POLYMER ADSORPTION–DRIVEN SELF-ASSEMBLY OF NANOSTRUCTURES

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Abstract Driven by prospective applications, there is much interest in developing materials that can perform specific functions in response to external conditions. One way to design such materials is to create systems which, in response to external inputs, can self-assemble to form structures that are functionally useful. This review focuses on the principles that can be employed to design macromolecules that when presented with an appropriate two-dimensional surface, will self-assemble to form nanostructures that may be functionally useful. We discuss three specific examples: (a) biomimetic recognition between polymers and patterned surfaces. (b) control and manipulation of nanomechanical motion generated by biopolymer adsorption and binding, and (c) creation of patterned nanostuctures by exposing molten diblock copolymers to patterned surfaces. The discussion serves to illustrate how polymer sequence can be manipulated to affect self-assembly characteristics near adsorbing surfaces. The focus of this review is on theoretical and computational work aimed toward elucidating the principles underlying the phenomena pertinent to the three topics noted above. However, synergistic experiments are also described in the appropriate context.

I. INTRODUCTION

The adsorption of macromolecules onto two-dimensional surfaces has been considered since ancient times. For example, inks have included naturally occurring substances that we now understand to be polymers that adsorb onto the dye molecules and prevent their aggregation and precipitation from solution. In modern times, polymer adsorption has been the focus of much attention because of its importance in a host of practical applications and because developing a proper understanding of the pertinent phenomena presents some fundamental challenges in statistical physics.

Examples of traditional technological applications wherein polymer adsorption plays a crucial role include paints, coatings, boundary lubricants, ceramics processing, and adhesives. The fundamental interest in polymer adsorption stems
from the fact that in addition to a short-range primary structure defined by the chemical identity of the monomers polymers are long flexible objects over larger length scales. Long flexible molecules can adopt a large number of conformations, and there is a significant entropy associated with sampling this multitude of conformations. Many macroscopic properties of polymers are dominated by entropic effects determined by their many possible molecular conformations. Adsorption of a flexible macromolecule onto an impenetrable surface reduces the number of accessible conformations that a macromolecule can adopt. The balance between the reduction in entropy due to adsorption and the energetic advantage of binding determines the molecular conformations (and hence, properties) of adsorbed polymers. Understanding how this balance is influenced by the nature of the polymer and the surface from a fundamental standpoint has been, and continues to be, a challenge. It is essential to develop such an understanding if we are to learn how to manipulate the properties of adsorbed polymers by appropriate choice of polymer and surface.

The adsorption of homopolymers (i.e. polymers with only one kind of monomer unit) onto chemically homogeneous surfaces has been studied extensively for over three decades. Experiments, theory, and computer simulations have elucidated the conformational statistics of adsorbed homopolymers and their implications for properties. These important advances have been reviewed many times (e.g. 1–3). In the preceding two decades, the adsorption of diblock copolymers onto homogeneous surfaces has also received much attention. These are amphiphilic polymers wherein two contiguous blocks of chemically distinct monomers are connected at a well-defined junction point. The adsorption of diblock copolymers with one block being well-solvated in the solvent adjacent to the solid surface and the other exhibiting a preferential affinity for the surface has been studied extensively using a battery of experimental tools, theory, and computer simulations (e.g. 4–6). In this instance, the poorly solvated block binds strongly to the surface, while the well-solvated block extends out into the solvent. The number of adsorbed polymer chains per unit area is called the grafting density. For sufficiently high grafting densities, adsorbed diblock copolymer layers are referred to as polymer brushes because the strong stretching of the individual chains makes them resemble this object in everyday use. Studies of the adsorption of homopolymers and diblock copolymers have advanced our understanding of polymer conformational statistics while assisting the design of effective polymers for applications (e.g. colloid stabilization). With the exception of systems where the monomers carry an electric charge (7, 8), however, it is fair to say that our understanding of such systems is fairly mature.

Many current and prospective technologies demand materials that can function with precision over length scales ranging from nanometers to microns. Functional materials of this type could be realized if the response of the material's molecular constituents to a particular set of conditions is to self-assemble into a structural motif that is functionally interesting. Such self-assembly into nano- and micro-scale structures that perform important functions is ubiquitous in biology. In
many instances, evolution has led nature to use macromolecules as the molecular building blocks that self-assemble into functionally useful nanostructures. Thus, exploring whether the sequence and architecture of synthetic polymers can be manipulated so that we can control their self-assembly characteristics appears to be a fruitful avenue to pursue in taking steps toward the design of functional nanostructures.

Research aimed toward designing polymeric materials that can self-assemble into functional nanostructures in response to external stimuli is just beginning to emerge. A number of different environments and target applications are being employed. In this article, we restrict attention to situations involving polymers interacting with surfaces. Specifically, we discuss three examples where polymeric molecules form self-assembled nanostructures upon being exposed to certain types of surfaces. The first example concerns the development of strategies that may enable polymeric molecules to recognize target patterns of binding sites on a surface (Section II). The second example illustrates how interactions of an adsorbed polymer layer with biomolecules can affect nanomechanical motion, which might prove useful in sensing applications (Section III). The third example considers how nanometer-scale periodic patterns can be induced by the self-assembly of certain molten polymers due to interactions with a similarly patterned surface (Section IV).

Discussion of these examples also illuminates interesting aspects of the effects of sequence on the statistical physics of long polymer chains. While the focus of this review is on theoretical and computational research, synergistic experiments are described in the appropriate context.

II. BIOMIMETIC RECOGNITION BETWEEN POLYMERS AND SURFACES

Many important biological processes such as intracellular signaling are initiated by a protein searching for and recognizing a particular pattern of binding sites (a receptor) on a cell surface. Three important hallmarks of such recognition events are that (a) a sharp discrimination exists between patterns of binding sites to which the macromolecule binds strongly and those to which it binds weakly; (b) the biopolymer is not kinetically trapped in metastable states for long periods by adsorbing to the nontarget patterns of binding sites on the surface; and (c) adsorption on the target pattern occurs in a particular conformation (note that the pattern has a length scale commensurate with chain dimensions). Adsorption of synthetic macromolecules with ordered sequence distributions from solution does not exhibit all the features that characterize recognition. The following question presents itself: Since nature does it all the time, why can we not?

One way to mimic recognition in synthetic systems is to attempt to reproduce the detailed chemistries to which nature has been led via evolution. This strategy would be very difficult to implement for a synthetic system even if the mechanisms that lead to recognition were known. This prompts us to ask whether there are any
essential (and universal) ingredients that would allow synthetic systems to mimic recognition.

It is important to remark that the work reviewed here does not aim to describe recognition in biological systems. However, coarse-grained observations concerning biological systems provided the inspiration for deducing candidate strategies that could be used to mimic recognition. In the context of protein folding, for example, many coarse-grained representations of protein sequences have been developed. An example is the HP model (9), wherein amino acids are considered to belong to two classes, hydrophobic (H) and polar (P). When protein sequences are represented using this or other coarse-grained models, it has been observed that in most instances the sequence of Hs and Ps is not periodically repeating (or ordered) (10–12). Similarly, while the pattern of binding sites that constitute a receptor are very specifically arranged, there is usually no periodically repeating pattern. These observations led to the following speculation: Is it possible that the disorder (in polymer sequence and pattern of binding sites) and competing interactions due to multiple types of segment-site interactions are the essential ingredients required to mimic recognition in synthetic polymeric systems? It is worth remarking that while coarse-grained observations concerning biological systems inspired this question, one can ask it independent of such observations.

Investigating the interactions of disordered heteropolymers (DHPs) with surfaces bearing binding sites of more than one type provides a good model system to explore the question noted above. Figure 1 is a schematic depiction of a DHP bearing two kinds of segments interacting with a surface that has two kinds of sites. The white (gray) segments interact favorably with the white (gray) sites on the surface. This introduces competing interactions while disorder is embodied in the sequence and surface site distribution.

DHP sequences are described statistically, and hence they encode a statistical rather than specific pattern. Similarly, binding sites on a surface can be arranged in a pattern that is also described statistically. For example, the average density of sites, the fraction of each type of site, and a two-point correlation function that measures the probability of finding sites of the same type a certain distance

Figure 1  Cartoon representation of DHP interacting with a surface onto which two types of sites have been distributed. A pattern matched conformation is shown.
away could be specified. In nature, when the specific pattern encoded in the biopolymer sequence and the pattern of binding sites are related in a special way (i.e. matched), recognition occurs. The question that has been asked (13–19) for the class of synthetic systems depicted in Figure 1 is, If the statistics characterizing the DHP sequence and the surface site distribution are related in a special way, will the ensemble of DHP sequences in question be able to recognize the statistical pattern of binding sites? In other words, is statistical pattern matching sufficient to mimic recognition?

