Confined crowded polymers near attractive surfaces
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We present results from molecular dynamics simulations of a spherically confined neutral polymer in the presence of crowding agents, studying polymer shapes and conformations as a function of the confining potential, solvent quality and the density of crowders. The conformations of the polymer under good solvent conditions are largely independent of crowder density, even when the polymer is strongly confined. However, for poor solvents and attractive walls, the polymer shows a transition between an adsorbed extended state to a globular conformation on the surface as a function of crowder particle density. This state differs from both the desorbed globular conformation in the absence of any wall interactions and the adsorbed globular conformation at low values of the attractive wall interactions. We revisit the earlier understanding of the adsorption of confined polymers on curved, attractive walls in the light of these results.

Keywords: confined walls, polymers, dynamical properties, entropic effects

I. INTRODUCTION

For an unconfined neutral polymer, the nature of the solvent determines whether the polymer adopts, on average, an extended or a collapsed conformation. If confined, the polymer experiences a loss of conformational entropy, favouring a subset of configurations that can now also depend sensitively on the shape and other properties of the confining volume1−8. A number of polymers in biological contexts face varying degrees of confinement. The approximately 2m of DNA in the nucleus of eukaryotic cells must be restricted to a nucleus that is ≈10µm in radius, while the packaging of viral DNA into sub-micron-sized protein capsids is often dense enough to induce local crystallinity.5−11. Cargo transported along axons by molecular motors typically consists of specific protein molecules encapsulated in vesicles of diameter 30−80nm, comparable in dimension to the larger peptide neurotransmitters that such vesicles must accommodate12.

Biological polymers in vivo also inhabit highly crowded environments. The presence of crowders can affect the compaction and higher-order organization of single polymers, as well as promote aggregation in polymer solutions13−18. Adding explicit crowders can induce similar conformational changes19. At high crowder concentration, neutral polymers undergo a continuous extended-to-collapsed transition20,21. Incorporating attractive interactions between crowder particles and macromolecules leads to the formation of complex aggregates. These can be observed directly22. Although repulsive interactions do not promote the formation of complexes, they can affect reaction rates and conformations via the Asakura Oosawa depletion interaction23. Experiments24 show that small molecules such as polyethylene glycol (PEG) can condense DNA. Although DNA is confined and crowded within the nucleus, it is not structureless and the interaction between polymer shape, confinement and crowding can potentially accentuate certain aspects of such structure while attenuating others. Within the cell, the presence of a heterogeneous mixture of proteins, organelles, water and ions can influence the loss of conformational entropy in ways that are particularly hard to predict14,25−28.

The ability to accurately describe the phase behavior of polymers in confined, crowded regimes is thus central to an improved understanding of a number of biological processes29−32. In addition, understanding polymer adsorption onto surfaces as solvent conditions are varied is relevant both to the efficiency of biosensors33 as well as to the formulation of protein resistant coatings34,35. For a confined polymer, where the interactions of the polymer with the confining surface are important to account for, the competition between monomer−monomer, monomer−solvent and monomer−surface interactions can lead to interesting conformational behaviour. Earlier simulations studying polymer confinement, e.g. the work of Ref.4, in which the confinement sphere radius was varied but explicit crowder particles were absent, also stressed the importance of confinement. A number of theoretical and simulation studies have examined the interaction of neutral and charged polymers with surfaces36−40. Using atomistic simulations to study the effects of crowder particles on the statics and dynamics of realistic bio-polymers is computationally expensive. However, coarse-grained simulations of biological polymers in the presence of crowders can be performed far more easily41,42. Previous studies have largely used a neutral polymer description, even though biologically relevant polymers such as DNA are typically weakly charged in solution. It is conventionally argued that the screening of the charges through counterions and other charged

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species around the biological polymer of relevance renders the effective electrostatic interaction short-ranged.

The interplay between chain entropy, monomer-monomer interactions and monomer-surface interactions should determine the conformational landscape of polymers near surfaces. Using phenomenological arguments, Rajesh et al. concluded that for low values of attraction between the monomers and the surface as well as between the monomers, the polymer is desorbed and extended. Upon increasing the monomer-monomer attraction, a desorbed collapsed phase results. If the interaction strength between monomer and surface is increased, the polymer can assume either an adsorbed-extended or an adsorbed-collapsed conformation, depending on the monomer-monomer interaction. These authors also predicted a “surface attached globule” state, in which the number of contacts between the both collapsed and globular conformations of the polymer in proximity to the surface differ significantly from those in the adsorbed collapsed phase.

