Binding of molecules to DNA and other semiflexible polymers

Haim Diamant* and David Andelman
School of Physics and Astronomy, Raymond and Beverly Sackler Faculty of Exact Sciences, Tel Aviv University, Ramat-Aviv, 69978 Tel Aviv, Israel
(Received 21 October 1999)

A theory is presented for the binding of small molecules such as surfactants to semiflexible polymers. The persistence length is assumed to be large compared to the monomer size but much smaller than the total chain length. Such polymers (e.g., DNA) represent an intermediate case between flexible polymers and stiff, rodlike ones, whose association with small molecules was previously studied. The chains are not flexible enough to actively participate in the self-assembly, yet their fluctuations induce long-range attractive interactions between bound molecules. In cases where the binding significantly affects the local chain stiffness, those interactions lead to a very sharp, cooperative association. This scenario is of relevance to the association of DNA with surfactants and compact proteins such as RecA. External tension exerted on the chain is found to significantly modify the binding by suppressing the fluctuation-induced interaction.

PACS number(s): 61.25.Hq, 87.15.Nn, 87.14.Gg

I. INTRODUCTION

Aqueous solutions containing polymers and small associating molecules such as folded proteins and amphiphiles (surfactants) are commonly found in biological systems and industrial applications. As a result, extensive efforts have been devoted in the past few decades to the study of polymer-surfactant interactions [1,2]. In addition, there has been growing interest in the interactions between DNA macromolecules and surfactants, lipids, and short polyamines [3–10]. These interactions are relevant to various biochemical applications such as DNA extraction and purification [8–10] and genetic delivery systems [11]. Association of folded proteins (e.g., RecA) with DNA plays a key role in genetic regulatory mechanisms. Structural details of this association have been studied in recent experiments [12,13].

Recently, we have presented a general theory for the self-assembly in aqueous solutions of polymers and smaller associating molecules [14,15]. Two different scenarios emerge, depending on the flexibility of the polymer. If the polymer is flexible enough, it actively participates in the self-assembly, resulting in mixed aggregates jointly formed by the two species. The polymer conformation changes considerably upon self-assembly but remains extended on a global scale, as the chain undergoes only *partial collapse* [14–16]. On the other hand, if the polymer is stiff, partial collapse is inhibited.

The criterion determining the ''flexible'' vs ''stiff'' scenarios concerns the polymer statistics on a mesoscopic length scale characterizing correlations in the solution (usually a few nanometers). It was found [14,15] that the flexible (stiff) scenario holds if the exponent ν, relating the number of monomers N to the spatial size R they occupy, $R \sim N^{\nu}$, is smaller (larger) than $2/d$ on that length scale (d being the dimensionality). This distinction is analogous to the one made in the critical behavior of certain disordered systems [17,18]—if the critical exponent ν of a system satisfies $\nu < 2/d$, the critical behavior is smeared by impurities (in analogy to the partial collapse), whereas if $\nu > 2/d$, the critical point remains intact. Indeed, neutral flexible polymers in three dimensions, having $\nu \simeq 3/5 < 2/3$, are found by scattering experiments to associate with surfactants in the form of a ''chain of wrapped aggregates'' [19,20]. On the other hand, stiff DNA molecules, having $\nu = 1$ on the relevant length scale, are found either to remain unperturbed by surfactant binding [6,9], or to undergo a discontinuous coil-to-globule transition [5], provided the chain is much longer than the persistence length.

In previous publications [14,15] we concentrated on the flexible case and the corresponding partial collapse, where the polymer degrees of freedom play an important role. In the opposite extreme limit of stiff, rodlike molecules, the conformational degrees of freedom of the polymer can be neglected and the chain may be regarded as a linear ''binding substrate.'' Models for stiff polymers, inspired by the Zimm-Bragg theory [21], treat the bound molecules as a one-dimensional lattice-gas (or Ising) system with nearest-neighbor interactions [22]. They have been widely used to fit experimental binding isotherms for polyelectrolytes and oppositely charged surfactants [23]. Recently, more detailed electrostatic models have been proposed for the interaction between rodlike polyelectrolytes and oppositely charged surfactants [24,25]. In addition, a theoretical work focusing on the *specific* binding of proteins to DNA has been presented recently [26], treating a pair of bound proteins as geometrically constraining inclusions on the DNA chain.

In the current work we address the intermediate case of *semiflexible* polymers. The polymer we consider is stiff in the sense defined above, i.e., its persistence length, l_p, exceeds several nanometers and, hence, the polymer is characterized by $\nu = 1 > 2/3$ on that length scale. The total chain length, however, is considered to be much larger than l_p, and therefore the entire polymer cannot be regarded as a single rigid rod. This case corresponds, in particular, to experiments on long DNA molecules [3–10], whose persistence length is typically very large (of order 50 nm), but much smaller than the total chain length (which is usually larger than a micron)

*Present address: The James Franck Institute, The University of Chicago, 5640 South Ellis Avenue, Chicago, IL 60637.

[27]. We argue that such an intermediate system may, in certain cases, be governed by different physics. Although the polymer is too stiff to change conformation and actively participate in the self-assembly, its degrees of freedom induce attractive correlations between bound molecules. Those fluctuation-induced correlations are weak but have a long spatial range (of order l_p) and, hence, may strongly affect the binding thermodynamics.

The model is presented in Sec. II. Bound molecules are assumed to modify the local features of polymer conformation, e.g., change its local stiffness. In the limit of weak coupling, our model reduces to the Kac-Baker model [28–30], which is solvable exactly. This limit is discussed in Sec. III. Although turning out to be of limited interest in practice, the weak-coupling limit provides insight into the mechanism of association, and helps us justify further approximations. Section IV presents a mean-field calculation for an arbitrary strength of coupling. This analysis leads to our main conclusions, and in Sec. V it is extended to polymers under external tension. The results are summarized in Sec. VI, where we also discuss several relevant experiments involving DNA and point at future directions.

II. THE MODEL

Small molecules bound to stiff polymers are commonly modeled as a one-dimensional lattice gas (or Ising system) [22]. Each monomer serves as a binding site, which can either accommodate a small molecule or be empty, and the surrounding dilute solution is considered merely as a bulk reservoir of small molecules. In the current work we stay at the level of a one-dimensional model, assuming that the polymer is still quite stiff (yet not infinitely stiff), i.e., the persistence length is much larger than the monomer size. In addition, a dilute polymer limit is assumed, where interchain effects can be neglected. We focus on the effect of introducing the polymer degrees of freedom and, hence, seek a simple meaningful coupling between the polymer and the bound lattice gas.

A polymer configuration is defined by a set of vectors, $\{\mathbf{u}_n\}_{n=1,\ldots,N}$, specifying the lengths and orientations of the N monomers. In addition, each monomer serves as a binding site which can be either empty ($\varphi_n=0$) or occupied by a small molecule ($\varphi_n=1$). A configuration of the entire system is defined, therefore, by specifying $\{\mathbf{u}_n,\varphi_n\}_{n=1,\ldots,N}$.

Since the polymer is assumed to be locally stiff, a natural choice would be to couple φ_n with the square of the local chain curvature, $\varphi_n(\mathbf{u}_{n+1}-\mathbf{u}_n)^2$, thus modifying the local chain stiffness. However, in the usual Kratky-Porod wormlike-chain model of semiflexible polymers [31], chain segments are taken as rigid rods of fixed length ($|\mathbf{u}_n|=\text{const}$), and each squared-curvature term contains only one degree of freedom (e.g., the angle θ_n between $\mathbf{u}_n$ and $\mathbf{u}_{n+1}$). Consequently, this coupling, $\varphi_n\cos\theta_n$, would leave $\{\varphi_n\}$ uncorrelated, leading merely to a trivial shift in the chemical potential of bound molecules [32]. One option to proceed is to consider higher-order extensions of the wormlike-chain Hamiltonian, involving three consecutive monomers. This will introduce correlations between bound molecules at different sites.

