Soft Matter

Transcription rates in DNA brushes

Journal:	*Soft Matter*
Manuscript ID:	SM-ART-12-2014-002871.R1
Article Type:	Paper
Date Submitted by the Author:	18-Feb-2015
Complete List of Authors:	Yamamoto, Tetsuya; Weizmann Institute of Science, Materials and Interfaces Safran, S; The Weizmann Institute of Sci, Materials and Interfaces

ARTICLE TYPE www. rsc.org/xxxxxx | XXXXXXXX

Transcription rates in DNA brushes†

Tetsuya Yamamoto*[a]‡ and S. A. Safran[a]

Received Xth XXXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
First published on the web Xth XXXXXXXXXX 200X
DOI: 10.1039/b000000x

We theoretically predict the rate of transcription (TX) in DNA brush by introducing the concept of TX dipoles that takes into account the unidirectional motion of enzymes (RNAP) along DNA during transcription as correlated pairs of sources and sinks in the relevant diffusion equation. Our theory predicts that the TX rates dramatically change upon the inversion of the orientation of the TX dipoles relative to the substrate because TX dipoles modulate the concentrations of RNAP in the solution. Comparing our theory with experiments suggests that, in some cases, DNA chain segments are relatively uniformly distributed in the brush, in contrast to the parabolic profile expected for flexible polymer brushes.

1 Introduction

The first step in expressing the genetic information encoded in the sequence of bases of DNA is transcription by which the complementary sequences of RNA are synthesized by enzymes called RNA polymerase (RNAP)[1]. Each transcribed unit (TX unit) is preceded and terminated by two non-coding regions, a promoter and a terminator. Transcription is initiated when RNAP in a solution (nucleoplasm) is bound to the promoters of TX units; the special sequence of the promoters stabilizes RNAP-DNA complexes against dissociation. The enzymes then move from site to site along the TX units, polymerizing nucleoside triphosphates into a chain of RNA, until these enzymes reach the terminators, where they unbind and are released to the solution. The motion of RNAP along DNA is *unidirectional* due to irreversible steps in the RNA polymerization[2–4].

DNA is densely packed in both prokaryotic and eukaryotic cells and the rates at which the code of a TX unit is transcribed (TX rate) are, in part, regulated by the local packing density of DNA in the vicinity of the TX unit. DNA brushes, in which DNA is end-grafted to a solid substrate (see fig. 1), are simple synthetic systems that allow quantitative control of the local packing density of DNA to determine how this modifies the TX rates of DNA[5,6]. Experiments on DNA brushes showed that TX rates are limited by the dynamics of binding of RNAP to the promoters of TX units; the local concentrations of RNAP at the positions of the promoters are the key parameters that determine TX rates in DNA brush[5,6]. Moreover, the TX rates of DNA brushes were observed to be sensitive to the orientations of TX units (that are defined by the unit vector that points from the promoter to the terminator), but not to its position along the DNA[5]. These experimental results cannot be attributed to the interactions between DNA chain segments and RNAP alone because the concentration profile of RNAP due to these interactions is approximately uniform on the length scale of a TX unit; reversing the orientation of TX units does not change the local concentration of RNAP at the promoter location. The directional motion of RNAP along TX units during transcription may modulate the local concentration of RNAP and thus TX rate in DNA brush[5]. In this paper, we introduce the concept of transcription (TX) dipoles that takes into account the directional motion of RNAP in the relevant diffusion equation. We use this concept to predict that the directional motion of RNAP is indeed the physical mechanisms of the observed dependence of TX rates on the orientations of TX units.

