THE BEHAVIOR OF FUNCTIONALIZED CARBON NANOTUBES IN WATER

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Abstract. Due to the cytotoxicity of carbon nanotubes (CNTs), there is an increasing need for functionalized CNTs (fCNTs) nowadays. Although a number of studies have been conducted to investigate the cytotoxic effects of fCNTs, their behavior in an aqueous medium has not been sufficiently studied. In this simulation-based research, the atomic level mechanisms of the interaction of pristine (non-functionalized) and fCNTs with water molecules were studied. The computational results showed that an increase in the number of functional groups in fCNT leads to an increase in its interaction energy with the water environment. This, in turn, results in a decrease in the cytotoxicity of fCNT. Overall, the results of the study contribute to the understanding at the molecular level of the transport and delivery of biological drugs using CNTs in the field of biomedicine.

Keywords: *single wall carbon nanotubes, functional groups, binding energy, water environment, interaction energy, molecular dynamics.*

Introduction

Carbon nanostructures are widely used in various fields as promising materials due to their unique physical, chemical and biological properties [1]. Especially, carbon nanotubes (CNTs) among them, are rapidly used in many fields due to their excellent electrical and mechanical properties [2]. In particular, they have been used in the field of biomedicine in the transport and delivery of biological drugs and as biosensors [3-7]. CNTs are used as membrane channels in cells, and they have shown excellent transport properties for DNA and other drug delivery across the cell membrane [8-11]. Especially, in cancer treatment, CNTs are considered as promising carriers [12] since they reduce harmful effects of therapy, i.e., drug toxicity [12-15], and deliver more drugs to the place where the tumor is located [16]. This, in turn, helps to reduce the damage to the healthy tissues of patients.

Pristine or non-functionalized CNTs are hydrophobic and tend to aggregate [17] in aqueous solutions due to their insolubility in water [18, 19]. The hydrophobicity of the surface of the aggregated CNTs leads them to chemically bind nutrients necessary for cell growth in a specific way and, as a result, has an indirect cytotoxic effect on cells (i.e., cell damage and death) [20]. In particular, it was observed that the cases of poisoning due to pristine CNTs in the lungs increased, as observed in experiments conducted with test animals [21, 22]. This limits the practical use of pristine CNTs in biomedicine and makes it necessary to reduce their toxicity by increasing their solubility in an aqueous environment.

An effective way to reduce the toxicity of CNTs is to add biocompatible organic materials to the surface of pristine CNTs, that is, to bind water-soluble functional radicals to them. In particular, experiments conducted using CNTs functionalized with formic acid (-CO2H) radical (i.e., carboxylated CNTs) showed that these CNTs do not have a cytotoxic effect [23]. In addition, in many studies, it was found that the solubility of nanotubes increases significantly after their modification by functionalized groups [24-30]. In particular, quantum mechanical calculations showed that an increase in the number of functional groups on the surface of carboxylated single-walled CNT (SWNT) leads to an increase in the Gibbs free energy of solvation and dipole moment of SWNT [28], meaning that the solubility of SWNT in water increased [28].

The molecular dynamics (MD) simulation-based study showed that the diffusion coefficient of carboxylated SWNT in water was lower than that of pristine SWNT (pSWNT), indicating that the hydrophilicity of SWNT increased [31]. Note that, in the above-mentioned computational studies, SWNTs with finite lengths (≤ 11 Å) and terminated edges with hydrogen atoms were chosen as model systems, that is, their physicochemical properties differ from those of sufficiently long SWNTs obtained by experimental

observations. In addition, the molecular-level mechanisms related to the diffusion of functionalized SWNT (fSWNT) have not been studied sufficiently in these investigations.

Based on the above considerations, in this study, the atomic level mechanisms of the interaction of pristine and functionalized (with different levels of formic acid radicals) SWNTs with the water environment are studied using reactive MD simulations.