We take a simpler route, however, and modify the wormlike-chain model by allowing the monomer length to fluctuate. This modification was originally presented by Harris and Hearst [33], using a single global constraint for the average chain length. The modified model was shown to successfully reproduce the results of the Kratky-Porod model as far as thermodynamic averages (e.g., correlation functions, radius of gyration) were concerned. It was less successful, however, in recovering more detailed statistics of the wormlike chain (e.g., distribution function, form factor), particularly in the limit of large stiffness. The Harris-Hearst model was later refined by Lagowski *et al.* [34] and Ha and Thirumalai [35,36], replacing the single global constraint by a set of local constraints for the average segment lengths. This further modification was shown to be equivalent to a stationary-phase approximation for the chain partition function, yielding reliable results for average quantities, as well as more detailed statistics [35]. We note that a similar approach was used in a recent model of semiflexible polymer collapse [37]. It should be borne in mind that, despite its success in the past, the constraint relaxation remains essentially an uncontrolled approximation. In the current work we restrict ourselves to thermodynamic averages, such as monomer-monomer correlations and free energies, for which the modified model with a single global contraint can be trusted.

Thus, the rigid constraints of the original Kratky-Porod model, $u_n^2=1$, are relaxed into thermodynamic-average ones, $\langle u_n^2\rangle=1$, where the root-mean-square monomer size is taken hereafter as the unit length. Using the modified model for the chain, each $\varphi_n(\mathbf{u}_{n+1}-\mathbf{u}_n)^2$ term involves two consecutive monomers (and not merely the angle between them), leading to a meaningful coupling between binding and polymer conformation.

The partition function of the combined system of polymer and bound molecules is written, therefore, as

$$Z=\mathrm{Tr}_{\{\varphi_n=0,1\}}\int\prod_{n=1}^{N}\mathrm{d}\mathbf{u}_n\exp(-\mathcal{H}),$$

$$\mathcal{H}=\frac{3}{4}l_p\sum_{n=1}^{N-1}(1+\epsilon\varphi_n)(\mathbf{u}_{n+1}-\mathbf{u}_n)^2+\sum_{n=1}^{N}\lambda_n u_n^2-\mu\sum_{n=1}^{N}\varphi_n. \tag{1}$$

In Eq. (1) l_p is the persistence length of the bare chain, characterizing its intrinsic stiffness. It is assumed to be much larger than the monomer size, $l_p\gg 1$. The coupling is introduced through the stiffness term, assuming that a bound molecule modifies the local stiffness by a fraction $\epsilon>-1$, which may be either negative or positive but cannot change the positive sign of the overall stiffness term [38]. The second term contains a set of multipliers λ_n to be chosen so that the constraints $\langle u_n^2\rangle=1$ are satisfied. However, replacement of the entire set $\{\lambda_n\}$ by a single multiplier λ can be shown to yield a nonextensive correction [35], which becomes negligible in the limit $N\to\infty$. Hence, we use hereafter a single multiplier λ. Finally, the system is assumed to be in contact with a reservoir of solute molecules. The last term in Eq. (1) accounts for this contact along with any other factors that couple linearly to the degree of binding. Typically, μ contains the chemical potential of the solute reservoir and the

direct energy of solute molecule-monomer binding. (All energies in this work are expressed in units of the thermal energy k_BT.) Note that we have not included in Eq. (1) any direct short-range (e.g., nearest-neighbor) interactions between bound molecules. Thus, all interactions in the model arise from the coupling to the polymer degrees of freedom. Short-range interactions between bound molecules do exist in physical systems. Yet, in the limit of $l_p \gg 1$ and $|\epsilon| \gtrsim 1$, which is of interest to the current work, such direct interactions have a minor effect on binding, as is demonstrated in the following sections. Hence, we omit them for the sake of brevity.

As a reference, let us start with the previously studied partition function of the bare polymer [35],

$$Z_p = \int \prod_n d\mathbf{u}_n \exp\left(-\frac{3}{4} l_p \sum_n (\mathbf{u}_{n+1} - \mathbf{u}_n)^2 - \lambda \sum_n u_n^2 \right). \tag{2}$$

It is a Gaussian integral which can be calculated either by transforming it to Fourier space and integrating, or by analogy to the path integral of a three-dimensional quantum oscillator [39]. The result in the limit $N \to \infty$ and for $l_p \gg 1$ is

$$Z_p^{1/N} = \left(\frac{4}{3\pi l_p} \right)^{3/2} \exp(3 - \sqrt{3\lambda / l_p}). \tag{3}$$

The multiplier λ can now be determined according to

$$-\frac{1}{N} \frac{\partial \ln Z_p}{\partial \lambda} = \langle u_n^2 \rangle_p = 1 \Rightarrow \lambda = \frac{3}{4 l_p}, \tag{4}$$

where $\langle \cdots \rangle_p$ denotes a thermal average over the bare chain statistics (i.e., using Z_p). The corresponding free energy per monomer (in the ensemble of *constrained* $\mathbf{u}_n$) is

$$f_p = -\frac{1}{N} \ln Z_p - \lambda = \frac{3}{2} \ln l_p + \frac{3}{4 l_p} + \text{const.} \tag{5}$$

Various correlations in the bare chain can be calculated. The pair correlation between segment vectors along the chain sequence is

$$\langle \mathbf{u}_m \cdot \mathbf{u}_n \rangle_p = e^{-|m-n|/l_p}, \tag{6}$$

which explains why the parameter l_p has been defined as the persistence length. Two higher-order pair correlations are calculated as well,

$$g_1 \equiv \langle (\mathbf{u}_{n+1} - \mathbf{u}_n)^2 \rangle_p = \frac{2}{l_p} + O(l_p^{-2}),$$

$$g_2(m,n) \equiv \langle (\mathbf{u}_{m+1} - \mathbf{u}_m)^2 (\mathbf{u}_{n+1} - \mathbf{u}_n)^2 \rangle_p - g_1^2$$

$$= \frac{8}{3 l_p^3} e^{-2|m-n|/l_p} + O(l_p^{-4}), \tag{7}$$

and will be of use in the next section, where we reexamine the coupled system.

III. WEAK COUPLING

Let us return to the full partition function (1), which can be equivalently written as

$$Z = Z_p \, \mathrm{Tr}_{\{\varphi_n\}} \exp\left(\mu \sum_n \varphi_n \right) \times \left\langle \exp\left(-\frac{3 l_p \epsilon}{4} \sum_n \varphi_n (\mathbf{u}_{n+1} - \mathbf{u}_n)^2 \right) \right\rangle_p . \tag{8}$$

First we consider the weak-coupling limit, $|\epsilon| \ll 1$, where the partition function (8) can be treated by a cumulant expansion. In this limit the model becomes analogous to the exactly solvable Kac-Baker model [28–30], and we show that identical results are derived from a simple mean-field calculation. We then use this observation to justify a mean-field calculation for an arbitrary value of ϵ.

