Investigation of Screening Effect of Bio-molecules on pH Sensitivity of SOI-ISFET Biosensor

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Abstract. A behavioral macromodel of the SOI-ISFET has been developed in HSPICE® to simulate the electrolyte-oxide-semiconductor structure of the ISFET in a solution with an additional membrane layer. This paper studies the Debye screening of bio-molecules and its effect on the single-gate sensitivity as well as dual-gate sensitivity of the SOI-ISFET based biosensor using the macromodel developed. The analysis has been done for different sensing materials for the ISFET such as SiO_2, Si_3N_4 and Al_2O_3.

Keywords: SPICE, SOI ISFET, Modeling, Biosensor, Debye Screening

INTRODUCTION

ISFET is a popular biochemical sensor, similar to a MOSFET with the additional capability to exhibit different threshold voltages for different external chemical environments around the device [1-3]. The device is sensitive to the concentration of ions and the pH of the solution in which the reference electrode is inserted. The SOI-ISFET has been investigated recently because of the advantages it presents such as lower leakage currents, reduced parasitic capacitances, stable performance and ability to operate in dual gate mode to increase the sensitivity beyond the Nernstian limit [4-5]. In this paper, a behavioral macromodel of the SOI-ISFET has been designed and simulated using HSPICE. This paper studies the Debye screening of bio-molecules and the resulting reduced sensitivity to pH for different sensing materials.

Conventional ISFETs have an upper limit of 59 mV/pH on their sensitivity to pH variations [6]. However, this limitation can be overcome by dual-gate operation of SOI-ISFET [4-5]. The SOI-ISFET can also be used to as a biosensor to detect different kinds of biological species [7]. This paper investigates the Debye screening of bio-molecules and their effect on the pH sensitivity of the biosensor, for different sensing films such as SiO_2, Si_3N_4 and Al_2O_3.

BEHAVIORAL MACROMODEL OF SOI-ISFET

Fig.1 shows a schematic of ISFET and all the layers at the electrolyte-oxide interface. Considering these layers with the help of site-binding theory and electrical double layer theory, the ISFET has been modeled in HSPICE®. In the model, we have assumed that the membrane layer (i.e. the biological layer to be sensed, such as DNA/proteins) is charged. This assumption is related to the screening lengths in the membrane layer [8].

The SOI-ISFET can be modeled appropriately using the equations provided by the site-binding theory and the electrical double layer theory. The electrolyte-oxide interface is considered to behave as a pH-dependent voltage source ψ_0 [6].

ψ_m is the membrane potential, q is the elementary unit charge, N_{sil} and N_{nit} are the surface densities of the silanol and amine binding sites respectively, $[H^+]$ is the proton concentration, k is the Boltzmann constant, T is the absolute temperature, K_+, K_- and K_N are the binding site dissociation constants and C_{Helm} is given by:

$$\psi_0 = \psi_m + \frac{qN_{sil}}{C_{Helm}} \frac{[H^+]^2 e^{\frac{-2q\psi_0}{kT}} - K_+K_-}{[H^+]^2 e^{\frac{-2q\psi_0}{kT}} + K_+[H^+]^2 e^{\frac{-q\psi_0}{kT}} + K_+K_-} + \frac{qN_{nit}}{C_{Helm}} \frac{[H^+]^2 e^{\frac{-q\psi_0}{kT}}}{[H^+]^2 e^{\frac{-q\psi_0}{kT}} + K_N} \tag{1}$$

$$C_{Helm} = \frac{\varepsilon_{IHP}\varepsilon_{OHP}}{\varepsilon_{IHP} d_{OHP} + \varepsilon_{OHP} d_{IHP}} \tag{2}$$