Answering these questions requires that both thermodynamic and kinetic issues be analyzed. Theoretical studies, computer simulations, and recent experiments have provided partial answers to some of the pertinent questions. In this section, we discuss some of this progress.

Thermodynamic issues were first considered using a toy model (13). While these were primitive, later studies have shown that this model contains much of the essential physics. Imagine that the segment-surface interactions are so much stronger than the intersegment interactions that the latter can be ignored. In this circumstance, the Edwards Hamiltonian for the situation depicted in Figure 1 can be written as:

\[ -\beta H = -\frac{3}{2l} \int_0^N dn \left( \frac{dr}{dn} \right)^2 - \int_0^N dr \times k(r)\delta(r(n) - r)\theta(n)\delta(z), \]

where \( r(n) \) is the spatial position of the nth polymer segment in three-dimensional space. \( \theta(n) \) equals +1 if the nth segment is of type A and is −1 if it is a B-type segment. \( k(r) \) is the interaction strength with a surface site located at \( r \). The Hamiltonian is written such that if a surface site is attractive to one type of DHP segment, it is equally repulsive for the other kind of segment. This is for simplicity only; the qualitative physics does not change as long as one type of segment interacts preferentially with one type of site while the other type of segment prefers the other kind of site. The factor of \( \delta(z) \) in the Hamiltonian restricts the sites to a two-dimensional manifold.

Since the sites on the surface and the DHP sequence are disordered, \( k(r) \) and \( \theta(n) \) are fluctuating variables. Their fluctuations are described statistically, and the statistics encode the pattern carried by the surface sites and the DHP sequence. In the simplest scenario, \( k(r) \) and \( \theta(n) \) are taken to be random variables described by Gaussian statistics. The statistics are therefore described by the variance, which is trivially related to the average composition of the DHP or the average total density of the two types of sites on the surface. In the high temperature limit, this description is equivalent to an uncorrelated discrete distribution characterized by a mean value. For DHP sequences, using this representation also generalizes the results to sequences with more than two types of segments.

Let us employ this simplest version of statistical patterns to examine some elementary ideas concerning pattern recognition between polymers and surfaces. We will soon examine more complicated statistical patterns. The probability
distributions for $k(r)$ and $\theta(n)$ are:

$$
P[k(r)] \propto \exp\left[-\frac{1}{2\sigma_1^2} \int dr \, k^2(r)\right]
$$

$$
P[\theta(n)] \propto \exp\left[-\frac{1}{2\sigma_2^2} \int dn \, [\theta(n) - (2f - 1)^2]\right].  \tag{2}
$$

where $\sigma_1^2$ and $\sigma_2^2$ are the variances for the distributions. $\sigma_1^2$ is proportional to the total number density of surface sites; $\sigma_2^2$ equals $4f(1 - f)$, where $f$ is the average composition characterizing the DHP sequence.

Depending on the preparation conditions, the distribution of surface sites could either change in response to interactions with the DHP chains (annealed) or not (quenched). In the former case, an interesting question is how the final pattern adopted by the surface sites is related to the sequence of the DHP. This would tell us whether it is possible to transfer information from the DHP to the surface. How much entropic loss of information would occur? In the latter case, the issue is whether DHPs with a particular statistical class of sequences can recognize a prescribed pattern of binding sites.

For disorders external to the fluid of interest (the surface sites, in our case), in the thermodynamic limit, treating this disorder as quenched or annealed leads to the same equilibrium properties. This has been argued in many contexts (e.g. 20–22). However, it is important to note that quenched external disorders exhibit the same thermodynamics if the sample is sufficiently large and the observation time is sufficiently long. Quantifying this statement for a given problem is difficult, and the dynamics are certainly different for quenched and annealed disorders external to the fluid. For the moment, we restrict attention to thermodynamic properties and imagine that the surface is sufficiently large and the DHP has sufficient time to sample the surface sites. In this case, we can integrate out the external disorder to obtain the following influence functional (23, 24):

$$
expl[-\beta H_{eff}] = \int \int Dk(r) \exp\left[-\frac{1}{2\sigma_1^2} \int dr \int dr' \, k(r)k(r')\delta(r-r')\delta(z)\delta(z')\right]
$$

$$
\times \exp\left[-\frac{3}{2\eta} \int dn \left(\frac{dr}{dn}\right)^2 - \int dn \int dr \, k(r) \delta(r(n) - r)\theta(n)\delta(z)\right].  \tag{3}
$$

The quenched disorder embodied in the DHP sequence, however, is carried by the fluid of interest. The arguments made above for the external disorder no longer apply, and we must explicitly treat the sequence as quenched even for thermodynamic properties. This is to say that the partition function is not self-averaging with respect to $\theta(n)$; the free energy is. One way to carry out this quenched average is to use the replica trick (25, 26). Replicating the effective Hamiltonian, $H_{div}$, in Equation 3 and carrying out the functional integral over the
distribution of \( \theta(n) \) leads to the following m-replica partition function:

\[
\langle G^m \rangle = \prod_{\alpha=1}^{m} \int D\mathbf{r}_\alpha(n) \int Dk_\alpha(r) \exp \left[ -\frac{3}{2l} \sum_{\alpha=1}^{m} \int \frac{dn}{dn} \left( \frac{dr_\alpha}{dn} \right)^2 \right] \times \exp \left[ -\frac{1}{2\sigma_1^2} \sum_{\alpha,\beta} \int d\mathbf{r} \int d\mathbf{r}' k_\alpha(r) \delta_{\alpha\beta} \delta(r - r') k_\beta(r') \delta(z) \delta(z') \right] \times \exp \left[ \frac{\sigma_2^2}{2} \sum_{\alpha,\beta} \int dn \int d\mathbf{r} \int d\mathbf{r}' k_\alpha(r) k_\beta(r') \times \delta(r_\alpha(n) - \mathbf{r}) \delta(r_\beta(n) - \mathbf{r}') \delta(z) \delta(z') \right].
\]

4.

Let us define the following order parameter that measures the conformational overlap in the plane of the surface between the various replicas:

\[
Q_{\alpha\beta}(\mathbf{r}, \mathbf{r}') = \int dn \delta(r_\alpha(n) - \mathbf{r}) \times \delta(r_\beta(n) - \mathbf{r}') \delta(z) \delta(z').
\]

5.

In terms of \( Q_{\alpha\beta} \), the replicated partition function can be rewritten as:

\[
\langle G^m \rangle = \int DQ_{\alpha\beta} \exp(-E[Q_{\alpha\beta}] + S[Q_{\alpha\beta}])
\]

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

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

6.

where

\[
P_{\alpha\beta}(\mathbf{r}, \mathbf{r}') = \frac{\delta(\mathbf{r} - \mathbf{r}') \delta(z) \delta(z')}{\sigma_1^2} - \sigma_2^2 Q_{\alpha\beta}(\mathbf{r}, \mathbf{r}').
\]

7.

The expression above shows that \( S \) equals the logarithm of the number of chain conformations that have a particular surface overlap function while obeying the connectivity constraint. Thus, it is the entropy corresponding to a particular \( Q_{\alpha\beta} \). Then, \( E \) must be the energy.

Physical systems characterized by competing interactions and quenched disorder can, under certain circumstances, have thermodynamic properties that are determined by a few dominant conformations. In other words, phase space can be partitioned into different parts with very large free energy barriers separating the different regions. DHPs exhibit this kind of behavior, wherein a few conformations are thermodynamically important, in a number of different contexts.
We admit the possibility of such thermodynamic states in the mathematical analysis by allowing for broken replica symmetry. Parisi pioneered the way to think about broken replica symmetry in spin glass physics (35). We follow this line of thinking and its adaptation to DHPs by other workers (27, 28). It has been argued that DHPs can exhibit characteristics akin to the random energy model (REM) or p-spin models with \( p > 2 \) (e.g. 36). This has been the basis for employing a one-step replica symmetry breaking (RSB) scheme (26) to examine thermodynamic states with only a few dominant conformations. We use such an analysis here.

In a one-step RSB scheme, replicas are divided into groups. Replicas within a group have perfect conformational overlap (in our case, in the plane of the surface), while replicas in different groups have no conformational overlap. The energy in Equation 7 is obtained by evaluating the Gaussian integral, and it equals the logarithm of the determinant of the matrix \( P \). The computation of this quantity, while allowing for broken replica symmetry, has been detailed by Mezard & Parisi (37). Following their method, for a one-step RSB scheme, we find that

\[
E = \frac{1}{2} \left[ -\ln \sigma_1^2 + \frac{1}{x_0} \ln(1 - C_1 \bar{\sigma}_x) \right]
\]

where \( x_0 \) is the number of replicas in a group, \( A \) is the surface area, and \( p \) is the number of segments in contact with the surface. The derivation of Equation 8 involves approximating the total segmental density on the surface to be uniform.

