

Molecular Simulation of Surface-modified Polymer Vesicle Designed for Gene and Drug Delivery : Monte Carlo Simulations of Grafted Polymers between Two Walls

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Abstract

Monte Carlo simulation of coarse-grained models of polymers is introduced and employed to study grafted polymers brushes using two walls of tethered chains to form top and bottom boundaries. For a non-interacting brush, profiles of monomer density and free end density, bond orientation, and average monomer position along a chain were investigated. The profile of the inner bead, chain end density, mean chain conformational path and bond orientation were seen to exhibit universal law in agreement with the prediction of analytical Self-Consistent Field (SCF) theory. For interacting grafted systems at fixed chain length and grafting density, the density profiles of compressed brushes was determined, focusing on the change of brush height and density under compression, the degree of interpenetration, and the end-segment distribution. The thickness of the layer was thin enough that the two interfacial regions could overlap. The widths and density of the polymer brushes were found to decrease initially and then increase as a function of wall separation. In addition, local and chain properties were not changed monotonically with the wall separation either.

Introduction

Targeted gene and drug delivery holds a great potential for the successful treatment of many diseases. Approaching the tumor via blood circulation should allow several advantages over the local intratumoral injection such as reaching multiple distant metastases. One of the considerable problems preventing the creation of such a gene delivery carrier is inefficient site-specific targeting. Modification of nanoparticles with polymer e.g. poly(ethylene glycol) offers a reduction of non-specific binding to cell surfaces and improves the circulation time of the gene/drug delivery vehicles in blood. In this work, a novel computer simulation technique capable of probing the structure of the interface between the solid substrate and grafted polymer brushes at a prescribed grafting density σ is developed. This simulation method allows us to obtain detailed information about the conformational (chain orientation and packing), structural (bond ordering), and thermodynamic (local density, distributions of chain ends, energetics) properties near the solid substrate, while avoiding many of the assumptions invoked in the mesoscopic, SCF models, in analytical brush theories and past simulations of bead-spring or ideal chains. Our interest in this study is to see how compression affects the behavior of the very thin confined brushes. The confinement can be simply introduced in the simulation by placing the grafted polymer melts between two parallel hard walls separated a distance d apart. The thickness of the layer varies from $\sim 2h^*$ to $\sim 1.5h^*$, which is thin enough that the two interfacial regions can overlap. The compressed system can be simply achieved by changing the separation between two impenetrable walls with other variables unchanged, which results in a change of the density and interfacial profile in the confined geometry.

II. Model and Simulation Method

The simulation employs the bridging technique that allows the interconversion between a fully atomistic representation of a structure in continuous space and a coarse-grained version of the same structure in the discrete space of a high coordination lattice. The lattice structure is a coarse grained version of a diamond lattice discarding every second site in the lattice. Each occupied site on the 2nd lattice represents a $-\text{CH}_2\text{CH}_2-$ unit. The coarse-grained representation retains every second carbon atom on a lattice with $10i^2 + 2$ sites in shell i . Systems of monodisperse grafted polymers, each chain containing N ethylene units, with $20 < N < 40$ i.e. chain of $\text{C}_{80}\text{H}_{162}$ is represented by 40 beads on the lattice was studied. To model the conformational characteristics of a polymer chain, the Rotational Isomeric State (RIS) formalism was used to model the short-range intramolecular interactions on the lattice. The original RIS model for polyethylene was modified for the coarse-grained simulations. Long-range intra- and intermolecular interaction among nonbonded units were incorporated into the simulations using the Lennard-Jones potential for ethylene units with $\epsilon/k_B = 185$ K and $\sigma = 0.44$ nm. The second virial coefficient expression was utilized to assign an average interaction energy for each neighboring shell around a lattice site. This simulation uses the first, the second, and the third shell interaction parameters, which are 14.122, 0.526, and -0.627 kJ/mol, respectively. Only three shell interaction parameters are used for the computational efficiency, implying a cutoff distance of 7.5 Å in the long-range interaction. The lattice model consists of a distorted cubic lattice of dimensions $L_x \times L_y \times D$ with $L_x = L_y = 40$ (surface area = 86.6 nm²). Five kinds of wall separations, from $H = 32l$ to $H = 48l$, were used. These wall separations correspond to the length scale ranging from $\sim 2h^*$ to $\sim 1.5h^*$. We choose periodic boundary conditions only in the x and y directions. Two impenetrable solid walls parallel to the xy direction were placed at lattice planes $z = 0$ and $z = D$. Beads were not allowed to move from $z = 0$ to -1 or from $z = D$ to $D+1$ which means the substrate was considered as an impenetrable wall. The grafting density (σ) was ranged from 0.92 to 1.85 nm⁻². Single bead and pivot moves on the lattice were employed in the simulation with the restriction that a chain cannot pass through itself, as in a self-avoiding random walk and are accepted according to the Metropolis MC algorithm. The probability of a move of a bead within a chain is given by $P_{\text{move}} = \min[1, P_{\text{LR}}P_{\text{new}}/P_{\text{old}}]$ where $P_{\text{LR}} = \exp(-\Delta E_{\text{LR}}/RT)$ is the probability from the change in the long-range interaction energy and $T = 450$ K. $P_{\text{new}}/P_{\text{old}}$ is the ratio of the probability change with a new bead position according to the short-range interaction component. For the equilibration, 5 million Monte Carlo steps were performed, with one Monte Carlo step defined as the simulation length when every bead has attempted one move, on average. Analysis of the static properties is obtained by an ensemble average of the subsequent 10^7 MCS after equilibration of an initial structure. A snapshot is taken every 10,000 MCS during this period and used for analysis of the static properties. All computations were carried out using a Pentium IV (3.2 GHz, 1 GB RAM) computer, and approximately 120 h CPU time was consumed for the generation, the relaxation, and the data gathering from the 5 million steps of Monte Carlo simulation for each system.