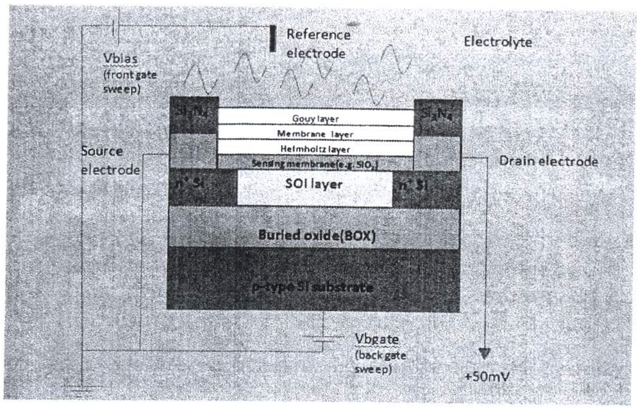


FIGURE.1. Schematic showing pH sensing ISFET

The membrane potential can also be related to the pH-dependent voltage source as [7]:

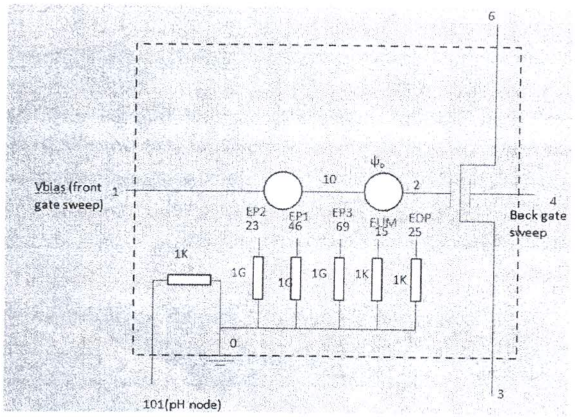


FIGURE.2. HSPICE sub-circuit schematic of SOI-ISFET

$$\psi_m = \psi_0 - \frac{sign(\psi_m)\sqrt{4n_0 kT\varepsilon_m} \times [\cosh\frac{q\psi_m}{kT} - \cosh\frac{q\psi_{DP}}{kT} - (\psi_m - \psi_{DP})\sinh\frac{\psi_{DP}}{kT}]^{0.5}}{C_{Helm}} \tag{3}$$

$$\psi_{DP} = \sinh^{-1}(\frac{vN_m}{2zn_0}) = \ln(\frac{vN_m}{2zn_0} + \sqrt{1 + (\frac{vN_m}{2zn_o})^2} \tag{4}$$

where n_0 is the salt concentration, ε_m is the dielectric constant of the membrane, v is the valency of the membrane charge, z is the valency of the salt ions and N_m is the membrane charge density. Fig.1 shows a schematic of the biological layers formed at the electrolyte-oxide interface. The developed macromodel in HSPICE has been depicted in Fig. 2.

DEBYE SCREENING OF BIO-MOLECULES

The Debye length in an electrolyte is defined as the measure of charge carrier's net electrostatic effect in a solution and is expressed as [7]:

$$\lambda_{DP} = \sqrt{\frac{\varepsilon\varepsilon_o kT}{2q^2 n_o}} \qquad (5)$$

where ε is the dielectric constant, ε_o is the dielectric constant of free space, k is the Boltzmann constant, T is the absolute temperature, q is the elementary unit charge and n_0 is the salt concentration. Equations (1) and (3) are based on the assumption that charge neutrality will be achieved in the membrane [8]. Charge neutrality will exist only if the screening length inside the membrane is shorter than the screening length inside the electrolyte. This will depends on the values of the membrane charge and the salt concentration. When the value of the membrane charge exceeds the value of the salt concentration i.e. $N_m >> n_o$, the screening length inside the electrolyte starts exceeding the screening length inside the membrane based on equation (5). Due to this screening effect, the effective charge of the biological membrane as seen by the biosensor reduces. This results in a reduced sensitivity of the biosensor as membrane charge increases. [7].

When SOI-ISFET is used as a pH sensor, the membrane charge is taken to be zero. However, in the case of biosensors, there is an appreciable amount of membrane charge present, so that it can be comparable or even greater than the salt concentration [7]. In such cases, we shall observe a decrease in the single-gate sensitivity as well as the dual-gate sensitivity of the SOI-ISFET. The further section of the paper summarizes the results and demonstrates the reduced sensitivity due to screening of biosensors.

