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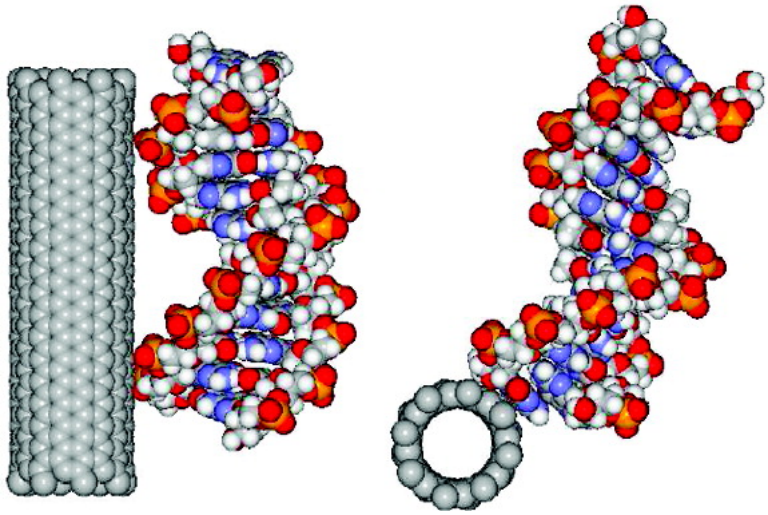

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Simulation of Adsorption of DNA on Carbon Nanotubes

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Abstract: We report molecular dynamics simulations of DNA adsorption on a single-walled carbon nanotube (SWNT) in an aqueous environment. We have modeled a DNA segment with 12 base pairs (Dickerson dodecamer) and a (8,8) SWNT in water, with counterions to maintain total charge neutrality. Simulations show that DNA binds to the external surface of an uncharged or positively charged SWNT on a time scale of a few hundred picoseconds. The hydrophobic end groups of DNA are attracted to the hydrophobic SWNT surface of uncharged SWNTs, while the hydrophilic backbone of DNA does not bind to the uncharged SWNT. The binding mode of DNA to charged SWNTs is qualitatively different from uncharged SWNTs. The phosphodiester groups of the DNA backbone are attracted to a positively charged SWNT surface while DNA does not adsorb on negatively charged SWNTs. There is no evidence for canonical double-stranded DNA wrapping around either charged or uncharged SWNTs on the very short time scales of the simulations. The adsorption process appears to have negligible effect on the internal stacking structure of the DNA molecule but significantly affects the A to B form conversion of A-DNA. The adsorption of A-DNA onto an uncharged SWNT inhibits the complete relaxation of A-DNA to B-DNA within the time scale of the simulations. In contrast, binding of the A-DNA onto a positively charged SWNT may promote slightly the A to B conversion.

1. Introduction

The interaction of biomolecules with single-walled carbon nanotubes (SWNTs) has generated a great deal of interest in the past few years. There are concerns about the biological safety, activity, and compatibility of SWNTs.[1−5] Such issues are relevant to the proposed applications of SWNT in drug or gene delivery[3−9] and any situation that may result in human exposure to SWNTs. Recent work has shown that single-stranded DNA (ssDNA) interacts very strongly with SWNTs; adsorption of ssDNA onto a mixture of different types of nanotubes can be used to separate and purify SWNTs.[10−14] The purification mechanism involves ssDNA wrapping around individual SWNTs, separating them from the bundle and facilitating dispersion into solution. The DNA-wrapped nanotubes can then be separated by their diameters and helicities through ion-exchange chromatography.[11−14] Furthermore, size-exclusion chromatography can be used to sort ssDNA-wrapped SWNTs according to lengths.[15] ssDNA-wrapped SWNTs have been used to probe the excitonic relaxation of (6,5) SWNTs.[16,17] Gigliotti et al.[18] have recently shown that completely random sequences of long ssDNA can be very effective at dispersing SWNTs as long as care is taken to remove complementary strands of DNA. The hybridization of complementary strands was thought to compete with binding to the SWNTs.[18]

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Using SWNTs as biosensors and in other bioengineering applications has recently attracted significant research attention.[2,19−26] Aligned SWNTs have been used in atomic force microscopy as probe tips for imaging biomolecules.[27,28] It has been found that aligned bundles of SWNTs exhibit superior resolution compared with conventional tips when probing DNA fragments.[28] This finding may be employed in techniques for fast haplotyping of DNA.[28,29] SWNTs have been used as DNA immobilization platforms and hybridization detection.[20,25] Strano et al.[26] have monitored a secondary structure conformation change of a 30-base pair (dGdT) DNA by observing changes in the dielectric environment of SWNTs around which the DNA is wrapped. This DNA−SWNT system was shown to be a very sensitive probe of ionic concentration. Notwithstanding the many potential applications of SWNTs with biomolecules, there is a lack of molecular-level information on the thermodynamic, structural, and dynamic/kinetic aspects of SWNT−biomolecule interactions.[30]

Molecular simulations can provide insights into the fundamental interactions between SWNTs and biomolecules. However, there is a relatively small number of papers in the literature dealing with interactions of DNA and SWNTs. Molecular dynamics (MD) simulations of Gao et al.[31,32] indicate that the association between ssDNA and SWNTs is very strong. They found that ssDNA can readily be adsorbed from solution inside a SWNT of appropriate diameter due to the hydrophobic parts of the ssDNA being attracted to the interior of the SWNT. The insertion process for a short ssDNA segment occurs very rapidly, usually within 1 ns. Insertion of ssDNA into SWNTs from solution has subsequently been observed experimentally.[33] Okada and co-workers used a radio frequency electric field to stretch ssDNA and a concurrent DC electric field to provide a driving force for the ssDNA to migrate toward the SWNTs, which were deposited on the anode of the cell. The encapsulation of ssDNA in the SWNTs was observed indirectly, through shifts in the Raman spectra, and directly, through imaging of DNA@SWNT with high-resolution transmission electron microscopy.[33]

Yeh and Hummer studied the electrophoretic transport of ssRNA through a hypothetical SWNT membrane using MD simulations with and without an applied electric field.[34] In the absence of the field the ssRNA was trapped in the SWNTs by hydrophobic forces, even considering the large entropic penalty for confining the ssRNA inside the nanotube. Application of an electric field provided a driving force for translocation of ssRNA through a short SWNT membrane. Translocation rates through the model SWNT membrane were found to be sequence dependent because of different affinities of the base groups with the nanotube.

