Adsorption-Freezing Transition for Random Heteropolymers near Disordered 2D Manifolds due to "Pattern Matching"

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We study the simplest model for random heteropolymers near chemically disordered surfaces, and predict a new phenomenon that may have implications for pattern recognition applications. As the strength of surface fluctuations increases a smooth adsorption transition occurs first, with a multitude of chain conformations being sampled. More interestingly, beyond a larger threshold value of the strength of surface fluctuations, a sharp second adsorption transition is observed that is accompanied by the polymer freezing into a few dominant conformations that match the pattern of the surface fluctuations. [S0031-9007(96)01346-4]

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Random heteropolymers (RHPs) are an interesting class of soft matter where a quenched disorder (the sequence distribution) is *carried* by the fluid of interest. In recent years, it has also been recognized that RHPs are the simplest physical models of proteins (e.g., [1–3]). This has sparked enormous interest in the behavior of RHPs (e.g., [4–8]).

One motivation for the study of RHPs in the vicinity of disordered 2D surfaces is provided by biosensor and pattern recognition applications. RHPs (and real biomolecules) carry a pattern encoded in their sequence distribution. A properly chosen randomly functionalized surface may be able to "recognize" this information on the RHP and adsorb it strongly.

In spite of these interesting applications and possibilities, the behavior of RHPs near disordered 2D manifolds has never been studied. The physics of homopolymers [9,10] and RHPs [11,12] in 3D random media have been considered before. Studies of RHP adsorption to homogeneous surfaces [6,7], homopolymer adsorption to disordered [13] and ordered patterned surfaces [14] have also been reported. In this Letter, we study the simplest model for RHPs near disordered surfaces. Specifically, we imagine that in the absence of the surface the RHP is a Gaussian chain. The surface is considered to be made up of randomly placed sites which have distinctly different interactions with chemically different segments (see Fig. 1). We consider the bare RHP to be Gaussian for simplicity, and find a hitherto unknown phenomenon pertinent to pattern recognition that seems consistent with recent experiments [15].

The physical situation described above corresponds to the following Hamiltonian:

$$-\beta H = -\frac{3}{2l}\int_0^N dn\left(\frac{d\mathbf{r}}{dn}\right)^2 - \int_0^N dn \int d\mathbf{r} \times k(\mathbf{r})\delta(\mathbf{r}(n) - \mathbf{r})\theta(n)\delta(z), \qquad (1)$$

where $\mathbf{r}(n)$ represents chain conformation, l is the usual statistical segment length, $k(\mathbf{r})$ is the strength of interactions with surface sites, and the factor $\delta(z)$ ensures that these sites live on a 2D surface. $\theta(n)$ represents the identity of the chain segment at position n. For a RHP made up of only two kinds of units ($\theta = \pm 1$), Eq. (1) is written in a manner such that a given surface site that is attractive to one type of segment imposes a repulsive potential of equal strength on segments of the other type. A corresponding physical system is a polyampholyte (in a salt solution that renders all interactions short ranged) interacting with a solid surface that is made up of randomly located positively and negatively charged sites. Such surfaces can be prepared [16].

Since the surface is disordered, $k(\mathbf{r})$ is a fluctuating quantity. For simplicity, we consider the surface to be overall neutral, and take the fluctuations in k to be described by a Gaussian process with short-ranged correlations (variance $= \sigma_1^2$).

In order to proceed, we must average over the quenched sequence distribution and the surface fluctuations.

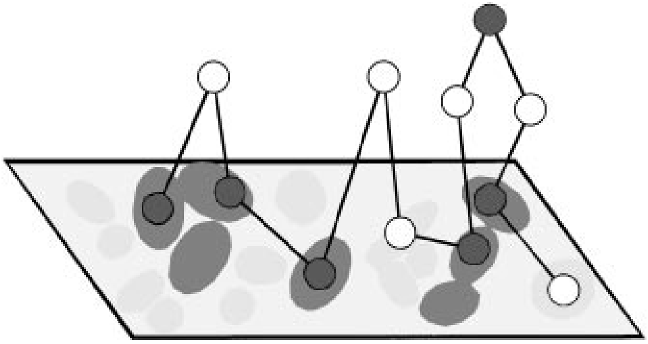

FIG. 1. Schematic representation of the physical system. The sites shaded gray attract the white segments and repel the black segments. The black sites attract the black segments and repel the white segments.

