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Evidence for the extended de Gennes regime of a semiflexible polymer in slit confinement

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Abstract

We use off-lattice, pruned-enriched Rosenbluth method (PERM) simulations to compute the confinement free energy of a real wormlike chain of effective width w and persistence length l_p in a slit of height H . For slit heights much larger than the persistence length of the polymer and much smaller than the thermal blob size, the excess free energy of the confined chain is consistent with a modified version of the scaling theory for the extended de Gennes regime in a channel that reflects the blob statistics in slit confinement. Explicitly, for channel sizes $2l_p \lesssim H \lesssim 0.2l_p^2/w$, the difference between the confinement free energy of the real chain and that of an ideal chain scales like w/H .

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I. INTRODUCTION

When a polymer is confined in a channel or a slit, excluded volume interactions cause the polymer to swell in the unconfined direction [1]. The extent of this swelling depends on the length scale H characterizing the confinement, the persistence length l_p of the polymer, and the effective width w of the polymer backbone. A region of phase space of considerable recent interest is the so-called “extended de Gennes” regime [2], corresponding to confinement length scales H lying between the polymer Kuhn length $2l_p$ and the thermal blob size l_p^2/w . Although the existence of this regime was known for quite some time through various less descriptive terms [3–5], the moniker extended de Gennes emphasizes that the scaling law for the size of a chain confined in a channel or slit where $H > l_p^2/w$ (normally called the de Gennes regime) “extends” to channel or slit sizes below the thermal blob size [2]. In the context of blob theory, the extended de Gennes regime is characterized by anisometric blobs [4, 5], with the subchain inside the blob existing at the border between ideal and real behavior. As such, there is a strong connection between the thermodynamics of the extended de Gennes regime for a confined polymer and the theory of marginal polymer solutions [6], with the extended de Gennes regime corresponding to confined version of marginal solution theory [7, 8].

The extended de Gennes regime for channel confinement has attracted substantial attention over the past several years [2, 6, 9–16]. Here, fluctuations about the average extension of the chain along the channel axis provide a simple way to distinguish the extended de Gennes regime and de Gennes regime — the variance in chain extension is independent of the channel size D in the extended de Gennes regime [2, 10–12], whereas the variance scales like $D^{1/3}$ in the de Gennes regime [1, 2]. Importantly, this quantity can be measured experimentally using DNA as a model polymer. Recent experimental work indicates that the variance in chain extension is indeed independent of channel size [14, 15], confirming a key prediction of the extended de Gennes regime in channels.

In contrast, the extended de Gennes regime in slit confinement has attracted considerably less attention [17]. One possible reason is that the average value of the end-to-end distance of a polymer in slit confinement is zero, whereas excluded volume leads to a non-zero average extension in channel confinement [18]. Rather, the size of a chain in slit confinement is measured by the root-mean-square (RMS) end-to-end distance of the chain. The problem

of determining the size of a semiflexible chain in slit confinement has been the subject of extensive experimental work using DNA as a model polymer [19–27], along with concomitant simulations [17, 19, 27–47], and theory [1, 3, 5, 45, 48]. A key conclusion emerging from this body of work is that the scaling law prediction for the RMS size of a chain of length L [1],

$$\langle R^2 \rangle^{1/2} \cong L^{3/4} \left(\frac{l_p w}{H} \right)^{1/4} \quad (1)$$

indeed holds for channels where $H > 2l_p$, with small corrections at smaller channel sizes due to orientation of the chain by the walls [5, 17, 45]. In practice, one typically measures the in-plane radius of gyration or in-plane end-to-end distance, as these are experimentally accessible and provide better correspondence with the theory in the limit of relatively small chains.

Inasmuch as the RMS size of the chain is already a measure of the variance in the chain size about its zero average value, the strategy used to demonstrate the existence of the extended de Gennes regime in channels [2, 10–12, 14, 15], i.e., from the scaling for the second moment of the span of the chain in a nanochannel, cannot be applied to slits. Thus, a previous claim of the existence of an extended de Gennes regime in slits [17] rests upon the lack of contradictory evidence from an exceptionally thorough exploration of the phase space for $\langle R^2 \rangle^{1/2}$. In the present contribution, we provide affirmative evidence in support of the extended de Gennes regime in slits by adopting the free-energy based strategy used by Dai *et al.* [6] for channel confinement.

