33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Design of a High Sensitive Double-gate Field-effect Transistor Biosensor for DNA Detection

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Abstract—**The study of interactions between organic biomolecules and semiconducting surfaces is an important consideration for the design and fabrication of field-effect-transistor (FET) biosensor. This paper demonstrates DNA detection by employing a double-gate field effect transistor (DGFET). In addition, an investigation of sensitivity and signal to noise ratio (SNR) is carried out for different values of analyte concentration, buffer ion concentration, pH, reaction constant, etc. Sensitivity, which is indicated by the change of drain current, increases non-linearly after a specific value (~1nM) of analyte concentration and decreases non-linearly with buffer ion concentration. However, sensitivity is linearly related to the fluidic gate voltage. The drain current has a significant effect on the positive surface group (-NH_2) compared to the negative counterpart (-OH). Furthermore, the sensor has the same response at a particular value of pH (5.76) irrespective of the density of surface group, although it decreases with pH value. The signal to noise ratio is improved with higher analyte concentrations and receptor densities.**

I. Introduction

MODERN label free detection of bioanalytes using field-effect-transistor biosensor has attracted interests because of its ultrasensitive, low-cost and high-throughput analysis of biological processes. This type of biosensing is considered as an alternative detection technology to the traditional chemical detection schemes with a potential for on-chip integration [1]. The FET biosensor is a charged-based detection scheme which gives an indication of the presence of biomolecules based on their intrinsic characteristics. The technology can be employed in various applications including detection of proteins [2], DNA [3], pH [4] and gas [5]. Among these, DNA detection using a FET structure offers more sensitive means as DNA carries negative charge under normal physiological conditions while the net charged carried by proteins depends on the pH of the solutions and other factors (e.g., ionization of the R groups of the amino-acids) [6].

DNA detection is an important means for many of the diagnosis applications and a number of methods including cantilever DNA bisensor [7], surface plasmon resonance biosensor [8], and impedimetric detection[9] have been achieved. However, these techniques suffer from complex, expensive, and time-consuming operation. Detection of DNA using the FET approach can address some of these issues; it is thus being currently investigated by many researches [10-12].

Recently, research on the FET-based DNA detection is tremendously motivating for the nanosensing applications. However, a wide study has been investigated on single-gate FETs and only a few attempts [13, 14] have focused on double-gate FETs (DGFETs). Nair et al. [15] performed a performance analysis of a FET nanobiosensor and reported the performance analysis in terms of incubation time and the analyte density. They focused on the channel geometry in terms of cylindrical, planar and spherical shape of the silicon nanowire channel to analysis the performance parameter for their study. However, the performance parameters can further be improved by employing a DGFET. The added advantage of the floating gate in this approach is that the charge in solution can be further modulated by applying biasing arrangement to the terminal. In addition, the floating gate is assumed to be charged when a biomolecule attaches to it or the pH of solution is changed.

Sensitivity which is an important parameter can be improved by considering the device geometry (e.g., carbon nanotube channel, planar silicon nanowire channel). However, dealing with the geometry modification encounters some unwanted results including loss of detection accuracy and complexity to the device miniaturization [16]. For example, unlike carbon nanotube (CNT) FET biosensor which requires precise control and manipulation of the CNT to form the channel region, the silicon DGFET does not involve the complex manipulation arrangement. In this work, the performance parameters for a DGFET biosensor are investigated in terms of the analyte concentration, buffer ion concentration, pH of the solution, dissociation constant of surface groups and fluid gate voltage, etc., rather than the taking into account the device structure which has been addressed in the published work. In addition, an optimum value of pH for the different values of the density of surface groups is found by employing a number of experimental studies.

II. Kinetics of DNA Hybridization

The principles underlining the DNA detection is simple in which untagged single-stranded DNAs (ssDNA) are functionalized onto the sensor surface, which interacts with the complementary DNA (cDNA) (Fig. 1). The electrostatic interaction between these two charged particles produces a diffusion of the target DNA throughout the sensor volume

Manuscript received April 15, 2011.

