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# Solvation of alanine and histidine functionalized carbon nanotubes in aqueous media: A Monte Carlo simulation study

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ABSTRACT

In this research, the effect of adsorption of two amino acids on the solvation of carbon nanotubes is investigated. The complexes of β-Alanine and Histidine with armchair single wall carbon nanotube are studied by density functional theory. Then, the outcomes of Monte Carlo simulations of these nanotubes immersed in water to look at the effects of nanotube type on the solvation in water are reported. It is found that the binding energy of the interaction of β-Alanine with nanotube is larger than Histidine. The results of computer simulation in aqueous solution indicate that amino acid functionalization increases the intermolecular interactions of carbon nanotube and water. Computed solvation free energies are in this order: CNTAlanine > CNTHistidine > pure CNT.


## 1. Introduction

Carbon nanotubes (CNTs), due to their one dimensional structure and remarkable mechanical, thermal, optical, and electronic properties, may find many applications in materials and life sciences [1]. The well-defined shape and size of carbon nanotubes (CNTs) make them attractive candidates for theoretical and experimental studies of various nanoscopic phenomena such as protection and confinement of molecular species as well as transport of molecules through their interior pores. Nanotubes are believed to open the road toward different modern fields, either technological or biological. CNTs have recently become promising materials in various biological applications such as drug delivery [2], tumor therapy [3], biosensors [4], and templates for biomolecule assembly [5]. However, the applications of nanotubes have been badly impeded for the poor solubility in water which is especially essential for studies in the presence of living cells. Therefore, water soluble samples are in demand candidates for theoretical studies of various nanoscopic phenomena such as protection and confinement of molecular species as well as transport of molecules. However, there are still challenges facing the carbon nanotube industry, such as how to effectively disperse CNTs in solution, and how to assemble CNTs and other molecules into useful nanostructures [6–8].

An important technique to increase the solubility and reactivity of CNT is through functionalization, which increases the electrical dipole moments [9]. A theoretical study of the functionalization of SWCNTs with some organic molecules has shown the changes in the NT properties due to the functionalization [10]. Among numerous functional species, functionalization of NTs with the assistance of biological molecules (such as nucleic acids and proteins) improves the solubility in aqueous, thus facilitating the application of NTs in biotechnology, biomedicine, and bioengineering. Theoretical studies on DNA bases [11] and functionalized CNTs with DNA bases [12] indicate the enhancement of solubility of NTs in water through favorable changes in the solvation energy.

Some specific proteins/peptides have been proven to bind to CNTs in experiments, thus can be used to disperse CNTs through their interior pores [13–15], At the same time the wide biomedical applications raise the biosafety concerns of CNTs due to their unintended interactions with proteins and other biological molecules [16–18].

Despite their technological and biological interest there is not enough detailed theoretical analysis of the interactions of CNTs and biological molecules such as amino acids. As a starting point in understanding interactions with much more complex biological systems, we carried out the interaction of CNTs and two amino acids β-Alanine and Histidine (two amino acids in the structure of carnosine dipeptide). Carnosine has protective functions additional to anti-oxidant and free radical scavenging roles. It extends cultured human life span, kills transformed cells, protects cells against aldehydes and an amyloid peptide fragment and inhibits in vitro, protein glycation and DNA/protein cross linking. Carnosine is an aldehyde scavenger, a likely lipofuscin (age pigment) precursor and possible modulator of diabetic complications, atherosclerosis and Alzheimer's disease [19–25].

It has been shown that CNTs can be used as liquid filled nanoparticles for drug delivery tool improves the bioavailability of carnosine. This is an example of the potential applications of carbon nanotubes in biomedicine as drug or vaccine carriers and biomolecular recognition [26].

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In this study we investigate the interaction of armchair (5, 5) carbon nanotube and the amino acids β-Alanine and Histidine in gas phase and aqueous solution within density functional theory calculations and Monte Carlo simulation. Since carnosine dipeptide structure consists of β-Alanine and L-Histidine, we are interested in these amino acids. Details on the model as well as on the computational methods employed are explained more thoroughly in the proceeding section.

## 2. Computational method

This study comprised two sections: quantum mechanics (QM) and Monte Carlo (MC) simulation. In the quantum mechanical part, isolated molecules (CNT, β-Alanine and L-Histidine functionalized CNTs and isolated β-Alanine and L-Histidine) were optimized. Then it has been applied Monte Carlo simulation for dilute solutions of nanotubes in water.

Therefore the study was divided into four parts: (i) Geometry optimization of the amino acids, and (5, 5) CNT; (ii) interactions of amino acids with substrate (CNT); (iii) stability analysis structure of the CNTAlanine (CNTAla) and CNTHistidine (CNTHis) complexes in gas phase: and (iv) stability analysis structure of the CNTAla and CNTHis complexes in water medium.

In the first step of our investigation it was important to find the most stable isomers of β-Alanine and L-Histidine. As mentioned before, we were interested to study the interaction of alanine and histidine with CNT, because these two amino acids participate in carnosine dipeptide structure. Therefore, the sites of amino acids that take part in peptide bonding were blocked to prevent interacting with CNT. The sections that would form part of the peptide bonding have all been replaced by terminating hydrogen. This approach has been utilized in other researches before [27].

