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Meso-scale Simulations of Poly(N-isopropylacrylamide) Grafted Architectures

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ABSTRACT

Poly(N-isopropylacrylamide) (PNIPAM) is a thermosensitive polymer that is well-known for its behavior at a lower critical solution temperature (LCST) around 305 K. Below the LCST, PNIPAM is soluble in water, and above this temperature, polymer chains collapse and transform into a globule state. The conformational dynamics of single chains of polymer in a solution is known to be different from those of grafted structures that comprise of an ensemble of such single chains. In this study, we have carried out MD simulations of a mesoscopic nanostructure of PNIPAM polymer chains consisting of 60 monomer units grafted onto gold nanoparticles of different diameters, to study the effect of temperature and core particle size on the polymer conformations. Additionally, we have also studied the effect of grafting density on the coil-to-globule transition exhibited by PNIPAM through the LCST. The systems investigated consisted of ~3 and ~6 million atoms. Simulations were carried out below and above the LCST of PNIPAM, at 275K and 325K. Simulation trajectories were analyzed for radius of gyration of PNIPAM chains.

INTRODUCTION

Poly(N-isopropylacrylamide) (PNIPAM) undergoes a coil-to-globule transition when the temperature is raised from below to above its lower critical solution temperature (LCST), typically near 305 K.[1] Coil-to-globule transitions shown by such macromolecules can have a number of practical applications, including drug delivery, medical diagnostics, biomolecule separations, etc.[2] Recent advancements in synthetic chemistry have allowed us to alter the LCST of these polymers by copolymerizing these temperature sensitive polymers with other polymers that are hydrophilic or hydrophobic in nature, by modifying the end groups of these polymers with different ionic groups or attachment of biomolecules, for example. Addition of salts and electrolytes in solvent, such as salt ions or co-solvents can also modify the LCST of these polymers.[3] With the aid of recent synthetic techniques, these macromolecules can be built up into mesoscopic nanostructures with arbitrary architectural complexity, which allows us to incorporate building blocks of different chemical functionality or biomolecule (DNA, peptides etc.) in well-controlled positions.[4] A "polymer brush" structure is a classic example of such a mesoscopic macromolecular nanostructure. Polymer brushes are essentially flexible macromolecular chains that are strategically anchored by special linkers to a substrate at sufficiently high grafting density such that different chains interact.[5] A precise control of the make-up of such macromolecular chains of temperature-sensitive copolymer sequences (block or

graft) as a part of a polymer brush architecture is fascinating because of their remarkable phase behavior in aqueous solutions.[6]

Our understanding of the aggregation behavior or solvation properties of nanoparticles is limited, which makes controlled processing of nanoparticles difficult. One of the most acceptable and widely used methods to overcome these issues is the functionalization of these nanoparticles with different polymeric materials or small organic molecules.[5] Functionalizing either organic or inorganic nanoparticles with polymer chains can prevent agglomeration and is becoming a preferred method for controlled synthesis of nanoparticles for a wide range of applications.[7]

Successful efforts have been made to functionalize nanoparticles with thermo-sensitive polymers. For example, grafting of gold nanoparticles with PNIPAM can result in a water-soluble material that changes its morphology (shape, size, and texture) based on the surrounding temperature.[8] Experimental studies suggest a decrease in the mean distance between the nanoparticles above the LCST of PNIPAM.[8] This decrease was attributed to the collapse of the PNIPAM chains. The molecular structure and grafting density of the attached PNIPAM defines the structural and functional properties of these functionalized nanoparticles.[7] The exact atomic-level structure of these composites of PNIPAM and the nanoparticles, however, is not very well understood. Experimentally, it is very difficult to obtain the atomistic details of the effect of grafting density, temperature, and chain-length of PNIPAM on the structure and conformation of these mesoscopic nanostructures. Additionally, the mechanism, geometry, morphology, and dynamics of self-assembly of these nanoparticles in presence of external stimuli, such as temperature, is also not very well understood.

