

Spontaneous Insertion of DNA Oligonucleotides into Carbon Nanotubes

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ABSTRACT

We report molecular dynamics simulations showing that a DNA molecule could be spontaneously inserted into carbon nanotube (CNT) in a water solute environment. The van der Waals and hydrophobic forces were found to be important for the insertion process, with the former playing a more dominant role in the DNA–CNT interaction. Our study suggests that the encapsulated CNT–DNA molecular complex can be further exploited for applications such as DNA modulated molecular electronics, molecular sensors, electronic DNA sequencing, and nanotechnology of gene delivery systems.

Functionalization of novel nanoscale materials with chemical or biological molecules could lead to new types of miniature devices for chemical/biological applications^{1–5} such as probes and sensors. In the case of carbon nanotubes (CNTs), much interest has been devoted to utilizing or controllably modifying their intrinsic chemical and physical properties by attaching molecules^{6–10} to the outside. In addition to the sidewall or tip functionalization, it has been found that molecules such as C₆₀,¹¹ metallofullerenes,¹² water,¹³ or gas molecules¹⁴ can be encapsulated inside nanotubes, suggesting alternative ways to functionalize CNTs. Recent molecular dynamics simulations¹³ demonstrated that single-wall carbon nanotubes (SWCNTs) could be realized as molecular channels for water transport. Here we report molecular dynamics simulations of the dynamic processes of encapsulating deoxyribonucleic acid (DNA) inside CNTs in a water solute environment. Our results indicated spontaneous insertion and confinement of single-strand DNA oligonucleotide under a combined action of the van der Waals and hydrophobic interaction forces.

The designed DNA–CNT system consists of a homogeneous single-strand DNA oligonucleotide with 8 adenine bases and an uncapped armchair (10,10) carbon nanotube (2.95 nm long and 1.36 nm in diameter). As initial configurations, CNT and DNA were aligned along the nanotube axis and separated by 0.6 nm. The CNT–DNA complex was solvated in a water reservoir and its dynamics

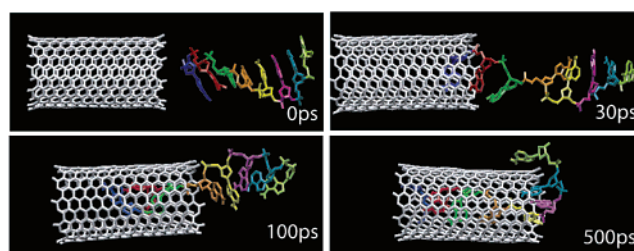


Figure 1. Simulation snapshots of a DNA oligonucleotide (8 adenine bases) interacting with a (10,10) carbon nanotube at 0, 30, 100, and 500 ps. Water molecules are not displayed for clarity.

was simulated for 2 ns at temperature 400 K and pressure 3 bar.^{15–17} A time-step of 1 fs was used and full-precision trajectory was recorded every 1 ps. The snapshots of the oligonucleotide–nanotube system shown in Figure 1 indicated a very fast insertion process of oligonucleotide into nanotube. At $t = 30$ ps, the first base of the oligonucleotide has begun to enter the nanotube. After 500 ps, five of the eight DNA bases are fully inside the nanotube and the first base has reached the opposite end of the tube. The last DNA base remains outside and attached to the sidewall. Correspondingly, the center of mass (COM) distance d (Figure 2) between oligonucleotide and carbon nanotube rapidly decreases with time up to 500 ps. The nearly constant d afterward indicated that the system has reached equilibrium.

To reveal the physical mechanisms of the insertion process of oligonucleotide, we plot the normalized radial density profiles of water and oligonucleotide within nanotube in

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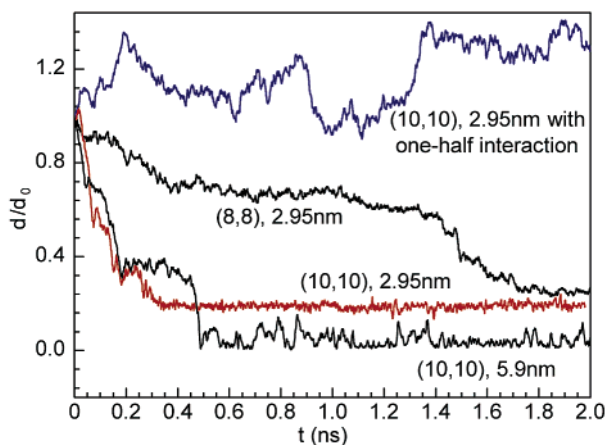


Figure 2. Normalized center-of-mass distances between the oligonucleotide and carbon nanotube as function of simulation time. d_0 is the initial center-of-mass separation.

