Effects of fluid flow on the oligonucleotide folding in single-walled carbon nanotubes

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This paper presents molecular-dynamics (MD) simulations of DNA oligonucleotide and water molecules translocating through carbon nanotube (CNT) channels. An induced pressure difference is applied to the system by pushing a layer of water molecules toward the flow direction to drive the oligonucleotide and other molecules. This MD simulation investigates the changes that occur in the conformation of the oligonucleotide due to water molecules in nanochannels while controlling the temperature and volume of the system in a canonical ensemble. The results show that the oligonucleotide in the (8,8)–(12,12) CNT channel forms a folded state at a lower pressure, whereas the oligonucleotide in the (10,10)–(14,14) CNT channel forms a folded state at a higher pressure instead. The van der Waals forces between the water molecules and the oligonucleotide suggest that the attraction between these two types of molecules results in the linear arrangements of the bases of the oligonucleotide. For a larger nanotube channel, the folding of the oligonucleotide is mainly dependent on the solvent (water molecules), whereas pressure, the size of the nanotube junction, and water molecules are the considering factors of the folding of the oligonucleotide at a smaller nanotube channel. For a folded oligonucleotide, the water distribution around the oligonucleotide is concentrated at a smaller range than that for the distribution around an unfolded oligonucleotide.

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I. INTRODUCTION

Single-walled carbon nanotubes (SWNTs) are important structures for studying fillings of various species in their interior. This is because SWNTs have well-defined morphologies, thickness, etc. Iijima and Ichihashi found that atomic iron particles are important catalysts in assisting the formation of single-shell carbon nanotubes [1], whereas Bethune *et al.* produced single-walled tubules using cobalt as catalysts [2]. The areas of carbon nanotube (CNT) applications cover a wide range, from diagnostic tools and devices to biopharmaceutics, implantable materials and devices, and surgical aids [3]. Numerous studies have focused on properties and functionality of CNTs, due to the vast potential of CNTs as modal structures. Molecular transporters, DNA detectors, and sensors are a few of the many potential biomedical applications [4–9]. The hybrid system of biomolecules and CNTs has also shown promising prospect for bioelectronic, nanocircuitry, etc [10]. One of the growing interests in the application of CNTs is to use a CNT as a flow channel for fluid [11]. The nanoscale behavior of fluid flow in a CNT has much to be explored before practical applications can be realized.

Molecular transport in CNTs can be determined by various factors [12]. For example, pore size and hydrophobicity play a crucial role in the speed of molecular transportation and the ease of the molecules to enter the nanotube [13]. Molecules, such as DNA, RNA, peptides, and methanol [13–16], are a few of the many nanomaterials that are essential for simulation cases of nanoscale flow in CNTs. DNA, in particular, has attracted attention in recent studies, especially in the understanding of the dynamical behavior of the oligonucleotide due to applied forces [17,18], during the translocation processes of the oligonucleotide along nanopores [19,20], and the conformation of the oligonucleotide in nanofluidic channels [21,22]. The possibility of encapsulating a single-stranded DNA (ssDNA) molecule into a single-walled CNT was demonstrated by Okada *et al.* [23]. Water molecules, on the other hand, are often integrated into CNTs as the fluid molecules that solvate the molecules of interest during simulation. Thus, the behavior of water molecules in a CNT channel provides insightful information regarding the fluid-fluid and fluid-channel wall interaction. Striolo [24] performed the simulation of water diffusion through an infinitely long narrow CNT, which shows that the concerted motion of water molecules depends not only on the interaction between water-water and water-carbon but also on the number of molecules and the temperature of the system. These conditions affect the speed of the diffusion and also the effectiveness of the diffusion. Hummer *et al.* [25] also suggested that a CNT might be exploited as a unique molecular channel for water and protons.

The application of forces to a system of molecules is often performed in molecular-dynamics (MD) simulations such that various methods of driving fluid flow are induced to the system of interest. However, in some cases, the driving force such as a pressure or density gradient is achieved through a source and sink relationship [26]. The source is maintained at a constant density and temperature by introducing the required particles, while the sink region is maintained at vacuum. Other methods that use pressure gradient to drive fluids include the reflecting particle method [27], the fluidized piston model, and the ice piston model [28].

In this work, we investigate the folding of an ssDNA oligonucleotide in CNT channels due to the effects of the fluid flow by MD simulations, using an induced pressure difference as the driving force. The induced pressure is achieved by applying forces on a layer of water molecules, acting as a piston to the entire system. The resulting movement of these water molecules will cause the oligonucleotide in the channel to flow in the direction of the forces applied. Two CNT channels are used for comparing their size effects on the dynamical behavior of the oligonucleotide. Besides

addressing the flow distribution of water molecules around the ssDNA in a CNT channel under an induced pressure difference, the folding of the DNA molecule is investigated in more detail in this work in order to understand the effects of the induced pressure, fluid flow, and the size of CNTs on the oligonucleotide more clearly. Because the pressure is applied on the water molecules and not on the oligonucleotide directly, the translocation of the oligonucleotide depends highly on the interaction between the water molecules and the oligonucleotide. The investigation of the van der Waals forces between the water molecules and the oligonucleotide is thus necessary to understand the changes in forces that would occur between them. Further investigation has also looked into the resultant interaction between the bases of the oligonucleotide due to folding. The shape of the oligonucleotide is compared using the radius of gyration of the biomolecule. The study helps to understand the flow behavior of the oligonucleotide in CNT channels and the effects of water molecules on the oligonucleotide.

