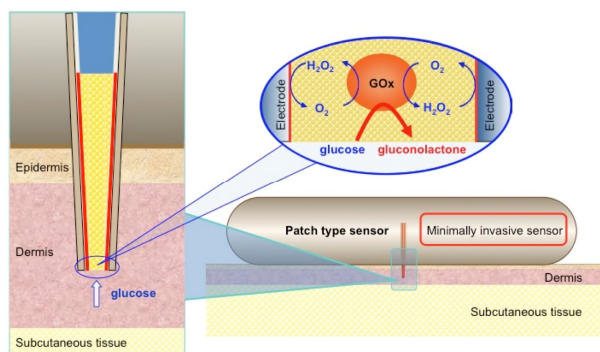


Figure 1. Schematic illustration of fine needle tube type glucose sensor implanted inside the skin.

Sensor Preparation

Platinum-iridium (Pt 90%) tube with the outer diameter of 0.5 mm and inner diameter of 0.3 mm was employed as a starting material. One end of Pt-Ir tube was filled with solvent soluble polymer for protection and the outside surface of tube was coated with dielectric film.

Polymer filled at one end was removed and glucose oxidase (GOx) (244 U/mg, purified from *Aspergillus niger*, Biozyme laboratories) was immobilized inside the tapered tube using the combination of electrodeposition and electropolymerization, according to the procedure of Matsumoto et al. [1] That is, a 10 mg/mL GOx 0.05 M

phosphate buffer solution (pH 7.0) containing 0.8 mM Triton X-100 was poured inside Pt-Ir tube and a potential of 1.3 V (vs Ag/AgCl) was applied for 1 h to form GOx layer on the surface. GOx immobilized Pt-Ir tube was then putted into a degassed 50 mM *o*-phenylenediamine 0.1 M phosphate buffer solution (pH 7.4) and a potential of 0.7 V (vs Ag/AgCl) was applied for 15 min to induce the electropolymerization reaction.

Sensor Response Measurement

The amperometric responses of the prepared electrodes to glucose were examined at 25°C in a 0.1 M phosphate buffer solution (pH 7.4) containing 0.1 M NaCl, by measuring the electrooxidation current at a potential of 0.6 V (vs. Ag/AgCl) for hydrogen peroxide detection. Amperometric measurements were performed with a Potentiostat Model 3104 (Pinnacle Technology Inc.).

The calibration of the sensor was carried out by adding increasing amounts of glucose to the measuring solution. The current was measured at the plateau (steady-state response), and was related to the concentration of the analyte.

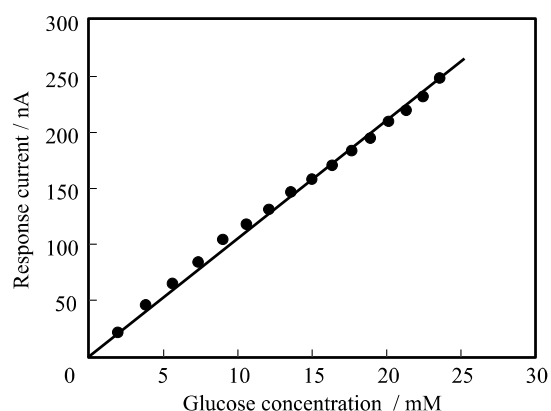


Figure 2. Typical calibration curve of Pt-Ir tube type glucose sensor having sensing region inside the tube tip in a 0.1 M phosphate buffer solution (pH 7.4) containing 0.1 M NaCl at 25°C.

Figure 2 shows typical calibration curves of prepared tube electrode. The response current increased with increasing concentration of glucose. Good linear relationship was obtained up to the glucose concentration of 22.4 mM, which was actually higher than normal sensor without outer film for permeability restriction. This may due to high concentration of oxygen obtained by sufficient reproduction and maintenance oxygen, since both electrochemical and enzymatic reactions occur in the tube and the release of oxygen can be restricted.

In vivo evaluation using experiment animals is under way.

Acknowledgment

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References

- [1] N. Matsumoto, X. Chen and G. S. Wilson, *Anal Chem*, 74, 368 (2002).