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"An Integrated SOS/FET Biosensor"

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(Summary)

A monolithically integrated biosensor has been realized using SOS/FET (Silicon on Sapphire/Field Effect Transistor) technology, which makes it possible to measure a very small sample and to make measurements in a body, such as in a vein.

The integrated biosensor proposed in this paper (Fig. 1) adopts SOS/ISFET (Silicon on Sapphire/Ion Sensitive Field Effect Transistor), which is fabricated in a silicon island on the sapphire substrate and is sensitive to hydrogen ions (H^+). The silicon island is easily isolated from the other FETs and a measured solution, because sapphire is a good dielectric material. Its inherent dielectric isolation property makes SOS/FET very suitable for use in chemical sensors and biosensors, which are used for making measurements in a solution.

The integrated SOS/FET biosensor consists of two kinds of SOS/ISFETs, which are made on the same chip. One SOS/ISFET has an immobilized enzyme (urease) membrane on the surface. The other has a membrane which has inactivated enzyme. A gold layer is deposited on the sapphire back surface and works as a pseudo reference electrode.

At the immobilized enzyme membrane, urease catalyzes the hydrolysis of urea according to the following reaction and changes pH.

$$\begin{matrix} H_2N \\ H_2N \end{matrix} > C{=}O + 2H_2O + H^+ \xrightarrow{\text{urease}} 2NH_4^+ + HCO_3^-$$

By measuring a differential output between the two SOS/ISFETs, only pH change due to urea hydrolysis can be detected.

SOS/FET technology has also made it possible to integrate the biosensor by using conventional IC (Integrated Circuit) fabrication processes, such as spin coating and photolithography. Main integrated SOS/FET biosensor fabrication processes are;

1) Etch an island from the Si layer
2) Boron (B) ion implantation to Si
3) Phosphor (P) ion implantation to source and drain region
4) Gate oxidation (1000Å thick SiO_2)
5) Phosphor (P) ion implantation to gate region for a threshold voltage control
6) Chemical vapor deposition of a silicon nitride (Si_3N_4) layer, which works as an ion sensitive membrane
7) Sputter deposition of gold (Au) on the sapphire backsurface to make a pseudo reference electrode

8) Spin coat an acetyl cellulose layer containing glutaraldehyde and 1,8 diamino-4-aminomethyloctane

9) Immobilize urease

10) Inactivate immobilized urease except at the gate region for the urea sensitive SOS/FET

11) Scribe the wafer and connect wires.

As shown above, the proposed integrated SOS/FET biosensor was fabricated by IC technology, which contributes to miniaturization of the biosensors and to obtaining uniform sensor characteristics.

A measurement circuit for the proposed biosensor is shown in Fig. 2. Figure 3 shows the response curves for the urea concentration measurement. In Fig. 3, line Sl shows the output from the urea sensitive SOS/FET and line S2 shows the differential output between the two SOS/FETs on the same chip. Drift caused by the potential change in the solution is cancelled in line S2. Figure 4 shows a relationship between urea concentration and the differential output. Urea concentrations in the from 10 to 100 mg/dl range were detected by the differential response.

These results show that a miniaturized biosensor can be easily achieved by SOS/FET technology, which enables a direct IC fabrication process application. The proposd integrated SOS/FET biosensor can be set in a catheter or in a needle. It becomes very useful in medical application fields.

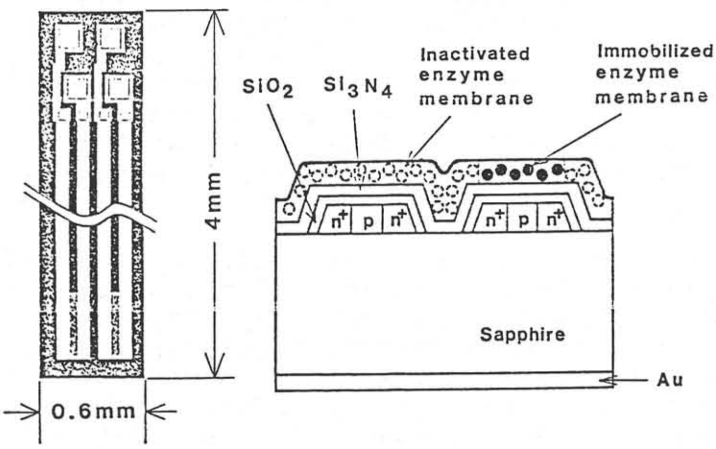

Fig. 1 Proposed integrated SOS/FET biosensor structure.

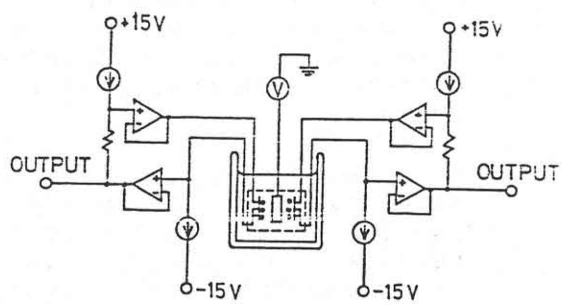

Fig. 2 Proposed biosensor measurement circuit.

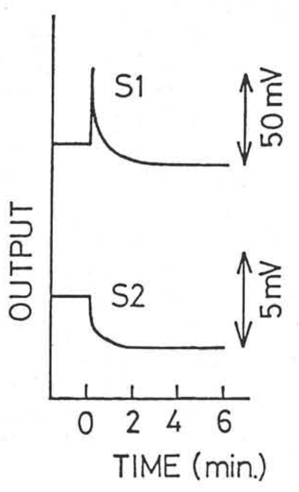

Fig. 3 Response curves for urea FET (Sl), and differential output (S2). Urea is added into the buffer solution at time=0.

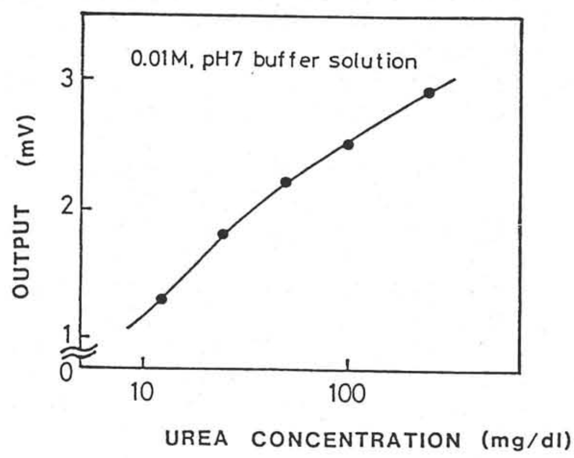

Fig. 4 Relationship between differential output and urea concentration