Interaction of DNA with Single-Walled Carbon Nanotubes: Implication to the Bio-Sensors

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ABSTRACT

The sensing mechanism of DNA with carbon nanotube–field effect transistor sensors is investigated by first-principles electronic structure calculations. We have investigated the interaction of individual DNA nucleobases (especially guanine and cytosine) with single walled carbon nanotubes (SWNTs), and compared the binding energies of various configurations including π-stacking and direct bonding ones. Secondly, we have also simulated the interaction of the thiolated nucleotides with gold nanoparticles. Comparing the calculated results of above two systems, we tried to propose the mechanism of sensing the binding of single-stranded DNA (ss-DNA) on the SWNTs and the hybridization of complementary DNA on the pre-bound ss-DNA.

Keywords: CNT, DNA, electronic structure, calculation, sensing mechanism

1 INTRODUCTION

A field effect transistor (FET) sensor consisting of a bare single-walled carbon nanotube (SWNT) has been actively studied with a view to using them in ultrasensitive chemical and biological sensors. Electronic detection of analyte can be advantageous in a sense that it can be easily miniaturized for point of care testing, and does not require additional expensive equipments. Recent years have seen a large number of research results reporting the highly sensitive detection of bio-molecules by using one-dimensional nanowires or nanotube field effect transistors. Already, the detection of single virus, small molecules and multiplexed detection of tumor markers using Si nanowires [1,2] and highly sensitive detection of proteins using single walled carbon nanotube field effect transistors (SWNT-FET) were successfully demonstrated as well.[3-6]

SWNTs functionalized with biomolecular complexes hold great promise as molecular probes and sensors targeted for chemical species and biological agents that interact weakly or not at all with bare carbon nanotubes.[7,8,9] Among the molecules that can bind to the surface of SWNTs, the most widely used one is DNA, [10,11,12] which is regarded as an excellent candidate for the molecular targeting layer because it can be easily engineered, using directed evolution, for affinity to a wide variety of targets, including small molecules and specific proteins. DNA-coated CNTs are attractive materials for a range of applications, such as highly specific nanosensors,[13] or as a vehicle to disperse, efficiently separate CNTs according to their structures and pattern CNTs for microelectronics.[14] There was also a theoretical suggestion that it is possible to discriminate between nucleosides on CNTs based on measurement of electronic features.[15]

Recently, Star *et al*. demonstrated the label-free detection of DNA hybridization using nanotube network transistors.[12] In their case, the probe single stranded DNAs (ssDNA) were non-specifically adsorbed on carbon nanotubes by π-stacking interaction between DNA bases and the sidewalls of SWNTs. They reported that the current between the source and drain in CNT-FET decreases and the threshold voltage (V_{th}) shifts to the negative values when the probe ssDNA is stacked onto the CNT surface. The current is further reduced and the V_{th} goes into more negative values when the complementary DNA hybridizes with the pre-bound ssDNA. That is to say, electrical detection is a useful technique not only to detect the interaction between the ssDNA and the CNT wall but also to identify the hybridization between the target DNA with the complementary ssDNA which is non-specifically adsorbed on carbon nanotubes.

Such non-specifically adsorbed ssDNA molecules cannot easily bind with their complementary strands; one needs more robust immobilization method for capture probes onto the surface of CNT. In that respect, we have performed some experiments for label-free detection of DNA hybridization with the Au-cluster decorated SWNT-FETs as a sensor platform. Thiolated ssDNA binds with the Au clusters deposited on SWNTs, and Au clusters do not disturb the excellent electrical properties of SWNTs. In that way, we can covalently attach DNA capture probes without disturbing the excellent electrical characteristics of SWNTs, and measure electrical response upon hybridization. The transport behavior is different from that of non-specifically adsorbed DNA-CNT by π-stacking interaction between DNA bases and the sidewalls of SWNTs. Upon deposition of Au clusters, the current is increasing and the V_{th} shifts into positive values compared with that of unmodified CNT. When the single stranded DNA oligomers covalently attached to the Au clusters deposited on SWNT-FET, the

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decrease of conductance occurs. The current between the source and drain in CNT-FET further decreases when the DNA hybridization occurs between the probe ssDNA pre-bound onto Au cluster and the target complementary DNA. The result looks inconsistent with that previously reported.[12]