2 Model

2.1 Transcription dipole

We treat a DNA brush in a solution of RNAP, where each DNA chain has one TX unit at the s_0-th chain segment (originating at the grafted end of the chain), see fig. 1. Above the brush region, $z > h$, the concentration ρ_0 of RNAP is uniform and this region plays the role of a reservoir of RNAP (z is the distance from the substrate and h is the height of the brush). In the solution *within* the brush, the local concentrations $\rho(z,t)$ of RNAP are derived from an effective diffusion equation that has the form

$$\frac{\partial}{\partial t}\rho(z,t) = -\frac{\partial}{\partial z}J(z,t) - k_{\rm on}(z)\rho(z,t) + k_{\rm off}(z,t). \qquad (1)$$

† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

[a] *Department of Materials and Interfaces, Weizmann Institute of Science, Rehovot 76100, Israel. E-mail: tetsujava@hotmail.com*
‡ Present address: Center of Soft Matter Physics and its Applications, Beihang University, Xueyuan Road 37, Beijing 100191, China.

The first term is due to the flux $J(z,t)$ of RNAP in the solution in the brush; this flux includes the contributions of the interactions between RNAP and DNA chain segments (see eq. (2)). $k_{\rm on}(z)$ is the rate at which RNAP is bound to the promoters of DNA from the solution in the brush (per unit concentration of RNAP) and $k_{\rm off}(z,t)$ is the rate at which RNAP is released from the terminators of DNA to the solution in the brush. With the second and third terms, the promoters and terminators of DNA are treated as the sinks and sources of RNAP relative to the solution; these terms account for the directional motion of RNAP during transcription.

The flux of RNAP has the form

$$J(z,t) = -D\left[\frac{\partial}{\partial z}\rho(z,t) + v\rho(z,t)\frac{\partial}{\partial z}\Phi(z)\right]. \qquad (2)$$

The first term is due to (entropically driven) diffusion and the second term arises from the interactions between DNA chain segments and the RNAP (the derivation is shown in Supplementary Information). For simplicity, we consider the case in which the concentration of RNAP within the solution in the brush is relatively small; interactions between RNAP molecules are negligible. D is the diffusion constant of RNAP within the solution in the brush region. v is the second virial coefficients that account for excluded volume interactions between the DNA chain segments and the RNAP. $\Phi(z)$ is the local concentration of the DNA chain segments (see below).

The binding rate $k_{\rm on}(z)$ (to promoters) has the form $\lambda g_{s_0}(z)$, where λ is the rate constant for the binding of RNAP to the promoters and $g_{s_0}(z)$ is the local concentration of promoters on the chains at height z (see fig. 1). In general, the unbinding rate $k_{\rm off}(z)$ from terminators does not have a simple form and depends on the model of DNA brush because of the correlations involved in the fact that RNAP is released from the terminator of a TX unit only when it is be bound to the promoter of the same unit beforehand; the unbinding rate of RNAP from the terminator of a TX unit, depends on the local concentration of RNAP at the position of the promoter of the same TX unit, at a time before the delay time τ of transcription. However, one can use a simple and generic treatment for the case in which the TX unit is relatively short. In the asymptotic limit that the length $l_{\rm TX}$ of TX units tends to zero, $-k_{\rm on}(z)\rho(z,t)+k_{\rm off}(z,t)\to 0$, because RNAP that is bound to the promoters is released at the corresponding terminators (that are infinitesimally close) with negligible travel time. When the length $l_{\rm TX}$ is finite (but still smaller than the Kuhn length $l_{\rm a}$), the promoters and terminators of TX units can be treated as the dipoles of sinks and sources of RNAP that are separated by $l_{\rm TX}$ (the TX dipoles): We expand the unbinding rate $k_{\rm off}(z,t)$ in eq. (1) with respect to the separation $l_{\rm TX}$, $k_{\rm off}(z,t) \simeq \langle k_{\rm on}(z-l_{\rm TX}\cos\theta)\,\rho(z-l_{\rm TX}\cos\theta,t-\tau)\rangle \simeq k_{\rm on}(z)\,\rho(z,t-\tau) - l_{\rm TX}\langle\cos\theta\rangle\frac{\partial}{\partial z}(k_{\rm on}(z)\,\rho(z,t-\tau))$, where $\langle\rangle$ is the (local) statistical average of the orientation of the TX dipoles (defined by the unit vector that points from the promoters to the terminators), θ is the angle between TX dipoles and the normal to the substrate, and τ is the delay time due to transcription. This leads to an approximate diffusion equation (see also sec. S2 in the Supplementary Information for a formal derivation)