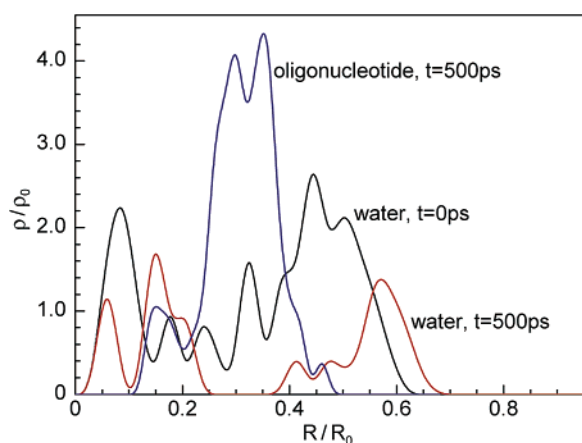


Figure 3. Radial density profiles of water and oligonucleotide within nanotubes in units of the water bulk density ρ_0 , averaged over cylindrical shells centered at the axis of the nanotube, with radius r , and height determined by the carbon atoms at the nanotube rim. $R_0 = 0.68$ nm is nanotube radius.

Figure 3. Due to the hydrophobic property of carbon nanotubes, water molecules inside CNTs exhibit a continuous radial distribution only up to $R \sim 0.7R_0$ ($R_0 = 0.68$ nm) after equilibration at 0 ps. The radial density of water inside CNT gradually decreased during the simulation. The water density profile at 500 ps showed a discontinuous region between $0.25R_0$ and $0.35R_0$, where the radial density of oligonucleotide entering the nanotube exhibits a maximum. This demonstrated that during the insertion of oligonucleotide some of water molecules inside the nanotube have been repelled out of the nanotube. The water molecules inside nanotubes are three-dimensionally structured and the induced difference in the hydrogen-bond energy of water should be negligible. Since the water molecules were initially trapped inside CNTs due to van der Waals attraction,¹³ the repelling of water molecules to the outside of CNTs is energetically costly and provides an effective resistance for DNA insertion. It was further observed that the oligonucleotide entering CNT formed a hydrophobic tubular-like shell within the nanotube, with the remaining water molecules inside the CNT confined

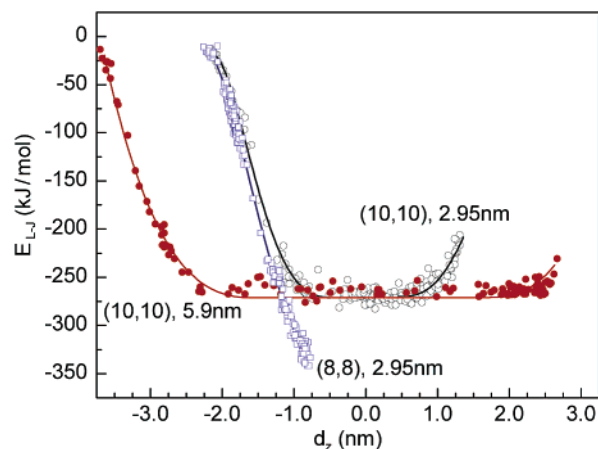


Figure 4. van der Waals energy between nanotubes and the first DNA base entering the nanotube as a function of their axial direction projected COM distance d_z .

near the nanotube center along the tube axis and between the tube wall and the oligonucleotide.

Strong hydrogen-bond interaction among water molecules is known to produce hydrophobic forces that cause hydrophobic solutes (both CNT and DNA) to aggregate to reduce solvent–solute interface energy. This hydrophobic effect alone is, however, found to be insufficient to encapsulate DNA due to resistance from water molecules inside the CNT. On the other hand, the carbon nanotube and oligonucleotide will also experience an attractive force from each other due to van der Waals interaction when their separation is about 1 nm or smaller. This attractive interaction is found to play a dominant role in the DNA insertion process. The derived van der Waals energy between nanotube and the first DNA base entering the nanotube (Figure 4) confirmed the rapid decrease in the interaction potential energy with distance. The flat bottom of the van der Waals potential well in the middle of the nanotube is about 2 nm in width, which traps the DNA molecule inside the CNT. The importance of van der Waals force is demonstrated by the following analysis. We reduced the interaction between carbon nanotube and oligonucleotide atoms¹⁷ and repeated the simulation. We found that the insertion process of oligonucleotide is dramatically slowed by a small reduction of van der Waals force. With 50% reduction in the interaction, as indicated by the derived COM distance in Figure 2, the oligonucleotide only made random motion around the nanotube and no base entered the nanotube. To clarify the role of hydrophobic force, we simulated carbon nanotubes interacting with polypeptide molecules. The attraction of a hydrophilic polypeptide toward a CNT was found to cause peptide insertion into the CNT but the process is severely hindered in comparison with DNA oligonucleotides, despite the comparable van der Waals interaction in both cases. These observations suggest that both van der Waals attraction and hydrophobic interaction between nanotube and DNA play important roles in encapsulating molecular clusters or nanoparticles inside CNT. In the case of DNA, the van der Waals attraction force is found to be dominant.

