

Random heteropolymer adsorption on disordered multifunctional surfaces: Effect of specific intersegment interactions

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Biopolymers adsorb on cell and virus surfaces with great specificity. Recently, theoretical and computational studies have inquired as to whether there are any universal design strategies that nature employs in order to affect such recognition. Specifically, the efficacy of multifunctionality and quenched disorder as essential design strategies has been explored. It has been found that when random heteropolymers interact with disordered multifunctional surfaces, a sharp transition from weak to strong adsorption occurs when the statistics characterizing the sequence and surface site distributions are related in a special way. The aforementioned studies consider the intersegment interactions to be much weaker than the surface site interactions. In this work we use nondynamic ensemble growth Monte Carlo simulations to study the effect of the competition between frustrating intersegment and segment-surface interactions. We find that as the intersegment interactions become stronger, the transition from weak to strong adsorption occurs at higher surface disorder strengths. This trend is reversed beyond a threshold strength of the intersegment interactions because interactions with the surface are no longer able to “unravel” the dominant conformations favored by the intersegment interactions. © 1998 American Institute of Physics.

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I. INTRODUCTION

Random heteropolymers (RHPs) are polymers with chemically different monomer units distributed along the backbone in a disordered sequence. They are used in technological applications, and also serve as coarse grained models for proteins,¹⁻⁹ since they exhibit a phase transition akin to protein folding. RHPs are a class of quenched disordered materials since the disordered sequence distribution cannot change in response to changes in the environment without chain cleavage occurring. This quenched disorder, along with chain connectivity and competing interactions (between the different types of monomers and/or between the monomers and the environment) make RHPs quintessential examples of a frustrated system. Frustration is the origin of many of the interesting properties exhibited by these materials.

The physics of RHPs has been considered in many contexts in recent years. For example, their phase behavior in the molten state,¹⁰⁻¹³ freezing transitions in the compact state,^{1-3,5,8,13-15} adsorption onto homogeneous surfaces,¹⁶⁻²⁰ behavior at interfaces,²¹⁻²⁴ “folding” kinetics,²⁵⁻²⁸ and their behavior in three-dimensional disordered media²⁹⁻³¹ have been studied.

Recently, our laboratory has considered the adsorption

of RHPs onto multifunctional disordered surfaces.³²⁻³⁵ Proteins and other biopolymers (which carry a specific pattern encoded in their sequence distribution) recognize cell and virus surfaces bearing specific patterns.³⁶⁻⁴⁰ The hallmark of recognition is a sharp discrimination between surfaces onto which the chain molecules adsorb strongly, and those onto which they do not adsorb. RHPs also carry a pattern encoded in their sequence distribution; however, unlike proteins, the sequence distribution, and hence the pattern, is only described statistically. Similarly, surfaces with multiple types of sites can also carry a statistical pattern. Our work on RHP adsorption onto disordered multifunctional surfaces has been motivated by the following question: is a sharp adsorption transition that mimics recognition possible if the statistics characterizing the sequence and surface site distributions are related in a particular way? In other words, is matching statistics sufficient to mimic recognition? Issues pertinent to pattern matching have also been considered recently by Muthukumar.⁴¹

Using replica field theory,³² a simple physical model,³⁴ and Monte Carlo (MC) simulations,^{33,35} Chakraborty and co-workers have found that a sharp adsorption transition from weak to strong adsorption occurs when the statistics characterizing the sequence and surface site distributions are related in a special way. Therefore, by appropriate choice of the statistics characterizing the surface site distribution, one may discriminate between chains bearing different statistical

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patterns.³³ Such a phenomenon can perhaps be profitably exploited in a range of applications including the development of sensors, chromatographic materials,³⁷ and viral inhibition agents.^{39,40} This motivates further work exploring this phenomenon.