Consider the latter issue first. If the sites on the surface can anneal in response to the presence of the RHP, then the partition function is self-averaging with respect to fluctuations in $k(\mathbf{r})$. If the external disorder fluctuations are quenched, then the partition function is self-averaging only under restricted conditions that have been elaborated extensively (eg., [17–20]). Our model applies under all conditions to annealed surface randomness (can be realized experimentally), and to quenched surface randomness when the conditions noted in [17–20] are met. Following Feynman [21], the Boltzmann factor after averaging over the surface disorder is thus written as

$$\exp[-\beta H_{\mathrm{dis}}] = \iint Dk(\mathbf{r}) \exp\left[-\frac{1}{2\sigma_1^2}\int d\mathbf{r}\int d\mathbf{r}'\, k(\mathbf{r})\delta(\mathbf{r}-\mathbf{r}')k(\mathbf{r}')\delta(z)\delta(z')\right] \times \exp\left[-\frac{3}{2l}\int_0^N dn\left(\frac{d\mathbf{r}}{dn}\right)^2 - \int dn\int d\mathbf{r}\, k(\mathbf{r})\delta(\mathbf{r}(n)-\mathbf{r})\theta(n)\delta(z)\right]. \tag{2}$$

The partition function is not self-averaging with respect to the quenched sequence fluctuations, and we use replica methods [22] to carry out this average. We consider the sequence fluctuations to be Gaussian with mean equal to $2f - 1$ and variance σ_2^2; f is the average composition which we take to be $1/2$ for simplicity. Using a Gaussian process rather than a lattice gas distribution does not affect the qualitative physics [23], and generalizes our results to RHPs with more than two kinds of monomers.

If we define an order parameter, $Q_{\alpha\beta}(\mathbf{r},\mathbf{r}')$, that measures the conformational overlap *on the surface* between replicas in the following manner,

$$Q_{\alpha\beta}(\mathbf{r},\mathbf{r}') = \int dn\, \delta(\mathbf{r}_\alpha(n) - \mathbf{r}) \times \delta(\mathbf{r}_\beta(n) - \mathbf{r}')\delta(z)\delta(z'), \tag{3}$$

the m-replica partition function after averaging over the sequence fluctuations can be written as a functional integral over the overlap order parameter fields as follows:

$$\langle G^m\rangle = \iint DQ_{\alpha\beta} \exp(-E[Q_{\alpha\beta}] + S[Q_{\alpha\beta}]), \tag{4}$$

where

$$E = -\ln\prod_{\alpha=1}^{m}\iint Dk_\alpha(\mathbf{r}) \times \exp\left[-\frac{1}{2}\int d\mathbf{r}\int d\mathbf{r}'\, k_\alpha(\mathbf{r})P_{\alpha\beta}(\mathbf{r},\mathbf{r}')k_\beta(\mathbf{r}')\right], \tag{5}$$

$$S = \ln\prod_{\alpha=1}^{m}\iint D\mathbf{r}_\alpha(n)\exp\left[-\frac{3}{2l}\sum_{\alpha=1}^{m}\int dn\left(\frac{d\mathbf{r}_\alpha}{dn}\right)^2\right] \times \delta\left[Q_{\alpha\beta}(\mathbf{r},\mathbf{r}') - \int dn\,\delta(\mathbf{r}_\alpha(n)-\mathbf{r}) \times \delta(\mathbf{r}_\beta(n)-\mathbf{r}')\right], \tag{6}$$

and

$$P_{\alpha\beta}(\mathbf{r},\mathbf{r}') = \frac{\delta(\mathbf{r}-\mathbf{r}')\delta_{\alpha,\beta}}{\sigma_1^2}\delta(z)\delta(z') - \sigma_2^2 Q_{\alpha\beta}(\mathbf{r},\mathbf{r}'). \tag{7}$$

