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Computational Aspects of the Three-Dimensional Feature-Scale Simulation of Silicon-Nanowire Field-Effect Sesnsors for DNA Detection

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Computational aspects of the three-dimensional feature-scale simulation of silicon-nanowire field-effect sensors for DNA detection

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Abstract In recent years DNA-sensors, and generally biosensors, with semiconducting transducers were fabricated and characterized. Although the concept of so-called BioFETs was proposed already two decades ago, its realization has become feasible only recently due to advances in process technology. In this paper a comprehensive and rigorous approach to the simulation of silicon-nanowire DNAFETs at the feature-scale is presented. It allows to investigate the feasibility of single-molecule detectors and is used to elucidate the performance that can be expected from sensors with nanowire diameters in the deca-nanometer range. Finally the computational challenges for the simulation of silicon-nanowire DNA-sensors are discussed.

Keywords DNAFET · BioFET · Simulation · Silicon-nanowire

1 Introduction

The basic idea of the ISFET (ion-selective field-effect transistor) was already realized more than three decades ago. In an ISFET the gate structure of a MOSFET is replaced by an ion-selective layer, aqueous solution, and a references electrode [1, 2]. Hence ISFETs can measure the concentration of certain ion species in the solution and determine its pH value. Of course this concept is readily generalized to biosensors like EnFETs (enzyme FETs) ImmunoFETs, and DNAFETs (also called GenFETs) that contain layers of immobilized enzymes, antibodies, and DNA strands, respectively, instead of the ion-selective layer. All these devices can be classified as BioFETs (biologically sensitive FETs, cf. Fig. 1).

Recently experimental silicon-nanowire DNAFETs and BioFETs were manufactured and their functioning was verified [3, 4]. These devices consist of a silicon-nanowire core, an enveloping silicon-oxide layer, and surface receptor molecules. Experimental results can be attributed to a field-effect: when a ssDNA oligomer attaches to its complementary immobilized ssDNA counterpart, the local charge distribution changes and modulates the conductance of the nanowire. However, alternative mechanisms, e.g., leakage current through the functionalized layer, are conceivable [5]. This question will be addressed in the discussion of simulation results.

BioFETs are highly selective sensors since binding between two biomolecules (a protein and an antibody, for example) is equivalent to a biological function. Furthermore extremely high detection sensitivity in the pg/ml regime has been reported in the case of silicon-nanowire sensors [3]. Hence it can be expected that arrays of BioFETs will be able to sense a huge class of biomolecules. The main advantage of BioFETs is the label-free operation, as opposed to marking the analyte with fluorescent molecules. Further advantages are the real-time and continuous operation.

Because of these advantages the following application areas are notable. First sensors in the single-digit nanometer range can advance proteomics by measuring the expression of hundreds and thousands of protein in living cells. A healthcare application of utmost importance is the detection of minute concentrations of several cancer markers in parallel and in serum, if possible. It is well-known that reliable early diagnosis must rely on the measuring several indicators at the same time. It is conceivable that BioFETs will eventually be used in point-of-care applications. Arrays of DNAFETs enable

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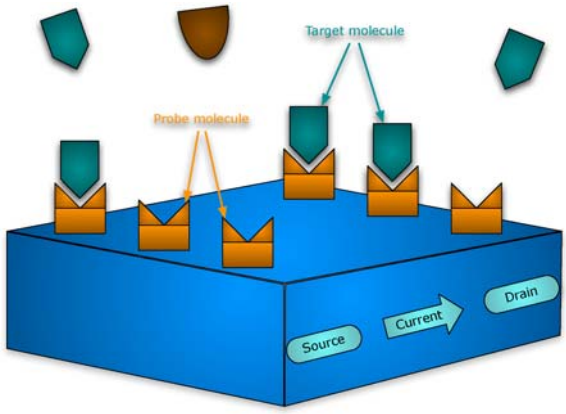

Fig. 1 This figure shows how BioFETs work in principle. The highly specific binding of target molecules to immobilized probe molecules on the oxide surface modulates charge transport through the semiconducting substrate

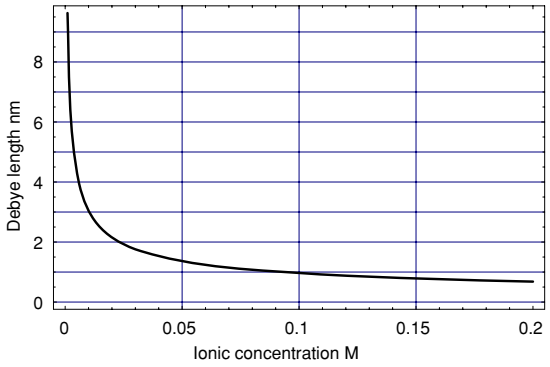

Fig. 2 Debye length as a function of Na^+Cl^- concentration. Physiologically relevant concentrations correspond to a 150 mM or 160 mM solution

the detection of single-nucleotide polymorphisms and thus of hereditary diseases.

