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Size-selective, non-covalent dispersion of carbon nanotubes by pegylated lipids: a coarse-grained molecular dynamics study

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ABSTRACT

Phospholipids with tethered poly(ethylene glycol) chains (PL-PEGs) offer efficient, non-covalent dispersion of carbon nanotubes (CNTs). Important questions concern the relation between micellar and CNT-assembled PL-PEG structures, and the influence of PEG length on assembly and dispersion. We explore these questions here via coarse-grained molecular dynamics simulation. Employing two representative CNT diameters and a range of PEG molecular weights, we find (i) PL-PEG aggregation number to vary inversely with PEG chain length, consistent with recent experiments, (ii) an assembled morphology to vary from micellar-like to monolayer-like, depending on PEG chain length and CNT diameter, (iii) micellar coatings to
result in greater CNT dispersion ability, with a higher barrier for interparticle aggregation (84 kJ/mol) compared to monolayer coatings (60 kJ/mol), and (iv) good agreement between simulation and scaling theories of a brush-type PEG.

KEYWORDS

size-selective separation, molecular simulation, MARTINI, amphiphilic di-block biopolymer, adsorption, aggregation barrier

**Introduction**

Carbon nanotubes (CNTs) are thought to be promising candidates for optical, electrical, mechanical, and chemical applications.\(^1\)-\(^3\) In addition, CNTs are being considered for many biological applications, including cell scaffolds and drug and gene delivery vehicles.\(^4\) Achieving isolated CNTs remains a key challenge, as they tend to aggregate in many solvents, particularly the more polar solvents such as water.\(^5\) Ultrasonic shock waves can be used to de-aggregate CNTs, but unless a barrier is present, re-aggregation generally occurs. To stabilize isolated CNTs, two approaches have been taken: chemical functionalization with hydrophilic groups\(^6\),\(^7\) and coating with amphiphilic molecules such as lipids,\(^8\)-\(^13\) surfactants,\(^14\),\(^15\) proteins,\(^16\),\(^17\) and polymers.\(^18\)-\(^24\) Chemical functionalization, while effective at dispersion, introduces CNT defects, which may compromise desired properties. Amphiphilic species, on the other hand, leave the CNTs intact, and therefore are particularly attractive.

Poly(ethylene glycol) (PEG) is a hydrophilic polymer often end-grafted to material surfaces so as to prevent surface deposition.\(^25\)-\(^28\) PEG chains may be grafted to the hydrophilic head groups of phospholipids (PL-PEGs), such that assembled structures become stabilized against self-
aggregation. PL-PEGs have been used to disperse and functionalize CNTs. Brahmachari et al. have found even short PL-PEG (PEG M\textsubscript{W} 550) to inhibit aggregation.\textsuperscript{29} Liu et al. have developed covalent and PL-based non-covalent methods of CNT PEG functionalization,\textsuperscript{30-32} and considered the blood circulation and organ uptake ratios as a function of PEG length.\textsuperscript{33} Sacchetti et al. determined the protein adsorption to PEG grafted and PL-PEG coated CNTs to depend more sensitively on PEG chain length than on any specific properties of the protein.\textsuperscript{34} Our earlier work showed PL-PEG to significantly influence the degree of CNT bundling, which in turn strongly influenced the thickness and antimicrobial character of layer-by-layer assembled CNT-polyelectrolyte films.\textsuperscript{35}

