Modeling the Electrical Characteristics of FET-type Sensors for Biomedical Applications

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ABSTRACT

Selective detection of biological pathogens is of great importance in health care. Early detection of infections can help isolate diseases at earlier stages and therefore facilitates early containment and eradication. Fluorescent DNA microarrays have been used extensively to detect pathogens with specific gene expressions. Recently, gate-modified transistors (BioFETs) have been used for direct electrical detection of DNA hybridization. This paper addresses a model that describes the electrical response of the BioFET to charged DNA strands, and provides some insight on the noise characteristics as limiting factors for the sensitivity of such sensors.

Keywords: FETs, BioFETs, Modeling, Biosensors, DNA, Hybridization.

1 INTRODUCTION

Optical DNA microarrays have shown high sensitivities in selective detection of specific oligonucleotides which leads to accurate detection of specific pathogenic micro-organisms in a solution [1]. However, the requirement of expensive labels and laser scanners renders the economic feasibility of such sensors low to all but the most advanced labs. It is desired to achieve biosensors with equivalent or superior performance to that of the optical methods without the need for optical methods of detection. If such devices could be operated with very low power, portable handheld biosensors could be realized. Recently, MOSFET devices have been modified to operate as DNA hybridization sensors by attaching DNA probes to the dielectric material and detecting a signal due to hybridization of the target oligonucleotides [1], [2], and a recent review of BioFET-type sensors is presented in [3]. DNA molecules contain negative charges on their sugar backbones that enable them to modify the charge carrier population of a semiconductor when placed in close proximity to them. In a BioFET, shown in Figure 1, this change can be detected as change in the drain current. In order to quantify the signal of a BioFET, accurate physical modeling must be carried out to account for the various phenomena that occur within the BioFET structure.

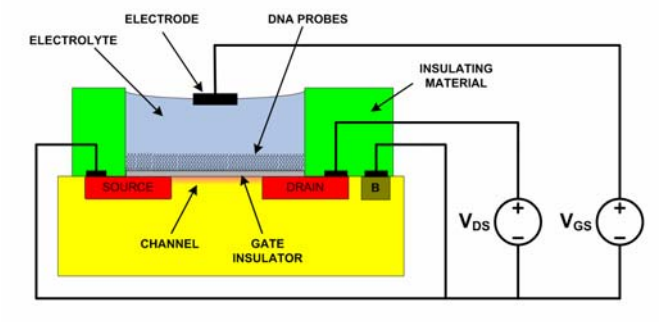

Figure 1 Simplified diagram of a BioFET

2 PHYSICAL MODELING

DNA molecules in electrolytic solutions are surrounded by a diffuse of ionic counter-charge. This can lead to screening of the DNA charge from the semiconductor surface. This can drastically reduce the sensitivity of the DNA sensor, specifically for high ionic concentrations. In addition, the surface of the insulator can aid in screening DNA charges. If there are sites that favorably react with protons, then these adsorbed protons can further aid in the screening and reduction of the BioFET's sensitivity. In a recent model [4], these effects were included into the general modeling of the device. A sample potential diagram of a BioFET is shown in Figure 2.

The ionic distribution around macromolecules in an electrolyte follows the nonlinear charge-perturbed Poisson-Boltzmann equation, which is given by:

$$\nabla \bullet \varepsilon(\boldsymbol{r}) \nabla \psi(\boldsymbol{r}) = q\left(2n_0 z \sinh(z\beta\psi(\boldsymbol{r})) - N_m\right) \qquad (1)$$

where r is the position vector, ψ is the potential, ε is the local permittivity, z is the ionic valence for a balanced electrolyte, N_m is the volumetric charge density of the DNA membrane, n_0 is the molar concentration of the electrolyte under no potential, and β is the inverse thermal voltage. Equation (1) is used together with a non-perturbed Poisson-Boltzmann equation for the

region of the electrolyte solution that is not permeated by DNA:

$$\nabla \cdot \varepsilon(\boldsymbol{r}) \nabla \psi(\boldsymbol{r}) = 2qn_0 z \sinh(z\beta\psi(\boldsymbol{r})) \qquad (2)$$

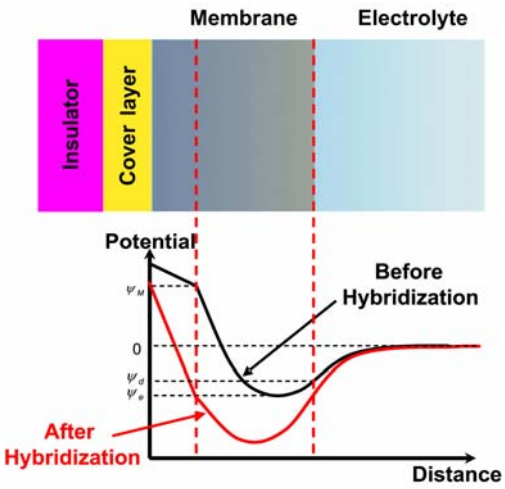

Figure 2 sample potential diagram of the electrolyte in a BioFET

Equations (1) and (2) can be solved with appropriate boundary conditions to arrive at an effective charge density on the electrolyte. Another contribution to electrolyte charges results from surface states in the insulator capturing spurious ions. This can be described by a protonation equilibrium relationship which results in a pH-dependent charging of the insulator surface. The relationship between the potential and the stored charge is given by [3]:

$$\sigma_0 = qN_s \left(\frac{A - B}{1 + A + B} \right) \qquad (3)$$

where N_s is the density of protonation sites on the surface of the insulator, and the values A and B are related to the bulk proton concentration, and to the protonation-deprotonation equilibrium constants by the following relationships:

$$A = \frac{[H^+]_0}{K_a} e^{-\beta\psi_0}, B = \frac{K_b}{[H^+]_0} e^{\beta\psi_0} \qquad (4)$$

Equations (1-3) can be coupled with the equation for semiconductor inversion layer which, for an N-type substrate (PMOS), is given by:

$$\sigma_s = \mathrm{sgn}(-\psi_s)\sqrt{2kT\varepsilon_s n_i} \left(\begin{array}{l} e^{-\beta\phi_F}\left(e^{\beta\psi_s} - \beta\psi_s - 1\right) \\ +e^{\beta\phi_F}\left(e^{-\beta(\psi_s - V_{CB})} + \beta\psi_s - e^{\beta V_{CB}}\right) \end{array} \right)^{1/2} \qquad (5)$$

where V_{CB} is the bias of the source (C=S) or drain (C=D). Equation (5) must be calculated twice, once for the drain bias and once for the source. Two more equations that complete the system of equations to be solved are the charge balance equation and the potential balance. The charge balance is given by:

$$\sigma_s + \sigma_f = \sigma_0 + \sigma_m + \sigma_d \qquad (6)$$

In equation (6), σ_s, σ_f, σ_0, σ_m, and σ_d are the charge densities of the semiconductor channel, the fixed charges on the insulator surface, the adsorbed proton charges, the DNA membrane charge, and the residual diffuse charge outside the DNA region, respectively. The final equation is the potential balance, given by:

$$V_{GB} = \chi_{sol} - \chi_{Si} - \frac{u_{sol}}{q} + \frac{u_s}{q} - \psi_0 - \frac{\left(\sigma_s + \sigma_f\right)}{C_{eff}} + \psi_s \qquad (7)$$

Figure 3 shows a sample solution of the BioFET potential profile, showing how the DNA density can affect the total potential profile, and the corresponding charge on the semiconductor.

Once the semiconductor surface potential on the source and drain has been obtained, we can use the charge-sheet model approximation of MOSFETs to calculate the corresponding drain current of the BioFET. The charge sheet model for drain current, including both diffusion and drift current components, results in the following expression for an inverted PMOS device:

$$I_D = K \left(\begin{array}{l} \frac{1}{\beta}\left(\begin{array}{l} \psi_{00} - \psi_{0L} + \psi_{sL} - \psi_{s0} \\ +\gamma\left(\sqrt{-\psi_{s0}} - \sqrt{-\psi_{sL}}\right) \end{array} \right) \\ + \left(\begin{array}{l} \left(V_{GB} - V_{FB} + \frac{1}{2}\left(\psi_{00} + \psi_{0L}\right) \right) \\ \left(\psi_{s0} - \psi_{sL}\right) \\ -\frac{1}{2}\left(\psi_{s0}^2 - \psi_{sL}^2\right) \\ -\frac{2}{3}\gamma\left(\left(-\psi_{s0}\right)^{3/2} - \left(-\psi_{sL}\right)^{3/2}\right) \end{array} \right) \end{array} \right) \qquad (8)$$

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where ψ_{00}, ψ_{0L}, ψ_{s0}, and ψ_{sL} are the source and drain surface potentials of the electrolyte and the semiconductor, respectively, V_{FB} is the flatband voltage, γ is the body effect coefficient, and K is defined as:

$$K = \frac{WC_{eff}\,\mu_{eff}}{L} \tag{9}$$

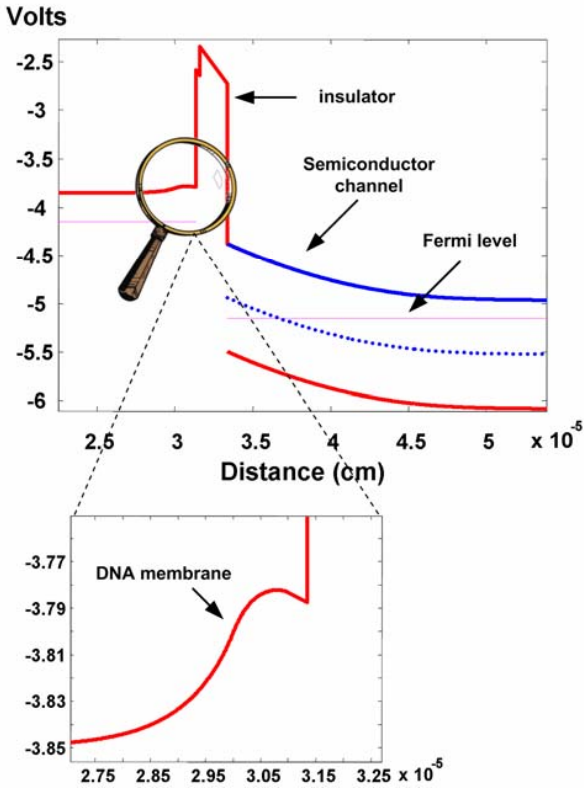

Figure 3 Simulated BioFET potential diagram

Figure 4 shows a plot of the change in drain current due to immobilization, and hybridization of DNA strands.

3 NOISE IN BIOFETS

Once the BioFET current change due to DNA hybridization has been determined, we can calculate the expected signal-to-noise ratio using MOSFET noise theory. At the low frequencies of sensing, both the channel's thermal noise and the *1/f* noise contribute to the total sensitivity of the BioFET [5]. In the correlated mobility-number theory of carrier fluctuation, the gate-referred noise spectral density is given by:

$$S_{VG} = \frac{qkTN_t\lambda}{fWLC_{eff}^2}\left[1+\left(\alpha\mu_{eff}C_{eff}\frac{I_D}{g_m}\right)\right]^2 \tag{10}$$

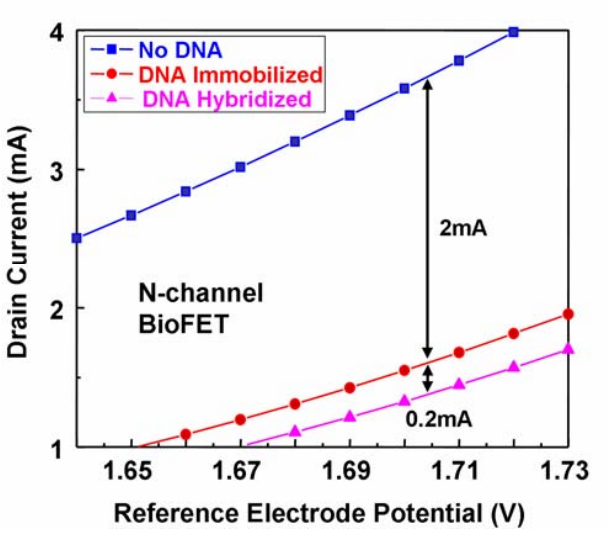

Figure 4 Current shift due to immobilization of probes and hybridization

where N_t is the trap density, α is the correlation coefficient, g_m is the transconductance, λ is the tunneling parameter, and f is the frequency. The thermal noise for a PMOS is given by:

$$S_{VG-th} = \frac{4kT\,\mu_{eff}C_{eff}}{g_m^2L^2}(Q_I) \tag{11}$$

where Q_I is the total inversion charge in the channel of the BioFET. Equations (10) and (11) allow the total noise of the BioFET to be calculated. Figure 5 shows the results of plotting the signal to noise ratio as a function of the gate bias. It can be seen that there exists an optimum biasing condition around threshold voltage that would maximize the SNR. This biasing point is quite important for ultra-highly sensitive circuits, such as BioFET-modified opamps.

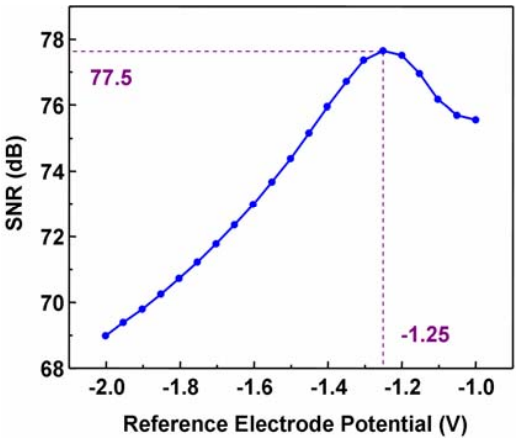

Figure 5 Simulated signal-to-noise ratio for a BioFET

4 CONCLUSION

The BioFET potential profile allows calculation of the response to a uniform DNA density charge. Using this model, several different methods of operation can be employed. Although the model shown here can be used to determine the sensitivity limits of the BioFET, it is worth noting that very low DNA densities can cause 2-D effects that are not accounted for in this model, and that can provide more realistic limits for sensitivity. Such models will be the basis upon which the optimum sensitivity of these devices can be modeled.

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