Virtual Molecular Design of an Environment-Responsive Nanoporous System

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ABSTRACT

Molecular dynamics simulations have been used to explore a "smart" nanoporous system that can open and close in response to environmental conditions. The dynamic pore sizing capability is produced by a rod–globule transition in comb polymer molecules that are anchored to the inside of a nanometer-scale pore. The simulations indicate that changing the solvent quality can produce a significant change in pore opening, which in turn can be used to selectively trap large molecules while allowing smaller molecules to diffuse freely through the pore. The simulation results suggest that nanoporous systems of this type could be designed to respond to changes in environmental conditions such as pH, temperature, and solute concentration, with a variety of potential applications including smart drug delivery, controlled chemical release, ultrafiltration, and as molecular sieves.

Introduction. Materials that contain pores of molecular size have a variety of applications including filtration, size-sorting biomolecules, and chemical separation. The conventional transport selectivity of such materials is based on features such as charge, chemical interaction and molecular size. Recent experiments by Park, Ito, and Imanishi[1] have shown that additional selectivity can be built into nanoporous materials such that signal responsive liquid permeation is achieved. In one set of experiments, the permeation of toluene through pores in a glass filter was controlled by UV/vis irradiation that induces a collapse transition in a polymer brush. In this experiment, a polymer brush was made by grafting a spiropyran-substituted methyl methacrylate/methyl methacrylate copolymer on to a glass filter. The optically active functional group associated into the polymer chains formed a stable Zwitterion upon UV irradiation, whereas the uncharged structure was recovered by irradiation with visible light in combination with heat. Toluene acts as a good solvent for the brush in its uncharged state, but a poor solvent when the brush contains Zwitterions. Hence, the brush swells in its uncharged state in toluene, filling the pores and significantly reducing the flow of toluene. In the charged state the brush collapses, opening the pores and allowing solvent flow. In a second set of experiments,[2] polypeptide brushes were self-assembled onto a gold plated nanoporous membrane. The permeability of water was controlled via a helix-coil transformation that was driven by solvent pH.

Motivated by the experiments of Park, Ito, and Imanishi, we have been using molecular simulations to explore the functionality of other systems that could potentially act as smart molecular valves. The design discussed here is based on a rod-globule transition in polymer comb molecules. Polymer comb molecules, also termed brush polymers or molecular bottlebrushes, consist of densely grafted side-chains extending from a polymer backbone. Comb polymers can be either copolymer or homopolymer macromolecular structures. For example, polymacromonomers based on polystyrene and poly-(2-vinylpyridine) side chains grafted on a methacrylate backbone are known to form a cylindrical brush.[3] The excluded volume interaction of the side chains causes stretching of the main chain such that it adopts a cylindrical brush structure. Depending on the length and density of the side chains, and the interaction between them, comb polymers can attain very high stiffness,[4] Kuhn statistical segment length of the order of 1000 Å. In a poor solvent, a comb polymer can undergo a conformational transition. In a molecule with a flexible backbone, collapse of the side chains will result in axial contraction of the whole molecule and may result in a globular state as compared to a fully stretched cylindrical brush in a good solvent.[5]

In the proposed structure polymer brush molecules are grafted to the interior of a slit nanopore (Figure 1). In the presence of a good solvent the grafted comb molecules are stretched away from the grafting surface, forming a network of obstacles for molecular diffusion through the pore. Upon exposure to a poor solvent, the polymer comb molecules

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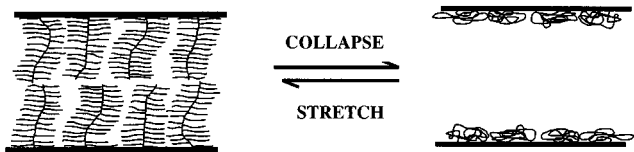
Figure 1. Illustration of the proposed nanoporous system.

undergo a collapse transition, leaving the pore open, thereby reducing resistance to diffusing molecules. In principle, by a proper selection of solvent-polymer comb combination one can design a molecular gating system that can be opened and closed by varying the solvent quality. Using comb polymer molecules has the potential advantage over linear polymer chains such as those used in the Park, Ito, and Imanishi experiment with the gold-covered nanoporous membrane that comb molecules might form a more effective network of obstacles.