The results from our MD simulations show the magnitude of the van der Waals forces between the oligonucleotide and the water molecules is affected by the strength of the applied pressure. The folding of the oligonucleotide is dependent on the interaction between the water molecules and the oligonucleotide. However, the folding of the oligonucleotide is also affected by the sizes of the CNT junctions. The decreasing diameter along the junction acts as a resistance to the changes that would occur on the oligonucleotide. The radius of gyration of the oligonucleotide is affected not only by the strength of the pressure employed but also by the diameter of the nanotube channel. By comparing the shape of the oligonucleotide based on the radius of gyration, we can understand how the cross-sectional diameter of the oligonucleotide affects the amount of the water molecules flowing through the nanochannel.

II. COMPUTATIONAL MODEL AND CONDITIONS

MD simulations are performed in this study for the translocation of the oligonucleotide and water molecules through CNT channels. In the simulations, the oligonucleotide and water molecules are confined within a CNT channel modeled as a nonpolarized, single-walled, and armchair CNT. The structure of the CNT channel consists of two CNT junctions, each joined by two nanotubes of different diameters. The connecting joint of the CNT can be connected by a pentagon and heptagon pair of carbons [29]. For this simulation study, two carbon nanotube channels were chosen for comparison: (8,8)–(12,12) and (10,10)–(14,14) CNT channels. The (8,8)–(12,12) CNTs have 1688 carbon atoms, with a diameter of 10.8 Å for the (8,8) nanotube and a diameter of 16.2 Å for the (12,12) nanotube. The (10,10)–(14,14) CNTs consists of 1980 carbon atoms, with a diameter of 13.6 Å and 18.9 Å for the (10,10) and (14,14) nanotubes, respectively. Both CNT channels are approximately 100 Å in length.

There are in total two systems that were set up for this study. The first system consists of an ssDNA molecule enclosed within a (8,8)–(12,12) CNT channel, with water molecules and sodium ions. The second system has the same ssDNA molecule enclosed in a (10,10)–(14,14) CNT channel. In order to understand the dynamical phenomena of the oligonucleotide that represents the basic unit of the genetic code, three nucleotides are considered for the construction of the oligonucleotide. The ssDNA consists of cytosine, guanine, and cytosine.

The transferable intermolecular potential three point (TIP3) water model [30] is used with sodium counter ions to fill the carbon nanotube channel. There are a total of 257 water molecules in the (8,8)–(12,12) CNT channel, whereas the (10,10)–(14,14) CNT channel is filled with 411 water molecules. The rectangular periodic boxes of the sizes $102 \times 20 \times 20$ Å and $99 \times 20 \times 25$ Å are set up for the periodic boundary conditions of the (8,8)–(12,12) and (10,10)–(14,14) CNTs, respectively. Periodic boundary conditions are applied in the x direction of the CNT channel, parallel to the flow of the fluid. The center of the periodic box is set as the origin of the coordinates. The radial distribution of water molecules at the center region of the CNT channels is determined using the VMD program [31].

The CNT channels are fixed in space. The carbon atoms of the CNT channel are modeled as uncharged Lennard-Jones particles, with $\sigma_{cc}=3.80$ Å and $\varepsilon_{cc}=0.105$ kcal/mol [32]. The carbon-carbon bond length is maintained at 1.42 Å and bond angles of 120° are maintained by a harmonic cosine angle. For simulating the translocation process in a solvent environment, the oligonucleotide was solvated in a water reservoir. The Chemistry at Harvard Macromolecular Mechanics force field [33] was used for the oligonucleotide and sodium ions. The oligonucleotide was initially placed within the CNT channel. Before the nonequilibrium MD simulations were performed, energy minimization and equilibrium MD runs had been made. A strong hydrogen-bond interaction between water molecules is known to cause the oligonucleotide to aggregate due to hydrophobic forces [34]. The formation of a hydrophobic tubularlike shell of the encapsulated oliognucleotide would lead to reconfiguration of the oligonucleotide molecules, which may result in repositioning of the oligonucleotide caused by the repulsive interactions of water. During the energy minimization and equilibrium runs, one of the atoms from the oligonucleotide was fixed to prevent the molecule from being pushed out of the CNT channel due to the hydrophobic effects of the water. The parallel molecular-dynamics code NAMD [35] was used for the simulation runs.