In the present study, we have used atomistic molecular dynamics (MD) simulations to investigate the effect of size of PNIPAM grafted nanoparticles on its morphology and coil-to-globule transition of PNIPAM. Multi-million atom MD simulations of PNIPAM grafted gold nanoparticle and water system were carried out using CHARMM force-field at a range of temperatures from 275 K to 325 K. PNIPAM chains consisting of 60 monomer units were grafted on gold nanoparticles, of 6 and 10 nm diameter, to study the effect of curvature and temperature on the polymer conformations. Simulation trajectories consisting of trajectories of ~ 3 to ~ 6 million atoms were analyzed for radius of gyration (R_g) of PNIPAM chains at 275 K and 325 K to study the coil-to-globule transitions in these polymers.

THEORY DETAILS

To study the coil-to-globule transition in PNIPAM grafted gold nanoparticles, we have used a fully atomistic model of PNIPAM and water. CHARMM force-field has been successfully employed in the past to study different biomolecules and polymer systems.[9] In the present study, we have used CHARMM-27 force-field to study the coil-to-globule transition in PNIPAM grafted on gold nanoparticles of ~ 5 and ~ 10 nm diameters in presence of water. TIP3P water model was used with CHARMM force-field to conduct simulations of solvated PNIPAM. The combination of CHARMM with TIP3P has been effectively used by the CHARMM community to understand the structural and dynamic properties of proteins, nucleic acid and carbohydrates.

In the first step of structure generation, a monomer unit was generated and was repeated to generate an isotactic-rich chain of PNIPAM consisting of 60 monomer unit (60-mer). One end of the PNIPAM was terminated with a CH_3 group and the other with a hydrogen atom. This chain was initially equilibrated for 100 ps in vacuum using CHARMM force-fields. In the case of gold nanoparticle with ~ 5 nm diameter 28 and 42 chains were grafted. 99 chains of PNIPAM

were grafted on the gold nanoparticle with ~ 10 nm diameter. Hydrogen atom of a CH_3 termination was grafted on a gold nanoparticle. The gold nanoparticle was represented by a fixed atom with a diameter of ~ 5 nm and ~ 10 nm. This was followed by random insertion of TIP3 water molecules. Systems with ~ 5 nm and ~ 10 nm diameter consist of ~ 3 M and ~ 6 M atoms, respectively. Simulations were carried out at 275 and 325 K under constant NPT condition at 1 atm pressure. The NPT condition is maintained using Langevin thermostat and Nose-Hoover Langevin piston pressure control. The NAMD simulation package with periodic boundary conditions was used to conduct all the simulations. A spherical cut-off of 12 Å was used for all non-bonded interactions. Simulations were carried out for ~ 35 ns with a time step of 1 fs. The atomic trajectories (atom positions, velocities, temperature, pressure, velocities) were accumulated and stored every 1 ps. Trajectory files obtained from these simulations were analyzed for structural and dynamical properties. The structural evolution of polymer chains in presence of explicit water model at different temperatures was followed by analyzing the change in radius of gyration (R_g) over time.

RESULTS AND DISCUSSION

Conformation Snapshots

The trajectories obtained from our large-scale, atomistic MD simulation were used to obtain insights into the collapse of a PNIPAM brush structure consisting of 28 and 42 chains of PNIPAM 60-mer grafted onto a ~ 5 nm diameter gold nanoparticle. **Figure 1** shows the snapshots of the PNIPAM brush structure consisting of ~ 28 chains at the end of ~ 35 ns. Figure 1(a) and (b) represent conformations below (275 K) and above (325 K) the LCST observed for single chains, respectively. We see a clear coil-to-globule transition in the conformation of the grafted PNIPAM chains at 325 K compared to 275 K. Initial observation of snapshots suggests that at 325 K PNIPAM chains are both collapsed and agglomerated.