The number of ways in which replicas in a group can be arranged such that they have perfect conformational overlap on the surface and \( p \)-adsorbed segments can be calculated as follows. The conformations of adsorbed polymers are comprised of loops, trains, and tails (see Figure 2). Trains are a contiguous set of adsorbed segments. Loops are made up of a contiguous set of unbound segments between two bound segments. Tails extend away from the surface. In the long chain limit, tails can be ignored. Furthermore, trains can be considered to be composed of a number of consecutive loops, each one segment long. Let the probability for a loop of length \( n \) to begin at a position \( r_i \) and end at \( r_i + 1 \) be \( f_n (r_{i+1} - r_i) \). Then, the number of ways to arrange \( x_0 \) replicas that overlap perfectly on the surface and have the first segment adsorbed at \( r_1 \) is:

\[
Z(r_1) = \sum_{n_1, n_2, \ldots, n_p} \int dr_2 \int dr_3 \int \int \int \cdots \int \int f_{n_1} (r_2 - r_1) f_{n_2} (r_3 - r_2) \cdots f_{n_p} (r_p - r_{p-1})
\]

\[
\times \delta(n_1 + n_2 + \cdots + n_p - N).
\]

The entropy that we seek is obtained by integrating this restricted partition function,
$Z$, over $r_1''$ and taking the negative logarithm. The Dirac delta function in Equation 9 enforces a constant chain length equal to $N$.

This computation is done most easily by defining the Fourier-Laplace transform of Equation 9. The Laplace transform is conjugate to chain length and the Fourier transform is defined with respect to the two-dimensional spatial coordinates in Equation 9. Taking advantage of the convolution structure of Equation 9 yields

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

where $k$ and $\lambda$ are Fourier and Laplace variables. Different functions are used for $f_1$ and $f_i$ for all $i \neq 1$. For $i = 1$, we use the well-established expression due to Hoeve et al. (38); i.e.,

$$f_1(r) = \omega \delta(r - l).$$

For larger values of $i$, we imagine that the loops extending away from the surface are Gaussian (38, 39). Using these expressions for $f_i$, and following the steps noted earlier, we can obtain the entropy as a function of $\mathcal{P}$ and $x_0$. Combining this expression with Equation 2 yields the free energy $F$.

$$F = \frac{1}{2} \left[ -\ln \sigma_1^2 + \frac{1}{x_0} \ln(1 - C_1 \mathcal{P} x_0) \right] - \frac{1}{x_0 N}$$

$$\times \ln \left[ \sum_{q=0}^{\mathcal{P} N} \left( \frac{2\pi l^2}{3x_0} \right)^q C_q x_0 \mathcal{P}^{N-q} x_0^{q-1} \frac{\Gamma(q((4 - 3x_0)/2))}{\Gamma(q(4 - 3x_0)/2)} \right]$$

$$\times [N - (\mathcal{P} N - q)][(4 - 3x_0)/2]^{q-1} \right].$$

In deriving this expression, the discrete sum over loop lengths was replaced by a continuous integral.
Mean field predictions for $p$ and $x_0$ are obtained by extremizing the free energy expression with respect to these order parameters. The quantity $p$ is just the adsorbed fraction and measures the extent of adsorption. The parameter $x_0$ has been interpreted to be $1 - \sum_i P_i^2$, where $P_i$ is the probability of occurrence of conformation $i$. When a multitude of conformations are sampled, $x_0$ is, therefore, unity. Values of $x_0$ smaller than unity signal a thermodynamic state with a few dominant conformations.

Let us study the behavior of $p$ and $x_0$ for a given statistical ensemble of DHP sequences interacting with different surfaces. In this simple model, this implies varying the total number density of sites (loading, measured by the parameter $C$). Figure 3 shows the variation of $p$ and $x_0$ with $C$; note that every point on the abscissa of this figure corresponds to a different surface. There is no adsorption on surfaces that have small loadings. This is simply because the energetic advantage of binding to a few sites is insufficient to overcome the entropic penalties associated with adsorption. When the loading is sufficiently high, Figure 3 shows a continuous transition to adsorbed states. At this stage, $x_0$ remains unity. This is similar to the phenomenon that is observed for adsorption of chains with ordered sequence distributions. Figure 3 makes a much more interesting prediction when the surface

![Figure 3](image.png)

**Figure 3**  The order parameters $\bar{p}$ (dashed line) and $x_0$ (solid line) plotted as a function of $C$. For the calculation described in the text, each point on the abscissa represents a different statistically patterned surface.
loading exceeds a higher threshold value. The adsorbed fraction exhibits a sharp transition to strongly adsorbed states. This sharp transition from weak to strong adsorption is accompanied by $x_0$ acquiring values smaller than unity, signaling that only a few adsorbed conformations are thermodynamically important.

Consider the situation when the loading is sufficiently large to induce adsorption, but not large enough to cause the sharp transition from weak to strong adsorption. In this scenario, since the loading is not large, it is relatively easy for adsorbed chains to avoid unfavorable segment-surface contacts while still making favorable ones. Furthermore, there are many adsorbed conformations that can acquire the same energy by having different combinations of the same number of favorable segment-surface interactions. Thus, the system minimizes free energy by sampling these adsorbed conformations and $x_0$ equals unity. As the loading increases, the adsorbed fraction increases. However, larger values of the adsorbed fraction and the loading imply that it becomes increasingly difficult to avoid unfavorable interactions. Imagine generating arbitrary adsorbed conformations for a particular adsorbed fraction when the loading is high. Intuitively it is clear that most of these arbitrary conformations will have a rather high energy because of many unfavorable segment-surface contacts. However, there will be a few conformations that carefully avoid these unfavorable contacts. These few conformations are much lower in energy than the other adsorbed conformations. Sampling only these states is entropically not favored, however. As the loading increases, the energy gap between the few pattern-matched conformations and the others increases. (We use the term pattern-matched conformations to refer to those conformations that exhibit a high degree of registry between complementary segments and surface sites.) When this energy gap becomes much larger than the thermal energy, the system prefers to sacrifice the entropic advantage of sampling a multitude of conformations and so adopts the few energetically favorable ones. Of course, these pattern-matched conformations are strongly adsorbed. This is the physical origin of the transition from weak to strong adsorption leading to a thermodynamic state with a few dominant conformations.

The arguments above are very similar to those that describe the behavior of the random energy model (REM) in spin glass physics. It is worth remarking that the system we have been studying is more frustrated than the two-letter DHP in solution by itself (39a). This is because the competing interactions are confined to a two-dimensional manifold. It is important to note that this does not mean that the dimensionality of the system that we have been describing is two. This is because the polymer chains can escape into a third dimension by forming loops. The importance of these loops and their fluctuations will be made vivid later.

Figure 3 shows that the transition from weak to strong adsorption is sharp. In fact, replica mean-field theory predicts the transition to be first order (13). In such a theory, $x_0$ acquiring values less than unity corresponds to broken replica symmetry of the underlying Hamiltonian. The mean-field theory shows that there are two free energy minima, one that is replica symmetric and the other with broken replica symmetry. When the loading acquires the value required for a transition
from weak to strong adsorption, the global free energy minimum switches from
being the replica symmetric one to that with broken replica symmetry. The mean-
field prediction of the order of the transition could be incorrect because fluctuations
could change the order of the transition. It is worth noting, however, that Monte-
Carlo simulations are also suggestive of a first order transition (16–18).