Simulation details

Reactive MD simulations are performed using the ReaxFF potential to investigate the interaction mechanisms of pSWNT and fSWNT with water at the atomic level [32]. Using ReaxFF, MD simulations have been performed on various model systems, including water [33], CNT [34], etc. In our study, the parameter set of the ReaxFF developed by Zou et al. [35] is used. It has been shown that this set of parameters can describe SWNT very well (i.e., accurately and reliably) [34]. This parameter set can also describe accurately the water environment [33].

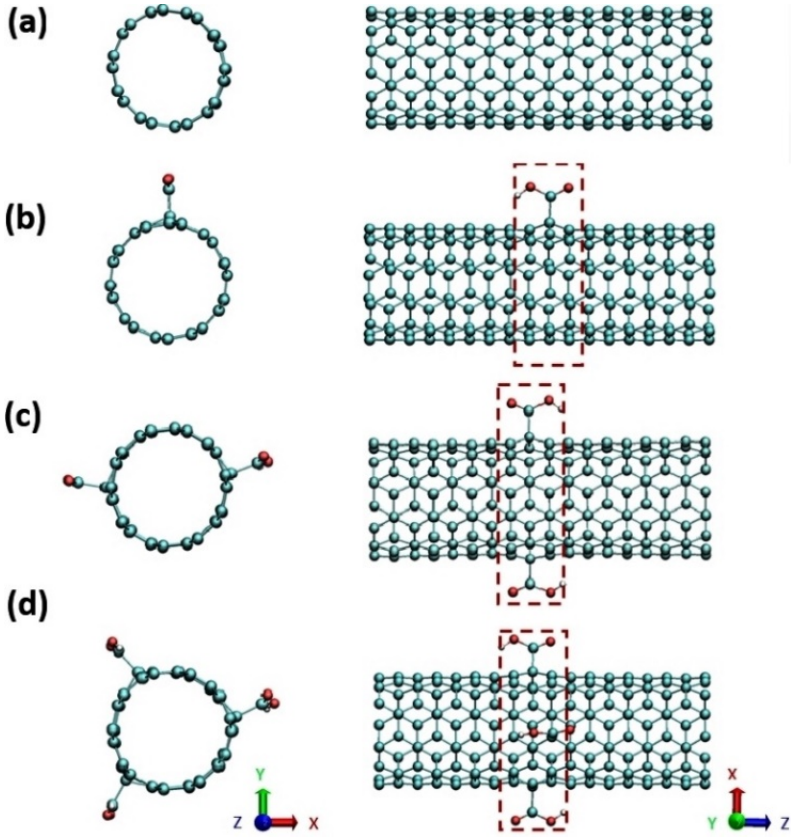

Fig. 1. Top (left) and side (right) views of pristine (a) and functionalized SWNTs with one (b), two (c) and three (d) formic acid (-CO_2H) radicals. The red dashed rectangles show the areas where the functional groups are located in SWNT.

As a model system, a pSWNT with (5,5) chirality, length of 22 Å, and diameter of 6.8 Å is created using the Nanotube Modeler software (Fig. 1(a)). To form fSWNT, one, two, and three formic acid (-CO_2H) radicals are covalently bonded to the surface of pSWNT (Fig. 1(b-d)). These functional groups are connected to the middle areas of pSWNT in the direction of the z-axis. Subsequently, these four model systems are surrounded by water molecules. Thus, pSWNT and fSWNT together with surrounding water molecules are placed in a simulation box with a size of 22 × 22 × 22.68 $Å^3$. Periodic boundary conditions are applied along the three directions of the simulation box: this allows the SWNTs to be considered long enough to mimic the experimental studies. Initially, the energy of the model systems is minimized using the conjugate gradient method. Then, the temperature of the systems is gradually heated up to 310 K (with a heating rate of 1 K/ps) using the NpT ensemble under a pressure of 1 atm for 0.31 ns. To control the temperature and pressure of the system the Berendsen thermostat and barostat are applied with corresponding dumping constants of 0.1 and 5 ps, respectively [36]. Subsequently, the temperature of the

model systems is kept for 1 ns using the Berendsen thermos-barostat in the NpT ensemble. A time step of 0.25 fs is chosen in all MD simulations.