In the previous studies noted above, the bare intersegment interactions were either absent or taken to be merely nonspecific excluded volume interactions. In this paper, we employ MC simulations to study the effects of specific and competitive intersegment interactions on the phenomenon of recognition between RHPs and multifunctional surfaces due to statistical pattern matching. We model RHPs made up of two types of units (*A* and *B*). We study the adsorption of such RHPs from an infinitely dilute solution onto a surface functionalized with two kinds of sites. One kind of surface site interacts more favorably with the *A* segments and the other kind with the *B* segments. Like segments also interact with each other more favorably than with segments of the other type. Our simulations show that the inclusion of distinct types of intersegment interactions enriches the picture described in earlier efforts.^{32–35} Competition between the frustrating intersegment interactions and the segment–surface interactions leads to some phenomena that may, at first, appear to be counterintuitive. We find that as the intersegment interactions become stronger, the transition from weak to strong adsorption occurs at higher surface disorder strengths. This trend is reversed beyond a threshold strength of the intersegment interactions because interactions with the surface are no longer able to “unravel” the dominant conformations favored by the intersegment interactions.

This paper is organized as follows. In Sec. II we describe our simulation method and the model that we have simulated. In Sec. III we analyze and discuss our main results. Some concluding remarks are offered in Sec. IV.

II. MODEL DESCRIPTION AND MC SIMULATIONS

Our simulations are carried out on a cubic lattice using the ensemble growth MC method developed originally by Higgs and Orland.⁴² Our adaptation of this method to study RHPs near disordered manifolds has been described elsewhere in detail.^{35,43} M monomers are randomly placed on the lattice according to Boltzmann statistics. We perform $6M$ attempts at adding *A*- or *B*-type segments (dictated by the chosen sequence). M dimers are then chosen according to Boltzmann probabilities. The potential energy is determined by intersegment interactions and by interactions of the segments with sites on the disordered surface. This process is continued until M chains with the desired length N are obtained. For $M \gg N$, a canonical distribution results⁴² and properties can be calculated as nonweighted averages over the ensemble. Typical values of M and N in our simulations are $M = 66\,000$ and $N = 32$.

Many populations of the same sequence are simulated for improved statistical accuracy, and the same procedure is then repeated for several realizations of the sequence distribution. The average over different realizations of the surface sites is done analytically, and the pre-averaged Hamiltonian is used in the simulations. In doing so, we treat the surface disorder as annealed. The surface disorder is assumed to cor-

respond to a Gaussian process with zero mean and variance $\sigma^2 = \langle (\beta u)^2 \rangle$, where u denotes local segment–surface potential.³² The variance in the segment–surface potential equals the square of the segment–site interaction, u_1 , times the variance in the number of surface sites in the area occupied by an adsorbed segment, $\langle (\delta n)^2 \rangle$. For uncorrelated disorder, $\langle (\delta n)^2 \rangle$ equals the surface loading defined as the average number of sites, $\langle n \rangle$, per segment area, l^2 . The dimensionless quantity, σ^2 , is therefore a direct measure of the surface loading, $\langle n \rangle$. Averages over quenched disorder have been shown to be equivalent to those obtained in the annealed case if the surface is sufficiently large and observation times are long.^{44–46} A large surface can be divided into many subsurfaces, each of them being larger than any relevant correlation length in the problem. A sufficiently mobile polymer will visit the subsurfaces, each having a different configuration of the disorder, within a time scale over which averages are made. Thus, for sufficiently large surfaces and long observation times, the quenched and annealed averages over the external disorder are equivalent. Carrying out the average of the site disorder in our simulations explicitly for sufficiently large surfaces gave statistically equivalent results as using the preaveraged Hamiltonian.^{34,35} Notice that the above arguments do not make the quenched and annealed averages equivalent when the disorder is carried by the fluid whose statistical properties are of interest (i.e., the RHP chains).

The statistics of the RHP sequence distribution may be described by the average composition, f , and by λ , a measure of the strength of correlations characterizing the sequence distribution.⁴⁷ Positive values of λ correspond to statistically blocky sequences (runs of like segments occur with high probability within a certain correlation length), while negative values of λ correspond to statistically alternating type sequences. In previous work, we have shown how these statistical measures of pattern can be manipulated to discriminate between different statistical patterns. In this work, however, our purpose is to study the effects of the interplay between the frustrating intersegment and segment–surface interactions. In order to focus on the essential physics, we study the adsorption of RHPs with fixed statistics ($f = 1/2$ and $\lambda = 0$) onto surfaces with different statistics. Specifically, again with a view toward studying the essential physics, we consider surfaces with the distribution of different types of sites being described by short-ranged correlations. Thus the total number density of sites per unit area (the loading) is the only measure of the statistics for surfaces with symmetric compositions. The surface sites are such that one type of site interacts more favorably with the *A*-type segments, while the other type of site interacts more favorably with the *B*-type segments. Both the surface–segment and intersegment interactions are taken to be short-ranged. The intersegment interactions are of three types: V_{AA} , V_{BB} , and V_{AB} , where V_{IJ} is the interaction potential between *I*-type and *J*-type segments when the two segments occupy adjacent lattice sites, and are zero otherwise. These interaction strengths can be grouped into two physically relevant parameters; nonspecific excluded volume interactions, $v_0 = (V_{AA} + V_{BB} + 2V_{AB})/2$, and specific intersegment interactions that