From a practical standpoint, what is important is that the transition is sharp. This
implies a sharp discrimination between weakly and strongly adsorbing surfaces—
one of the previously mentioned hallmarks of recognition. The arguments noted
above do not provide a reason for the sharpness of the transition or its order.
An intuitive argument, and associated phenomenological model, suggests that the
physical origin of the sharp transition is the strong suppression of loop fluctuations
when adsorption occurs in pattern-matched conformations (40). The basic idea is
this: Consider homopolymer adsorption on a chemically homogeneous surface. All
segment-surface contacts are favorable, so the loop lengths and distance between
loop ends on the surface can change without changing the nature of the segment-
surface interactions. Thus, strong loop fluctuations occur leading to a lower free
energy. Now consider the problem we are considering—a DHP interacting with
a heterogeneous surface with a disordered distribution of sites. Now, there are
two types of contacts with the surface: favorable and unfavorable. Concomitantly,
there are two kinds of loops: those associated with good contacts at both ends,
and the others. For loops associated with good contacts, only certain values of
loop lengths and distances between loop ends on the surface are allowed. Loops
associated with good contacts require favorable segment-surface contacts at both
ends. This indicates that the fluctuations of this type of loop are suppressed due to
competing interactions and quenched disorder. These loops are thus fundamentally
different in character from the other type of loops or the strongly fluctuating loops
associated with homopolymer adsorption on homogeneous surfaces. The allowed
values of loop lengths and distance between loop ends for loops associated
with good contacts are intimately related to the probabilities of finding certain types
of sites and segments at different locations on the surface and along the chain be-
cause favorable segment-surface contacts must be established. When the statistics
of the DHP sequence and the surface site distribution are related in such a way that
there is a high probability of forming good contacts, it is reasonable to suppose
that loop fluctuations are strongly suppressed. Suppression of loop fluctuations
is tantamount to making the chain stiffer. Sufficiently stiff chains are known to
undergo first-order adsorption transitions (39), and thus, suppression of loop fluc-
tuations is argued to be the origin of the sharp adsorption transition depicted in
Figure 3.

The analysis described above predicts that when the statistics characterizing the
distribution of surface sites and those characterizing the DHP sequence are related
in a special way, a sharp adsorption transition accompanied by the adoption of a few
thermodynamically important conformations occurs. A sharp transition implies
sharp discrimination between surfaces, one hallmark of recognition. Thus, one
hallmark of recognition is realized when the statistics of the DHP sequence and
surface site distribution are matched. This has been shown for a very simple model where the statistics for uncorrelated surface site and sequence distributions are measured by total loading and average composition, respectively. Monte-Carlo simulations have shown that the same phenomenon occurs for more complicated and interesting statistical patterns (16). The thermodynamic principles described above cause DHPs bearing a particular statistical pattern encoded in their sequence to sharply distinguish between surfaces bearing complementary statistical patterns and those that do not. The complementarity condition, based upon thermodynamic considerations, is found to be (16):

$$\sum_{m=1}^{N} P_s(m) P_c(m) = \Gamma,$$

where $P_s(m)$ is the probability of finding a patch of size $m$ of like sites at an arbitrary point on the surface, $P_c(m)$ is the probability of finding a contiguous “run” of like segments of length $m$ at arbitrary locations along the chain, and $\Gamma$ is a threshold number that depends strongly on chain flexibility and the strength of the interactions. $P_s(m)$ and $P_c(m)$ can be determined from the statistics of the DHP sequence and surface site distribution.

Our discussion so far has been concerned with thermodynamics. If recognition is to occur due to statistical pattern matching, a DHP bearing a particular statistical pattern encoded in the sequence, when exposed to a surface bearing different statistical patterns in different regions, should be able to find the target pattern without getting kinetically trapped in the wrong parts of the surface. Whether or not this can occur, and if so, what the pertinent principles for designing DHP sequences and surface site distributions are, can only be understood by studying the dynamics of DHP chains near surfaces bearing multiple types of statistical patterns. This has recently been done using kinetic Monte-Carlo simulations (19).

The simplest way to create statistical patterns that go beyond the completely uncorrelated distributions we have considered so far is to introduce two point correlations. The statistical patterns carried by chemically synthesized DHPs can be characterized naturally in terms of the chemical reactivities of the segments. If only two point correlations are included, the statistics of two-letter DHP sequences can be characterized by the average composition and a $2 \times 2$ matrix of reaction probabilities. An element of this matrix, $P_{ij}$, is the probability of finding a segment of type $j$ immediately following a segment of type $i$. This matrix has one nontrivial eigenvalue (41), $\lambda = P_{AA} + P_{BB} - 1$. Positive values of $\lambda$ imply that, below a certain correlation length $q$, contiguous runs of the same type of segment occur with high probability. We shall refer to this type of statistical pattern as statistically blocky. Negative values of $\lambda$ correspond to sequences where, for lengths smaller than $q$, there is a propensity to form blocks of alternating segments. We shall refer to this type of sequence as statistically alternating. The value of $q$ is set by the absolute magnitude of $\lambda$. Examples of statistically blocky and alternating DHP sequences are depicted schematically in Figure 4a.
Figure 4b depicts statistically alternating and blocky distributions of A- and B-type surface sites. The simplest statistical measures of such site distributions are the correlation length, the total number density of A- and B-type sites, and the fraction of sites of each type (always equal to half in the following discussion). Such surface patterns can be generated by simulating an Ising-like Hamiltonian using a Monte-Carlo algorithm. Details are provided in (19). These types of patterned surfaces can be prepared in practice by self-assembly of mixed molecular adsorbents or molten DHPs on solid surfaces (42–44).

Figure 5 shows a surface divided into four quarters. The pattern of sites in the top right corner is statistically alternating, while that in the bottom left corner is statistically blocky. In the other two quarters the distribution of sites is completely random (i.e. uncorrelated). If a solution with a mixture of DHPs carrying statistically alternating and statistically blocky sequences is exposed to this surface, will the statistically alternating (blocky) chains rapidly find and bind strongly to the complementary statistically alternating (blocky) patch of the surface? An affirmative answer to this question would indicate that a phenomenology that mimics recognition can occur due to statistical pattern matching.

Figure 6 shows typical trajectories of the center of mass for a statistically alternating and a statistically blocky DHP generated by kinetic Monte Carlo simulations carried out on a lattice. The parameters characterizing the DHP and the surface site patterns are detailed in the figure caption. A standard Verdier-Stockmayer algorithm (45) is used to carry out the simulations. The interaction energy between complementary segments and surface sites is \(-kT_{\text{ref}}\), and the unfavorable interactions are equal but of opposite sign. Only nearest neighbor interactions are allowed. As is clear, both trajectories start out in parts of the surface characterized by random site distributions. Each trajectory first samples wrong parts of the surface, but ultimately finds the target pattern and binds strongly. For \(T/T_{\text{ref}} = 0.6\), separation due to statistical pattern matching is over 90% efficient (1000 trials) for a simulation time corresponding to the order of one second of real time. (Local motion on the scale of monomers occurs in \(10^{-10} - 10^{-11}\) sec depending on solvent conditions and monomer size.) These phenomenological results demonstrate that recognition due to statistical pattern matching can be successful, and it may be possible to exploit this notion in applications where biomimetic specificity is desired.

The DHPs do adsorb onto the wrong parts of the surface. These adsorbed states are, however, short lived compared to the length of the trajectories. In contrast, once strong binding occurs in the target region of the surface, the chains do not desorb in simulation time scales [or, it is estimated (19), on any time scale of experimental interest]. Figure 7 shows the free energy landscape that a statistically alternating DHP negotiates when interacting with the surface shown in Figure 6. This has been computed by extensive Monte Carlo simulations. As is evident, the free energy barriers separating local minima in the wrong parts of the surface are relatively small. The target region of the surface is, however, characterized by a few deep minima. Each such minima exhibits a rugged topography. This free
energy landscape makes clear why the chain traverses the wrong parts of the surface relatively fast and ultimately finds and binds strongly to a region corresponding to one of the deep free energy minima in the target region of the surface.

The strength of the segment-surface interactions is set by the chemical identities of the chain segments and the surface sites. For our model, this chemistry sets the value of $T_{\text{ref}}$. The temperature of the system relative to the strength of the segment-surface energetics ($T/T_{\text{ref}}$) plays an important role in determining the behavior of the system. If the temperature is too high, entropic factors will prevent appreciable adsorption to all parts of the surface due to thermodynamic reasons. If the temperature is too low, then the free energy minima in the wrong parts of the surface will serve as long-lived kinetic traps. The existence of an optimal value of $T/T_{\text{ref}}$ suggests that, given the chemical identity and statistics characterizing

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Figure 7  Free energy landscape (in arbitrary units) as a function of DHP center of mass position generated for an alternating DHP interacting with the surface shown in Figure 5. The deep free energy minima on the right side of the figure are artifacts of periodic boundary conditions.
the surface site distribution, the chemical identity of the monomers that make up
the statistically pattern-matched DHP sequences can be chosen in an optimal way.
This could provide guidelines for design and synthesis of devices exploiting the
notion of recognition due to statistical pattern matching.

One example of such an application is work being done by Whitesides and
coworkers aimed toward designing copolymeric viral inhibition agents (47–49).
The idea is to choose the chemistry and sequence of synthetic copolymers that
could recognize and bind strongly to the pattern of receptors on a specific virus,
thereby inhibiting its ability to interact with cells. Using copolymers made of
sugars and acrylic acid, experiments suggest that a range of compositions (i.e.
sequence) leads to optimal inhibition of the influenza virus (49). We briefly men-
tion current efforts to develop computational tools that may prove useful in design-
ing optimal DHP sequences that can recognize specific patterns of binding sites
(e.g. a receptor).

