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HIGH-PERFORMANCE CARBON NANOTUBE FIELD-EFFECT TRANSISTORS FOR HIGH-SENSITIVE BIOSENSORS

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ABSTRACT
Carbon nanotube field-effect transistors (CNTFETs) with local electrolyte gated in solution provided high performance in terms of subthreshold slope and transconductance, resulting from the modulation of the conduction in the carbon nanotube channel and the large gate capacitance. Using the CNTFETs, label-free protein biosensors have been fabricated to detect immunoglobulin E (IgE), in which CNT channels were modified with aptamers. Since aptamers are artificial oligonucleotides, the aptamers are smaller in size than the Debye length. Therefore, the biosensors are expected to detect IgE with high sensitivity. After the 5'- amino modified aptamers were covalently immobilized on the CNT channels, the electrical properties of the CNTFETs were monitored in real time. The introduction of target IgE at various concentrations caused a sharp decrease in the source-drain current and gradual saturation at lower values. From electrical measurements in IgE concentration dependent, the association constant between IgE molecules and IgE aptamer could be calucated to be 5.14×10^8 (M^{-1}) using the Langmuir adsorption isotherm.

KEY WORDS
carbon nanotube field-effect transistors, local electrolyte gate, channel conductance modulation, label-free protein biosensors, aptamers, association constant

1. Introduction

Label-free electrical monitoring of biorecognition events provides a promising platform, which is simpler, less expensive and requires less energy. Rapid testing of different proteins is also required in various applications, including clinical diagnostics, environmental testing, food analysis, bioterrorism detection technologies, etc [1].

Carbon nanotubes (CNTs) are one of the most attractive materials in terms of both fundamental science and technology due to their unique characters [2]. CNTs are quasi-one-dimensional conductors or semiconductors with reduced carrier scattering rates [3], high current densities, and high carrier mobilities [4]. Hence, SWNTs are also promising materials for building nanoscale electronic devices and microelectrodes [5-11]. In particular, carbon nanotube field-effect transistors (CNTFETs) are promising candidates for high-sensitive label-free biosensors due to their unique geometries with high surface-to-volume ratio. The detection of biomolecules such as proteins has been successfully performed using CNTFETs [12-16].

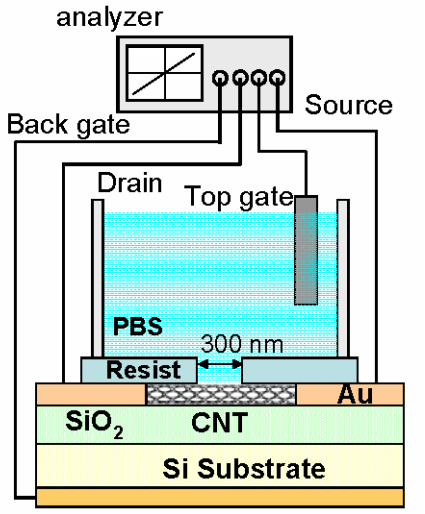
In this study, we have fabricated localelectrolyte-gated CNTFETs, in which switching occurs by the modulation of the SWNT channel conductance. In a CNTFET, a narrow groove on the SWNT channel, which is made of resist, acts as a local electrolyte gate in the solution. Since the electrolyte solution functions as a very thin and high-κ insulator [17, 18], a local-top-gate voltage is effectively applied to the CNTFET through the groove in the solution. Moreover, using the CNTFETs, label-free protein biosensors have been fabricated to detect immunoglobulin E (IgE), in which CNT channels were modified with aptamers.

