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Label-Free Protein Biosensor Based on Aptamer-Modified Carbon Nanotube Field-Effect Transistors

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We have fabricated label-free protein biosensors based on aptamer-modified carbon nanotube field-effect transistors (CNT-FETs) for the detection of immunoglobulin E (IgE). After the covalent immobilization of 5′-amino-modified 45-mer aptamers on the CNT channels, the electrical properties of the CNT-FETs were monitored in real time. The introduction of target IgE at various concentrations caused a sharp decrease in the source-drain current, and a gradual saturation was observed at lower concentrations. The amount of the net source-drain current before and after IgE introduction on the aptamer-modified CNT-FETs increased as a function of IgE concentration. The detection limit for IgE was determined as 250 pM. We have also prepared CNT-FET biosensors using a monoclonal antibody against IgE (IgE−mAb). The electrical properties of the aptamer- and antibody-modified CNT-FETs were compared. The performance of aptamer-modified CNT-FETs provided better results than the ones obtained using IgE−mAb-modified CNT-FETs under similar conditions. Thus, we suggest that the aptamer-modified CNT-FETs are promising candidates for the development of label-free protein biosensors.

Label-free electrochemical monitoring of biorecognition events provides a promising platform, which is simple, cost-effective, and requires no external modification on the biomolecules.[1,2] Carbon nanotube field-effect transistors (CNT-FETs) are one of the promising candidates for the development of label-free biosensors.[3−7]

Debye length is simply defined as the typical distance required for screening the surplus charge by the mobile carriers present in a material.[8] If a molecule is placed a Debye length away from the surplus charge, its effects on the mobile charges of the material are no longer felt. Debye length varies as the inverse square root of the ionic strength (I), and it is $\sim 0.32 I^{-1/2}$ nm in water. For this reason, the strict adjustment of I conditions is necessary for sensitive detection of biomolecules using FET-based sensors. The typical size of an antibody may vary between 10 and 15 nm,[9,10] and the size of immunoglobulin E (IgE) was reported to be ∼10 nm.[11] Thus, the binding of an anti-IgE monoclonal antibody (IgE−mAb) with IgE would easily exceed the Debye length. In this study, we have detected IgE using CNT-FETs, in which CNT channels were modified with 45-mer aptamers and mAbs. Since the aptamer that we used in this report is self-complementary with 12 bp, its size was significantly smaller than that of IgE−mAb. Under similar I conditions, the immunorecognition may have occurred outside the electrical double layer in solution, since the IgE−mAbs are much larger in size than the Debye length as illustrated in Figure 1a. Thus, the charges of the bound protein may be "screened" by the double layer, and their effect on the equilibrium carrier distribution would then be vanishingly small. However, they are no more or no less "canceled" in the sense of being paired with an ion from the solution of opposite charge that they would be if much closer to the electrode. On the other hand, aptamers enable sensitive detection possibilities, partly derived from their small size.

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(1) Drummond, T. G.; Hill, M. G.; Barton, J. K. *Nat. Biotechnol.* **2003**, *21*, 1192−1199.

(2) Kerman, K.; Kobayashi, M.; Tamiya, E. *Meas. Sci. Technol.* **2004**, *15*, R1−R11.

(3) Maehashi, K.; Matsumoto, K.; Kerman, K.; Takamura, Y.; Tamiya, E. *Jpn. J. Appl. Phys.* **2004**, *43*, L1558−L1560.

(4) Kaminishi, D.; Ozaki, H.; Ohno, Y.; Maehashi, K.; Inoue, K.; Matsumoto, K.; Seri, Y.; Masuda, A.; Matsumura, H. *Appl. Phys. Lett.* **2005**, *86*, 113−115.

(5) Kerman, K.; Morita, Y.; Takamura, Y.; Tamiya, E.; Maehashi, K.; Matsumoto, K. *Nanobiotechnology* **2005**, *1*, 65−70.

(6) Grüner, G. *Anal. Bioanal. Chem.* **2006**, *384*, 322−335.