The optimum in $T/T_{\text{ref}}$ results from the importance of both kinetics and ther-
modynamics in determining the efficacy of recognition due to statistical pattern
matching. This can also be demonstrated by comparing two situations: (a) the
behavior of a statistically alternating DHP interacting with the surface shown in
Figure 5 and (b) a surface with two regions, both bearing random site distributions
with loadings equal to 20% and 40% exposed to DHP sequences that strongly favor
the latter region on thermodynamic grounds. Recall that our replica field theory
showed that, on thermodynamic grounds, DHPs with random sequences could
differentiate sharply between surfaces that have different loadings of randomly
distributed sites (13).

Monte Carlo simulations show that the window of $T/T_{\text{ref}}$ over which successful
recognition occurs (defined as $>80\%$ efficiency) is 50% wider for scenario (a)
compared to scenario (b). This is so even though the equilibrium adsorbed fraction
in the target region is the same for both cases. The reason is that, for uncorrelated
sequence and surface site distributions, the free energy landscape that the chains
negotiate is uncorrelated and rife with optima that serve as kinetic traps. (It is
amusing to remark that similar arguments have been made in the context of species
evolution on fitness landscapes (50).)

The free energy landscape shown in Figure 7 suggests that the dynamics of
DHP chains traversing it should exhibit interesting features on different scales
of length and time. To begin, consider the distribution of first passage times
for a chain starting in the random part of the surface to find the target region
and adsorb strongly. Strong adsorption is quantified by an energy cut off ($-20$
kT in the discussion to follow). Figure 8 shows the first passage time distribu-
tion for a 100-segment statistically alternating DHP interacting with the surface
shown in Figure 5. After the usual turn-on time, the distribution of first passage
times is decidedly nonexponential. In fact, a stretched exponential function with
a stretching parameter equal to 0.43 best fits the simulation results. This indi-
cates that highly cooperative events occur during the phenomenon that we are
simulating.
Figure 8 First passage time distribution for alternating DHP interacting with the surface shown in Figure 5. An exponent of $\beta = 0.43$ was used to generate the curve shown.

The event in question can be naturally divided into two events that occur in succession: center of mass motion from the random part of the surface to the edge of the target region followed by motion leading to strong adsorption. Simulation results show that only the first passage time distribution for the second event is nonexponential. It is also important to note that single-particle Kramers diffusion on the free energy landscape shown in Figure 7 does not lead to nonexponential first passage time distributions. This last observation suggests that the DHP center of mass is not the slowest dynamic mode through the duration of the entire event.

Further insight into the origin of the cooperative dynamics (data in Figure 8) is obtained by examining the distribution of loops during the course of a typical trajectory. This is shown in Figure 9 for a typical trajectory of a statistically alternating chain interacting with the surface shown in Figure 5. The distribution of loops is quantified by a quantity, $P_n$, which is the probability of a randomly chosen segment belonging to a loop of length $n$. This probability distribution is shown for different time periods in the trajectory. During the early stage of the trajectory, when the DHP center of mass lies above the wrong parts of the surface (first panel), the probability distribution is essentially structureless and the values of $P_n$ are uniformly small. This is because different adsorbed conformations are energetically similar, and so the DHP minimizes free energy by sampling a multitude of conformations (and thus, loop lengths). Thus, no particular adsorbed conformations are greatly favored, leading to an essentially structureless distribution for $P_n$. As the trajectory enters the statistically pattern-matched region (second panel), we find that the distribution $P_n$ begins to acquire structure. By the time the DHP is strongly adsorbed in a deep free energy minimum in the target region of the surface (last panel) the distribution resembles a spectrum, indicating that the DHP
Figure 9  Loop length distributions, $P_n$, for different time windows along a typical trajectory: (a) DHP in the wrong region of the surface, (b) DHP center of mass entering the pattern-matched region, and (c) DHP strongly adsorbed in the pattern-matched region.
is bound in a class of conformations (or shapes). This is because in the statistically pattern-matched region, with high probability, there exist a few dominant conformations that can bind very strongly by carefully avoiding unfavorable interactions. However, most arbitrary conformations correspond to many unfavorable interactions because of the disordered sequence and competing interactions. Thus, the DHP sacrifices the entropic advantage of sampling a multitude of conformations, and adsorbs in a class of shapes. This is reminiscent of biopolymers binding to specific receptors in particular shapes.

These findings suggest that the time scales associated with loop fluctuations may be very different in different parts of the trajectory. This is seen clearly in the simulation results shown in Figure 10 for the time correlation function $\langle P_n(t)P_n(t + \tau) \rangle$. Specifically, we plot the time in which these time correlations decay along the trajectory. Only one value of $n$ (corresponding to a peak in Figure 9) is considered in Figure 10, but the results are similar for other values of $n$ corresponding to peaks in the distribution of $P_n$. In the wrong parts of the surface, these correlations decay very fast, and on the scale of the plot in Figure 10, the decay time is essentially zero (data not shown). As we enter the statistically pattern-matched region, the decay time begins to rise and ultimately oscillates about a large value as in a crystal. This implies that once adsorption occurs in a particular class of shapes, $\langle P_n(t)P_n(t + \tau) \rangle$ decays very slowly as these adsorbed shapes persist for long times.

Chain dynamics are thus very different in the wrong and target regions of the surface. In the wrong regions, the loop fluctuations are very fast, and the center of mass motion is the slowest dynamic mode. In the target region of the surface, once

![Figure 10](image-url)  
**Figure 10** Relaxation time, $\tau^*$ (time for $\langle P_n(t)P_n(t + \tau) \rangle$ to relax to within 5% of its equilibrium value) for loops of length 26, calculated for same trajectory as Figure 9. During the time window shown, the polymer is in the statistically pattern-matched region.
the chain center of mass localizes over a region corresponding to a deep free energy minimum, the center of mass essentially stops. On the time scale of observation, it is effectively equilibrated. Now, the loops rearrange to acquire the conformation that corresponds to the bottom of the free energy minimum. This rearrangement takes place over long time scales, as there are many important entropic barriers that must be surmounted. These entropic barriers are made vivid in a movie that shows an animation of a trajectory for a DHP chain searching and finding a target pattern. These entropic traps have also been considered by Muthukumar (51, 52) in the context of a polyelectrolyte binding to a patterned array of charges of the opposite sign, and he has called a related phenomenon topological dereliction. Figure 11 shows snapshots from the movie mentioned above, and the fact that many adsorbed shapes are sampled in the wrong parts of the surface and only a few in the target region is made vivid.

After the chain center of mass has localized over a deep free energy minimum, the chain center of mass is the fastest degree of freedom, and the loop fluctuations are the slow dynamic modes. This explains why Kramer’s dynamics for a particle on the free energy landscape parametrized by the center of mass coordinates does not reproduce the first passage time distribution observed in the simulations. The center of mass is not the slowest dynamic mode during the course of the trajectory.

Careful experimental studies of these issues pertinent to dynamics in frustrated systems and the phenomenon of statistical pattern matching are under way. One study aims to synthesize polymers made up of two naturally occurring amino acids and disordered sequences (SJ Muller, JD Keasling, personal communication, 2000). Following the methods pioneered by Tirrell et al (54), carefully controlled sequences can be synthesized. Studying the adsorption characteristics of such polypeptides on patterned surfaces created by mixed self-assembled monolayers is expected to address issues similar to those described in the text. Another study focuses on the characteristics of synthetic DHPs adsorbing onto patterned surfaces prepared by casting molten films of the same DHP onto silicon wafers. Neutron and X-ray reflectivity studies of the adsorption characteristics are planned (TP Russell, personal communication, 2000).

While these careful experiments have been initiated, three classes of experiments that provide coarse-grained information are worth mentioning. We have already mentioned the viral inhibition experiments carried out by Whitesides and coworkers (47–49). Recently, Gunning et al (56) have used time-resolved AFM to study the dynamics of a single plant polysaccharide chain interacting with a mica surface with a random distribution of charges. The dynamics they observe is reminiscent of our simulation results. In fact, movies of their AFM observations (56) and animations of our simulation results resemble each other in important ways. Further work comparing this class of experiments and theoretical results are suggested. Finally, some experimental studies of horse cytochrome c adsorption on surfaces bearing a disordered distribution of copper
(which favorably interacts with the histidine residues of the protein) exhibits adsorption characteristics that are similar to expected from statistical pattern matching. For example, it is found (57, 58) that a plot of adsorbed fraction versus loading of copper sites is strikingly similar to the prediction of the replica field theory (Figure 3).