$$0 = -\frac{\partial}{\partial z}J(z) - \frac{\partial}{\partial z}P_{\rm TX}(z) \qquad (3)$$

that is applicable for steady states ($\partial\rho(z,t)/\partial t \to 0$). $P_{\rm TX}(z)$ is the local density of TX dipoles and has the form

$$P_{\rm TX}(z) = \lambda\rho(z)l_{\rm TX}S_1(z)g_{s_0}(z), \qquad (4)$$

where $\lambda\rho(z)l_{\rm TX}$ is the moment of each dipole at z, $g_{s_0}(z)$ is the number of dipoles per unit volume, and S_1 ($\equiv\langle\cos\theta\rangle$) is the local average projection of DNA chain segments along the z direction. TX dipoles are directed inwards ('IN', $S_1<0$) or outwards ('OUT', $S_1>0$) from the substrate, dependent on which end of DNA is end-grafted to the substrate, see fig. 1. This orientational order parameter is a *vector*, not a tensor, in contrast to the situations of force dipoles[8] and liquid crystals[9], because terminators and promoters are point sources $\lambda\rho(z)$ and sinks $-\lambda\rho(z)$ that are scalars. The TX dipoles account for the correlations due to the causality involved in the binding of RNAP to the promoter of a TX unit and the subsequent unbinding from the terminator of the same unit.

We solve eq. (3) with two boundary conditions: (i) RNAP cannot penetrate the substrate and thus the flux of RNAP is zero at $z=0$, $J(0)+P_{\rm TX}(0)=0$. (ii) The chemical potentials of RNAP are continuous at the height $z=h$ of the brush, $\rho(h)=\rho_0 e^{-v\Phi(h)}$ (see also Supplementary Information). The TX rate in a DNA brush is defined by the sum of the rate $\lambda\rho(z)$ at which RNAP is bound to a promoter over all of the promoters in the system,

$$R = \int_0^h dz\lambda\rho(z)g_{s_0}(z). \qquad (5)$$

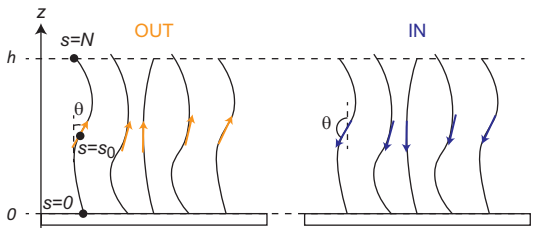


Fig. 1 The geometry of a DNA brush: Each DNA chain in the brush has one TX unit at the s_0-th chain segment (originating at the grafted end). The unit vector from the promoter to the terminator of the TX unit is directed outward from the substrate (left) or inwards, towards the substrate (right).

The forms of the local concentrations $\Phi(z)$ of chain segments, the local concentrations $g_{s_0}(z)$ of the TX units, and the orientational order parameter $S_1(z)$ depend on the applicable brush model for a given situation. The TX rate R depends on the orientations and positions of TX units via the local orientational order parameter $S_1(z)$ and local concentration $g_{s_0}(z)$ of the TX units.