The above studies indicate the PL chemical structure, and the morphology of the assembled PL-PEG coatings, to greatly influence the dispersion efficiency. However, molecular details on PL-PEG assembly to CNT are scarce. A few molecular scale, thermodynamic theories have been developed,\textsuperscript{36,37} but are in need of molecular level inputs. Molecular computer simulation has been widely used as a form of “computational microscopy” to study the formation of self-assembled aggregates on a molecular or even atomic level. In particular, all-atom\textsuperscript{13,38-43} and coarse-grained (CG)\textsuperscript{44-46} molecular dynamics (MD) simulations and mesoscale dissipative particle dynamics (DPD) simulations,\textsuperscript{47-49} have provided molecular scale insight into CNT-lipid and CNT-surfactant aggregation. Furthermore, the interactions between CNT-lipid complexes and lipid bilayers\textsuperscript{50,51} have been simulated, providing insight into the structural perturbations induced in cell membranes from exposure to coated CNTs. A few recent studies have specifically addressed PL-PEG coatings. In particular, Lee et al. have shown CNT interparticle aggregation to differ between grafted\textsuperscript{52} and PL-assembled\textsuperscript{53} PEG coatings, and for lipid structure and PEG length to play key governing roles the PL-PEG systems. Bobadilla et al. have studied
PEG-grafted CNTs with atomistic detail, and showed that grafted PEG may suppress the wrapping of the CNTs by free polymer.\textsuperscript{54}

In this work, we employ molecular dynamics simulation to investigate the influence of PEG chain length on PL-PEG micellization and CNT-PL-PEG assembly and dispersion efficiency. We consider (10,0) and (18,0) CNTs, of diameters 0.7 and 1.4 nm, respectively, 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[hydroxy(polyethylene glycol)] (PL-PEG) at 0.13 w/v concentration (above the critical micelle concentration), and PEG molecular weights 500, 1000, 2000, and 5000. We find the PL-PEG assembly morphology to be quite similar to that of pure PL-PEG micelles under conditions of small CNT diameter and short PEG length, but to switch to a monolayer-like morphology for larger diameter CNT and/or longer PEG length. Furthermore, we find the micellar-like assembled structures to offer superior CNT dispersion.

**Computational Methods**

**System setup**

In all simulations, the PL-PEG molecule used is DSPE-PEG-OH (IUPAC name (propyl-polyethyleneglycol)-carbamyl-distearoylphosphatidyl-ethanol). The PEG chain length varied as 12, 24, 48, or 114 monomers, corresponding to molecular weights \(M_w = 500, 1000, \) and 2000, and 5000 respectively, while the PL part was kept intact. The PL-PEG molecules of different PEG chain length are referred to PL-PEG12, PL-PEG24, PL-PEG48, and PL-PEG114, respectively. The simulation box size was (21x21x20) nm\(^3\) and in all simulations the PL-PEG concentration was kept fixed at 0.13 w/v, which is well above the experimentally reported CMC (in the micromolar range).\textsuperscript{55} Thus, 454, 339, 225, or 117 PL-PEG molecules were simulated, depending on the chain length. As an increase in solute concentration accelerates micellar self-
assembly, the elevated concentration selected for the simulations enabled the study of micellar aggregation in detail. The simulations were carried out both in pure PL-PEG—water solution and in the presence of either a (10,0) CNT with a diameter of 0.7 nm, or an (18,0) CNT with a diameter of 1.4 nm. The PL-PEG molecules were inserted randomly into the simulation box with their respective Na\(^+\) counterions (to maintain electroneutrality). When present, the CNT spanned the periodic simulation box in the z-direction. Simulation details are given in Table 1, and a representative snapshot of the initial configuration is shown in Figure 1.

Free energy calculations to estimate the dispersion barrier height were performed for the PL-PEG24 system with (10,0) CNT and (18,0) CNT. In these calculations, the final configuration representing a fully PL-PEG coated CNT from a prior simulation was used. Two such coated CNTs were inserted parallel to each other into a larger simulation box of size (26x26x20) nm\(^3\), with initial inter-tube separation of 13 nm. The CNTs were pulled radially towards each other at a rate of 0.1 pm/ps. A set of 44 windows (structures) was taken from the pulling simulation. The windows were spaced 0.22 nm apart, spanning the range of inter-tube center-of-mass (COM) distance 1–10 nm. For each window, a simulation in which the CNTs were radially restrained with a biasing potential was performed. The potential of mean force (PMF) with respect to the inter-tube COM distance was extracted from these biased simulations to estimate the re-aggregation barriers.