2. Carbon nanotube field-effect transisitors

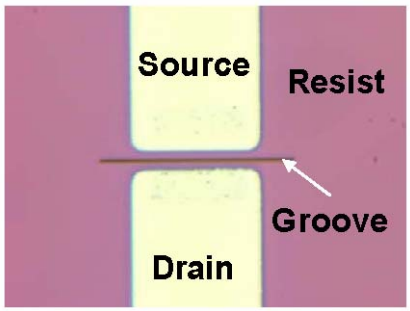
The CNTFET devices were fabricated using positioncontrolled growth process. CNTs were synthesized by the ethanol CVD method using a patterned Co chemical catalyst [19], which was formed by conventional photolithography and liftoff process technology, on heavily doped p^+-Si substrates capped with 150-nm-thick SiO_2, which was used as a back gate. The spacing between the source and drain electrodes was about 3 μm. Source and drain contacts (Ti/Pd) were formed on the patterned chemical catalyst after the growth of the CNTs [20, 21]. After the devices were covered by 300-nm-thick waterproof resist (ZEP520A), a 300-nm-wide groove was formed on the center of the SWNT channel by electronbeam lithography. This groove leads to the formation of a local electrolyte gate in the solution.

The schematic structure of the experimental setup of a local-electrolyte-gated CNTFET is shown in Fig. 1(a). The optical plan view image of a CNTFET with groove is also shown in Fig. 1(b). The CNTFETs were incubated in 10 mM phosphate buffer solution (PBS). A saturated calomel reference electrode (BAS Inc.) was used as the top-gate electrode to minimize the effects of the environment [22]. The electrical properties of the local-

electrolyte-gated CNTFETs were measured with the top gate in PBS, while those of back-gated devices were all measured in air. All electrical measurements were carried out at room temperature using semiconductor parameter analyzer.



(a)



(b)

Figure 1. (a) Schematic structure of the experimental setup of a local-electrolyte-gated CNTFET and (b) optical plan view image of a CNTFET with groove.

The gate transfer characteristics of the localelectrolyte-gated and back-gated CNTFETs were measured using the same SWNT devices, as shown in Fig. 2. The top-gate bias (relative to the source) of the local electrolyte gate was swept from 0.5 to -0.5 V to avoid undesirable oxidation or reduction reactions. Leakage currents to the reference electrode were negligible in the solution under the bias range. On the other hand, the back-gate bias in air was swept from 1 to -1 V, as shown in Fig. 2. The results reveal that the device exhibited ptype FET characteristics with the top gate in PBS as well as with the back gate in air. The drain current of the localelectrolyte-gated CNTFET was smaller than that of the back-gated CNTFET at the gate bias of 0 V, resulting from the electrostatic-voltage shift at the interface between the calomel electrode and the saturated KCl solution. Then, the net top-gate bias was positively shifted from the input top-gate voltage. This result reveals the good subthreshold characteristics of the local-electrolytegated devices, as shown in Fig. 2, were due to the channel-conductance-modulation effect. The transconductances of the back-gated and top-gated FET were estimated to be 1.0 μS (V_D = 0.1 V) and 6.9 μS (VD = 0.1 V), respectively. These results indicate that the local-electrolyte-gated CNTFETs exhibit the smaller subthreshold slope and better transconductance than that of the back-gated CNTFETs. Therefore, carbon nanotube field-effect transistors (CNTFETs) with local electrolyte are useful for detection of biomolecules.

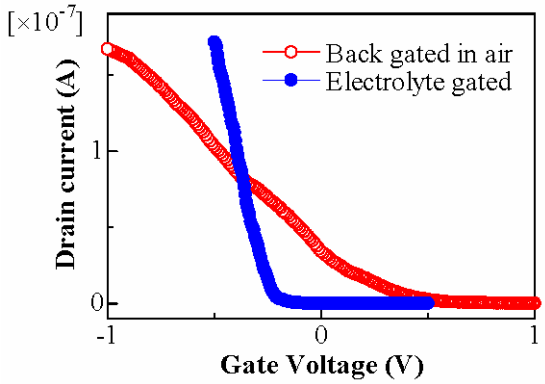


Figure 2. Gate transfer characteristics of the localelectrolyte-gated and back-gated CNTFETs.

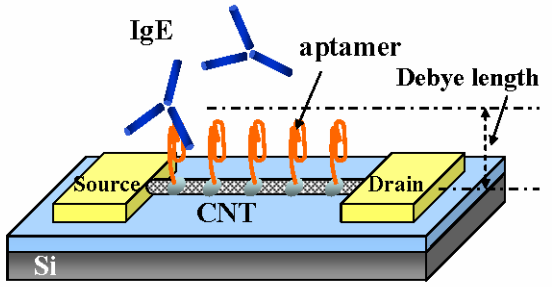


Figure 3. Schematic structure of protein biosensors based on an aptamer-modified CNTFET.