In this paper, we will show the theoretical investigations to resolve the apparent inconsistencies in the transport characteristics experiments and to better understand the DNA sensing mechanism of CNT-FET sensors by first-principles electronic structure calculations. Firstly, we have discussed the interaction of nucleobases (especially guanine and cytosine) with CNTs, and compared the binding energies of various configurations including π-stacking and direct bonding ones. Secondly, we have also simulated the interaction of the thiolated nucleotides with gold nanoparticles. The gold nanoparticle is used not only as a sensitivity enhancer of SWNT-FET sensor but also as a receptor of DNA via alligating clip atom, sulfur. Comparing the calculated results of above two systems, we tried to propose the mechanism of sensing the binding of single-stranded DNA (ss-DNA) on the SWNTs and the hybridization of complementary DNA on the pre-bound ss-DNA.

2 COMPUTATIONAL METHODS

We attempted to explain the changes in the *I-V* characteristics of CNT-FET sensor that occur as a result of DNA-CNT and DNA-DNA interactions by carrying out a series of first principles calculations. The calculations were carried out in the framework of density functional theory with a plane wave basis set. To obtain stable atomic geometries and binding energies, we used the Vienna *Ab initio* Simulation Package (VASP)[16] with ultrasoft pseudopotentials.[17] This approach makes carrying out numerous computations feasible even for systems with a large number of atoms per unit cell. We expanded the electronic eigenstates in plane waves up to a maximum cutoff energy of 287 eV. For some of the calculations, the cutoff energy was increased up to 29.1 Ry (396 eV) to check the convergence of the results. Further, we determined the exchange-correlation potential within the generalized gradient approximation (GGA)[18] and chose only Γ point in the Brillouin zone for k-point mesh.

3 RESULTS AND DISSCUSSIONS

3.1 Non-specific Binding

For the modeling of non-specific adsorption of DNA on CNTs by π-stacking interaction between DNA bases and the sidewalls of SWNTs, only the fragmented DNA nucleobases are used because of the computing power limit. Since only the semiconducting CNTs are used in SWNT-FET sensors, we chose a (10, 0) zigzag nanotube. In order to model the interaction between isolated nucleobase and the CNT, we put a (10, 0) CNT, which has the nucleobase (guanine or cytosine) nearby, in a supercell of size 30 Å x 30 Å x 25.7 Å, which contains twenty-four layers of CNT along the tube axis (z-axis).

We have performed a series of calculations to determine the possible adsorption structures of guanine or cytosine on the CNT, including not only the π-stacking geometries but also the line bonding, where the plane of nucleobase is not parallel to the CNT wall. The optimized geometries of stable configurations obtained in calculations both in π-stacking and line bonding are showed in Figure 1. In line bonding geometries the specific atoms in nucleobases bind with the carbon atoms in CNT wall. The calculated binding energy and the nearest neighbor distances are tabulated in Table 1. Previous reports discussed only about π-stacking configurations, but the binding energies of line bonding geometries are comparable. Considering the small binding energy difference, the DNA will be in multi-configuration binding geometries on CNT surface including both π-stacking and line bonding, in real experimental situations.

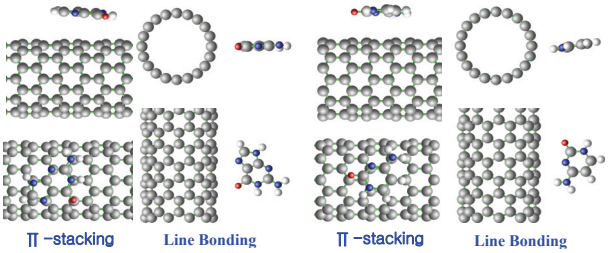

Figure 1: The stable configurations of guanine (left) and cytosine (right) on the single walled carbon nanotube surface.

base	Config.	E_b (eV)	d(base-CNT) (Å)
guanine	π-stacking	0.121	3.3
	Line bonding	0.115	2.9
cytosine	π-stacking	0.100	3.3
	Line bonding	0.148	2.6

Table 1: The binding energies (Eb) in the nearest neighbor distance between the DNA and the CNT wall.