**Force Field and Models**

The framework of the MARTINI CG force-field\(^{56,57}\) was used in all simulations. As MARTINI excels in reproducing partitioning free energies between polar and apolar phases,\(^ {56}\) it is well-suited for studying hydrophobicity-driven self-assembling systems such as PL-PEG-CNT
complexes. Originally the MARTINI force-field was developed for lipids and detergents,\textsuperscript{56,57} but has been extended later to proteins,\textsuperscript{58} lipoproteins,\textsuperscript{59} fullerenes,\textsuperscript{60,61} graphene\textsuperscript{62} and CNTs\textsuperscript{53}.

In the MARTINI model, the atoms of a molecule are replaced with specific interaction centers: on average one interaction center consists of four non-hydrogen atoms. Interaction sites are categorized into four different main types: charged, polar, non-polar, and apolar, and within these groups to subtypes based on, for example, polarity or hydrogen-bonding capabilities. The viability of the MARTINI CG approach for polymers has been tested for biopolymers, such as PL-PEG,\textsuperscript{63-65} triblock polymers such as PPO-PPO-PEO,\textsuperscript{66} as well as synthetic polymers such as polystyrene.\textsuperscript{67,68} The molecular level CG modeling based scheme is chosen for this work because, compared to fully atomistic models, it allows larger systems and longer timescales to be studied, with the same computational effort, while preserving the underlying chemical nature.

The speed-up is mainly due to the CG approach smoothing out the interaction potential, enabling the use of a longer time-step. Additionally, the CG simulation time corresponds to a significantly longer actual time. For MARTINI, a factor of 4 based on, e.g., water diffusion rates is typically used in converting the simulation time to real time.\textsuperscript{56,69} The simulation times reported in this work are multiplied by this factor and hence represent real time.

The model for the PL-PEG, DSPE-PEG-OH, was constructed by modifying the standard MARTINI DSPE lipid\textsuperscript{56} to include the new MARTINI PEG tail introduced and verified previously.\textsuperscript{65} CG CNT models represent atomistic (10,0) and (18,0) CNTs, with diameters \textasciitilde0.7 nm and 1.4 nm, and are described by a 3-to-1 mapping with CG bead-to-bead distance of 2.84 Å (the atomistic carbon-carbon separation is 1.42 Å). This CG model preserves CNT chirality and other symmetries. The interaction model and the force constants of the CNT beads have been described previously,\textsuperscript{53} and shown to accurately predict the amount of adsorbed
lyosphosphadidylcholine on a CNT surface. Due to the large radius of curvature in the coarse-grained tubes, the CNT bead distances were further constrained by the Lincs algorithm. For water and counterions, standard MARTINI water and ion beads were used. The MARTINI force field is known to underpredict the CMC of a pegylated alkane model by about an order of magnitude. Concentrations employed here are well above the experimental CMC, so this discrepancy is expected to have a negligible influence on system behavior.