Monte-Carlo simulation studies on neutral spherically confined polymers suggest that for low temperatures, the polymer adsorbs on the wall of the sphere and tends to form layer-like structures. At higher temperatures, the polymer was found to desorb, assuming an extended conformation. The effect of solvent conditions on polymer conformations near the surface have also been studied. Under good solvent conditions a grafted polymer on a flat surface is adsorbed on the surface at low temperatures, while it assumes a desorbed conformation at higher temperatures. In poor solvent conditions, for lower temperatures, it takes a globular adsorbed conformation, while for higher temperatures, the polymer desorbs from the surface. Using multi-canonical Monte Carlo simulations, a phase diagram consolidating the observed behaviour has been proposed. In this phase diagram, for low temperatures and for a small value of monomer-surface interaction energy, the polymer assumes a desorbed collapsed conformation. With increasing surface interaction, the polymer undergoes a transition from an amorphous globular conformation to a more layered internal structure. The layering, in those simulations, covered regimes between a 4-layered adsorbed structure to a monolayer adsorbed structure. There appear to be four dominant “phases” that describe the behaviour of neutral polymers near attractive walls and under different solvent conditions. These are the desorbed-extended (DE), desorbed-collapsed (DC), adsorbed-extended (AE) and adsorbed-collapsed (AC) phases. The nature of the transition between these phases has been studied , but we note that these are largely performed on polymers of relatively short chain length. Different structures could possibly be stabilized, or the boundaries between the states proposed earlier altered, when long chain polymers are adsorbed at a surface, as opposed to short ones. In addition, confining polymers and adding crowders to the system adds further dimensions of complexity, but represent a limit that is more relevant to biophysical situations.

To examine these questions, this paper explores how confinement, powder density, solvent conditions and surface interaction combine to influence polymer conformations, using simulations of a simple model system. Our work extends previous results through its incorporation of the effects of crowder density, specifically, in the confined case with wall interaction. We point out that solvent quality and crowder density complement each other in determining configurations, and that the effects of these are most prominent in the poor solvent case. We characterize the “crumpling” of polymer conformations under the combination of high crowder density and poor solvent. Although the parameter space is large, our results provide a benchmark for the nature of polymer conformations in each of these different regimes, providing physical arguments for why they should be stabilized.

This paper is organized as follows: in Section II, we discuss the procedures by which we set up our systems, describing the simulation protocols employed and the methods used for our calculation. Our results are presented in section III. This is followed by a discussion that summarizes the conclusions we draw from our study and provides suggestions for future work.

II. METHODS

We study, using molecular dynamics simulations, a single long self-avoiding polymer chain of 400 monomers, confined to the interior of a hollow sphere. The simulated volume also contains crowders i.e. particles that interact non-specifically with the monomers constituting the chain as well as with themselves. In our simulations, we vary solvent quality across the extreme limits of good and poor solvents. Our monomers and particles have the same size.

We define the total volume fraction as , with being the total number of both monomers and crowders together, the volume of a monomer or crowder particle and the volume of the spherical confining region. We vary between 0.05 to 0.45 in steps of 0.05, by changing the number of crowder particles between 950 and 12,150. To be able to compare results for the confined and the unconfined cases, we also perform simulations using periodic boundary conditions, applied across a cubical simulation box.

The interaction between the monomers, between monomer and crowder, as well as between crowder and crowder is taken to be of the Weeks-Chandler-Andersen (WCA) form,

\[
V_{ij}^{WCA}(r_{ij}) = \begin{cases} 
4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right] + \epsilon & r < r_c \\
0 & r \geq r_c
\end{cases}
\]

(1)

where , refers to the monomers and crowder particles respectively, and is the distance between two
particles. (By definition $\epsilon_{ij}$ is a symmetric matrix and the quantities $\epsilon_{ij}$ and $\sigma_{ij}$ define the corresponding interaction parameters.) The interaction among monomers, and between crowders and monomers, determines the effective solvent condition. The interaction of the monomer with the wall is described by a Lennard-Jones potential. Both repulsive and attractive wall interactions between monomers and wall are considered. The interaction of the crowder particles to the wall is set to be repulsive regardless of solvent condition. The strength and sign of the interaction of the polymer with the wall can be varied, so that the full range between repulsive and attractive wall strengths is accessed. The parameters used in this study are given in Table S1.

