Simulation of Field-Effect Biosensors (BioFETs) for Biotin-Streptavidin Complexes

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Abstract. Biologically sensitive field-effect transistors (BioFETs) are a promising technology for detecting pathogens, antigen-antibody complexes, and tumor markers. A BioFET is studied for a biotin-streptavidin complex. Biotin-streptavidin is used in detection and purification of various biomolecules. The link between the Angstrom scale of the chemical reaction and the micrometer scale of the field effect device is realized by homogenized interface conditions.

Keywords: BioFET, field-effect biosensor, biotin-streptavidin, simulation, multi-scale problem, interface conditions.
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INTRODUCTION

Detection of pathogens, tumor markers, and antigen-antibody complexes is an expensive, time consuming, and complex task [1, 2]. A typical procedure for detecting a certain DNA strand consists of several steps: increasing the DNA concentration by PCR (polymerase chain reaction) or RT (reverse transcription), labeling of the molecule, and applying it to a microarray. Then the microarray is read out in an optical procedure with laser beams. Making optical detection superfluous by an electrical signal has several advantages. Using BioFETs also makes it possible to integrate additional circuits for amplifying and analyzing the signal on the same chip. Therefore BioFET microarrays save time, space, and equipment, enabling their use outdoors to control the spread of diseases and environmental pollution, without the need of an expensive lab [3].

The components of a BioFET are a semiconductor transducer, a dielectric layer, a functionalized surface with immobilized biomolecule receptors where the analyte binds, and an electrolyte with an electrode (Figure 1). When analyte molecules bind to the receptors, their charges change the potential near the transducer-surface and thus the conductance of the field-effect transistor channel. The change of the potential happens at the Angstrom length scale, while the device dimensions are on the micrometer length scale. Therefore it is essential to have an appropriate model to describe the transducer-solution interface.

SIMULATION METHOD

A homogenized interface model [4, 5, 6, 7, 8] is studied on a common nMOS device to show the generality of the modeling approach for biomolecular detection. For this simulation a biotin-streptavidin complex was chosen because of its use in purification and detection of various biomolecules. The strong streptavidin-biotin binding can also be used to attach various biomolecules to one another or onto a solid support. The charges of the biomolecules were modeled using a bottom-up approach [9], and the charge and dipole moment of a single molecule from the protein data bank [10] are calculated. These values are related to surface densities by choosing the mean distance between the molecules. The connection between the surface silicon oxide and the aqueous solution is realized by two homogenized interface conditions:

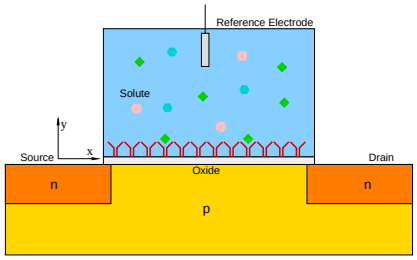

FIGURE 1. Schematic diagram of a BioFET.

$$\varepsilon_0\varepsilon_{Oxid}\,\partial_y\psi(0-,x)-\varepsilon_0\varepsilon_{Ana}\,\partial_y\psi(0+,x)=-C(x), \quad (1)$$

$$\psi(0-,x)-\psi(0+,x)=-\frac{D_y(x)}{\varepsilon_{Ana}\varepsilon_0}\,. \quad (2)$$

The x-axis of the device is parallel to the oxide, while the y-axis is pointing into the solute. $\psi(0-,x)$ describes the potential in the oxide, while $\psi(0+,x)$ is the potential

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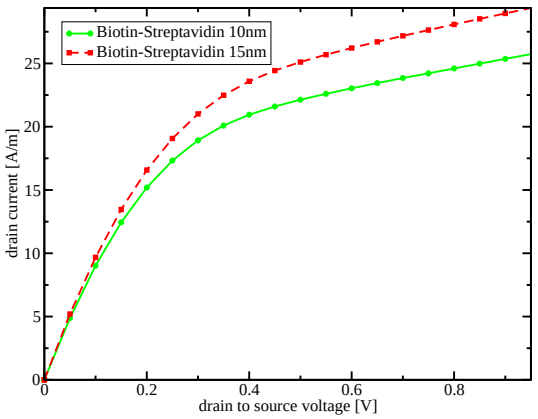

FIGURE 2. Output characteristics for bound state (biotin-streptavidin) at $\lambda = 10$nm and $\lambda = 15$nm.