Lau et al. have used MD to study the encapsulation of canonical double-stranded DNA (dsDNA) into large SWNTs, 30 and 40 Å in diameter.[35] They showed that the structure of DNA is not significantly perturbed if the counterions are included inside the nanotube. If counterions are excluded from the nanotube interior, then the structure of DNA was seen to deviate significantly from either A- or B-form DNA.[35] They did not, however, study the encapsulation process, so it is not known from their calculations if dsDNA will spontaneously adsorb inside the hydrophobic nanotube.

Lu and co-workers have studied a system composed of an infinitely long (periodic) DNA molecule interacting with an array of SWNTs.[36] They used molecular dynamics to optimize the DNA−SWNT complex in the absence of water or counterions. They used hydrogen passivation on the DNA phosphate groups to create uncharged DNA. The electronic structure of the relaxed periodic system was then calculated using a density functional theory-based tight-binding formalism.[37] Their calculations show that (10,0) SWNTs fit inside the major groove sites of DNA and that the resulting system can exhibit states involving charge flowing through both DNA and the SWNTs simultaneously. They speculate that such DNA/SWNT systems could be used as nonvolatile random access memory or for ultrafast DNA sequencing.

Meng and co-workers have investigated the interaction of individual nucleosides with a carbon nanotube in a vacuum, both with and without an externally applied gate voltage.[38] They proposed a scheme to discriminate between different nucleosides on SWNTs based on measurements of electronic features through a local probe such as scanning tunneling spectroscopy. They performed quantum mechanical calculations to demonstrate that the electronic feature measurements can have high efficiency in identifying nucleoside bases. They proposed the use of such systems for ultrafast DNA sequencing using electrical measurements. However, it is not clear if their results can be generalized from individual uncharged nucleosides to charged DNA nucleotides in solution with counterions. In particular, it is not clear that nucleotides in dsDNA will bind to nanotubes in the way that isolated nucleosides in vacuum were observed to bind to nanotubes in the study of Meng et al.[38]

From the above examples it is fairly clear that ssDNA will readily adsorb inside a SWNT and that this is due to ssDNA having exposed hydrophobic sites. The simulations involving dsDNA and SWNTs are not conclusive. The work of Lau and co-workers does not address the question of whether DNA will be attracted to a SWNT, since in their simulations the DNA was constrained to be inside the nanotube.[35] The simulations of Lu et al. do not include water, counterions, or charges on the DNA, so that hydrophobic and electrostatic forces are not considered.[36] It is therefore not clear if the SWNTs will be

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attracted to the major groove sites of the DNA if explicit water, counterions, and charged DNA are included in the system.

The question of whether dsDNA will be attracted to the external surface of an uncharged carbon nanotube in solution has not yet been fully resolved, by either experiments or simulations. The work of Strano et al. indicates that associated poly-(dGdT) does indeed wrap around individual nanotubes.[26] However, poly-(dGdT) cannot form canonical Watson−Cricks base pairs observed in dsDNA but does form weaker G−T wobble pairs.[39] There is some evidence that ssDNA interacts more strongly with SWNTs than dsDNA,[30] but this has not been quantified. One might suppose that the hydrophilic nature of the external surface of DNA would preclude favorable interactions with the hydrophobic nanotube surface. On the other hand, van der Waals attractive forces between DNA and a SWNT might be sufficient to cause the DNA to adsorb on the SWNT. In contrast, positively charged SWNTs would be expected to interact very favorably with DNA, because of the negative charges on the phosphate groups along the backbone of DNA. Nanotubes can be charged in various ways, such as by applying a voltage bias to a SWNT AFM tip or doping nanotubes with *p*-type dopants to produce positively charged nanotubes.[40−42]

In this paper we report simulation results for the interactions of a dsDNA segment in an aqueous solution with a SWNT. The questions we address are as follows: (1) Does dsDNA adsorb on an uncharged SWNT from solution? (2) How does charging the SWNT affect the adsorption of DNA? (3) How does adsorption on a SWNT change the structure of DNA? (4) Does adsorption affect the characteristics of the A to B transition of DNA? Our molecular simulations provide a detailed look at DNA−SWNT interactions for a simple model system consisting of a short 12 base pair DNA molecule interacting with an (8,8) SWNT in a solution of water and counterions.