The paper is organized as follows. After an explanation of the fundamental limiting factor of BioFET operations, we describe our three-dimensional feature-scale simulation method. The performance of a realistic silicon-nanowire DNAFET is then investigated and computational aspects are discussed using this example.

2 The fundamental limitation: the Debye length in saline solution

The fundamental problem of semiconducting transducers was realized early: the Debye length of the partial charges of the analyte is a function of the ionic concentration of the solution, and it decreases rapidly as the ionic concentration increases. At the salt concentration of blood or serum the Debye length is less than 1nm (cf. Fig. 2). This is the reason why experimental investigations have only become feasible in recent years as ultra-thin oxide layers can be manufactured. Furthermore the probe molecules must be attached as close as possible to the oxide surface. This can be realized nowadays after advances in the understanding of silicon-oxide surface and biomolecular chemistry.

Of course one could try to decrease the salt concentration in the analyte solution. This procedure however would make measurements more complicated and increase their cost. A more important reason why this is not desirable is the fact a certain salt concentration is necessary for DNA hybridization and the DNA hybridization energy in turn determines the sensitivity of the sensors.

Because of these conditions on BioFET operation a successful and predictive simulation method must necessarily model the electrostatics of the probe and target molecules and the solid-state sensor very carefully. Due to the small dimensions of the silicon-nanowires used in experiments (with diameters in the range of 20 nm down to 5 nm) quantum-mechanical charge transport effects are of great importance as well.

3 Simulation method

Generally there are three states of a sensor that should be simulated. In the first state no probe molecule is attached to the transducer, in the second state a functioning sensor is produced by immobilizing a probe molecule (ssDNA in the case of a DNAFET) on the transducer surface, and in the third state both a probe and a target molecule (dsDNA in the case of a DNAFET) are attached.

In our simulation method first the electrostatic potential due to the partial charges of the probe and target molecules is calculated with atomic precision. Given an arbitrary sequence of Watson-Crick base-pairs, we construct single- and double-stranded oligomers of B-DNA using the atomic coordinates of the nucleotides [6]. Then the partial charges of the oligomers are calculated using a GROMACS force-field [7]. In this work we assume an uncharged linker between the probe molecule and the silicon-oxide surface. The correctness of the DNA structure files was validated by comparison with a known structure (5′-D(CGTGAATTCACG)-3′, PDB-id 1D28 [8]).

Having determined the coordinates and partial charges of the molecules, the electrostatic potential is obtained by solving the three-dimensional Poisson-Boltzmannequation in the second step. The simulation domain includes the sensor and enough aqueous solution around the sensor so that the error due to the open boundary conditions is negligible. The Poisson-Boltzmann equation is a modified Poisson equation with additional exponential terms for each ion species. The exponential terms include the screening

of each ion species according to Boltzmann statistics. In the case of a 1:1 electrolyte, as e.g. Na^+Cl^-, the two exponential terms can be combined into a sinh term and the Poisson-Boltzmann equation reads

$$-\nabla \cdot (\varepsilon(x)\nabla u(x)) + \kappa(x)^2 \sinh u(x) = \frac{4\pi q^2}{kT} \sum_{k=1}^{N} z_i \delta(x - x_i). \quad (1)$$

Here $u(x) = q\varphi(x)/(kT)$ is the dimensionless unknown, $u(\infty) = 0$, $\varphi(x)$ is the potential, q is the elementary charge, $\varepsilon(x)$ gives the permittivities of the materials, $\kappa(x)$ includes the ionic strength of the solution and the accessibility of ions to the solute interior, N is the number of point charges present, and x_i and z_i are their positions and charges [9]. The mobile electrolyte charges are therefore included in a continuum approximation. After building the structure of the sensor, we use an adaptive finite-element solver to perform the numerical calculations [9].

Unless the pH value of the analyte solution equals the isoelectric point (pI) of the transducer surface, an electric double layer forms. Since $pI(SiO_2) \approx 2$, this effect is quite profound and must be included in simulations. At a pH value of 7, which we assume in the following, the surface potential is ≈ -0.165 V.

In the third and last step both the electrostatic potential arising from the molecules and the potential due to the electric surface layer are added to yield the boundary condition for the device simulation. For calculating the $I(V)$-characteristics we use a three-dimensional self-consistent ballistic effective-mass uncoupled mode-space NEGF (non-equilibrium Green function [10]) simulator [11].