Hence, among the possible isomers, the protonated form of these two amino acids (Fig. 1) has been used. It should be noticed that these protonated forms of amino acids are stable under their isoelectric pH [28]. The protonated forms of histidine and alanine were fully optimized to confirm the stability of related structures. Then separately optimized geometries were used in the combined system.

To perform an accurate QM calculation to a nanosized system without ending up in a prohibitively large computation, an approach is the cluster model. Most of the previous attempts to study this phenomenon are using a cylindrical part of the tube while dangling bonds at the ends of the tube were saturated with hydrogen atoms to minimize the edge effect [29]. Similar methodology was used successfully to study the gas adsorption to CNTs [30,31].

The ab initio study of the interaction of glycine amino acid and CNT has used the same approach [32]. A large part of an armchair (4, 4) and a zigzag (8, 0) CNT containing 64 carbon atoms (or 3 hexagon layers) were separated and treated as an individual system. In the study of DNA-base Li doped SiC nanotubes [12], 5 hexagon layers of SiC nanotubes have been used.

In our research a large adequate part of an armchair (5, 5) CNT containing 100 carbon atoms was separated and treated as an individual system. Five layers of carbon ring hexagons along the tube axis were modeled where the two edge dangling bonds are saturated by hydrogen atoms to emulate the bulk properties. Then interactions of amino acids with the central ring were studied.

Each species (amino acid, CNT and their complexes) was optimized by the DFT/B3LYP method using the 6–31 G* [33,34] basis set. The length of the tube has been chosen constant (equal to 11 Å). In all calculations, nanotubes were capped with hydrogen atoms. All structural optimization for the nanotube-amino acid systems was performed by using the GAMESS-US quantum chemistry package [35].

Then investigations of the structural properties of water surrounding nanotubes (containing CNT, CNTAla and CNTHis) were studied by performing fully atomistic Monte Carlo simulation in water. The FORTRAN code developed by the corresponding author [36] was used in simulation.

In all separate MC simulations performed here, throughout a standard manner the Metropolis sampling technique [37] in canonical (T, V, N) ensemble was used. Each setup includes two sections: a solute fragment and water molecules. All calculations were performed in a cubic box at the experimental density of water, 1 g/cm$^3$. The optimum edges of the box were 50 × 50 × 50 Å, which corresponds to almost 4000 $H_2O$ molecules of pure solvent. The interactions between the solute and the water molecules were defined by a site–site interaction potential consisting of a LJ potential to represent the short range interactions and a long range Coulomb potential with parameters, $\varepsilon_i$, $\sigma_i$, and $q_i$ for each atoms in nanotube and amino acids:

$$E^{AB} = 4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right] + \frac{q_i q_j e^2}{r_{ij}} \quad (1)$$

$E^{AB}$ is the interaction energy between two molecules, A and B, which are expressed by the pair wise sum of their interaction contributions. Appropriate Lennard–Jones parameters for atoms in CNT [38] and amino acids [39,40] are given in Table 1. The Transferable intermolecular potential function (TIP3) [41] was applied for modeling water molecules. Periodic boundary conditions were employed in computation. The system was thoroughly equilibrated using $10^7$ configurations.

To calculate the solvation free energies of the nanotubes, the thermodynamic perturbation method was applied in these computations. The free energy difference between two states A and B of a system may be derived from classical statistical mechanics [42] allowing this difference to be expressed as Eq. (2) as the free energy perturbation (FEP) master equation.

$$\Delta G = G_B - G_A = -RT \ln\langle \exp -(E_B - E_A)/RT\rangle \quad (2)$$

$(E_B - E_A)$ is the potential energy difference ($\Delta E$) between states A and B of the system. $R$ is the molar gas constant, $T$ is the absolute temperature,

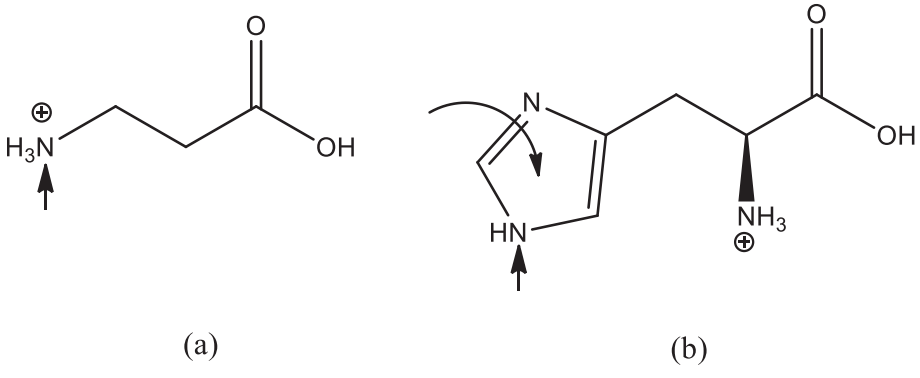


**Fig. 1.** Amino acids (a) β-Alanine and (b) Histidine.