2. Simulation Methods

We employed the AMBER force field and simulation package,[43] which has been successfully used to study DNA segments and other biomolecules in solution.[43−46] We used an empirical potential for SWNTs similar to that used to study SWNT−water interactions.[34,47,48] We modeled charged SWNTs by introduction of localized partial charges on each carbon atom of the SWNT, as has been done previously.[49]

We have chosen to model a short DNA segment consisting of 12 base pairs, d[CGCGAATTCGCG]$_2$, about 40 Å in length. This segment is known as the Dickerson dodecamer, which has previously been studied using molecular simulations.[50−52] We have studied an (8,8) "armchair" SWNT,[53] 10.7 Å in diameter and 44.3 Å in length (18 unit cells) containing 576 carbon atoms. We have used the 1999 version of the AMBER force field,[43] which is an all-atom potential including van der Waals, electrostatic, bond vibration, bond angle, and dihedral distortion energies, to model the DNA molecule. The carbon atoms in the SWNT were modeled as Lennard−Jones (LJ) particles with a well depth of $\epsilon_C/k_B = 43.2$ K, where k_B is the Boltzmann constant, and a diameter of $\sigma_C = 3.40$ Å.[47] We performed simulations of charged SWNTs with nominal charges on each carbon atom of $q = +0.01e$, $q = +0.05e$, and $q = -0.05e$. The actual charges on each carbon atom for these simulations were slightly different from the nominal charge in order to give an integer total charge on the SWNT. Thus, the total charges on the nanotubes were $+6e$, $+28e$, and $-28e$. This allowed us to maintain charge neutrality of the system by adding an integer number of counterions having integer charge. The actual charges, corresponding nominal charges, and the neutralizing ions added for each system are reported in Table 1. The LJ parameters for Na^+ are $\sigma = 3.328$ Å, $\epsilon/k_B = 1.393$K,[54] and for Cl^- are $\sigma = 3.471$ Å, $\epsilon/k_B = 133.2$K.[55] The values of these parameters are the built-in default values in AMBER 7. The DNA and SWNT were initially placed so that their long axes were parallel to each other in the simulation box for most simulations. The SWNT and DNA were similar in length; the DNA segment has a diameter nearly twice as large as that of the SWNT. The initial distance between the axes of the DNA and SWNT was set to 20 Å; the corresponding average distance between the outside surfaces of the nanotube and DNA was about 9 Å. This distance gave a boundary of about three layers of water molecules between the SWNT and DNA at the start of the simulation, while limiting the simulation box to a computationally manageable size. The DNA/SWNT system was solvated in about 4600 to 5000 water molecules, with a typical starting simulation cell of about $70 \times 65 \times 70$ Å^3. We used the TIP3P potential for water[56] because previous simulations of DNA using the TIP3P potential have been shown to give results in reasonable agreement with experimental data.[45,46] Periodic boundary conditions[57] were applied in all three directions. The solvated box had water buffer layers at least 12 Å thick between the solute surface and simulation box boundary in all three directions. The SWNT carbon atoms were held fixed throughout the simulations by applying a harmonic potential with spring constants of 500 kcal mol^{-1} Å^{-2} on each carbon−carbon bond. The DNA, counterions, and water molecules were free to move. The LJ cross interactions between different atoms were calculated from the Lorentz−Berthelot combining rules. The cutoff distance for LJ interactions was 9.0 Å. Molecular dynamics simulations were performed in the isothermal−isobaric ensemble[58] at 1 bar and 300 K using the AMBER 7 suite of programs.[43] The particle-mesh Ewald method[59] with

Table 1. Nominal Charges, Corresponding Actual Charges, and the Number and Types of Counterions Used in the Simulation

simulation	nominal charge (*e*/C)	actual charge (*e*/C)	counterion	no. of ions used
uncharged			Na^+	22
charged	+0.05	+0.0486	Cl^-	6
	−0.05	−0.0486	Na^+	50
	+0.01	+0.0104	Na^+	16

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a fourth order interpolation and grid spacing of about 1 Å was applied to calculate electrostatic interactions. The real space cutoff in the Ewald sum was set to 9 Å, and the direct sum tolerance was set to 10−5. The SHAKE algorithm[60] was used to constrain the bonds containing hydrogen atoms, while other bonds were modeled by the standard harmonic bond potential employed in the AMBER package. Each simulation included 5000 steps for energy minimization, 40 ps of solvent relaxation, 5 cycles of solute relaxation with each cycle including 1500 steps of energy minimization, 20 ps of equilibration, and 3 to 6 ns of production. A time step of 2 fs was used, as suggested in the literature.[45] The structural configurations were saved every 2 ps. Visualization and analysis of the configurations were performed with the VMD package[61] and the utility packages included in AMBER.

3. Results and Discussion

The exterior surface of the dsDNA backbone is hydrophilic, whereas the interior of the double helix is hydrophobic. The graphene surface of a SWNT is also hydrophobic. We therefore expected that the double helix form of DNA would not readily adsorb onto the external surface of an uncharged SWNT from solution because the desolvation penalty of the hydrophilic DNA surface would be prohibitive. Interestingly, simulations show that one end of the Dickerson dodecamer adsorbs onto the surface of the SWNT within a few hundred picoseconds. This is due to the hydrophobic nature of the exposed ends of the dodecamer. The hydrophobic interaction between the DNA end base pair planes and the SWNT wall surface drives either of the identical DNA ends to attach to the SWNT. The other end of the DNA segment did not attach to the nanotube. The two ends of the Dickerson dodecamer are symmetric; therefore, there is no preference for which end attaches to the nanotube. The simultaneous attachment of both ends of the segment to the SWNT would require the dsDNA to bend into a horseshoe shape; the bending energy required for this to occur for the relatively short dodecamer is prohibitively high, at least for the B form DNA structure. The hydrophilic backbone of the DNA was not observed to attach to the uncharged SWNT. The adsorption process is illustrated by the dynamics of the DNA/SWNT system displayed in Figure 1a. The normalized distances between the SWNT and three different base pairs on the Dickerson dodecamer are plotted as a function of time for 3 ns. The dashed line is the normalized distance between one end (C1−G24 pair) of the DNA and the SWNT. This distance is seen to drop to about 60% of its initial value within the first 200 ps of the simulation. The opposite end of the segment is seen to move away rapidly from the nanotube (dotted line), while the relative distance between the middle segment and the SWNT increases only slightly (solid line). A snapshot of the ending configuration for the DNA segment adsorbed on an uncharged SWNT is shown in Figure 2a. The water molecules and ions are not shown for clarity.

