Conformational Transitions of Non-Grafted Polymers Near an Adsorbing Substrate

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We have performed multicanonical chain-growth simulations of a polymer interacting with an adsorbing surface. The polymer, which is not explicitly anchored at the surface, experiences a hierarchy of phase transitions between conformations binding and non-binding with the substrate. We discuss the phase diagram in the temperature–solubility plane and highlight the transition “path” through the free-energy landscape.

PACS numbers: 05.10.-a, 87.15.Aa, 87.15.Cc

The recent developments in single molecule experiments at the nanometer scale, e.g., by means of atomic force microscopy (AFM) and optical tweezers, allow now for a more detailed exploration of structural properties of polymers in the vicinity of adsorbing substrates. The possibility to perform such studies is of essential biological and technological significance. From the biological point of view the understanding of the binding and docking mechanisms of proteins at cell membranes is important for the reconstruction of biological cell processes. Similarly, specificity of peptides and binding affinity to selected substrates could be of great importance for future electronic nanoparticle circuits and pattern recognition devices. Since single-molecule experiments allow monitoring of polymer chains adsorbed at surfaces, the investigation of structural deformations of the polymer shape near substrates is a central aspect of experimental, computational, and theoretical studies.

In computer simulations and analytical approaches, typically, one end of the polymer is anchored at a flat substrate and the influence of adhesion and steric hindrance, pulling forces or external fields on the shape of the polymer is considered. The question how a flexible substrate, e.g., a cell membrane, behaves as a reaction of a grafted polymer, was, for example, addressed in Refs. Proteins exhibit a strong specificity as the affinity of peptides to adsorb at surfaces depends on the amino acid sequence, solvent properties, and substrate shape. This was experimentally and numerically studied, e.g., for peptidelmetal and peptide-semiconductor interfaces. Binding/folding and docking properties of lattice heteropolymers at an adsorbing surface were subject of a recent numerical study.

In this work we investigate in detail the temperature and solubility dependence of adsorption properties for a polymer which is not fixed at the surface of the substrate with one of its ends. This model was inspired by the experimental setup used in Refs., where the peptides are initially freely moving in solution before adsorption. Therefore, there are two main differences in comparison with studies of polymers explicitly grafted at the substrate: First, the chain can completely desorb from the substrate allowing for the investigation of the binding/unbinding transition. Second, adsorbed conformations are possible, where none of the two polymer ends is in contact with the surface.

We use a lattice model for a polymer near an adsorbing substrate where nearest-neighbor contacts between monomers (nonadjacent along the chain) and contacts between monomers and the substrate are assigned different energy scales. The polymer energy is given by

\[ E = -\varepsilon_s n_s - \varepsilon_m n_m, \]  

where \( n_{s,m} \) are the numbers of contacts with the surface and between the monomers, respectively. The associated energy scales are set to \( \varepsilon_s = 1 \) and \( \varepsilon_m = s \), for convenience. The solvent parameter \( s \) takes account of the goodness of the implicit solvent and rates the two energy scales. As a first guess, \( s > 0 \) for a poor solvent, where globular conformations of the polymer are preferred. For \( s = 1 \), adsorption and collapse are equally attractive for the polymer. Negative values of \( s \) refer to good solubility and stretched conformations dominate. The partition sum per surface area \( A \) for the polymer with the described properties at inverse temperature \( \beta = 1/k_B T \) (\( k_B \equiv 1 \) in the following) can be written as

\[ Z(\beta, s)/A = \sum_{n_{s,m}} g_{n_{s,m}}^u e^{\beta (n_s + sn_m)}, \]  

where \( g_{n_{s,m}}^u \) stands for the density of unbound conformations, whereas \( g_{n_{s,m}}^b \) is the density of surface and intrinsic contacts of all conformations bound to the substrate. Since the number of unbound conformations in the half-space accessible to the polymer is unrestricted, \( g_{n_{s,m}}^u \) formally diverges. For regularization, we introduce an impenetrable (but neutral, i.e., non-adhesive) wall at a sufficiently large distance \( z_w \) from the substrate, in order to keep its influence on the unbound polymer small.