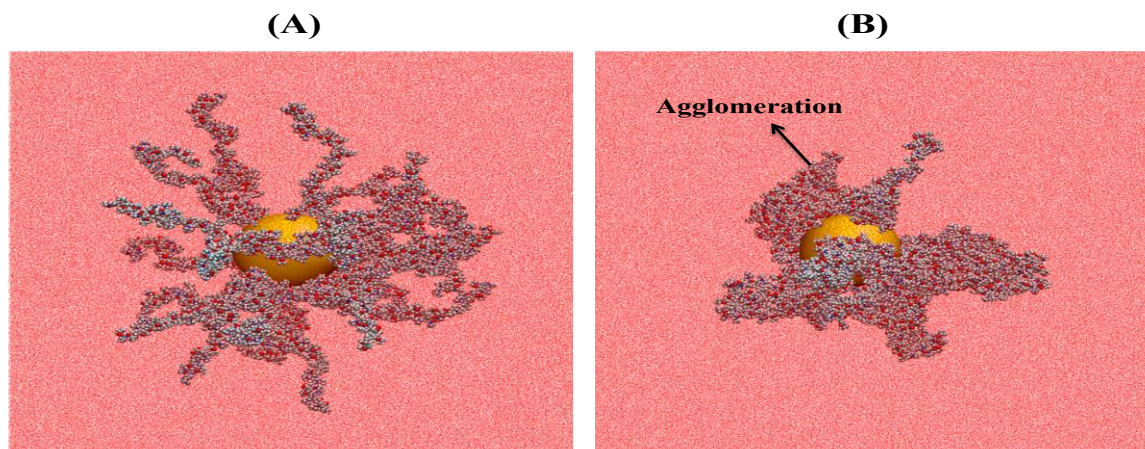


Figure 1: Snapshot of a brush structure of 28 chains of PNIPAM grafted on ~ 5 nm diameter at (a) 275 K and (b) 325 K at the end of ~ 35 ns. The central sphere represents the Au nanoparticle with ~ 5 nm diameter. Water molecules are shown in red.

Figure 2 shows the conformation snapshots of the PNIPAM brush structure consisting of ~ 42 chains at the end of ~ 35 ns, below (275 K) and above (325 K) the LCST observed for single chains. We see a clear coil-to-globule transition in the conformation of PNIPAM chains at 325 K compared to 275 K. At 275 K, we observe that PNIPAM chains are entangled and yet remain in a

coil-state. At 325 K, however, PNIPAM chains are both collapsed and agglomerated as compared to 275 K. **Figure 2** also suggests that with increase in the grafting density of polymer chains onto the nanoparticle surface, the extent of coil-to-globule transition above its LCST is reduced. This suggests that the apparent degree of the coil-to-globule transition in PNIPAM brush structures strongly depends on the grafting density. The total collapse of the many of the polymer chains appears to be hindered due to steric effects from neighboring chains.

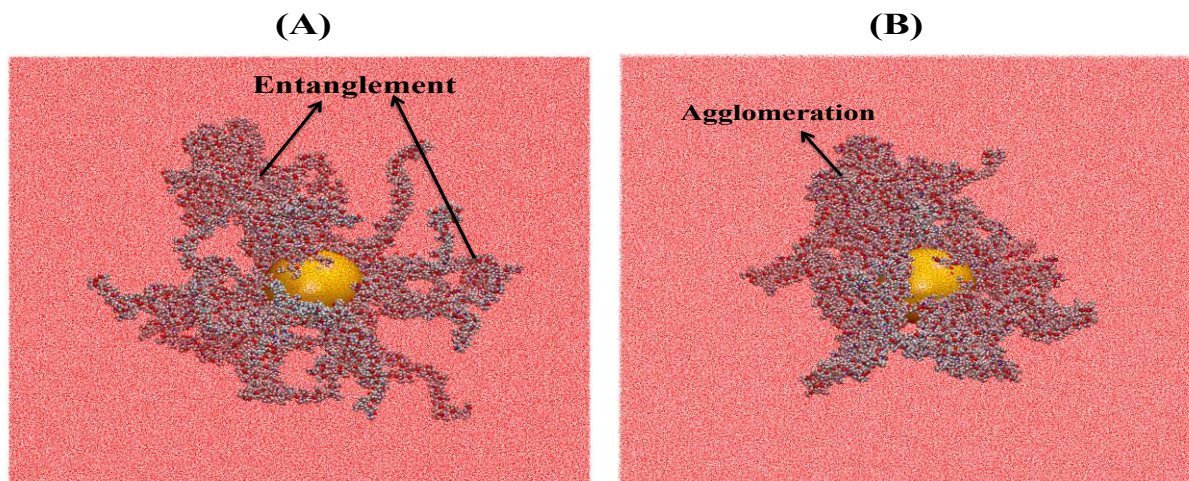


Figure 2: Snapshot of a brush structure of 42 chains of PNIPAM grafted on ~5 nm diameter at (a) 275 K and (b) 325 K at the end of ~35 ns. The central sphere represents the Au nanoparticle with ~5 nm diameter. Water molecules are shown in red.