Simulation Protocols

Simulations were performed within the NPT ensemble using the GROMACS 4.6.4 simulation package. For thermostating, the stochastic velocity rescaling thermostat of Bussi et al. was employed with temperature $T=298K$. A pressure of 1 bar was maintained with the Parrinello-Rahman pressure control using $\tau_p = 12$ ps semi-isotropically with the CNT axial direction pressure controlled separately. A cut-off of 1.2 nm was employed for the Lennard-Jones (LJ) potential and electrostatic interactions. The LJ interactions were shifted to zero smoothly between 0.9 nm and 1.2 nm, and the Coulombic interactions between 0 nm and 1.2 nm. The time step was 20 fs. This simulation protocol corresponds to the standard MARTINI protocol. For each simulation, energy minimization was carried out with the steepest descent algorithm. The above conditions were used both during the normal simulation and during the umbrella sampling runs. The umbrella sampling algorithm was used to carry out the potential of mean force (PMF) calculations to estimate the free energy profile. The umbrella sampling windows were generated using the pull code of GROMACS with a force constant of 3000 $kJ \text{ mol}^{-1} \text{ nm}^{-2}$, starting from an initial inter-tube distance of 13 nm.
A total of 44 windows were created, and each window was simulated for 400 ns. The bias potentials from the umbrella windows were removed with the weighted histogram analysis method\(^\text{76, 77}\) (WHAM). Based on the extent of sampling employed here (see above), a certain level of statistical uncertainty is present in the simulated potentials of mean force. However, further sampling to reduce uncertainty is impractical, as motion of non-grafted PL-PEG molecules acts to disrupt the CNT coating and thus influence the PMF.

**Results**

**Pure PL-PEG**

We begin by considering PL-PEG in pure water, focusing on the effect of PEG chain length. PL-PEG spontaneously forms micelles with aggregation number varying inversely with the PEG chain length. In Figure 2, we show images of self-assembled micelles following 4 μs simulation time. Aggregation numbers of \(N_{\text{AGG}} = 68, 24, 21,\) and 18 correspond to PEG chains of 12, 24, 48, and 114 monomers (see Table 2). The resulting gyration radii (\(R_G\), Table 2), a measure of micellar size, are somewhat smaller than the experimentally determined radii of \(8.4 \pm 0.2\) nm and \(12 \pm 1\) nm for PL-PEG micelles of 45 and 113 monomer PEG chains, respectively.\(^\text{55}\) A simulation in lower concentration (\(6.7 \times 10^{-3}\) w/v) was realized by taking pre-formed micelles and solvating them in excess water. We note an increase in \(R_G\), reflecting the greater extension of PEG chains into solution.

**PL-PEG with CNT**

To investigate the adsorption behavior of PL-PEG on a CNT, a \((10,0)\) or \((18,0)\) CNT is inserted into the aqueous PL-PEG solution. The starting condition of randomly dispersed PL-
PEG molecules in the simulation box approximates the experimental conditions immediately after rigorous ultrasonication. The PL-PEG molecules near the CNT individually adsorb on the surface, whereas the ones further away first aggregate into micelles. The micelles then diffuse in contact with the CNT, and adsorb. We find a stepwise increase in the number of adsorbed molecules on the CNT, indicating micellar adsorption (Figure 3). The number of adsorbed molecules and the morphology of the adsorbed layer are observed to reach steady states, indicating an approach to equilibrium. However, the simulation time scale is not sufficient to observe equilibrium between adsorption and desorption events. Consistent with the pure PL-PEG case, longer PEG chains result in smaller aggregation numbers. As shown in Figure 4, we find PL-PEG of short PEG length to adsorb to the smaller diameter CNT as a micelle, of size comparable to a pure PL-PEG micelle. As the PEG length increases, the size of the micelle-like structure decreases, until the adsorbed structure becomes essentially monolayer-like for long PEG chains. As in the case of pure PL-PEG, these structural changes reflect a destabilization of the micelle with longer PEG chain length. PL-PEG adsorbed to the larger diameter CNT also evolve from a more micelle-like structure at low PEG chain length, to a more monolayer-like structure at high PEG length. The transition appears to take place at a lower PEG chain length, suggesting the larger CNT diameter to favor the monolayer-like structure. An interesting ramification is the significantly higher adsorbed amount on the smaller CNT for intermediate PEG length – owing to the micelle-like structure. For longer PEG chains, we find the larger diameter CNT to generally adsorb more PL-PEG molecules because of its larger surface area (250 nm$^3$ vs 160 nm$^3$, Table 3). The different adsorbed morphologies are consistent with our earlier work on isolated and bundled CNTs, and can be explained by steric considerations. While the thinner (10,0) CNT readily fits inside of the hydrophobic core of the PL-PEG24
micelle, the wider (18,0) CNT perturbs the micellar structure enough to induce the micelles to form a monolayer.