The feasibility of the proposed system depends on several factors. These factors include the time required to respond to stimuli, the volume difference between the extended and globule state of the grafted chains, the range of stimuli over which the chains respond (e.g., the temperature range for a thermal transition), and the efficacy of the system for inhibiting flow of solute molecules depending on their size. A bead-spring molecular model has been used to explore these factors, with the main objective being to provide a proof-of-concept for the proposed nanoporous system. The first part of this report discusses the nature of the rod-globule transition in an isolated polymer brush molecule as predicted by the model, including the difference in volume between the two states, the time scale associated with the transition, and the order of the transition. In the second part of the report, opening and closing of the pore by the grafted system and transport of chain molecules through this nanopore as a function of solvent quality is modeled.

Method. The simulations were carried out using the DL_POLY_2.12 molecular dynamics code.[6] The polymer brush molecules were simulated using a bead-spring model[7] with the mass of each bead taken as 14 AMU. Nonbonded pair interactions, which were included between all pairs of beads except the nearest neighbors, were modeled using a Lennard-Jones shifted force potential of the form

$$U_{SF}(r_{ij}) =$$

$$\begin{cases} U_{LJ}(r_{ij}) - U_{LJ}(r_c) - (r_{ij} - r_c)\left(\dfrac{dU_{lj}(r_{ij})}{dr_{ij}}\right)_{r_{ij}=rc} & r_{ij} \le r_c \\ 0 & r_{ij} > r_c \end{cases} \quad (1)$$

where $U_{LJ}(r_{ij})$ is the Lennard−Jones potential given by

$$U_{LJ}(r_{ij}) = 4\epsilon_{ij}\left\{\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right\} \quad (2)$$

and r_c is the cutoff distance beyond which the interaction is zero. The quantities ϵ_{ij} and σ_{ij} are the respective energy and distance parameters corresponding to the particular pair of

particles i and j. Values of $\epsilon_{ij} =0.5$kJ/mol and $\sigma_{ij} = 2.7$A° were used for all pair interactions (unless stated otherwise). The truncation distance r_c in eq 1 for the nonbonded interactions was taken as either $2^{1/6}\sigma$ or 2.5σ. The former distance truncates the potential such that only repulsive interactions are included, whereas the latter allows attractive forces to be modeled. Neighboring monomers along a chain interact via a harmonic bond potential with the value of spring constant $k = 40\epsilon/\sigma$ and equilibrium distance $r_o = \sigma$.

The molecular dynamics simulations used a time step of 5fs and unless otherwise stated were carried out at constant energy. Each system was initially equilibrated for a minimum of 5×10^4 time steps during which velocities were scaled to obtain the desired temperature. After equilibration data was typically obtained over runs of 10^5-10^6 time steps. The size of a polymer chain consisting of N monomers is defined using the mean square end-to-end distance

$$\langle R^2 \rangle = \langle (R_N - R_1)^2 \rangle \quad (3)$$

Where R_N and R_1 are coordinates of monomer N and 1 respectively, and the mean square radius of gyration

$$\langle R^2_g \rangle = \frac{1}{N}\sum_{i=1}^{N} \langle (R_i - R_{COM})^2 \rangle \quad (4)$$

where R_i is the coordinate of monomer i, R_{COM} is the coordinate of center of mass of the molecule, and the brackets indicate an average over the equilibrium dynamics of the system. Radii referred to below correspond to either the entire molecule or just the backbone monomers.