A harmonic potential between nearest neighbours along the chain enforces chain connectivity. It is defined through,

$$V_{\text{bond}}^{\text{bond}}(r_{ij}) = \frac{1}{2} k_{\text{bond}} (r_{ij} - r_0)^2.$$  \hspace{1cm} (2)

The equation of motion is integrated for $10^8$ steps using a velocity-Verlet algorithm. The step size is taken to be $\delta t = 0.001 \tau$, where $\tau = \sigma \sqrt{m/\epsilon}$, $m$, $\sigma$ and $\epsilon$ are units of mass, length and energy respectively. All simulations are performed under constant volume and temperature (T) conditions ($T = 1.0$) using a Nose-Hoover thermostat. The MD implementation is from the LAMMPS software package. Snapshots of the system were taken using the VMD package and used to first qualitatively assess changes in configurations across parameter values, prior to quantitative analysis.

The system’s initial configuration is constructed using the pizza-py toolkit. At higher volume fractions, the system’s initial configuration was unstable. We thus used a harmonic wall interaction initially for $10^4$ steps, subsequently restarting the system with the desired wall interaction potential and parameters. The bond length $r_0$ for the polymer is taken to be 1.122, and the size of the monomer and of the crowder particles are both taken to be 1.0, in the units set above. The polymer and crowder particles are enclosed in a confining spherical shell of radius $R = 15.0$, a choice explained in the following section.

We calculated a number of quantities, among them the radius of gyration which describes the overall spread of the polymer is, defined as

$$R_g^2 = \frac{1}{2N^2} \sum_{i=1}^{N} \sum_{j=1}^{N} |(\vec{r}_i - \vec{r}_j)|^2.$$  \hspace{1cm} (3)

We also compute contact maps of polymer configurations, counting a valid contact as when any two monomers are within a distance of $2\sigma$. The results are averaged over a large number of configurations corresponding to $5 \times 10^6 \tau$. For the confined, adsorbed case, we count the average fraction of monomers adsorbed on the surface as well as a height function that measures the height of the adsorbed configuration relative to the confining sphere surface. To calculate the height of the polymer stacks, we calculated the distance of each monomer from the centre of the confining sphere. We then subtracted this quantity from the radius of the confinement. The largest number thus obtained, after averaging over a large number of configurations, is a measure of the height of the polymer stack in each snapshot, and is termed $H$.

The pair radial distribution function $g(r)$ is computed in order to understand how density varies with distance from any reference particle. It measures the probability of finding a particle at a distance $r$ from the reference particle. In order to compute $g(r)$, the distance between each such pair of particles is calculated and an appropriately normalized histogram plotted.

In order to understand the effect of the curvature of the confinement on the conformation of the polymer, we also performed simulations with a larger sphere of radius $R = 30.0$, for the same volume fractions, potential and other parameters. In all cases, we performed a large number of simulations starting from different initial conditions and with the same parameters to ensure good statistical averaging.

III. RESULTS

A. Confined, crowded polymers in a good solvent with a repulsive wall interaction

To understand the effects of crowder particle density on polymer conformation, we simulated the neutral polymer in a good solvent condition in a confining sphere with repulsive walls. We also performed simulations using periodic boundary conditions with a cubical simulation box. Repulsive walls were used so we could first isolate the effects of crowder particles. Our results are shown in Figure 1. Even for the smallest crowder particle densities, the $R_g$ value of the polymer in the confined sphere is significantly lower than that in the unconfined case. The radius of the confining sphere was chosen based on the typical $R_g$ value of the polymer in the unconfined case. The polymer, in the confined case, undergoes large fluctuations in its conformations. This is captured through the $R_g$ values, as shown with the corresponding error bars, obtained by averaging over at least 5 different initial conditions.

