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Nucleobase adsorbed at graphene devices: Enhance bio-sensorics

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Graphene as a good material for sensing single small molecules is hardly believed to identify bio-molecules via electrical currents. This is because bio-molecules tend to bind to graphene through non-covalent bonds, such as π-π stacking interaction, which is not customarily considered to induce a clear perturbation of the graphene electronic structure. In contrast to these expectations, we demonstrate that oxygen in nucleobases adsorbed on graphene with π-π stacking interaction can clearly alter the electric current even in water at room temperature. This property allows us to devise the strategies employing graphene as material of choice in bio-sensorics, bio-chips. © *2012 American Institute of Physics*. [doi:10.1063/1.3681579]

Ability to detect single bio-molecules with high accuracy and efficiency is of central importance in many areas of biology, chemistry, and environmental science.[1–7] Efficient bio-sensors are expected to contribute to the improvement of medicine and medical treatment.[3] It is, however, uncertain whether traditional chemical techniques can be simultaneously fast and inexpensive.[4] Nano-materials can form an excellent technological platform for single-molecule recognition due to their extreme sensitivity of the electron-transport properties in confined materials to external perturbations.[8–12]

Recently, graphene nano-ribbon (GNR) has emerged as suitable candidates for making sensors for single small molecules,[13] such as H_2, H_2O, and NO. The concept is based on measuring a variation in the source-drain current of a GNR-based field-effect transistor originating from the covalent bond formed between the molecule to be detected and a defect (or an edge) of GNR. However, few reports exist on the use of GNRs as bio-sensors. One of reasons for this lack of information is that bio-molecules do not usually bind to GNRs via covalent bonds, meaning that the electrical perturbation induced by a bio-molecule on a GNR is too weak to be detected. Although graphene has been proposed for DNA sequencing by adsorbing single-stranded DNA (ssDNA) via π-π stacking with photosignal,[14] conventional wisdom suggests that the stacking interaction, a typical non-valence bond, is hardly expected to be the basis of devices with clear electrical responses.

In this letter, we show an unexpected observation that nucleobases can induce a distinguishable signal in the electric current through a GNR even in water at room temperature. Further analysis reveals the oxygen in the nucleobases is inducing such electronic signal, while still the π-π stacking interaction exploited to mechanically stabilize the bio-molecules on the device.

A seven-armchair GNR was applied for our conducting channel. Along the small ends, the lattice had a zigzag configuration, and it was connected by sulfur atoms to the hollow sites of the Al(111) electrodes. These formed the device[15] for studying the effects of nucleobases on GNR. Then we placed a nucleobase (adenine A, thymine T, guanine G, or cytosine C) in the center of the nano-ribbon and performed geometry optimization based on density functional theory (DFT) as implemented in the SIESTA package[16] without allowing relaxation of the device itself (only the nucleobase was allowed to relax). Figure 1 illustrates the final conformation of an adenine on GNR, showing that the adsorbed nucleobase aligned nearly parallel to the nano-ribbon surface. To clearly present the parallel alignment, we calculated the averaged distance between the atoms in the nucleobase and the GNR surface. The distance fluctuations were only ± 0.1 Å for A and C, ± 0.4 for T, and ± 0.2 for G with an average distance of 3.0 Å for all nucleobases. The weak fluctuations strongly indicate that the nucleobases are parallel to the GNR surface.

To investigate the adsorption stability, we calculated the adsorption energy of each nucleobase on GNR by the formula $E_{\text{adsorption}} = -[E(\text{nucleobase} + \text{device}) - E(\text{nucleobase}) - E(\text{device})]$. From the results reported in Table I, we can