We apply the powerful multicanonical chain-growth algorithm, originally introduced for the simulation of lat-
The whole phase diagram can in principle be constructed by reweighting the density of contacts with respect to quantities such as, e.g., the specific heat are obtained on PERM chain-growth \[20\], the contact distributions for unravelling the detailed structure of the phase diagram, in particular, at low temperatures, where most energetic difficulties. In order to break correlations being inherent in the chain-growth process, we averaged over independent simulations (including the determination of the multicanonical weights), and a total statistics of more than 10\(^n\)mer near an attractive substrate and the steric wall in also investigated polymers with up to 200 monomers \[22\]. For confirmation, we distinguish six thermodynamic phases, four for the adsorbed (AC1, AC2, AE1, AE2) and two for the desorbed (DC, DE) polymer \[23\]. In the adsorbed-collapsed phase AC1, all monomers are in contact with the substrate and the two-dimensional (single-layer) conformation (“film”) is very compact. The transition from AC1 to AC2 is the layering phase transition from single to double-layer conformations. The white transition lines within AC2 indicate pseudo-transitions to compact conformations with more than two layers. These transitions are expected to disappear in the thermodynamic limit. The transition line between AC1 and the adsorbed-expanded phase AE1 is the two-dimensional \(\Theta\) collapse. It separates the compact single-layered conformations in AC1 from the dissolved, but still basically two-dimensional conformations. White lines in AE1 indicate conformational transitions to unstructured conformations extending partially into the third dimension. The substrate-contacting layer is dissolved and although several layers can form, no explicit layering transitions are observed in this region. In contrast to AE1, the conformations dominating phase AE2 possess a very compact surface layer but less compact upper layers. As in AE1, the formation of higher-order layers is not accompanied with noticeable conformational transitions. The difference between AE1 and AE2 becomes more apparent when approaching the unbinding transition line to the phases DE and DC, where the polymer has completely desorbed from the substrate: In the desorbed-expanded phase DE random-coil conformations dominate, while in the desorbed-collapsed phase DC globular conformations are favored. Phases DE and DC are separated by the transition line indicating the three-dimensional \(\Theta\) collapse.

The main difference to a polymer which is explicitly anchored at the substrate with one of its ends, is the occurrence of the strong binding/unbinding transition between the A and D phases. In the D phases, the polymer can move freely within the cavity, restricted only by the presence of the two impenetrable walls. This transition influences, however, also the conformational behavior of the polymer in the phases AE1 and AE2, the latter not being present for the anchored polymer. In fact, phases AC2, AE2, and DC lie within the DC/SAG (surface-attached globule) regime of the anchored polymer, whose precise phase structure is not yet completely clarified. The phases AE1, AC1, and AC2 approximately coincide in the two systems for low temperatures, although the system in our study has more entropic freedom since also adsorbed conformations are possible, where none of the ends is anchored at the substrate. This may have consequences for the location of transition lines.

Apart from the thermodynamic transitions in the traditional meaning we also see pseudo-transitions being specific to the chosen number of monomers (e.g., a reorientation transition from the 5 \(\times\) 5 \(\times\) 4 cube with 25 surface contacts to the rotated cube exhibiting only 20 contacts with the substrate, which occurs within phase AC2 at \(T \approx 0.7\)). We are convinced that growing experimental capabilities will allow the observation of these effects also.
for short synthetic or naturally occurring polymers (e.g., peptides). Details of the different conformational phases will be reported elsewhere [22].

Thermodynamically, the conformations dominating a certain phase correspond to the minimum of a suitably coarse-grained free energy depending on a few characteristic observables of the system. The complexity of the free energy landscape and its dependence on external parameters such as temperature or solvent strongly influences the kinetics of phase transitions. For the polymer near an adsorbing surface we choose the numbers of monomer-substrate contacts, \( n_s \), and those between monomers, \( n_m \), as system observables. According to Eq. (2), the probability for a polymer conformation is given by \( p(n_s, n_m) \propto g_{n_s,n_m} \exp([n_s + sn_m]/T) \) and the contact free energy reads as

\[
F_{s,T}(n_s, n_m) = -T \ln p(n_s, n_m), \tag{3}
\]

where the temperature \( T \) and the solubility \( s \) are fixed external parameters.

In Fig. 2 we have included all minima of the contact free energy for the parameter set \( T \in [0, 4.0], s \in [-2.0, 4.0] \). Given a fixed solubility \( s \), the stability of a conformation with minimal free energy is connected with the range of temperatures \( \Delta T \) over which the associated free energy is actually the global free energy minimum. We have included into Fig. 2 for several fixed solubilities the “paths” of free energy minima hit when increasing the temperature from \( T = 0 \) up to \( T = 4 \), that is moving from right to left.