For the confined polymer, $R_g$ depends on the crowder density. It shows a further reduction in its values at the highest crowder densities considered in this study. Snapshots of polymer conformations with and without confinement and at the highest crowder density are shown in Figure 1 (b) and (c) respectively.

Earlier studies, both theoretical and computational, have shown that the primary effect of confinement, with or without crowders, is to reduce the conformational space available to the polymer. The results shown in Figure 1 are in agreement with these results.
For higher crowder densities, depletion forces could cause further compaction of the polymer, even in good solvent conditions. This is both as shown here as well as seen in earlier studies. How polymer-wall interactions further modify the landscape of polymer configurations under different conditions of solvent and crowder particle densities will be explored in later sections.

B. Confined polymers in good and bad solvents with attractive walls

We next examine the effects of attractive wall strength on the polymer conformations, in good as well as in poor solvent conditions. We first explore the case of low crowder densities, showing snapshots of terminal simulation configurations in Figure 2. At these densities, we find that the polymer is extended in good solvent conditions (Figure 2 (a) and (b)), while it is collapsed in a poor solvent ((Figure 2 (c) and (d))). However, the polymer is positioned differently with respect to the wall, depending on the solvent condition, even at low crowder densities. Across multiple initial conditions, for poor solvents, we find that the polymer remains in close proximity to the attractive wall, while also staying collapsed. This remains true even for the smallest interaction strengths, consistent with earlier studies. In contrast, for a polymer in a good solvent, there appears to be a threshold interaction strength for the polymer to associate to the attractive wall. As the attractive wall strength is increased further ($\epsilon_{mw} = 10.0$), the polymer spreads on the wall surface under both solvent conditions. The conformations they assume, however, are very different in each case. Typical conformations at the attractive wall for good solvent conditions do not vary significantly with an increase in interaction strength beyond a critical attractive wall interaction once the polymer adsorbs on the wall. In contrast, for poor solvents, the polymer adopts a more extended conformation at higher attractive wall interactions.

Coverage in poor solvent conditions differs significantly from that in good solvent conditions. This can be understood in terms of two opposing effects. The polymer wants to maximize its (attractive) interactions with the wall, but this competes with the tendency towards compaction, exacerbated by the presence of crowder particles, that is present even for low crowder densities. For low crowder density, in a good solvent condition, as well as in the poor solvent condition, the fraction of adsorbed monomers ($f_{ad}$) on the surface of the sphere increases as $\epsilon_{mw}$ varies from $\epsilon_{mw} = 1.0$ to 20.0 (see Figure S1).

C. Confined polymers with attractive walls in good and poor solvents: The role of crowder density

To understand the role of crowder density on polymer conformations, we explored higher crowder particle densities. These results are shown in Figure 3. Here, the strength of the attractive wall interaction is kept fixed ($\epsilon_{mw} = 10.0$), while crowder density is varied across both
good and poor solvent conditions.

As in Figure 1, we find that the typical conformation of the polymer in good solvent conditions (Figure 3(a)) is largely unchanged as a function of crowder density, apart from a small reduction in $R_g$ towards the highest crowder densities we explored. This suggests that crowder density has only a small impact on the polymer conformation in a good solvent. However, for poor solvents, the polymer adapts an extended conformation on the confinement surface even at lower crowder density (Figure 3(b)). As the crowder density is increased, the polymer configurations undergo a second transition from extended to collapsed at the surface.

We contrast this to the case for low crowder density (Figure 2), where as the attractive wall strength is increased, a first transition from collapsed to extended conformation (AC to AE phase) in poor solvent is observed. While that transition was driven by the attractive wall strength, the transition from extended to collapsed shown in Figure 3 in the poor solvent case is driven by the crowder density.

FIG. 3. The snapshots of the polymer (a) for good solvent condition (b) for poor solvent condition at different volume fractions $\phi_T = 0.05, 0.25, 0.35, 0.45$ for attractive wall strength $\epsilon_{mw} = 10.0$. (c) Fraction of adsorbed monomers on the surface of confinement vs total volume fraction in good and poor solvent condition. The fraction of adsorbed monomers remains constant for good solvent condition as the volume fraction increases because almost all the monomers are already adsorbed on the surface of confinement. It drops significantly for the poor solvent case as the polymer makes a transition from adsorbed layer to an adsorbed globule.