The quantity E is the effective energy for a given overlap order parameter. S is the entropy, as it is the logarithm of the number of ways in which the replicas can arrange themselves in 3D space with the constraint that the overlap between replicas on the 2D surface is $Q_{\alpha\beta}$.

RHPs in 3D exhibit thermodynamics similar to the random energy model (REM) or the Potts glass with a large number of discrete states [2,5]. Thus, under certain circumstances, the thermodynamics of RHPs is determined by a few dominant conformations that are energetically very favorable rather than the usual situation where an infinitude of conformations is sampled. Within the framework of replica calculations the formation of such phases is signaled by replica symmetry breaking (RSB) [5,11,23], and, as in the REM, one step of the hierarchical Parisi scheme [22] proves to be sufficient [5]. Recent simulation studies [12] lend strong support to the use of one-step RSB calculations for studying the qualitative behavior of RHPs in 3D, and here we devise such a mean-field theory. This is a reasonable first approximation (and reveals exciting physics) even though the present problem has both 2D and 3D aspects.

We divide replicas into groups. Replicas within a group have perfect overlap *on the surface*, and replicas in different groups have no surface overlaps. With this RSB scheme, following Mezard and Parisi [24], the energy per segment after taking the replica limit is evaluated by computing the Gaussian functional integral in Eq. (5) to yield

$$\begin{aligned} E &= \frac{1}{2}\left[-\ln\sigma_1^2 + \frac{1}{x_0}\ln(1 - C_1\overline{p}x_0)\right], \\ \overline{p} &= p/N, \\ C_1 &= \sigma_1^2\sigma_2^2 N/A, \end{aligned} \tag{8}$$

where p is the number of contacts with the surface, x_0 is the number of replicas in a group, and A is the surface area of the solid.

To obtain the entropy [Eq. (6)], we first need to compute the number of ways in which x_0 replicas can be arranged such that they overlap perfectly on the surface. In the long chain limit we ignore tails and allow for the formation of loops and trains only. Let $f_{ni}(\mathbf{r}_\| - \mathbf{r}'_\|)$ be the probability that a loop of length ni (range, 1 to N) starts at $\mathbf{r}_\|$ on the surface and ends at $\mathbf{r}'_\|$. The restricted partition function (Z) for x_0 replicas in the same group is then

$$Z(\mathbf{r}_1^{\|}) = \sum_{n1,n2,\ldots,np} \int d\mathbf{r}_2^{\|} \cdots \int d\mathbf{r}_p^{\|} f_{n1}^{x_0}(\mathbf{r}_2^{\|} - \mathbf{r}_1^{\|}) \cdots \times f_{np}^{x_0}(\mathbf{r}_p^{\|} - \mathbf{r}_{p-1}^{\|}) \times \delta(n1 + n2 + \cdots + np - N). \qquad (9)$$

The entropy of x_0 replicas in a group is obtained by integrating Z over all positions $\mathbf{r}_1^{\|}$, and then taking the logarithm. We define a Laplace transform conjugate to N, and a Fourier transform corresponding to the 2D coordinates on the surface. Taking advantage of the convolution theorem, we can write the Fourier-Laplace transform of Eq. (9) to be

$$Z(\mathbf{k}, \lambda) = \left[\sum_{n=1}^{N} f_n^{x_0}(\mathbf{k}) e^{-\lambda n}\right]^p, \qquad (10)$$

where $\mathbf{k}$ and λ are the Fourier and Laplace variables, respectively.

