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PSPICE Simulation Model for Biomolecule Detection with Silicon Nanowire Biosensors in both Potentiometric and Impedimetric Readout Mode

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Abstract

In this work we present a PSPICE behavioral model to interpret pH sensing and biotin-streptavidin binding experiments in both potentiometric and impedimetric readout mode using top-down fabricated silicon nanowire sensors. The model is based on the electrical level 7 PMOS SPICE model combined with the well-known site-binding model to explain qualitatively the pH responses and changes in the liquid-solid interface of the sensor upon biomolecule binding with a previously described ion-permeable membrane model. Our model should aid data interpretation and extract relevant biosensor parameters out of the respective recordings.

1. Introduction

Silicon nanowires (SiNW) are a promising transducer for label-free detection of various biomolecules [1][2]. The most commonly used readout principle is based on a potentiometric approach of either monitoring the wire's conductance or monitoring the respective threshold voltage shifts upon binding of charged molecules to the SiNW surface. Normally, the recording signal will suffer from sensor drift, temperature drift, differences in ionic composition of the electrolyte solution, reference electrode position, and Debye screening effect. The impedance method is on the other hand based on the measurement of the impedance of the whole system, which can serve as an alternative technique to work around the drawbacks of the potentiometric method in biomolecular applications [3].

In pH sensing experiments the site-binding theory is the commonly accepted model to describe the interaction of protons from the solution with the commonly used dielectric surface of the field-effect transistor (FET) devices [4]. A theoretical model for FET-based sensors to detect charged molecules was previously presented as a planar ion-permeable membrane expressed in a first approach by a linearized Poisson-Boltzmann equation [5]. Another approach is to simulate ISFET-based biosensors by the electronic circuit simulation program SPICE [6]. To the author's best knowledge, so far there are only a few publications available for simulating SiNW-based biosensors for example in Verilog A by Paolo et al. [7] and in SPICE by authors in the past [8]. In these works a simple MOSFET model was employed to simulate the behavior of the SiNW-sensors, which can be regarded as long-channel FETs. Our SiNW sensors were fabricated on silicon-on-insulator (SOI) wafers combining nanoimprint lithography and wet anisotropic etching in a top-down approach. The simple SPICE model is in some cases sufficient to investigate parasitic parameters of the sensors or to model pH sensing, however, it normally leads to high errors in the FET characteristics due to poor parameter fittings. Moreover, to our knowledge there is no publication about a SPICE model for biomolecule detection with SiNW devices in impedimetric readout mode available.

In this work, we present a PSPICE simulation model for SiNW sensors in both potentiometric and impedimetric detection mode for pH- and biomolecules sensing. A PMOS level 7, which is mainly based on physical parameters, was used to model the characteristics of the devices. We employed the site-binding theory to explain the experiments in terms of pH sensing and the planar ion-permeable membrane theory to interpret the experiments for biotin-streptavidin detection.

2. Experimental setup and results

SiNW chips

The SiNW chips (28×2 arrays) used in this work were fabricated by a processes that combined nanoimprint lithography and tetra methyl ammonium hydroxide (TMAH) etching, which was explained in earlier works [9][10]. The advantage of this approach is to achieve wafer-scale, high-density SiNW array sensors with high sensitivity and chip-to-chip reproducibility. We employed two kinds wire dimension of 200 nm width and 10 or 20 µm length, respectively (mask measures)

Readout devices

The amplifier system utilized in this work is a new version of the readout device, that was formerly described [8]. The current version is a multifunctional solution, which is adaptable to different kinds of FET devices with current ranges from 100 nA up to 1 mA. It allows to read out the devices in both potentiometric (*dc*) and impedimetric (*ac*) modes for up to 32-channel FET arrays.

PSPICE simulation model

The simulation model was divided into two parts: basic pmos transistor model and the site-binding theory-based model for pH sensing [4] or/and the ion-permeable membrane model for biomolecule sensing [5]. We employed the PSPICE level 7 to simulate characterization measurements

of the devices and achieved good agreement with our experimental results (Fig. 1).

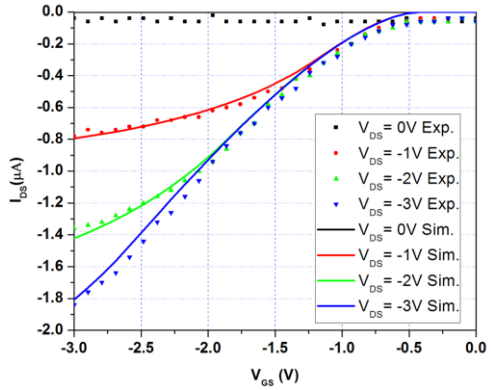

Fig. 1 Characterization measurement and corresponding simulation results

Biotin-streptavidin impedance measurement

Fig. 2 shows the surface modification protocol to implement the biotin-streptavidin experiments. At first, the SiNW sensor was cleaned and activated by Piranha acid to obtain a high density of hydroxyl groups on the silicon dioxide surface. Then the chip was kept under a mild vacuum condition (0.6 mPa) followed by evaporation of (3-Aminopropyl)triethoxysilane (APTES) at 70°C for two hours to form a thin amino silane layer on the SiNW surfaces.

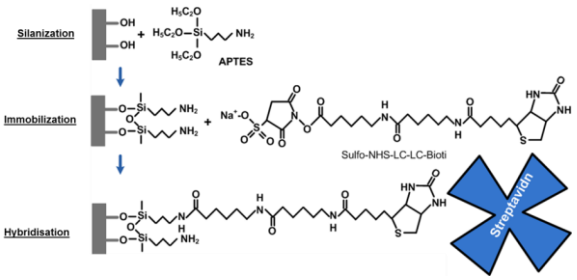

Fig. 2 Surface modification protocol for the biotin-streptavidin experiments

These amino groups can covalently bind to a linker molecule (Sulfo-NHS-LC-LC-Biotin (Thermo Fisher Scientific Inc.)) during the immobilization process. For detection of streptavidin proteins (Sigma-Aldrich Co. LLC.) it is then binding to biotin. Streptavidin is a protein with an isoelectric point (pI) of 6.4-7 and charges are unevenly distributed over the entire molecule. After each step of silanization, biotinylation and streptavidin binding we measured the impedance of the whole system from reference electrode via the wires to the first amplification stage. The experimental result shows that the impedance spectrum can distinguish each described steps (Fig. 3). After biotinylation, the resonant point in the impedance spectra increases, while after streptavidin binding this point decreases.

3. Conclusions

We presented a PSPICE simulation model that can better simulate characteristic measurement of SiNW that fabricated on SOI wafer.

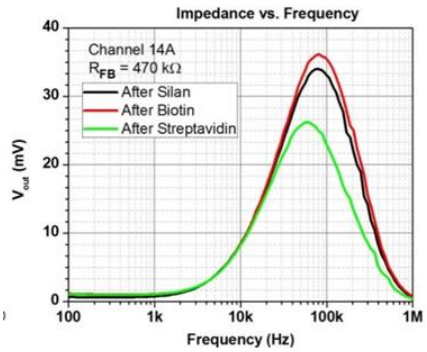

Fig. 3 Detection of biomolecules by the impedimetric readout method (with 0.001× PBS solution at pH 7.5).

The pmos model was then combined with the site-binding model presenting the oxide/liquid interface to simulate pH sensing with an ion-permeable membrane model describing biomolecule binding. The simulation results showed a good agreement with the experimental data in all cases.

Acknowledgements

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