To quantify the spreading of the polymer on the attractive wall, we calculated the fraction of monomers adsorbed to the wall ($f_{ad}$) as a function of crowder density for poor solvent conditions (Figure 3(c)). These results are to be contrasted to those for good solvent conditions, as in Figure S1. We consider a monomer to be adsorbed on the surface if it is within $1.5\sigma$ of the wall. Each point in the plot represents an average of 5 initial conditions and is averaged over $5 \times 10^6$ time steps.

We find that the fraction of adsorbed monomers of the polymer at the surface in good solvent conditions is largely the same even as the crowder density is increased. This fraction is lower than that obtained for poor solvent conditions for all crowder densities except the largest. For poor solvent conditions, however, the fraction of adsorbed monomers at the attractive wall decreases sharply beyond a crowder density of $\phi_T = 0.35$. This reflects the extended to collapsed transition shown in Figure 3(b) ($\phi_T = 0.35 \rightarrow 0.45$).

Contact maps for polymers under poor solvent conditions as a function of increasing crowder density are shown in Figure 4. The contact maps show that as the crowder density increases, the number of contacts increase in general. There are also significant contacts between monomers which are far apart along the sequence, consistent with the visual identification of the collapse of the polymer with increasing crowder density.

D. A crumpling transition induced by crowders

To better characterize the “crumpling” of the polymer under the combination of poor solvent conditions and high crowder densities, we plotted the maximal height of the polymer from the surface as a function of crowder density, for all wall interaction strengths (see Figure 5(a)).

Some intuition for the maximal height can be obtained from side-views of the system as a function of crowder density, as shown in Figure 5(b). At low crowder densities, increasing the strength of the attractive interac-
tions between monomers and wall results in the polymer spreading on the surface. This is evident in the height profile at the smallest crowder density considered \((\phi_T = 0.05)\). The highest height is achieved for the smallest wall attraction strength, where the polymer assumes a collapsed conformation. When the attractive strength of the wall is small \((\epsilon_{mw} = 1.0)\), the height function is largely independent of the crowder density except at the largest crowder density, where the compactness of the polymer increases. However, for other attractive wall strengths, the dependence of the height function on the crowder density is more complex. For an attractive wall strength of \(\epsilon_{mw} = 5.0\), the initial configuration of the polymer is more extended (as can be seen from the difference in heights even at the smallest crowder density). However, the extended-to-collapsed transition is initiated at a lower volume fraction than in the case of \(\epsilon_{mw} = 1.0\). For higher wall interactions, the extended-to-collapsed transition occurs at higher crowder densities.

Our results suggest the following: The polymer in poor solvent conditions near an attractive wall experiences two competing forces. These favour, independently, compaction and spreading on the wall. The propensity to collapse would lead to a higher height function. This is primarily driven by crowder particles. The propensity of the polymer to spread along the surface arises from its attractive interactions with the surface. The interplay between these determines the eventual conformational landscape of the polymers at the interface.

For low attractive wall strength \(\epsilon_{mw} = 5.0\), a smaller threshold crowder density is required for collapse (for \(\phi_T < 0.25\)). We thus see an increase in the height function. As the strength of the attraction towards the wall is increased, the threshold crowder density after which the polymer starts to collapse moves towards higher crowder density, as seen for \(\epsilon_{mw} = 10.0, 20.0\). At the highest crowder densities \((\phi_T = 0.45)\), irrespective of wall interactions, the polymer under poor solvent conditions is predominantly in a collapsed state, as evident in the height function.

Snapshots of the collapsed polymer in poor solvent conditions and at the highest crowder density are shown in Figure 3 (b) and Figure 5 (b). These indicate an increased tendency to order in the polymer conformation. This is absent in the collapsed conformation of the polymer at very low crowder density (See Figure 2). To probe whether the collapsed conformations of the polymer under poor solvent conditions across low and high crowder density are similar, we calculated the pair distribution function for the two collapsed phases. These results are shown in Figure S2. The presence of strong peaks in the distribution function, in the case of high crowder density \((\phi_T = 0.35)\), clearly indicates increased structure in the collapsed conformations compared to the case for lower crowder density \((\phi_T = 0.05)\). This strongly suggests that the collapsed conformations of the polymer under poor solvent conditions at lowest and highest crowder densities are dissimilar and that the crowder particles induce local structure in the collapsed polymer conformation.