(7) Li, C.; Curreli, M.; Lin, H.; Lei, B.; Ishikawa, F. N.; Datar, R.; Cote, R. J.; Thompson, M. E.; Zhou, C. *J. Am. Chem. Soc.* **2005**, *127*, 12484−12485.

(8) Debye, P. *Chem. Rev.* **1936**, *19*, 171−182.

(9) Rudikoff, S.; Potter, M. *Proc. Natl. Acad. Sci. U.S.A.* **1976**, *73*, 2109−2112.

(10) Teillaud, J. L.; Desaymard, C.; Giusti, A. M.; Haseltine, B.; Pollock, R. R.; Yelton, D. E.; Zack, D. J.; Scharff, M. D. *Science* **1983**, *222*, 721−726.

(11) Kane, P. M.; Holowka, D.; Baird, B. *J. Cell Biol.* **1988**, *107*, 969−980.

10.1021/ac060830g CCC: $37.00
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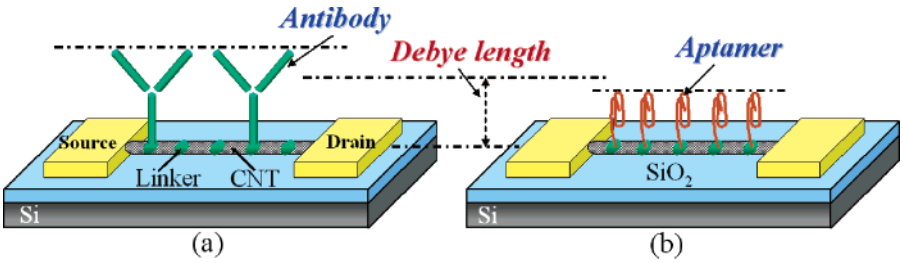

Figure 1. Schematic representation of label-free protein biosensors based on CNT-FETs: (a) antibody-modified CNT-FET; (b) aptamer-modified CNT-FET.

Aptamers are synthetic oligonucleotides that can be generated to recognize amino acids, drugs, and proteins with high specificity.[12−16] Aptamers are usually isolated from combinatorial libraries of synthetic nucleic acids by a process of adsorption, recovery, and amplification coined SELEX for systematic evolution of ligands by exponential procedure.[12−15] Some of the aptamers have several advantages over their corresponding antibodies.[17] Since the aptamers can be engineered in vitro easily, their mass production is relatively cost-effective. Moreover, while antibodies are sensitive to temperature and denaturate easily upon contact with surfaces, leading to limited shelf-lives, aptamers are stable to long-term storage. Aptamers have already been employed in a range of analytical techniques,[18,19] including affinity capillary electrophoresis,[20,21] capillary electrochromatography,[22] HPLC,[23] fluorescence,[24] and AFM.[25] An RNA aptamer, specific for the protein transactivator of transcription of HIV-1, was used as the biorecognition element to develop biosensors based on piezoelectric quartz crystal microbalance (QCM) and surface plasmon resonance.[26,27]

In terms of FET technology, the aptamers provide a preferable choice, because they are smaller in size than the Debye length as illustrated in Figure 1b. As a result, the binding event between the aptamers and the target proteins can occur within the electrical double layer in buffer solution, and therefore, changes in the charge distribution within proximity to the CNT can easily be detected by FET.[28,29] Moreover, the density of the immobilized aptamers on the CNT channels can be controlled, and a high density of aptamers can easily be prepared.

IgE is an antibody subclass, found only in mammals. IgE is capable of triggering the most powerful immune reactions.[30] Most of our knowledge of IgE has resulted from research into the mechanisms of type-1 hypersensitivity.[31] Rapid detection of IgE is of great interest in dealing with patients with allergy-mediated disorders.[32,33] IgE is found at low levels in human serum (~1 nM); however, it significantly increases in patients afflicted with allergic asthma, atopic dermatitis,[34] and other immune deficiency-related diseases, such as AIDS.[35]