The cutoff distance for the nonbonded interactions among the oligonucleotide, water, and CNTs was set at 12 Å. A pressure difference was induced into the system to drive the oligonucleotide and water molecules to translocate along the CNT channel. The simulations were performed at a constant temperature of 310 K [36].

The purpose of inducing a pressure difference in this simulation study is to create a virtual piston by applying a constant force onto a layer of water molecules. These molecules would move along the direction of the force applied and subsequently push the rest of the molecules in the system through repulsive interactions. This initial pressure created by the groups of water molecules is similar to the pressure exerted by a piston. The length of the "piston" used was 20 Å (not shown here). There are in total three magnitudes

TABLE I. Simulation conditions.

Cases	CNT channels	Applied forces kcal/(mol Å)	Duration simulated
1	(8,8)–(12,12)	0.1	10 ns
2	(8,8)–(12,12)	0.3	10 ns
3	(8,8)–(12,12)	0.5	10 ns
4	(10,10)–(14,14)	0.1	3 ns
5	(10,10)–(14,14)	0.3	3 ns
6	(10,10)–(14,14)	0.5	2 ns

of forces used to drive the water molecules: 0.1, 0.3, and 0.5 kcal/(mol Å), which correspond to pressures of 1.11×10^{-25}, 3.33×10^{-25}, and 5.55×10^{-25} kcal/(mol Å^3). These forces are applied onto the oxygen atoms of the water molecules. The applied forces on the hydrogen atoms are ignored in this simulation method. The water molecules at the end of the periodic box are applied with forces and translated into the box from the opposite side. This ensures that the pressure is fed into the system from the beginning. The radius of gyration of the oligonucleotide is used as a reference for determining the changes that occur in the cross-sectional radius of the molecule. The radius of gyration r_g is defined as [37]

$$r_g^2 = \frac{\sum_i m_i (r_i - r_c)^2}{\sum_i m_i}, \quad (1)$$

where m is the mass of the atom, r_i is the position of the ith atom, and r_c is the position of the center of mass.

The simulation cases for the translocation of oligonucleotide and water molecules through CNT channels are summarized in Table I. Each case consists of a combination of different CNT channels with the applied forces used to drive the water molecules for the induction of a pressure difference. The simulation time step is set at 1 fs. According to de Groot *et al.*, "real time" visualization of water molecules migrating through a channel is achieved when simulations were run for 10 ns. Hence, the maximum simulation duration for our study is set at 10 ns. Cases 1, 2, and 3 are simulated for 10 ns. Cases 4 and 5 are simulated for 3 ns. Lastly, case 6 is simulated for only 2 ns due to the highly repetitive translocating process that has occurred.

III. RESULTS AND DISCUSSION

The investigation of the simulation focuses on the conformational changes in the DNA oligonucleotide and water flow in CNT channels due to the pressure and size effects of carbon nanotube junction. The oligonucleotide is initially situated in the CNT channel and positioned with the tube axis aligned. The translocation of the oligonucleotide is based on the pressure difference created by the water molecules in the CNT channel. The different magnitudes of pressures denote the different simulation cases as shown in Table I.

Due to the presence of the oligonucleotide, the permeation of water molecules in the (8, 8)–(12, 12) CNT channel

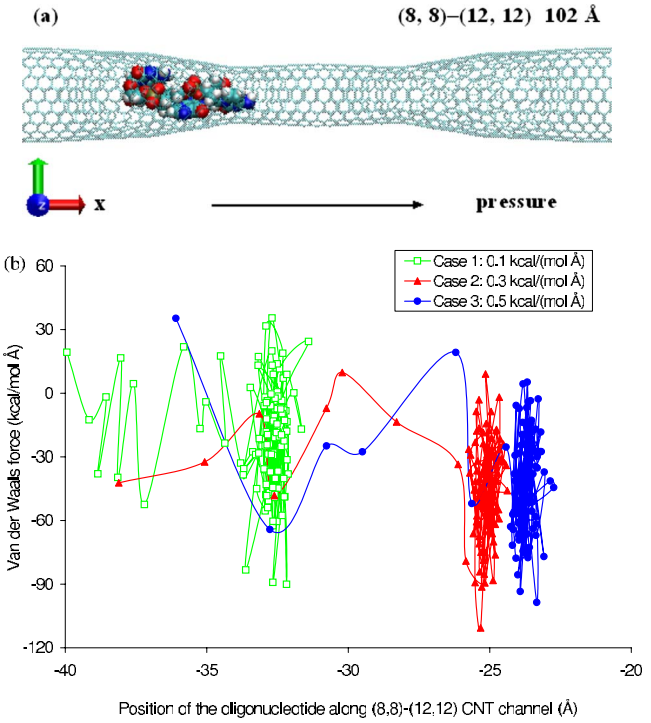

FIG. 1. (Color online) Translocation of the oligonucleotide in the (8,8)–(12,12) nanotube. (a) A snapshot taken at 2.68 ns in case 3. (b) Van der Waals forces between water molecules and the oligonucleotide in the (8,8)–(12,12) CNT channel.