The geometry of the DNA−SWNT complex for a charged SWNT is different from that of the uncharged case. The DNA segment binds so that the segment axis is roughly parallel to the charged SWNT. The exterior surface of the DNA backbone is attracted to the SWNT by the charges on each of the nanotube carbons. The normalized distance plot is shown in Figure 1b for a SWNT with a nominal charge of $q = +0.05e$ per carbon.

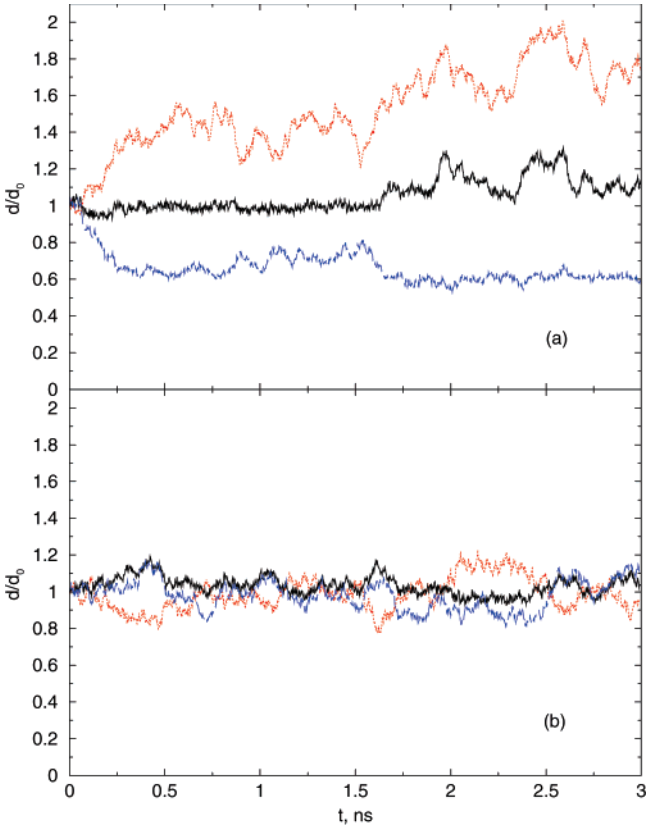

Figure 1. Normalized distance between the centers of mass of the SWNT and the head (C1−G24 pair, red dotted line), tail (G12−C13 pair, blue dashed line), and one middle group (T8−A17 pair, black solid line) of the DNA. (a) DNA on an uncharged SWNT; (b) DNA on a positively charged SWNT ($q = +0.05e$ per carbon atom).

The backbone of the DNA segment is attracted to the charged nanotube wall due to the strong Coulombic interactions between the positive charges on the SWNT and the negatively charged DNA backbone. The corresponding ending configuration of DNA adsorbed on a charged SWNT with a nominal charge of $q = +0.05e$ per carbon is shown in Figure 2b. Close examination of the distance plot reveals that the two ends of the dodecamer undergo a slight "rocking" motion, whereby the head and tail groups are alternately closer and farther from the SWNT center of mass. Additional simulations were performed for DNA with a SWNT with a nominal charge of $q = +0.01e$ per carbon. The general behavior of this system is similar to that of DNA on the SWNT with a charge of $q = +0.05e$ /C.

We have carried out simulations of DNA interacting with a negatively charged SWNT ($q = -0.05e$ per C) in solution. As expected, we observe that the DNA is repelled by the negatively charged nanotube; the entire DNA segment rapidly moves away from the SWNT, and no adsorption is observed.

As noted above, the hydrophilic nature of the charged DNA backbone[62−64] inhibits it from adsorption onto the hydrophobic surface of uncharged SWNTs. Most of hydrophobic sites of a DNA double helix (located on the base rings) are wrapped inside the helices, except for those at the ends of the helices. Therefore, only the exposed hydrophobic base groups at the ends of the DNA segment adsorb onto the uncharged SWNT. In contrast,

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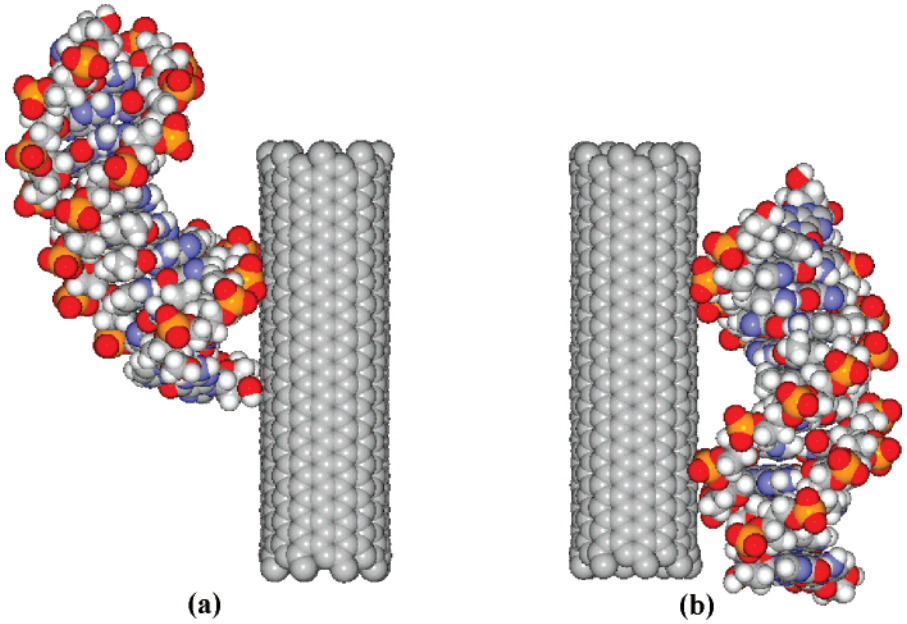