Collapse Transition in Isolated Comb Molecules. The equilibrium size of a comb polymer molecule depends on the number of monomers in the main chain N, the number of monomers along the side chain n, the number of monomers between subsequent side-chains m, and the type of solvent. For example, Rouault and Borisov[8] have used free energy calculations to estimate the equilibrium size of the main chain and the side chains in a good solvent. The relation,

$$R \cong N^{3/5}a\left(1 + \frac{n}{m}\right)^{2/5} \quad (5)$$

where a is the monomer size, indicates that the effective size of a polymer brush molecule can be tuned by changing the size and grafting density of the side chains. Poor solvent conditions, either due to a reduced temperature or the presence of a solvent with relatively less affinity, can induce a collapse transition to a globule structure in these molecules. In the globular state, it is expected that the brush size R, including the side chains and the backbone, will scale as

$$R \cong \left[N\left(1 + \frac{n}{m}\right)\right]^{1/3} a \quad (6)$$

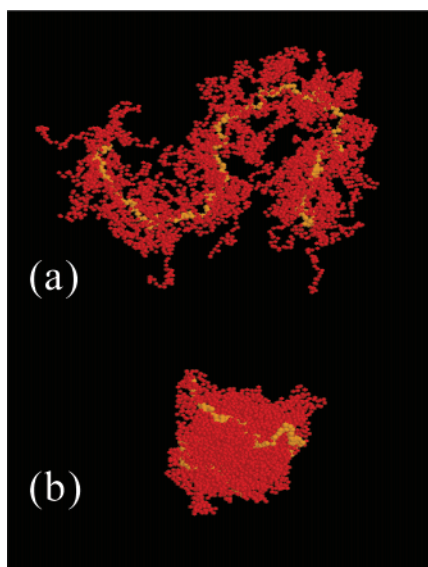where N, n, and m are as above. From the above equations

Figure 2. Snapshots from molecular dynamics simulations of (a) stretched, and (b) collapsed comb polymer. Color code: side-chain (red), backbone (yellow).
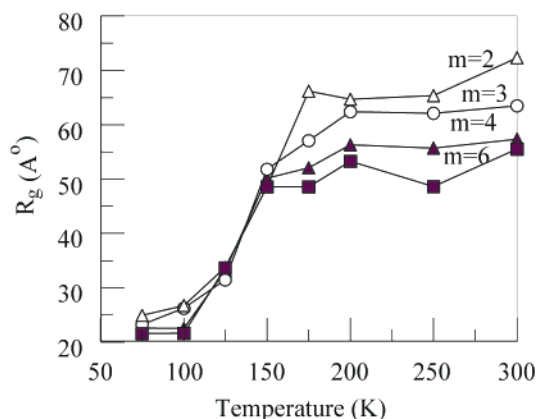

Figure 3. Radius of gyration of the whole molecule as a function of temperature for side chain grafting distances m = 2, 3, 4, and 6.

Figure 4. Probability distribution of the end-to-end distance R for isolated comb polymer with N = 200, m = 2, and n = 40, at temperatures T = 125, 150, 175, 200, 250, and 300 K.

the size change associated with a rod-globule transition can be easily estimated. For example, the radius of a comb polymer with N = 200, n = 40, and m = 4 will be reduced by about 50% upon collapse.

To characterize the nature and time scale of the transition, isolated polymer brush molecules consisting of N = 200 monomers in the backbone and n = 40 monomers along the side chains with spacer length m = 2, 3, 4, and 6 were simulated. All nonbonded interactions involving the backbone monomer pairs (i.e., backbone−backbone and side chain−side chain) were taken to be purely repulsive, while an attractive nonbonded interaction was included between monomers in the side chains.