Results and discussion. In order to evaluate the interaction of hydrophilic functional groups with nanotubes, the binding energy E_b of these groups to the surface of SWNT is determined as follows:

$$E_b = E_{SWNT-(CO_2H)_n} - (E_{SWNT} + E_{(CO_2H)_n}) \quad (1)$$

where, n is the number of functional groups ($n = 1-3$), $E_{SWNT-(CO_2H)_n}$ is the potential energy (eV) of the system consisting of SWNT and functional group(s), E_{SWNT} and $E_{(CO_2H)_n}$ are the potential energies (eV) of pSWNT and functional group(s), respectively. Using the formula (1), the binding energy of –CO2H radical(s) to the surface of SWNT is calculated for vacuum and aqueous media (see Table 1).

Table 1.

The binding energy of -CO2H radical(s) to the surface of SWNT in a vacuum and water environment. The values given in parentheses are the binding energy corresponding to one -CO2H radical.

Number of -CO_2H radicals	Binding energy (eV)	
	In vacuum	In water
1	-4.56	-4.58
2	-9.12 (-4.56)	-9.16 (-4.58)
3	-13.62 (-4.54)	-13.74 (-4.58)

It can be seen from the table that in both vacuum and water cases, the binding energy corresponding to one radical is nearly unchanged with an increase in the number of radicals. Namely, the binding energy corresponding to one radical in a vacuum environment is equal to -4.56, -4.56 and -4.54 eV for SWNTs with one, two and three functional groups, respectively, while in the aqueous environment, this value is -4.58 eV for all cases. Previous quantum mechanical calculation results showed that the increase in the number of radicals on the surface of SWNT leads to a decrease in their binding energy to SWNT (i.e., weakening of the bond) [28]. The difference between the results of this work and the quantum-mechanical calculations can be explained by the size of the SWNT and the hydrogen-based termination of its edges. In other words, in quantum-mechanical studies, a model structure of SWNT with a finite length of 8.65 Å was selected, and the edges of the nanotube were completely terminated with hydrogen atoms. The interaction of these hydrogen atoms with the functional groups in SWNT through non-bonding (i.e. Van der Waals and Coulomb) forces can affect the binding energy of these groups with SWNT. In our research, the absence of hydrogen atoms in the structure of SWNT eliminates the possibility of their interaction with functional groups, and therefore, the binding energy does not change (see Table 1). In addition, the long enough length (~22 Å) of SWNT prevents them from interacting with functional groups even if there are hydrogen atoms on its edges (i.e., hydrogen atoms and functional groups are outside the cut-off radius of interactions, i.e., 10 Å). Indeed, our test simulations with long enough (~22 Å) SWNT structures terminated with hydrogen atoms fully confirmed our above hypothesis. Namely, the binding energy corresponding to a single radical in a vacuum environment is equal to -4.61, -4.62 and -4.59 eV for terminated SWNTs with one, two and three functional groups, respectively.

In order to analyse the geometrical and electronic changes that can lead to better solubility of functionalized nanotubes, one can focus on their dipole moment. Determining the dipole moment of a given molecule can estimate its solubility in a solvent. The average dipole moments of pSWNT and fSWNT with one, two and three formic acid radicals are shown in Fig. 2.

It is obvious that the average dipole moment of pSWNT is almost 0 D, and this indicates that pSWNT is insoluble in polar solvents such as water [28]. The main reason for this is that the partial charges of carbon atoms of pSWNT are almost zero. On the other hand, the average dipole moment of fSWNT significantly increases compared to that of pSWNT. In particular, the average dipole moments of pSWNT and fSWNT with one, two and three –CO_2H radicals are 0.001, 3.793, 1.946 and 1.541 D, respectively. A decrease in the average dipole moment with an increase in the number of functional groups can be explained by the fact that the dipole moments of the functional groups remain in opposite directions, thereby attenuating each other. In general, the functionalization of SWNT with –CO_2H radicals increases its dipole moment and this, in turn, can change its interaction with a polar solvent such as water.