Figure 2. Adsorption geometries of DNA on a SWNT at $t = 3$ ns, for initial configurations with axes of DNA and SWNT parallel to each other. (a) DNA on an uncharged SWNT; (b) DNA on a positively charged SWNT ($q = +0.05e$ per carbon atom).

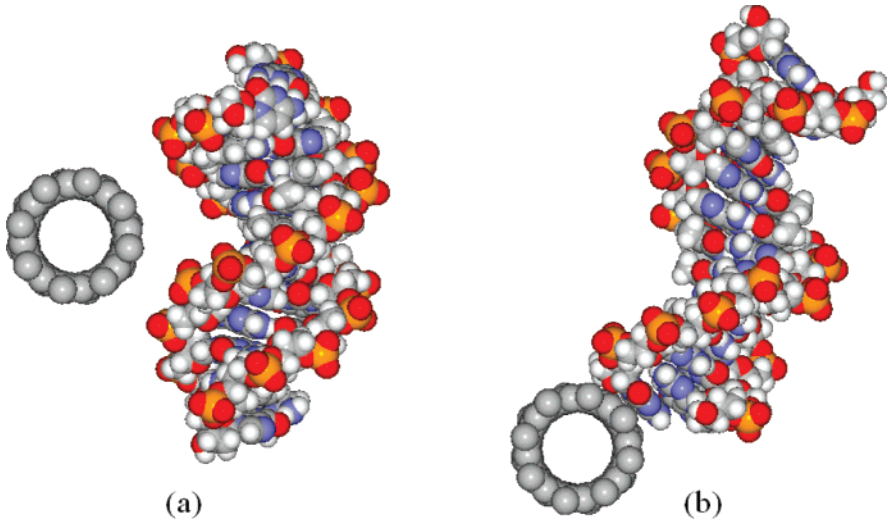

Figure 3. Initial and final geometries of DNA on an uncharged SWNT, for initial configurations with axes of DNA and SWNT perpendicular to each other. (a) The initial configuration; (b) the final configuration at $t = 3$ ns.

ssDNA has been found to interact strongly with uncharged SWNTs, in both experiments[10−14,18] and simulations.[31] The exposed base rings on the nucleotides of ssDNA are available to interact with the hydrophobic surface of a SWNT; ssDNA has experimentally been observed to wrap around SWNTs.[10−14,18] Simulations indicate that ssDNA, which is relatively flexible, can adsorb inside a SWNT with a sufficiently large diameter.[31] However, in our study we found that the double-stranded Dickerson dodecamer does not wrap onto the (8,8) SWNT, at least at short times, because the dsDNA segment has fewer exposed hydrophobic interaction sites, resulting in a relatively weak attraction between the DNA segment and the uncharged nanotube. This result is consistent with the experimental observation by Gigliotti et al. that complementary strands of ssDNA must be removed in order to allow ssDNA to wrap around SWNTs.[18] Likewise, dsDNA does not have a large energetic driving force to adsorb inside a SWNT, although we have not tested this, since the (8,8) SWNT studied in this work is far too narrow to accommodate the dsDNA inside.

We have tested the sensitivity of our results to the initial conditions of the simulation by starting with the DNA segment oriented perpendicular, rather than parallel, to the SWNT, as shown in Figure 3a. The final configuration for the uncharged SWNT case is shown in Figure 3b. We observe a very similar binding pattern to that seen when the DNA and SWNT are parallel—one end of the DNA is bound to the SWNT wall with the other end free. A movie of the binding process for this case is available in the Supporting Information.

We have investigated the change in the structure of DNA upon adsorption onto a SWNT in our simulations. We found that adsorption has a negligible effect on the internal stacking structure and the relative positions of the nucleotides within DNA. This is true for DNA adsorbed on either uncharged or positively charged SWNTs. The average center of mass distance