To investigate the emerging structure in the conformation of the extended polymer at high wall interaction strength, we calculate the radial distribution function \(g(r)\). For monomer-wall interaction \(\epsilon_{mw} = 10.0\), as \(\phi_T\) is increased, the order in the structure increases (see Figure 6 (a)). To understand the positioning of the polymer relative to the wall, we plot the density function of the polymer vs. the radial distance \(r\). To calculate density function, we split the spherical volume in a large number of thin shells and count the number of particles in each shell. This is then normalized with respect to the average density, considering that monomers are distributed uniformly throughout the volume.

This method allows us to probe layering in the system. For lower crowder density, there are fewer layers. As we increase the crowder density in the system, more layers begin to appear, as seen in Figure 6 (b)). This can be understood in the following way. In poor solvent conditions, as we increase the number of crowder particles in the system, the polymer tries to collapse in order to avoid the exposure to the crowder particles. However, since monomers are attracted towards the wall, a fully globular conformation cannot be sustained. This leads to a partial layering near the wall and hence to the peaks in the density plot.

To investigate whether there is a difference in the col-

![Graph](attachment:image.png)

**FIG. 5.** (a) The maximum height of the polymer stack along the radial direction. The height of the stack decreases as the strength of the attraction increases and more and more monomers are recruited along the wall of the confinement. (b) The snapshots of the polymer conformation in poor solvent condition for the different volume fractions \(\phi_T = 0.05, 0.25, 0.35, 0.45\).
E. Neutral polymers on an attractive surface: The role of the strength of the wall interaction

In this section, we probe the role of attractive wall strength on the polymer conformation. For crowder densities, $\phi_T = 0.05$, and for smaller monomer-wall attractive strength $\epsilon_{mw} = 1.0$, the polymer assumes a globular conformation on average. As $\epsilon_{mw}$ is increased from 1.0 to 5.0, the polymer assumes an extended conformation, accommodating itself to the surface. In this case, most of the monomers stick to the wall. Further increasing the value of $\epsilon_{mw}$ to 10.0 and 20.0 does not lead to any significant difference in polymer conformation. (see Figure 7(a).) These results are qualitatively captured in the contact maps between monomers and are shown in Figure S4.

On the other hand, for a higher crowder density $\phi_T = 0.35$ and for a smaller value of $\epsilon_{mw}$, the polymer sticks to the wall, while assuming a largely globular form. As we increase the value of attractive strength $\epsilon_{mw}$ from 1.0 to 5.0, the height of the globule decreases. Further increasing $\epsilon_{mw}$ to 10.0, we see that the height continues to decrease. For $\epsilon_{mw} = 20.0$, most monomers are now attached to the surface. Unlike the case for lower crowder density, the extended conformation of the polymer has some amount of internal structure at higher crowder densities. (see Figure 7(b).) This structuring of the polymer at high, as compared to low, crowder densities can be seen in the increased number of peaks emerging in pair distribution function between monomers. This is shown in Figure 8. The effect of changing the attractive wall strength on the radius of gyration of the polymers as a function of crowder density is shown in Figure S5. This shows that, at very high crowder density, the polymer is in a collapsed phase under poor solvent conditions, regardless of surface attraction.

Consolidating these results affords us a global picture of possible conformations of a neutral polymer in the $\phi_T - \epsilon_{mw}$ space under poor solvent conditions; see Figure 9. A reduced attraction towards the wall leads to an adsorbed globular (AG) structure. Upon increasing the crowder density, the polymer maintains the AG structure. As the attraction of the polymer towards the wall is increased, the AG state opens up. There is a transition towards an adsorbed, layered structure at low crowder density.
If we now increase crowder density, the polymer tries to collapse in order to avoid exposure to the crowder particles. The competition between the attractive interactions between monomer and wall and the repulsive interaction between the polymer and the crowder particles now governs polymer shape and internal structure. For intermediate $\epsilon_{mw}$ values, the crowder interaction appears to be dominant while for higher values of $\epsilon_{mw}$, the attraction wins. In this case, there is no layering even at higher crowder densities.