is affected by the size of the oligonucleotide and the magnitude of the induced pressure. Because the diameter 10.8 Å is the critical diameter for an oligonucleotide [32], the oligonucleotide does not pass through the center of the (8, 8)–(12, 12) CNT channel. The oligonucleotide remains at the CNT channel junction and blocks off most of the water molecules flowing through the channel. Figure 1(a) shows a simulation snapshot of the oligonucleotide in case 3. The main observable phenomenon from the simulation snapshots from case 1 (not shown here) to case 3 [as shown in Fig. 1(a)] is that the oligonucleotide is positioned much closer to the junction as the magnitude of the induced pressure is increased. The position of the oligonucleotide in the CNT channel is defined based on the placement of the center of mass of the oligonucleotide along the x axis of the channel. The blockage of the oligonucleotide at the CNT junction affects the amount of water molecules flowing across the CNT channel. The detailed descriptions of the permeation of water molecules are described by Lim *et al.* [38]. Another factor affecting the flow of water molecules across the carbon nanotube junction is the change in the cross-sectional area of the oligonucleotide due to folding. The cross-sectional area of the oligonucleotide becomes larger due to folding of the bases of the molecule. This creates a greater blockage to the water molecules entering the center region of the nanochannel.

Figure 1(b) shows the van der Waals forces between the water molecules and the oligonucleotide along the x direction of the (8,8)–(12,12) CNT channel. The positive values in the forces mean that the water molecules and the oligonucleotide are experiencing an overall repulsive force, whereas

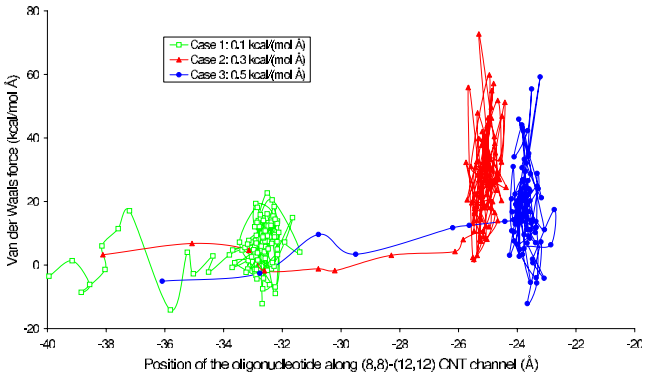

FIG. 2. (Color online) Van der Waals forces between the bases (guanine and cytosine) of the oligonucleotide in the (8, 8)–(12, 12) CNT channel.

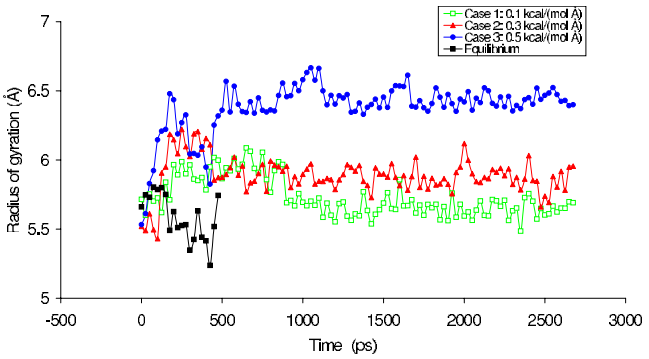

FIG. 3. (Color online) Radius of gyration of the oligonucleotide in the (8,8)–(12,12) nanotube channel for different forces applied.

negative values mean that there is an overall attractive force between the water molecules and the oligonucleotide. Figure 1(b) indicates that the van der Waals forces in cases 1, 2, and 3 are almost similar. However, the slight difference in the values of the forces indicates that as the induced pressure increases, the van der Waals forces between the water molecules and the oligonucleotide are inclined toward an attractive phenomenon. Although the repulsive effect exists at the ending of the oligonucleotide near the (12,12) nanotube, the flow of some water molecules into the (8,8) nanotube forms a more dominant attractive effect on the oligonucleotide at that narrow junction. This suggests that there is lesser folding of the oligonucleotide at a high pressure, resulting in sufficient space between the oligonucleotide for the flow of water molecules.

As the pressure in the nanochannel increases, water molecules pass through the oligonucleotide much quickly. The repulsive forces induced by water molecules also push the oligonucleotide to move closer toward the CNT junction. The decrease in the van der Waals forces could partly contribute to the change in the shape of the oligonucleotide, especially in the folding of the oligonucleotide. The higher attractive forces between the water molecules and the oligonucleotide would cause the oligonucleotide to fold lesser, due to the stretching of the oligonucleotide along the flow direction of the water molecules. The higher pressure results in a deeper insertion of the oligonucleotide into the narrower channel. Since the nanotube junction is too small for the oligonucleotide to flow through, the blockage by the junction resists the oligonucleotide from folding, forming a less folded shape of the oligonucleotide. The position of the oligonucleotide along the (8,8)–(12,12) CNT channel is also shown in Fig. 1(a), where a higher pressure (case 3) shows a further displacement of the oligonucleotide toward the CNT junction at around −24 Å.