3. Carbon nanotube biosensors

Using CNTFETs, we have fabricated label-free protein biosensors in which CNT channels were modified with aptamers, and have tried to detect IgE. Aptamers are artificial oligonucleotides that can be generated to recognize amino acids, drugs, and proteins with high specificity [23]. The aptamers can be engineered in vitro easily, and therefore are relatively inexpensive. Moreover, the aptamers are smaller in size than the Debye length, as shown in Fig. 3. As a result, formations of aptamers and target proteins occur inside the electrical double layers in buffer solution, and the aptamers can be immobilized in dense on the CNT channels. They have also demonstrated stronger and more selective affinity for their target proteins than the corresponding antibodies. Therefore, aptamer-modified CNTFET biosensors are expected to detect target proteins with high sensitivity and high

selectivity. IgE is an antibody subclass, found only in mammals. IgE is capable of triggering the most powerful immune reactions.

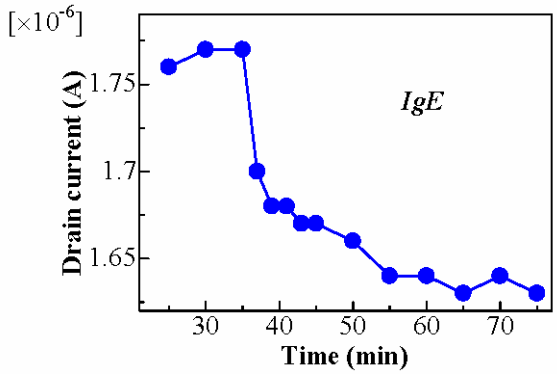


Figure 4. Time dependence of drain current of the CNTFET after the introduction of target IgE at 20 nM onto the IgE aptamer-modified CNTFET.

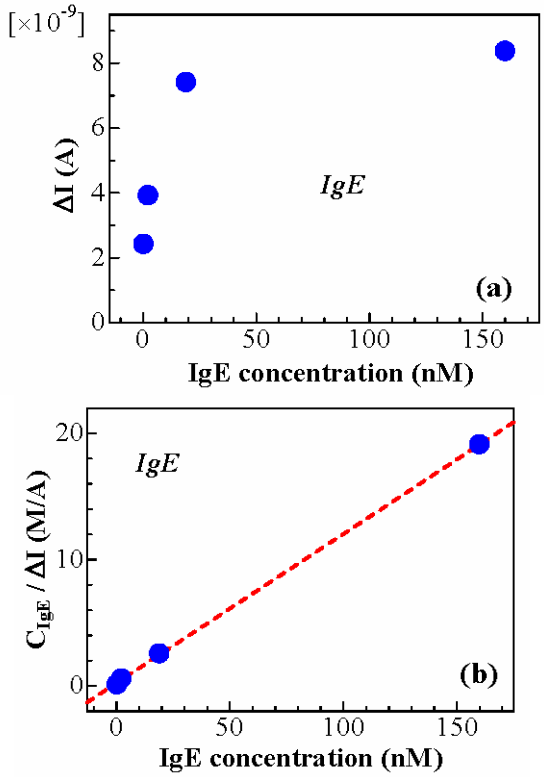


Figure 5. (a) Amount of net drain current as a function of IgE concentration, and (b) IgE concentration / amount of net drain current as a function of IgE concentration.