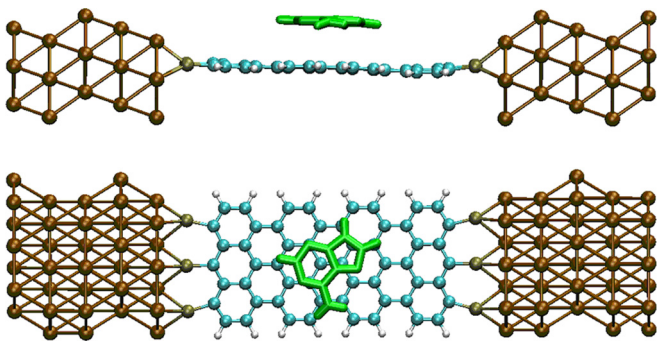

FIG. 1. (Color online) Molecular geometry of the GNR-based device with a color code: Al = brown, C = light blue, H = white, S = yellow. An adenine molecule (green fragment) is adsorbed to the GNR. The upper panel shows a side view, and the top view is in the lower panel (enhanced online) [URL: http://dx.doi.org/10.1063/1.3681579.1].

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TABLE I. Adsorption energy ($E_{adsorption}$) of a nucleobase (A, T, G, or C) on the GNR-based device.

	Adenine	Thymine	Guanine	Cytosine
$E_{adsorption}$ (eV)	0.624	0.649	0.823	0.620

see that all of the adsorption energies are greater than 0.6 eV. Considering the average kinetic energy of one base at room temperature is less than 0.1 eV, we conclude that all of the nucleobases are efficiently confined to GNR.

For understanding the origin of this substantial confining energy, we calculated the electronic-density re-distribution over GNR induced by the adsorbed nucleobase. This value was defined as

$$\Delta D = D(\text{nucleobase} + \text{device}) - D(\text{nucleobase}) - D(\text{device}),$$

with D indicating the electron charge density. The results are presented in Fig. 2, in which the blue regions indicate $\Delta D > 0$ (the electronic density is enhanced by the adsorption) and the red regions indicate $\Delta D < 0$ (the electronic density is reduced by the adsorption). We observed that the blue cloud appeared clearly between the nucleobase and the GNR, indicating that the electron density in this area increased as a consequence of the adsorption. This result provides evidence for a π-π stacking interaction between the p-orbitals residing on the nucleobase aromatic rings and the delocalized π-electrons of graphene.[17]

Next, we studied the effect of the adsorbed nucleobase on the electronic transport property of GNR, based on DFT and the non-equilibrium Green's function method (NEGF-DFT), as implemented in the Smeagol code.[18] We introduced bias voltages (V_{bias}) between the two terminals of the device in the interval of 0.00-0.60 V and explored five different cases: (a) a pristine GNR; (b) a GNR with an adsorbed adenine (A-on-GNR); (c) a GNR with an adsorbed thymine (T-on-GNR); (d) a GNR with an adsorbed guanine (G-on-GNR); and (e) a GNR with an adsorbed cytosine (C-on-GNR).

The results for the transport are presented in Fig. 3(a). The currents are similar for all of the structures when $V < 0.30$ V. After that, the current becomes dependent on the specific case. The saturation current is about 4.1 μA for the pristine GNR and the A-on-GNR after $V = 0.55$ V but drops to about 3.6 μA for the T-on-GNR, the G-on-GNR, and the C-on-GNR. These follow a more general trend in which the currents are almost identical for all of the investigated structures up to voltages of around 0.30 V, after which there are clear differences between A-on-GNR and the structure containing the other nucleobases. The current of A-on-GNR always remains close to the current of the pristine GNR; we conclude that the adenine cannot be detected clearly in this manner. In contrast, the current of the remaining three nucleobases at 0.60 V was approximately 0.5 μA lower than that of the pristine GNR, as shown in Fig. 3(b). Because this difference is considerably larger than the pico-ampere electrical sensitivity for carbon-based two-probe devices,[8] we conclude that T, G, and C are detectable. In what follows, we also show that this result is robust with respect to the thermal motion of the nucleobase in water.