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978-1-4244-4122-8/11/$26.00 ©2011 IEEE

and modulates the electrical characteristics (e.g., conductivity and drain current) of the FET channel.

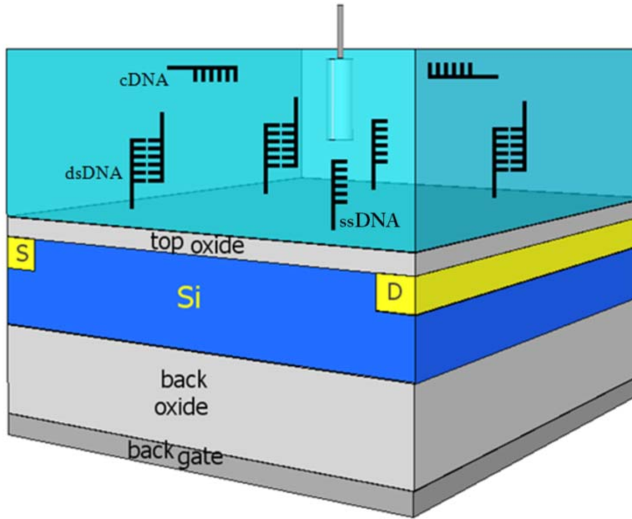

Figure 1. Schematic structure of the double-gate FET biosensor with receptors functionalized to the surface. (dsDNA corresponds to double-stranded DNA)

The change of the drain current signifies the presence of desired target DNA molecules in the analyte. However, the capturing of the target molecules occurs in the sensor surface only when the target is specific and inclusive complement to the receptors. The capture of the target molecules by the receptor molecules follows two steps [17]: transport of the target molecules and hybridization with the receptor molecules. For the DGFET operation, a linear transport is assumed whereas target-receptor hybridization is treated as a first-order chemical reaction. The dynamic of the diffusion-capture model describing biomolecule conjugation is treated as a first-order chemical reaction, and determined by the following equation [15]:

$$\frac{d\rho}{dt} = D\nabla^2\rho \tag{1}$$

and

$$\frac{dN}{dt} = k_F\,(N_0 - N)\rho_s - k_R N \tag{2}$$

where D and ρ are the diffusion coefficient and the concentration of the analyte, respectively. N and N_0 are the density of the conjugated receptors, and the total receptor density on the sensor surface, respectively. k_F and k_R are the capture and dissociation constants, and ρ_s is the concentration of analyte particles at the sensor surface. Eq. (1) represents the diffusion of target molecules to the sensor surface whereas (2) denotes the capture of biomolecules.

Assuming a large value of k_F/k_R (~ 10^5 for specific target receptor hybridization) [15] and N_0 (~ 10^5 μm^{-2}), (2) can be rewritten as:

$$\frac{dN}{dt} = k_F\,N_0\rho_s \tag{3}$$

whereas the solution of (1) can be found as follows [15]:

$$-\frac{k_F N_0 + E - k_F N_{equi}}{k_F\rho_0 + k_R}\log\left(1-\frac{N}{N_{equi}}\right) + \frac{k_F}{k_F\rho_0 + k_R}N = Et \tag{4}$$

where E= $(N_{avo}C_D(t))/A_D$, N_{avo} is the Avogadro's number, C_D (t) is the time dependent diffusion equivalent capacitance, A_D is the dimension dependent area of the sensor and

$$N_{equi} = \frac{k_F\,N_0\rho_s}{k_F\rho_0 + k_R} \tag{5}$$

is the equilibrium concentration of the conjugated biomolecules.