An experimental setup for detection of IgE using CNTFETs was carried out as follows. First, the CNT channels were incubated into 1-pyrenebutanoic acid succinimidyl ester in dry dimethylformamide solutions (linkers) for 1 hour in a 5 mM solution before the IgE aptamer immobilization. Next, in order to covalently immobilize IgE aptamers on the CNT channels, the devices were submerged into the 5'- amino modified aptamers in a 12 μg/ml solution overnight. Then, unreacted linkers were blocked by ethanolamine (100 μM solution, 30 min). Afterwards the aptamer-modified channels in the CNT-FETs were immersed into 10 mM phosphate buffer solutions. An Ag/AgCl reference electrode (Bioanalytical Systems, West LaFayette, IN) was used as a gate electrode to minimize the environmental effects. Finally, the electrical properties of the CNTFETs were measured in real time by Semiconductor Parameter Analyzer after introduction of IgE at various concentrations.

Figure 4 shows time dependence of source-drain current of CNTFETs at the source-drain bias of 0.2 V and at the gate bias of 0 V after the introduction of target IgE at 20 nM onto the IgE aptamer-modified CNTFET while monitoring in real time. Adding the target IgE caused a sharp decrease in the source-drain current and then gradual saturation at lower values. This result indicates that the positive charges of the IgE molecules were detected by the CNT channel conductance modulation in the aptamer-modified CNTFET.

Next, target IgE molecules with various concentrations were introduced onto the IgE aptamermodified CNTFET while monitoring source-drain current in real time. The source-drain current sharply decreased after adding the target IgE for every concentration. The amount of the net source-drain current before and after IgE introduction for every concentration is plotted in Fig. 5(a). The results reveal that the amount of the net sourcedrain current increased as a function of IgE concentration of 0.25, 2.2 and 19 nM. However, at IgE concentration of 160 nM, the amount of the net source-drain current was almost saturated, as shown in Fig. 5(a). According to the results in Fig. 5(a), IgE concentration (C_{IgE}) / the amount of the net source-drain current (ΔI) was plotted as a function of IgE concentration, as shown in Fig. 5(b). The experimental results were fitted well by a linear curve, indicating that adsorption of IgE molecules to IgE aptamar on CNT channels follows the Langmuir adsorption isotherm. It is given by

$$\frac{\Delta I}{\Delta I_{max}} = \frac{KC_{IgE}}{1 + KC_{IgE}} \quad (1)$$

where K is the association constant between IgE molecules and IgE aptamer, Δ_{Imax} is the amount of saturated drain current. From eq. (1), the Langmuir adsorption isotherm of the linear form is described as

$$\frac{C_{IgE}}{\Delta I} = \frac{1}{\Delta I_{max}} C_{IgE} + \frac{1}{K\Delta I_{max}} \quad (2)$$

Using eq. (2), the Langmuir adsorption isotherm well fitted the experimental results, as shown in Fig. 5(b). From the fitting, K was estimated to be 5.14×10^8 (M^{-1}). As compared to the association constant between antibodies and antigens for serum albumin group, which ranges from 2.5×10^6 to 5.2×10^7 (M^{-1}) [24-27], the

reactions between IgE molecules and IgE aptamer have much better affinity. These results indicate that IgE at 250 pM could be effectively detected using the aptamermodified CNTFET. Therefore, the biosensors can detect IgE molecules with high sensitivity.

4. Conclusion

We have fabricated local-electrolyte-gated CNTFETs, in which channel modulation effect is dominant to the switching. With high transconductances and small subthreshold slopes, local-electrolyte-gated CNTFETs have the high performance. Using CNTFETs, we have detected IgE, in which CNT channels were modified with aptamers. After the 5'- amino modified aptamers were covalently immobilized on the CNT channels, the electrical properties of the CNTFETs were monitored in real time. The source-drain current sharply decreased, and gradually saturated at lower values after the introduction of target IgE at various concentrations onto the aptamermodified CNTFET while monitoring in real time. The amount of the net source-drain current before and after IgE introduction increased as a function of IgE concentration and finally saturated. The feature of IgE molecules on IgE aptamer could be explained based on the Langmuir equation isotherm. As a result, the association constant could be calucated using the Langmuir equation fitting, indicating that the reactions between IgE molecules and IgE aptamer have good affinity.

Our aptamer-based CNTFET biochip is a promising candidate for the development of an integrated, high-throughput, multiplexed real-time biosensor for medical, forensic and environmental diagnostics.

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