In order to understand the effect of the van der Waals forces between the water molecules and the oligonucleotide, the van der Waals forces between the bases (guanine and cytosine) of the oligonucleotide in cases 1–3 are shown in Fig. 2. Figure 2 shows the bases of the oligonucleotide are more repulsive to each other as the pressure of the system increases and the highest repulsive force occurs in case 2. Although the oligonucleotide is less folded at a higher pressure system (cases 2 and 3), the oligonucleotide is sandwiched between the nanotube junction and the pressurized water molecules. This is because the oligonucleotide is unable to flow through the center region of the (8,8) CNT channel any further as mentioned earlier. The pressure exerted by the water molecules forces the bases of the oligonucleotide to squeeze closer with each other toward the nanotube junction, hence, increasing the van der Waals forces between the bases. In case 2, the insertion of the oligonucleotide into the (8,8) nanotube region is lesser than that in case 3. Due to the built-up pressure at one end of the oligonucleotide, the distances between the bases are shortened in a linear fashion and thus cause greater interactions between them. As for case 3, the insertion of the oligonucleotide into the (8,8) nanotube region is deeper. When the pressure at one end of the oligonucleotide is built up, the "squeezing effect" between the bases is compensated by the forward insertion of the other end of the oligonucleotide. This reduces the repulsive effect between the bases. Since some water molecules are able to flow freely through the oligonucleotide and across the CNT junction, the increased pressure would not result in the increase in forces between water and the oligonucleotide that are of the same magnitude as that between the bases.

Figure 3 shows the radius of gyration of the oligonucleotide in the (8, 8)–(12, 12) CNT channel under the influence of different pressures. When the radius of gyration of the oligonucleotide increases, the cross-sectional area of the oligonucleotide is decreased due to the linear arrangement of the bases of the oligonucleotide. The cross-sectional area is defined as the area parallel to the diameter of the nanotube. The radius of gyration of the oligonucleotide decreases when the oligonucleotide folds. Likewise, the radius of gyration of the oligonucleotide increases when the oligonucleotide unfolds. Figure 3 shows the folded oligonucleotide is formed when the oligonucleotide is under the influence of a lower pressure. The result from the radius of gyration of the oligonucleotide has confirmed that folding of the oligonucleotide is less prominent as the pressure increases. The state of the oligonucleotide after equilibration at 0 ps is indicated as the "equilibrium" stage of the oligonucleotide and is used to compare with the other cases. The oligonucleotide in the (8, 8)–(12, 12) CNT channel has shown an overall increment in the unfolding of the oligonucleotide, compared to the initial equilibrium state. Because the radius of gyration of the oli-

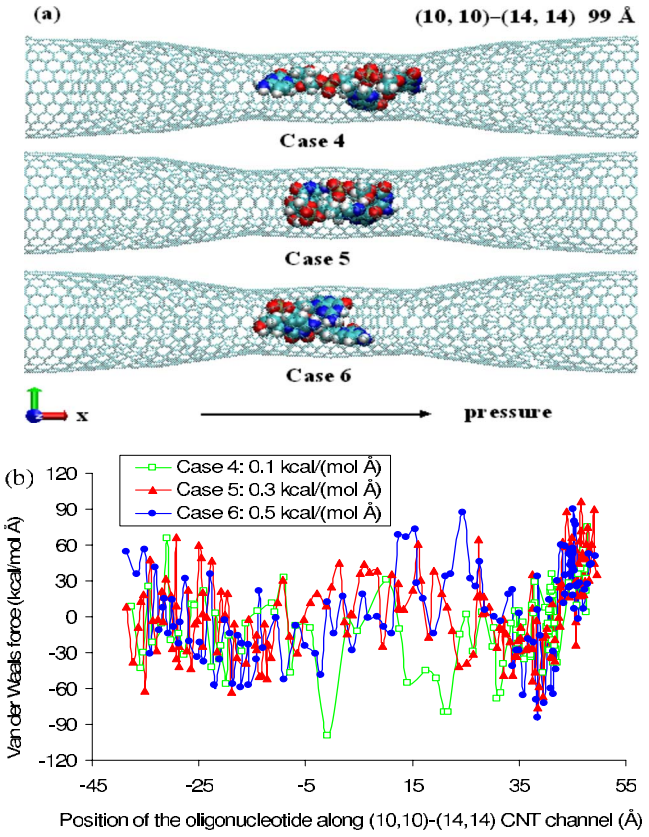

FIG. 4. (Color online) Translocation of the oligonucleotide at the center of the (10,10)–(14,14) nanotube. (a) Snapshots of the oligonucleotide in cases 4 (at 5.75 ns), 5 (at 5.22 ns), and 6 (at 5.13 ns), respectively. (b) Van der Waals forces between water molecules and the oligonucleotide in the (10,10)–(14,14) CNT channel.