Wiegand and co-workers[36] isolated a SELEX-based high-affinity D17.4 DNA aptamer for IgE and applied it in affinity probe capillary electrophoresis. In order to stabilize the structure of the aptamer, Liss et al.[37] extended both the 5′- and 3′-ends of D17.4 by adding 5′-GCGC-3′ sequences, allowing formation of a longer stem and, consequently, a more stable tertiary structure. This strategy reduced the dissociation constant of the aptamer to 3.6 nM, thus improving its binding characteristics. We have employed this engineered aptamer, called D17.4ext (extended) in this report. Liss and co-workers[37] developed their aptamer-based QCM biosensor for IgE detection with a limit of detection of 500 pM. A fluorophore-labeled aptamer was employed for the detection of IgE by German et al.[38] An aptamer-based IgE detection method in connection with a DNA intercalating light switch complex has been reported by Jiang et al.[39] Electrochemical impedance spectroscopy on aptamer-modified array electrodes for

(12) Tuerk, C.; Gold, L. *Science* **1990**, *249*, 505−510.
(13) Robertson, M. P.; Joyce, G. F. *Nature* **1990**, *344*, 467.
(14) Ellington, A. D.; Szostak, J. W. *Nature* **1990**, *346*, 818−822.
(15) O'Sullivan, C. K. *Anal. Bioanal. Chem.* **2002**, *372*, 44−48.
(16) Li, C.; Curreli, M.; Lin, H.; Lei, B.; Ishikawa, F.; Datar, R.; Cote, R.; Thompson, M.; Zhou, C. *J. Am. Chem. Soc.* **2005**, *127*, 12484−12485.
(17) Jayasena, S. D. *Clin. Chem.* **1999**, *45*, 1628−1650.
(18) Luzi, E.; Minunni, M.; Tombelli, S.; Mascini, M. *Trends Anal. Chem.* **2003**, *22*, 810−818.
(19) Tombelli, S.; Minunni, M.; Mascini, M. *Biosens. Bioelectron.* **2005**, *20*, 2424−2434.
(20) Berezovski, M.; Krylov, S. N. *J. Am. Chem. Soc.* **2003**, *125*, 13451−13454.
(21) Buchanan, D. D.; Jameson, E. E.; Perlette, J.; Malik, A.; Kennedy, R. T. *Electrophoresis* **2003**, *24*, 1375−1382.
(22) Rehder-Silinski, M. A.; McGown, L. B. *J. Chromatogr., A* **2003**, *1008*, 233−245.
(23) Michaud, M.; Jourdan, E.; Ravelet, C.; Villet, A.; Ravel, A.; Grosset, C.; Peyrin, E. *Anal. Chem.* **2004**, *76*, 1015−1020.
(24) Rajendran, M.; Ellington, A. D. *Nucleic Acids Res.* **2003**, *31*, 5700−5713.
(25) Jiang, Y.; Zhu, C.; Ling, L.; Wan, L.; Fang, X.; Bai, C. *Anal. Chem.* **2003**, *75*, 2112−2116.
(26) Minunni, M.; Tombelli, S.; Gullotto, A.; Luzi, E.; Mascini, M. *Biosens. Bioelectron.* **2004**, *20*, 1149−1156.
(27) Tombelli, S.; Minunni, M.; Luzi, E.; Mascini, M. *Bioelectrochemistry* **2005**, *67*, 135−141.
(28) So, H.-M.; Won, K.; Kim, Y. H.; Kim, B.-K; Ryu, B. H.; Na, P. S.; Kim, H.; Lee, J. O. *J. Am. Chem. Soc.* **2005**, *127*, 11906−11907.
(29) Guo, X.; Huang, L.; O'Brien, S.; Kim, P.; Nuckolls, C. *J. Am. Chem. Soc.* **2005**, *127*, 15045−15047.
(30) Sutton, B. J.; Gould, H. J. *Nature* **1993**, *366*, 421−428.
(31) Ravetch, J. V.; Kinet, J.-P. *Annu. Rev. Immunol.* **1991**, *9*, 457−492.
(32) Poole, J. A.; Matangkasombut, P.; Rosenwasser, L. J. *J. Allergy Clin. Immunol.* **2005**, *115*, S375−S385.
(33) Hamilton, R. G.; Adkinson, N. F., Jr. *J. Allergy Clin. Immunol.* **2004**, *114*, 213−225.
(34) DeWitt, C. A.; Bishop, A. B.; Buesher, L. S.; Stone, S. P. *J. Am. Acad. Dermatol.* **2006**, *54*, 855−865.
(35) Rancinan, C.; Morlat, P.; Chene, G.; Guez, S.; Baquey, A.; Beylot, J.; Salamon, R. *J. Allergy Clin. Immunol.* **1998**, *102*, 329−330.
(36) Wiegand, T.; Williams, P. B.; Dreskin, S. C.; Jouvin, M.; Kinet, J.; Tasset, D. *J. Immunol.* **1996**, *157*, 221−230.
(37) Liss, M.; Petersen, B.; Wolf, H.; Prohaska, E. *Anal. Chem.* **2002**, *74*, 4488−4495.
(38) German, L.; Buchanan, D.; Kennedy, R. T. *Anal. Chem.* **1998**, *70*, 4540−4545.
(39) Jiang, Y.; Fang, X.; Bai, C. *Anal. Chem.* **2004**, *76*, 5230−5235.

