

DNA confined in a two-dimensional strip geometry

AIQUN HUANG and ANIKET BHATTACHARYA

Department of Physics, University of Central Florida - Orlando, FL 32816-2385, USA

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Abstract – Semiflexible polymers characterized by the contour length L and persistent length ℓ_p confined in a spatial region D have been described as a series of “spherical blobs” and “deflecting lines” by de Gennes and Odjik for $\ell_p < D$ and $\ell_p \gg D$, respectively. Recently new intermediate regimes (*extended de Gennes* and *Gauss-de Gennes*) have been investigated by Tree *et al.* (*Phys. Rev. Lett.*, **110** (2013) 208103). In this letter we derive scaling relations to characterize these transitions in terms of universal scaled fluctuations in d -dimension as a function of L , ℓ_p , and D , and show that the Gauss-de Gennes regime is absent and the extended de Gennes regime is vanishingly small for polymers confined in a 2D strip. We validate our claim by an extensive Brownian dynamics (BD) simulation which also reveals that the prefactor A used to describe the chain extension in the Odjik limit is independent of the physical dimension d and is the same as previously found by Yang *et al.* (*Phys. Rev. E*, **76** (2007) 011804). Our studies are relevant for optical maps of DNA stretched inside a nanostrip.

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Conformations and dynamics of DNA inside a nanochannel have attracted considerable attention among various disciplines of science and engineering [1]. Important biomolecules, such as, chromosomal DNAs, or proteins whose functionalities are crucially dependent on the exact sequence of the nucleotides or amino acids usually exist in highly compact conformations. By straightening these molecules on a two-dimensional sheet [2–4] or inside a nanochannel [5–10] it is possible to obtain the structural details of these molecules. It is believed that a complete characterization of the DNA sequence for each individual and a proper understanding the role of genetic variations will lead to personalized medicine for diseases, such as, cancer [11]. DNA confined and stretched inside a nanochannel offers significant promise towards this goal. Unlike traditional sequencing using Sanger’s method [12], which requires fragmentation and replication, the analysis of a single DNA will be free from statistical errors and sequence gaps during reconstruction [11]. Naturally quests for efficient but low-cost techniques have attracted considerable attention. Along with optical maps [2,7], DNA melting characteristics inside a nanochannel have recently been studied showing further promises [9]. These recent experiments have generated renewed interest in theoretical and computational studies of confined polymers [13–24].

Confined DNAs inside nanochannels were often studied in high salt concentrations [1] where the charges of the individual nucleotides are heavily screened [5,16]. Besides, the resolution of optical studies set by the diffraction limit is typically of the order of 100 base pairs. Under these conditions a double-stranded DNA is often described as a worm-like chain (WLC) [25] whose end-to-end distance $\langle R_{bulk}^2 \rangle = 2\ell_p L (1 - \frac{\ell_p}{L} [1 - \exp(-L/\ell_p)])$ interpolates from a rod ($\langle R_{bulk}^2 \rangle \sim L^2$ for $L \ll \ell_p$) to a Gaussian coil ($\langle R_{bulk}^2 \rangle \sim 2L\ell_p$ for $L \gg \ell_p$). However, for a very long chain eventually the excluded-volume (EV) effect becomes important [26,27], and for $L \gg \ell_p$ the end-to-end distance in d dimensions should be characterized by the bulk conformation of a swollen semiflexible chain [28,29],

$$\sqrt{\langle R_{bulk}^2 \rangle} = a \left(\frac{L}{a} \right)^{\frac{3}{d+2}} \left(\frac{\ell_p}{a} \right)^{\frac{1}{d+2}}, \quad (1)$$

where a is the effective width of the chain. It is noteworthy that while in 3D there is a broad Gaussian regime for $L \gtrsim \ell_p$ [26,27] before EV effects become important, in two dimensions (2D) the intermediate Gaussian regime is absent due to the severe dominance of the EV effect [30,31].

