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Separation of chiral nanotubes with an opposite handedness by chiral oligopeptide adsorption: A molecular dynamics study

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ABSTRACT

The separation of enantiomeric chiral nanotubes that can form non-covalent complexes with an unlike stability upon adsorption of chiral molecules is a process of potential interest in different fields and applications. Using fully atomistic molecular dynamics simulations, we report in this paper a theoretical study of the adsorption and denaturation of an oligopeptide formed by 16 chiral amino acids having a helical structure in the native state on both the inner and the outer surface of the chiral (10, 20) and (20, 10) single-walled carbon nanotubes having an opposite handedness, and of the armchair (16, 16) nanotube with a similar diameter for comparison. In the final adsorbed state, the oligopeptide loses in all cases its native helical conformation, assuming elongated geometries that maximize its contact with the surface through all the 16 amino acids. We find that the complexes formed by the two chiral nanotubes and the chosen oligopeptide have a strongly unlike stability both when adsorption takes place on the outer convex surface of the nanotube, and when it occurs on the inner concave surface. Thus, our molecular simulations indicate that separation of chiral, enantiomeric carbon nanotubes for instance by chromatographic methods can indeed be carried out using oligopeptides of a sufficient length.

1. Introduction

Carbon nanotubes, including multi-walled and in particular single-walled carbon nanotubes (SWNT), have spurred a large interest in the last years for their most peculiar structure, leading to new and unusual electronic and structural properties, relevant for nanoscience in general, but in particular for electronic, mechanical and biomaterials applications [1–4]. SWNT can be structurally described as the cylindrical wrapping of a single graphene sheet, and are structurally characterized with two indices, (n, m): in particular, if $n = m$ one gets the so-called armchair nanotubes, which are electrically conducting, whereas for $n \neq m$ one gets the chiral nanotubes, where the nanotube chirality is akin to the chirality of the isotactic stereoregular polymers having a helical conformation in the solid state. The latter SWNTs (which are in most cases semiconducting, apart from special combinations of the n, m indices) are often denoted as nanotubes with different chiralities with reference to the chiral vector characterized by the (n, m) values which describe how the graphene sheet is wrapped up [5]. In a more rigorous chemical language, however, a different chirality indicates molecules that are non-superimposable to their mirror images, so that it refers to individual enantiomeric (n, m) and (m, n) nanotubes [6], which accordingly differently respond to circularly polarized light. Incidentally, we also mention that enantiomeric nanotubes are sometimes denoted as *M* and *P* nanotubes with a single set of values (n, m) and $n > m$ [7].

Because of this feature, enantiomeric SWNTs may in principle interact with chiral molecules by forming complexes with an unlike stability, thus allowing separation of left-handed from right-handed nanotubes for instance through appropriate chromatographic procedures with suitable stationary phases. Such separation of enantiomeric carbon nanotubes was first achieved experimentally by using chiral nano-tweezers formed by two porphyrin rings joined by a 1,3-substituted phenyl ring, each carrying two asymmetric substituents [7,8]. Another successful separation technique employed density gradient ultracentrifugation using a chiral sodium cholate surfactant [9]. The chiral recognition of nanostructured carbon allotropes (nanotubes or fullerenes) is thus an emerging area of great potential interest [10], related also to their effect in the formation of chiral molecules in certain chemical reactions [11]. On the other hand, such experimental achievements were quite unexpected on the basis of earlier theoretical results for the adsorption of *trans* 1,2-substituted cyclopropane and cyclohexane on chiral SWNT [12]. In the latter work, a united atom model

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Table 1
The sequence of residues in the selected amino acid sequence with the corresponding hydropathy indices.

Residue	Hydropathy index[a]
GLU16	−3.5
GLU17	−3.5
ASN18	−3.5
PHE19	2.8
LYS20	−3.9
ALA21	1.8
LEU22	3.8
VAL23	4.2
LEU24	3.8
ILE25	4.5
ALA26	1.8
PHE27	2.8
ALA28	1.8
GLN29	−3.5
TYR30	−1.3
LEU31	3.8

[a] [29].

was adopted for the adsorbates interacting with the SWNT through a Lennard-Jones potential. Using a hybrid Monte Carlo method at a constant temperature and considering chiral SWNT of different diameters, the difference in stability of the chiral adsorbates inside the enantiomeric nanotubes was always found to be smaller than about 65 J/mol, but with an even larger statistical uncertainty which indicated than no enantioselectivity should actually be possible. Since this result is clearly at variance with the abovementioned experimental results, we can speculate that the number of asymmetric chiral atoms present in the experimentally used adsorbate molecules and their flexibility can explain this discrepancy, and furthermore that using a fully atomistic theoretical model could also be most relevant.

