Transient State in the Affinity-Based Biosensor: A Simulation and Experimental Study

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Abstract—**We present a simulation and experimental study of a transient state of the system consisting of the electrolyte and the metal electrode including the electric double layer (EDL). The motivation of the study on the transient state is to remove the charge screening effect, thereby enhancing the sensitivity of the electrical biosensor. The Poisson equation and drift-diffusion equation are calculated on transient state. Both the de-ionized water (DIW) and phosphate buffered saline (PBS) buffer are considered as the electrolyte solution, yielding distinct results due to the difference of the ion concentrations. From the transient simulation and measurement after the step-pulse, the sensitivity enhancement can be achieved.**

Keywords-Biosensor; Electrical double layer; Transient state; Sensitivity

I. INTRODUCTION

In the affinity-based biosensors for label free electronic detection, the surface of the semiconductors (or gate oxide) are functionalized by the probe molecules, which are complementary to target molecules[1,2]. Because most biological processes involve electrostatic interactions, the probe-target bound molecules induce the modulation of the carrier density, thereby the conductivity, in the semiconductor channel.

However, there exists a space charge layer called the electric double layer (EDL) at the interface between the solution and the electrode, which screens the electrostatic field induced from the charged molecule over the Debye length[3]. General sensing environment involves the buffer solution, where the Debye length is ~1 nm in, while the size of biomolecule is several nanometers. In this case, large part of the charges from the biomolecules is screened and the sensitivity of the sensor is sacrificed.

In this study, we propose a new sensing method based on 'the transient state' measurement, where the electric current is measured after the step pulse voltage is applied across the electrodes, in our case, the source and drain. The mobility of the ions in electrolyte solution is quite lower than that of electrons and holes in semiconductor, thus the RC time constant of the sensor system, the time required reaching the steady state after disturbance, is large enough to perform the transient electrical measurements. After the step-pulse bias, the EDL is extended instantaneously, the screening counter-ions around the target molecule are swept away on transient state.

In order to verify the idea, we have simulated performed the transient simulation using the numerical simulators developed in-house. In addition, we report initial measurements results applied to the DNA sensor platform developed in our group[4].

II. GOVERNING EQUATION FOR SIMULATION

The electrical potential and charged carriers in the electrolyte solution are governed by the Poisson equation,

$$\nabla \cdot \varepsilon(-\nabla \psi) = q([n^+]-[n^-]), \tag{1}$$

where ε is the permittivity of electrolyte solution, ψ is the electrical potential, and $[n^+]$ and $[n^-]$ are the cation and anion in the electrolyte solution, respectively.

In the electrolyte solutions, ion carriers accelerate through the drift and diffusion similar to the transport of the electrons and holes in the semiconductor. Accordingly, the ion flux is represented by

$$F_{[n^\pm]} = \pm\mu_{n^\pm}[n^\pm]\nabla\psi - D_{n^\pm}\nabla[n^\pm], \tag{2}$$

where $\mu_{n\pm}$ and $D_{n\pm}$ are the mobility and the diffusion coefficient of cation and anion, respectively, in the electrolyte solution.

The continuity equation for ion carriers can be written as

$$\frac{\partial[n^\pm]}{\partial t} = -\nabla \cdot F_{[n^\pm]}. \tag{3}$$

In the steady state, the left term of Eq. (3) becomes zero, yielding the Boltzmann distribution for ions,

$$[n^\pm] = n_0 \exp(\mp\psi / V_t), \tag{1}$$

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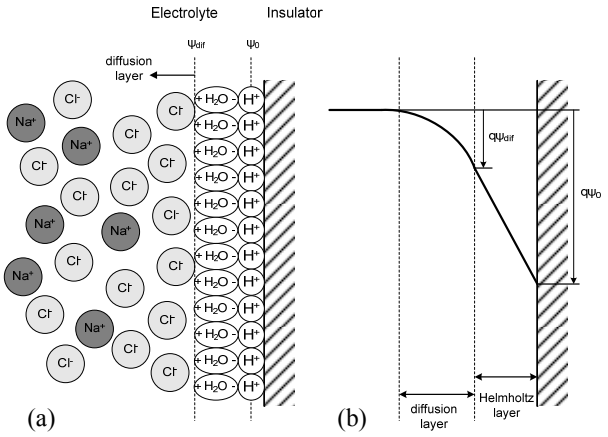


Figure 1. Schematic diagrams of (a) the EDL, and (b) the energy diagram across the EDL for the electrolyte containing Na^+ and Cl^- ions. EDL consists of two layers, the diffuse and Helmholtz layers.

where n_0 is bulk ion concentration of the electrolyte solution. The diffuse layer is derived from this distribution, suggested by Gouy and Chapman[5,6].