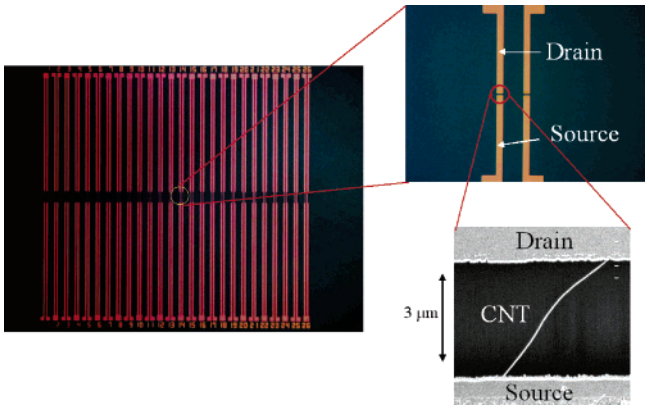

Figure 2. Images of the biochip containing 26 arrayed CNT-FET devices. Inset images show the single-walled carbon nanotube connecting the source and drain electrodes.

the detection of IgE was reported by Xu et al.[40] In this paper, we have fabricated aptamer- and IgE−mAb-modified CNT-FET biosensors, and the electrical properties of the CNT-FETs have been monitored and compared in real time after the introduction of IgE at various concentrations.

EXPERIMENTAL SECTION

Materials. DNA aptamer (D17.4ext) with 5′-amino modification was custom-synthesized by Fasmac Co. (Kanagawa, Japan), and its base sequence is as follows:

D17.4ext: 5′-NH_2-GCG CGG GGC ACG TTT ATC CGT
CCC TCC TAG TGG CGT GCC CCG CGC-3′

Monoclonal anti-IgE antibody (IgE−mAb, human) was purchased from Biogenesis Ltd. (Poole, U.K.). The analyte, IgE purified from human myeloma (Biogenesis Ltd.), was diluted from a 20 g/L stock in PBS (10 mM PBS, pH 7.4) and stored at −20 °C until use. Bovine serum albumin fraction V (BSA) was obtained from Sigma (Tokyo, Japan), and dissolved in PBS to a final concentration of 20 nM.

Apparatus. Reference electrode (Ag/AgCl, Bioanalytical Systems, West LaFayette, IN) was used as the gate to minimize the environmental effects. Finally, the electrical properties of the CNT-FETs were measured in real time using an Agilent 4156C Precision Semiconductor Parameter Analyzer (Palo Alto, CA) in connection with the shield case LC-361F (Measure Jig Co. Ltd.). The regulated dc power supply (PAS60-12) was purchased from Kikusui Co.