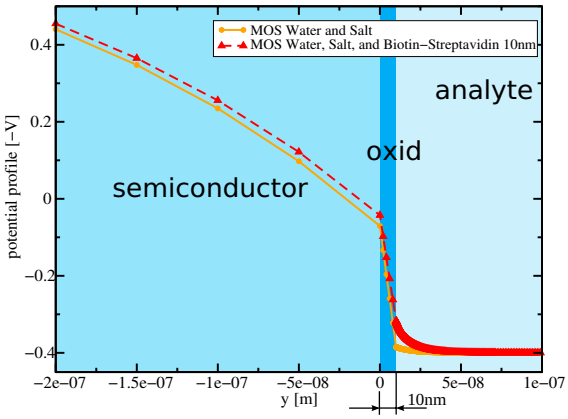

FIGURE 4. Potential profile at the interface (from left to right: semiconductor, oxide, solute).

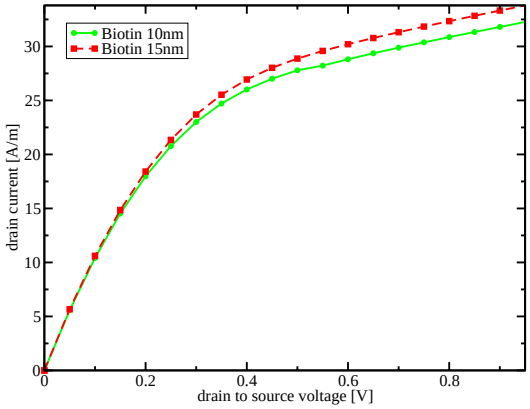

FIGURE 3. Output characteristics for prepared but unbound state (biotin only) at $\lambda = 10$nm and $\lambda = 15$nm.

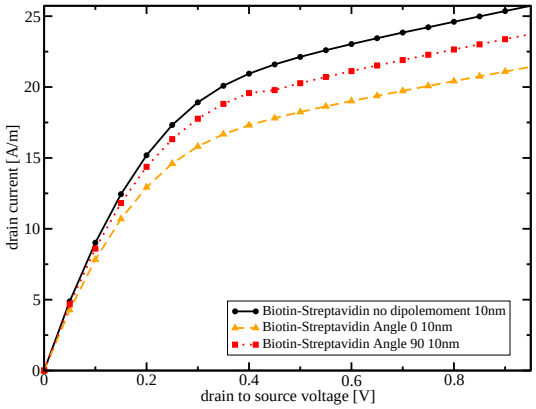

FIGURE 5. Output characteristics for bound state (biotin-streptavidin) at $\lambda = 10$nm including the effect of different molecule orientations.

in the solute. The first equation describes the jump in the field, while the second introduces a dipole moment causing a shift of the potential which is taken into account by adjusting the potential in the solute.

RESULTS AND DISCUSSION

The model shows a strong dependence on surface charges and indicates a relatively small shift in the threshold voltage depending on their orientation relative to the surface. The bound state (biotin-streptavidin), shown in Figure 2, is negatively charged with 5 elementary charges compared to the unbound state (biotin only), shown in Figure 3, which is negatively charged with 1 elementary charge. This leads to a reduced conductivity after binding. The shift of the potential profile (Figure 4) and the change in the output characteristics due to different molecule orientations (0 degrees - biotin is perpendicular to surface, 90 degrees - biotin parallel to surface), depicted in Figure 5, indicate that the orientation of the molecules can also be resolved.

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