II. SCALING THEORY

Computing the confinement free energy of a polymer is a problem of long-standing interest [49], owing to its connection with size exclusion chromatography [50]. Note that, while Flory theory provides the correct scaling law in Eq. (1) for the size of the confined chain [17], it fails to provide the correct confinement free energy.

Let us begin with the blob theory argument [1] for the de Gennes regime $H \gtrsim l_p^2/w$, as it makes clear the approach required to modify the theory for the extended de Gennes regime [6]. The confinement free energy in the de Gennes regime is approximately equal to the number of blobs N_b ,

$$\beta \Delta F_r \cong N_b \quad (2)$$

where $\beta^{-1} = k_B T$ is the inverse Boltzmann factor. In the latter, ΔF_r is measured relative to a reference state of an unconfined real chain [1], and the subscript “r” denotes that this quantity refers to the confinement free energy of a real chain. For the de Gennes regime, the blob size is equal to the slit height [1] and given by real chain statistics,

$$R_b \sim H \sim L_b^{3/5} w^{1/5} l_p^{1/5} \quad (3)$$

where L_b is the contour length within a blob. Noting that the number of blobs is $N_b = L/L_b$, we arrive at [42]

$$\beta \Delta \hat{F}_r \cong \frac{l_p^{4/3} w^{1/3}}{H^{5/3}} \quad (4)$$

where $\Delta \hat{F}_r = \Delta F_r l_p / L$ is the free energy per persistence length.

In the extended de Gennes regime, Dai *et al.* [6] proposed that the confinement free energy consists of two terms,

$$\beta \Delta F_r \cong N_b \left(\frac{L_b l_p}{H^2} \right) + N_b \quad (5)$$

The bracketed quantity in the first term is the free energy required to compress a blob containing a contour length L_b from its unconfined size $(L_b l_p)^{1/2}$ to a smaller size H . This is the dominant term, and appears in a previous scaling theory by Hsu and Binder [42]. Noting that $L = L_b N_b$, the first term in Eq. (5) can also be written as [6]

$$\frac{L l_p}{H^2} \cong \beta \Delta F_i \quad (6)$$

where ΔF_i is the confinement free energy required to compress an ideal semiflexible chain of length L in a slit of size H , using an unconfined ideal chain as the reference state. The second term in Eq. (5), which is small and does not appear in the theory by Hsu and Binder [42], is the free energy cost required to arrange the N_b anisometric blobs in the plane, and is analogous to Eq. (2). In the extended de Gennes regime, it is assumed that the blobs have ideal chain scaling [4],

$$H \cong (L_b l_p)^{1/2} \quad (7)$$

and that the z -parameter characterizing the excluded volume interactions is unity [17],

$$z = \frac{L_b w}{H B^2} \cong 1 \quad (8)$$

where B is the in-plane size of the anisometric blob in a slit. Solving these two equations for B and L_b [17], and then inserting the result into Eq. (5) yields the confinement free energy

$$\beta\Delta F_r \cong \beta\Delta F_i + \frac{Lw}{Hl_p} \quad (9)$$

In our analysis, it proves convenient to define the excess free energy per persistence length as

$$\beta\Delta\hat{F}_{\text{ex}} \equiv \beta(\Delta\hat{F}_r - \Delta\hat{F}_i) \cong \frac{w}{H}. \quad (10)$$

The extended de Gennes regime is most relevant for highly anisotropic chains, $l_p \gg w$, so that a broad window exists between the lower bound at $H \cong 2l_p$ and the upper bound at $H \cong l_p^2/w$ [17]. As the slit height H approaches the lower bound at $H \cong 2l_p$, the first term in Eq. (9) approaches L/l_p and thus becomes large compared to the second term [6]. At the upper bound for the slit height, both terms are comparable in magnitude and eventually merge with the result in Eq. (4) when $H = l_p^2/w$. Thus, there is a gradual transition in the extended de Gennes regime from almost ideal chain confinement to real chain confinement. Although detecting such subtle changes in confinement free energy can be quite challenging [1], the success of this approach in channel confinement [6] makes it worth attempting here for slit confinement.

