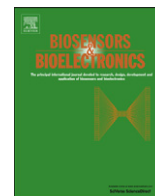




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## Label-free detection of DNA hybridization using transistors based on CVD grown graphene

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### ABSTRACT

The high transconductance and low noise of graphene-based field-effect transistors based on large-area monolayer graphene produced by chemical vapor deposition are used for label-free electrical detection of DNA hybridization. The gate materials, buffer concentration and surface condition of graphene have been optimized to achieve the DNA detection sensitivity as low as 1 pM ( $10^{-12}$  M), which is more sensitive than the existing report based on few-layer graphene. The graphene films obtained using conventional PMMA-assisted transfer technique exhibits PMMA residues, which degrade the sensing performance of graphene. We have demonstrated that the sensing performance of the graphene samples prepared by gold-transfer is largely enhanced (by 125%).

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### 1. Introduction

Exploring the interaction between deoxyribonucleic acids (DNA) and nanomaterials is helpful for developing biosensors. The development of nanomaterials for DNA detection such as inorganic nanoparticles (Drummond et al., 2003; Zhang et al., 2007), silicon nanowires (Patolsky and Lieber, 2005; Xie et al., 2012), nanoporous membranes (Li et al., 2003), and nanocarbon materials (Li et al., 2011; Muller et al., 2010; Schrand et al., 2009) is growing rapidly over the past few years. The majority of DNA detection technology has relied on optical or electrochemical transductions; however, these methods require fluorescent or electrochemical tags. Label-free electrical detection is considered as a candidate for development of cost-effective and sequence-selective DNA sensors. Carbon nanotube transistors show great promise in detecting ATP (Huang et al., 2009), DNAs (Gui et al., 2006; Tang et al., 2006; Dong et al., 2008; Fu et al., 2010; Sorgenfrei et al., 2011), proteins (Byon and Choi, 2006), and bacteria (Villamizar et al., 2008) on account of the high sensitivity and specificity. However, recent studies have revealed the potential cytotoxicity and genotoxicity of carbon nanotubes at the cellular level (Zhu et al., 2007; Allen et al., 2007). Another issue

for carbon nanotubes is the coexistence of metallic and semi-conducting carbon nanotubes in available ensembles, and it is of great challenge to obtain pure metallic or semiconducting nanotubes for the fabrication of field-effect transistors (FETs). An attractive alternative nanocarbon, graphene, has found fascinating applications in biosensor technology because of its large surface area and pronounced ambipolar characteristics (Fu and Li, 2010). Due to its atom-thick nature, the electrical properties of graphene are highly sensitive to the interaction of graphene surface and adsorbed foreign molecules. Graphene FETs fabricated with mechanically-exfoliated graphene or reduced graphene oxide have been used in the recognition of proteins (Ohno et al., 2009), bacteria (Mohanty and Berry, 2008), and single-stranded DNAs (Lin et al., 2010). However, the size of reduced graphene oxide is small ( $\approx$  hundreds nanometers) and the electrical properties significantly vary with the preparation conditions (Su et al., 2009). In contrast, large-area single-layer graphene films grown by chemical vapor deposition (CVD) are more favorable for device fabrication, since the CVD process exhibits better reproducibility compared to the chemical exfoliation process (Li et al., 2009; Reina et al., 2009; Chen et al., 2012).

Detection of DNA molecules in dry state by bottom-gated graphene FETs have been reported, where DNAs act as negative potential gating agents (Lin et al., 2010; Lu et al., 2010). In these devices, the transfer characteristics show resistor-like behaviors (very small on/off current ratio), which can be attributed to the low gate coupling efficiency and the gapless feature of graphene.

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In this respect, our previous results indicated that label-free detection of DNA hybridization can be accomplished using liquid-gated FETs with few-layer graphene sheets prepared by CVD (Dong et al., 2010). The high transconductance and low noise of graphene FETs operated in liquid gating mode make them more attractive for biosensing purposes. So far, the interaction between biomolecules and graphene in aqueous solutions is still not fully understood. This may be figured out by examining the ambipolar characteristics of FETs in details because it is strongly related to graphene/electrolyte interface properties. In this study, we constructed liquid-gated FETs based on single-layer CVD graphene. The transfer curve change upon DNA immobilization and hybridization under various environments are investigated. These devices can achieve high sensitivity to detect as low as 1 pM ( $10^{-12}$  M) of target DNA. Meanwhile, the material of gate wires, the concentration of buffer solution, and the surface condition of graphene would obviously affect the sensing performance and surface charge state of the devices. The results shown in this contribution provide better understanding and useful information for the design of graphene-based DNA sensors.

## 2. Material and methods

### 2.1. Preparation and transfer of CVD graphene

Centimeter-scale graphene films were grown by CVD on 25  $\mu\text{m}$  copper foils (Alfa Aesar, item no. 13382, purity 99.8%). The tube furnace was preheated to 1000 °C under  $\text{H}_2$  flow to remove the native oxide of copper, and then a mixture of 60 sccm  $\text{CH}_4$  and 15 sccm  $\text{H}_2$  was introduced into the system to grow graphene. A transfer process was carried out to separate graphene from the foil by dissolution of Cu and put on insulating substrates using poly(methyl methacrylate) (MicroChem, PMMA 950K A4) as a capping layer. Firstly, PMMA was spin-coated on graphene/copper sheets, and then copper was etched in ferric nitrate solution (50 g/L, J.T.Baker ACS reagent, 98.0%). A transparent PMMA/graphene thin film can be obtained after removal of copper and cleaning. The films were transferred onto  $\text{SiO}_2$  (300 nm)/Si substrate, and PMMA was dissolved in hot acetone (60 °C) overnight. In order to ensure no PMMA remained on the surface, graphene films were annealed at 450 °C in a mixed atmosphere ( $\text{H}_2$ : 20 sccm + Ar: 80 sccm) to decompose the polymers.

