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DNA Aptamer-Based Biosensing of Immunoglobulin E Using Carbon Nanotube Field-Effect Transistors

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1. Introduction

Carbon nanotube field-effect transistors (CNTFETs) are promising candidates for the high-sensitive label-free biosensors due to their excellent electrical transport properties. However, conventional FET biosensors based on antigen-antibody reactions, using antibodies as probes, have an inevitable problem on the size of probes. Since the size of antibodies is larger than that of the Debye length in buffer solutions as shown in Fig. 1(a), most of the protein charges can be canceled in buffer solutions. As a result, proteins can not be detected easily with such FET biosensors.

In this paper, we have detected Immunoglobulin E (IgE) with CNTFETs, in which aptamers are used as probes. Aptamers are artificial oligonucleotides that have the ability to recognize specific ligands by forming binding pockets. The aptamers are smaller in size than the Debye length, as shown in Fig. 1(b). They have also demonstrated stronger and more selective affinity for their target proteins than the corresponding antibodies. Recently, various aptamers, which can bind to nucleic acids, proteins or small organic compounds, have been found. IgE is the type of antibody and most instrumental in allergic reactions. Hence, detection of IgE is very important in terms of immunology. Moreover, IgE is contained only low amount in human blood. Therefore, high-sensitive detection is required in medical scene.

2. Experimental

CNTFETs have been fabricated on a Si substrate, as shown in Fig. 2. A schematic cross section of the CNTFET used for biosensing is also shown in Fig. 3. CNTs were synthesized with alcohol chemical vapor deposition method, and were employed as channels in CNTFETs. First, the side-walls of CNT channels were modified with linkers (1-pyrenebutanoic acid succinimidyl ester). Next, the 5'- amino modified aptamers were covalently immobilized on the CNTs. Then, unreacted linkers were blocked by ethanolamine. Figure 4 shows a schematic diagram for the electrical detection system. The aptamer-modified channels in the CNTFETs were incubated into 10 mM phosphate buffer solutions (PBS). A reference electrode (Ag/AgCl) was used as a gate electrode.

3. Results and Discussion

The electrical properties of the CNTFETs were measured in real time at room temperature. Before modification of linkers, the fabricated samples still showed *p*-type characteristics in 10 mM buffer solutions as shown in Fig. 5. Figures 6(a) and 6(b) show the drain current-drain bias characteristics of the CNTFET at the gate bias of 0 V before and after modification of IgE aptamers on the CNT channel, respectively. The current increased at the source-drain bias of 0.2 V after the IgE-aptamer modification. The increase in conductance for the p-type CNTFET devices comes from an increase in negative charge density on the CNT channel. This result is consistent with the fact that aptamers are negatively charged oligonucleotides. Therefore, the result indicates that IgE aptamers were successfully modified on CNT channels. Spontaneously, it is confirmed that no current to a reference electrode were measured, as shown in Fig. 6(c).

Then the different concentrated IgE solutions were introduced into the samples, and the electrical properties were measured in real time. Figure 7 shows the time dependence of source-drain current at source-drain voltage of 0.2 V, source-gate voltage of 0 V. In the figure, arrows show the point of adding IgE solutions, and the concentrations of IgE after adding are by turns 0.25, 2.2, 18.5, and 159 nM. After introduction of IgE, source-drain current sharply decreased, and gradually saturated at lower values. This indicates that the changes in conductance of CNTs after aptamer-IgE binding on channel were detected by CNTFETs. Therefore, IgE at 0.25 nM could be detected by CNTFETs.

4. Conclusions

High-sensitive and real-time IgE detection has been performed using CNTFETs modified with aptamers. For 45-mer DNA aptamer probe, IgE with concentration as low as 0.25 nM solution could be effectively detected. Our aptamer-based CNTFETs are promising for future generations of biosensors which are compact and realize easily real-time detection in medical, forensic and environmental diagnostics.

Acknowledgments

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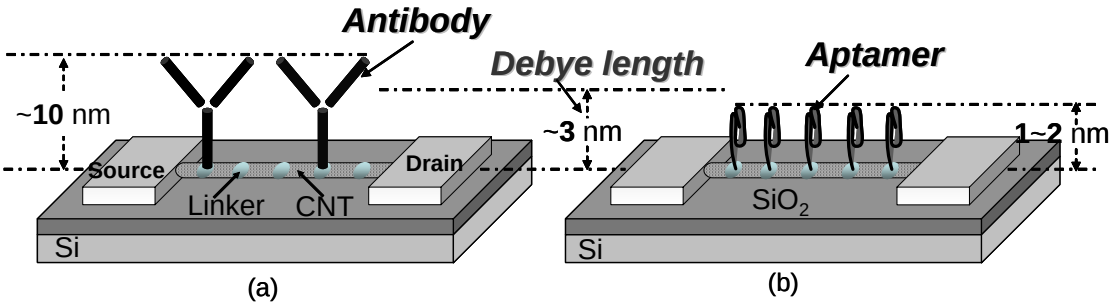

Fig. 1. Schematic structure of protein biosensors based on CNTFETs;
(a) an antibody-modified CNTFET, and (b) an aptamer-modified CNTFET.