We observe the aliphatic PL tails to be strongly attracted to the hydrophobic CNT surface, while the PEG chains typically extend into water. In Figure 5, we show the cross-sectional radius of gyration ($R_G$) of the PL-PEG--CNT complexes to first decrease, and then increase, with PEG chain length. The initial decrease is due to the transition to a monolayer-like structure, while the increase is due to the enhanced extension of the longer chains. Radial distribution functions (RDFs) of adsorbed PL-PEG molecules (Figure 6) suggest the PL tails to orient along the CNT axis in the monolayer morphology, and to extend radially in the micellar morphology.

**PEG conformational effects**

To further investigate the conformation of the PEG chains, we consider the scaling of PEG chain $R_G$ values obtained in the simulations of pure PL-PEG micelles and CNT-adsorbed PL-PEG (Table 2 and Figure 7). For shorter PEG chains (PL-PEG $M_W \leq 2000$), the data for both adsorbed and micellar systems obey the scaling relation $R_G = 0.12^*N^{0.65\pm0.02}$, where $N$ is the number of monomers (or $R_G = 0.10^*M_W^{0.65\pm0.02}$, where $M_W = $ PEG chain weight). Over the full range of PEG chain lengths, the scaling relations in high (0.13 w/v) and low (6.7*10^{-3} w/v) concentration are $R_G = 0.13^*N^{0.61\pm0.01}$ and $R_G = 0.11^*N^{0.68\pm0.01}$, respectively. For PL-PEG adsorbed on CNTs, the corresponding relation is $R_G = 0.10^*N^{0.70\pm0.01}$.

Next, we compare our scaling results with predictions from popular polymer theories. The mean field approach by Flory\textsuperscript{78-80} estimates the size of isolated, mushroom-like conformations to scale as $R_G \sim N^{3/5}$. In the mushroom regime, polymers are approximated as isolated chains in a good solvent, occupying roughly a half-sphere with a radius comparable to $R_G$. When the
number of chains on the surface increases, chain-chain interactions become more important, resulting in a net extension of the chains away from the surface. de Gennes has shown the thickness of a layer of polymer grafted (to a flat surface), $L$, to scale linearly with monomer number, $L \sim N$, when the grafted chains are separated by a distance less than the radius of gyration.\(^{79}\) A third approach for estimating the size of a spherical PL-PEG micelle is obtained from theories developed for star-like polymers,\(^{81,82}\)

\[
R_G = \left[ NL^{1/\nu} \frac{8f(1-\nu)/2\nu}{3\nu^4} + R_d^{1/\nu} \right]^\nu,
\]

where $R_G$ is the PL-PEG micelle radius, $l$ is the thermal blob length of the polymer, equivalent to the bond length 0.33 nm, $\nu$ is the Flory exponent (fit to the data presented in Figure 7), $R_d$ is the radius of the hydrophobic micelle core (values shown in Table 2) and $f$ is the aggregation number (values shown in Table 2).

A comparison between our simulated scaling exponents and those of the Flory and de Gennes theories suggests our systems to behave as something between an isolated polymer and a polymer brush. Such behavior is likely strongly influenced by the curvature in our systems – polymer extension away from a curved surface is expected to be less pronounced than that away from a flat surface\(^{81}\) – and is consistent with recent experiments.\(^{55,83,84}\) The somewhat elevated scaling exponent for CNT-adsorbed PL-PEG likely reflects greater chain crowding associated with the cylindrical versus spherical curvature. Faller and Yang\(^{85}\) have previously observed similar behavior of PEG chain extension under structural change from curved micelles to planar bilayers. In their CG simulation study of mixtures of pure and PEGylated DOPC lipids, the self-assembled lipid mixtures also experienced morphological changes upon an increase in pressure. Conversely, the lower scaling exponent observed in aqueous micelles at high concentration is
closer to that found in the mean-field case, suggesting a polymer layer compaction due to crowding by other micelles. Equation (1) predicts $R_G$ values of 3.36 nm, 3.54 nm, 4.83 nm, and 6.67 nm, respectively, for the PL-PEGs with PEG chains of 12, 24, 48, and 114 monomers (in the absence of CNT). Compared to Table 2, the $R_G$ values obtained by Equation (1) somewhat overestimate the micelle sizes.