Procedure. Figure 2 shows images of the arrayed CNT-FETs on the chip. CNTs were grown using a thermal chemical vapor deposition (CVD) approach as we described previously.[41] The CNTs were synthesized by ethanol CVD using the patterned Co chemical catalyst, which were formed by the conventional photolithography and liftoff process technology, on heavily doped p^+-Si substrates capped with 100-nm-thick SiO_2. The spacing between the source and drain electrodes was ~3 μm, as shown in Figure 2. The source and drain contacts (Ti/Au) were formed on the patterned chemical catalyst after the growth of the CNTs. The fabricated samples were *p*-type CNT-FETs at room temperature in air.

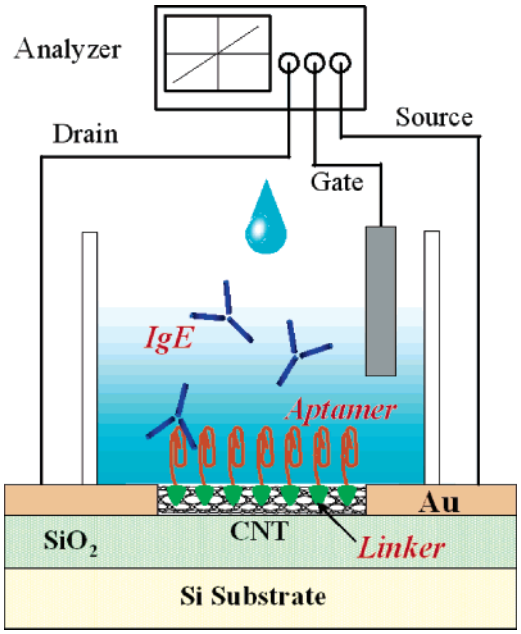

Figure 3. Schematic structure of the experimental setup for the detection of IgE using an aptamer-modified CNT-FET device.

Figure 3 shows the experimental setup for the detection of IgE using CNT-FETs. First, the CNT channels were incubated with 5 mM 1-pyrenebutanoic acid succinimidyl ester (Aldrich) in dry dimethylformamide solutions (linker) for 1 h, followed by rinsing with PBS. Next, in order to covalently immobilize IgE aptamers on the CNT channels, the devices were exposed to the 5′-amino-modified aptamers at 12 μg/mL in PBS overnight. After rinsing with blank PBS, to deactivate and block the excess reactive groups remaining on the surface, 100 mM ethanolamine was added onto the resulting electrodes and incubated for 30 min. After rinsing with PBS, 100 μL of blank PBS was injected into the incubation chamber for electrical measurements.

We also prepared IgE−mAb-modified CNT-FET devices. After the covalent activation step using the linker molecule, all the CNT channels were incubated with 10 μg/mL IgE−mAb overnight. The procedures for the surface blocking using 100 mM ethanolamine and reaction with IgE were performed under similar conditions as described above.

RESULTS AND DISCUSSION

The electrical properties of the CNT-FETs were measured in real time at room temperature. The experimental configuration shown in Figure 3 reveals that the electric field applied to the CNT via the reference electrode bias (relative to the source and drain) will not have the simple perpendicular-to-conduction path geometry that is more typical in "real" FETs. Rather, the field will be nonuniform from one end of the CNT to the other and directed toward or away from the source and drain electrodes,

(40) Xu, D.; Xu, D.; Yu, X.; Liu, Z.; He, W.; Ma, Z. *Anal. Chem.* **2005**, *77*, 5107−5113.
(41) Maehashi, K.; Ohno, Y.; Inoue, K.; Matsumoto, K. *Appl. Phys. Lett.* **2004**, *85*, 858−860.