RESULTS AND DISCUSSION

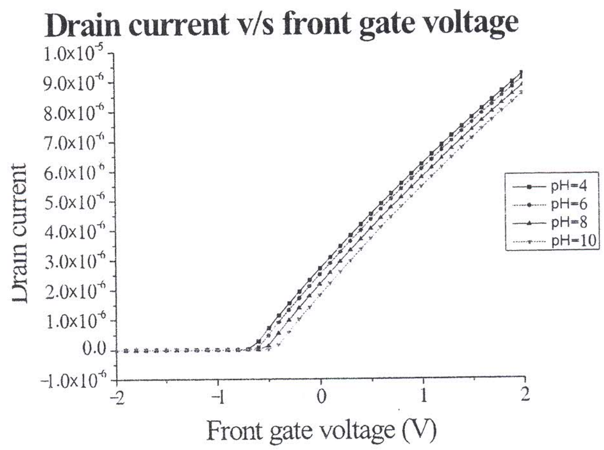
Ion concentration has been kept low, at 0.001M throughout the analysis. SOI layer of SOI-ISFET in consideration is 150 nm thick, buried oxide thickness is 700 nm and the sensing film oxide thickness is 20nm.

The analysis has been done for three different sensing films: SiO_2, Si_3N_4 and Al_2O_3 Table I summarizes the sensing film characteristics and their values to be substituted in the HSPICE netlist [9].

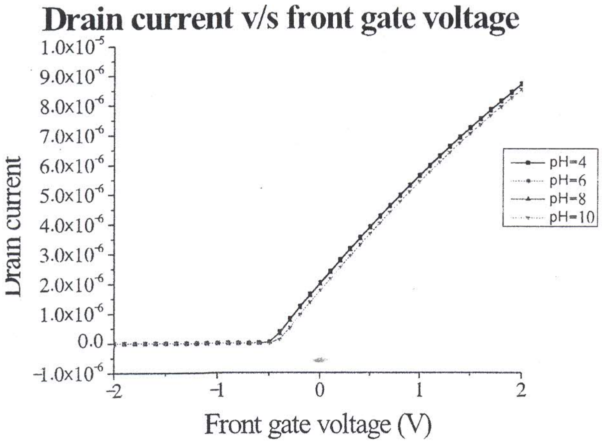
TABLE 1. Parameters for different sensing films [9]

Material	K_+	K_-	K_N	N_{sil}	N_{nit}
SiO_2	15.8	63.1e-9	-	5.0e+18	-
Si_3N_4	15.8	63.1e-9	1.0e-10	4.5e+18	5.0e+17
Al_2O_3	12.6e-9	79.9e-10	-	8.0e+18	-

Fig. 3 and 4 show the output current characteristics of the biosensor for different values of membrane charges. In Fig. 3, the output current is shown against front gate voltage for membrane charges of 1.0 x 10^{22} m^{-3} and 1.0x $10^{27} m^{-3}$, keeping back gate grounded. Fig.4 shows the values of output current against back gate voltage for membrane charges of 1.0 x $10^{22} m^{-3}$ and 1.0x $10^{27} m^{-3}$ with front gate grounded. The reduced sensitivity to pH can be clearly seen in Fig. 5. There is an appreciable decrease in the single-gate sensitivity as well as the dual-gate sensitivity with increase in the membrane charge. It can also be observed that the charge screening is prominent SiO_2 in sensing film while Al_2O_3 sensing film is least affected by membrane charge.