**Free energy calculations**

To probe the influence of micelle-like vs. monolayer-like PL-PEG assemblies on CNT aggregation, we calculate the Gibbs free energy versus separation (Figure 8). 24 segment PEG chains are considered, so that structures are micelle-like on the (10,0) CNT and monolayer-like on the (18,0) CNT. We observe the micelle-like morphology to result in a higher barrier for CNT aggregation (84 versus 60 kJ/mol), due to the higher PEG chain density (Table 3) and the greater PEG chain extension from the surface (Figure 5). The difference in barrier height ($\Delta E = 24\text{kJ/mol}$) indicates a ratio of barrier crossing probabilities of $P = e^{-\Delta E/kT} = 6.2 \times 10^{-5}$. This value also reflects the predicted ratio of characteristic aggregation times between the monolayer and micellar-coated CNTs.

In Figure 9, we show the peak in the free energy barrier to occur when the PEG density between the two tubes reaches a maximum, suggesting the repulsive barrier to be due to the steric pressure arising from the repulsion of the PEG chains, as described in previous theoretical models.\textsuperscript{37,86,87} This repulsion is of entropic origin, as interdigitating polymer chains have less conformational freedom. Additionally, we observe an attractive regime to emerge in the case of short inter-tube distances, due to the ability of the hydrophobic PL chains to bind CNTs together. This attractive regime may be difficult to observe experimentally, as thermal energy is generally
insufficient to overcome the large barrier. Our results are also in agreement with the experiments of two PEGylated lipid layers (M_w=750) by Kenworty et al., who report a sharp increase in steric pressure at an inter-bilayer distance of 7 nm, with a maximum pressure plateau occurring below a 4 nm separation.

**Discussion**

Studies treating the phase behavior of PEG lipid/phospholipid systems indicate short PEG chains (M_w=350) to lead to lamellar phases, and longer PEG chains to lead to various micellar structures. Here, based on molecular simulation, an inverse relation is observed between micellar aggregation number and PEG chain length. The values correspond qualitatively with both experimental and theoretical PL-PEG micellar sizes. In particular, our simulations slightly underestimate equilibrium aggregate size compared to experiments. Finite simulation time may contribute here, owing to the slow dynamics of long polymers. In addition, the R_G values obtained from dynamic light scattering are typically larger than those obtained from simulations, as some hydrating water is typically included in experimentally reported sizes of poorly draining micelles. Furthermore, larger aggregates scatter more light, which may shift the average observed size to a larger value.

PL-PEG has proven to be an excellent solubilization agent for CNTs as well as other nanoparticles. Furthermore, a variety of PL–PEGs with different functional groups are commercially available. The self-assembled structures of PL-PEG–nanoparticle complexes are of particular interest, since a variable surface density and the presence of functional groups may reduce nonspecific interaction with proteins, achieve desirable in vivo biodistribution of
nanoparticles, and significantly enhance the ability of nanoparticles to target specific disease markers.