We take the functions f_n to be of two types. The form of f_1 that we use is that employed by Hoeve *et al.* [25]; viz.,

$$f_1(r) = \omega \delta(r - l), \qquad (11)$$

where ω is the partition function for one adsorbed segment, and is a constant that depends upon specific chain properties. Since in our simple model the RHP is Gaussian in the absence of the surface, f_n for longer loop lengths is given by

$$f_n(r) = \frac{C}{n^{3/2}} \exp\left[-\frac{r^2}{2nl^2}\right]. \qquad (12)$$

C is a normalization constant that measures chain stiffness.

We now substitute the Fourier transforms of Eqs. (11) and (12) into Eq. (10), integrate over all $\mathbf{r}_1^{\|}$, and invert the Fourier and Laplace transforms. [In the long chain limit, we replace the sum in Eq. (10) by an integral.] Taking the logarithm of the result and noting that there are m/x_0 groups of replicas, the entropy corresponding to Eq. (6) is computed. Combining this result with Eq. (8) obtains the free energy density (F) to be

$$F = \frac{1}{2}\left[-\ln\sigma_1^2 + \frac{1}{x_0}\ln(1 - C_1\overline{p}x_0)\right] + \frac{D\overline{p^3}}{6} - \frac{1}{x_0 N}\ln\left[\sum_{q=0}^{\overline{p}N}\binom{\overline{p}N}{q}\left(\frac{2\pi l^2}{3x_0}\right)^q C^{qx_0}\omega^{(\overline{p}N-q)x_0)}\frac{\Gamma^q((4-3x_0)/2)}{\Gamma(q(4-3x_0)/2)} \times [N - (\overline{p}N - q)]^{[(4-3x_0)/2]q-1}\right], \qquad (13)$$

where Γ is the gamma function, and we have also added nonspecific three-body repulsions on the surface (proportional to D) which may be necessary for stability when $\overline{p}$ is large. The first two terms in Eq. (13) represent energetic contributions, and the last term is a measure of entropy. We extremize Eq. (13) with respect to the order parameters $\overline{p}$ and x_0 for a mean-field solution.

The order parameter $\overline{p}$ is simply the fraction of adsorbed segments. The order parameter x_0 has been interpreted to be $(1 - \sum_i P_i^2)$, where P_i is the probability associated with conformation, i [11,22,23]. Thus, when x_0 is unity, the RHP samples a multitude of conformations. Values of x_0 less than unity signal the formation of a frozen phase where the thermodynamics is determined by a few dominant adsorbed conformations. We shall now fix all chain parameters (l, C, ω, etc.), and study adsorption (by following $\overline{p}$) and freezing (by following x_0) as a function of C_1. C_1 is the strength of the surface fluctuations, and in our simple model it measures the total density of surface sites shown in Fig. 1. Physically, C_1 can be adjusted by changing the total number of sites on the surface (e.g., by preparing surfaces as in [15] by adsorption from solutions of different concentrations).

$C_1 = 0$ implies a uniform neutral surface, and so neither chain adsorption nor freezing (on the 2D plane) into a few conformations can occur ($\overline{p} = 0, x_0 = 1$). Above some value of C_1, Fig. 2 shows that some adsorption occurs with a multitude of adsorbed conformations being sampled ($x_0 = 1$). At this point there are a sufficient number of sites that are attractive to the different types of RHP segments to overcome the entropic penalty for adsorption, and a smooth adsorption transition occurs. Since the number of sites is still small it is easy to avoid unfavorable interactions, and there are many different conformations that the RHP can adopt that lead to roughly the same energetic advantages due to interactions with attractive sites. This resembles homopolymer adsorption. At this stage, the energetic advantage due to favorable

