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Three-dimensional Simulation of DNA Sensing by Ion-Sensitive Field-Effect Transistor: Optimization of DNA Position and Orientation

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1. Introduction

Label-free electrical DNA sensor element using ion-sensitive field-effect transistors (ISFETs) has gained increasing attention recently. ISFET is used to read out the flatband voltage shift, ΔV_{FB}, due to the inherent DNA charges from the phosphate ions. The analysis by a simulation is useful in predicting the experimental results, and improvement of the sensing characteristic. Although some simulation studies of DNA detection using ISFET have been reported [1-3], the influence on ΔV_{FB} due to DNA position and orientation has not been taken into consideration. A three-dimensional (3D) simulation has also been reported [4], but it analyzes ordered position and upright orientation only. In this work, 3D numerical analysis of DNA arrangements with various position and orientation is persented, and then condition for the improvement in the sensing characteristic is presented.

2. Simulation Model

ISFET is a semiconductor device similar to metal-oxide-semiconductor field-effect transistor (MOSFET) with its gate replaced by electrolyte. In this simulation, the space which consists of electrolyte, DNAs, stern layer, linker molecules, and insulator is applied to the model shown in Fig. 1. At the insulator/semiconductor interface, zero electric field is imposed to simulate the flatband condition, the potential there is regarded as flatband potential (ψ_{FB}) which is read out to evaluate flatband potential shift ($\Delta\psi_{FB}$) caused by DNA immobilization and hybridization. Mirror boundary condition at the side walls is imposed to make the state where many DNAs stand on an infinite plane. DNAs are immobilized through the linker molecules which form self-assembled monolayer (SAM), so the monolayer through which ion in electrolyte can't pass is applied to the model. Since the center of the ion in electrolyte can't approach the SAM surface less than 4nm due to aggregate of water molecules around ion, the 0.4nm stern layer without any charges is applied to the model [4]. DNA is modeled as a cylindrical insulator which has a stern layer in the surroundings. Equalizing charge distribution of DNA within the cylinder for simplification, it is presupposed that double-strand (ds) DNA has a twice as many negative charge as single-strand (ss) DNA. DNA density is determined by cubical side length of ISFET model and DNA number.

3. Simulation Method

ISFET applies the principle of MOSFET operation and reads out the threshold voltage shift (ΔV_{TH}) due to the charge of insulator interface (Fig. 2). Since the ΔV_{TH} in ISFET is almost equal to ΔV_{FB}, ΔV_{FB} due to the immobilization and hybridization of DNA is calculated in this work. ΔV_{FB} is simply given by $\Delta V_{FB} = -\Delta\psi_{FB}$. Poisson's equation is solved using finite element method for the model shown in Fig. 1. This simulation is performed on the condition that nine DNAs of 17 bases exist in the plane whose side length is 60nm, namely DNA density is $0.25\times10^{12}\mathrm{cm}^{-2}$. The salt concentration of electrolyte is 1.0mM.

4. Results & Discussions

In an experiment, DNA position and orientation are considered to be random. Fig. 3 shows cumulative probability of ΔV_{FB} by immobilization and hybridization from 100 samples of a unit cell containing nine DNAs with totally random position and orientation. Since ΔV_{FB} changes a lot with DNA density [4], if the DNA density in an experiment is not known, it is difficult to make simulation data correspond with experimental data. Fig. 4 shows influence on ΔV_{FB} due to DNA position. Flatband potential shift of the model (a) which has uplight DNAs arranged equally, (b) arranged at random, and (c) arranged densely is calculated about each of ssDNA and dsDNA, and ΔV_{FB} due to hybridization is calculated. (b) is calculated 100 samples. Flatband voltage shift becomes the largest when upright DNAs are arranged equally, and ΔV_{FB} becomes the smallest when DNAs is arranged densely. Fig. 5 shows influence on ΔV_{FB} due to DNA orientation. The ΔV_{FB} increases as DNA becomes nearly parallel to the insulator interface. Fig. 6 shows ΔV_{FB} due to hybridization of the model (a) which has DNAs tilted 90 degrees and arranged equally, (b) arranged at random, and (c) arranged densely. (b) is calculated 100 samples. From these results, ΔV_{FB} due to hybridization becomes the largest by tilting all DNAs 90 degrees, and arranging them equally.

5. Conclusion

Full 3D simulation of DNA detection by ISFET provides consideration of DNA position and orientation, and be useful to optimize experimental conditions. For prediction of an experiment, although ΔV_{FB} is sharply changed by the difference in DNA density [4], rough prediction is possible.

References

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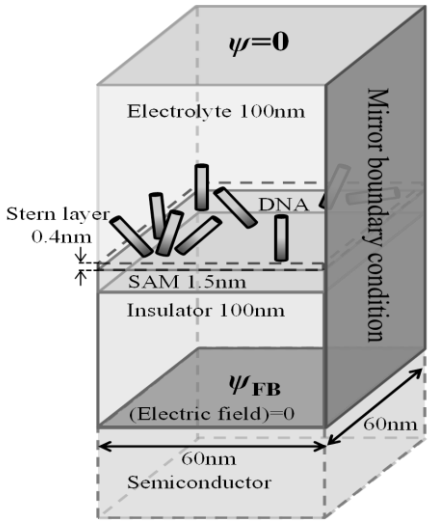

Fig. 1 Schematic illustration of ion-sensitive field-effect transistor (ISFET) model.