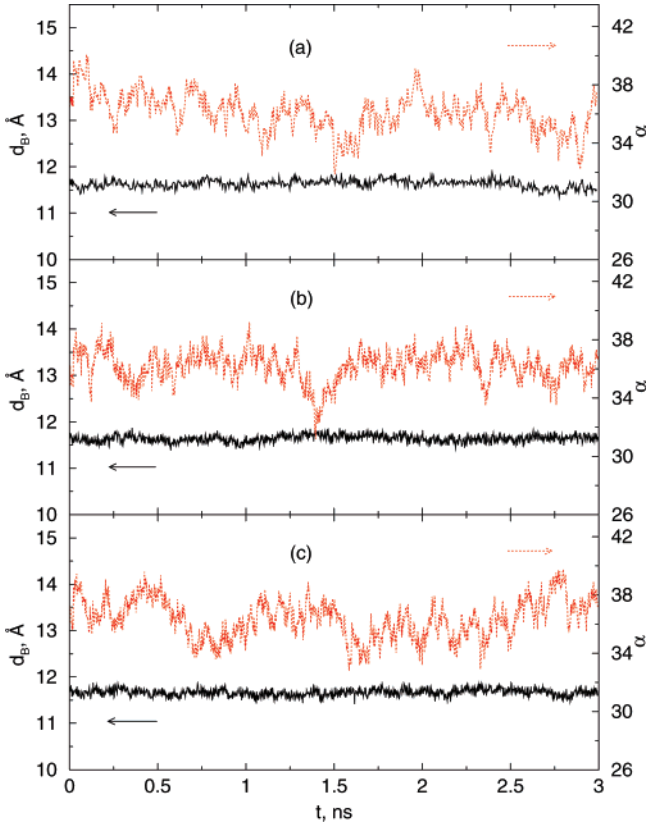

Figure 4. Average center of mass distance between the base pairs (black solid line) and the average rotation angle per base pair (red dotted line) of the DNA strand. (a) DNA in water, without the SWNT; (b) DNA with an uncharged SWNT in water; (c) DNA with a positively charged SWNT ($q = +0.05e$ per carbon atom) in water.

between the 12 base pairs and the average rotation angle per base pair of the DNA are plotted in Figure 4 as a function of simulation time. The structural parameters for DNA adsorbed on either an uncharged SWNT [Figure 4b] or a SWNT with a charge of $q = +0.05e$ per carbon. [Figure 4c] are very similar to the values for DNA in water without a SWNT [Figure 4a]. This indicates that the interaction between the DNA and the SWNT is not strong enough to disrupt either the hydrogen bonds between the base pairs or rotation frame of the double helix, at least over the 3 ns of the simulation.

The A to B transition of DNA is a well-known feature of dsDNA[65−68] that has been successfully observed in MD simulations.[69,70] We have investigated how adsorption of A-DNA onto a SWNT influences the A to B conversion. The spontaneous A to B transformation has been observed to happen in simulations at ambient conditions within a few hundred picoseconds.[45] Our simulation of A-DNA in water without a SWNT have confirmed this. In Figure 5 we present the end-to-end DNA length, L, as a function of simulation time for the DNA starting from the A form. L is defined as the distance between the centers of mass of the two end base pair groups. Hence, A-DNA for the Dickerson dodecamer has $L = \sim 28$ Å, while L for the B-form is about 38 Å. Therefore, the A to B transition can be observed as an increase in L of about 10 Å (about 36%).

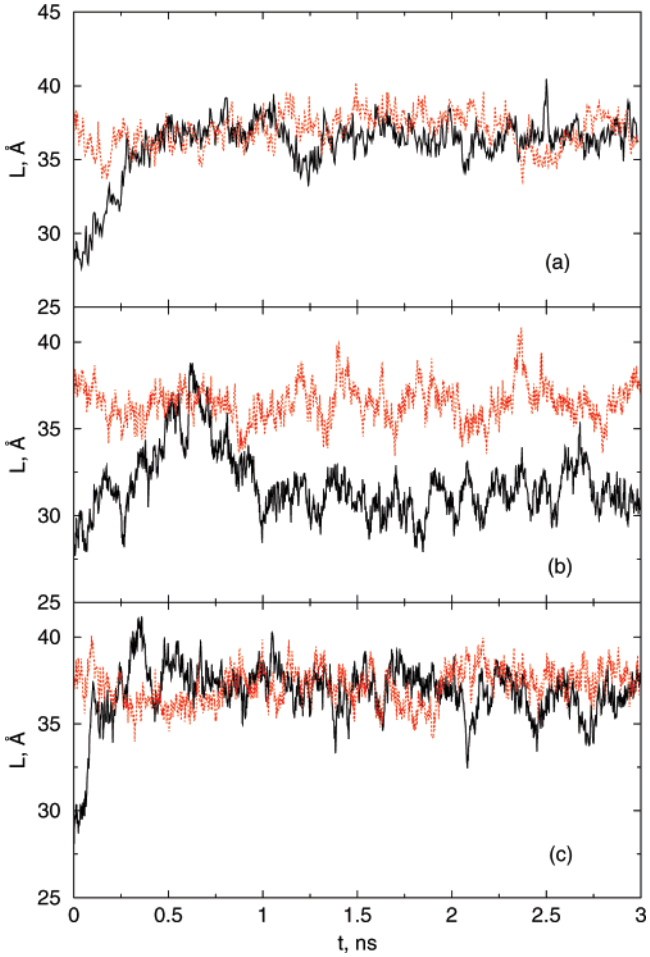

Figure 5. End-to-end length of A-DNA (black solid lines) and B-DNA (red dotted lines) under three different conditions. (a) DNA in water without a SWNT; (b) DNA with an uncharged SWNT in water; (c) DNA with a charged SWNT ($q = +0.05e$/C) in water.

Several parameters may be used to monitor the A−B conversion, including the end-to-end length, the minor groove width, and the base pair inclination.[45] We chose L as the representative indicator because we found that it had much better statistical behavior than the width of the minor groove and the base pair inclination, which we also monitored. These last two indicators gave results that were consistent with L but were plagued by large statistical fluctuations (see Figures S1 and S2 in the Supporting Information for plots of the minor groove width and the inclination angle).