4 Simulation of silicon-nanowire DNAFETs with varying diameters

Although silicon-nanowires with diameters of 100 nm were already grown more than 40 years ago [12], they received wider attention only recently due to difficulties in device assembly. In the following we investigate the influence of nanowire diameter on the performance of single-molecule DNAFETs whose structure is shown in Fig. 3. Arranging these sensors or similar structures in high-density arrays will enable the ultra-sensitive and label-free detection of single-nucleotide polymorphisms.

In the simulations the length of the undoped silicon-nanowire is 30 nm. The B-DNA-dodecamer CGTGAATTCACG was attached by a 2 nm uncharged linker to the 2 nm thick oxide. A pH value of 7 and an Na^+Cl^- concentration of 10 mM were assumed. The diameters of the silicon-nanowire were 10, 12, and 14 nm.

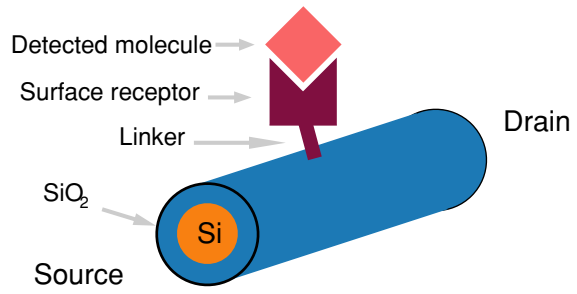

Fig. 3 The structure of a single-molecule silicon-nanowire

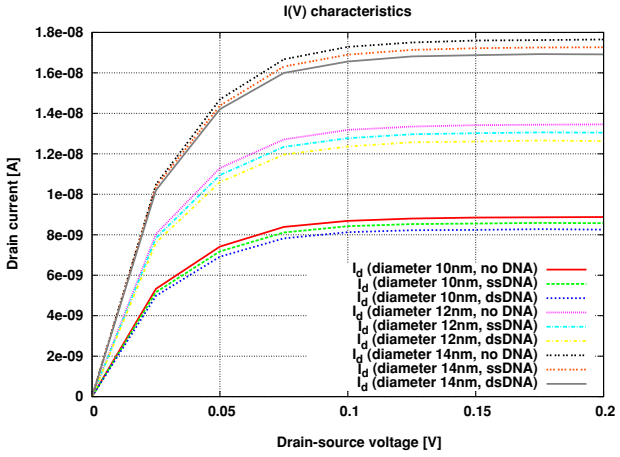

Fig. 4 The $I(V)$ characteristics of three sensors with different diameters: 10 nm (lower-most three curves), 12 nm (curves in the middle), and 14 nm (upper-most three curves)

10 nm wire, change from ssDNA to dsDNA	−3.57%
12 nm wire, change from ssDNA to dsDNA	−2.95%
14 nm wire, change from ssDNA to dsDNA	−1.77%

Fig. 5 This table summarizes the small-signal AC analysis of the three devices for low frequencies. The difference in conductance between the attachment of the probe strand and the attachment of the probe and target strands is shown

The current-voltage characteristics are shown in Fig. 4.For each of the three diameters, the characteristics imply that the differences in current between the three states allow to discern if a functional device was produced and if a target strand is attached to the probe strand.

More significant for practical applications is the small-signal AC analysis of the devices. Figure 5 shows the sensitivity for low frequencies as obtained by numeric differentiation from the current-voltage characteristics. As expected the results show that as the diameter increases, the sensitivity decreases. The conductance change is in the measurable range and the results indicate that even single-molecule detectors can be realized as field-effect devices.

5 Computational aspects

In the three-dimensional mode-space effective-mass NEGF charge transport calculations it is observed that the ratio of time spent in the Poisson and NEGF parts of the self-consistent loop is 1:10. If scattering is included using Büttiker probes, the ratio increases to 1:100. In the simulations a distance of 0.2 nm between slices was assumed. It is indispensable to solve the Schrödinger equation for each slice in parallel.

The silicon-nanowires used in experiments can have lengths in the micrometer range. Therefore scattering must be included, which makes the simulation of long nanowires extremely time consuming. Hence the major challenge for the simulation of nanowire devices using the NEGF approach is to devise fast algorithms for self-consistent simulations including scattering.

6 Conclusion

The conductance changes simulated using the presented method are in qualitative and quantitative agreement with published results [13]. Hence the feature-scale simulations show that the observed conductance change is indeed a field-effect. This conclusion provides the theoretical basis of BioFET simulation and enables us to engineer devices by simulation.

The simulation results also show the theoretical possibility of single-molecule detectors. The main remaining manufacturing problems are the close placement of ohmic contacts on the nanowire and the functionalization of a single surface sensor site.

Readers can run simulations of various DNAFET structures online at http://www.nanohub.org.

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