The simulations indicate that the comb polymer model undergoes a rod-globule transition that depends on temperature. Illustrated in Figure 2 are typical snapshots of stretched and collapsed comb polymers. Plotted in Figure 3 is the radius of gyration of the whole molecule as a function of temperature for different values of m. The transition from a swollen state at high temperatures to a collapsed state at low
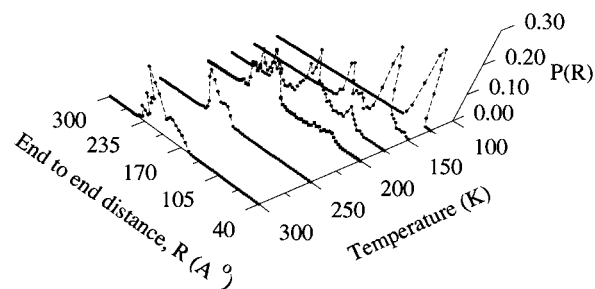
temperatures is exhibited over a relatively narrow range of temperature, approximately 50 K. Plotted in Figure 4 is the probability distribution of the end-to-end distance of the backbone for an m = 2 comb polymer at different temperatures. Each plot represents a time average of a single comb polymer molecule after equilibration. Double peaks are apparent in the probability distributions in the vicinity of the transition temperature. This is a clear indication that there are two preferred states at the transition, which is characteristic of a first-order transition. The conclusion of a first-order transition for a structure of this type is consistent with results from recent bond-fluctuation model based Monte Carlo simulations.[9] It is also consistent with the experimental results reported by Sheiko et al.[10] of a rod-globule transition of poly (n-butyl acrylate) brush molecules adsorbed on a water layer. In this experiment, a discrete transition occurred upon lateral compression of the monolayer that was visualized using scanning force microscopy. They observed coexistence of rod and globule phases at the critical point, which indicates a first-order transition.

To characterize the time scale of the collapse transition, simulations were carried out in which the temperature of brush molecules with different m values was quenched using a Nose' thermostat from an average temperature of 300 K to 100 K (i.e., from above to below the transition temperature range). Plotted in Figure 5 is the average radius of gyration R_g for the backbone as a function of time for molecules with different m values calculated from these simulations. Each plot represents average over five starting configurations. For reference, the temperature averaged over the simulations as a function of time is also plotted. In all the cases the molecules relax from their initial extended structures to the final globule structure in less than about 0.5 ns. This time value provides an estimate for the response time of a smart valve created from these structures.

Brush Molecules Inside the Slitpore. When attached to the interior walls of a slit pore comb polymers form a planar brush with individual molecules stretching away from the attachment points due to excluded volume interactions. The system modeled consists of comb polymer molecules (B) of N=100, m=4 and n=30, end-attached to two opposing walls. The in-plane x and y dimensions of the slit pore are $52\sigma \times 54\sigma$, respectively, and each wall is separated in the z direction by 74σ. The pore walls are modeled with frozen atoms placed on a (111) plane of a face centered cubic lattice with lattice
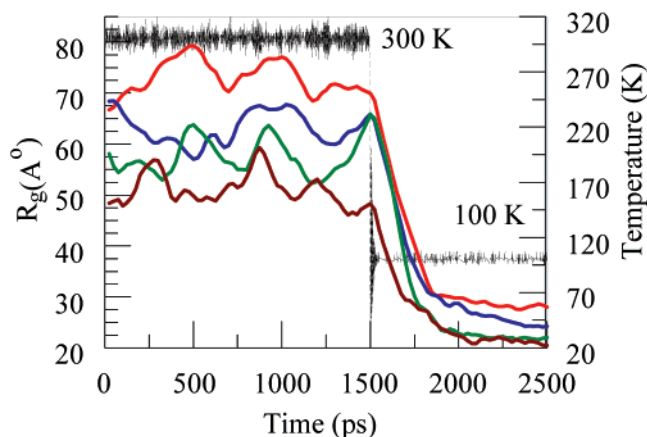
Figure 5. Plot of R_g vs time for a comb polymer with $N = 200$, $n = 40$ and $m = 2$ (red), 3 (blue), 4 (green), and 6 (brown). The isolated molecules were quenched from a temperature T = 300 K to 100 K. Temperature of the system as a function of time is shown in black for reference.