2.2 Uniform DNA brush

We consider the biologically relevant case in which the solution contains high concentration of salt ions; in this case, DNA in the brush can be treated as a neutral semiflexible polymer[10,11]. We first use a simple model of a DNA brush in which the concentration of DNA chain segments are uniform in the brush region (uniform brush); $\Phi(z) = \Phi_0$ $(\equiv N\sigma/h)$ for $0 < z < h$, where the height h of the brush is Nl_aS_1, σ is the grafting density (number of chains per unit area) of DNA in the brush, N is the number of chain segments of each DNA chain, and l_a is the Kuhn length of double-stranded DNA ($l_a \simeq 100$ nm for fully neutralized DNA[12]). The distribution function $n(\mathbf{u})$ ($\mathbf{u}$ is the orientation of DNA chain segments) is determined by minimizing the free energy that has the form

$$\frac{F}{N\sigma T} = \int d\Omega\, n(\mathbf{u}) \log n(\mathbf{u}) + \frac{1}{2}\Phi_0 \int d\Omega_i \int d\Omega_j\, \beta_{ij} n(\mathbf{u}_i) n(\mathbf{u}_j). \quad (6)$$

The first term is due to the orientational entropy of the DNA chain segments and the second term is due to the (anisotropic) excluded volume interactions between these segments; this free energy takes into account the semiflexibility of DNA (the inextensibility of DNA and the anisotropic excluded volume interactions between DNA chain segments)[13,14] in an extension of a free energy of the Alexander model for flexible polymer brushes[15–17] (see also Supplementary Information). $\beta_{ij} \equiv \frac{4w}{\pi}|\mathbf{u}_i \times \mathbf{u}_j|$, where w is the second virial coefficient that accounts for the excluded volume interactions between DNA chain segments[13,14]. The integral $d\Omega$ is over all possible orientations $\mathbf{u}$ of chain segments and the subscripts i and j represent two interacting chain segments; this treats the excluded volume interactions among the chain segments near the substrate in the same manner as the rest of the brush. In this model, the substrate plays a role in breaking the symmetry of the system; the chain segments of DNA are stretched only towards the outward normal to the substrate, where the solvent is found. Eq. (6) is effective for relatively small concentrations of RNAP in which the chain conformations of DNA in the brush are only negligibly modified by interactions between DNA chain segments and RNAP. We use a variational approach[18] to derive an approximate form of the orientational order parameter S_1 (defined after eq. (4)) as a function of the grafting density of DNA (see Supplementary Information).

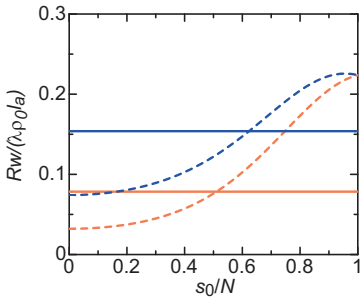


Fig. 2 Rescaled TX rates $Rw/(\lambda\rho_0 l_a)$ are shown as a function of the segment index s_0/N of TX units with the OUT (orange) and IN (blue) orientations and for the cases that the local concentrations of DNA chain segments are uniform (the solid curves) and parabolic functions (the broken curves) of the distance from the substrate. The values of v/w, $\lambda l_{TX} l_a/(Dw)$, and $\sigma w/l_a$ used for these calculations are 1.5, 1.0, and 1.0, respectively.

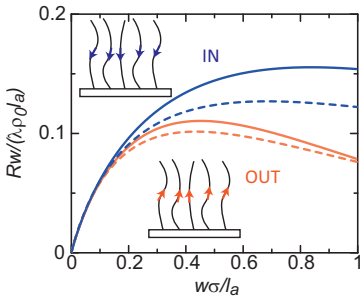


Fig. 3 The rescaled TX rate $Rw/(\lambda\rho_0 l_a)$ is shown as a function of the rescaled grafting density $w\sigma/l_a$ for the OUT (orange) and IN (blue) configurations and for the cases that the local concentrations of DNA chain segments in the brush is uniform (solid curves) and parabolic functions of the distance z (broken curves). The values of v/w, $\lambda l_{TX} l_a/(Dw)$, and s_0/N used for the calculations are 1.5, 1.0, and 0.5, respectively.