The A to B transition for DNA in water (no SWNT) is plotted in Figure 5a. The evolution of the end-to-end length for A-DNA adsorbed on an uncharged SWNT in solution is plotted in Figure 5b. Note that L initially increases to about the correct length for the B form but then decreases and stabilizes at about $L =$ 31 Å. Hence, it appears that the A−B transformation is frustrated by adsorption onto an uncharged SWNT, at least over a time scale of 3 ns. However, we did note that clear major and minor grooves, which are indicators of the B-form, developed during the simulation. Hence, adsorption of A-DNA onto an uncharged SWNT appears to stabilize a form of DNA that is between the A- and B-forms, at least for short times. The ending configu-

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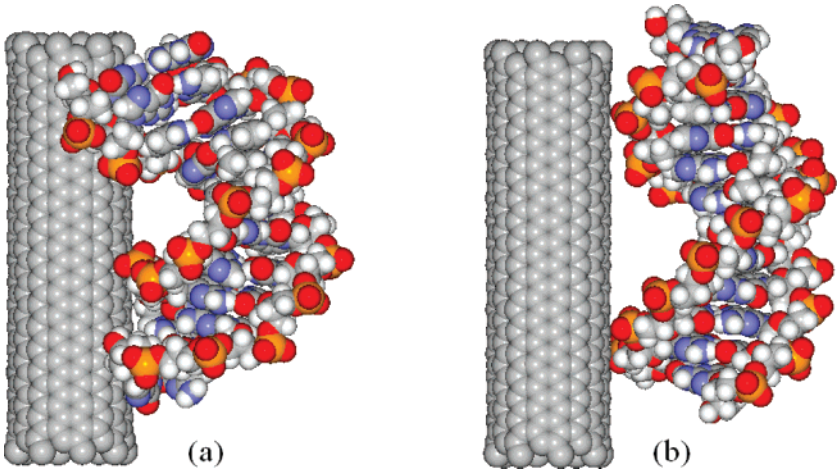

Figure 6. Adsorption geometries of A-DNA on a SWNT. (a) A-DNA on an uncharged SWNT; (b) A-DNA on a positively charged SWNT ($q = +0.05e$/C).

ration of A-DNA adsorbed on an uncharged SWNT is shown in Figure 6a.

The incomplete A−B-form transformation observed in A-DNA/uncharged SWNT can be explained by the adsorption configurational difference between A-DNA/uncharged SWNT and B-DNA/uncharged SWNT. For the B-DNA adsorption on an uncharged SWNT, one end of the DNA binds with the SWNT and the other end is unbound, as can be seen in Figure 2a. When the A-DNA adsorbs on an uncharged SWNT, both ends of the A-DNA bind with the SWNT through a "rocking" motion similar to that noted for B-DNA on a charged SWNT [Figure 1b], but with a much larger amplitude, as seen in Figure 7a. The plane containing the end group base pairs is nearly parallel to the SWNT axis when the A-DNA end groups bind to the nanotube, as seen in Figure 6a. This relative geometry between the A-DNA and the SWNT gives substantial contact between the hydrophobic SWNT wall and the hydrophobic DNA end base pair planes.

Note that the end groups of DNA adsorbed on the charged nanotube are oriented so that the planes of the end group base pairs are roughly perpendicular to the nanotube axis, meaning that the hydrophobic parts of the end groups are actually not binding to the charged nanotube [compare Figures 2b and 6a]. Thus, the apparent "rocking" noted in Figure 1b is very different from that displayed in Figure 7a, where the driving force for the rocking is binding of the hydrophobic end groups to the nanotube. One important difference between the A and B structures is that the two end base pair planes for B-DNA are parallel to each other, while those for A-DNA are tilted toward one another. Therefore, the A-form is able to have both end groups binding to the SWNT without incurring a large bending energy penalty.

We found that the adsorption of A-DNA on a positively charged SWNT ($q = +0.05e$ per carbon) does not inhibit but may promote slightly the A to B conversion. The end-to-end length relaxation of the A-DNA adsorbed on the charged SWNT to the B-DNA form happens remarkably quickly, faster than the conversion of the A-DNA in water without a SWNT [compare Figure 5c to 5a]. This observation is consistent with the claim that SWNTs could cause the A to B transition for some DNA fragments,[30] assuming the nanotubes are charged. The promotion of the A to B conversion on the positively

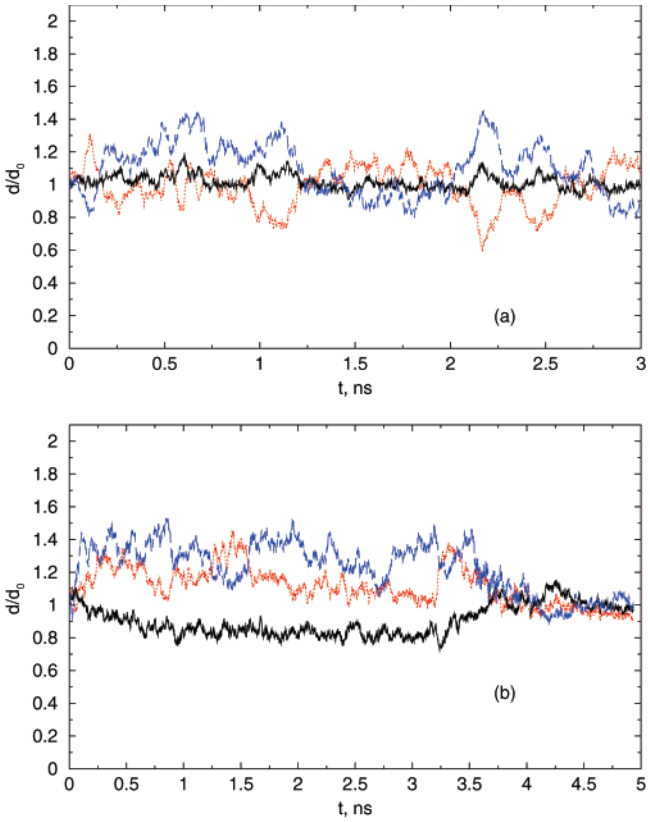

Figure 7. Normalized distance between the centers of mass of the SWNT and the head (C1−G24 pair, red dotted line), tail (G12−C13 pair, blue dashed line), and one middle group (T8−A17 pair, black solid line) of DNA initially in the A-form at the start of the simulation. (a) A-DNA on an uncharged SWNT; (b) A-DNA on a positively charged SWNT ($q = +0.05e$ per carbon atom).