The surprisingly different behavior of adenine relative to the other nucleobases can be traced back to the electronic-density redistribution of the nano-ribbon induced by nucleobase adsorption. We need further analyzing the information in Fig. 2. It is observed that in addition to the blue regions ($\Delta D > 0$) corresponding to the excess of electrons participating in the π-π stacking interaction, there are the depletion regions where $\Delta D < 0$ (red surfaces in the figure). These red surfaces are always localized around the oxygen atoms in the nucleobase, and they are almost absent for adenine. We then conclude that it is the presence of the oxygen in a nucleobase inducing the base electrically detectable. Oxygen produced the largest electrical perturbations over the charge density of the ribbon and then alters the current the most. Thus, although the π-π stacking interaction between the aromatic rings of the nucleobase and the nano-ribbon alone is not sufficient to produce a detectable electrical response in GNR, the presence of oxygen can do it. Expanding on this finding, one can imagine situations in which each different bio-molecule (such as nucleobase) is functionalized with different atoms (or small molecular fragments), yielding distinct and detectable perturbations of GNR. This scheme may represent a valuable tool for individual bio-molecule sensing.

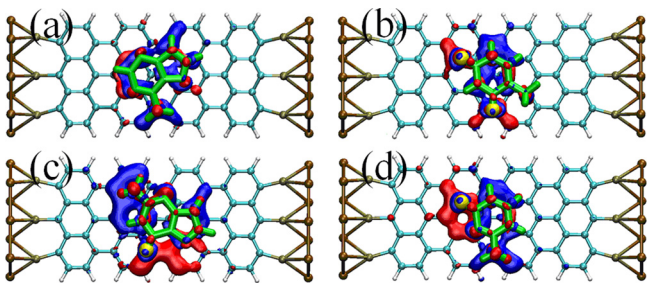

FIG. 2. (Color online) GNR electronic-density re-distribution induced by nucleobase adsorption. The blue cloud denotes regions accepting electrons ($\Delta D > 0$), the red cloud denotes regions losing electrons ($\Delta D < 0$). The four panels represent the four different nucleobases: (a) A, (b) T, (c) G, and (d) C. Color code is the same as Fig. 1. The green fragment over the GNR stands for the nucleobase, in which the yellow sphere denotes the oxygen of the base (enhanced online) [URL: http://dx.doi.org/10.1063/1.3681579.2].

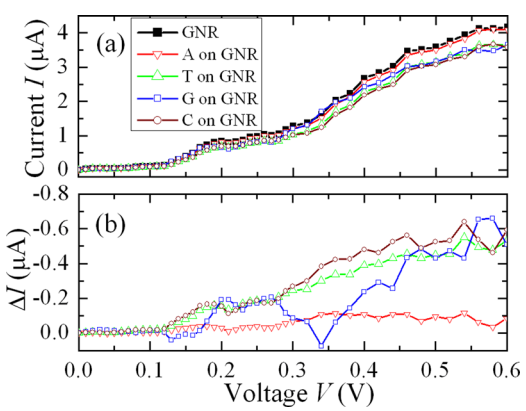

FIG. 3. (Color online) (a) I-V curves for a pristine GNR (■) and GNRs with an adenine (▽), a thymine (Δ), a guanine (□) or a cytosine (○) adsorbed at the center. (b) The current difference (ΔI) between the current though the GNR adsorbing a base and through the pristine GNR.

Finally, we investigated whether thermal noise suppresses our ability to detect the nucleobases. This research was performed with a combination of molecular dynamics (MD) simulations and transport calculations. We concentrated only on C-on-GNR and A-on-GNR. A 2-ns MD simulation was performed with a time step of 2.0 fs.[15] Our results showed the nucleobase (C or A) was efficiently confined to GNR and skated on the surface.[15]

Next, we took one snapshot every 20 ps and calculated the electric current at $V = 0.6$ V for every snapshot. It has been reported that the thermal-motion-induced conformational changes of the nucleobases in water are the dominant source of the noise in the current,[19] while the direct effect of water is mainly that of shifting the conductivity at a given gate voltage due to the dielectric environment,[20] which is expected not to influence the contrast between the transport fingerprints of the different bases. Thereby, just focusing us on the influence of thermal noise on the current signal, we performed NEGF-DFT calculations without explicitly including the water molecules in the simulation cell.