gonucleotide in case 3 is larger, the possibility of deeper insertion to the smaller nanochannel would be greater. This shows that the depth of insertion is mainly caused by the magnitude of the induced pressure in the system, the interaction of the oligonucleotide and the water molecules, and also the shape of the oligonucleotide. The radius of gyration has indicated the changes in the cross-sectional diameter of the oligonucleotide at different pressures, as shown in Fig. 3. The result from the radius of gyration rectifies the uncertainty of the shape of the oligonucleotide in different simulation cases reported by Lim *et al.* [38].

In order to further inspect the size effect of the CNT channel on the dynamics of the oligonucleotide, the (10,10)–(14,14) CNT channel is used to repeat the MD simulations. According to the findings of Wang *et al.*, the static properties of water confined in CNTs are mainly affected by the sizes of the tube diameter rather than the helicity effect of the tubes [39]. Since water properties are not affected by the helicity effect, the dynamics of the oligonucleotide due to water molecules is considered to be dependent on the effect of the tube diameter as well, instead of the helicity effect. The translocation of the oligonucleotide through the (10,10)–(14,14) CNT channel is shown in Fig. 4(a), where three simulation snapshots show the oligonucleotide located at the center of the CNT channel. The position of the oligonucleotide is presented in three simulation cases (cases 4, 5, and 6) to show the difference in the folding of the oligonucleotide. Figure 4(a) shows that the oligonucleotide is less folded under a lower-pressure condition (case 4), as compared to the higher-pressure conditions (cases 5 and 6). The phenomenon of the folding of the oligonucleotide can be further clarified using the explanation of the van der Waals forces between the water molecules and the oligonucleotide. As shown in Fig. 4(b), the van der Waals forces between the water molecules and the oligonucleotide at the center region of the (10,10)–(14,14) CNT channel (approximately between −20 Å and 20 Å) increase as the pressure increases in the system.

The increase in the van der Waals forces indicates a repulsive nature between the water molecules and the oligonucleotide as mentioned earlier. Since the van der Waals forces along the center region of the CNT channel change significantly as compared to the forces at both ends of the tube (approximately ≤ -20 Å and ≥ 20 Å), the conformation of the DNA is therefore affected more greatly by the water molecules while translocating along the center tube. This possibility is reasonable since the diameter of the center tube region is smaller than the diameters at the two ends of the CNT channel and, therefore, decreases the space for the distribution of water molecules around the oligonucleotide. When cases 4, 5, and 6 are compared, it is obvious that the increase in the van der Waals forces at the center region of the tube in case 4 is less significant than that in cases 5 and 6, as shown in Fig. 4(b). The lower force has led to the lesser folding of the oligonucleotide in case 4. Due to the forces by the water molecules that are inclining more toward the attractive nature to the oligonucleotide, the oligonucleotide is less folded while translocating along the narrower tube region. The flow of the water molecules leads to a more linear arrangement of the bases of the oligonucleotide in case 4. This phenomenon is in fact different from the behavior of the oligonucleotide in the (8,8)–(12,12) CNT channel, where a higher pressure leads to a lesser folding of the oligonucleotide.

When comparing the van der Waals forces in the (8,8)–(12,12) CNT channel with the forces in the (10,10)–(14,14) CNT channel, it is evident that the forces in the (10,10)–(14,14) CNT channel are more repulsive. As more space is available between the oligonucleotide and the (10,10) tube region, more water molecules are able to form hydrogen bonding between water molecules around the oligonucleotide and the effect of hydrophobic forces on the oligonucleotide is more prominent. The surface contact between the oligonucleotide and water has also increased due to the spacing available in the (10,10) nanotube region. Water molecules are able to "wrap" around the oligonucletoide in the (10,10) nanotube region, whereas the interaction between water molecules and the oligonucleotide at the (8,8)–(12,12) CNT channel junction occurs only between water and the exposed oligonucleotide to the solvent. At the (8,8)–(12,12) CNT channel junction, the amount of water molecules flowing toward the oligonucleotide and repelled by the oligonucleotide is minimal, whereas attraction between water and the oligonucleotide at the narrow junction is more dominant. Since the oligonucleotide in the (10,10) CNT interacts with more amount of water molecules, the number of water molecules repelled away from the oligonucleotide is also in-