A cumulant expansion of Eq. (8) to second order in ϵ leads to

$$Z \simeq Z_p \, \mathrm{Tr}_{\{\varphi_n\}} \exp\left[\left(\mu - \frac{3 l_p \epsilon}{4} g_1 \right) \sum_n \varphi_n + \frac{1}{2} \left(\frac{3 l_p \epsilon}{4} \right)^2 \sum_{m,n} g_2(m,n) \varphi_m \varphi_n \right], \tag{9}$$

where the correlations g_1 and g_2 were defined in Eq. (7). Substituting expressions (7), the partition function is decoupled into a polymer contribution and an effective contribution from the bound solute molecules,

$$Z \simeq Z_p Z_s = Z_p \, \mathrm{Tr}_{\{\varphi_n\}} \exp(-\mathcal{H}_s),$$

$$\mathcal{H}_s = \frac{1}{2} \sum_{m \neq n} V_{mn} \varphi_m \varphi_n - \hat{\mu} \sum_n \varphi_n , \tag{10}$$

where

$$V_{mn} \equiv -\frac{3\epsilon^2}{2 l_p} e^{-2|m-n|/l_p},$$

$$\hat{\mu} \equiv \mu - \frac{3\epsilon}{2} + \frac{3\epsilon^2}{4 l_p}. \tag{11}$$

The introduction of the polymer degrees of freedom and their coupling to the binding ones have led to two effects, as compared to previous lattice-gas theories. First, there is a shift in the chemical potential, $\mu \to \hat{\mu}$. This is equivalent to an effective change in the affinity between the small molecules and the chain. As expected, if binding strengthens the local stiffness of the chain ($\epsilon > 0$), the affinity is reduced (i.e., the isotherm is shifted to higher chemical potentials), whereas if it weakens the stiffness ($\epsilon < 0$), the shift is to lower μ. [Recall that for small ϵ, the linear term in Eq. (11) is the dominant one.] The second, more interesting effect is that bound molecules experience an attractive potential V_{mn} along the chain. The amplitude of this effective interaction is small ($\sim \epsilon^2 / l_p$), but its range is large—of order l_p. When l_p is increased there are two opposing consequences: the interaction amplitude diminishes, while the interaction range is

extended. The overall effect on the thermodynamics of binding, therefore, has to be checked in detail.

A. Analogy with the Kac-Baker model

The effective Hamiltonian of the bound solute, $\mathcal{H}_s$, is a lattice-gas version of the Kac-Baker model [28–30], which is exactly solvable. Moreover, the procedure relevant to our semiflexible polymer, i.e., increasing l_p while keeping $1 \ll l_p \ll N$, is precisely the one studied in detail by Kac and Baker. Their results, as applied to our binding problem, can be summarized as follows. For any finite l_p, the bound molecules are always in a disordered state along the polymer chain, as in any one-dimensional system with finite-range interactions. Consequently, the binding isotherm, i.e., the binding degree $\varphi \equiv \langle \varphi_n \rangle$ as a function of μ [see, e.g., Fig. 2(a) below], is a continuous curve. However, in the limit $l_p \to \infty$, taken *after* the infinite-chain limit $N \to \infty$, there is a critical value of coupling above which the binding exhibits a discontinuous (first-order) transition. According to Baker's rigorous calculation [30], the critical value of the potential amplitude multiplied by l_p (equal, in our case, to $3\epsilon_c^2/2$) is 4, i.e.,

$$\epsilon_c^{\pm} = \pm \sqrt{8/3} \simeq \pm 1.63. \tag{12}$$

Note that the symmetry with respect to the sign of ϵ is merely an artificial consequence of our second-order expansion, Eq. (9). In general, the results should not be the same if the stiffness is weakened ($\epsilon < 0$) or strengthened ($\epsilon > 0$), as is demonstrated in Sec. IV.

The negative critical value in Eq. (12), $\epsilon_c^- \simeq -1.63$, lies outside the range of validity of the original polymer binding model, $\epsilon > -1$ [cf. Eq. (1)]. The positive value, $\epsilon_c^+ \simeq 1.63$, does not satisfy the assumption of weak coupling, $|\epsilon| \ll 1$, which led to the analogy with the Kac-Baker model in the first place. Thus, the sharp binding isotherms obtained from the Kac-Baker model for $|\epsilon| > \epsilon_c$ do not apply, strictly speaking, for our polymer binding problem. The weak-coupling calculation does demonstrate, however, how fluctuations in polymer conformation induce long-range attraction between bound molecules. This basic feature is expected to remain when one considers stronger coupling, $|\epsilon| > 1$, and the resulting many-body terms omitted in Eq. (9). This is further discussed in the following sections.

Finally, the polymers we consider have a large but finite l_p. For example, the persistence length of a DNA macromolecule is typically of order 50–100 nm, whereas the length of a single base pair is 0.34 nm. Hence, l_p is of order 10^2 (in units of monomer length). It is worth checking to what extent the sharpness of binding in the Kac-Baker model for $|\epsilon| > \epsilon_c$ is affected by finite l_p. For this purpose, let us define a *cooperativity parameter* for the binding, measuring the maximum slope of the binding isotherm,

$$C \equiv \left. \frac{\partial \varphi}{\partial \mu} \right|_{\max} - \frac{1}{4}. \tag{13}$$

This parameter is equivalent to the zero magnetic field susceptibility in the analogous spin system, and is commonly measured from the slope of binding isotherms obtained in potentiometric experiments [1,2]. It has been defined in Eq. (13) so as to yield zero for vanishing interaction ($\epsilon = 0$) and diverge at a critical point. (In the current weak-coupling limit, the maximum $\partial\varphi/\partial\mu$ is obtained for $\langle \varphi \rangle = 1/2$.) Given l_p and ϵ, the cooperativity is numerically calculated using Kac's exact solution [28,29], as is explained in the Appendix. Figure 1 presents the results for $l_p = 10$ and 50. For $l_p = 50$ the binding becomes highly cooperative for $|\epsilon| > \epsilon_c$. For even larger values of $l_p \sim 10^2$ (relevant, e.g., to DNA) the binding will be hardly distinguishable from that of an infinite l_p.

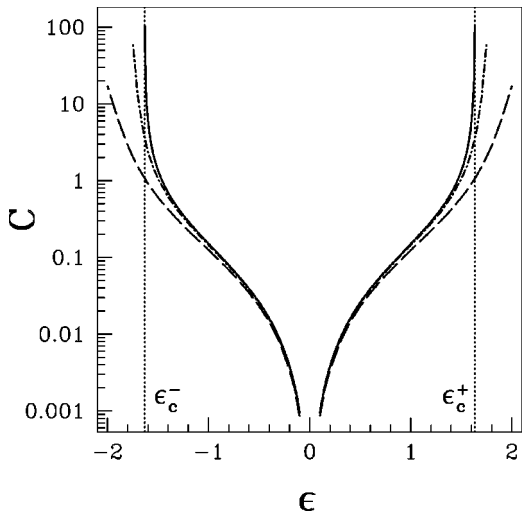

FIG. 1. Binding cooperativity as function of ϵ according to the Kac-Baker model, plotted on a semilogarithmic scale. The dashed and dash-dotted curves are results of numerical calculations for $l_p = 10$ and 50, respectively. The solid curves show analytic results for $l_p \to \infty$ as obtained by a mean-field calculation [Eq. (15)]. The critical points are at $\epsilon_c^{\pm} = \pm\sqrt{8/3}$ (dotted lines).

B. Mean-field calculation

In fact, the results of the Kac-Baker model in the limit $N \to \infty, l_p \to \infty$, while keeping $l_p < N$, can also be obtained from a simple mean-field calculation [28,40]. The heuristic argument for this agreement is the following: as l_p is increased, the range of interaction is extended and each bound molecule interacts with an increasing number of neighbors. As a result, the averaging assumption underlying the mean-field approximation is justified, and becomes *exact* when the range of interaction is taken to infinity. The correspondence between infinite-range models and mean field was rigorously proved by Lebowitz and Penrose for a more general class of potentials [41].

