ELECTRICAL DETECTION OF DNA HYBRIDIZATION USING TRANSISTORS BASED ON CVD-GROWN GRAPHENE SHEETS

Lain-Jong Li[1], Xiaochen Dong[2], Peng Chen[3] and Yumeng Shi[2]*

[1] Research Center for Applied Science, Academia Sinica, Taipei, Taiwan.
[2] School of Materials Science and engineering, [3] School of Chemical and Biomedical Engineering, Nanyang Technological University, Singapore

Introduction

The interface between biosystems and nanomaterials is emerging for detection of various biomolecules and subtle cellular activities. Graphitic nanocarbon materials, such as carbon nanotubes, graphene oxide and graphene layers, have been employed as biosensors because they are biocompatible, extraordinarily sensitive and promising for large-area detection. In particular, the development of cost-effective and sequence-selective DNA detection is urgent for diagnosis of genetic or pathogenic diseases. The label-free electrical detection of the presence of biomolecules such as DNAs[1-2] and dynamic secretion of biomolecules such as ATP[3] and catecholamines[4] from living cells have been realized using carbon nanotube-based transistors. Graphene is another promising materials for these purposes. Comparing to one-dimensional carbon nanotubes, graphene is expected to excel carbon nanotubes because it offers large detection area, biocompatibility, and exceptional and unique electronic properties such as ultra-high mobility and ambipolar field-effect. The developing of graphene-based biosensors becomes practical with the recent advent of chemical vapor deposition (CVD) of large-sized graphene film (up to wafer size)[5-7]. Here, we fabricate long-channel and large-sized graphene transistors by transferring the as-grown CVD graphene films from Ni to arbitrary substrates. We show that these devices show well-defined ambipolar transfer characteristics. They are able to electrically detect the hybridization of target DNAs to the probe-DNAs pre-immobilized on graphene with detection sensitivity of 0.01 nM. These devices are capable of distinguishing the single-base mismatch. The detection mechanism is attributed to the electronic–doping (*n*-doping) introduced by target DNAs, which is in clear contrast to the electrostatic gating mechanism used by graphene oxide based sensors[8].

Experimental

Graphene film was synthesized by ambient pressure chemical vapor deposition (APCVD) on polycrystalline Ni (300 nm) coated Si substrates. Graphene film was consisting of ~60% single-layered and ~40% few-layered graphene domains as revealed by optical contrast microscopy. To transfer graphene films to the desired substrates, the as-grown graphene films on Ni were spin-coated with a thin layer of poly(methyl methacrylate) (PMMA). After etching of the Ni film, the PMMA/Graphene film detached from Si substrate was transferred to glass substrates. To fabricate graphene transistor, silver paint was used as the source (S) and drain (D) electrodes at the two ends of the graphene film (size ~3mm×10mm). Polydimethylsiloxanes (PDMS) was then used to insulate the source and drain electrodes and create a solution chamber (~ 4 mm × 5 mm) as illustrated in Fig.1. The typical optical image of the graphene film is also shown.

The probe, complementary and one-base mismatched DNA strands (sequences shown in Fig.1) were dissolved in the phosphate buffered saline (PBS, pH 7.4) containing 0.25 M NaCl and 10 mM phosphate. Before the addition of probe DNA molecules, pure PBS (40μL) was added in the chamber to measure transfer curve, i.e., drain current I_d vs. gate voltage V_g applied by a Ag wire to the PBS solution. Probe DNAs with a high concentration (1μM in 40μL PBS buffer) were added in the chamber for 16 hr to allow the saturate attachment to graphene surfaces, followed by rinsing with PBS buffer to remove the weakly bound DNA molecules. 40 μL of complementary or one-base mismatched DNAs (with desired concentration) was then added to the probe-DNA immobilized graphene device for 4h for hybridization, followed by water rinsing and drying. Subsequently, the transfer curve was obtained after adding 40μL of fresh PBS buffer solutions to the dried devices.

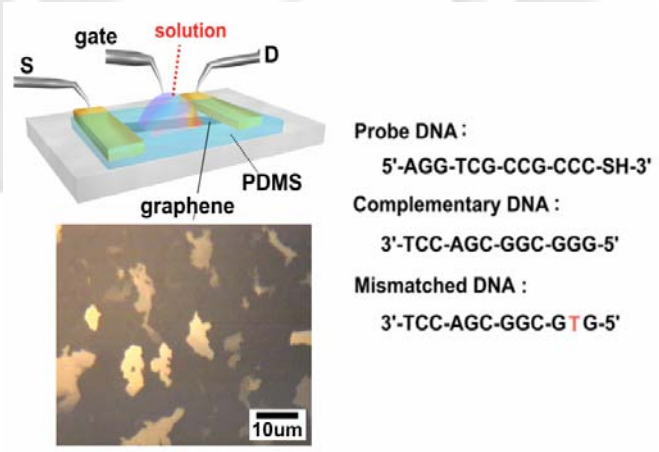

Fig. 1 Schematic illustration of the graphene device operated by liquid gating. The optical micrograph of the graphene film and the DNA sequences used are also presented .