For uniform DNA brushes, TX rate has the form

$$R = \frac{D}{l_{TX}S_1}\rho_0 e^{-v\Phi_0}\left(1 - e^{-\lambda l_{TX}S_1\sigma/D}\right). \quad (7)$$

This expression is obtained by using eq. (5), where the local concentration of RNAP is derived from eqs. (2) and (4) for the case in which the local concentration of DNA chain segments is Φ_0 (constant). The form of eq. (7) indeed does not depend on the specific form of the local concentrations $g_{s_0}(z)$ of the TX units (see also Supplementary Information); the TX rate in the DNA brush thus does not depend on the position s_0 of TX units, see also the solid curves in fig. 2.

3 Results and Discussion

Our theory predicts the rescaled TX rate $Rw/(\lambda\rho_0 l_a)$ as a function of the rescaled grafting density $w\sigma/l_a$ of DNA as well as the positions s_0/N (along DNA chains) and orientations of TX units. This rate also depends on the ratio v/w of the second virial coefficients and the rescaled rate constant $\lambda l_{TX} l_a/(Dw)$, where the values of these parameters are of order unity for physiologically relevant salt concentrations (see also Table 1 in the Supplementary Information). For relatively small grafting densities of DNA, the TX rate increases linearly with increasing the grafting density of DNA, simply because the number of TX units increases, see the solid curves in fig. 3. The TX rate is not very sensitive to the orientation of the TX dipoles because, in this limit, the density of the TX dipoles is too small to modulate the local concentration of RNAP in the brush region. For larger grafting densities, the TX rate is always smaller for the OUT configuration than for the IN configuration. This is because, for the OUT configuration, both the directional motion of RNAP and the excluded volume interactions between RNAP and DNA chain segments (the osmotic pressures of the brush) tend to expel RNAP from the brush region; this decreases the local concentrations of RNAP in the vicinity of the promoters and thus suppresses the TX rate in DNA brush. In contrast, for the IN configuration, the TX dipoles tend to accumulate RNAP near the substrate and thus increase the concentration of RNAP in the brush region, relative to the OUT configuration. This result is in agreement with experiments[5,6] and thus demonstrates that the directional motion of RNAP during transcription plays an important role in the TX rate in DNA brushes.

Our theory predicts that for the IN configuration, the TX rate shows a plateau at relatively large grafting densities, when the ratio v/w of the second virial coefficient is as large as the rescaled rate constant $\lambda l_{TX} l_a/(Dw)$, see fig. 3*. This is because the fluxes of RNAP due to excluded volume interactions between RNAP and DNA chain segments (which tend to expel RNAP from the brush) are as large as localizing effects of the TX dipoles (that tend to accumulate RNAP near the substrate). In contrast, when the ratio v/w is small or negative, TX rate does not show plateau and continues to increase monotonically with increasing the grafting density of DNA. Experiments (that are performed at physiologically relevant salt concentrations for the IN configuration) show that TX rate saturates for large grafting densities[5]. The experimentally relevant ratio v/w is thus positive and somewhat large for these salt concentrations (it is estimated to be ~ 1 from the dimension of a DNA chain segment and a T7 RNAP[19]). In this case, our theory predicts that the concentration of RNAP is smaller in the solution in the brush region than in the bulk solution (for both the OUT and IN configurations). Moreover, for the OUT configuration, the TX rate decreases as the grafting density of DNA is increased, see fig. 3, because both TX dipoles and excluded volume interactions (between RNAP and DNA chain segments) tend to expel RNAP from the brush. These results are indeed in agreement with experiments[6,7].