Recently confined polymers in rectangular, cylindrical and triangular channels have been studied by several

groups [13–24]. One first sees the effect of the confinement (described by the length of the cross-section of the channel D) for $D < R_g$, where R_g is the radius of gyration of the chain. This limit has been identified as the Flory-de Gennes regime where chain conformations can be described as a series of spherical blobs of size D [32,33]. A further decrease of the ratio D/R_g first leads to an extended de Gennes regime with anisotropic blobs followed by a Gaussian regime analogous to the 3D bulk case, which has been referred to as the Gauss-de Gennes regime [17]; for extreme confinement when $\ell_p \gg D$, the blob picture breaks down and the chain enters into the Odjik regime [34,35] where the chain conformations are described as a series of straight segments deflected from the confining wall [15]. While both de Gennes and Odjik regimes are well established, the characteristics of the transition regions (the extended de Gennes and the Gaussian regimes) have been the main subject of several recent studies [15–17,19]. However, the extension of the confined DNA in the extended de Gennes regime has been determined to be the same as in the de Gennes regime by minimizing the free energy [1,16,19], so making a difference of these two regimes has been either difficult or not evident [16,17].

Confined chains inside 3D nanochannels exhibit analogous regimes as found in their respective bulk counterparts [17]. In this letter we study confined DNA in a 2D strip geometry. As mentioned before, that unlike in 3D, the bulk Gaussian regime does not exist for semiflexible chains in 2D [30,31]. Therefore, one wonders, if regimes of confined DNA in 2D will follow their corresponding bulk counterpart. The second motivation comes from the observation that the Flory exponent in 2D (0.75) is significantly larger than the corresponding exponent in 3D (0.588) which implies that a chain is more elongated in a 2D strip rather than in a tube of the same width D . Therefore, the elongation would be more profitable by further reducing the physical dimension of the region. Finally, in the Odjik limit, prior theoretical and numerical results [13] have indicated that the prefactor A in the expression for the chain elongation (see eq. (9)) is nearly independent of the shape of the nanochannel. By studying elongation along a 2D strip, we further observe that this constant is almost the same as the values in 3D indicating that this constant is independent of the spatial dimension. While in 3D the extended de Gennes limit is somewhat controversial, we provide scaling arguments for a 2D strip and validate by carrying out the BD simulation that the extended de Gennes regime is vanishingly small. This result along with the absence of a Gaussian regime in a 2D strip geometry implies that a 2D strip is a cleaner system to study a stretched chain as the conformations interpolate between de Gennes and Odjik regimes only, and, therefore, it is another reason to think about designing DNA elongation experiments inside a 2D strip.

de Gennes regime: The starting point of our theoretical analysis is the ansatz for the normalized free energy

$\mathcal{F}/k_B T$ of confinement along a tube axis first proposed by Jun, Thirumalai, and Ha [36], later used for a square channel [16] and a slit [19], and is given by

$$\mathcal{F}/k_B T = \frac{X^2}{(L/L_{blob})D^2} + D \frac{(L/L_{blob})^2}{X}, \quad (2)$$

and the expression for the end-to-end distance of a swollen semiflexible chain as given by eq. (1). Here X is the extension along the tube/strip axis, and L_{blob} the contour length of the chain in a blob [32,33], k_B is the Boltzmann constant, and T is the temperature. The dimension dependence comes from the chain statistics for L_{blob} (eq. (1)). In order to contrast the results for polymers confined in a 2D strip with those for cylindrical, square, and rectangular channels, in the following we derive expressions in terms of d spatial dimensions ($d = 2$ for a strip and $d = 3$ for a tube). By differentiating eq. (2) with respect to X , one can easily check i) $X = Dn_{blob}$, where $n_{blob} = L/L_{blob}$ is the number of blobs, ii) $\mathcal{F}/k_B T \sim n_{blob}$, and iii) $\mathcal{F}/k_B T \sim L$. For the de Gennes regime monomers inside the blob are described by the conformation of a swollen chain either in $d = 2$ (strip) or $d = 3$ (tube), so that $D = L_{blob}^{3/d+2} \ell_p^{1/d+2} a^{d-2/d+2}$ (eq. (1)). It is then easy to check that the elongation is given by

$$\langle X \rangle_{de\ Gennes} = Dn_{blob} = L \left(\frac{D}{a} \right)^{\frac{1-d}{3}} \left(\frac{\ell_p}{a} \right)^{\frac{1}{3}}. \quad (3)$$

Likewise, the second derivative of eq. (2) gives the effective stiffness constant k_{eff} for the DNA polymer [1,6] under confinement, so that the longitudinal fluctuation of the extension $\langle \sigma^2 \rangle$ can be obtained as

$$\langle \sigma^2 \rangle = \frac{k_B T}{k_{eff}} = La \left(\frac{\ell_p}{a} \right)^{\frac{1}{3}} \left(\frac{D}{a} \right)^{\frac{4-d}{3}}. \quad (4)$$