In this section we have described how to roughly design ensembles of sequences that can discriminatingly bind to target patterns of binding sites by statistical pattern matching. For this notion to be useful in applications, however, the following question needs to be addressed: Can the optimal DHP sequence for binding to a target pattern be determined? Or conversely, can the optimal pattern of binding sites to elicit adsorption of a DHP with a specific sequence be determined? Consider the first question. The design of such DHPs is complicated by the fact that the adsorbed conformation is a priori unknown.

In natural systems, this optimization is continuously being carried out by molecular evolution. Currently, calculations are being performed that utilize an algorithm designed to mimic directed molecular evolution (59). In these simulations, trajectories are run that evolve not only in real space, but also in DHP sequence space. This algorithm generates DHP sequences optimal for binding to a target pattern. Such a computational tool may find use in applications such as viral inhibition (47–49).

III. NANOMECHANICAL MOTION DUE TO BIOPOLYMER BINDING AND ADSORPTION

Interactions between biomolecules are often translated into motion that is crucial for biological function. Understanding the mechanisms by which such molecular motors work in physiological processes is a subject of great current interest (60–68). Recent experiments have also demonstrated how interfacing molecular biology with microcantilever technology and biopolymer adsorption can result in controlled nanomechanical motion (69, 70). Quantitative differences in the generated motion can be related to differences in the biochemistry of the involved macromolecules. This observation, and its origin, suggests ways in which this class of phenomena can be exploited to devise diagnostic tools that can accurately detect the presence of specific biomolecules in solution. Such devices may prove useful for rapid and accurate detection of pathogens and proteins implicated as causes of certain diseases.

Here, we describe only one set of experiments (69) that illustrates the basic phenomenon, its origins, and its potential for applications. The experimental setup consists of a transparent fluid cell within which a gold-coated silicon nitride cantilever is mounted. Only one side of the cantilever is coated with gold. The cantilevers are typically 200 μm long and 0.5 μm thick, with each leg being 20 μm wide. A laser reflected off the cantilever and focused onto a
position-sensitive detector is used to measure cantilever deflection. This methodology for measuring cantilever deflection is commonly used in atomic force microscopy (e.g., 71, 72).

Phosphate buffer, which maintains a desired pH, is first injected into the cell. Figure 12 (69) shows the measured deflection as a function of time upon injecting 50-nucleotide-long single stranded (ss) DNA molecules that are end-thiolated with HS-(CH$_2$)$_6$. These molecules form a self-assembled monolayer on the gold-coated side of the microcantilever. As Figure 12 shows, adsorption (or end-grafting) of the ssDNA molecules leads to a downward deflection of the microcantilever (see Figure 13). The inset in Figure 13 makes clear that the steady state deflection increases as the number of nucleotides (length) of the adsorbing DNA molecules increases.

Figure 14 shows the deflection that results upon subsequently injecting a solution containing ssDNA molecules, which are complementary to the end-grafted molecules and hence bind to them with great specificity. This process of complementary ssDNA molecules binding to form double-stranded (ds) DNA is called

![Figure 12](image.png) Change in cantilever deflection as a function of time. The data suggest exposure to either 0.1 M phosphate buffer or unthiolated probe ssDNA causes very little change in cantilever deflection while exposure to probe ssDNA thiolated at the 5' end does generate deflection (all ssDNA concentrations approximately 3.2 μM). The effect of the length of the probe molecule on the steady state deflection is shown in the inset.
Figure 13  Interactions generated by adsorption of molecules to the cantilever surface can be designed to result in repulsive forces between adsorbed species. These forces may be large enough to generate nanomechanical motion in the form of the deflection of the cantilever as shown.

Figure 14  Change in cantilever deflection due to hybridization of a complementary target fragment of ssDNA with the probe ssDNA at its distal end. Results are shown for several target fragment lengths—20, 15, 10, and 9 nucleotides (nt). The degree of deflection increases with the length of the complementary fragment. Results for a typical noncomplementary fragment show little impact on cantilever deflection.
hybridization. While results are shown for only 20-nucleotide-long adsorbed DNA molecules, the same behavior is observed for adsorbed DNA molecules containing 30–50 nucleotides. The experimental data shows that hybridization leads to upward motion of the microcantilever. The upward deflection at steady state is directly related to the length of the complementary ssDNA that is injected into the solution after creating the original adsorbed layer. The longer the length of these target DNA molecules, the greater the extent of upward deflection. Thus, measurement of the deflection can be used to distinguish between small (the data indicates 1 nucleotide) changes in the number of nucleotides in the target DNA. The data shown in Figure 14 (69) correspond to situations where the target DNA molecules are all distally complementary. However, recent experiments (A Majumdar, T Thundat, personal communication, 2000) show that the deflection is also sensitive to the sequence and the number of complementary nucleotides on target DNA molecules of the same overall length. This again is suggestive that such observations could be exploited in diagnostic applications.

The origin of the downward deflection of the microcantilever upon end-grafting biopolymers onto one surface has been argued to be the compressive stress created by the intermolecular repulsion between adsorbed polymer chains. Since the polymers are end-grafted only to one side of the microcantilever, the repulsive interactions and concomitant compressive stress are alleviated by bending the cantilever at the expense of the strain energy required for bending the microcantilever by a certain amount.

Quantitative cantilever deflections for both the end-grafting step and the hybridization step are found to depend on the concentration of the buffer (the ionic strength) in the solution. This suggests that repulsive electrostatic forces and their screening play an important role. Since each nucleotide carries a net negative charge, one would expect hybridization to further increase the repulsive forces between the adsorbed macromolecules, and hence cause the cantilever to bend further. Clearly, the opposite is observed in the experiments. Thus, steric and electrostatic repulsions between the adsorbed macromolecules cannot be the sole reason underlying the observed phenomenon.

At the ionic strengths used in the experiments (0.05–1 M), ssDNA is known to have a persistence length on the order of 0.75 nm (corresponding to two nucleotides) (74). When these chains are end-grafted onto a surface, if the grafting density is sufficiently high, each chain will occupy a region of space that is smaller than its natural size due to the intermolecular repulsions. This reduction in the configurational entropy can be alleviated by adsorption onto a convex surface. This is because the curvature allows each chain to occupy a larger region of space as distance from the surface increases. Thus, in addition to intersegment repulsions, there is an entropic driving force that balances the strain energy of the cantilever and enhances the extent of bending. In contrast to ssDNA, at the experimental conditions, dsDNA has a persistence length of 50–80 nm (74), which is approximately 150 base pairs. Thus, the dsDNA is effectively a rod at the
experimental conditions, and the configurational entropy gain by forming a curved surface is inconsequential compared to the adsorbed ssDNA molecules. Therefore, the cantilever strain energy and intersegment repulsions are balanced at a lower cantilever deflection (or curvature). This explains the upward deflection upon hybridization.

The qualitative energy-configurational entropy balance described above is supported by the following experiment (69). ssDNA molecules were end-grafted with a buffer concentration of 1 M. The ionic strength was then reduced by an order of magnitude reduction in the buffer concentration. The grafting density resulting from adsorption at the higher buffer concentration is too high at the lower ionic strength because now the range of the intersegment repulsions is larger. This can cause the DNA chains to reduce the configurations sampled and to maximize the distance between neighboring grafted molecules by adopting the stretched configurations. In this instance, subsequent hybridization should lead to minimal changes in configurational entropy. The increased intersegment repulsions between the dsDNA molecules should be dominant, leading to a downward deflection upon hybridization. This is exactly what is observed in experiments (69). In addition to supporting arguments pointing to the importance of configurational entropy of adsorbed macromolecules in generating nanomechanical motion, this experiment also indicates that the direction of such motion can be controlled by tuning the conditions.

A quantitative analysis of the entropic and energetic contributions that determine cantilever bending can be easily carried out for sufficiently long chains using methods described in the polymer adsorption literature (e.g. 75–78). However, the DNA chains used in the experiments are short, and so a quantitative analysis is more delicate. It can be carried out, however, and should lead to a quantitative method for predicting and analyzing nanomechanical motion generated by biomolecular binding to polymers adsorbed on microcantilevers. Such an analysis, in conjunction with more extensive experiments, can prove useful in understanding how to control and manipulate nanomechanical motion generated by biomolecule binding to adsorbed layers.