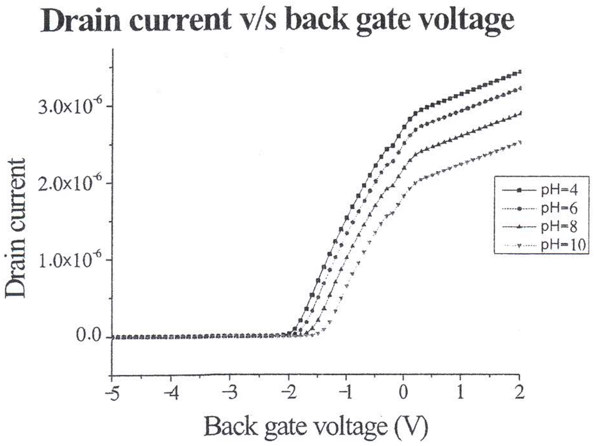


(a)



(b)

FIGURE 3. Output current against front gate voltage for membrane charge of (a)1.0×10^{22} $m^{-3}$and (b)1.0×10^{27} m^{-3}



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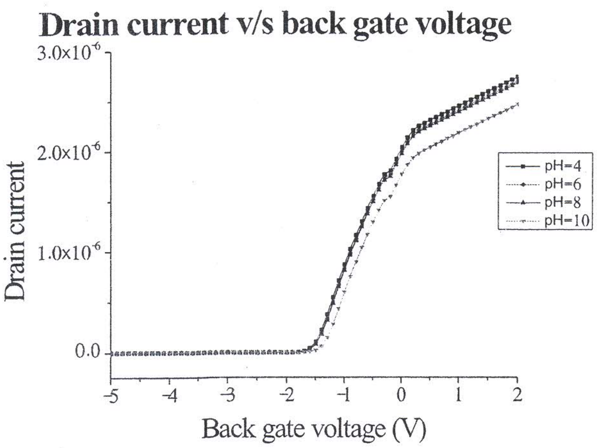
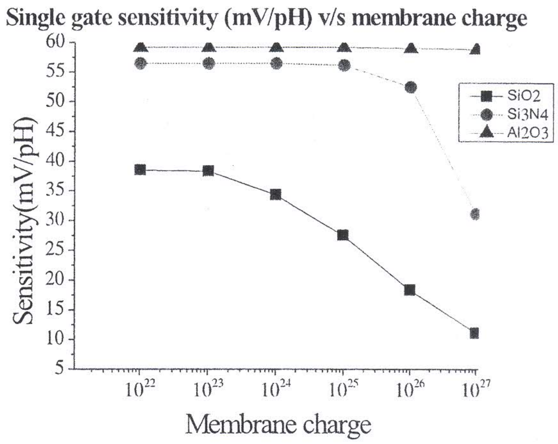


(b)

FIGURE 4. Output current against back gate voltage for membrane charge of (a)1.0×10^{22} $m^{-3}$and (b)1.0×10^{27} m^{-3}



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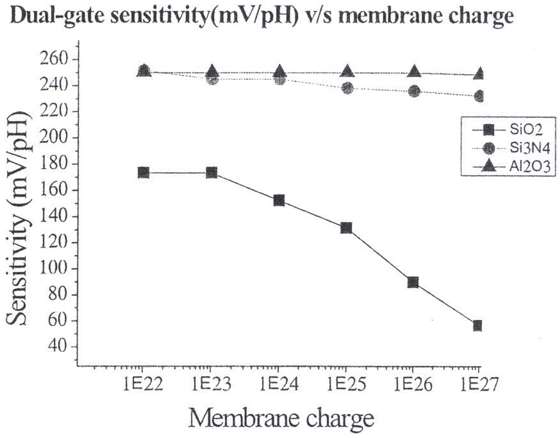

(b)

FIGURE.5. Variation of single-gate sensitivity and dual-gate sensitivity with membrane charge

Due to sensing film characteristics, the amount of decrease in the sensitivity is different for different sensing films. In our analysis, sensitivity of an SOI-ISFET having sensing film of Al_2O_3 will not reduce much, however appreciable decrease in sensitivity will be observed for SOI-ISFETs having sensing films of SiO_2 or Si_3N_4.

CONCLUSIONS

The graphs obtained show significantly reduced sensitivity due to Debye screening of bio-molecules. As $N_m >> n_0$, the effect of screening can be clearly seen through the sensitivity graphs. These observations are in accordance with the predictions as stated in literature [2]. Hence, we can conclude that the Debye screening effect has been correctly modeled in our behavioral macromodel and our output is as expected.

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