Therefore, in order to tackle this issue, we decided to consider an oligopeptide formed by natural amino acids that contain multiple chiral centers and form a α-helix in the native state, and to model its adsorption on enantiomeric SWNTs with fully atomistic molecular mechanics (MM) and molecular dynamics (MD) methods. We recently modeled the adsorption of larger protein subdomains comprising 60 amino acids mostly structured in three α-helices on achiral, armchair SWNT, more precisely the (30, 30), (40, 40) and (50, 50) nanotubes, considering both the outer convex and the inner concave surface to understand the effect of an unlike nanoscale topography (the different radii of curvature), and the adsorption a single oligopeptide within the much smaller (8, 8) and (10, 10) SWNT [13]. Conversely, the aim of the present study is to determine whether a chiral oligopeptide formed by natural amino acids can discriminate between two chiral enantiomeric SWNTs, namely the (10, 20) and (20, 10) nanotubes, of opposite handedness by forming non-covalent complexes with an unlike stability. Adopting throughout the same methodology as in our previous work [13], in this study the chosen oligopeptide is a hydrophobic sequence with a native α-helix structure taken from human serum albumin (HSA), more precisely helix A2A formed by 16 residues, from GLU16 to LEU31 as reported in Table 1, previously employed also to model the interaction with the (8, 8) and (10, 10) SWNT [13]. This α-helix belongs to a subdomain close to the outer HSA envelope (see Fig. 1 of ref. [14]), but still it is quite hydrophobic, as shown by the hydropathy indices of the individual residues reported in Table 1.

It should be added that all residues in the chosen sequence contain a chiral C_α atom, since glycine is not present. The selected nanotubes are two uncapped chiral SWNT (n, $2n$) and ($2n$, n), with $n = 10$, having a diameter of 20.71 Å, but for comparison we also modeled adsorption on an achiral armchair (16, 16) SWNT with a diameter of 21.70 Å. In all cases, we considered the oligopeptide interaction with the inner concave and with the outer convex nanotube surfaces, thus having two unlike topographies but the same surface chemistry of sp^2 carbon atoms. In either case, however, we assumed an unbiased interaction by placing the starting oligopeptide helix with different initial arrangements close to the lateral surface and to the open end of the nanotubes, not assuming any a priori insertion within the SWNT. Thus, surface adsorption or encapsulation of the oligopeptide would only take place within the MD runs if indeed the surface interaction is favorable.

In the following, after a short description of the simulation methodology, we discuss the oligopeptide interaction strength with the outer or the inner nanotube surfaces and the general stability of the resulting adducts after its adsorption and spreading with complete denaturation. Afterwards, we describe in more detail the interaction geometries, first inside the SWNT on the concave surface, and then outside the SWNT on the convex surface, considering the system energy and the adsorbate conformation through the Ramachandran maps. Further details about the simulations results can be found in the Supplementary data. The present simulations are carried out in an effective dielectric medium using a distance-dependent dielectric constant as done in previous papers [13–17]. This approach allows probing lengthy large-scale surface rearrangements thanks both to the smaller system size and to the much faster relaxation rate due to the lack of friction with the solvent molecules. Such approach was already supported by a comparison with our previous simulations in explicit water, where the changes in the solvation energy was estimated to amount to about 10% [17], and with our simulations of molecular recognition phenomena in supramolecular host–guest complexes [18]. Moreover, using MD simulations in explicit water [19,20], Szeifler et al. [19] recently showed that atomistic MD simulations of protein adsorption (lysozyme) on a hydrophobic surface (namely crystalline polyethylene) require huge simulation times because of lengthy dehydration processes, but eventually, after an initial diffusion to the surface, the protein–surface interaction leads to their dehydration on timescales of the order of tens of nanoseconds, eventually followed by local denaturation mostly involving the loss of α-helices. Moreover, Zhou et al. [20] showed that a much smaller protein (the villin headpiece, comprising only 35 residues) on graphene in explicit water lead to a very large, though not yet fully complete, surface spreading. Such adsorption processes, accompanied by very lengthy protein dehydration close to the surface, produced final arrangements very similar to those obtained by us on graphite with the effective dielectric medium, thus supporting our use of an implicit solvent as a way to significantly speed up computationally the protein adsorption process on these materials without introducing significant artifacts.

2. Simulation method

The simulations were performed using the same methodology adopted in our previous papers, using the InsightII/Discover, the Materials Studio and the Discovery Studio programs [21] with the consistent valence force field CVFF [22], as previously done in similar studies [13–17]. We considered uncapped chiral (10, 20) and (20, 10) SWNTs with a diameter $D = 20.71$ Å and a length of 67.63 Å, and an armchair (16, 16) SWNT with $D = 21.70$ Å and a length of 61.49 Å. The selected oligopeptide sequence was taken as the hydrophobic A2A α-helix of human serum albumin (described in more detail in ref. [14] and previously modeled also in ref. [13]) containing 16 residues (all with a chiral C_α atom, since glycine is not present) with the appropriate charges for the ionizable residues at the physiological pH = 7.4. The native α-helix was optimized close to the surfaces in four unbiased trial orientations both close to one open end of the uncapped SWNTs, not assuming a priori any inclusion