It is worthwhile to compare the de Gennes and extended de Gennes scaling theories to the theory of Casassa [49], which has been used recently [27] to model the confinement of relatively short DNA molecules. Casassa's calculation of the confinement free energy [49] is valid for flexible, ideal chains as the confinement passes from $H > R_g$, where the polymer easily fits into the slit but experiences a depletion near the slit walls, to $H < R_g$, where the polymer must adopt a pancake-like configuration to fit inside the slit. The de Gennes and extended de Gennes theories only apply for the case $H < R_g$, such that the confined chain can be modeled as a chain of compression blobs. For cases $H < R_g$ that are in the de Gennes regime, there is a distinct difference with the Casassa theory; the confined chain experiences substantial excluded volume interactions, which lead to a confinement free energy in Eq. (4) that is markedly different than Casassa's ideal polymer theory. For the extended de Gennes regime with $H < R_g$, the situation is subtler. The leading-order contribution to the confinement free energy in Eq. (9) is that of an ideal chain. However, there is an important distinction between the two theories in that ΔF_i from Casassa's theory [49] is that of a flexible chain, while ΔF_i in the extended de Gennes regime is for a semiflexible

chain [48]. The situation surrounding the excess free energy is much clearer; inasmuch as Casassa's theory is for ideal chains, it predicts no excess free energy of confinement.

III. SIMULATION METHOD

To test whether Eq. (9) indeed provides a probe for the extended de Gennes regime, we performed Pruned-Enriched Rosenbluth Method (PERM) simulations [51, 52] of a discrete wormlike chain model, following our previous work in this area [9, 11, 18, 45]. Both our implementation of off-lattice PERM and the discrete wormlike chain model have been described in detail elsewhere [9, 53], so we will be brief here. The chain consists of $N + 1$ touching beads of size b such that the contour length of the chain is $L = Nb$. Both bead-bead and bead-wall excluded volume are modeled with a hard-core potential of size w . The stiffness of the chain results from a potential

$$\beta U_{\text{bend}} = \kappa \sum_{n=1}^{N-1} (1 - \cos \theta_n) \quad (11)$$

where θ_n is the angle formed by the bead trio starting with bead n . The bending constant κ is related to the persistence length of the chain by [54]

$$\frac{l_p}{w} = \frac{\kappa}{\kappa - \kappa \coth(\kappa) + 1} \quad (12)$$

The chain is confined between two parallel plates separated by some distance H_{wall} . In the theory described above, the quantity H refers to the slit that is accessible to the chain. For real chains, $H = H_{\text{wall}} - w$. To test Eq. (9), we also need to simulate ideal chains. In our code, this is accomplished by setting $w = 0$, whereupon $H = H_{\text{wall}}$.

PERM is a biased chain growth method that avoids the attrition problem during chain growth, making it well suited for self-avoiding random walks and polymers in confinement [55]. For our purposes here, one of the most important points about PERM is that it provides a direct measure of the free energy during chain growth relative to a reference state [51]. In our implementation, the reference state is an unconfined, ideal wormlike chain [9]. For a given combination of H , l_p , and w , we perform three PERM simulations: (i) a real, unconfined chain, (ii) a real, confined chain, and (iii) an ideal, confined chain. The quantity ΔF_r is obtained as the difference of the free energies computed from the first two simulations, whereas ΔF_i is obtained directly from the third simulation.

TABLE I. Table of simulation parameters range used in PERM. For the real chains, the bead size used is $b = 1$ with $w = b$. For the ideal chains, we used the same parameters but set $w = 0$.

l_p/w	H/w	L/w
[3.5-100]	[10 - 1200]	[40,000 - 100,000]

We have used a wide range of H/w , l_p/w , and L/w ratios, which are tabulated in Table I. These values were selected to provide almost 3 orders of magnitude of distributed data points in Hw/l_p^2 while keeping $H > 2l_p$ and maintaining a reasonable values for the contour length within a blob, L_b , for computational tractability. The contour lengths were set such that each data point produces free energies that are proportional to the contour length, with the largest contour length being $N = 10^5$.