Extended de Gennes regime: It was argued [1,15,16] that the scaling relation eq. (1) for each spherical blob in the de Gennes regime only holds true when the channel size D and chain length L both are above certain critical values D_{**} and L_{**} , respectively, to be determined in the following manner. When $D < D_{**}$, the EV repulsion becomes less significant resulting in a local ideal chain behavior in each blob, while it is strong enough to sustain the global picture of linearly ordered blobs, each turning into an ellipsoid characterized by its major axis H (and of volume $\sim D^{d-1}H$) along the long axis of the nanochannel¹. The critical length L_{**} and the critical channel width D_{**} can be obtained by equating the size of an ideal chain and a Flory coil in the bulk: $D_{**} \simeq (L_{**}\ell_p)^{1/2} \simeq \ell_p^{\frac{1}{d+2}} L_{**}^{\frac{3}{d+2}}$, from which we get

$$L_{**} \simeq a \left(\frac{\ell_p}{a} \right)^{\frac{d}{4-d}} \quad \text{and} \quad D_{**} \simeq a \left(\frac{\ell_p}{a} \right)^{\frac{2-d}{4-d}}. \quad (5)$$

¹In this case one can use the same free-energy expression of eq. (2) replacing $D \rightarrow H$ [17].

Notice that $L_{**} \simeq \ell_p^3 a^{-2}$, $D_{**} \simeq \ell_p^2 a^{-1}$ in 3D while $L_{**} \simeq D_{**} \simeq \ell_p$ in 2D. Both ideal and EV effects coexist in this regime [15]. This balance of ideal and EV behavior is obtained by setting $a^{d-2} L_{blob}^2 / H D^{d-1} = 1$ from which the length H can be obtained as follows:

$$H = \sqrt{L_{blob} \ell_p} = a^{d-2} \frac{L_{blob}^2}{D^{d-1}}. \quad (6)$$

Denoting L_{blob} as L_{ellip} , from eq. (6) we get

$$L_{ellip} = \ell_p^{\frac{1}{3}} \left(\frac{D^{d-1}}{a^{d-2}} \right)^{\frac{2}{3}} \quad \text{and} \quad H = \ell_p^{\frac{2}{3}} \left(\frac{D^{d-1}}{a^{d-2}} \right)^{\frac{1}{3}}. \quad (7)$$

Replacing $D \rightarrow H$, $L_{blob} \rightarrow L_{ellip}$ in eq. (2) and minimizing with respect to X , we get $X = H(L/L_{ellip})$, and substituting L_{ellip} and H by eq. (7) we obtain eq. (3). This completes the proof that the de Gennes regime and the extended de Gennes regime cannot be differentiated from the elongation of the chain.

However, by repeating the same procedure we note that, unlike eq. (4), in the extended de Gennes regime the fluctuation is different and is given by $\langle \sigma^2 \rangle = L \ell_p$. Therefore, the de Gennes regime and the extended de Gennes regime can be differentiated by measuring the characteristic fluctuations in their respective chain extensions [16]. The lower bound D_* of the extended de Gennes regime where it merges with the Gauss-de Gennes regime, following Odijk's scaling analysis [15] (which is also valid in 2D) is given by $D_* \simeq c \ell_p$, where the prefactor $c \gtrsim 1$ (in [16] it was found to be ≈ 2). Using eq. (5) we note that while the range for the extended de Gennes regime being $[D_*, D_{**}] = [c \ell_p, \ell_p^2]$ is broad in 3D, it would be either very narrow or vanishingly small to be observed in $[c \ell_p, D_{**} \simeq \ell_p]$ in 2D.

Gauss-de Gennes regime: Upon further decrease of the confining region, for $D < D_*$ the EV effect plays no role, and the DNA behaves as a Gaussian chain [15,17], so that $D = (L_{blob} \ell_p)^{1/2}$ [17]. Then according to eq. (2), we have the extension

$$\langle X \rangle_{Gauss-de\ Gennes} = L \frac{\ell_p}{D}, \quad (8)$$

which holds both in 2D and 3D. It is easy to check that in this regime the fluctuation $\langle \sigma^2 \rangle = L \ell_p$, the same as in the extended de Gennes regime.

While eq. (8) has been recently tested to be true for 3D [17] channels, similar studies have not been carried out for confined polymers in 2D strips. Considering the absence of Gaussian regime for a bulk 2D swollen chain [30,31] one wonders if this new Gauss-de Gennes phase will be observed in a 2D strip. The universal fluctuations from our BD simulation studies (fig. 4) will provide conclusive evidence for the absence of a Gaussian regime inside a 2D strip.