Indeed, employing a mean-field approximation for the potential (11) in the limit of very large l_p,

$$\sum_{mn} V_{mn} \varphi_m \varphi_n \to -\frac{3\epsilon^2}{2l_p} \left(\sum_{mn} e^{-2|m-n|/l_p} \right) \varphi^2 \simeq -\frac{3\epsilon^2}{2} N \varphi^2,$$

where φ is an average, uniform binding degree, we are led to the following mean-field free energy per monomer:

$$f = f_p + f_s \simeq f_p + \varphi \ln \varphi + (1-\varphi)\ln(1-\varphi) - \frac{3\epsilon^2}{4}\varphi^2 - \hat{\mu}\varphi \quad \text{for } l_p \to \infty. \tag{14}$$

It is easily verified that the critical point of this free energy is $\epsilon_c^2 = 8/3$, in agreement with the rigorous result, Eq. (12). The cooperativity parameter can be calculated as well from Eq. (14), yielding

$$C = \frac{\epsilon^2}{4(\epsilon_c^2 - \epsilon^2)} \quad \text{for } l_p \to \infty. \tag{15}$$

This expression shows the usual critical behavior obtained from mean-field theories, $C \sim |\epsilon - \epsilon_c|^{-\gamma}$ with $\gamma = 1$. The dependence of C on ϵ according to Eq. (15) is shown by the solid line in Fig. 1. The curves obtained from Kac's solution approach it, as expected, when l_p is increased. Recall that expressions (14) and (15) correspond to the original problem of bound molecules only in the limit of small ϵ.

IV. STRONG COUPLING

The interesting part of our theory requires $|\epsilon| \gtrsim 1$ and thus limits the interest in the analogy to the Kac-Baker model. Nevertheless, based on the heuristic argument given above, it is reasonable to assume that, in the limit $l_p \gg 1$, the mean-field approximation is good for larger values of $|\epsilon|$ as well [42]. The preceding section, discussing the Kac-Baker model in the weak-coupling limit, may be regarded, therefore, as a justification for using the mean-field approximation for one-dimensional models with large l_p and $|\epsilon| \gtrsim 1$. Applying a mean-field approximation to the binding degrees of freedom φ_n in our starting point, Eq. (1), the tracing over u_n can be done exactly. The resulting free energy is composed of the polymer free energy f_p evaluated with an effective persistence length $l_p \to l_p(1+\epsilon\varphi)$ and the entropy of mixing for φ,

$$f = f_p|_{l_p \to l_p(1+\epsilon\varphi)} + \varphi \ln \varphi + (1-\varphi)\ln(1-\varphi) - \mu\varphi. \tag{16}$$

Using Eq. (5), we obtain

$$f = \varphi \ln \varphi + (1-\varphi)\ln(1-\varphi) + \tfrac{3}{2}\ln[l_p(1+\epsilon\varphi)] + \frac{3}{4l_p(1+\epsilon\varphi)} - \mu\varphi. \tag{17}$$

For $\epsilon \ll 1$ and $l_p \gg 1$ this expression reduces, as expected, to our previous result for the weak-coupling limit, Eq. (14).

In the limit of only $l_p \gg 1$ the critical points of the free energy (17) are

$$\epsilon_c^- = \tfrac{2}{3}(2 - \sqrt{10}) \simeq -0.775, \quad \epsilon_c^+ = \tfrac{2}{3}(2 + \sqrt{10}) \simeq 3.44, \tag{18}$$

both of which lie within our general range of validity, $\epsilon > -1$. (Note the loss of symmetry with respect to the sign of ϵ, which was a consequence of the weak-coupling approximation in Sec. III.) The corresponding critical chemical potentials are

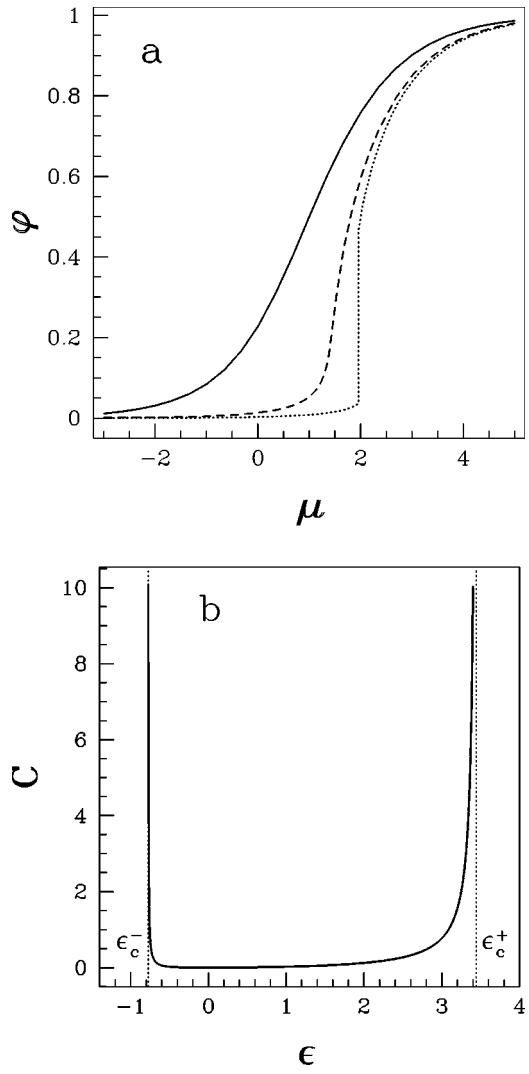

FIG. 2. (a) Binding isotherms obtained from the mean-field theory [Eq. (20)] for three different values of ϵ: $\epsilon = 1$ (solid line), $\epsilon = 3$ (dashed), and $\epsilon = 4$ (dotted), the last being beyond the critical point $\epsilon_c^+ \simeq 3.44$. The chemical potential μ is given in units of $k_B T$. (b) Binding cooperativity as function of ϵ according to the mean-field calculation [Eq. (21)]. The cooperativity diverges at the two critical points $\epsilon_c^\pm = 2(2 \pm \sqrt{10})/3$ (dotted lines), beyond which binding isotherms exhibit a first-order transition [see dotted curve in (a)].

$$\mu_c^\pm = \frac{3\epsilon_c^\pm(\epsilon_c^\pm + 2)}{4(\epsilon_c^\pm + 1)} - \ln(\epsilon_c^\pm + 1) \simeq \pm 1.67. \tag{19}$$

The binding isotherm, $\varphi = \varphi(\mu)$, as derived from Eq. (17), satisfies

$$\mu = \ln\frac{\varphi}{1-\varphi} + \frac{3\epsilon}{2(1+\epsilon\varphi)}, \quad l_p \gg 1. \tag{20}$$

Figure 2(a) shows three binding isotherms for three different values of ϵ below and above the critical point. The corresponding binding cooperativity is

$$C = \frac{8(1+\epsilon)^2}{3(2+\epsilon)^2(\epsilon - \epsilon_c^-)(\epsilon_c^+ - \epsilon)} - \frac{1}{4}, \quad l_p \gg 1. \tag{21}$$