III. Numerical Modeling and Simulation

In this study, a modeling and simulation exercise [17] is carried out for the DGFET biosensor for DNA detection. A schematic of the proposed design is shown in Fig. 1. The device consists of a microfluidic channel for the liquid analyte and a top oxide layer to cover the semiconducting surfaces to protect the front-end complementary metal oxide semiconductor process from biological solution [18]. For the entire simulation, the device dimension is maintained unaltered which is: device length and width = 1 µm, top oxide thickness = 0.04µm, back oxide thickness = 15µm and silicon body thickness = 8 µm.

To determine the electrical response for the presence of DNA, the sensor surface is functionalized with specific receptors (e.g., ssDNA for cDNA) that recognize and bind only to the target biomolecules. Biomolecules which are introduced into the liquid solution are diffused and captured by the receptor molecules. DNA in liquid solution carries a negative charge, thereby the electrostatic interaction between the charge of target cDNA and the sensor surface results in the modulation of the sensor characteristics. Measuring the shift of the electrical characteristics (e.g., drain current and conductivity) the presence of the target biomolecules is identified.

IV. Results and Discussions

Sensitivity, adsorption efficiency, and signal to noise ratio (SNR), are the crucial parameters for determining the performance of biosensors. In this study, sensitivity and SNR are investigated. For the best performance of the DGFET biosensor, the values of these parameters are expected to be as high as possible.

A. Sensitivity

The sensitivity of a biosensor depends on a number of factors (e.g., reaction constants, target molecules densities, and device geometry) but in the context of this study, the sensitivity improvement is a result of modulating the charge of the sample by applying the fluid gate voltage, increasing analyte concentration and buffer ion concentration with different reaction constant of the particular functionalization group. To confirm the sensitivity performance of the

DGFET biosensor, the dependence of drain current (I_d) on analyte concentration, buffer ion concentration and pH of the solution is measured.

1) Influence of Analyte Concentration and Fluid Gate Voltage: The sensor response for different fluidic gate voltage (V_{fg}) and concentration of analyte is shown in Fig. 2. It is outlined that the sensor has a response only after a particular concentration of analyte which is about 1nM (Fig.2 (a)). The I_d change is not directly proportional to the concentration of the captured molecules, whereas, it is linearly proportional to the V_{fg} (Fig.2 (b)). The nonlinearity in the sensor response arises because of the electrostatic screening effect.