A PERM simulation consists of an ensemble of tours [51]. A tour comprises chain growth starting from a single bead with enrichment (copying) of chains and pruning (removal) of chains to enhance the sampling, with appropriate reweighting to remove the bias in the chain growth when computing ensemble averages such as the free energy. Each tour potentially can produce many configurations in the ensemble through the enrichment process, but these configurations are correlated. Configurations from different tours are uncorrelated. Each simulation was performed for $m = 10^5$ tours to provide sufficient statistics.

To validate the our code against known results, we computed the in-plane radius of gyration $\langle R^2 \rangle^{1/2}$ over a wide range of the phase space and the confinement free energy ΔF_r for $H > l_p^2/w$, which corresponds to the de Gennes regime. Figure 1 shows that our simulations furnish the expected scaling behaviors. Note that these figures only include chains that are sufficiently long such that $\langle R^2 \rangle^{1/2} \sim L^{3/4}$ and $\Delta F_r \sim L$. We found that the free energy converges more quickly than the chain size, which is convenient for our purposes. The predictions by de Gennes for both of the in-plane radius of gyration [17, 19, 28, 30, 31, 40, 42, 43, 46] and confinement free energy [29, 30], or equivalently the force of the confinement [31, 42], have been verified many times. There is one report [39] claiming that the de Gennes theory for the confinement free energy fails for long chains; our results correspond to very long chains simulated with a state-of-the-art methodology and the agreement of the data in Fig. 1b with Eq. (4) is quite good.

We have previously shown [45] that our PERM simulations provide essentially the same confinement free energy for ideal chains as the interpolation formula of Chen and Sullivan

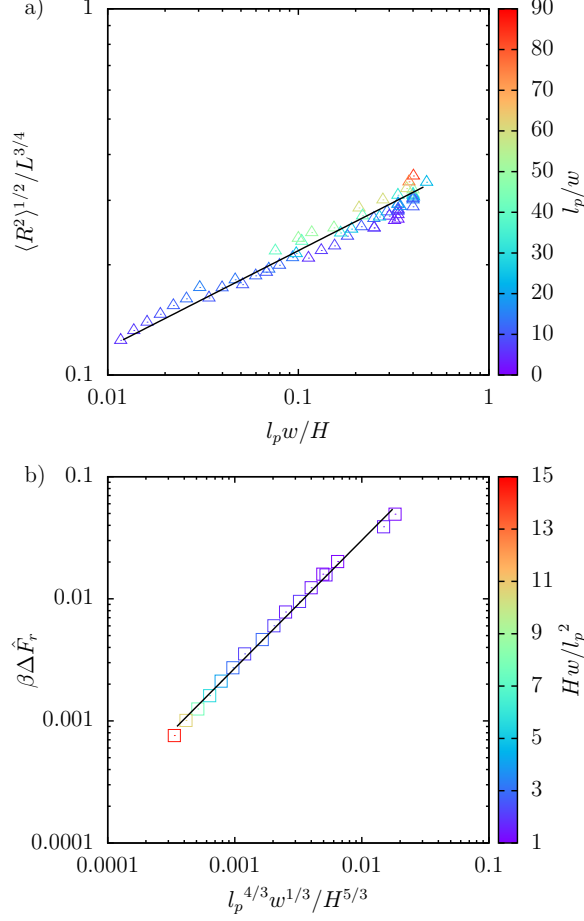


FIG. 1. (a) Normalized in-plane radius of gyration and (b) normalized confinement free energy per persistence length as a function of their scaling variables in Eq. (1) and Eq. (4), respectively. In (a), the colors correspond to the values of l_p/w and the solid line is Eq. (1) with a prefactor of 0.4 and exponent of 0.26. In (b), the colors correspond to Hw/l_p^2 and the solid line is Eq. (4) with a prefactor of 3.7 and exponent of 1.

