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Label-Free Immunosensors Based on Aptamer-Modified Graphene Field-Effect Transistors

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1. Introduction

Electrical biomolecule detection has been expected for biochips used at home for medical diagnosis. Carbon nanotubes are promising candidates for chemical and biological sensors due to their unique structural and electrical characteristics [1, 2]. Graphene, planar sheet of sp^2-bonded carbon atoms densely packed in a honeycomb crystal lattice [3], is also an attractive material for sensors. Several investigations have been conducted on the use of graphene for chemical and biological sensors [4-6]. In this paper, we report label-free immunosensors based on aptamer-modified graphene field-effect transistors (G-FETs). They electrically detected only target immunoglobulins.

2. Experimental procedure

Single-layer graphene flakes were obtained by micromechanical exfoliation using kish graphite with adhesive tape. The G-FETs were fabricated on a 280-nm-thick thermally grown SiO_2 layer on degenerately doped *p*-Si substrates. After confirming the number of the graphene layer by Raman spectroscopy, gold source and drain electrodes were formed on the single-layer graphene by conventional e-beam lithography and lift-off method. Figure 1(a) shows a typical optical microscope image of fabricated G-FET.

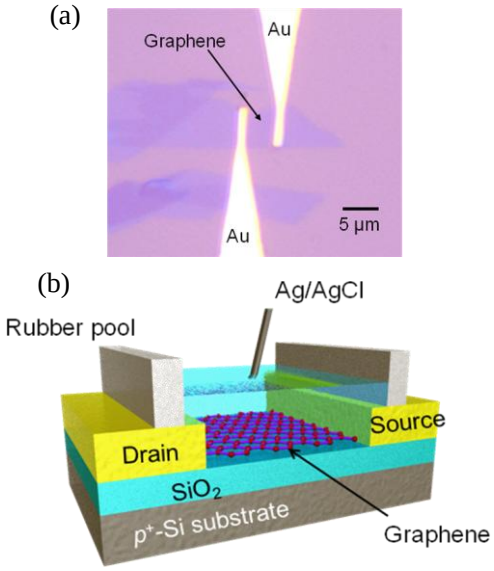

Fig. 1 (a) Optical microscope image of a G-FET. (b) Schematic illustration of measurement setup image.

Anti-immunoglobulin E (IgE) aptamer was used as a receptor in this work. Aptamers are artificial oligonucleotides and are produced in vitro. To immobilize the aptamers on the graphene surface, the G-FETs were immersed in 5 mM 1-pyrenebutanoic acid succinimidyl ester, which was used as linkers, in methanol for 1 hour. Then, the devices were immersed in 1 nM IgE aptamers in phosphate buffer solution (PBS) for 12 hours at room temperature. Finally, 100 mM ethanolamine was added onto the channel region of the G-FETs for 1 hour to deactivate and block the excess reactive groups remaining on the graphene surface. In sensing measurements, a silicone pool was put on the aptamer-modified G-FETs as shown in Fig. 1(b). Top-gate voltage was applied by Ag/AgCl reference electrode.

3. Results and discussion

Figure 2 shows atomic force microscope (AFM) images of a G-FET with (a) before and (b) after IgE-aptamer functionalization. The insets of Fig. 2 indicate the height profiles of the graphene channel. Before aptamer functionalization, approximately 0.3-nm-thick height was observed on the graphene channel, indicating that the number of the graphene layer was single. On the other hand, approximately 3-nm-thick structure was observed on the aptamer-modified graphene channel.

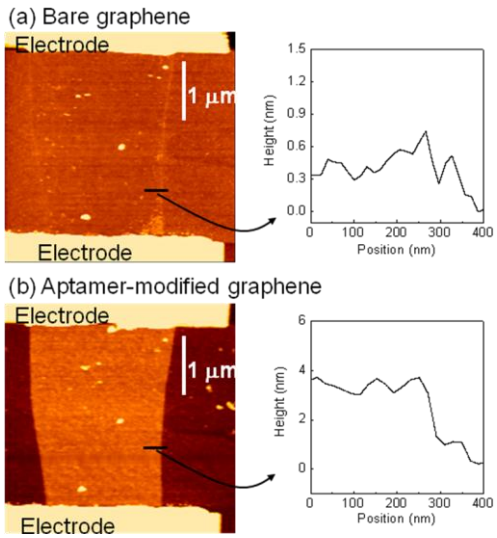

Fig. 2 AFM images of a G-FET (a) before and (b) after aptamer functionalization. The insets show the height profiles of the graphene channel.