constant $2^{1/2}\sigma$. The pore is grafted with nine brush molecules on a rectangular lattice with a grafting distance of 17.65σ between attachment points. The wall separation and grafting distances are about 2 times and one-half, respectively, of the end-to-end distance of a single comb molecule in its extended state, and about 8 and 2 times, respectively, of a comb molecule in its globule state. Purely repulsive non-bonded interactions using the parameters given above are used for the brush-wall and solvent-wall interactions. The brushes are immersed in monomeric solvent molecules (S) of the same size and mass as that of the beads of the comb molecules. Periodic boundary conditions are applied in the two directions parallel to the grafting surface. The total number of atoms in the system (excluding wall atoms) is N_t=96031 at a reduced number density of $N_t\sigma^3/V = 0.45$. The temperature of the system was chosen to be in the stretch-collapse transition region such that by proper choice of solvent-brush interaction pore opening and closing can be demonstrated. For a solvent with $\epsilon_{BS}/\epsilon_{BB} > 1$, the solvent-comb interaction is more attractive than the comb-comb interaction, thereby forming a good solvent for the combs. A solvent with $\epsilon_{BS}/\epsilon_{BB} < 1$ forms a poor solvent. For a solvent with $\epsilon_{BS}/\epsilon_{BB} = 1$, the B−B as well as B−S interactions are equally preferred and the brush is said to be in the theta condition. The nanopore system was studied under different solvent qualities, with ϵ_{BS} ranging from 0.1 to 0.8 kJ/mol ($\epsilon_{BS}/\epsilon_{BB}$ between 0.2 and 1.6).

Plotted in Figure 6 is the density of monomers belonging to comb molecules as a function of distance from the grafting surface at different solvent qualities. In a good solvent, the solvent molecules wet the grafted layer and the result is a stretched brush covering the entire volume across the pore. In a poor solvent, interaction among monomers of the comb polymers is preferred over interaction with solvent molecules and the comb polymer molecules collapse on the grafting surface, expelling the solvent molecules into the open space left in the pore. At the theta condition, the comb polymers adopt an intermediate structure, and the pore is partially open.
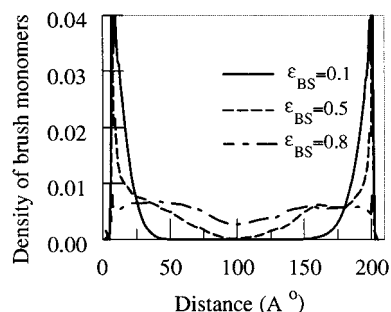

Figure 6. Density profiles of brush monomers across the pore at $\epsilon_{BS} = 0.1$, 0.5, and 0.8 kJ/mol.
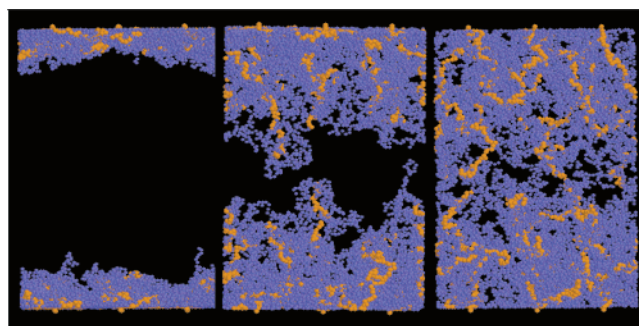

Figure 7. Snapshots from MD simulations of the nanoporous system for $\epsilon_{BS} = 0.1$ (left), 0.5 (center) and 0.8 (right) kJ/mol. Solvent molecules are not shown for better visualization of the brush structure. Color code: side chains (blue) and main chain (yellow)
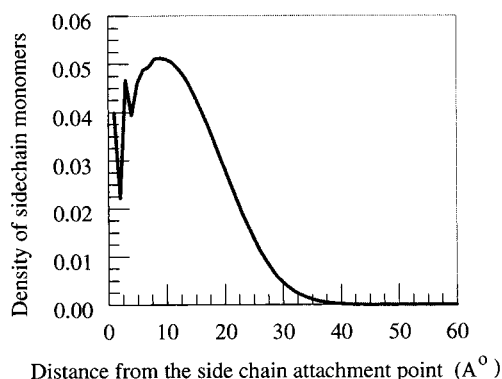

Figure 8. Density profile of side-chain monomers around the comb polymer. The number density of side-chain monomers is plotted as a function of xy-component (parallel to the grafting surface) of distance from the backbone under $\epsilon_{BS} = 0.8$ kJ/mol.