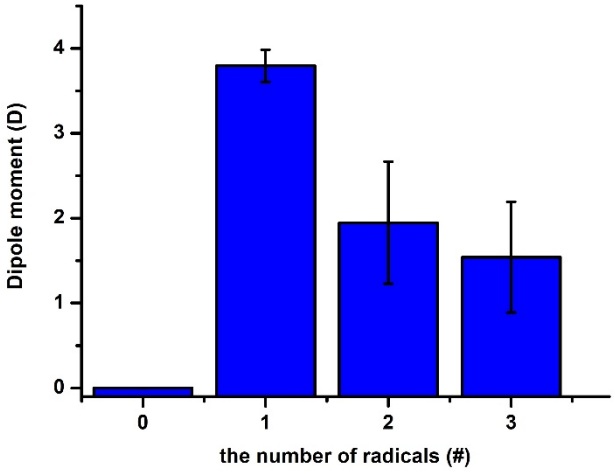

Fig. 2. The average dipole moments of pSWNT and fSWNT with one, two and three formic acid radicals.

Table 2 shows the interaction energies of pSWNT and fSWNTs with water molecules. It should be noted that these energies are calculated in the same way as the binding energy given in formula (1). In other words, the interaction energy between fSWNT and water is determined by subtracting the sum of the separately calculated potential energies of fSWNT and the water environment from the total potential energy of the aqueous system.

Table 2.

The interaction energies of pSWNT and fSWNTs with water molecules.

Nanotube	Interaction energy (eV)	Number of atoms in the system	Energy per atom of the system (eV)
SWNT	-6.13	180	-3.41×10-2
SWNT-CO2H	-6.46	184	-3.51×10-2
SWNT-(CO2H)2	-7.44	188	-3.96×10-2
SWNT-(CO2H)3	-8.72	192	-4.54×10-2

Table 2 shows that the interaction energy between pSWNT and water molecules is equal to -6.13 eV, and this energy increases with the increase in the number of functional groups in fSWNT. In particular, this energy is -6.46 eV, -7.44 eV and -8.72 eV for fSWNTs with one, two and three radicals, respectively. Also, the table indicates that the average values of these interaction energies per atom of the system increase with the increase in the number of functional radicals in fSWNT. Namely, the interaction energies of pSWNT and fSWNT with one, two, three radicals are -3.41×10^{-2} and -3.51×10^{-2}, -3.96×10^{-2}, -4.54×10^{-2}, respectively. Due to the increase in the interaction energies, the attraction of water molecules to the surface of the SWNT may hinder the movement of fSWNT in water and cause a decrease in its diffusion coefficient. Therefore, these results are in full agreement with the previous MD results [31] obtained on the diffusion of fSWNT in water and help us to understand the behavior of fSWNT in the water environment. In general, the functionalization of a nanotube with $–CO_2H$ radicals increases its dipole moment, thereby leading to an increase in its solubility eventually reducing its toxicity.

Conclusions

In this MD-based research work, the mechanisms of the interaction of pSWNT and fSWNT with the water environment were investigated at the atomic level. The results obtained showed that the binding energy corresponding to one functional group in SWNT in a vacuum and in an aqueous medium remained practically unchanged with an increase in the number of functional groups. This phenomenon was explained by the long length of SWNT and the termination degree of its edges. Simulation results also showed that the fSWNT dipole moment is inversely proportional to the number of functionalized groups, while in pSWNT it is almost zero. Moreover, obtained interaction energy per atom in SWNT increases with the

increase in the number of functional radicals. Hence, the increased interaction between fSWNT and water molecules improves the solubility of fSWNT, thereby leading to a decrease in its cytotoxicity.

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