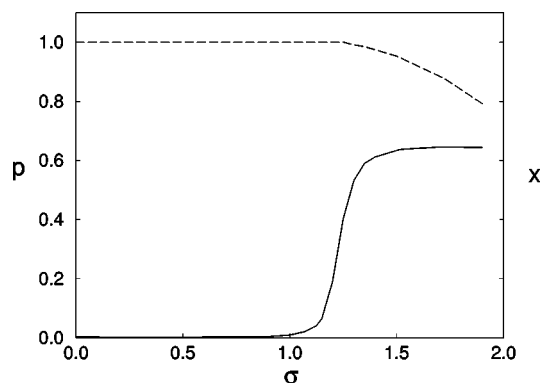


FIG. 1. Adsorbed fraction, \bar{p} (solid line), and order parameter x (dashed line) as a function of surface loading, σ , for a RHP with weak specific intersegment interactions ($b = -0.5$).

favor segregation of the two types of segments, $b = (V_{AA} + V_{BB} - 2V_{AB})/2$. We choose $V_{AA} = V_{BB} = -V_{AB}$ such that $b < 0$, which is tantamount to the Flory parameter, χ_F , being greater than zero and encourages segregation of like segments in absence of the surface.

In previous studies of RHP adsorption onto statistically patterned surfaces^{32–35} it has been observed that when the sequence and surface site distribution statistics are related in a special way, a sharp adsorption transition occurs which is accompanied by the thermodynamics being determined by only a few dominant conformations. Thus, in our simulations, we monitor a quantity, $x = 1 - \sum_i P_i^2$, where P_i is the probability of occurrence of a particular conformation. When a multitude of conformations are sampled, the probability, P_i , for each conformation is small and x asymptotically approaches unity. When the chains spend significant fractions of time in a few dominant conformations, however, the corresponding probabilities squared, P_i^2 , are no more negligible and the parameter x acquires values below unity. We present our simulation results by plotting the adsorbed fraction \bar{p} , and the order parameter x , as a function of surface loading measured in terms of the dimensionless parameter σ for various values of the strength of intersegment interactions, b .

III. RESULTS AND DISCUSSION

Figure 1 shows simulation results for a case with relatively weak intersegment interactions. As in earlier studies, we find that a smooth transition to weak adsorption occurs when the loading is sufficient to overcome the entropic penalty for adsorption. This resembles homopolymer adsorption. x is asymptotically unity at this stage; i.e., the chains sample a multitude of adsorbed conformations. Figure 1 shows that, beyond a threshold value of σ , a sharp transition from weak to strong adsorption occurs accompanied by the chains freezing into a few dominant adsorbed conformations. The physical reason for this type of phenomenon occurring when RHPs interact with disordered multifunctional surfaces has been pointed out before,³² and is as follows. When the site density is low, it is very easy for the chains to avoid unfavorable interactions, and there are many conformations with roughly the same adsorption energy gain. Thus, the chains

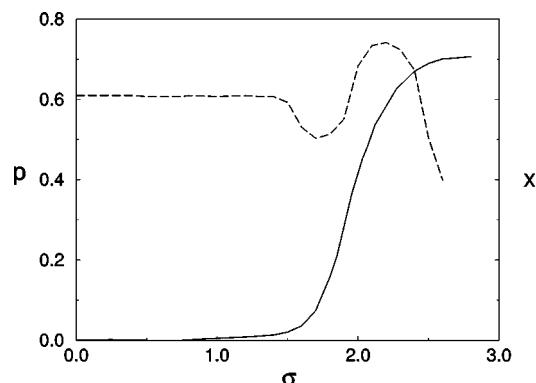


FIG. 2. Adsorbed fraction, \bar{p} (solid line), and order parameter x (dashed line) as a function of surface loading, σ , for a RHP with strong specific intersegment interactions ($b = -4$).