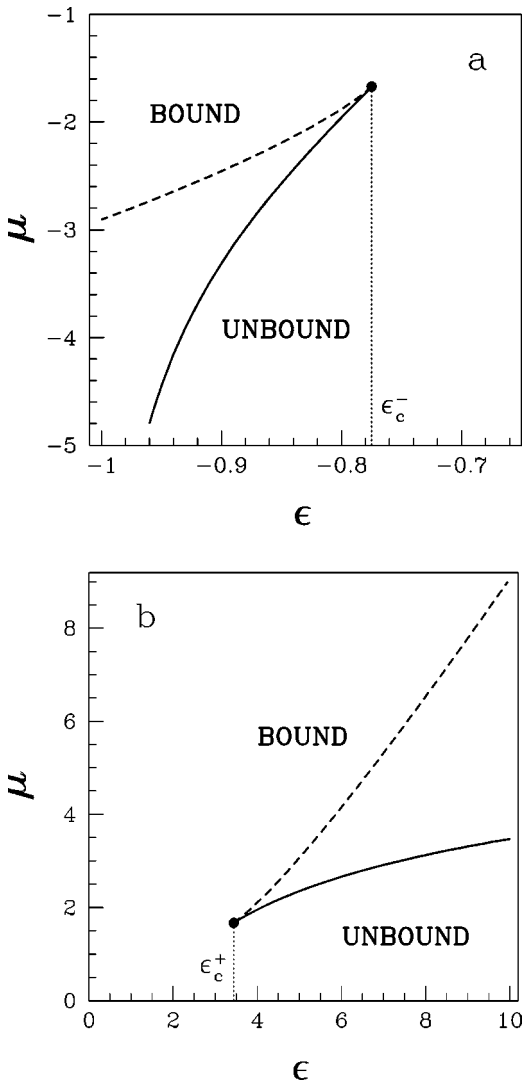

FIG. 3. Binding phase diagrams calculated from the free energy Eq. (17). (a) Phase diagram for stiffness-weakening binding ($-1<\epsilon<0$); (b) phase diagram for stiffness-strengthening binding ($\epsilon>0$). Solid and dashed lines indicate the binodal and spinodal, respectively. The lines meet at the critical points $(\epsilon_c^{\pm},\mu_c^{\pm})$ given by Eqs. (18) and (19). The chemical potential μ is given in units of k_BT.

As in Eq. (15), this expression exhibits the usual mean-field critical behavior, $C\sim|\epsilon-\epsilon_c|^{-\gamma}$ with $\gamma=1$. The dependence of C on ϵ is plotted in Fig. 2(b).

Finally, the binding phase diagram arising from Eq. (17) in the limit $l_p\gg1$ is depicted in Fig. 3. At the lower limit of model validity, $\epsilon\to-1$, the spinodal approaches a finite value, $\mu_{sp}=\ln(2/3)-5/2\simeq-2.91$, whereas the binodal diverges. Indeed, for $\epsilon\to-1$ the free energy (17) tends to $-\infty$ for $\varphi=1$, regardless of the value of μ, and the binodal is thus obtained at $\mu\to-\infty$. In this respect, the limit $\epsilon=-1$ for the bound molecules is similar to the limit of zero temperature—the induced interaction is so strong that the molecules condense for any value of the chemical potential. Note that in this special limit, $\epsilon\to-1$, $\varphi\to1$, the effective stiffness $l_p(1+\epsilon\varphi)$ becomes vanishingly small. This limit cannot be accurately treated within the continuum form of the semiflexible polymer Hamiltonian [38].

Equations (18)–(21) and the phase diagrams in Fig. 3 summarize the results obtained so far. They indicate that in cases of semiflexible polymers, where binding of small molecules significantly affects local chain features, the binding should be a very sharp process. For finite l_p the slope of the binding isotherm is finite, i.e., the binding is always continuous, yet for $l_p\sim10^2$ as in DNA, the behavior will be practically indistinguishable from a discontinuous phase transition.

It should be borne in mind that the sharp binding, obtained despite the one-dimensionality of the model, relies on the long range of the induced interaction. A direct short-range interaction between bound molecules could not produce a similar effect. Hence, such a short-range interaction (e.g., a nearest-neighbor interaction), which was omitted in Eq. (1) for the sake of brevity, does not have an important effect on the binding in the domain of interest, i.e., $l_p\gg1$ and $|\epsilon|\gtrsim1$.

V. CHAINS UNDER TENSION

In addition, we consider binding to semiflexible chains that are subject to external tension. This scenario is relevant to recent single-molecule manipulation experiments [12,13]. Since the tension suppresses chain fluctuations, it is expected to have a significant effect on the fluctuation-induced mechanism presented in the preceding sections.

In order to incorporate the external tension into our model, a term is to be added to the chain Hamiltonian [cf. Eq. (1)] [36],

$$Z=\mathrm{Tr}_{\{\varphi_n=0,1\}}\int\prod_{n=1}^{N}d\mathbf{u}_n\exp(-\mathcal{H}-\mathcal{H}_t),$$

$$\mathcal{H}_t=-\mathbf{t}\cdot\sum_{n=1}^{N}\mathbf{u}_n, \tag{22}$$

where $\mathcal{H}$ has been defined in Eq. (1), and $\mathbf{t}$ is the exerted tension (in units of k_BT divided by monomer length).

As in Sec. II, we begin with the previously studied problem of a bare semiflexible chain, yet it is now a chain under tension [36,43]. The additional tension term has not changed the Gaussian form of the polymer part of Z. It can be calculated, therefore, in a similar way to that of Sec. II, yielding

$$Z_{pt}^{1/N}=Z_p^{1/N}\exp(t^2/4\lambda), \tag{23}$$

where Z_p is the tensionless polymer partition function given in Eq. (3). The equation for the multiplier λ is, in this case,

$$\frac{1}{2}\left(\frac{3}{l_p\lambda}\right)^{1/2}+\frac{t^2}{4\lambda}=1, \tag{24}$$

which reduces to Eq. (4) for $t=0$. The resulting polymer free energy is

$$f_{pt}=\frac{3}{2}\ln l_p+\left(\frac{3\lambda}{l_p}\right)^{1/2}-\frac{t^2}{4\lambda}-\lambda, \tag{25}$$

where $\lambda=\lambda(l_p,t)$ is the solution to Eq. (24).

For $l_pt\ll1$, the solution for λ is

$$\lambda \simeq \frac{3}{4l_p}[1+\tfrac{8}{9}(l_p t)^2+O(l_p t)^4],$$

and the free energy becomes

$$f_{pt} \simeq f_p - \frac{l_p}{3}t^2 + O(l_p^3 t^4), \quad t \ll 1/l_p, \tag{26}$$

where f_p is the tensionless free energy given in Eq. (5). This is the elastic regime, where the energy is quadratic (i.e., the relative chain extension is linear) in tension [36,44]. Since we assume a large persistence length, this regime corresponds to very weak tension, $t \ll 1/l_p \ll 1$. In the opposite limit, $l_p t \gg 1$, the solution to Eq. (24) becomes

$$\lambda \simeq \frac{t}{2}\left[1+\frac{1}{2}\left(\frac{3}{2l_p t}\right)^{1/2}+O(l_p t)^{-1}\right],$$

and the corresponding free energy is

$$f_{pt} \simeq \tfrac{3}{2}\ln l_p - t + \left(\frac{3t}{2l_p}\right)^{1/2} + O(l_p^{-1}t^0), \quad t \gg 1/l_p. \tag{27}$$

In this regime the chain extension changes like the inverse square root of tension [36,45].