Microcantilever deflections upon immobilizing proteins and then binding complementary ligands to immobilized proteins as well as that due to antibody-antigen interactions have also been observed and quantified for a few systems (68, 69). These results and those described in more detail in this section suggest that the binding of biomolecules to adsorbed polymer layers, and an understanding of the principles that govern the chemomechanical phenomena, could be exploited to design medical diagnostic devices. For example, an array of microcantilevers bearing different adsorbed macromolecules could be fabricated. Serum containing a known pathogen could then be injected into the solution in which the array is immersed. The deflection of the specific cantilever bearing the adsorbed macromolecule complementary to the target pathogen could then be used as a way to accurately and simply detect the presence of this pathogen. Much progress in
measurement methods, fabrication, and theoretical analyses is required before such devices can be used in routine application. However, research aimed in this direction is fruitful, as the payoff could be substantial. It is also an arena where knowledge of polymer adsorption and molecular biology, acquired in the last three decades, can be used fruitfully toward creating useful medical diagnostic tools.

IV. ORDERING OF DIBLOCK MELTS NEAR PATTERNED SURFACES

As noted earlier, diblock copolymers are macromolecules consisting of two chemically distinct polymer chains covalently bonded together at one junction point. It is well known that a molten collection of these molecules microphase segregates below an order-disorder transition temperature (ODT) to form a myriad of interesting nano/microstructures (e.g. 79, 80). Efforts to exploit this ability to form regular nanoscale features in applications is an active research area. In this section we briefly review research aimed toward the creation of regular morphologies in thin films of diblock copolymers by utilizing interactions with patterned surfaces.

Molten diblock copolymers with symmetric compositions will spontaneously form lamellae with the stacking pattern AB–BA, and natural lamellar period \( L_b \) below the ODT (e.g. 79–82). In the case of a thin film (or slit), the lamellae may orient either parallel to the film or perpendicular to it (83–91) (see Figure 15). The case in which the lamellae orient perpendicularly is of particular interest, as the resulting exposed surface will bear a well-ordered repeating pattern on the scale of nanometers. This surface is potentially useful as a template for nanolithography.

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**Figure 15** Schematic depiction of symmetric DCP morphologies in thin slits. Panel a shows a perpendicular lamellar structure while panel b shows parallel lamellae. \( D \) is the slit thickness and \( L_b \) is the natural lamellar period.
Much work has been done in predicting the orientation of these lamellae, which is strongly dependent upon the nature of the confining surface(s) and the film thickness \(D\) \cite{83-85}.

Surfaces that interact preferentially with one block of the diblock copolymer induce wetting of the surface by that component, resulting in the formation of parallel lamellae. Depending on the nature of each of the surfaces (where the air-polymer interface of a film may be considered as a surface), either symmetric or asymmetric wetting will be favored, which have preferred film thicknesses of either \(nL_b\) or \((n + 1/2)L_b\), respectively. Molten diblock copolymers constrained to different film thicknesses will either (for slits) form lamellae with periods stretched or compressed from their unconstrained values or (for films) form islands or holes at the free surface. The formation of both parallel and perpendicular lamellae, as well as the formation of islands and holes at the free surface, has been observed experimentally by a number of researchers \cite{92-98}.

It has been suggested that patterning one of the surfaces with alternating stripes that interact preferentially with the two types of diblock segments can lead to stable perpendicular lamellar morphologies with a greater degree of lateral homogeneity than those formed on homogeneous surfaces \cite{99-107}. The remainder of this section is devoted to understanding how factors such as the natural bulk lamellar period \(L_b\), film thickness, surface interfacial energy, and surface patterning period \(L_s\) influence the morphology of the confined melt.

This problem has been studied theoretically by many researchers. Petera & Muthukumar employed both mean-field and self-consistent field theories \cite{99, 100} to examine the problem. Another coarse-grained model was proposed by Chen & Chakrabarti \cite{101}, who employed a Landau-Ginzburg free energy functional combined with the Cahn-Hilliard formalism to study a diblock melt confined between striped and neutral walls. Nath, Nealey & de Pablo \cite{106} utilized density functional theory to provide information on the length scale of the molecule. Wang and coworkers \cite{108} attacked the problem using exhaustive lattice Monte Carlo simulations. The most useful strategy appears to use phenomenological models, first employed by Pereira & Williams \cite{102-105, 107} and elaborated by Wang et al \cite{109}.

The essence of work in the area can be captured by briefly discussing the SCF theory, the phenomenological model, and their connections with experiments.

Petera & Muthukumar \cite{100} use a SCF theory to generate possible equilibrium structures for the molten diblock copolymers below the ODT between striped and neutral or (preferentially) attractive walls. They do this by slowly lowering the temperature of an initially disordered state through the ODT while allowing the system to relax to a free energy minimum. They find the ratio of parameters \(L_s\) (the surface pattern period) and \(L_b\) (the natural bulk lamellar period) to be important, as well as the film thickness \(D\). In addition to these geometrical parameters, the degree of chemical inhomogeneity \(\chi\) (where \(\chi_n\) is the Flory interaction parameter between segment types and \(n\) is the number of segments constituting each diblock) and the nature of the second wall (neutral or repulsive) also play pivotal roles in determining morphologies.
We begin a brief discussion of their theory by writing their Hamiltonian (H) for molten diblocks of length N (with n Kuhn segments of length l) composed of fn segments of type A.

\[ H = \sum_{i=1}^{N} \frac{1}{2l^2} \int_0^L d\tau \left( \frac{\partial \mathbf{R}_i(\tau)}{\partial \tau} \right)^2 + \sum_{i,j=1}^{N} \left[ \frac{\omega_{AA}}{2} \int_0^L d\tau \int_0^L d\tau' \delta(\mathbf{R}_j(\tau) - \mathbf{R}_i(\tau')) + \frac{\omega_{BB}}{2} \int_0^L d\tau \int_0^L d\tau' \delta(\mathbf{R}_j(\tau) - \mathbf{R}_i(\tau')) + \frac{\omega_{AB}}{2} \int_0^L d\tau \int_0^L d\tau' \delta(\mathbf{R}_j(\tau) - \mathbf{R}_i(\tau')) \right] \]

where \( \omega_{ij} \) is the segment-segment interaction energy and \( V_{si} \) is the segment-surface interaction energy.

Providing for weak compressibility with a quadratic term and introducing coarse grained density fields

\[ \rho_A(\mathbf{x}) = \sum_{i=1}^{N} \int_0^L d\tau \delta(\mathbf{x} - \mathbf{R}_i(\tau)) \quad \rho_B(\mathbf{x}) = \sum_{i=1}^{N} \int_0^L d\tau \delta(\mathbf{x} - \mathbf{R}_i(\tau)) \]

the Hamiltonian becomes

\[ H' = N \ln(N - 1) - N \ln S[\Phi_A, \Phi_B] \]

\[ + \int d^d x \left\{ \frac{\omega_{AA}}{2} \rho_A^2(\mathbf{x}) + \frac{\omega_{BB}}{2} \rho_B^2(\mathbf{x}) + \omega_{AB} \rho_A(\mathbf{x}) \rho_B(\mathbf{x}) \right\} \]

\[ + \frac{\lambda}{2} (\rho_A(\mathbf{x}) + \rho_B(\mathbf{x}) - \rho_o) \]

where

\[ S[\Phi_A, \Phi_B] = \]

\[ \int d\mathbf{R}(\tau) \exp \left[ \frac{-1}{2l^2} \int_0^L d\tau \left( \frac{\partial \mathbf{R}(\tau)}{\partial \tau} \right)^2 - \int_0^L d\tau (i\Phi_A(\mathbf{R}(\tau)) + V_{SA}(\mathbf{R}(\tau))) \right] \]

\[ - \int_0^L d\tau (i\Phi_B(\mathbf{R}(\tau)) + V_{SB}(\mathbf{R}(\tau))) \]

\[ \rho_o = \frac{nN}{V} \]
The functional integrals over the fields $\rho_A(x)$, $\rho_B(x)$, $\phi_A(x)$, and $\phi_B(x)$ are evaluated using the saddle point approximation. With the assumption $\omega_{AA} = \omega_{BB} = \omega$, this leads to the following SCF equations:

$\rho_A(x) = N \int_0^{\tau_n} d\tau q_1(x, \tau) q_2(x, n - \tau) / \int d^3x q_1(x, n)$

$\rho_B(x) = N \int_0^{(1-f)n} d\tau q_1(x, \tau) q_2(x, n - \tau) / \int d^3x q_2(x, n)$

Beginning with a homogeneously disordered density field, these equations are iterated until the density stops changing. To simulate the temperature decrease, the final state of a higher temperature calculation is used as the initial state of a lower temperature calculation. Resultant density fields for several different sets of parameters are displayed in Figure 16.