In good solvent conditions, provided $\epsilon_{mw}$ is small, the polymer takes an extended form and is not completely adsorbed on the wall. As the wall interaction $\epsilon_{mw}$ increased, the polymer adsorbs on the confining wall but its configurations are extended even as crowder densities are increased.

### IV. DISCUSSION AND CONCLUSION

In this paper, we used molecular dynamics simulations to describe the conformational landscape of a confined polymer in the presence of attractive walls as well as crowder particles for good and poor solvent conditions. We used a 400–monomer long polymer and varied the number of crowder particles, as well as interactions with the wall and the quality of the solvent. The confining wall attracted monomers while it repelled the crowder particles. We varied both the monomer-surface attraction and crowder particle numbers to explore different parts of configurational space preferentially explored as wall attraction and crowder density were changed.

The conformation of the polymer on a surface has been the subject of multiple earlier studies. The nature of polymer configurations depend on the curvature of the surface, solvent quality, boundary conditions, and the interaction energy between the surface and the polymer. Earlier Monte Carlo studies showed that polymers display a number of shape transitions near an attractive planar surface. This work suggested a pseudo phase-diagram in the $\epsilon_{mw} - T$ plane. According to this phase diagram, at low temperatures, the polymer assumes a layered adsorbed crystalline shape. At higher temperatures, the polymer is desorbed at smaller surface attraction, while it remains adsorbed for high surface attraction. Similar shape transitions are seen for polymers on curved surfaces. However, as we show here, the situation is considerably more complex when the polymer is confined.

We showed that for poor solvents, as the attractive interaction strength between the wall and the polymer was increased, the polymer exhibited a shape transition from adsorbed globule (AG) to adsorbed layered (AL). For intermediate values of $\epsilon_{mw}$, as the number of crowder particles was increased, polymer configurations changed from the AL state to an adsorbed collapsed (AC) state. In good solvents, for a reduced value of surface attrac-
tion, the polymer did not completely adsorb on the surface. As the surface attraction was increased the polymer adsorbed on the attractive surface.

The curvature of the confining sphere plays an important role in the selection of conformations. We observed layered structures in proximity to the wall, as seen from the difference in number of peaks (suggesting layers of stacked monomers) when the radius of confining sphere was doubled (see Figure 56); as the radius of the confining sphere is increases, the number of secondary peaks decreases. For the larger sphere, all the monomers are adsorbed on the surface at low \( \phi_T \); as the density of crowders is increased, a second layer appears. For the smaller system, there are multiple layers present even at the smaller volume fraction of crowders. These results suggest that the confinement and the relative ratio of confining sphere radius and length of the polymer can significantly alter the conformational landscape of the polymers. In particular, smaller confinement radii led to more substantial layering, presumably because the smaller sphere frustrates the formation of the adsorbed monolayer that is a feature of the sphere with larger radius. These features can all be tuned by the density of crowders, providing a second axis to adjust the properties of the adsorbed state.

In this study, in addition to the interacting surfaces and solvent condition, we discussed the role of another critical variable associated to crowding of the polymer chain by other monomeric particles. The quantity \( \phi_T \) was found to play an important role in determining the conformation of the polymer. In good solvent conditions, we found that the crowder particle density did not affect the conformations substantially. In poor solvent conditions however, for higher \( \epsilon_{mw} \), the increase in number of crowder particles leads to a more ordered structure. We suggest that this may be a general feature of crowded confined polymers in a poor solvent, when attracted by a wall, and that the ability to adjust solvent quality as well as crowder concentration may be key to stabilizing a polymer in the vicinity of a confining wall.

The addition of crowder particles adds additional complexity but presumably provides a better representation of a large number of biological situations. Indeed, the combination of confinement, crowding and wall interactions should be generic to a number of polymer systems of biological and pharmacological relevance. More detailed studies of these regimes, keeping specific systems in mind, should be of considerable interest.