Our results highlight the importance of the relative sizes of the PL-PEG micelle hydrophobic core (R_d) and the CNT diameter. Micelles with larger R_d are able to form around larger CNTs, resulting in a coating with higher PL-PEG density and PEG chain extension. On the other hand, if the CNT diameter is comparable to the diameter of the micellar hydrophobic core, micelles cannot form around the CNT and a sparser PL-PEG layer adsorbs. This result is in agreement with our previous experimental and simulation work with isolated and bundled CNTs. In addition, the micelle breakdown, on a smooth CNT surface, upon increasing CNT diameter, indicates the structural transition to be dominated by the ratio of the two length scales, as opposed to other factors such as surface roughness, and to result in preferential PL adsorption sites, induced by the CNT bundle groove sites. Since the hydrophobic core size decreases with PEG length, we observe a somewhat non-intuitive result: increasing the PEG length can decrease the extent of PEG adsorption, owing to the favored flatter adsorbed layer morphology. Although not explicitly investigated here, we suspect decreasing the lipid tail size (at constant PEG size) to have a similar effect. Indeed, related to our findings on characteristic lengths and PL-PEG adsorption morphologies, Calvaresi et al. observed cylindrical micellar, hemimicellar, and random adsorption aggregate morphologies by examining various hydrophobic tail lengths of model lipid-like surfactants, using a DPD simulation method. They observed smooth morphological transitions, upon changing concentration or surfactant tail length, which were dependent on the strength of surfactant-CNT interactions.

We also calculate the free energy barrier to CNT--PL-PEG aggregation. We find increased PEG density and chain extension of the micellar PL-PEG coating to lead to higher barriers due to
increased steric repulsion from PEG chains. Somewhat non-intuitively, the micelle-like surface morphology associated with this higher barrier is favored by a shorter PEG chain length. This increase in “steric pressure” with increasing PEG concentration, PEG size, and chain extension has previously been experimentally probed with PEG-lipid complexes. Our results are also in excellent agreement with previous theoretical, experimental, and coarse grained simulation studies, which show the repulsive barriers against aggregation to increase with polymer or surfactant density, allowing polymer-induced steric stabilization to selectively disperse CNTs.

In the current study, the repulsive barrier for monolayer-coated CNT is significantly smaller than the barrier for the micelle-coated CNT (24 kJ/mol or 28%). While in this particular case both coatings result in barriers larger than the thermal energy kT, indicating strong CNT dispersibility (and little difference in solubility), we expect with larger diameters or lower PEG concentrations, the barriers may become comparable to kT, and larger stability differences could result. In fact, we showed this experimentally in our previous study, where PEG-coated CNT bundles aggregated rapidly during LbL assembly, but PEG-coated isolated tubes were mostly water-soluble and resulted in thinner LbL assemblies. The experimental PEG concentrations were significantly lower, and the CNT size difference significantly higher, than in our simulations. The particular CNT diameters studied in this work were employed to capture the morphology transition. The high PL-PEG concentrations were necessary to accelerate the aggregation process to achieve fully coated CNTs on the simulation time scale. Nevertheless, the principles shown in the present study appear to apply to larger systems (as in Ref. 35) where size-selective dispersibility is achieved. Size-selective dispersion of non-covalently coated CNTs potentially enables the isolation of nanotubes with specific electronic properties.
Conclusions

We present here coarse grained molecular dynamics simulations of aqueous dispersions of CNTs with a biocompatible amphiphilic polymer, PL-PEG. We observe morphological transitions from dense, micelle-like structures to sparser, monolayer-like coatings of PL-PEG upon increasing CNT diameter and/or PEG chain length. The micelle-like structure results in a higher PL-PEG density and degree of PEG tail extension, and also to a higher steric repulsion and stabilization to aggregation. Chain conformations are observed to be in agreement with prior experiment, theory, and simulation. This study demonstrates the importance of PEG chain length to micellization and CNT adsorption, and ultimately to CNT dispersibility and stability. Furthermore, the ability to control the coating and resulting aggregation stability via a proper choice of polymer $M_w$ allows for dimensional selectivity, ultimately enabling a size-selective purification of CNTs with specific diameters from mixtures of non-nanoscale objects and CNTs of various diameters.
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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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References

(1) Baughman, R. H; Zakhidov, A. A; de Heer, W. A. Carbon nanotubes--the route toward applications. *Science* 2002, **297**, 787-792.