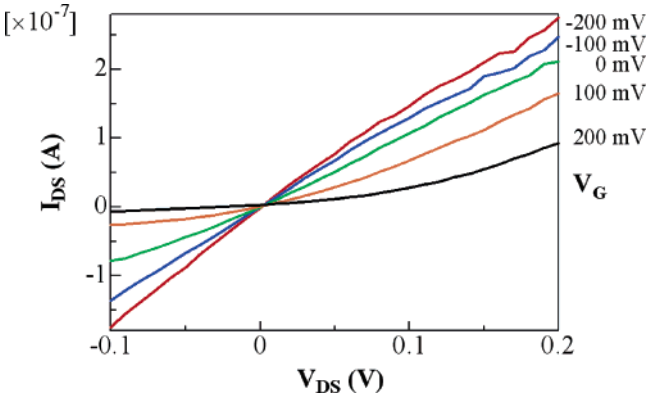

Figure 4. Electrical properties of CNT-FET devices before modification of linker molecule in phosphate buffer solution (10 mM PBS, pH 7.4).

depending on the relative potentials of the gate, source, and drain. It would be likely that the sensitivity to target binding would depend on where the target molecule binds (relative to source and drain contacts) and that this location-dependent sensitivity would vary with the selected source-drain bias as well as the chosen reference electrode (gate) potential. The characteristics of CNT-FETs in buffer solution were investigated as shown in Figure 4. With increasing gate bias using the reference electrode, the source-drain current was decreased at the source-drain bias of 0.2 V. This result indicated that this device showed *p*-type characteristics in blank PBS.

Figure 5A(a) and A(b) shows the drain current−drain bias characteristics of the CNT-FET at the gate bias of 0 V before and after the 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 CNT-FET 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 indicated that IgE aptamers were successfully modified on CNT channels. Simultaneously, it was confirmed that no current to the reference electrode was measured, as shown in Figure 5 A(c).

Electrical properties of the IgE−aptamer-modified CNT-FETs were carried out in order to investigate the stability and selectivity of the biosensors. Figure 5B shows time dependence of CNT-FET responses at the source-drain bias of 0.2 V and the gate bias of 0 V. No conductance change was observed after the addition of 100 μL of blank PBS into the chamber. Next, the selectivity of the responses was challenged by applying a control protein, BSA to the biosensor. BSA at 20 nM was introduced onto the aptamer-modified CNT-FET sensor. No change in the source-drain current was observed as shown in Figure 5B. The result indicated that the nonspecific binding of BSA was successfully suppressed in the biosensor with the treatment of 100 mM ethanolamine to suppress the covalently activated functional groups on CNTs as described in the Experimental Section.

Figure 6A shows the time dependence of source-drain current of CNT-FETs 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 of 250 pM, 2.2 nM, 18.5 nM, and 160 nM onto the

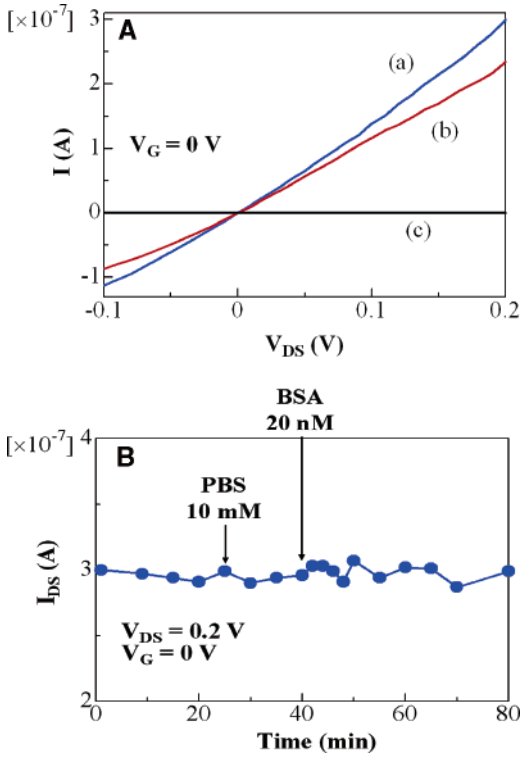

Figure 5. (A) Drain current-drain bias characteristics of the CNT-FET at the gate bias of 0 V (a) before and (b) after the immobilization of IgE aptamers on the CNT channel. The current (c) to the reference electrode is also shown. (B) Time dependence of source-drain current of the CNT-FET at the source-drain bias of 0.2 V and at the gate bias of 0 V after the introduction of blank buffer solution and nontarget BSA onto the IgE aptamer-modified CNT-FET. Arrows indicate the points of sample injections.