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Supplementary Information
Confined crowded polymers near attractive surfaces

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### S1 Simulation parameters

|        | Good solvent | Poor solvent |
|--------|--------------|--------------|
| $i-j$  | $\epsilon_{ij}$ | $\sigma_{ij}$ | $r_c$ | $\epsilon_{ij}$ | $\sigma_{ij}$ | $r_c$ |
| m-m    | 1.00         | 1.00         | (2)$^{1/6}$ | 1.00 | 1.00 | 2.5 |
| c-c    | 1.00         | 1.00         | (2)$^{1/6}$ | 1.00 | 1.00 | (2)$^{1/6}$ |
| m-c    | 0.50         | 1.00         | (2)$^{1/6}$ | 5.00 | 1.00 | (2)$^{1/6}$ |

Table S1: Table of parameters for WCA potential for good and poor solvent conditions.

The interaction between the particles and wall is given by the LJ potential,

$$V_{ij}^{LJ} = \begin{cases} 
4\epsilon_{ij} \left[ \left( \frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left( \frac{\sigma_{ij}}{r_{ij}} \right)^{6} \right] & r < r_c \\
0 & r \geq r_c 
\end{cases}$$

In case of repulsive confining wall, cutoff $r_c = 1.0$ is used and for the attractive confining wall $r_c = 2.5$ is used while $\sigma = 1.0$ is used in both the cases.

### S2 Effect of solvent condition on the fraction of adsorbed monomers

#### Figure S1: The fraction of adsorbed monomers on the surface of the confining sphere in (a) good solvent condition for $\epsilon_{mw} = 1.0, 5.0, 10.0, 20.0$ (b) poor solvent condition for $\epsilon_{mw} = 1.0, 5.0, 10.0, 20.0$
S3  Radial distribution function for low and high crowder density

Figure S2: The pair radial distribution function for $\phi_T = 0.05$ and $\phi_T = 0.35$ for $\epsilon_{mw} = 20.0$. For lower volume fraction value $\phi_T = 0.05$, the plot suggests less order while for the higher volume fraction $\phi_T = 0.35$, $g(r)$ shows many peaks indicating more order in the system.

S4  Average number of neighbours

Figure S3: Average number of neighbours for $\epsilon_{mw} = 20.0$ (a) for $\phi_T = 0.05$ and (b) for $\phi_T = 0.40$.

The average number of neighbours for higher density ($\phi_T = 0.40$) system is about 6 which is higher than that of lower density system ($\phi_T = 0.05$). This suggests that polymer is more ordered in higher density system than lower density system.
S5  Contact maps as a function of attractive wall strength

(a)

(b)

Figure S4: For poor solvent condition and \( \phi_T = 0.35 \) (a) the snapshots of the system for different \( \epsilon_{mw} \) and (b) the corresponding contact maps.

S6  Radius of gyration of polymer in bad solvent condition confined within sphere with attractive wall

Figure S5: Radius of gyration \( R_g \) of the polymer vs volume fraction \( \phi_T \) in poor solvent condition confined in a sphere with attractive wall for different wall attractive strength.

We see that for low attractive strength \( \epsilon_{mw} = 1.0 \), the radius of gyration remains almost constant with volume fraction \( \phi_T \), while for higher strength values (\( \epsilon_{mw} = 20.0 \))
5.0, 10.0, 20.0) the radius of gyration drops with $\phi_T$.

**S7 Effect of curvature on the conformation of polymer in bad solvent condition**

![Figure S6: The density function of the monomers in poor solvent condition confined within attractive walls. (a) for the sphere of radius $R = 15.0$ (b) for the sphere of radius $R = 30.0$.](image)

In order to understand the effect of the curvature on the conformation, we simulated the system of polymer of same length in a sphere with larger radius $R = 30.0$ with the total volume fraction from 0.05 to 0.45 for $\epsilon_{mw} = 10.0$. It is seen that increasing the radius of the sphere leads to the higher fraction of adsorption in the monomers. The density function describes normalized number of particles at a certain distance $R$ from the center of the confinement. The density function plots for monomers indicate that for the system with $R = 15.0$ and $\phi_T = 0.05$, there are two layers of monomer while increasing the $\phi_T$ to 0.30 leads to multiple peaks (see Figure S6(a)) which is an indication of beginning of collapse of the polymer to a globular conformation. In case of system with larger radius $R = 30$ and for $\phi_T = 0.05$, all the monomers are adsorbed on the surface while increase in $\phi_T$ value to 0.30, some of the monomers come on top of the monomer layer which is indicated by the second peak in the density function plot (see Figure S6(b)).