**Figure 1.** Left: Snapshot of the initial configuration of the PL-PEG24 simulation with a (18,0) CNT. The PL-PEG molecules reside randomly in the aqueous phase. Water is omitted for clarity. The PL portion is colored in green and the PEG chains are shown in yellow. Periodic boundary conditions are employed in the three mutually orthogonal directions. Right: Models of the PL-PEG molecules with PEG chain lengths 12, 24, 48, and 114 monomers (from left to right).
**Figure 2.** Snapshots of PL-PEG in aqueous solution following a 4 μs coarse-grained molecular dynamics (CGMD) simulation. From left to right: PL-PEG12, PL-PEG24 and PL-PEG48. Shorter PL-PEGs form larger micelles. Corresponding details are shown in Table 2.
Figure 3. The number of PL-PEG molecules adsorbed to the CNT surface versus time, as determined by CG MD simulation.
Figure 4. Representative side view and cross-section snapshots of PL-PEG assembly on (18,0) CNT (left) and (10,0) CNT (right), as determined by CGMD simulation. PEG chain lengths are 12, 24, 48, and 114 monomers (from top to bottom). The dashed lines show the borders of the simulation cell. CNTs appear silver, aliphatic PL tails green, and PEG chains yellow. Although present in the simulations, water, sodium counterions, and the PL-PEG micelles in solution are omitted for clarity.
**Figure 5.** Cross-sectional radii of gyration ($R_g$) of CNT-PL-PEG-complexes, as determined by CG MD simulation.

**Figure 6.** Radial distribution function (RDF) plots of PL-PEG adsorbed to (10,0) CNT (left) and (18,0) CNT (right), as determined by CG MD simulation. The RDFs are normalized by the number of monomers in the PEG chain. The entire PL-PEG RDF is shown in black, the PL tail RDF in green, and the PEG chain RDF in red.
**Figure 7.** PEG chain radius of gyration ($R_G$) versus PEG chain length, as determined by CG MD simulation of PL-PEG micelles at high (black circles) and low concentration (green diamonds), and of PL-PEG adsorbed on (10,0) CNT (blue plus-signs) and (18,0) CNT (red squares).
Figure 8. Gibbs free energy profiles of two parallel PL-PEG-CNT complexes, as determined by CG MD simulation with umbrella sampling. Black crosses represent a (10,0) CNT coated by micelle-like PL-PEG, and the red circles a (18,0) CNT coated by monolayer-like PL-PEG.
Figure 9. Two-dimensional molecular density plots of PL-PEG24 adsorbed to two parallel (18,0) CNT, as determined by CG MD simulation. The plots correspond to inter-tube distances of 10 nm.
(top), 4 nm (highest barrier, middle), and 3.4 nm (bottom). PEG and PL densities are plotted to the left and right, respectively.
Table 1. Simulation details: The number of water beads is rounded to the nearest thousand.

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Table 2. Properties of PL-PEG micelles

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<th>PEG length (monomers)</th>
<th>Aggregation number</th>
<th>Hydrophobic core $R_G$ (nm)</th>
<th>Micelle $R_G$ (nm) (0.13 w/v)</th>
<th>Micelle $R_G$ (nm) (6.7*10⁻³ w/v)</th>
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Table 3: PL-PEG adsorption number ($N_{ADS}$) on CNT

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<th>PEG length</th>
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<th>$N_{ADS}$ (18,0) CNT</th>
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<tr>
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<td>118</td>
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</table>
For Table of Contents use only. Manuscript: Size-selective, non-covalent dispersion of carbon nanotubes by pegylated lipids: a coarse-grained molecular dynamics study. Authors: Jukka Määttä, Sampsa Vierros, Paul R. Van Tassel, and Maria Sammalkorpi.