In order to explain the conductance change by the DNA-CNT interaction and the DNA-DNA hybridization, we have investigated the electronic structure changes by the adsorption of nucleobases onto the surface of CNTs. There are various scenarios on the sensing mechanism of CNT-FET sensors, including the gap opening at Fermi energy of metallic nanotubes upon metal adsorption,[19] orbital hybridization between adsorbates and CNT[20], Schottky barrier formation and modifications by work function change upon analyte adsorption[21], and charge transfer between adsorbed species and the CNT.[22] Among them, the charge transfer scheme is the simplest mechanism and applied to the wide variety of sensing mechanisms from gas sensor[22] to the biological detector.[23] To determine the amount of charge transfer, we have calculated the charge

density difference, Δρ, which is defined as the subtraction of sum of charge densities of consitituent agents from that of combined total system;, i.e., $\Delta\rho = \rho_{total} - \rho_{CNT} - \rho_{base(G\ or\ C)}$ is. The atomic geometries of the separated nucleobases and CNT are frozen in that of combined systems. The *xy-integrated* charge density difference Φ(z) is shown in Figure 2. The amount of charge transfer from the nucleobases to the CNT is -0.08 electrons for the guanine and 0.01 electrons for the cytosine. Since the amount of charge transfer is very small, the transferred charge effect on the transport characteristics of CNT-FET is negligible. Moreover, the sign of transferred charge is opposite in the guanine and the cytosine, so the effect of charge transfer is further compensated by different nucleobases in the native DNA, which has the random base sequence. The current variation in the non-specific adsorption experiments is explained by the negative gating effect exerted on the CNT by the negatively charged DNA backbone, PO_4^-. Upon hybridization, the negatively charged backbone of target DNA is added to that of previously stacked probe DNA, so the threshold voltage shifts into more negative values.

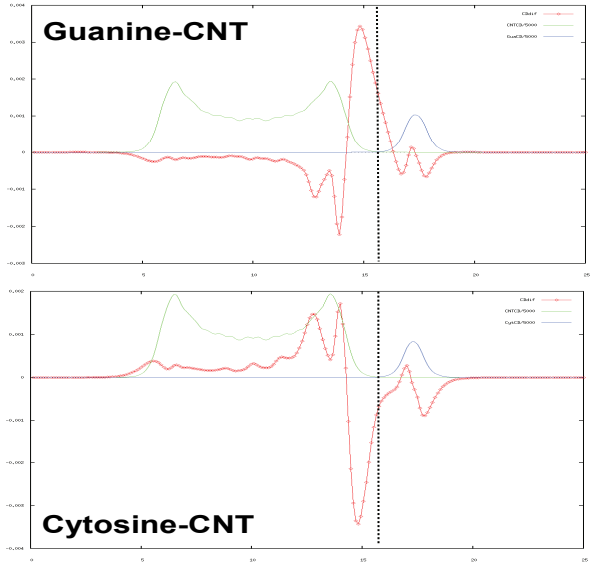

Figure 2: The calculated *xy-integrated* charge density difference Φ(z) for guanine (upper) and cytosine (lower) adsorbed CNT.

3.2 Specific Binding with Au Cluster

For the modeling of specific binding of thiolated DNA with Au cluster, we have used thiolated nucleotide monophosphate composed of two guanine bases which will bind to Au cluster via thol ligand. The hybridization effect is also investigated by hybridization with the complementary nucleotide composed of two cytosine bases. We have used only Au atom instead of cluster, because of the stable geometry of Au cluster is controversial. The obtained fully optimized structures of probe DNA (thiolated GG nucleotide) with Au atom and after hybridization with CC nucleotide are shown in Figure 3 (a) and (c), respectively. The atomic distance is 2.26 Å between gold and sulfur atom and is 2.07 Å between sulfur and phosphorus atom. The energy gain obtained by hybridization of guanine and cytosine is 1.265 eV and three hydrogen bondings are generated in G-C pair and the distances between O and H are 1.67 and 1.78 Å, and that between N and H is 1.82 Å. The atomic structure change upon hybridization is very small and the energy gain of structure relaxation is only 0.284 eV.