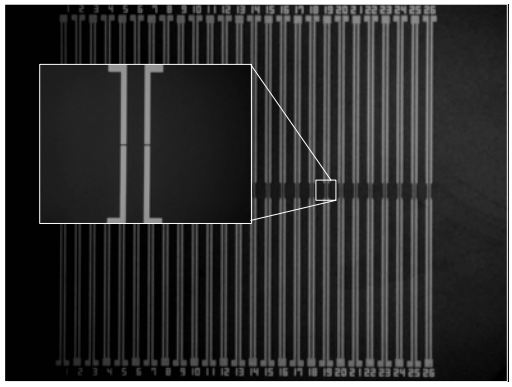

Fig. 2. Photo micrographs of the CNTFETs on a Si substrate.

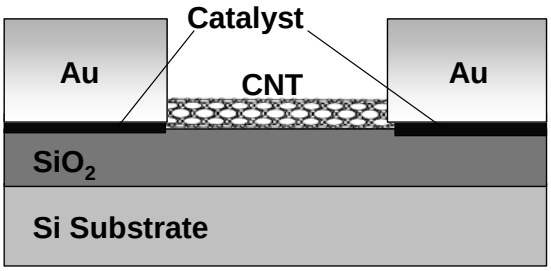

Fig. 3. Schematic cross section of the CNTFET.

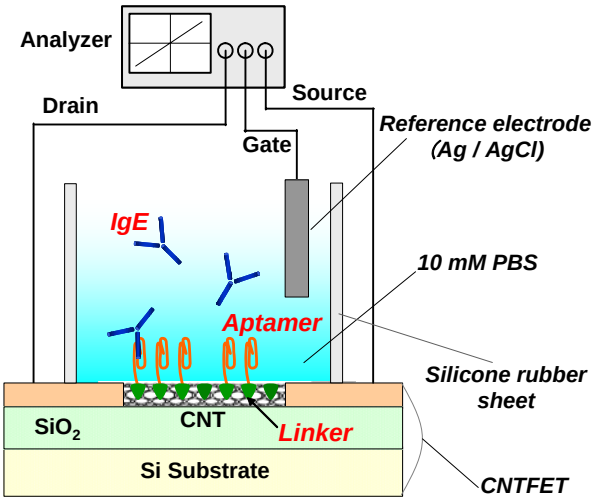

Fig. 4. Schematic structure of experimental setup for detection of IgE using an aptamer-modified CNTFET.

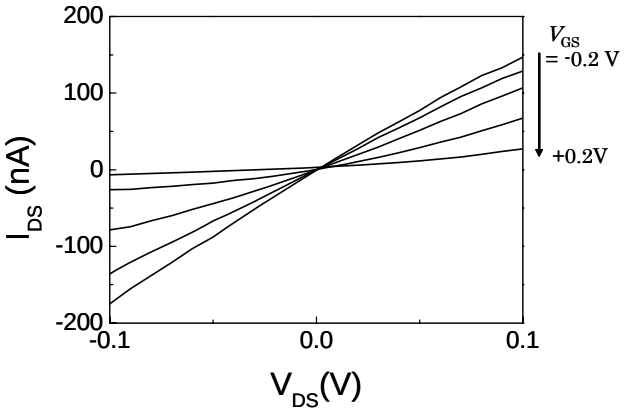

Fig. 5. Drain current-drain bias characteristics of the CNTFET in PBS solution.

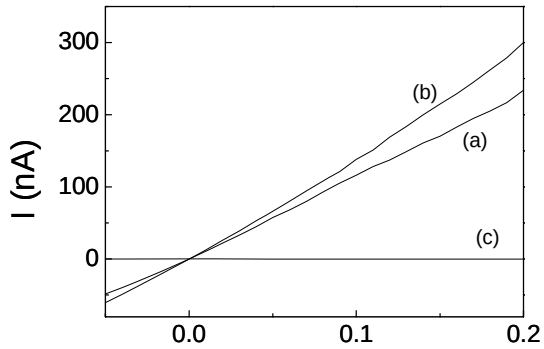

Fig. 6. Drain current-drain bias characteristics of the CNTFET in PBS at the gate bias of 0 V (a) before and (b) after modification of IgE aptamers on the CNT channel. The current (c) to a reference electrode are also shown.

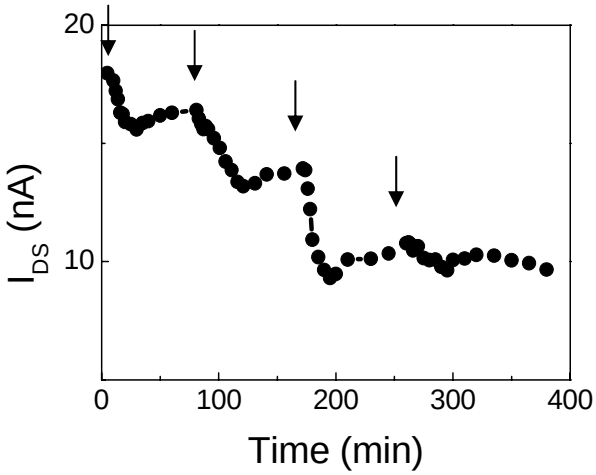

Fig. 7. Time dependence of source-drain current of the CNTFET at the source-drain bias of 0.2 V and at the gate bias of 0 V after the introduction of target IgE at various concentrations onto the IgE aptamer-modified CNTFET. Arrows indicate the point of adding IgE solutions.