Experiments show that the TX rate is not very sensitive to the position s_0 of TX units for $\sigma \sim 1100\ \mu\mathrm{m}^{-2}$ (that is an order of magnitudes larger than the inverse of square of Kuhn length)[5]. This is in agreement with the prediction of our theory for the case of a DNA brush, where the concentration of chain segments is uniform, see fig. 2. Such a uniform concentration profile has been predicted for strongly stretched polymer brushes due to the anisotropic excluded volume interactions between chain segments and/or the inextensibility of the polymers[20,21]. However, recent experiments have shown that DNA in brushes may not be strongly stretched even for the largest grafting density (that is used in the experiments) because the excluded volume of DNA chain segments is relatively small[10,25]. For a polymer brush that is moderately stretched, one expects the local concentration of DNA chain segments to be a quadratic function of the distance z from the substrate (parabolic brush)[20,21]. For a parabolic brush, the local concentration $\Phi(z)$ of DNA chain segments and the orientational order parameter S_1 have the forms

$$\Phi(z) = \frac{3}{2}\frac{\sigma N}{h}\left(1-\frac{z^2}{h^2}\right) \quad (8)$$

$$S_1(z) = \frac{\pi}{2}\frac{z}{N l_a}\cot\left(\frac{\pi s_0}{2N}\right), \quad (9)$$

where $h\ (= N l_a(\frac{4w\sigma}{\pi^2 l_a})^{1/3})$ is the height of the brush[22–24] (see also Supplementary Information). The local concentrations $g_{s_0}(z)$ of TX units are

$$g_{s_0}(z) = 3\sigma\frac{\chi^2 z\sqrt{h^2-\chi^2 z^2}}{h^3} \quad (10)$$

for $0 < z < \chi^{-1}h$ and zero for $\chi^{-1}h < z < h$, where we used a factor $\chi^{-1}\ (\equiv \sin(\frac{\pi s_0}{2N}))$[22–24] (see also Supplmentary Information)†. In contrast to uniform brushes, for parabolic brushes, our theory predicts that TX rate *is* sensitive to the position s_0 of TX units because the local concentrations of DNA chain segments are not themselves uniform, see the broken curves in fig. 2. This is not the case in the aforementioned experiments[5] that use brushes of DNA with the contour length of ~ 700 nm (~ 7 Kuhn segments); such DNA brushes show rather uniform concentration profile, even for the case in which the DNA is

* This 'plateau' is indeed not a saturation, but a relatively broad maximum unless the ratio v/w of the second virial coefficients and the rescaled rate constant $\lambda l_{TX} l_a/(Dw)$ are fine tuned (see also eq. (7) and fig. 3 in Supplementary Information).

† Eqs. (8) - (10) are applicable for relatively small concentrations of RNAP in which the chain conformations of DNA are only negligibly modified by the excluded interactions between the RNAP and the DNA chain segments.

stretched only moderately. This prediction may be tested more directly by experiments using total internal reflection fluorescence[7,28]. The general dependence of TX rate on the grafting density of DNA is not sensitive to the brush model, at least, for the values of rescaled grafting density $w\sigma/l_a$ that is smaller than unity, see fig. 3.

Our results suggest that the approximation of flexible polymer brushes is not relevant to DNA brushes, even for some cases in which the chains are longer than the Kuhn length and are only moderately stretched. Indeed, a theory of DNA solutions predicts that the structures of DNA are only slightly affected by the excluded volume interactions between DNA chain segments even in semidilute concentrations when the length of DNA is shorter than a length scale $\sim l_a^3/d^2$ (where d is the effective diameter of DNA chain segments, $\simeq 4$ nm)[25]. This is in agreement with recent experiments that use $< 50\ \mu$m long DNA in solutions[26,27]. This implies that the conformation of relatively short DNA chains in brushes may not be very different from a single DNA chain that is end-grafted to a substrate even for a relatively large grafting density[10‡]. The uniform concentration profile that is predicted by comparing our results with the experiments discussed here may be rationalized by taking into account the stiffness of DNA[28]. We here emphasize that our prediction that the TX rate of a uniform brush is not very sensitive to the positions of TX units along DNA chains is a generic result that does not depend on the specific form of the free energy, see sec. S3B in the Supplementary Information. Measurements of TX rate as a function of the chain length of DNA may provide further information about the physical mechanisms that stabilize the uniform concentration profile.