aptamer-modified CNT-FET. Adding the target IgE caused a sharp decrease in the source-drain current and then a gradual saturation at lower values. Supporting Information Figures 1 and 2 show the time dependence for source-drain current of the IgE aptamer-modified CNT-FET device at the source-drain bias of 0.2 V and the gate bias of 0 V after the introduction of target IgE at 20 nM and 250 pM, respectively. This decrease was attributed to two events in this report. First, the screening effect of IgE molecules on the negative charge of the aptamers might have caused the decrease in the response after the binding event. Moreover, the increase in Schottky barrier height between the metal electrodes[42] and CNT channel, which could be due to the adsorption of IgE molecules on CNT channels at the CNT−metal contacts, might have caused the drop in the electrical response.[43,44] Additionally, the increasing sequence of concentrations shown in Figure 6A were followed by a return to zero concentration of IgE to verify that the binding constant for IgE by the aptamer was as large as previously claimed.[32,33] After the injection of 160 nM IgE, the injection of zero concentration of IgE onto the CNT-FET device resulted in no change in the signals.

(42) Byon, H. R.; Choi, H. C. *J. Am. Chem. Soc.* **2006**, *128*, 2188−2189.
(43) Chen, R. J.; Choi, H. C.; Bangsaruntip, S.; Yenilmez, E.; Tang, X.; Wang, Q.; Chang, Y.-L.; Dai, H. *J. Am. Chem. Soc.* **2004**, *126*, 1563−1568.
(44) Chen, Z.; Appenzeller, J.; Knoch, J.; Lin, Y.-M.; Avouris, P. *Nano Lett.* **2005**, *5*, 1497−1502.

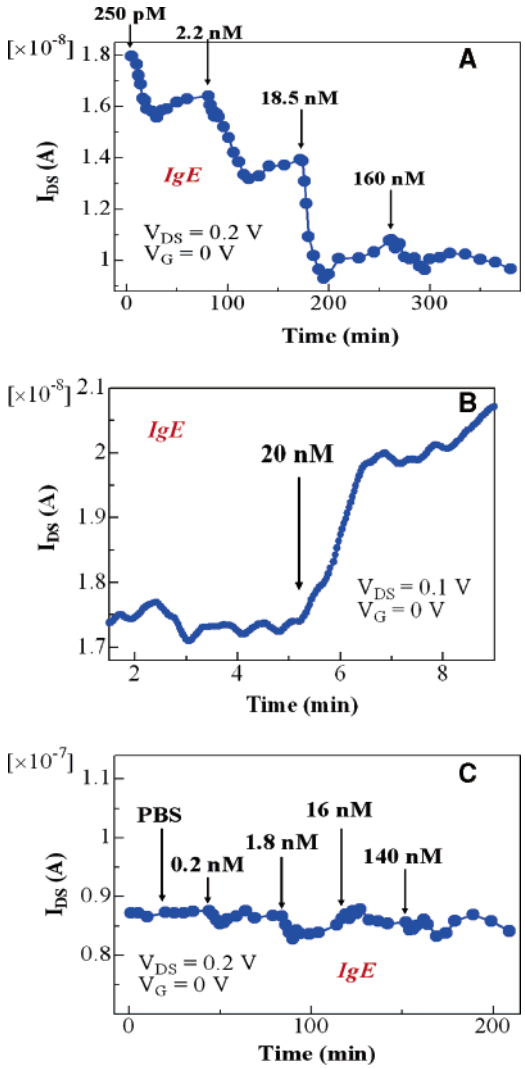

Figure 6. (A) Time dependence of source-drain current of the CNT-FET at the source-drain bias of 0.2 V and at the gate bias of 0 V after the introduction of target IgE at various concentrations onto the IgE aptamer-modified CNT-FET. Arrows indicate the points of IgE injections. (B) Time dependence of source-drain current of the CNT-FET at the source-drain bias of 0.1 V and at the gate bias of 0 V after the introduction of target IgE onto the bare CNT-FET. Arrow indicates the point of IgE injection. (C) Time dependence of source-drain current of the CNT-FET 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−mAb-modified CNT-FET. Arrows indicate the points of IgE injections.