Odijk regime: For $\ell_p \gg D$ Odijk [34,35] argued that the chain deflects back and forth off the wall with a deflection

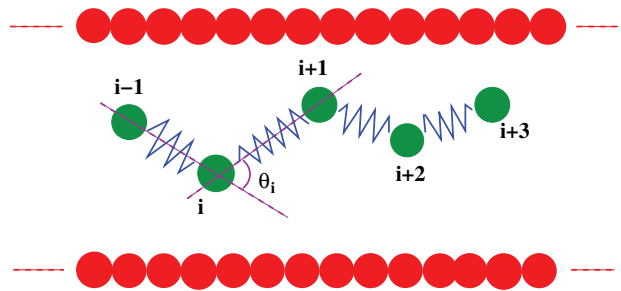


Fig. 1: (Colour on-line) Bead-spring model of a 2D polymer confined in a 2D channel.

length of $\lambda \simeq (\ell_p D^2)^{1/3}$, and the extension of the confined polymer can be written as²

$$\langle X \rangle_{Odijk} = L \left[1 - A \left(\frac{\ell_p}{D} \right)^{-\frac{2}{3}} \right], \quad (9)$$

where A is a “universal”³ prefactor [13,14]. In this limit it is easy to check that the free energy and fluctuations in chain length both in 2D and 3D are given by

$$F/k_B T = B \frac{L}{(\ell_p D^2)^{1/3}} \quad \text{and} \quad \langle \sigma^2 \rangle = \frac{L D^2}{\ell_p}. \quad (10)$$

Brownian dynamics (BD) simulation results: To provide further support to our scaling analyses we have performed Brownian dynamics (BD) simulation with a bead-spring model for a swollen chain having pairwise repulsive Lennard-Jones (LJ) interaction between any two monomers (excluded volume), a finitely extensible nonlinear elastic (FENE) potential between the successive beads (elastic-bond energy), and a three-body potential $U_{bend} = \kappa(1 - \cos \theta_i)$, where θ_i (fig. 1) is the angle between two consecutive bonds, and the parameter $\kappa = \frac{1}{2} k_B T \ell_p$ is a measure of the chain stiffness proportional to the chain persistence length ℓ_p . The DNA-wall interaction is also modeled as LJ. We observed that during simulation the average bond length stays at 0.97 with a fluctuation less than 0.2%, and the bending potential hardly affects the bond length. By monitoring $\langle \cos \theta \rangle$ we also find that $\ell_p = -1 / \ln(\langle \cos \theta \rangle) \equiv 2\kappa / k_B T$ to be the same as in a WLC [31]. Numerical integration of the equation of motion with respect to time in the canonical ensemble was done according to the algorithm developed by van Gunsteren and Berendsen [39]. In our simulation we have used reduced units of length, time, and temperature as a , $a\sqrt{\frac{m}{\epsilon}}$, ϵ/k_B , respectively. We have chosen a large number of combinations of $256 \leq N \leq 1024$, the chain persistence length $2 \leq \ell_p \leq 270$ (by varying κ from 1

²This result is valid both in two and three dimensions, as can be seen from the expansion of various averages for worm-like chains near the rod limit [37,38].

³Analytic calculations [13] for a cylindrical/square channel supported by numerical calculations indicate that this prefactor A is universal, although there is no general proof. Our results in this letter also support this claim.

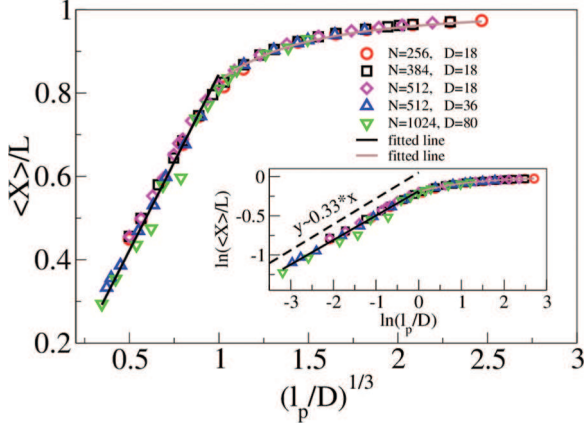


Fig. 2: (Colour on-line) Dimensionless chain extension $\langle X \rangle/L$ as a function of $(\ell_p/D)^{1/3}$ for various combinations of chain length N , persistence length ℓ_p , and width D of the confining strip. The inset is the log-log plot $\langle X \rangle/L$ as a function of ℓ_p/D showing excellent data collapse with initial slope of $1/3$ for $\ell_p \leq D$ verifying eq. (3).