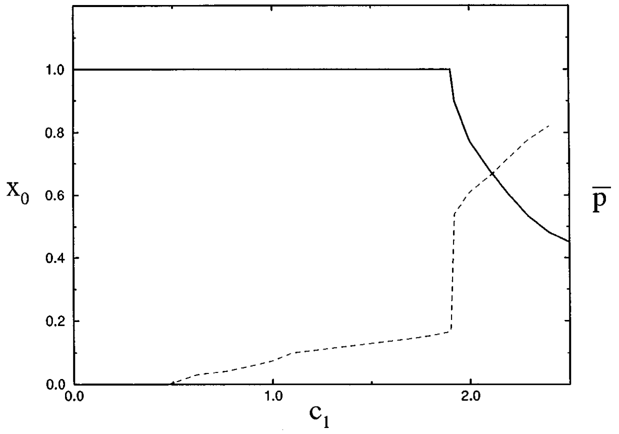

FIG. 2. x_0 (solid line) and $\overline{p}$ (dashed line) as a function of C_1. The values of the other parameters are fixed at $\omega = 0.5$, $l = 1$, $D = 20$, and $C = 0.01$.

interactions with surface sites is balanced by the entropic term in Eq. (13); this prevents all segments of a given type to adsorb on one favorable site.

As C_1 increases further, Fig. 2 shows an exciting heteropolymeric effect. Beyond a threshold value of C_1, we find a sharp transition where two things happen: x_0 becomes less than unity signaling the formation of a few dominant adsorbed conformations, and the fraction of adsorbed segments increases sharply. Both the freezing and the dramatic increase in adsorbed fraction are first order transitions, and have a simple physical explanation.

As C_1 increases, the number of sites on the surface that attract and repel segments of different types increases. The parameter C_1 scales as $1/d^2$ and $\overline{p}$ scales as L_{train}^2; d is the average distance between sites and L_{train} is the average length of adsorbed trains on the surface. Clearly, when L_{train} becomes of the order of d ($C_1\overline{p} \rightarrow 1$) it becomes very difficult to avoid unfavorable interactions. In other words, due to competing interactions and the random site and sequence distributions, as the surface loading increases it becomes increasingly difficult to avoid unfavorable interactions. When the above condition is realized, most adsorbed conformations have relatively high energy. However, there are a few adsorbed conformations that match the pattern of the sites on the disordered surface. By pattern matching we mean a registry between RHP segments and the corresponding attractive sites. These few pattern-matched conformations are energetically much more favorable than all others once $C_1\overline{p} \rightarrow 1$. Thus, the RHP sacrifices the entropic advantage of sampling many adsorbed conformations and adopts the few pattern-matched ones when the aforementioned condition is realized. These pattern-matched conformations adsorb strongly (large $\overline{p}$). Consistent with this physical argument, our equations and numerical results show that the adsorption-freezing transition occurs when $C_1\overline{p} \rightarrow 1$. We also find that there are two free energy extrema with respect to $\overline{p}$ on both sides of the transition, one corresponding to the replica symmetric (RS) solution of our equations and the other to a RSB solution. Before the transition the RS solution is the global extremum, and crossover to the RSB extremum being global occurs at the transition. We expect this result to be qualitatively correct for more complicated RSB schemes also. This is supported by recent Monte-Carlo simulations [26], which reveal the same qualitative physics.

Recently, Todd *et al.* [15] have studied the adsorption of horse cytochrome *c* on a hydrophobic surface that is randomly functionalized with copper. Hystidine residues on the protein bind to copper and not to the hydrophobic support. Their measurement of the adsorbed fraction (Fig. 5 of their paper) as a function of copper loading is in qualitative agreement with our results for $\overline{p}$. Thus, there appears to be some experimental support for the phenomenon revealed by our study.

Our results for parameters different from those used to generate Fig. 2 show the same qualitative features, and so does an asymptotic analysis of our equations in the limit of small $\overline{p}$ and x_0 close to unity (with $D = 0$). Only after the transition occurs and $\overline{p}$ becomes very large are finite values of D required for stability.

Our findings raise obvious possibilities for designing chemically heterogeneous surfaces that can "recognize" patterns on real biopolymers and adsorb them strongly. This type of phenomenon can perhaps be used profitably for chromatography [15] and biosensors.

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