Let us turn now to the effect of tension on the system of polymer and bound molecules, Eq. (22). As in Sec. IV, we employ the mean-field approximation, valid for $l_p \to \infty$. The resulting free energy is the same as Eq. (17), but with f_{pt} instead of f_p,

$$f = f_{pt}|_{l_p \to l_p(1+\epsilon\varphi)} + \varphi \ln \varphi + (1-\varphi)\ln(1-\varphi) - \mu\varphi. \tag{28}$$

Due to the additional degree of freedom, namely, tension, the binding phase diagrams of Fig. 3 become three-dimensional. In particular, the critical points $\epsilon_c^{\pm}$ become critical lines, $\epsilon_c^{\pm}(t)$. (Note that $\mathbf{t}$ is an external field coupled to $\{\mathbf{u}_n\}$ rather than $\{\varphi_n\}$, and hence it does not destroy the critical behavior.) The ''condensation'' of bound molecules in our model results from attraction induced by polymer fluctuations. By suppressing fluctuations, the tension should weaken the attraction and shift the critical coupling to higher values, i.e., increase the positive critical point ϵ_c^+ and decrease the negative one, ϵ_c^-. Using Eqs. (24), (25), and (28), the critical lines $\epsilon_c^{\pm}(t)$ can be calculated. The results are shown in Fig. 4.

Before examining the detailed effect of tension, we address the question whether the critical behavior can survive *any* strength of tension. In this respect there is an essential difference between stiffness-strengthening binding ($\epsilon > 0$) and stiffness-weakening binding ($\epsilon < 0$). In the former case, since the value of ϵ is unbound, there exists $\epsilon_c^+(t)$ for any value of t, such that the binding is a sharp transition for $\epsilon > \epsilon_c^+(t)$. In other words, the critical line $\epsilon_c^+(t)$ exists for any $0 \leqslant t < \infty$. Indeed, substituting $\epsilon \to \infty$ in Eq. (28) while using Eq. (27), we find that the free energy always describes a sharp transition, regardless of the value of t. On the other hand, in the case of stiffness-weakening binding, there is a lower bound for ϵ, $\epsilon > -1$, where the validity of the entire approach breaks (see the previous section). Substituting $\epsilon = -1$ in Eqs. (28) and (27), we find that a critical point exists only for $t < t^*$, where

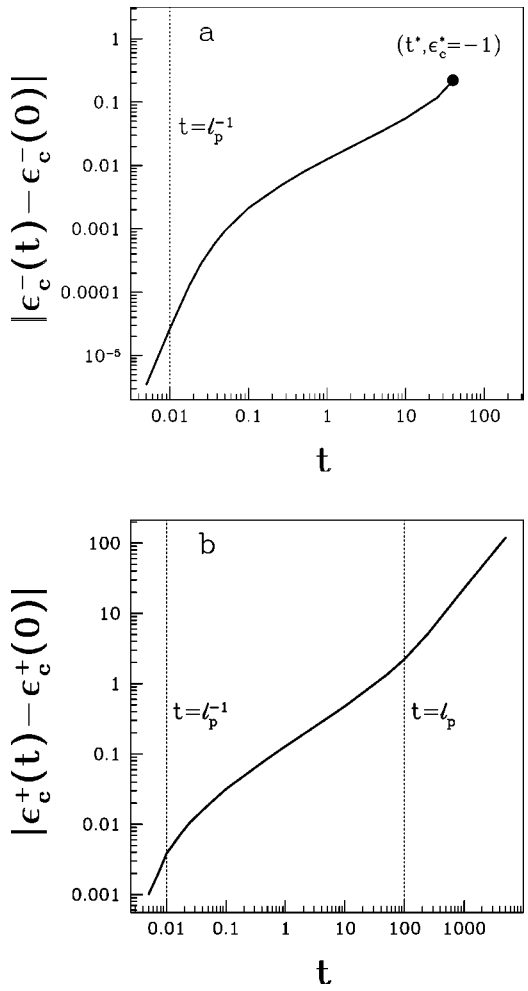

FIG. 4. Effect of tension on the critical behavior of binding. (a) Critical coupling $\epsilon_c^-(t) < 0$ as function of tension. Two regimes are found: for $t \lesssim 1/l_p$, $|\epsilon_c^-(t)|$ increases like t^4; for $t \gtrsim 1/l_p$, it increases like $t^{1/2}$. The critical line terminates at the point ($t^* \simeq 0.410 l_p$, $\epsilon_c^* = -1$), beyond which a sharp binding transition becomes unattainable. (b) Critical coupling $\epsilon_c^+(t) > 0$ as function of tension. Apart from the two regimes of (a) there is a third one for $t \gtrsim l_p$, where $\epsilon_c^+(t)$ increases linearly with t. The value taken for l_p in the numerical calculation is 100. The tension t is given in units of $k_B T$ divided by monomer length.

$$\frac{t^*}{l_p} = \tfrac{4}{9}(33 - 7\sqrt{21}) \simeq 0.410. \tag{29}$$

Thus, the critical line $\epsilon_c^-(t)$ terminates at the point (t^*, $\epsilon_c^* = -1$), beyond which a sharp binding transition cannot be attained. This situation is similar to a case where the critical temperature T_c coincides with $T = 0$ (e.g., in a one-dimensional Ising model), and the system is disordered at all temperatures $T > 0$.

Several regimes are found as function of tension. For very weak tension, $t < 1/l_p$, the leading-order term which couples binding and tension is found from Eqs. (26) and (28) to scale like $l_p t^2 \epsilon \varphi$, i.e., it is linear in φ. Hence, to leading order in

$l_p t$ there is no effect on the critical point. Although the tension influences chain fluctuations (e.g., causing the chain to extend linearly with t), it is too weak to affect the fluctuation-induced interactions between bound molecules. The next-order term scales like $l_p^3 t^4 (1+\epsilon\varphi)^3$, leading to a very small shift of $\sim l_p^3 t^4$ in the critical point (see also Fig. 4).

For $t > 1/l_p$, the leading-order term in the free energy, according to Eqs. (27) and (28), is $\sim (t/l_p)^{1/2}(1+\epsilon\varphi)^{-1/2}$. Here two regimes should be distinguished. For intermediate tension, $1/l_p < t < l_p$, the critical line scales like $(t/l_p)^{1/2}$, reflecting a more significant, yet still weak, effect of tension. Although the chain conformation is significantly stretched by tension in this regime, the induced interaction between bound molecules is not strongly affected. However, for $t > l_p$, the tension term in the free energy $\sim (t/l_p)^{1/2}(1+\epsilon\varphi)^{-1/2}$ becomes dominant, leading to a linear dependence of the critical point on tension, $\epsilon_c^+ \sim t/l_p$.

The above analysis for the dependence of the critical coupling on tension is summarized in the following expression:

$$|\epsilon_c^{\pm}(t) - \epsilon_c^{\pm}(0)| \sim \begin{cases} l_p^3 t^4, & t < 1/l_p \\ (l_p/t)^{1/2}, & 1/l_p < t < l_p \\ l_p/t, & t > l_p, \text{ relevant only to } \epsilon_c^+ . \end{cases} \tag{30}$$

The various regimes are also clearly seen in Fig. 4. Note that for the large values of l_p considered in this theory the intermediate tension region, $1/l_p < t < l_p$, is very wide.

VI. DISCUSSION AND CONCLUSIONS

We have considered the binding of small molecules to isolated semiflexible polymer chains, where the persistence length l_p is much larger than the monomer size but still smaller than the total chain length N. We have demonstrated that in such systems polymer fluctuations induce attraction between bound molecules. The long range of this interaction (of the same order as the persistence length) can lead to strong effects on the binding process. In particular, if bound molecules significantly affect local features of the chain, e.g., weaken or strengthen the stiffness by a factor of about 5 ($\epsilon < \epsilon_c^-$ or $\epsilon > \epsilon_c^+$), then the binding is predicted to be extremely cooperative, occurring as a transition for a sharply defined solute concentration. This is an unusual yet practical example for a one-dimensional system exhibiting a sharp transition due to long-range interactions. The results of the model should apply, in particular, to the association of DNA with smaller molecules such as surfactants and compact proteins.