It takes approximately 2×10^5 simulation time steps to open a closed pore, which is about 0.5 ns.

Snapshots of the system from the simulations in Figure 7 depict the pore structure at the three different solvent conditions. Solvent molecules are not shown for better visualization of the brush. Plotted in Figure 8 is side chain monomer density as a function of distance from the side-chain attachment point for a good solvent ($\epsilon_{BS} = 0.8$ kJ/mol). This plot suggests that the side chains form an impermeable structure of radius 10σ around the main chain causing a significant overlap of adjacent brush molecules that are grafted at a distance 17σ.

It is apparent from the snapshots of the nanopore structure that comb polymer molecules grafted inside the pore could
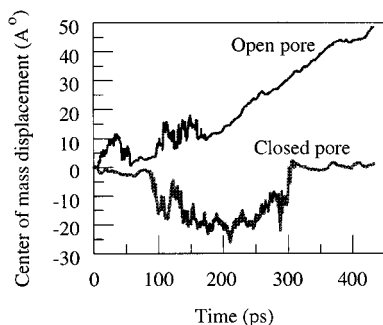
Figure 9. Center of mass displacement as a function of time for a free polymer chain of length $N_p = 200$, under an external force $F_e = 0.0162\epsilon/\sigma$ per monomer.
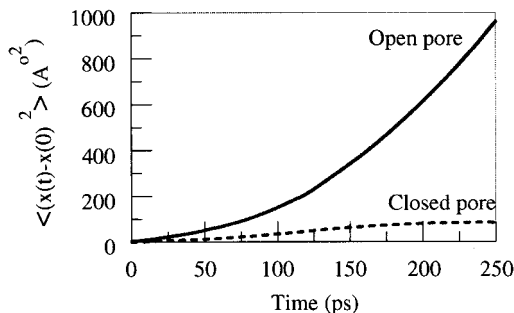

Figure 10. Mean square displacement of center of mass of the diffusing polymer chain ($N_p = 200$) as a function of time in closed and open pores. $F_e = 0.0162\epsilon/\sigma$ per monomer.

Figure 11. Center of mass displacement versus time for polymer chains of length $N_p = 20$, 50, 100, and 200, through a closed pore. $F_e = 0.0162\epsilon/\sigma$ per monomer.

act as barriers for large molecule transport in the presence of a good solvent. To characterize the selectivity of the system for molecular separation, the transport of free oligomers of different lengths through the system under an external force was modeled. The oligomer chains interact purely repulsively with all other species in the system. A constant force F_e was applied in the x-direction of the pore channel on each bead belonging to the free chains. This artificial external force is analogous to an electric field acting on a charged polymer or a field due to chemical potential gradient in the x-direction. Ideally, collapsed comb molecules in a poor solvent would offer little resistance to the transport of oligomers and the dynamics would reduce to transport of a free chain in a monomeric solvent under an external force.