After Stern's modification[7] that considers the Helmholtz layer due to the minimum distance between the ions and the electrode surface, the EDL has been regarded as a series capacitance made up of the Helmholtz layer and diffuse layer, as shown in Figure 1.[8]

III. Simulation Results

The parameters and simulation conditions used in this work are summarized in Table 1. The electrical potential ψ_0 is applied to the electrode with respect to bulk solution, which is grounded by the reference electrode. Generally, the semiconductors are employed as the electrode in the affinity-based biosensors to detect the charge induced by charged molecules.

TABLE I. Values Used for Variables and Constants Used to Calculate the Theoretical Value.

Parameter	Value	Note
ε	78 * ε_0	aqueous solution in room temperature
μ_{H+}	33.3 * 10^{-4} cm^2/V-s	
μ_{OH-}	18.8 * 10^{-4} cm^2/V-s	
μ_{Na+}	5.9 * 10^{-4} cm^2/V-s	
μ_{Cl-}	7.0 * 10^{-4} cm^2/V-s	
$D_{n\pm}$	$\mu kT/q$	Einstein relation
n_0	10-7 M 0.1 M	in DIW in PBS buffer
d_H	5 Å	thickness of Helmholtz layer

Figure 2 shows the normalized potential profiles in the DIW and PBS buffer condition in the steady state. Theoretical values for the Debye length in DIW and PBS buffer are about 1 μm and 1 nm, respectively. In the PBS buffer, the Helmholtz layer which has 5 Å-thickness can be observed. As the bias voltage increases, the screening length becomes shorter because the counter ions accumulate on the electrode surface exponentially to the electrode potential.

A. Steady State

The electrode surface charge induced by charged molecules is calculated from $Q = -\int D \cdot ds$. Note that the induced charges simulate the conductivity modulation if the electrode is used as the semiconductor channel. The size of molecules is set to be 4

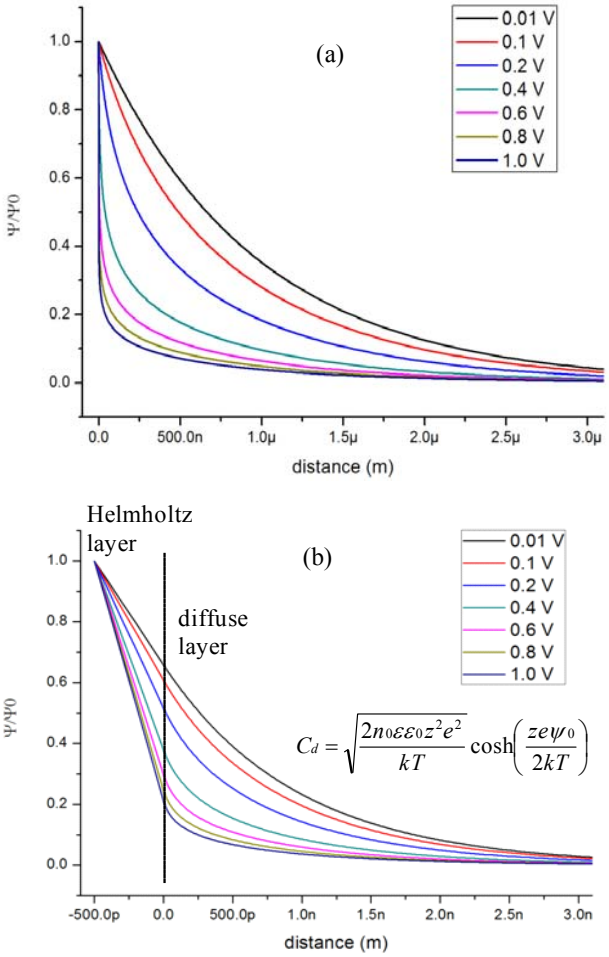
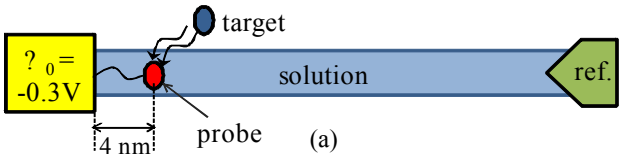
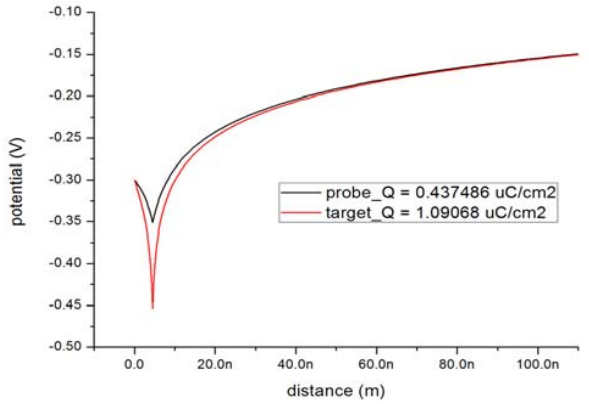