### 2.2. Transistor fabrication and characterizations

For device fabrication, silver paint (PELCO<sup>®</sup>, item no. 16034) was spread onto graphene films with  $1 \times 1$  cm in area set on  $\text{SiO}_2$  (300 nm)/Si substrate to make source and drain electrodes with diameter of 3 mm. The source and drain electrodes were protected from solution by covering with silicone rubber (Dow Corning<sup>®</sup> 3140) and a reservoir ( $8 \times 8$  mm in area) was also built in the same way to hold electrolyte. The test solutions were dropped on the surface of graphene from a micropipette and kept in silicone rubber reservoir. The size of the whole device is  $1.5 \times 1.5$  cm. Silver, graphite, and platinum wires (diameter: 1 mm) were used as the gate electrode, respectively. Single-stranded DNA molecules (Sigma Aldrich) with the sequences: 5'-AGG TCG CCG CCC-3' (as probe) and 3'-TCC AGC GGC GGG-5' (as complement "target") were tested. DNAs were dissolved to different concentrations in phosphate buffered saline (PBS, Uni-Region Bio-Tech). The composition of  $10 \times$  PBS is 1370 mM NaCl, 27 mM KCl, 43 mM  $\text{Na}_2\text{HPO}_4$ , and 14.7 mM  $\text{KH}_2\text{PO}_4$ .

The transfer characteristics of liquid-gated graphene FETs were measured by semiconductor parameter analyzer (Keithley, Model 4200-SCS). The liquid-gate voltage was controlled in a relatively

narrow range to avoid any side effects. Atomic force microscopy (AFM) images were taken by Veeco Dimension-Icon system. The quality of graphene films were determined by confocal Raman microscopic system (NT-MDT, laser wavelength: 473 nm, laser power: 0.5 mW, spot size:  $\approx 0.5 \mu\text{m}$ ). Silicon peak at  $520 \text{ cm}^{-1}$  was utilized as reference for wavenumber calibration.

## 3. Results and discussions

### 3.1. Configuration of liquid-gated graphene FETs

Single-layer CVD graphene was grown on copper foils at 1000 °C using  $\text{CH}_4/\text{H}_2$  gases as described elsewhere (Su et al., 2011; Lu et al., 2012). The graphene/Cu foil films were spin-coated with a supporting layer of PMMA, followed by etching Cu in  $\text{Fe}(\text{NO}_3)_2$  solution. The PMMA-supported graphene was then transferred onto insulating substrates, followed by removal of PMMA using acetone. The inset of Fig. 1a shows a photograph of a graphene sheet with  $1 \text{ cm}^2$  in area set on  $\text{SiO}_2$  (300 nm)/Si substrate. In Fig. 1a, Raman spectrum for as-transferred sample exhibits features of high-quality single-layer graphene: a symmetric 2D-band ( $\approx 2700 \text{ cm}^{-1}$ ) with a full width at half maximum of  $30.2 \text{ cm}^{-1}$  and a high  $I_{2D}/I_G$  ratio (1.95) (Li et al., 2009; Reina et al., 2009). After thermal cleaning in  $\text{H}_2/\text{Ar}$  environment (20/80 sccm) at 450 °C, a blue shift in G-band (from 1588.6 to 1592.0  $\text{cm}^{-1}$ ) and 2D-band (from 2701.9 to 2716.9  $\text{cm}^{-1}$ ) occurs, indicating that graphene is *p*-doped by annealing (Ryu et al., 2010). Some defects may be introduced to graphene by thermal treatment, resulting in the appearance of a weak D-band (at 1361.5  $\text{cm}^{-1}$ ) for the annealed sample.

The configuration of our graphene device is schematically shown in Fig. 1b. The liquid-gated FETs are fabricated by forming source and drain electrodes on graphene using silver paste. The silicone rubber is applied to cover the electrodes for the isolation of electrodes and solutions, and an external conducting wire is employed as a gate electrode. The conductance between source and drain varies in response to the surface electric potential of graphene. And the gate electrode coupled through the liquid electrolytes is used to control the on and off switching of the devices (Patolsky et al., 2006). The transfer curves (drain current  $I_d$  versus gate voltage  $V_g$ ) of the liquid-gated FETs with as-transferred and annealed graphene films are recorded in phosphate buffered saline (PBS) solutions. In Fig. 1c ambipolar characteristics can be clearly observed when a small range of gate voltage (from  $-0.1$  to  $0.8$  V) is applied to the solution. The charge neutrality point ( $V_{\text{CNP}}$ : the applied gate voltage corresponding to the minimum conductance) of the devices made of as-transferred and annealed graphene are at  $V_g = 0.21$  and  $0.52$  V, respectively. The right shift of  $V_{\text{CNP}}$  confirms the observation in Fig. 1a that the carrier density of graphene is increased (*p*-doped) after annealing.

### 3.2. Effect of gate materials

The gate electrodes made from different materials are examined. Fig. 2a compares the transfer curves of a graphene FET operated with various gate electrodes. When a device is gated by a silver wire, natural graphite needle, and platinum filament, their  $V_{\text{CNP}}$  are 0.12, 0.20, and 0.94 V, respectively. The applied  $V_g$  makes free mobile ions in PBS form an electrostatic double layer between graphene and electrolytes. The electrostatic double layer works as a top-gate dielectric layer ranging from a few angstroms to several nanometers in thickness described by the Debye-Hückel equation (Ohno et al., 2009). The potential across electrostatic double layer and graphene is determined by  $V_g$  and the interface voltage between gate electrode and electrolytes. Since the work function value is determined by the material used, the

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