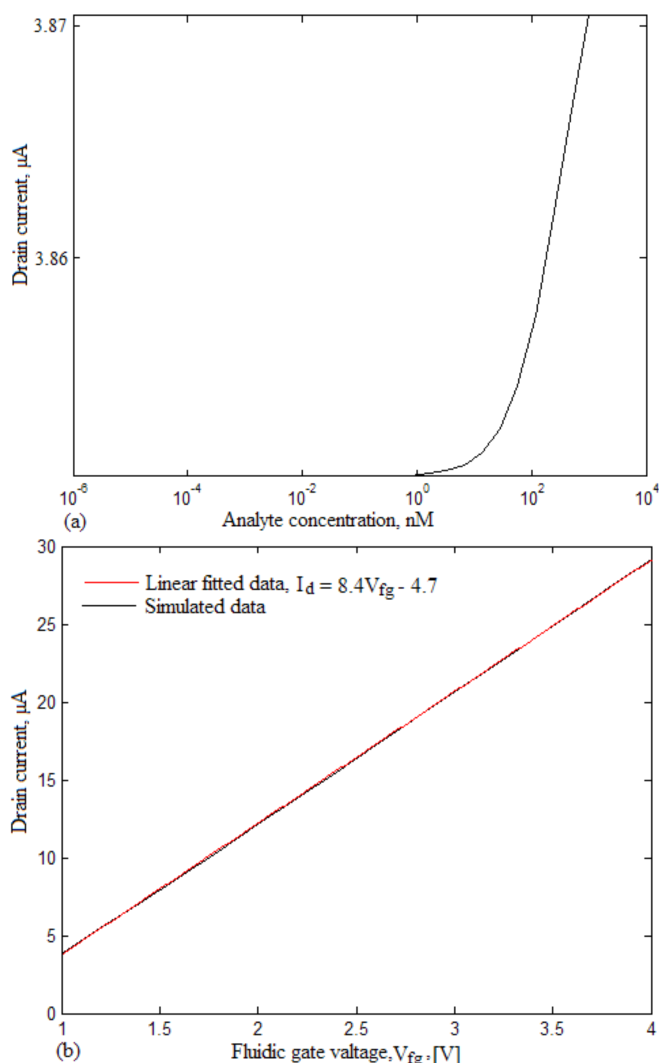

Figure 2. Sensor response with a constant supply voltage for different values of : (a) analyte concentration and (b) fluid gate voltage.

2) Influence of Buffer Ion Concentration: It is outlined that the drain current decreases with an increase in buffer ion concentration (Fig. 3). However, it is not linearly related to the ion concentration of buffer. It is noticed that the dependency of I_d is much enhanced by the amine group (-NH_2) compared to the hydroxyl group (-OH).

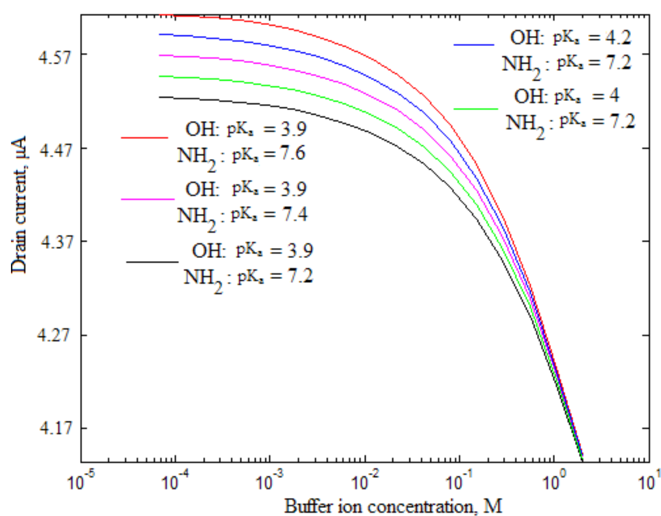

Figure 3. Variation of sensitivity with buffer ion concentration for different values of dissociation constants of the surface groups. $pK_a = -10\log_{10}(K_a)$, K_a is the dissociation constant of the particular functionalization groups.

3) Influence of pH of the solution: As shown in Fig. 4, the sensitivity (I_d) decreases with increase in pH of the solution which in not linear for the lower value of the density of surface group (black). However, it is almost linear for the higher values of the density of surface group (blue and red). The sensor has the same response at a particular value of pH (5.76) irrespective of the density of surface group.

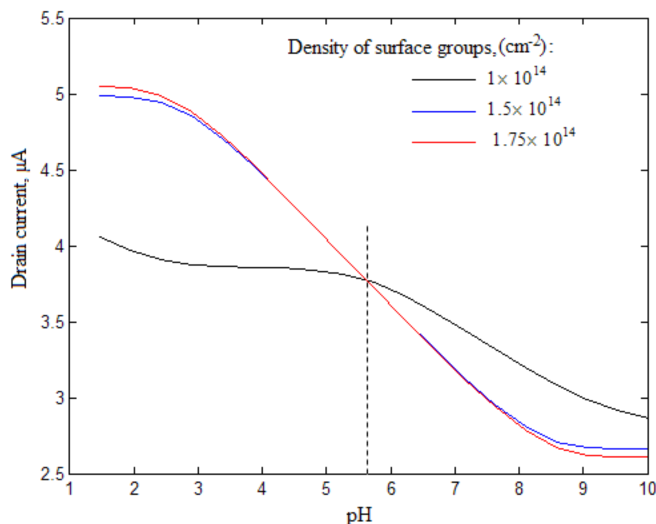

Figure 4. Graph illustrating the dependence of drain current on the pH of the solution and with different values of surface group density.