Results and Discussion

Density Profiles: Fig. 2 presents the variation with distance from the substrate of the density ρ of the C_{80} melt simulated, all chains of which were grafted on a hard substrate, as a function of relative position from the wall (Z/D). The densities were obtained from counting the beads as a function of Z/D and averaging over all configurations. It is seen that

for the grafting densities studied, $\rho(z)$ exhibits two zones of reduced density corresponding to the two boundaries of the system: the substrate/melt and the melt/vacuum interfaces. In contrast, in the bulk of the system, the density practically remains constant (about 0.74 g/cm^3) almost independent of D except at the lowest $D = 32l$ that shows higher density. The reduced $\rho(z)$ values near the solid are mainly entropic origin; they are caused by the presence of the boundary that limits the number of available conformation assumed by each grafted chain. The sigmoidal shape and the width of the profile at the free boundary of the melt in Fig. 2 is typical of a melt/vacuum interface. The simulation results are in contrast to the usual practice in analytical or numerical theoretical models of grafted melts which, in their majority, invoke the assumption of a constant density everywhere in the interfacial region. When the distance D between brushes is large (for example for $D = 48l$) there is only a very small interpenetration of the brushes, and the density distribution in each brush is very close to the distribution for one isolated brush (the density is equal to zero at the middle between the two grafting planes). When D is lower, the density distribution becomes uniform. The brush density slightly decrease and the interfacial profiles become broader for $D = 48l - 36l$, indicating a dominant attraction between grafted chains at two walls for small compression. When D is decreased further ($D < 36l$), the density start to increase and finally become larger than the equilibrium bulk density at the strongest compression. This behavior of the density is closed to the behavior of the total density distribution of one isolated brush with increasing surface coverage, but the inner structure is different. The main different is that in the system of two brushes the degrees of orientation and stretching of the chains decrease, whereas for one brush these quantities increase with increasing density.

Bead Distribution and Bond Orientation: Figs. 3 present data for the distribution of free ends for the fully grafted C_{80} melt for various wall separations. The curves in Fig. 3 show that as D decrease until the chains start to overlap, the extension of chains in the z direction initially increase if $D > 40l$ and then decrease and forces free ends to span a less distance. Clearly, the end monomers can be anywhere in the brush, and the highest probability occurs in the outer region where the average density of brush is already decreasing. Thus there is a systematic deviation from the prediction of the SCF theory which predicts no end bead at $z = 0$. More detailed information about the internal structure of polymer brushes can be obtained with the aid of the density distribution of different i th monomeric units along a chain of N units. Fig. 4 shows the mean z position of the i th monomeric unit along the chain versus its label i for different values of wall separation D in the system of two brushes. Decreasing the distance D between the grafting planes leads to an increase of the height of the i th unit for $D = 48l - 40l$. This imply that the polymer chains become more stretched resulting from attraction forces between brushes at each wall. For smaller values of $D < 40l$, the average height of monomer become smaller suggesting the compression of chains. The space confinement seems to dominate the effect of attraction at this wall separation. Similar information can be obtained from the decrease of the mean cosine of the i th monomeric unit along the chain with its label i . The perpendicular orientation of the chord vector connecting coarse-grained repeating units to the grafting site (Fig. 5) also becomes less pronounced with increasing label i (i.e., with increasing mean distance between the unit and the grafting plane). This mean cosine also increases with decreasing distance $D = 48l - 40l$. For smaller values of $D < 40l$, the mean cosine become smaller. These results are in accord with the change in mean z position as a function of D . Chains are stretched at $D = 48l - 40l$ and packed to a more ordered arrangement. With less value of D , the situation is