to 160), and the strip width $D = 18, 36$, and 80 such that the ratio ℓ_p/D is in the window $0.025 \leq \ell_p/D \leq 15$ and $1 \leq L/\ell_p \leq 400$. With these choices we cover experimental study scales (the commonly used λ DNA in experiments has a contour length $L = 16.5 \mu\text{m}$ with a persistence length $\ell_p \simeq 50$ nm, and the channel diameter ranges between 10 nm and 200 nm [1]) and fully interpolate from the de Gennes limit to the Odijk limit. The confined chains were equilibrated for several Rouse relaxation times before data were collected over a span of 10 – 25 Rouse relaxation times to ensure convergence.

Figure 2 shows the normalized chain extension. All the data for many combinations of L , ℓ_p , and D collapse onto one master curve and show a smooth transition from the de Gennes regime to the Odijk regime, which also indicates the absence of the Gauss-de Gennes regime predicted by eq. (8). For $\ell_p \leq D$ an excellent linear fit of $\langle X \rangle/L \sim (\ell_p/D)^{1/3}$ validates the theoretical prediction of de Gennes regime (eq. (3)). For $\ell_p > D$ we used eq. (9) to fit the data and the prefactor is determined to be $A_{strip} = 0.171$. With prior reported values for this prefactor $A_{square} = 0.183$ and $A_{cylind} = 0.170$ [13,14], it indicates that the constant A has little dependence on the physical spatial dimension and nearly universal, being consistent with the fact that one can show the validity of eq. (9) in both 3D and 2D. In the log-log plot shown in the inset of fig. 2, the $1/3$ power law dependence in the de Gennes regime expands to $\ell_p/D \simeq 1$ and the scaling relation, eq. (8), in the Gauss-de Gennes regime is not seen at all. Furthermore, around $\ell_p/D \simeq 1$ we find that both eq. (3) as well as eq. (9) give almost the same value for the extension, which shows that a description by eq. (8) is not necessary indicating that there is no Gauss-de Gennes regime between them.

We also observe another interesting feature by plotting chain extensions $\langle X \rangle$ normalized by the corresponding

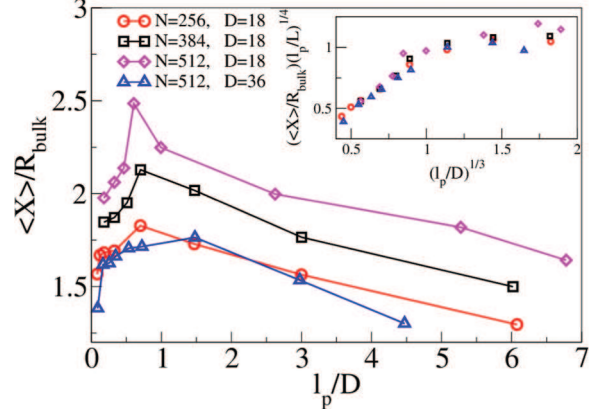


Fig. 3: (Colour on-line) Plot of the normalized extension by the end-to-end distance R_{bulk} in the bulk. The inset shows the plot of eq. (11a).

bulk end-to-end distance R_{bulk} as a function of ℓ_p/D which exhibits a peak for each curve as shown in fig. 3. This peak can be reconciled by noting that the normalized extensions in the de Gennes and Odijk limits can be expressed as

$$\frac{\langle X \rangle_{de\ Gennes}}{R_{bulk}} = \left(\frac{L}{\ell_p}\right)^{1/4} \left(\frac{\ell_p}{D}\right)^{1/3} = \tilde{L} \tilde{\ell}_p^{1/12}, \quad (11a)$$

$$\frac{\langle X \rangle_{Odijk}}{R_{bulk}} = \left(1 - A\tilde{\ell}_p^{-2/3}\right) \tilde{L}^{1/4} \tilde{\ell}_p^{-1/4}, \quad (11b)$$