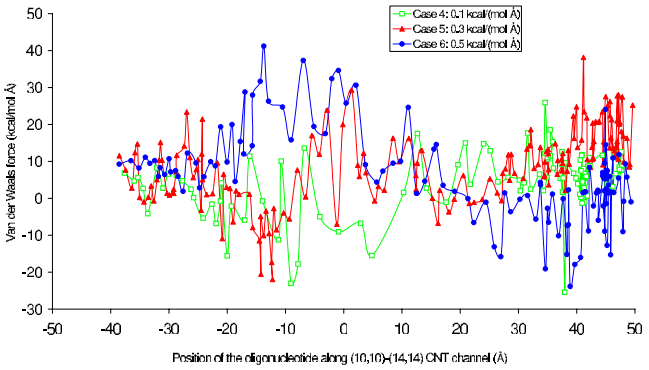

FIG. 5. (Color online) Van der Waals forces between the bases (guanine and cytosine) of the oligonucleotide in the (10,10)–(14,14) CNT channel.

creased. The resulting van der Waals forces between the oligonucleotide and water would therefore incline to more repulsive nature.

The interaction between the bases of the oligonucleotide is further emphasized in Fig. 5, showing the van der Waals forces between the bases (guanine and cytosine) of the oligonucleotide in the (10,10)–(14,14) CNT channel. Figure 5 shows that the less folded oligonucleotide in case 4 has led to a decrease in the van der Waals forces between the bases. The lower forces between bases of the oligonucleotide suggest that the interactions between the bases are less repulsive, possibly due to the less folding of the oligonucleotide.

Besides accounting the pressure as the contributing factor for the increasing amount of water molecules flowing along the (10,10)–(14,14) CNT channel, another possible factor is the blockage of the oligonucleotide. Figure 6 shows the radius of gyration of the oligonucleotide in the (10,10)–(14,14) CNT channel. Since the radius of gyration changes significantly along the entire channel, the main focus in Fig. 6 is the comparison of the radius of gyration along the center region of the (10,10)–(14,14) CNT channel only, between −20 Å and 20 Å. The radius of gyration of the oligonucleotide in the center region of the (10,10)–(14,14) CNT channel suggests that lesser folding occurs when the lowest pressure is induced to the system (case 4), as shown in Fig. 6. The decrease in radius of gyration of the oligonucleotide in Fig. 6 signifies a greater folding of the oligonucleotide as the

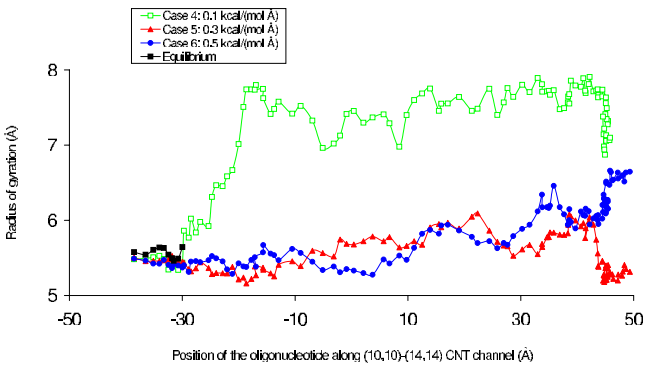

FIG. 6. (Color online) Radius of gyration of the oligonucleotide in the (10,10)–(14,14) nanotube channel in one translocation cycle.

pressure increases. The difference in the shape of the oligonucleotide influences the degree of blockage toward the number of water molecules flowing along the (10,10)–(14,14) CNT channel.

Based on the findings, we conclude that the folding of the oligonucleotide in the (8,8)–(12,12) CNT channel is due to the external force from the pressure applied, the effect of the nanotube junction, and the interactions between water molecules and the oligonucleotide. As for the oligonucleotide in the (10,10)–(14,14) CNT channel, the main effect of the folding is dependent on the water molecules and the pressure. When the cross-sectional area of the junction is sufficiently large, the folding of the oligonucleotide is more dependent on the pressure of the flow and the van der Waals forces between the water molecules and the oligonucleotide. Ponnuswamy and Gromiha [40] showed that there are two possible interactions involved in the unfolded chain of the oligonucleotide: the weakly formed hydrogen bonds between the nucleic acids chain and the solvent and the steric interactions among parts of the chain. Since the effect of electrostatic forces on the conformation of the oligonucleotide is very minimal [40], the electrostatic factor is therefore neglected in this study.

According to Rathore *et al.*, when the conformational space is limited, the unfolded state of the protein is destabilized by reducing the entropy of the protein [41]. However, the stabilization of the protein is dependent upon the relative magnitude of the change in enthalpy and entropy. The relationship of the energies can be expressed as $\Delta E = \Delta H - T\Delta S$, where E is the free energy, H is the enthalpy, and S is the entropy. In this study, the encapsulation of the oligonucleotide tends to decrease the entropy of the oligonucleotide [34]. In the case of the translocation of the oligonucleotide in the (8,8)–(12,12) nanotube channel, the increase in pressure results in a greater change in the van der Waals forces between water and the oligonucleotide. The decrease in van der Waals forces means that the total potential energy (enthalpy) is reduced and the net free energy is lower. Muthukumar showed that the escape of a polymer though a hole is achieved only when the polymer is able to overcome the free-energy barrier at the hole [42]. Since the net free energy at the nanotube junction is lower in the case of the oligonucleotide in the (8,8)–(12,12) nanotube channel at a high pressure, the insertion of the oligonucleotide into the narrow region of the channel has indeed deepened.