[48], the latter obtained from the ground-state approximation in a propagator approach. We have repeated these ideal chain simulations for additional values of H/l_p in the context of the present work and again obtained excellent agreement with Chen and Sullivan [48], essentially identical to our previous work [45] and that obtained using a different simulation method [27].

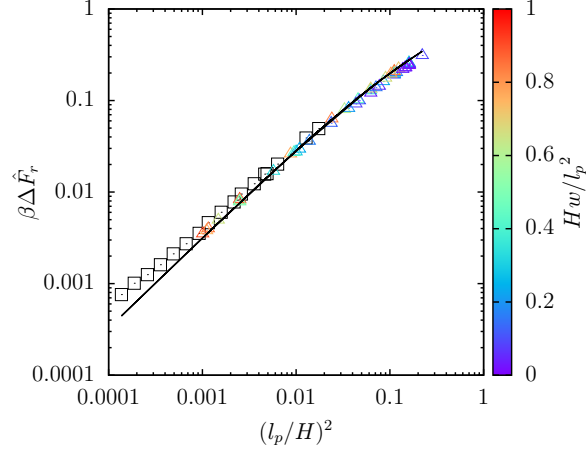


FIG. 2. Normalized free energy of confinement per persistence length for real chains as a function of the scaling variable for a confined ideal chain given by Eq. (6). The black squares are the data for the de Gennes regime ($Hw/l_p^2 > 1$) appearing in Fig. 1b. The triangles are data presumably in the extended de Gennes regime ($Hw/l_p^2 < 1$), where the color code indicates the value of Hw/l_p^2 . The solid line is the interpolation formula for the confinement free energy of an ideal chain in a slit from Chen and Sullivan [48].

IV. RESULTS AND DISCUSSION

Figure 2 compares the free energy of confinement of real chains in slits to the scaling for an ideal chain in Eq. (6). As we would expect, there is a substantial deviation between the real chain and ideal chain confinement free energies for the de Gennes regime, i.e. when $H > l_p^2/w$. Note that the prefactor demarcating the start of the de Gennes regime is somewhat arbitrary, since the crossover is gradual. For notational simplicity, we use a prefactor of unity here. As the slit size is decreased below the thermal blob size, the confinement free energies are increasingly closer to those for a confined ideal chain. To make this point even more clear, we have included the interpolation formula from Chen and Sullivan [48] as the solid line in Fig. 2; the free energy for the most strongly confined chains is almost indistinguishable from that of an ideal chain.

To test the prediction for the extended de Gennes regime, we simply need to compute the excess free energy from Eq. (10) by subtracting the solid line in Fig. 2 from the confinement free energy. Figure 3 represents the key result of our study. In this figure, we plot the data in a form similar to that used by Dai *et al.* [6] to analyze the excess confinement free energy

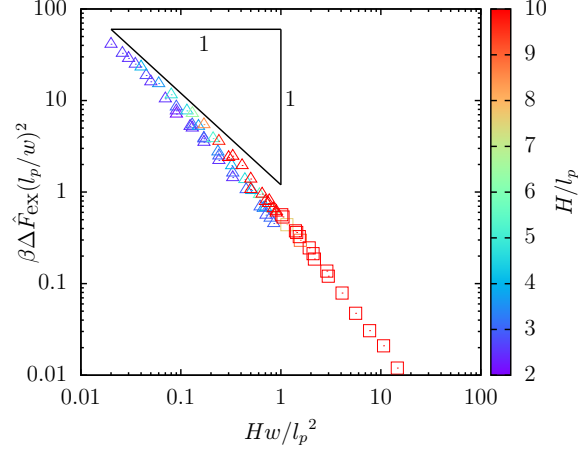


FIG. 3. Test of the extended de Gennes theory for the excess free energy in Eq. (10). The excess free energy of confinement per persistence length, $\beta\Delta\hat{F}$ is multiplied by the square of the monomer anisotropy, $(l_p/w)^2$, so that the data can be plotted as a function of Hw/l_p^2 [6]. The data for the de Gennes regime ($H > l_p^2/w$) are plotted as squares and the data for the extended de Gennes regime ($H < l_p^2/w$) are plotted as triangles to provide correspondence with Fig. 2. The data are colored according to their H/l_p values up to $H/l_p = 10$. The triangle indicates a -1 scaling.