Figure 2. Normalized potential profile in (a) DIW condition and (b) buffer condition. The screening length in buffer solution is very shorter than that in DIW, because of the difference of ion concentration. The bias dependence of the screening length corresponds to diffusion capacitance.

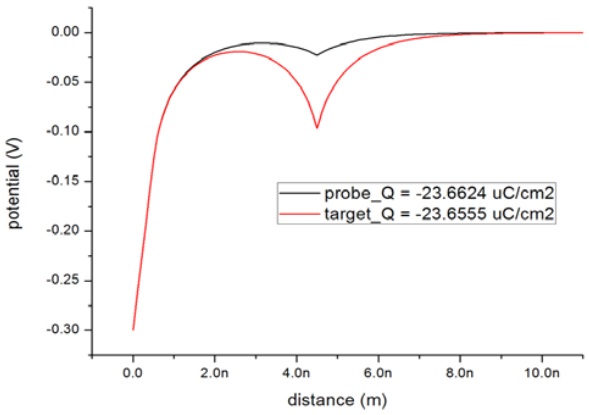
nm, and their charge density is considered as the sheet charge density. The sensor system detects the probe-target binding event by the difference of induced surface charge between before and after the event.

As shown in Figure 3(b), in the DIW condition, there is considerable variance of induced charge by the target binding because the screening length is quite longer than the size of the molecule. On the other hand, in PBS buffer condition as shown in Figure 3(c), the sensor cannot detect the target molecules due to relatively shorter screening length.





(b)



(c)

Figure 3. (a) Schematic diagram of the probe-target binding event in the affinity-based biosensor. Potential profiles in (b) DIW and (c) PBS buffer condition on steady state. The electrode bias voltage is set to -0.3 V and charged molecules are on the 4 nm from the interface. *Q* represents the induced charge on the electrode surface.

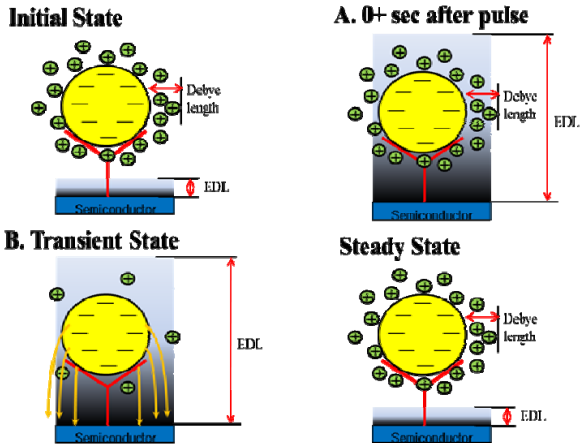


Figure 4. Conceptual scheme of affiinity-based biosensor after step pulse bias is applied between the semiconductor and the electrolyte.

Accordingly, in view of high sensitivity, the ionic solution with low ionic concentration is regarded as a better environment to detect the charged molecules.