Our results are presented in Fig. 4. In the case of C-on-GNR, the average value of the current was 3.8 μA with an average fluctuation of ± 0.2 μA. The thermal motion of the cytosine in water decreased the detection signal (the difference between the current for the pristine GNR and the current with the adsorbate at 0.6 V) from 0.5 to 0.4 μA. At the same time, the noise due to thermal motion in water at room temperature was modest, ± 0.2 μA, and was smaller than the current difference, which allows nucleobase detection. In the case of A-on-GNR, the average value of the current was 4.2 μA under these conditions, which is similar to the value of the current through the pristine GNR. The average fluctuation was only ± 0.1 μA, smaller than that of C-on-GNR. This demonstrate once again that the influence of the adsorbed adenine on GNR is weak compared to the cytosine, which reflects the rather mild sensitivity of the current to the geometry. The modest noise (i.e., fluctuation) of the current in both cases can be understood by the narrow full-width at half maximum of the atomic distribution in the direction vertical to the GNR surface[15] due to the thermal motion in water at room temperature.

Recent reports[14] have established that ssDNA can be stably adsorbed on graphene via π-π stacking interaction between the graphene and the nucleobases in the sequence, while the same is not true for double-stranded DNA (dsDNA). This difference suggests that a ssDNA fragment adsorbed on graphene can be removed by hybridization with its complementary strand. Because a similar mechanism can operate here, we envision a three-phase DNA detector operating as follows. First, a ssDNA segment is stably adsorbed on GNR. Next, it is detected via GNR as discussed herein. Finally, the ssDNA is removed by using its complementary strand, which is also detected by GNR. Therefore, with the help of the GNR's electric properties and the complementary ssDNA strand, we can determine the identity of the ssDNA sequence. It is noted that other adsorbants can hardly show this kind of behavior on the surface of graphene.

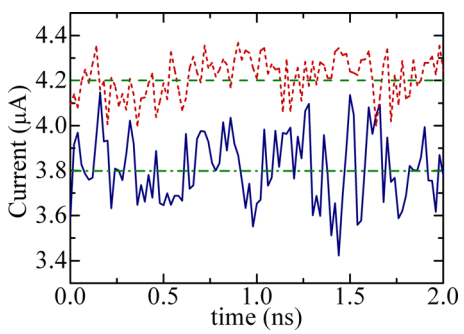

FIG. 4. (Color online) Electric current for C-on-GNR (blue solid line) and A-on-GNR (red dashed curve) at 0.6 V for the different molecular configurations obtained from a 2-ns molecular dynamics simulation. Data are plotted as a function of time with a resolution of 20 ps. The green horizontal dotted-dashed line indicates the average value of the current for C-on-GNR (A-on-GNR).

In summary, the effect of the adsorbed nucleobases on the electronic transport properties of GNRs has been investigated. On one hand, we find that adsorption of adenine alters little the electric current and therefore the nucleobase is undetectable. In contrast, on the other hand, the adsorption of T, G, and C surprisingly produces a clear fingerprint in the *I-V* property at 0.6 V, with the current being about 0.5 μA lower for the GNR with the adsorbed nucleobase than the current of the pristine GNR. Remarkably, this fingerprint is sufficient for detection and is rather robust with respect to thermal motion in water at room temperature. We have traced these observations to the presence of oxygen in the nucleobase. This discovery leads to the concept of deliberately functionalizing nucleobases to induce the distinguishable electronic signal on graphene, while still exploiting the π-π stacking interaction for mechanically stabilizing the biomolecules on the device. Considering that ssDNA can be dissociated from GNR by hybridization with its complementary strand, i.e., our GNR-based sensors are re-usable, we envision that this nanostructure may become the basis for biosensors, bio-chips, and even the protocols for fast DNA sequencing.

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[15]See supplementary material at http://dx.doi.org/10.1063/1.3681579 for the setup of the device (SI); the details of the corresponding calculations (SII); the details of the corresponding calculations (SIII); the details of molecular dynamics simulations (SIV); and the further discussion of nucleobase skating on the GNR surface (SV).
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