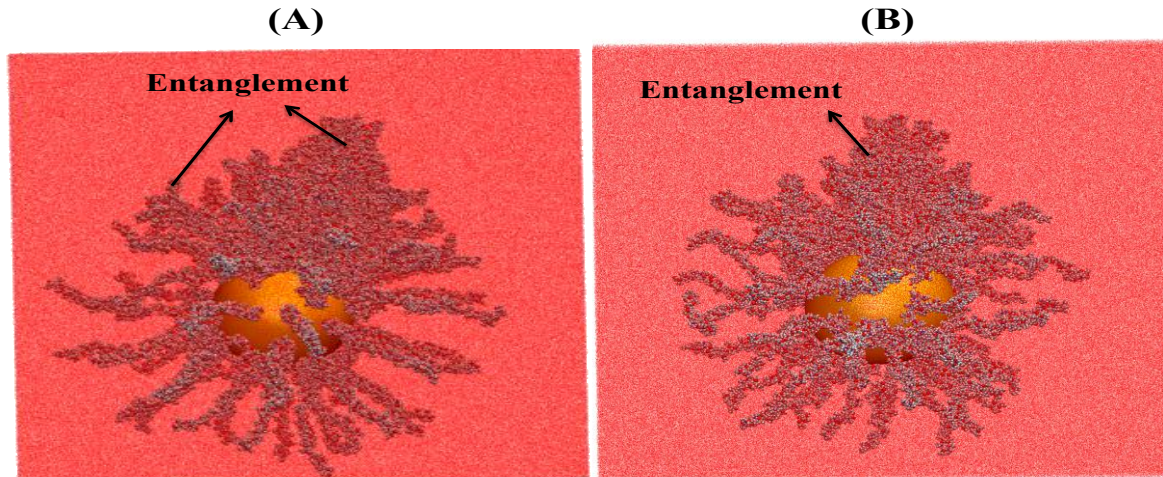


Figure 3: Snapshot of a brush structure of 99 chains of PNIPAM grafted on ~10 nm diameter at (a) 275 K and (b) 325 K at the end of ~10 ns. The central sphere represents the Au nanoparticle with ~10 nm diameter. Water molecules are shown in red.

Figure 3 shows conformation snapshots of the PNIPAM brush structure consisting of ~99 chains at the end of ~10 ns, both at 275 K and 325 K. These simulations are ongoing, and will be further continued up to ~35 ns of simulation time. This initial stage of these simulations suggest that even below the LCST at 275 K, PNIPAM chains are significantly entangled in the high-grafting density area and yet appear to still be in a coil-state.

Radius of gyration (R_g)

To obtain a more quantitative estimate of the collapse phenomena, we calculate the radius of gyration (R_g) of the PNIPAM chains. **Figures 1** and **2** clearly suggest that PNIPAM chains at 275 K remain in a random-coil-state and later at 325 K undergo a coil-to-globule transition by the end of a simulation run of ~ 35 ns. To better understand this coil-to-globule transition, we