As an example we consider the case \( s = 1 \) for the whole region of temperatures. In Table I we have listed the conformational transitions the 100mer experiences by increasing the temperature. We start at \( T = 0 \) with the ground state which is a lamellar two-dimensional conformation with 100 surface contacts and 81 monomer-monomer contacts. This is the maximal compact conformation that is possible in two dimensions. Note that with a conformation characterising a phase we mean all typical conformations

| phase | \( T \) | \( n_s \) | \( n_m \) | typical conformations |
|-------|-------|-------|-------|----------------------|
| I     | 0.0 – 0.2 | 100   | 81    |                      |
|       | AC1    | II    | 0.2 – 0.5 | 100 | 77±1                 |
|       |        | IV    | 0.6 – 1.1 | 61±4 | 95±5                 |
|       |        | V     | 1.1 – 1.4 | 53±2 | 88±2                 |
|       |        | VI    | 1.4 – 2.2 | 50±4 | 71±7                 |
|       |        | DE    | 2.2 – ∞   | 0    | \( \leq 62 \)       |

The labels I to VII refer to the pseudo phases in the case \( s = 1 \), described in detail in the text and in Table I. The lines are only guides to the eye.

FIG. 2: Map of free energy minima identified in the space of contact numbers \( n_s \) with the substrate and \( n_m \) between monomers. Also shown are exemplified “paths” through the free-energy landscape for different fixed solvent parameters \( s \). The labels I to VII refer to the pseudo phases in the case \( s = 1 \), described in detail in the text and in Table I. The lines are only guides to the eye.

FIG. 3: Probability distribution \( p(n_s, n_m) \) for the 100mer in solvent with \( s = 1 \) at \( T = 0.49 \), where the polymer experiences the layering transition from single to double layer.
There are in fact about $10^{14}$ (including all symmetries except translation) different realizations of the ground state. The ground-state conformation remains stable until $T \approx 0.2$, where the structures become less ordered. The lamellar structure is dissolved, but all in all they are still two-dimensional and very compact. The conformational changes in the transition from I to II are rather local — in contrast to the probably actual phase transition from II to III at $T \approx 0.5$, where the number of surface contacts is drastically reduced to about half the value of the ground-state conformation and thus a second layer forms. In Fig. 2 this transition appears as a jump from the surface state $(n_s, n_m) = (100, 77)$ to $(58, 108)$. As can be seen in Fig. 3 the probability distribution $p(n_s, n_m)$ exhibits two distinct peaks at these temperatures, which is interpreted as strong signal for a first-order transition. Entering regime IV, i.e., the adsorbed-expanded phase AE2, the dissolution of the surface-contacting layer begins. This process continues after passing the pseudo-transition line to section V, where higher-order layers form. Respective bottom layer and upper layers still form connected parts — in contrast to phase VI (which belongs to AE1), where upper layers can break apart and form isolated islands. Increasing the temperature further, we approach the second strong first-order-like transition line isolated islands. Increasing the temperature further, we have also missed the two-dimensional $\Theta$ collapse on the substrate. For this to happen, the quality of the solvent would have to be better (i.e., smaller values of $s$). From the free-energy perspective, both collapse transitions are of second order, since the free-energy minima of the 100mer at $(n_s, 100)$ (two-dimensional surface-layer conformations) and $(0, n_m)$ (three-dimensional conformations without contact to the surface) change continuously for increasing temperature (see Fig. 2).

In this work, we have qualitatively analysed the complete phase diagram for a polymer with 100 monomers in solvent near an adsorbing substrate. By means of an analysis of the global minima in the free-energy landscape we discussed conformational transitions in the temperature and solubility parameter space. Two types of transitions are experienced by the polymer, phase transitions in the thermodynamic sense and transition-type cross-over effects which are specific to the given finite number of monomers. In the first case, further simulations of longer polymers combined with finite-size scaling analyses will give estimates for the associated transition lines. Physically perhaps even more interesting, however, are the geometrically induced cross-over effects which are expected to become more and more important as the high-resolution experimental equipment allows concrete measurements in the nanometer range and the design of nanoscale devices will take advantage of the specific properties of finite-length polymers.

We thank Karsten Goede for interesting discussions on peptide adsorption at semiconductor surfaces. This work is partially supported by the German-Israel-Foundation (GIF) grant No. I-653-181.14/1999.

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