4 Conclusion

In this paper, we introduced the concept of TX dipoles to treat the directional motion of RNAP during transcription in a simple and generic manner. Our theory predicts that the directional motion of RNAP from the promoter to the terminator of the TX unit dramatically changes the local concentration of RNAP in the brush and thus is important in determining the TX rate in DNA brushes. The dipole approximation is appropriate for the case in which the length of TX units is smaller than the Kuhn length of DNA, which is the case of some experiments on DNA brushes[5]. The typical length of TX units in bacterial DNA is about 300 nm[4] and thus ~ 3 times longer than the Kuhn length of DNA. In such cases, the local density of TX dipoles has the form

$$P_{\rm TX}(z) = \lambda \rho(z) g_{s_0}(z) \langle z_t - z_p \rangle, \qquad (11)$$

where z_p and z_t are the real space positions of the promoter and terminator sites, respectively. This treatment takes into account the fact that the chain may fluctuate significantly in the region between the promoter and terminator; in that case, the (real-space) distance between the promoter and the terminator of a TX unit may be shorter than the contour length $l_{\rm TX}$ between these sites and the orientation of the unit vector from the promoter to the terminator may deviate from the tangent vector along the chain at the position of the promoter. Eq. (11) is effective for cases in which the length of TX units $l_{\rm TX}$ is much smaller than the entire length of DNA chains. TX dipoles may be thus still useful to approximately treat the directional motion of RNAP along TX units that are somewhat longer than the Kuhn length (but are still shorter than the entire length of a DNA chain). Otherwise, one should use eq. (1) to treat the directional motion of RNAP. An extension of the concept of TX dipoles may provide insight in other active transport processes, *e.g.* the transports of cargos by molecular motors along cytoskeletal filaments[29]. A unique feature of the directional motion of RNAP along TX units may be the fact that the starting and ending positions of the motion are prescribed in the base sequence of DNA.

‡ A self-consistent field theory predicts that the local concentration of chain segments tends to be more uniform than predicted by the classical theory as the stretching parameter $h^2/(Nl_a^2)$ is decreased[24]. Moreover, the self-consistent field theory also predicts that the tangent of the most probable conformation of DNA chains is directed towards the outward normal to the substrate more than predicted by the classical theory; the classical theory used here gives a lower bound on the order parameter $S_1(z)$. Both of these effects are underestimated in the classical theory since the entropic repulsion between the DNA chains and the substrate is not taken into account, while the self-consistent field theory does include this effect[24].

Acknowledgement

The authors thank P. A. Pincus, G. Shemer, R. H. Bar-Ziv, and B. Palmieri for helpful discussions. SAS is grateful for grants from the U.S.-Israel Binational Science Foundation, the Israel Science Foundation, the Schmidt Minerva Center and a research grant from Mr. and Mrs. Antonio Villalon. This research is made possible in part by the historic generosity of the Harold Perlman Family Foundation.

References

1 B. Alberts, A. Johnson, J. Lewis, *et al.*, *Molecular Biology of the Cell*, 5th ed., Garland Science, NY, 2002.
2 P. H. von Hippel, *Science*, 1998, **281**, 660.
3 F. Jülicher and R. Bruinsma, *Biophys. J.*, 1998, **74**, 1169.
4 R. Phillips, J. Kondev, and J. Theriot, *Physical Biology of the Cell*, Garland Science, NY, 2009
5 S. S. Daube, D. Bracha, A. Buxboim, and R. H. Bar-Ziv, *Proc. Natl. Acad. Sci. USA*, 2010, **107**, 2836.
6 A. Buxboim, S. S. Daube, and R. Bar-Ziv, *Mol. Syst. Biol.*, 2008, doi:10.1038/msb.2008.20.