B. Signal to Noise Ratio

The SNR corresponds to how accurately the resonance angle can be detected in relation to the noise level of the sensing medium. Noise usually arises from the statistical fluctuations in the density of captured molecules, unspecific adsorption, ion concentration etc. To increase the SNR, it is important to consider the factors which affect the specificity and target molecule and accuracy of the detected signals.

1) Influence of Analyte Concentration, Size and Density of Receptor: Fig. 5 shows that the SNR can be improved by

increasing the receptor density and concentration of target molecules. After a certain value of receptor density, the SNR becomes independent on the concentration of the target molecules. In addition, it can be further improved by increasing the dimension of the receptor. However, it has an negligible effect on the SNR for lower values of receptor density.

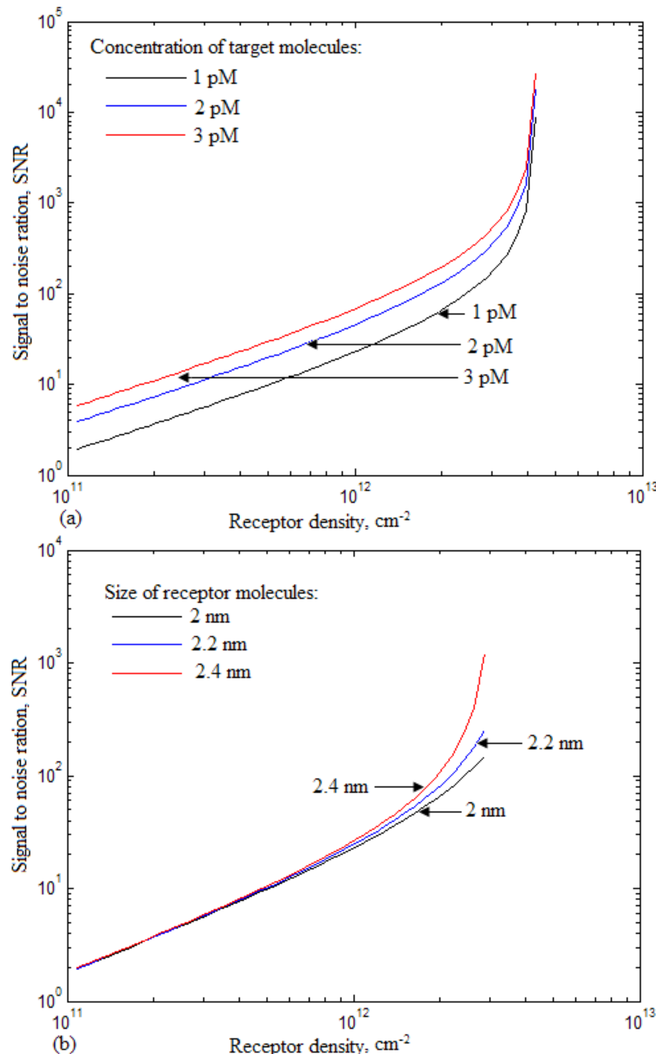

Figure 5. Graph illustrating the effect of the size and the density of receptor molecules, and the concentration of target molecules on signal to noise ratio:(a) SNR with receptor density and concentration of target molecules and (b) SNR with receptor density and size of receptor molecules.

V. CONCLUSION

This paper described the design of a DGFET biosensor with numerical simulation to predict the performance metrics for the DNA detection. The ssDNA was immobilized on to the sensor surface to specifically adsorb its complementary counterpart (cDNA) immersed in the buffer solution. It was demonstrated that the sensor response is significantly affected after a particular value of analyte concentration, pH value of the solution and buffer ion concentration. Additionally, the sensitivity is also greatly enhanced by the fluidic gate voltage. A linear relation is experimentally established between the fluidic gate voltage and the drain current. Apart from these, an improved SNR is obtained for higher value of receptor density and concentration of target analyte.

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