where we have used D as the unit of length (data points in each curve in fig. 3 have the same D) so that $\tilde{L} = L/D$ and $\tilde{\ell}_p = \ell_p/D$, respectively, eqs. (11a) and (11b) readily follow from eqs. (1), (3), and (9), respectively. One notices that ℓ_p/D increases, *i.e.* $\tilde{\ell}_p$ increases, and the extreme left and right side of the peak correspond to de Gennes and Odijk limits, respectively. But from eq. (11a) and (11b) we note that for small values of $\tilde{\ell}_p$ the normalized extension increases as $\sim \tilde{\ell}_p^{1/12}$ (de Gennes limit), whereas, for large values of $\tilde{\ell}_p$, the normalized extension decreases as $\sim \tilde{\ell}_p^{-1/4}$ (Odijk limit), which implies that for a finite extension of a chain, the normalized extension will exhibit a maximum as a function of ℓ_p/D . It is also noteworthy that this maximum occurs for $\ell_p/D \sim 1$ at the confluence of the de Gennes and Odijk limit. This description is also consistent with the critical channel width $D_* \simeq 2\ell_p$ which marks the onset of the Odijk regime. We also plotted eq. (11a) which is only valid in de Gennes regime (*i.e.*, for $\ell_p < D$) at the inset of fig. 3 showing a data collapse similar to that in fig. 2.

We now show simulation results for the fluctuation in the chain extensions and compare these results with the theoretical predictions. According to eq. (4) and eq. (10) the normalized fluctuation $\langle \sigma^2 \rangle/LD$ scales as $(\ell_p/D)^{1/3}$ and $(\ell_p/D)^{-1}$ in the de Gennes and Odijk limits, respectively. Indeed we find in fig. 4 that the fluctuation grows as $(\ell_p/D)^{1/3}$ in the de Gennes regime until $\ell_p \simeq 0.5D$, when it enters the Odijk limit and decays as $(\ell_p/D)^{-1}$ (inset).

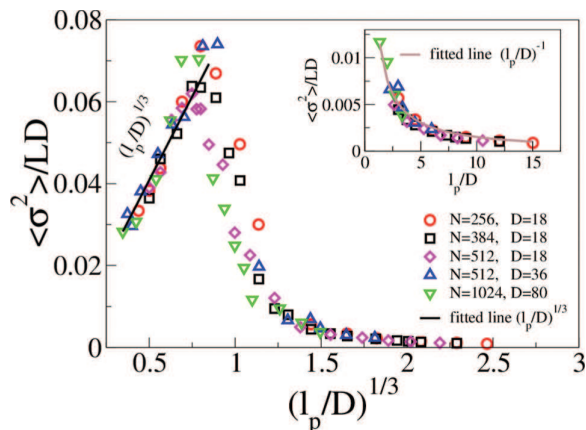


Fig. 4: (Colour on-line) Normalized fluctuation $\langle \sigma^2 \rangle / LD$ as a function of $(\ell_p / D)^{1/3}$ for the same combinations of N , ℓ_p , and D as in fig. (2). The inset shows the $(\ell_p / D)^{-1}$ dependence in the Odijk limit.

It is reassuring to note that since both the extended de Gennes and the Gauss-de Gennes regimes do not occur inside a 2D strip, in fig. 4 we do not see any intermediate regime where $\langle \sigma^2 \rangle / LD \sim \ell_p / D$, the characteristic fluctuations of both the extended de Gennes as well as the Gauss-de Gennes regimes. The excellent data collapse for the same combinations of N , ℓ_p , and D as in fig. 2 and the sharp peak signifies the onset of a transition from the de Gennes regime to the Odijk regime.

To summarize, in this letter we have provided a generalized scaling theory of confined DNA in d dimensions and compared/contrasted the behavior in 2D with those in 3D, recently reported in the literature. We validate the scaling analyses by the BD simulation where we identify each regime from excellent data collapse for the characteristic universal dimensionless extensions and fluctuations in terms of the dimensionless parameter ℓ_p / D . From the scaling analysis and results from the BD simulation reported in this letter, and prior work for 3D cylindrical and square channels, we concur that the different regimes of confined polymers follow their corresponding regimes in the bulk. We find that for a 2D strip, the Gaussian regime is absent and the extended de Gennes regime is vanishingly small, so that the chain conformations inside the channel are described either by the de Gennes or by the Odijk regime. Thus, the chain conformations for a straightened DNA inside a 2D strip are cleaner than for those of the 3D cylindrical and square geometries. Therefore, we believe that this work will motivate further experimental and theoretical work to study confined DNA inside nanostrips.

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