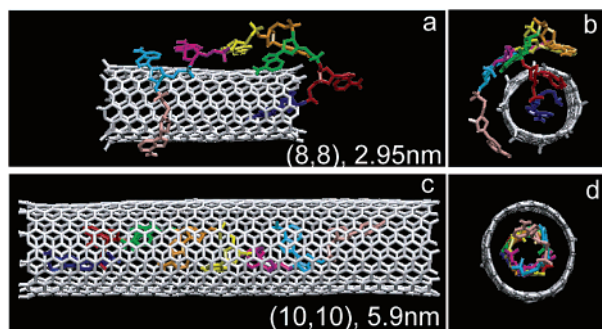


Figure 5. Snapshots (sideview a, c and top view b, d) of oligonucleotide–nanotube system simulated after 2 ns. Water molecules are not shown.

Since both the depth of the van der Waals potential well and the size of its flat region in the middle of the CNT depend on the diameter and length of CNT, the insertion process of the oligonucleotide is expected to be tube-size dependent. To explore the size effect of the insertion process, we repeated molecular dynamics simulations of the DNA–CNT system with two different carbon nanotubes: armchair (8,8) with 2.95 nm in length and 1.08 nm in diameter and (10,10) with doubled length (5.90 nm). The derived COM distances were also plotted in Figure 2, and the snapshots of the simulated oligonucleotide–nanotube systems at 2 ns were presented in Figure 5. Despite a van der Waals potential well deeper than the (10,10) tube, the (8,8) carbon nanotube cannot attract more than one DNA base into its inside. It was observed that for a time period up to 2 ns the remaining seven DNA bases gradually wrap around the outside of the (8,8) nanotube. A possible explanation is that the diameter of the (8,8) nanotube is too small and the oligonucleotide has to be severely deformed in order to enter the nanotube. The deformation-induced energy could overcompensate the reduction in van der Waals and hydrophobic interaction energies. It suggests that the diameter (1.08 nm) of the (8,8) nanotube is the critical size for inserting a single strand DNA into a CNT. For the (10,10) nanotube with doubled length, the flat part in its van der Waals potential well is much larger. The oligonucleotide completely entered the nanotube after 500 ps.

In conclusion, molecular dynamics simulations have indicated that DNA could be encapsulated inside carbon nanotubes in a water solute environment via an extremely rapid dynamic interaction process, provided that the tube size exceeds certain critical value. Both the van der Waals and hydrophobic forces are found to be important, with the former playing a more dominant role on DNA–CNT interaction. Our study has general implications on filling nanoporous materials with water solutes of molecular clusters or nanoparticles. Since carbon nanotubes possess many

unique electrical, chemical, mechanical and biological properties, the DNA–CNT or other CNT based bio-nano-complex can be further exploited for applications in molecular electronics, molecular sensors, electronic DNA sequencing, and nanotechnology of gene delivery systems. These studies are currently underway.

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- (17) Depending upon the nanotube length, the DNA–CNT systems were solvated in a periodic $5 \times 5 \times 9$ nm or $5 \times 5 \times 12$ nm box with SPC216¹⁸ water as solvent. The particle-mesh-ewald method¹⁹ with cubic-spline interpolation was applied to evaluate electrostatic interaction, and sodium ions were added as counterions to compensate negative net charges on the oligonucleotide. We used GROMACS force field based on GROMOS-87²⁰ to model atomic interactions in DNA–oligonucleotide and DNA–water interaction. The carbon atoms of nanotubes were treated as uncharged Lennard-Jones particles with $\sigma_{CC} = 0.385$ nm and $\epsilon_{CC} = 0.4396$ kJ/mol.²¹ The carbon–carbon bond lengths of 0.142 nm and bond angles of 120° were maintained by a Morse bond, a harmonic cosine angle, and a cosine torsion potential.²² The nanotube–water Lennard-Jones parameters were $\sigma_{CO} = 0.319$ nm and $\epsilon_{CO} = 0.3126$ kJ/mol.²³ Geometry average was taken as combination rules²⁴ for setting Lennard-Jones parameters for interactions between nanotube and DNA atoms. We also conducted simulations with reduced nanotube–DNA interaction by simply changing the value of σ_{CC} .
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