Results and Discussion

As shown in Fig.2, the conductance of our graphene devices exhibited ambipolar behaviors subjecting to the gate voltage applied to the bath solution. The $V_{g,min}$ that gives the minimum graphene conductance can be identified from the transfer curve, and be used to monitor the doping state of the graphene film. Figure 2 shows that the $V_{g,min}$ is sensitive to the

immobilization of probe DNAs and hybridization of the complementary target DNAs. Specifically, $V_{g,min}$ is significantly left-shifted with addition of DNA molecules, suggesting that DNA molecules *n*-dopes the graphene film. The binding between graphene and nucleotides has been attributed to the non-electrostatic stacking interaction. This explains how the probe DNAs are immobilized on graphene. Meanwhile, the left-shift of $V_{g,min}$ after DNA hybridization suggests that the complementary DNAs can also effectively interact with graphene and impose *n*-doping effect based on the graphene-nucleotide interaction. The shift in $V_{g,min}$ increased with the increasing concentration of the complementary DNA, specifically, 0.01nM and 10 nM DNA solutions caused >10 meV and >55 meV shift, respectively. The $V_{g,min}$ did not shift further at higher complementary DNA concentrations (>10nM) likely due to saturation in hybridization with the limited number of probe DNAs. Furthermore, Fig. 3 demonstrates that the complementary DNA and the one-base mismatched DNA can be easily differentiated because $V_{g,min}$ is much less sensitive to the mismatched DNA which only caused ~ 20 meV shift at a high concentration (500nM). These results prove that the large $V_{g,min}$ shift caused by the complementary DNA is not due to the non-specific binding between the complementary DNA and graphene[9]. Here we demonstrate that $V_{g,min}$ shift appears to be a good indicator for DNA hybridization and for detection of single-base mutation.

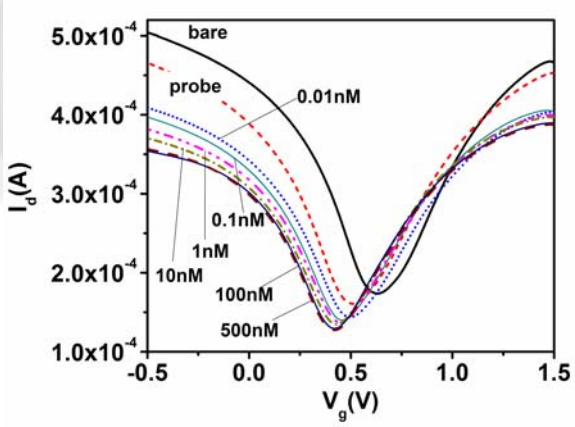

Fig. 2 Transfer characteristics for the graphene transistors before adding DNA, after immobilization with probe DNA, and after reaction with complementary DNA molecules with the concentration ranging from 0.01 to 500 nM.

Conclusions

This study demonstrates the emerging potentials of graphene based biosensors in sensitive and readily detection of biomolecules, particularly, in detection of single-base polymorphism that is thought as the key to diagnosis of genetic diseases and realization of personalized medicine.

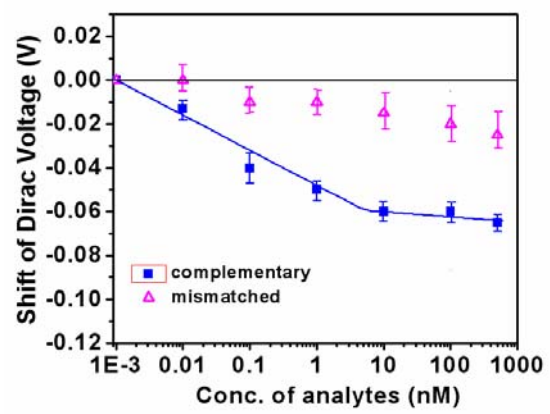

Fig. 3 The shift of $V_{g,min}$ for the probe DNA immobilized graphene transistors upon adding various concentrations of complementary or one-base mismatched DNA molecules.

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