Subjecting the polymer to external tension has been studied as well. By suppressing the fluctuation-induced interaction, the applied tension may strongly affect the binding. The effect is significant for sufficiently strong tension of order $t \sim l_p$. [For DNA this implies $t \sim 10^2 k_B T/(10\ \text{Å}) \sim 10^2$ pN.] In cases where binding weakens the chain stiffness, such a high tension should make the sharp binding transition disappear altogether (i.e., regardless of the strength of coupling or temperature). In cases where binding strengthens the chain stiffness, a tension of $t \gtrsim l_p$ significantly shifts ϵ_c^+ to higher values. It is worth mentioning that tension-induced pairwise interaction between *specifically* bound proteins on a DNA chain was studied in a previous work [26].

The interaction of DNA with oppositely charged cationic surfactants has been thoroughly studied by potentiometric techniques [3,4] and fluorescence microscopy [5,6]. Isotherms measured by potentiometry reveal a very cooperative, albeit continuous binding. Fluorescence microscopy convincingly demonstrated, however, that the binding to a *single* DNA molecule has a discrete nature resembling a first-order phase transition. It is usually accompanied by a coil-to-globule collapse of the DNA chain (which lies outside the scope of the current theory). The smoothness of potentiometric isotherms was shown to arise from averaging over an *ensemble* of DNA molecules, coexisting in bound and unbound states [5]. Similar results were obtained for the association of DNA with spermidine [7]. The microscopic origin of the observed cooperativity (or even discontinuous transition) has not been clarified. It is usually fitted to a phenomenological parameter describing strong interaction between nearest-neighboring bound molecules [22]. On the other hand, it is reasonable to expect that oppositely charged surfactants bound to DNA chains significantly modify the chain stiffness (probably weakening it). Thus, our model demonstrates that the strong cooperativity observed in experiments can be well accounted for by weak, yet long-range, interactions induced by polymer fluctuations.

Recently, the kinetics of nonspecific binding of RecA proteins to DNA has been studied by single-molecule manipulation [12,13]. RecA is a bacterial protein involved in DNA recombination and known to cause significant changes in the local structure of the double strand upon binding [46]. It was found to increase the DNA stiffness by a large factor, estimated to be around 10 in one study [12] and above 4 in another [13]. This corresponds to a large, positive ϵ in our model. A very cooperative nucleation-and-growth kinetics was observed, as expected from the current model. Moreover, in certain situations it was possible to achieve a smaller increase of stiffness by binding of RecA. This led, correspondingly, to a less cooperative process [13]. Yet probably the most compelling evidence is that the binding cooperativity was shown to be sensitive to external tension of order 10–100 pN. It was consequently deduced that DNA conformational fluctuations play a key role in RecA binding [12], in accord with the scenario suggested here.

The current work is restricted to one-dimensional interactions along the chain sequence, assuming that the polymer is locally stiff and obeys the wormlike-chain description. Apart from changing local properties of the polymer, an important feature not treated by the model is that bound molecules may also modify *volume* interactions between the monomers, thus affecting the three-dimensional conformation of the polymer. For example, binding of oppositely charged surfactants to a DNA molecule locally neutralizes the DNA charge. This should lead, indeed, to a modified stiffness, but also to a reduced second virial coefficient, which may drive a coil-to-globule collapse [5]. The collapse can be also driven by fluctuations in the concentration of ions adjacent to the chain, as has been demonstrated by recent theoretical studies [37,47].

In order to check the theory presented in this work more experiments are required, focusing, in particular, on the ef-

fect of persistence length and tension on binding. The fluorescence microscopy techniques, which have been successfully used for DNA-surfactant association, may be applied to chains under tension or flow, thus examining the role of fluctuations. It would be interesting to study a system consisting of a semiflexible polymer and bound molecules in computer simulations, and thereby check the applicability of our mean-field approximation. An important extension of the model, as mentioned above, would be to introduce volume interactions and obtain binding-induced collapse as observed in experiments.

ACKNOWLEDGMENTS

We greatly benefited from discussions and correspondence with R. Bar-Ziv, M. Feingold, A. Libchaber, R. Netz, A. Parsegian, R. Podgornik, M. Schwartz, V. Sergeyev, and K. Yoshikawa. Partial support from the Israel Science Foundation founded by the Israel Academy of Sciences and Humanities–Centers of Excellence Program, and the Israel-U.S. Binational Science Foundation (BSF), under Grant No. 98-00429, is gratefully acknowledged. H.D. would like to thank the Clore Foundation for financial support.

APPENDIX: NUMERICAL DETAILS

The aim of the numerical scheme is to calculate the results of the Kac-Baker model for finite l_p, which are presented in Fig. 1. Using Kac's solution [28,29], the partition function of bound solute molecules, Eqs. (10) and (11), is expressed in the limit $N\to\infty$ as

$$Z_s = \text{const}\times e_0^N, \tag{A1}$$

where e_0 is the largest eigenvalue of the following ''transfer kernel:''

$$K(x,y)=[(1+e^{\mu-3\epsilon/2+\sqrt{J}x})(1+e^{\mu-3\epsilon/2+\sqrt{J}y})]^{1/2} \times\exp\left(\frac{y^2-x^2}{4}-\frac{(y-e^{-2/l_p}x)^2}{2(1-e^{-4/l_p})}\right), \tag{A2}$$

where $J\equiv 3\epsilon^2/2l_p$ and $x,y\in(-\infty,\infty)$ are real variables.

We define a vector $\{x_i\}=\{(2i-M)d\}_{i=0,\ldots,M}$, where M is an even integer and d a real number, and use it to discretize the kernel $K(x,y)$ into a transfer matrix,

$$K_{ij}\equiv K(x_i,x_j). \tag{A3}$$

In addition, we define the diagonal matrix

$$A_{ij}\equiv x_i\delta_{ij}. \tag{A4}$$

Given l_p, ϵ, and μ, the transfer matrix K_{ij} is diagonalized and its largest eigenvalue e_0 is found.

The binding degree φ can be calculated in two ways. The first is by calculating the variation of $\ln e_0$ with respect to μ,

$$\varphi=\partial\ln e_0/\partial\mu. \tag{A5}$$

The second way is by using the equation

$$\varphi=\tilde{A}_{00}/(B\sqrt{J}), \tag{A6}$$

where $B\equiv\coth(1/l_p)$, and $\tilde{A}$ is the matrix A transformed to the basis where K is diagonal [48].

The cooperativity parameter C as defined in Eq. (13) is found by calculating the variation of φ with respect to μ around the point $\varphi=1/2$. The value $\mu=\mu_{1/2}$ which gives $\varphi=1/2$ is analytically found by transforming the lattice-gas partition function, Eqs. (10) and (11), into an Ising one ($\varphi_n\to s_n=2\varphi_n-1$), and requiring that the ''magnetic field'' coefficient should vanish. The result is

$$\mu_{1/2}=3\epsilon/2-JB/2. \tag{A7}$$

For each calculation (i.e., for each set of l_p, ϵ, and μ) the discretization parameters M and d were tuned until the result became insensitive to further refinement to six significant figures. In addition, the two methods for calculating φ were used and verified to yield identical results to six figures. All algebraic manipulations were performed using MATHEMATICA.