B. Transient State

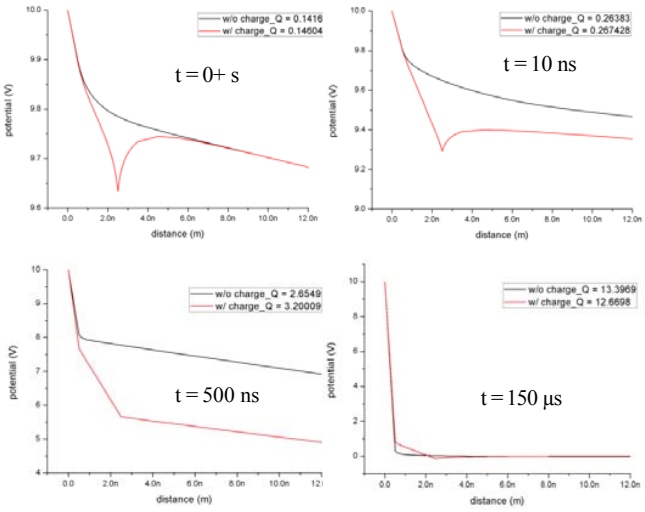
In figure 4, the sensitivity enhancement on transient state after step pulse bias is described. The counter-ions screening the charged target molecule in the initial state are swept away by high external electric field due to the extended EDL on transient state after pulse bias. At that moment, the charged molecule induces the image charge on the semiconductor surface.

Figure 5(a) demonstrates the potential profiles according to the time flow. At t = 0 sec, high bias voltage, 10 V, is applied to the electrode (distance = 0) in the PBS buffer condition. As discussed before, the high sensitivity cannot be achieved due to the short screening length for the case of the PBS buffer. However, high step pulse bias induces the electro-diffusion flow of mobile ions on transient state, so that the screening length is extended instantaneously. It may be noticed that after 500 ns from the pulse biasing, extended screening length makes the difference in the induced surface charge as shown in Figure 5(a).

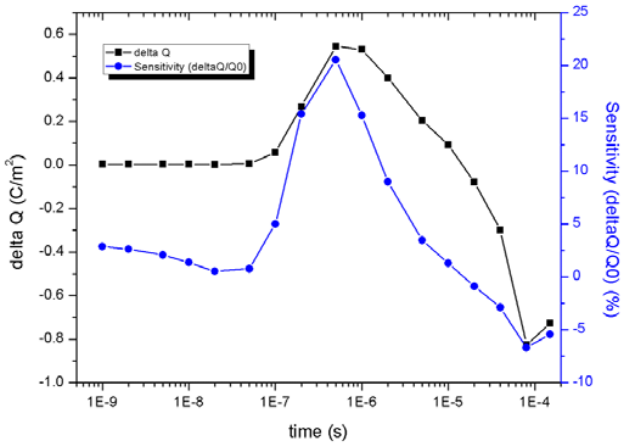
Figure 5(b) shows the change of the induced charge variation and the sensitivity with the time. As the screening length is extended, the sensitivity increased to reach the maximum, and decreases again as the system settles down at the steady state.

IV. TRANSIENT MEASUREMENT

We have applied the transient measurement scheme to the electrical DNA sensor consisting of CNT channel and concentric electrodes[4]. Comparing the transient responses of the channel conductivity between the cell before and after the DNA hybridization, the sensitivity of DNA sensor cells in the transient states can be plotted as shown in figure 6, where two



(a)



(b)

Figure 5. (a) Potential profiles at 0+ s, 10 ns, 500 ns and 150 µs. (b) Variance of induced surface charge and corresponding sensing ability with respect to time after step-pulse biasing in the buffer solution.

identically designed cells are measured. The sensitivity becomes maximum between 100 ns and 1 µs, which is similar to the simulation results shown in Figure 5. Although the simulation does not match with the experimental device structures, the agreement in the trend implies the justification of the transient method to mitigate the screening effect.

V. CONCLUSION

We have presented a numerical simulation for the response of the affinity-based electrical biosensor system to the step pulse voltage. From the simulation and experiments, we showed that the new sensing measurement scheme can mitigate the charge screening effect thereby achieve high sensitivity in the electrical biosensor.

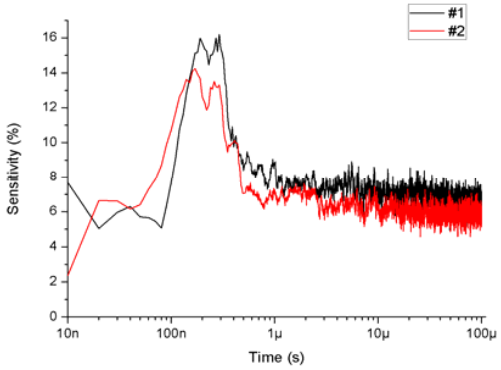


Figure 6. Measured sensitivity with respect to the time after step pulse bias in two identical sensor cells.

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