In the case of commensurate values of $L_s$ and $L_b$ (Figure 16a and b), perpendicular lamellae are only supported provided that the top wall is neutral. The presence of a preferentially attractive top wall was found to promote parallel lamellae in that region. This arrangement minimizes interfacial energy, as well as that through most of the film; very near the patterned surface, however, the diblocks align with the other surface to minimize its interfacial free energy. The authors also consider cases of incommensurability. When $L_s > L_b$ (Figure 16c and d) they find the lamellae tilt in order to minimize both the interfacial free energy and stretching free energy of the diblock chains. For $L_b > L_s$ (Figure 16e and f) they find that the chains undergo compression near the surface to match their period with that of the surface. This effect dissipates further into the film and parallel lamellae emerge unless the film is very thin ($D < 2 L_b$, as shown in f), whereupon the film cannot
Figure 16  Graphical depiction of self-consistent field theory results. Adapted from (100). Shading indicates density variations. (a) Commensurate case with neutral top surface. (b) Commensurate case with preferential top surface. (c) Neutral top surface with ratio $L_s/L_b = 1.5$. (d) Neutral top surface with ratio $L_s/L_b = 3$. (e) Neutral top surface with ratio $L_s/L_b = 0.75$. (f) Thinner slit with neutral top surface and ratio $L_s/L_b = 0.75$. 
support the high energy transition region between morphologies, and purely perpendicular lamellae persist throughout the film.

Some of these predictions are verified by experiments conducted by Rockford et al (110) for symmetric PS-PMMA diblock copolymer films on striped SiO$_2$-Au surfaces. The films are annealed under vacuum, corresponding to a neutral free surface. This study examines the regime in which $D < 2L_b$ for varying ratios of $L_b/L_s$. Only for the commensurate case are perpendicular lamellae formed that align with the surface pattern. For near commensurate cases, perpendicular lamellae are formed, but with significant structural defects. Cases in which $L_b$ and $L_s$ differ greatly show very little structure. Unfortunately, cases with $D > 2L_b$ are not studied, so the effects of the second surface and the possible formation of mixed lamellar structures have not been observed.

Forgoing a treatment that starts from a microscopic Hamiltonian (vide supra), many researchers have attempted to understand the morphologies present in thin diblock copolymer films by employing variants of essentially the same phenomenological theory. In this method, the free energy of the molten diblock copolymer film (in the strong segregation limit) is calculated as a sum of several contributions: a copolymer-copolymer interfacial contribution, copolymer-surface interfacial contribution, an elastic contribution and, if undulations in the lamellae are being considered, a bending contribution. In this method, a set of possible morphologies is proposed, and the free energy is calculated by summing the various contributions listed above. The theory predicts the melt to adopt the morphology that minimizes the free energy. With the variation of system parameters such as interfacial energies (segment-segment or segment-surface) and surface pattern periods, for example, a phase diagram for the melt may be constructed.

Pereira & Williams (102–105, 107) first applied this type of theory to the problem of a molten diblock copolymer confined in a thin slit with a heterogeneous surface. [This type of theory has been previously applied to molten diblock polymers (89, 111–115).] In their most inclusive study (105) they consider five different potential morphologies: perpendicular lamellae with period matching the surface pattern, perpendicular lamellae with the natural bulk period, parallel lamellae, and two mixed morphologies consisting of parallel lamellae over each of the two perpendicular lamellae (see Figure 17). Wang and co-workers (103) later applied the same type of theory to a more general set of eight morphologies that were observed in Monte Carlo simulations (108). Their set of morphologies is shown in Figure 18 and contains several that Pereira & Williams did not include, namely a checkerboard morphology, a mixed perpendicular lamellar morphology, and mixed checkerboard/lamellar structures.

In this section we have briefly discussed work that seeks to identify the regions of parameter space in which upon placing a diblock copolymer melt near a patterned surface, a regular periodic domain structure is induced at the exposed polymer surface. This work has been illustrated through both a SCF theory and a phenomenological model. The results give some general guidelines for the fabrication
Figure 17  Potential morphologies of Pereira & Williams (adapted from 104). They are: (a) Perpendicular lamellae with surface pattern period. (b) Perpendicular lamellae with natural period. (c) Parallel lamellae. (d) Mixed morphology with parallel lamellae near top surface and perpendicular surface-directed lamellae penetrating a distance $H_0$ from the patterned surface. (e) Mixed morphology with parallel lamellae near top surface and perpendicular natural lamellae penetrating a distance $H_0$ from the patterned surface. Periodic lines below bottom surface indicate surface patterning.

of such nanostructures. Efforts to fabricate such structures should concentrate on thin films between patterned-neutral surfaces with surface pattern periods commensurate with the bulk lamellar period of the diblock melt. Future efforts will illuminate whether or not the creation of defect-free nanostructures of this type is possible, and whether the fabrication of such nanoscale features is useful in applications.

CONCLUDING REMARKS

In the past three decades, much progress has been made toward understanding the fundamental physical chemistry of polymer adsorption processes. This understanding has also been harnessed for the creation of better commodity products where adsorbed polymer layers play a crucial role. It is expected that future
Figure 18  Potential morphologies of Wang et al (adapted from 109). They are (a) Natural perpendicular lamellae. (b) Surface directed perpendicular lamellae. (c) Checkerboard morphology. (d) Mixed morphology of surface lamellae near the patterned surface and bulk lamellae near the top surface. (e) Mixed morphology of checkerboard near the patterned surface combined with perpendicular bulk lamellae. (f) Parallel lamellae. (g) Mixed morphology of perpendicular surface lamellae near the patterned surface combined with parallel lamellae. (h) Mixed morphology of checkerboard morphology near the patterned surface combined with parallel lamellae. Periodic lines below bottom surface indicate surface patterning.

Applications will demand the creation and processing of information on short length scales (tens of nanometers). In response to external input (stimuli), nature often employs self-assembly processes to create specific structural motifs that are useful for a specific function. In other words, given certain inputs, self-assembly is used to process this information on short length scales and generate a specific function. In many instances, macromolecules are used as the molecular building
blocks that self-assemble into specific structures. A question that suggests itself is: Can we design synthetic macromolecular systems that can self-assemble into functionally useful nanoscale structures when stimulated by certain external conditions? Such processes may be found useful in prospective technologies where creation and processing of information on short length scales are desired.

In this article, we have briefly reviewed three examples where polymer adsorption processes can mediate self-assembly into specific nanostructures when particular external conditions are presented. In the first example, the external stimulus is a surface bearing a target pattern of binding sites. We have considered how the sequences of polymers can be designed such that they can rapidly search the patterns of binding sites on a surface, find the target pattern, and then bind to it in a class of conformations. In other words, we have considered the minimal requirements for biomimetic recognition between polymers and surfaces. In the second example, the external stimulus is provided by biological molecules (DNA) in solution that can bind with specificity to an adsorbed layer of complementary ssDNA immobilized on a microcantilever. The physical origins of strategies that allow the manipulation and control of nanomechanical motion of these cantilevers due to such specific biomolecular interactions were described. These strategies may prove useful in future applications requiring sensing and actuation on short length scales (e.g. medical diagnostic tools). The third example considered how surfaces bearing periodic patterns on the nanometer scale could be created by self-assembly of diblock copolymers adjacent to surfaces bearing periodic patterns on the nanometer scale.

The examples described in this review, and many others, constitute early attempts to develop functional materials that self-assemble in response to external inputs. Future research at the crossroads of physical chemistry, materials science, and biology, using theory, computer simulation, physical characterization experiments, and synthesis, should allow progress toward discovering strategies and implementing them in the creation of such responsive nanometer scale objects. Perhaps, some day, such studies will enable the design of synthetic systems that can mimic processes such as the assembly of micron-sized patterns of nanometer-size proteins that constitute synapses formed during exquisitely specific cell-cell recognition processes necessary for signal transduction and concomitant biological responses (116, 117).

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Figure 4  These panels show examples of statistical patterns. Panel a shows alternating and blocky surface patterns while panel b shows alternating and blocky DHP sequences.
Figure 5  Surface onto which four patterns with two types of sites have been put. The top right (bottom left) quadrant bears an alternating (blocky) pattern (within a correlation length of approximately 1.6 lattice units) while remaining two quadrants have a statistically uncorrelated distribution of sites (zero correlation length).
Figure 6  Surface from Figure 5 with typical polymer center of mass trajectories shown. The DHPs are characterized by \( f = 0.5 \) and \( \lambda = 0.4 \) or \( \lambda = -0.4 \). The black (white) trajectory is for a statistically alternating (blocky) DHP. Starting and ending positions are denoted by \( 1(1') \) and \( 2(2') \) respectively.
Figure 11  Six sequential snapshots taken from a typical trajectory. The top three panels depict the DHP in the wrong region of the surface, while the bottom three panels show the DHP strongly adsorbed in the pattern matched region.