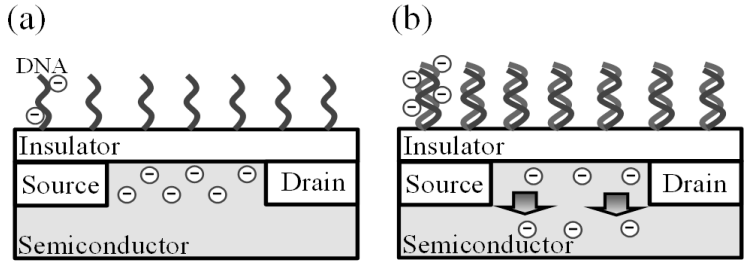

Fig. 2 Principle of DNA detection by ISFET.
(a) Immobilization
(b) Hybridization
ISFET applies the principle of operation of metal-oxide-semiconductor field-effect transistor (MOSFET). Negative charges of DNAs change the electrostatic potential at insulator interface, and it causes flatband voltage shift (ΔV_{FB}).

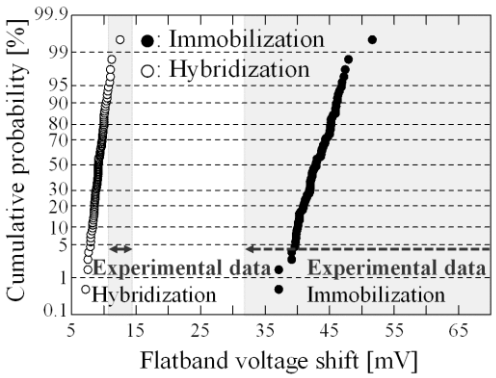

Fig. 3 Flatband voltage shift due to DNA whose position and orientation are random.
In experiment, threshold voltage shift is 32~100mV at Immobilization, 11~14mV at Hybridization [5-7].

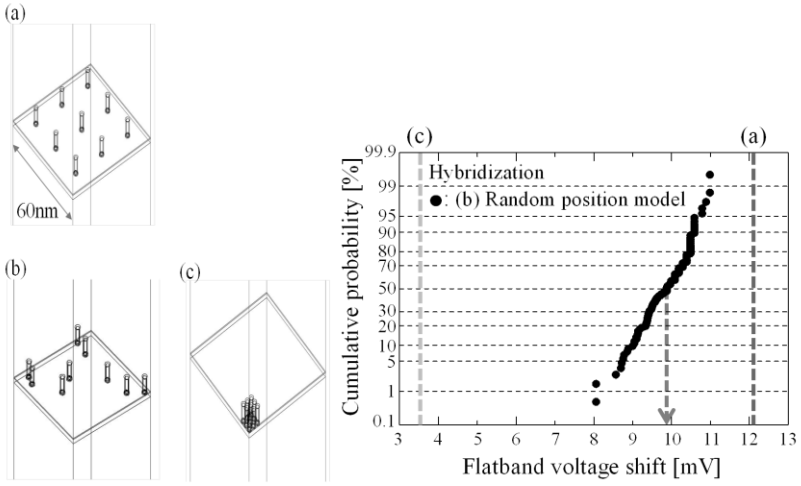

Fig. 4 Influence on flatband voltage shift due to position of upright DNA.
(a) Ordered position model (ΔV_{FB} = 12.1mV), (b) Random position model (median ΔV_{FB} = 9.89mV), (c) Dense position model (ΔV_{FB} = 3.53mV).

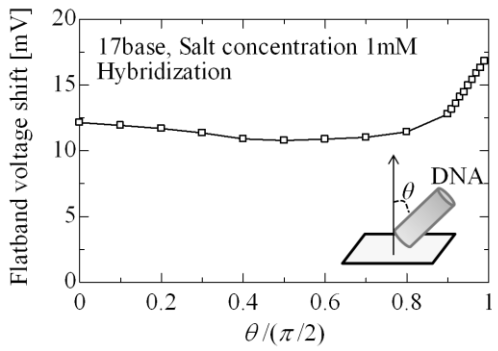

Fig. 5 Influence on flatband voltage shift due to DNA orientation angle θ.

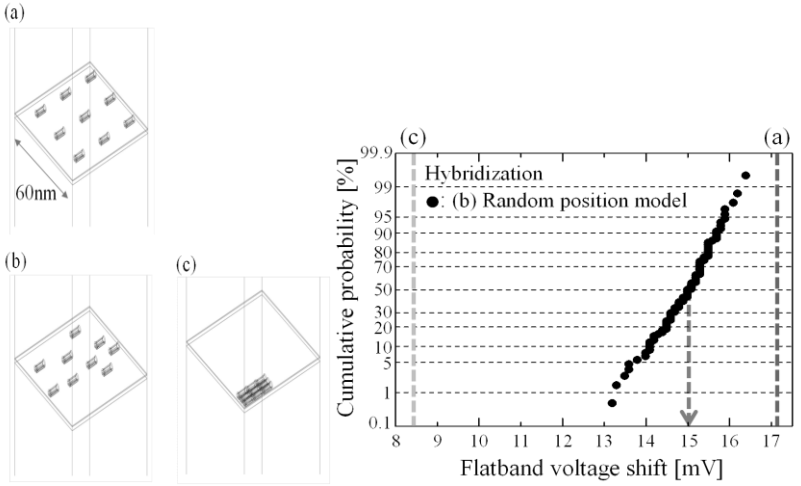

Fig. 6 Influence on flatband voltage shift due to position of DNA tilted 90 degrees.
(a) Ordered position model (ΔV_{FB} = 17.1mV), (b) Random position model (median ΔV_{FB} = 15.0mV), (c) Dense position model (ΔV_{FB} = 8.41mV).