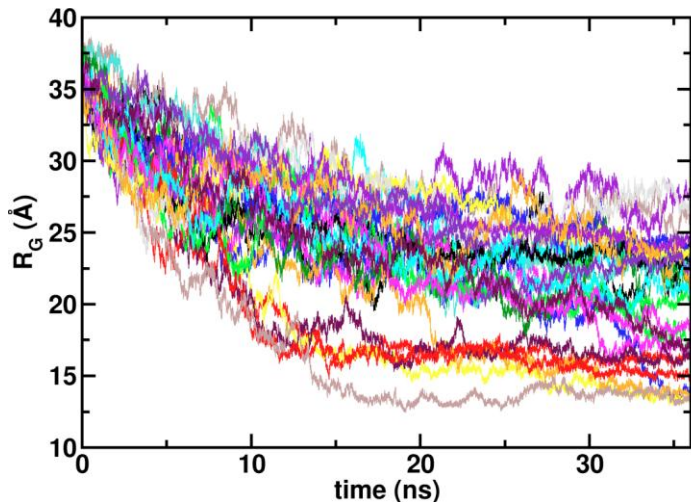


Figure 4: Instantaneous R_g of 28 chains of PNIPAM 60-mers grafted on ~ 5 nm gold nanoparticle at 325 K. A clear coil-to-globule transition can be observed for all PNIPAM chains, although the amount of change in R_g varies from chain to chain yet remains somewhat stable for each chain.

have calculated the R_g of the individual chains, for the system consisting of 28 PNIPAM chains grafted onto ~ 5 -nm-diameter gold nanoparticle, during the simulation run at 325 K. **Figure 4** shows the instantaneous R_g for the individual PNIPAM chains (28 chains) grafted on ~ 5 -nm-diameter nanoparticle at 325 K. It can be clearly seen from **Figure 4** that the R_g value for all the chains decreases during the simulation run and after the initial simulation time of ~ 10 ns, fluctuates around an average value associated with each individual chain. For example, for chains that show the greatest degree of coil-to-globule transition, the R_g value decreases from ~ 40 Å to ~ 12 Å, and after the initial ~ 10 ns, fluctuates around ~ 12 Å until the end of ~ 35 ns. In the case of

chains that are not as fully collapsed, perhaps due to agglomeration in the neighboring collapsed chains hindering conformational change, the R_g value decreases from ~ 40 Å to ~ 25 Å, and after the initial ~ 10 ns, fluctuates around ~ 25 Å until the end of ~ 35 ns. Interestingly, these spatial and temporal variations in the polymer morphology can be correlated to the analytical models developed by Daoud and Cotton¹⁰. In these analytical models for polymer brush structures on curved surfaces, it has been shown that the spatial variation radially can follow different scaling laws (depending on the number of monomers (N), number of branches (f), length of each chain (l)). The concentration of monomers in the vicinity of the spherical particles is very high and hence shows a dependence which can be characterized as $r < l^{1/2} * 1$. Away from the particle surface, the concentration decreases radially and the behavior corresponds to a single chain due to limited interaction between the different branches ($r < l^{4/3} * 1$). We have looked at the radial density distribution of the polymer brushes below the LCST. Consistent with the predictions of the analytical model, we observe that the density variation has a radial dependence that can be classified by different power laws in two regimes (vicinity near and away from the NP surface). Note that the analytical model does not have a temperature dependent term (except the Flory interaction parameter) and was not specifically developed for thermo-sensitive polymers. In our case, above the LCST, the free end of the branches collapses and hence the relative extent of the two regimes changes. In the case of system consisting of 42 chains of PNIPAM, at 325 K for fully collapsed and partially collapsed chains due to agglomeration the R_g value of decreases from ~ 40 Å to ~ 14 Å and from ~ 40 Å to ~ 27 Å the end of ~ 35 ns. Currently, we are in the process of further analyzing the trajectories of our simulations that will be presented in future

work. Our goal is to understand the change in overall morphology of the PNIPAM brush structures and compare this with the scattering data from experiments underway.

CONCLUSIONS

Our study is the first all-atom, mesoscale MD simulation of PNIPAM grafted onto gold nanoparticles. We have successfully conducted simulations of PNIPAM brushes at 275 K and 325 K, below and above the LCST of PNIPAM, to study the effect of the grafting density and the size of a nanoparticle on the coil-to-globule transition of the grafted PNIPAM. The behavior is more complex than that of single chains where a simple coil-to-globule transition occurs at 325 K. The conformational dynamics in the nanoparticle-grafted PNIPAM is strongly affected by the polymer grafting density, the polymer chain length, and the nanoparticle curvature. Our simulations suggest that at higher grafting densities of PNIPAM, perhaps due to steric hindrance, the extent of the coil-to-globule transitions is significantly reduced compared to that observed at lower grafting densities. In all cases, however, we observed entanglement versus agglomeration of the PNIPAM chains, at 275 K versus 325 K, respectively.

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