for a wormlike chain in channel confinement. The data in Fig. 3 show that the expected scaling of Eq. (10) only arises when the system is sufficient far from the boundaries of both the de Gennes regime at $H = l_p^2/w$ and the Odijk regime at $H = 2l_p$. Indeed, the transition between the confinement free energies for the de Gennes and extended de Gennes regimes is a gradual one, with the extended de Gennes regime requiring at least a decade in Hw/l_p^2 to emerge in a convincing manner. We performed a regression on the subset of data for $0.01 < Hw/l_p^2 < 0.2$ and recovered an exponent of -1.04 ± 0.05 , in excellent agreement with Eq. (10). Figure 4 shows that, for the extended de Gennes regime, the excess free energy is quite small, typically contributing around 5% of the total confinement free energy.

V. CONCLUSION

The simulation data provided here provide affirmative evidence in support of the existence of an extended de Gennes regimes in slits through the excess free energy of confinement. Inasmuch as this regime requires simultaneously satisfying $H \ll l_p^2/w$ and $H \gg l_p$, the scaling law predictions for the free energy of the extended de Gennes regime in a slit in

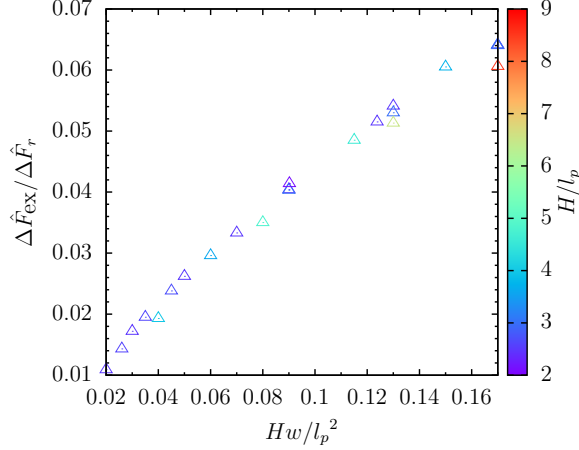


FIG. 4. Ratio of the excess free energy of confinement to the total free energy of confinement for $Hw/l_p^2 < 0.2$, where Fig. 3 indicates good agreement with the extended de Gennes excess free energy in Eq. (10). The data are colored according to their H/l_p values up to $H/l_p = 10$.

Eq. (9) only apply for highly anisotropic chains, $l_p \gg w$. Our data suggest that extended de Gennes excess free energy scaling is observed for $2l_p < H < 0.2l_p^2/w$. Taking $l_p = 50$ nm [56] and $w = 5$ nm [2, 57] as typical values for DNA at high ionic strength, the scaling law for the excess confinement free energy of the extended de Gennes regime would not be observable for DNA. Reducing the ionic strength does not improve the situation, as the ratio l_p/w decreases and ionic strength decreases [53]. Nevertheless, it would be interesting to see if recent experimental methods for experimentally measuring the free energy of confinement for DNA in slits [27, 58] can detect a deviation from the de Gennes regime that would indicate the existence of marginal solution behavior [7, 8]. We are cautiously optimistic, as experiments focused on the variance in DNA extension in a nanochannel [14, 15] have provided clear evidence for the extended de Gennes regime even though the restrictions on channel size noted above for nanoslits also apply in nanochannels [13]. Indeed, even if the scaling regime $\beta\hat{F}_{\text{ex}} \sim w/H$ is not reached, one can still compare the confinement free energy obtained in such an experiment to our data in Fig. 2. It would also be interesting to explore the possibilities engendered by confining highly anisotropic biopolymers, such as bottle-brush coated DNA [59], RecA-coated DNA [60], actin [61], or polyethylene-grafted methylcellulose [62], which will allow one to reach larger values of l_p/w than are possible with naked DNA.

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