Figure 3 shows drain current (I_D) plotted as a function of top-gate voltage (V_{TGS}) of a G-FET in PBS with pH 6.8 before (blue solid line) and after (red solid line) IgE-aptamer functionalization. Increased I_D was observed after aptamer functionalization. Since the carrier in the graphene channel is holes in this condition, this increased I_D comes from an increase in negative charge density on the graphene channel. These results show that the IgE aptamers were successfully immobilized on the graphene channel because the aptamers (oligonucleotides) are always negatively charged in solution due to the ionized hydroxyl of phosphoric acid. Moreover, slope of the I_D-V_{TGS} characteristics were almost the same, indicating that this aptamer-functionalization process was carried out without introducing defects on the graphene surface.

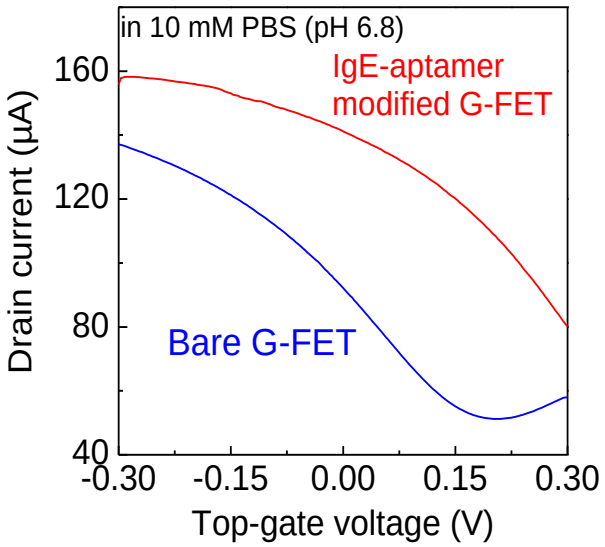

Fig. 3 I_D-V_{TGS} characteristics for before (blue solid line) and after (red solid line) aptamer functionalization.

Figure 4 shows time dependence of I_D of an aptamer-modified G-FET at source-drain voltage (V_{SD}) of 0.1 V and V_{TGS} of 0.1 V in PBS. After 10 and 30 min, nontarget proteins, which were 100 nM of bovine serum albumin (BSA) and streptavidin (SA), were added into the PBS, respectively, and target human IgE molecules were added after 50 min. When target protein was introduced on the graphene channel, the I_D suddenly decreased. On the contrary, in addition of nontarget proteins, the aptamer-modified G-FET shows almost constant in electrical conductance. These results show that selectively label-free immunosensors based on aptamer-modified G-FETs were successfully realized.

3. Conclusions

Aptamer-modified G-FETs were successfully fabricated for label-free immunosensors. IgE aptamers can be immobilized on the graphene surface using 1-pyrenebutanoic acid succinimidyl ester, which was confirmed by AFM and I_D-V_{TGS} characteristics. The aptamer-modified G-FETs were electrically detected only target IgE molecules. It was summarized that modified G-FETs have high potential for biological sensors.

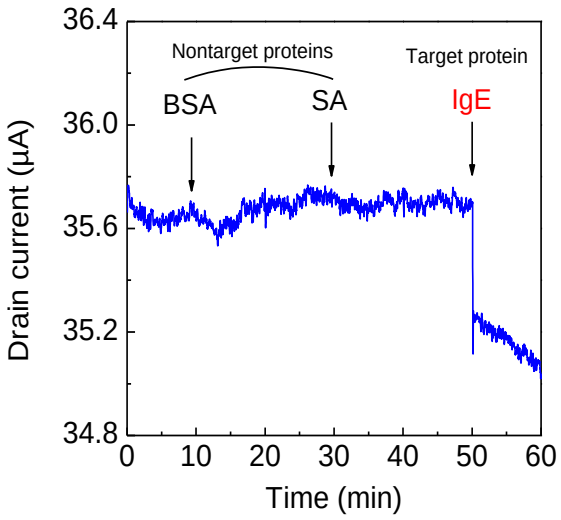

Fig. 4 Time dependence of I_D for an aptamer-modified G-FET. After 10 and 30 min, nontarget proteins (BSA and SA) were introduced, and 50 min, target IgE molecules were introduced on the aptamer- modified G-FET.

Acknowledgements

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