In the case of the translocation of the oligonucleotide in the (10,10)–(14,14) nanotube channel, the van der Waals forces between water and the oligonucleotide have shown to increase as the pressure is increased. The increase in van der Waals forces means that the total potential energy is increased and the net free energy should be higher. However, in order to maintain a lower free-energy barrier across the wider (10,10) nanotube, the change in the entropy of the oligonucleotide is increased instead and forms a more folded state of the oligonucleotide.

Lastly, the radial distribution of the water molecules around the oligonucleotide at the center region of the (10,10)–(14,14) nanotube channel is shown in Fig. 7. The flow of the solvent around the oligonucleotide is affected greatly by the shape of the oligonucleotide present in the

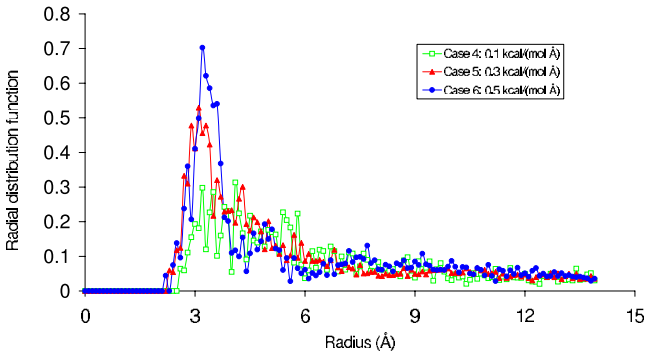

FIG. 7. (Color online) The radial distribution of water molecules around the oligonucleotide at the center region of the (10,10)–(14,14) nanotube channel for different forces applied.

narrow region of the CNT channel. Figure 7 shows that the distribution of the water molecules is concentrated more at the radius of 3 Å away from the center of the oligonucleotide when a high pressure is induced in the system (case 6). The center of the oligonucleotide is defined at the joining atom between guanine and cytosine. Since the folding of the oligonucleotide in case 4 is lesser, the distribution of water molecules is also less concentrated and varies at a wider range of the radius from the center of the oligonucleotide, between 3 Å and 6 Å, away from the center of the oligonucleotide.

IV. CONCLUSION

In conclusion, we conducted MD simulations of the solvated oligonucleotide translocating in CNT channels with an induced pressure difference. Three magnitudes of forces were applied onto water molecules to induce different pressures into the system. Two CNT channels of (8,8)–(12,12) and (10,10)–(14,14) were used as the nanochannels for studying the flow behavior of oligonucleotide and water molecules.

We have shown that the flow of the water molecules is affected by the blockage of the oligonucleotide at the (8,8)–(12,12) CNT channel, mainly, the cross-sectional area of the oligonucleotide. According to the calculations of the van der Waals forces between water molecules and the oligonucleotide, it is evident that the repulsion between water molecules and the oligonucleotide is lower when a higher pressure is induced into the system. Due to the inability of the oligonucleotide to flow through the middle tract of the (8,8)–(12,12) nanochannel, the CNT junction is able to resist the folding of the oligonucleotide at an induced higher pressure. The insertion depth of the oligonucleotide at the (8,8)–(12,12) nanotube junction is dependent on the induced pressure and also on the conformation of the oligonucleotide. The oligonucleotide is positioned nearer to the nanotube junction at a higher pressure than that at a lower pressure. As the pressure increases in the (8,8)–(12,12) nanochannel, the bases of the oligonucleotide repulse stronger against each other, due to the resistance of the CNT junction. The increase in the induced pressure results in a higher radius of gyration, meaning a more linear arrangement of the bases of the oligonucleotide in the (8,8)–(12,12) nanochannel.

The translocation of the oligonucleotide in the (10,10)–(14,14) CNT channel displays an increase in the van der Waals forces between the water molecules and the oligonucleotide as the pressure is increased in the system. The increment of the forces results in the folded arrangement of the bases of the oligonucleotide. The oligonucleotide is folded when a higher pressure is induced in the (10,10)–(14,14) CNT channel. The radius of gyration of the oligonucleotide is larger in a lower-pressured system, indicating an unfolded form of the oligonucleotide. The radial distribution of the water molecules is concentrated at a radius of approximately 3 Å away from the center of the oligonucleotide when a higher pressure is induced into the system. Due to the unfolded oligonucleotide present at a lower pressure, the water molecules are distributed more widely at a range between 3 and 6 Å away from the center of the oligonucleotide

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