[1] *Interactions of Surfactants with Polymers and Proteins*, edited by E. D. Goddard and K. P. Ananthapadmanabhan (CRC Press, Boca Raton, FL, 1993).
[2] *Polymer-Surfactant Systems*, edited by J. C. T. Kwak (Marcel Dekker, New York, 1998).
[3] K. Hayakawa, J. P. Santerre, and J. C. T. Kwak, Biophys. Chem. **17**, 175 (1983).
[4] K. Shirahama, K. Takashima, and N. Takisawa, Bull. Chem. Soc. Jpn. **60**, 43 (1987).
[5] S. M. Mel'nikov, V. G. Sergeyev, and K. Yoshikawa, J. Am. Chem. Soc. **117**, 2401 (1995); **117**, 9951 (1995); S. M. Mel'nikov, V. G. Sergeyev, Y. S. Mel'nikova, K. Yoshikawa, J. Chem. Soc., Faraday Trans. **93**, 283 (1997); S. M. Mel'nikov, V. G. Sergeyev, K. Yoshikawa, H. Takahashi, and I. Hatta, J. Chem. Phys. **107**, 6917 (1997).
[6] S. M. Mel'nikov and K. Yoshikawa, Biochem. Biophys. Res. Commun. **230**, 514 (1997).
[7] K. Yoshikawa, M. Takahashi, V. V. Vasilevskaya, and A. R. Khokhlov, Phys. Rev. Lett. **76**, 3029 (1996).
[8] V. G. Seregeyev, O. A. Pyshkina, M. O. Gallyamov, I. V. Yaminsky, A. B. Zezin, and V. A. Kabanov, Prog. Colloid Polym. Sci. **106**, 108 (1997).
[9] D. L. Reimer, Y.-P. Zhang, S. Kong, J. J. Wheeler, R. W. Graham, and M. B. Bally, Biochemistry **34**, 12 877 (1995).
[10] S. Bhattacharya and S. S. Mandal, Biochim. Biophys. Acta **1323**, 29 (1997).
[11] See, e.g., H. Gershon, R. Ghirlando, S. B. Guttman, and A. Minsky, Biochemistry **32**, 7143 (1993).
[12] J. F. Leger, J. Robert, L. Bourdieu, D. Chatenay, and J. F. Marko, Proc. Natl. Acad. Sci. USA **95**, 12 295 (1998).
[13] G. V. Shivashankar, M. Feingold, O. Krichevsky, and A. Libchaber, Proc. Natl. Acad. Sci. USA **96**, 7916 (1999).
[14] H. Diamant and D. Andelman, Europhys. Lett. **48**, 170 (1999).
[15] H. Diamant and D. Andelman, e-print cond-mat/9906271.

[16] P.-G. de Gennes, J. Phys. (France) **37**, L59 (1976); F. Brochard and P.-G. de Gennes, Ferroelectrics **30**, 33 (1980).
[17] M. E. Fisher, Phys. Rev. **176**, 257 (1968).
[18] A. B. Harris, J. Phys. C **7**, 1671 (1974).
[19] B. Cabane and R. Duplessix, J. Phys. (France) **43**, 1529 (1982).
[20] D. P. Norwood, E. Minatti, and W. F. Reed, Macromolecules **31**, 2957 (1998); E. Minatti, D. P. Norwood, and W. F. Reed, *ibid.* **31**, 2966 (1998).
[21] B. H. Zimm and J. K. Bragg, J. Chem. Phys. **31**, 526 (1959).
[22] I. Satake and J. T. Yang, Biopolymers **15**, 2263 (1976); K. Shirahama, H. Yuasa, and S. Sugimoto, Bull. Chem. Soc. Jpn. **54**, 375 (1981); K. Shirahama and M. Tashiro, *ibid.* **57**, 377 (1984).
[23] See, e.g., E. D. Goddard, in *Interactions of Surfactants with Polymers and Proteins* (Ref. [1]), Chap. 4.
[24] P. S. Kuhn, Y. Levin, and M. C. Barbosa, Chem. Phys. Lett. **298**, 51 (1998).
[25] A. J. Konop and R. H. Colby, Langmuir **15**, 58 (1999).
[26] J. Rudnick and R. Bruinsma, Biophys. J. **76**, 1725 (1999).
[27] Some experiments involve *short* DNA fragments, which requires a different approach. See A. V. Gorelov, E. D. Kudryashov, J.-C. Jacquier, D. M. McLoughlin, and K. A. Dawson, Physica A **249**, 216 (1998).
[28] E. H. Lieb and D. C. Mattis, *Mathematical Physics in One Dimension* (Academic Press, New York, 1966), Chap. 1.
[29] M. Kac, Phys. Fluids **2**, 8 (1959).
[30] G. A. Baker, Phys. Rev. **122**, 1477 (1961).
[31] O. Kratky and G. Porod, Recl. Trav. Chim. Pays-Bas. **68**, 1106 (1949); H. Yamakawa, *Modern Theory of Polymer Solutions* (Harper & Row, New York, 1971), Chap. II.
[32] That is also the reason why stiffness-modifying binding, considered by a previous work (Ref. [26]), did not produce any cooperativity effect without external tension.
[33] R. A. Harris and J. E. Hearst, J. Chem. Phys. **44**, 2595 (1966); **46**, 398 (1967).
[34] J. B. Lagowski, J. Noolandi, and B. Nickel, J. Chem. Phys. **95**, 1266 (1991).
[35] B.-Y. Ha and D. Thirumalai, J. Chem. Phys. **103**, 9408 (1995); Macromolecules **28**, 577 (1995); e-print cond-mat/9709345.
[36] B.-Y. Ha and D. Thirumalai, J. Chem. Phys. **106**, 4243 (1997).
[37] P. L. Hansen, D. Svenšek, V. A. Parsegian, and R. Podgornik, Phys. Rev. E **60**, 1956 (1999).
[38] In principle, the case of negative ''stiffness'' coefficient can be considered as well. In such a model the monomers tend to antialign (aggregate) instead of align. See H. Diamant and D. Andelman, e-print cond-mat/9804086. However, the continuum limit employed by wormlike-chain models, including the current model, implicitly assumes a large stiffness coefficient ($l_p \gg 1$). Consequently, the coefficient cannot be taken continuously from positive to negative values, and the case of zero stiffness becomes a singularity. Indeed, in the binding model presented here the limit $\epsilon \to -1$ is found to be similar to the limit of zero temperature, as shown in Sec. IV.
[39] R. P. Feynman and A. R. Hibbs, *Quantum Mechanics and Path Integrals* (McGraw-Hill, New York, 1965), Chap. 3.
[40] We are indebted to M. Schwartz for raising this point.
[41] J. L. Lebowitz and O. Penrose, J. Math. Phys. **7**, 98 (1966).
[42] Note that this statement, though plausible, is not rigorously proved. For values of ϵ which are not very small, the cumulant expansion of Eq. (8) would produce higher-order, many-body terms, whereas the proof by Lebowitz and Penrose, Ref. [41], applies to pair potentials only. On the other hand, all those higher-order terms have ranges proportional to l_p (it is the only length scale in the problem when N is infinite) and, hence, should satisfy the mean-field assumption for $l_p \to \infty$.
[43] J. F. Marko and E. D. Siggia, Macromolecules **28**, 8759 (1995).
[44] P.-G. de Gennes, *Scaling Concepts in Polymer Physics* (Cornell University Press, Ithaca, 1979), Chap. I.
[45] T. Odijk, Macromolecules **28**, 7016 (1995).
[46] A. Stasiak, E. Di Capua, and Th. Koller, J. Mol. Biol. **151**, 557 (1981).
[47] R. Golestanian, M. Kardar, and T. B. Liverpool, Phys. Rev. Lett. **82**, 4456 (1999).
[48] See, e.g., J. J. Binney, N. J. Dorwick, A. J. Fisher, and M. E. J. Newman, *The Theory of Critical Phenomena* (Oxford University Press, Oxford, 1993), Chap. 3.2.