Control experiments were performed in order to confirm that the nonspecific binding of IgE could be suppressed. IgE molecules were introduced onto the bare CNT-FETs without aptamers. Figure 6B shows time dependence of source-drain current of a CNT-FET at the source-drain bias of 0.1 V and at the gate bias of 0 V. The increase in conductance of the CNT-FET was clearly observed after introduction of 20 nM IgE onto bare CNT-FET without aptamers. Since IgEs were nonspecifically interacted with the bare CNT channels, their entire bodies could be placed inside the Debye length. IgEs were negatively charged under our experimental conditions (pH 7.4), which was relatively higher than the isoelectronic point of IgEs. For this reason, the increase in conductance of the CNT-FET was obtained after the introduction of IgE onto bare CNT-FET without aptamers, as shown in Figure 6B. On the other hand, when IgEs were introduced onto the aptamer-modified CNT-FETs, they were attracted to the CNT surface with the aptamers, as illustrated in Figure 3. Since only the bound part of IgEs with the negatively charged aptamers was placed inside the electrical double layer in the buffer solution, local positive charge in IgE molecules could be detected using CNT-FETs. As a result of the net positive charge of the IgE−aptamer complex on CNT, the conductance of CNT-FETs decreased as shown in Figure 6A. Therefore, the decrease in conductance was mainly attributed to the screening effect of IgE molecules on the aptamer-modified CNT-FETs. Furthermore, the results in Figure 6A and B revealed that the source-drain currents were changed in the opposite directions after introduction of IgE molecules, indicating that the nonspecific binding of IgE was successfully suppressed in the aptamer-modified CNT-FETs.

The results in Figure 6A revealed that the net source-drain current increased as a function of IgE concentration at 250 pM, 2.2 nM, and 18.5 nM. The detection limit for IgE was determined as 250 pM using the aptamer-modified CNT-FET. However, after the addition of 160 nM IgE into the chamber, a small change in conductance could be observed. This net current value for 160 nM IgE was much lower than the expected one. Almost all the IgE aptamers were considered to be already bound with IgE molecules after the addition of 18.5 nM IgE. Thus, the linear dynamic range was determined to be from 250 pM to 20 nM. Atopic individuals (people who suffer from IgE-mediated allergies) can have up to 10 times the normal level of IgE (~10 nM) in their blood as do the patients of hyper-IgE syndrome. Thus, we suggest that the dynamic range of our biosensor would be applicable for the detection of IgE.

For comparison of the performance between aptamers and antibodies, we fabricated IgE−mAb-modified CNT-FETs and performed similar experiments for IgE detection. Figure 6C shows the time dependence of source-drain current after IgE introduction onto the IgE−mAb-modified CNT-FET. After the introduction of IgE at various concentrations, the source-drain current seemed to slightly decrease at 0.2 and 1.8 nM IgE. Therefore, when compared with the results obtained using aptamer-modified CNT-FETs under similar conditions, we determined that the aptamer-modified device would be a promising tool for the detection of IgE.

CONCLUSIONS

We have detected an important immunoglobulin, IgE, using CNT-FET devices, in which CNT channels were modified with aptamers and monoclonal antibodies. Aptamers displayed a better performance for the detection of IgE than the monoclonal antibodies did under similar conditions. Our aptamer-based CNT-FET device is a promising candidate for the development of an integrated, high-throughput, multiplexed real-time biosensor. As the development and optimization studies of our aptamer-modified CNT-FET device continue, we predict that sensitive multiplexed detection of numerous clinically important biomolecules would become possible in a rapid and high-throughput format.

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SUPPORTING INFORMATION AVAILABLE

Additional information as noted in text. This material is available free of charge via the Internet at http://pubs.acs.org.

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