sample these many conformations to minimize the free energy. As the loading increases, it becomes increasingly difficult to avoid unfavorable interactions because of chain connectivity and the disordered sequence and site distributions. Beyond a threshold loading, most adsorbed conformations experience many unfavorable interactions with the surface. However, there are a few adsorbed conformations for which unfavorable interactions with the surface are minimized and favorable ones are maximized. These few conformations are energetically far more favorable than all other conformations. At this stage, the continuous energy spectrum of most conformations is separated by a gap from the energetically much lower pattern-matched conformations. When the gap is much larger than the thermal energy, the chains give up the entropic advantage of sampling many conformations and adopt these few entropically favored ones. Consistent with this picture, Fig. 1 shows that the sharp adsorption transition is accompanied by the thermodynamics being determined by a few dominant adsorbed conformations (i.e., $x < 1$). Increasing the ensemble we sample does not change this behavior.

Figure 2 shows results for a relatively large value of $|b|$; i.e., a RHP with strong specific intersegment interactions. Even before adsorption occurs, $x < 1$. This indicates that for sufficiently large values of $|b|$ the polymer is already “frozen” in a few dominant conformations before it adsorbs on the surface. This is akin to the adsorption of a folded protein from solution. The adsorbed fraction curve displays the same qualitative features as the previous case except that the transition occurs at higher surface loadings. Physically, this is so because stronger specific intersegment interactions lead to RHPs being in lower energy states in solution compared to cases wherein intersegment interactions are weak. Thus, compared to cases where $|b|$ is smaller, stronger (more favorable) segment–surface interactions are required for strong adsorption to become favorable. Interesting physics is revealed by the curve showing the variation of x in Fig. 2. The few conformations that are adopted in solution (i.e., before adsorption occurs) are dictated by the nature of the intersegment interactions and the sequence statistics. As the loading is increased beyond the point where a continuous transition to weak adsorption occurs, x decreases even further. This is so because even though the polymers are essentially in the

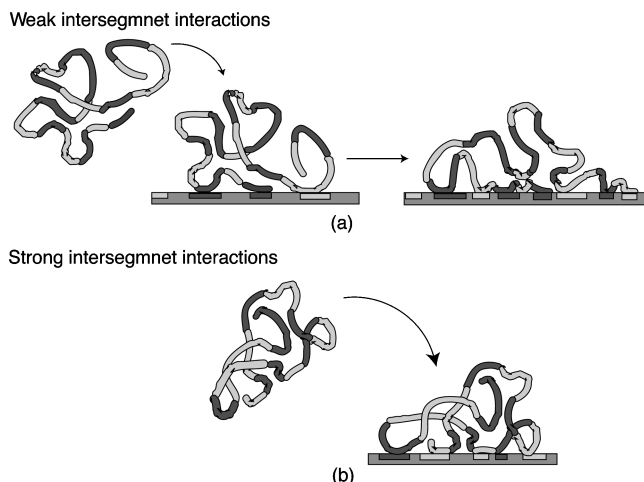


FIG. 3. Schematic depiction of the behavior of a RHP as it adsorbs on the disordered surface. (a) RHP with intermediate intersegment interaction strengths. While in solution the RHP is frozen into a few conformations that are determined by the intersegment interactions. Once adsorbed, the interactions with the surface are sufficient to “unravel” the RHP and cause it to “refold” into conformations determined by the surface–segment interactions. (b) RHP with very strong intersegment interactions. The RHP “folds” into a few conformations while in solution. At these interaction strengths, the interactions with the surface are not sufficient to unravel the RHP, and it remains in conformations determined by the intersegment interactions.

same frozen conformations as in solution, adsorption to the surface eliminates a few more conformations from being sampled. When the density of sites on the surface is increased such that a sharp adsorption transition from weak to strong adsorption occurs, we find that x first increases and then decreases. This is due to the following physical reason. As the segment–surface interactions increase in strength (due to a higher density of surface sites), they compete favorably with the intersegment interactions. Thus, the energetic advantage associated with adopting the few dominant conformations favored by the intersegment interactions is no longer large. Thus, the polymers sample other conformations in order to gain entropy and thereby reduce free energy. In other words, the few dominant chain conformations favored by the intersegment interactions “unravel” due to interactions with the surface. As the strength of the surface sites increases further, interactions with the surface dominate, and the chains adopt a few dominant adsorbed conformations favored by segment–surface interactions (i.e., the segment and surface site distribution statistics), which leads to a reduction in x . The above physical picture is made vivid in Fig. 3.