reversed as chains become more random conformation. Packing is less efficient and it causes less ordering of bond orientation.

Energetics: The conformational change and the subsequent bead distribution can be reflected through the energetics. The top, middle, and bottom panels of Figure 6 represent the average energies and the short-range energy from the RIS scheme and long-range energy from the Lennard-Jones potential contributions, respectively, as a function of z . These energies are normalized by the number of beads and volume in each bin. As shown in Fig. 6, the clear maximum of the total interaction is found at $Z/D = 0.5$ with the short- and long-range interaction shows a maximum and minimum at the same separation. The short-range interaction dominates the trend for the total energy. Next, we study the change in short- and long-range interaction as a function of wall separation (Fig 7 and 8). The long-range energy per bead per volume drops monotonically with the wall separation except at the large value of $D = 40 - 48l$ that the data show relatively constant values. Brushes gain more attractive interaction with the wall compression. From Fig. 4, it can be seen that brushes start to overlap at $D = 40l$ where the long-range energy start to deviate from the constant value. Even at the highest compression, there is no sign of increasing interchain interaction. Thus, it cause structure denser and the density should higher than that of the unperturbed bulk as seen in Fig 2. For the change in intramolecular interaction with wall separation, short-range energy slightly decreases from $D = 48l$ to $40l$. This is because the chains adopt more *trans* conformation resulting from the attraction between polymers grafted at the opposite wall. When the compression is larger ($D < 40l$), chain conformation become more random and higher short-range energy can be expected. These results are in accord with bead distribution and bond orientation described in the previous section.

Conclusion

Computer simulation by the method of lattice Monte Carlo Simulation of realistic polymer chain is applied to study two brushes attached to two parallel impenetrable planes at different wall separation. The interplay between interpenetration of the brushes and the configurational properties of the grafted chains can be illustrated clearly with this method. It was found that some of these properties are not change monotonically with the wall separation.

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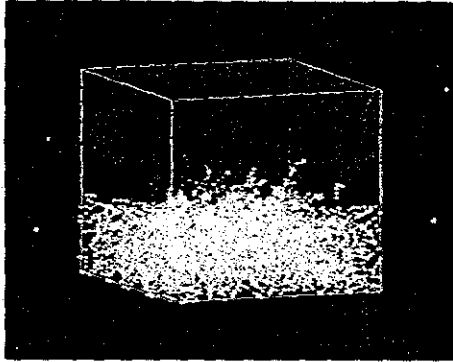


Fig. 1 Schematic representation of the molecular model of C_{80} for grafted polymer melts with surface coverage $\sigma = 1.85 \text{ nm}^{-2}$ at wall separation $D = 44$.

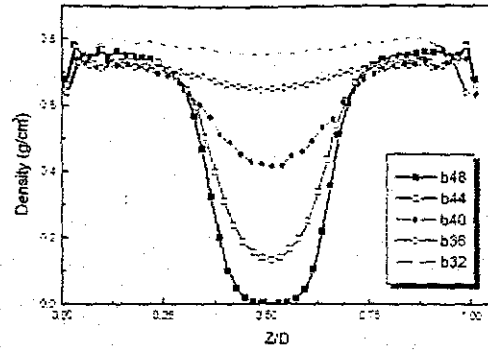


Fig. 2 Density distribution function for the system of two brushes with surface coverage $\sigma = 1.85 \text{ nm}^{-2}$ and for different wall separation.