Conversely, in a good solvent the network of stretched brush molecules would trap a diffusing chain that is larger than the open space remaining in the pore. Plotted in Figure 9 is the center-of-mass mean square displacement in the direction of the pore channel as a function of time for an oligomer chain containing 200 monomers drifting under an external field $F_e = 0.0162 \; \epsilon/\sigma$. For the open pore (corresponding to the solvent conditions for the system illustrated in the left frame of Figure 7), the chain is able to move through the pore, whereas for the closed pore chain diffusion is not apparent. Plotted in Figure 10 is the mean square displacement of the oligomer center of mass from the simulation averaged over a large number of starting points. In the open pore averaged mean-square displacement of the chain varies with time as t^2, characteristic of a drift-like motion under an applied force. In the case of the closed pore
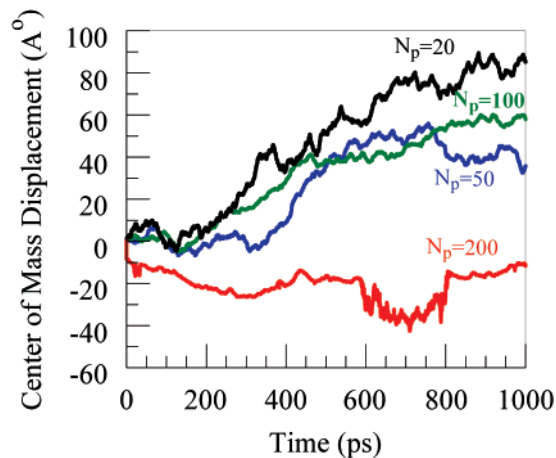
the applied force attempts to push the molecule through the comb structure. As the process has to compete with the relaxation dynamics of the brush molecules, which is very slow, the polymer chain gets trapped in the brush network. The average size of the oligomer chain is $R_g \approx N_p 3/5a = 24\sigma$, which is larger than the distance between two grafted brush molecules. This implies that the polymer chain cannot migrate as a sphere through the structure, and has to translate by reptation, a much slower process compared to free translation.[11]

It is expected that a chain with a size smaller than the grafting distance d between the brush molecules can migrate easier than an oligomer larger than the grafting density. A molecule with $R_g < d$ could make its way through the region between the grafted comb polymers which is less densely occupied by chains of the comb polymers. To test this expectation, simulations were used to characterize the transport behavior of oligomer chains of different sizes through the system containing a good solvent. The center-of-mass displacement in the direction along the pore channel as a function of time is plotted in Figure 11 for oligomer chains of size $N_p = 20$, 50, 100, and 200 under an external force $F_e = 0.0162\epsilon/\sigma$ per monomer. The $N_p = 20$ chain, which has an average size $R_g \approx 6.034\sigma$, translates through the system at a fairly steady velocity. For the $N_p = 50$ and 100 oligmers, with $R_g \approx 10.45\sigma$ and 15.85σ, respectively, the center-of-mass displacement plot shows a migration over a distance of about 50 Å followed by a plateau. This distance of free translation of $\sim18\sigma$ approximately corresponds to the grafting distance $d = 17.65\sigma$, suggesting that the molecules are large enough to be hindered by the brush molecules as they diffuse. For $N_p = 200$, the size $R_g \approx 24\sigma$ is larger than d, and the center-of-mass displacement does not indicate translation. However, as noted earlier, large molecules can reptate in the direction of the field, which is a slower mechanism that is not observed in the time scale of our simulations. It may be noted that Figure 11 shows a higher displacement for $N_p = 100$ oligomer than for $N_p = 50$ oligomer, which is out of the general trend. The reason for this discrepancy is that, in this set of simulations, $N_p =$

50 oligomer finds itself trapped by a grafted brush molecule along its trajectory before $N_p = 100$ oligomer does. Better statistics of trapping events are needed to further characterize the size dependency of oligomer diffusivity in the long time regime. This could be achieved through longer simulations or multiple simulations with different initial oligomer positions.

Conclusions

A stimuli-responsive nanoporous system whose functionality is based on a rod-globule transition in comb polymer molecules has been characterized using molecular dynamics simulations. The design consists of comb polymer molecules attached to the inside of a slit pore. The comb structures collapse in a poor solvent to open the pore and stretch in a good solvent to close the pore. Simulations of stretch-collapse transitions in isolated comb polymers indicate two-phase behavior characteristics of a first order transition, and that the transition can be completed in about 1 ns. Simulations of comb brushes attached to the inside surfaces of a slitpore immersed in a pool of explicit solvent molecules demonstrated the feasibility of opening and closing a pore in response to solvent quality. Simulations of oligomer chains in the pores also demonstrated that pore closing can be used to inhibit diffusion, and in a closed pore chains with sizes smaller than the grafting distance between the comb polymers can drifted relatively easily as compared to chains that are larger in size. Future work will target specific applications where environmental variables such as pH and temperature are used to tune the system operation.

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