7 D. Bracha, E. Karzbrun, S. S. Daube, and R. H. Bar-Ziv, *Account. Chem. Res.*, 2014, **47**, 1912.

8 U. S. Schwartz and S. A. Safran, *Rev. Mod. Phys.*, 2013, **85**, 1327.

9 P. G. de Gennes and J. Prost, *The Physics of Liquid Crystals*, 2nd ed., Oxford University Press, UK, 1993.

10 D. Bracha, E. Karzbrun, G. Shemer, P. A. Pincus, and R. H. Bar-Ziv, *Proc. Natl. Acad. Sci. USA*, 2013, **110**, 4534.

11 J. F. Marko and E. D. Siggia, *Macromolecules*, 1995, **28**, 8759.

12 C. G. Baumann, S. B. Smith, V. A. Bloomfield, and C. Bustamante, *Proc. Natl. Acad. Sci. USA*, 1997, **94**, 6185.

13 L. Onsager, *Ann. NY Acad. Sci.*, 1949, **51**, 627.

14 T. Odijk, *Macromolecules*, 1986, **19**, 2313.

15 S. Alexander, *J. Phys. France*, 1977, **38**, 983.

16 P. G. de Gennes, M̂acromolecules, 1980, **13**, 1069.

17 S. T. Milner, *Science*, 1991, **251**, 905.

18 S. A. Safran, *Statistical Thermodynamics of Surfaces, Interfaces, and Membranes*, Westview Press, CO (2003).

19 A. Polyakov, E. Severinova, and S. A. Darst, *Cell*, 1995, **83**, 365.

20 M. Deng, Y. Jiang, H. Liang, and J. Z. Y. Chen, *Macromolecules*, 2010, **43**, 3455.

21 D. F. K. Shim and M. E. Cates, *J. Phys. France*, 1989, **50**, 3535.

22 S. T. Milner, T. A. Witten, and M. E. Cates, *Macromolecules*, 1988, **21**, 2610.

23 E. B. Zhulina, O. V. Borisov, and L. Brombacher, *Macromolecules*, 1991, **24**, 4679.

24 R. R. Netz and M. Schick, *Macromolecules*, 1998, **31**, 5105.

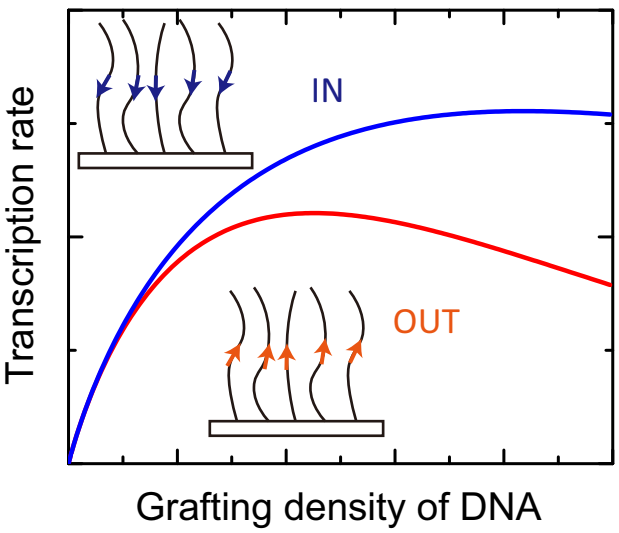
25 D. W. Schaefer, J. F. Joanny, and P. Pincus, *Macromolecules*, 1980, **13**, 1280.

26 E. Shafran, A. Yaniv, and O. Krichevsky, *Phys. Rev. Letts.*, 2010, **104**, 128101.

27 M. Nepal, A. Yaniv, E. Shafran, and O. Krichevsky, *Phys. Rev. Letts.*, 2013, **110**, 058102.

28 M. Lindner, G. Nir, S. Medalion, H. R. C. Dietrich, Y. Rabin, and Y. Garini, *Phys. Rev. E*, 2011, **83**, 011916.

29 A. Caspi, R. Granek, and M. Elbaum, *Phys. Rev. Letts.*, 2000, **85**, 5655.


IN
OUT
Transcription rate
Grafting density of DNA