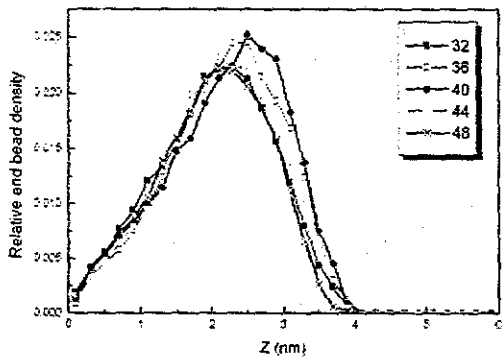


Fig. 3 Relative end bead density distribution for the system of two brushes with surface coverage $\sigma = 1.85 \text{ nm}^{-2}$ and for different wall separation.

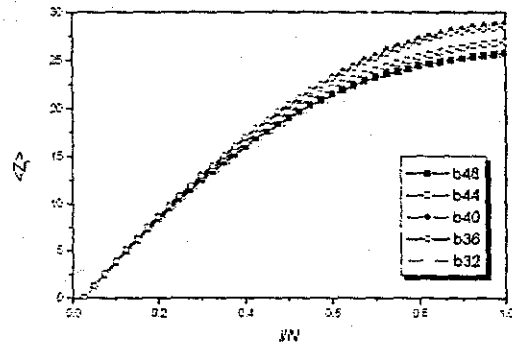


Fig. 4 Normalized mean height in z-direction as a function of the normalized bead coordinate along chain contour for the system of two brushes with surface coverage $\sigma = 1.85 \text{ nm}^{-2}$ and for different wall separation.

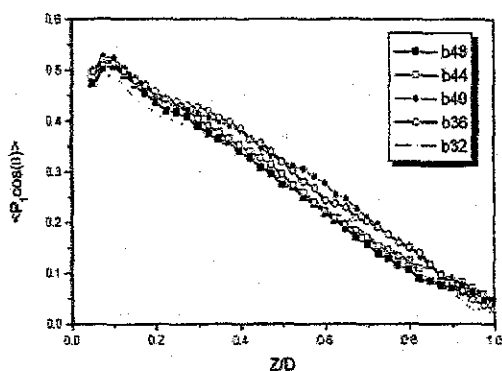


Fig. 5 Bond order parameter evaluated as a function of bond distance from the substrate for the system of two brushes with surface coverage $\sigma = 1.85 \text{ nm}^{-2}$ and for different wall separation.

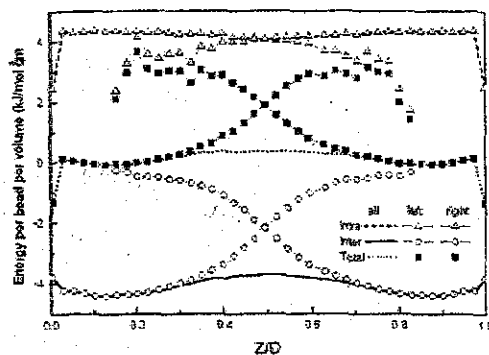


Fig 6. Average contribution of a bead to the total energy and the contributions from the short-range intramolecular interactions and the intermolecular interactions, as a function of the distance of the bead from the substrate

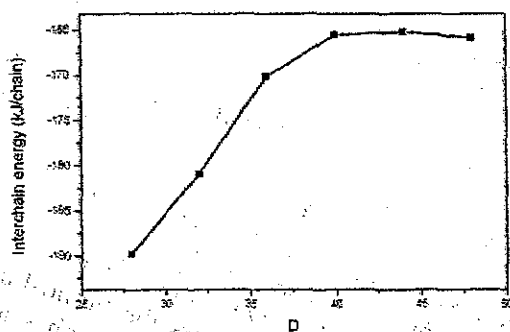


Fig 7. Changes in short-range intramolecular interaction of the brushes as a function of wall separation.

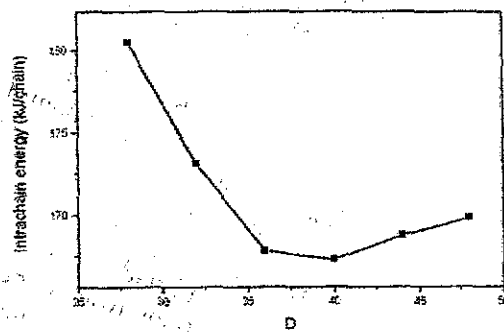


Fig 8. Changes in long-range intermolecular interactions of the brushes as a function of wall separation.

References

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