Our simulation results show another interesting feature when the strength of intersegment interactions is increased further beyond the value of $|b|$ corresponding to the situation depicted in Fig. 2. We illustrate this by presenting our results in the form of Fig. 4. Specifically, we plot the strength of the surface disorder at which the transition from weak to strong adsorption takes place as a function of the strength of specific intersegment interactions. The region below the curve corresponds to weak adsorption, and the parameter space above the curve corresponds to strong adsorption. As the strength of the intersegment interactions increases, at first,

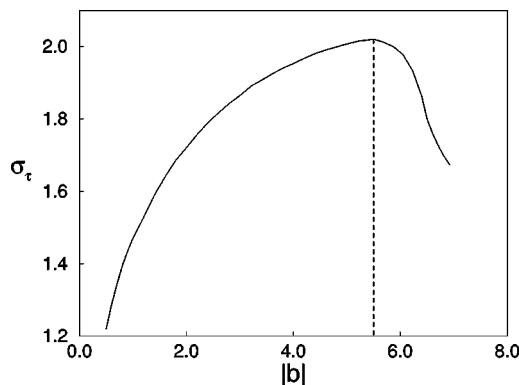


FIG. 4. Adsorption phase diagram of RHPs with specific intersegment interactions. The value of the surface loading (σ_τ) at the sharp transition is plotted as a function of the magnitude of intersegment interactions ($|b|$). Below the curve the RHP is weakly adsorbed to the surface; above the curve it is strongly adsorbed. The dashed line represents the threshold value of b above which the trend of increasing σ_τ with $|b|$ is reversed due to reasons described in the text.

the strength of the surface disorder required for the adsorption transition to take place also increases (also illustrated in Figs. 1 and 2, and discussed earlier). However, we find that beyond a threshold value of $|b|$ (indicated by the dashed line), this trend is reversed. The physical reason for this non-monotonic behavior is the following. For values of $|b|$ that are larger than that corresponding to the dashed line, the RHP in solution is in a very low entropy state as it adopts only a few dominant conformations. The entropy difference between the non-adsorbed state and the adsorbed state is thus small, and decreases even further with increasing values of $|b|$. Therefore, at these high values of specific intersegment interactions, the entropy penalty for adsorption is small, and the RHP undergoes the sharp transition to strong adsorption more and more readily with increasing magnitude of b . However, for these large values of $|b|$, the interactions with the surface are not sufficient to “unravel” the RHP, and it remains essentially in conformations determined by the specific intersegment interactions. The condition for statistical pattern matching is different in character for RHPs with very strong intersegment interactions. This is so because now only the surface of the few frozen conformations in solution are exposed to the disordered surface. This issue needs to be explored further for statistical patterns that are interesting, as has been done for RHPs with weak intersegment interactions. Differences in the dynamics characterizing the adsorption transition for RHPs with weak and strong intersegment interactions would also be intriguing to examine.

IV. CONCLUDING REMARKS

We have carried out nondynamic ensemble growth Monte Carlo simulations in order to study the effects of distinct intersegment interactions on the adsorption of random heteropolymers near a disordered surface that is functionalized with two types of sites. It has been found that when a threshold density of surface sites is reached, the heteropolymer undergoes a sharp transition from weak to strong adsorption. When the intersegment interactions are relatively

weak, we find that the threshold loading increases with increasing intersegment interaction strengths. This is because a chain with stronger intersegment interactions is at a lower energy state and thus stronger interactions with the surface are needed for strong adsorption to become favorable. However, this trend is reversed when the intersegment interactions become stronger than a threshold value. The reason is that the entropy penalty due to adsorption is very small since the heteropolymer with very strong intersegment interactions already exists in a very low entropic state in solution (i.e., in only a few dominant conformations).

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