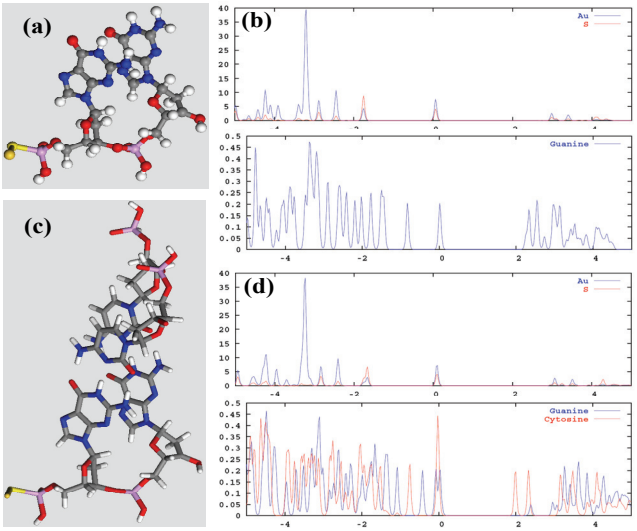

Figure 3: The fully optimized atomic geometries of thiolated nucleotide composed of two guanine bases binding with Au atom (a) and hybridized one with nucleotide with 2 cytosine bases (c). The calculated site-projected density of states (DOS) are also plotted in (b) and (d).

The conductance increase of CNT-FETs upon Au cluster deposition is well explained by the charge transfer driven by work function difference. Since the work function of metal Au (≈ 5.2 eV) is higher than that of semiconducting CNT (≈ 4.7 eV) [24] the charge transfer occurs from the CNT to the Au cluster, thus create hole carriers in the semiconducting CNT. It is well known that hole is the majority carrier of semiconducting CNT, so the charge transfer occurred by deposition of Au cluster results in the increase of current carriers and finally the conductance increase. Encouraged by this successful explanation of conductance increase upon Au cluster deposition, we will attempt to explain the conductance decrease upon binding of probe ssDNA and the conductance decrease with hybridization by electronic density redistribution. In order to investigate the electronic structure change upon hybridization, the calculated density of states (DOS) of probe DNA only and hybridized nucleotide pairs are shown in Figure 3 (b) and (c), respectively. From the calculated partial DOS plot, it is evident that the lowest unoccupied molecular orbital of hybridized GG-CC pairs is mainly located in the cytosine,

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and the conduction band is lowered compared with that of GG nucleotide only. Since the work function of metal is generally higher than that of organic molecular systems, the thiolated nucleotide provides electrons to the Au cluster. The Au cluster interacting with ssDNA gets some electrons from DNA, thus less electrons are taken from the CNT. This results in the decrease of hole carriers in the CNT (or less hole carrier generation by Au cluster), and finally the conductance decrease.

When the ssDNA hybridizes with complementary DNA, a number of hydrogen bonding is generated. For the pairing of guanine-cytosine, three hydrogen bonding is generated, and two bonding is needed for adenine-thymine pair. The additional bonding needs some more charge density between interacting atoms. The charge redistribution upon G-C hybridization is investigated by plotting the charge density difference. As shown in Figure 4, electron-density buildup occurs in hydrogen bonding regions. The consumption of additional electron in hydrogen bonding results in the smaller amount of electron transfer from the probe DNA (thiolated GG-nucleotide) to the Au cluster when hybridization occurs. The Au cluster needs more electrons to align Fermi level, and take more electrons from the CNT compared with non-hybridized case. This will increase the hole carrier density in the CNT, and finally increase of conductance compared with the CNT-FET interacting only probe DNA case.

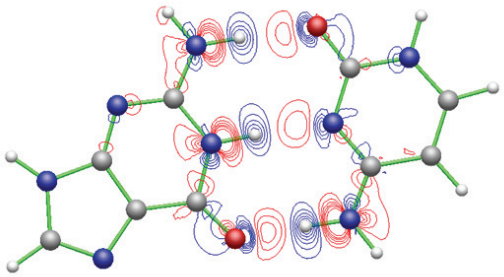

Figure 4: The plot of calculated charge density difference upon G-C hybridization, which is obtained by subtraction of charge density sum of the isolated guanine and cytosine from that of hybridized DNA.

In conclusion, we have successfully explained the sensing mechanism of DNA interaction with the CNT and hybridization with complementary DNA by the charge transfer scheme with the help of electronic structure calculations. Combining a series of calculations, we have settled down apparently inconsistent conductance change of CNT-FET sensor in the non-specific and specific bindings of the DNA on the CNT.

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