charged SWNT can be explained by the adsorption mechanism. The negatively charged backbone of the A-DNA binds to the positively charged wall of the SWNT. This can be seen from the dynamics of the middle groups, shown in Figure 7b. Adsorption of the backbone of the A-DNA to the SWNT facilitates the A−B transformation by providing an additional energetic driving force for the elongation, since the longer B-form has a larger contact area between the negative backbone and the positive SWNT. This is in stark contrast to the case for

A-DNA adsorbed on the uncharged SWNT, where binding of both ends to the SWNT inhibits the A−B transition.

The A to B elongation is followed by a slower relaxation to the ending configuration for A-DNA on the SWNT with a charge of $q = +0.05e$ per carbon. After about 4 ns the ending configuration is very similar to that observed for B-DNA on the SWNT with $q = +0.05e$/C studied previously [compare Figure 7b to Figure 1b, and Figure 6b to Figure 2b].

4. Conclusion

We have performed MD simulations of a Dickerson dodecamer DNA molecule interacting with a SWNT in an aqueous solution. Our simulations show that DNA will weakly adsorb onto an uncharged SWNT. Either end of a DNA molecule will adsorb onto a SWNT because of the partially exposed hydrophobic base pairs at the ends. Only one end of the DNA adsorbs onto the nanotube in our simulations because the Dickerson dodecamer is so short that binding of both ends to the nanotube would require a large bending energy. We expect that longer DNA segments should be able to have both ends bind to a long SWNT.

The DNA segment adsorbs onto a positively charged SWNT in a roughly parallel configuration. The charges on the SWNT attract the hydrophilic phosphodiester linkages to promote binding between the DNA backbone and the SWNT wall. Lu et al. speculated that electrostatic attraction between a charged SWNT and a DNA molecule would be adequate to displace water molecules between the DNA−SWNT pair. Our simulations indicate that this is true only at select points of contact between the DNA backbone and the nanotube. Most of the DNA is still solvated by water when adsorbed on the SWNT. The nature of the electrical contact between DNA and a charged nanotube in solution is still not clear, but it appears to be intermittent contact between the charged DNA backbone and the charged SWNT.

The initial binding between the DNA and the SWNT occurs on a time scale of a few hundred picoseconds, for both the positively charged and uncharged nanotubes. The adsorption process has negligible effect on the structure of the B-form DNA segment. The average base pair distance and the rotation angle per residue are not changed appreciably when DNA adsorbs onto uncharged or positively charged SWNTs.

In contrast, the adsorption process does affect the A to B conversion of A-DNA. The adsorption of the A-DNA onto an uncharged SWNT inhibits the complete relaxation of A-DNA to B-DNA over a time scale of 3 ns; this is due to the binding of both A-DNA ends to the SWNT wall. However, the adsorption of A-DNA on a positively charged SWNT appears to promote the A to B conversion. This is accomplished by the backbone of DNA adsorbing to the SWNT, which provides additional driving force for the elongation.

We note that simulations of DNA/SWNT systems without water performed by Lu and co-workers predicted that nanotubes would fit within the major groove of DNA.[36] The nanotube we studied is somewhat smaller in radius than that used by Lu et al. However, we see no evidence of attraction between the DNA major groove and the nanotube, with either neutral or charged nanotubes. Moreover, charged nanotubes would be more attracted to the backbone of the DNA rather than the major groove. Comparison of our results with those of Lu et al. highlights the need for inclusion of explicit water, counterions, and correct charges on the DNA.

We have found that nucleotides in dsDNA do not bind to either charged or uncharged SWNTs in the way that uncharged nucleosides were found to adsorb on SWNTs in a vacuum by Meng et al.[38] Moreover, Meng and co-workers noted that application of a gate voltage to the SWNT did not significantly alter the adsorption structure of nucleosides.[38] In contrast, we have found that the binding mode of dsDNA on SWNTs is dramatically affected by the presence of charges on the SWNT.

Calculation of the free energy of binding between DNA and a SWNT could be performed by computing the potential of mean force associated with binding of DNA to a SWNT.[45] This method, coupled with umbrella sampling,[71] has recently been used to examine polymer folding in water, allowing identification of entropic and enthalpic contributions to polymer collapse.[72] A similar approach could be applied to the DNA/SWNT problem but would require the identification of a set of conformational windows that span the binding process, which is less well defined in our case than in the polymer folding system.

In closing, we note that the two main limitations of our work are the very short time scales we are able to simulate within standard molecular dynamics and the accuracy of the potential models used. Specifically, the potentials we used do not account for polarization of the nanotube. Polarization could be important for describing accurately the interaction between charged DNA and the nanotube. The effect of polarization would be to increase the attractive potential between a SWNT and the DNA molecule. This enhanced attraction will not change qualitatively the conclusions and observations of this work. DNA would still adsorb onto uncharged or charged nanotubes if nanotube polarizability was included.

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Supporting Information Available: Complete ref 43, a movie of the binding of DNA to an uncharged nanotube starting from a configuration where the DNA and SWNT axes are perpendicular. Plots of the evolution of the minor groove width and base pair inclination angles for A and B DNA in solution, adsorbed on an uncharged SWNT, and adsorbed on a charged SWNT. This information is available free of charge via the Internet at http://pubs.acs.org.

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