Thermophoretic stretch of nano-confined polymers: model and simulations

Martin Bertrand and Béla Joós*
Institut de physique Ottawa-Carleton
Campus de l'Université d'Ottawa
Ottawa, Ontario, Canada, K1N 6N5
(Dated: September 29, 2011)

We present a novel approach to model the effects of a non-uniform force field stretching a nano-confined polymer using blobs and the Flory free-energy. We use it to describe the thermophoretic stretch of polymers exposed to symmetric thermal gradients in nano-confined geometries as demonstrated in Thamdrup *et al.*, Nano Lett., 10, 2010. We validate our model with experimental data and molecular dynamics simulations. Excluded volume interactions are shown to play a key role especially when temperatures are close to the solvent's θ value.

Being able to manipulate single biopolymers is of utmost importance for the study of their properties. In particular, we often wish to extend these to perform force response measurements or to expose the backbone of the chains to study the binding activity of external agents such as enzymes with DNA. Some common techniques are: optical and magnetic tweezers, and atomic force microscopy [1]; fluid flow [2], and electrophoretic forces [3]. All these techniques require the binding of one or both ends of the polymers to specific sites or colloids, which is not always convenient. Confinement of biopolymers such as DNA to nano-channels can also result in uniaxial extension and has many advantages as reported in [4], none the least being able to forgo the binding procedure. However, polymer insertion becomes one of the main challenges which Thamdrup *et al.* [5] recently overcame by thermophoretic manipulation of single DNA molecules in both micro- and nano-channels. They successfully inserted double-stranded DNA (dsDNA) in nano-channels using thermophoretic forces originating from highly localized thermal gradients and also showed that, once in, DNA can be symmetrically stretched under thermophoresis (see Fig. 1). Although it is not the first time thermophoretic forces have been used to stretch DNA [6, 7], the particular way they do it in [5] facilitates the study of thermophoresis.

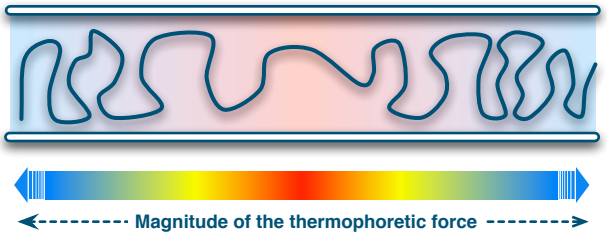

FIG. 1. A representation of the symmetric thermophoretic stretch of a polymer under a thermal gradient and confined to a nano-channel. The monomer concentration is lower in the central region and increases toward the ends.

The Soret coefficient $S_T = -1/c(\mathrm{d}c/\mathrm{d}T)$, where c is the particle concentration and T, the temperature, characterizes the strength of thermophoresis [8]. For particles suspended in gases in the quasi-hydrodynamic regime and under a thermal gradient, the general form of S_T has been analytically derived [9]. However, for colloids in solution, the picture is incomplete [8]. For instance, although an effective thermophoretic force proportional to the temperature gradient and acting on all suspended particles in a given solution can often be measured, its strength has been shown to be highly sensitive to molecular interactions whether they be particle-solvent or particle-particle [10–12]. In fact Duhr and Braun recently found evidences that support a theory of thermophoresis based on solvation entropy [13]. This leads to thermal diffusion from hot to cold (thermophobic behaviour), as expected, but also from cold to hot (thermophilic behaviour), which defies our naive intuition of the phenomenon.

We present a novel approach to describe nano-confined polymers symmetrically stretched by the action of a non-uniform force field originating in our case from thermophoretic forces as in Fig. 1. We construct a simple model that incorporates thermophoresis in a theory of blobs and Flory free-energy which accurately reproduces the observed monomer concentration profile. Temperature dependent excluded volume interactions (EVI) can also be included. We show that the particular shape of the monomer concentration profile such as the one reported in [5] can be obtained without the intervention of strong thermophoretic forces. To demonstrate this and give strength to our model, we fit the latter to data from molecular dynamics (MD) simulations in which we use a temperature profile similar to the one measured in [5] and an explicit thermophoretic force that we can tune. From a theoretical standpoint, we think the study of thermophoretic effects on nano-confined polymers, that is collections of linked monomers, can help shed light on the true nature of thermophoresis in viscous media. Indeed, the metastable state of equilibrium reached by the single polymer system studied here gives us a unique op-

portunity to look at collective effects in thermophoresis. From a practical standpoint, a better understanding of thermophoresis and temperature dependent EVI in the context of nano-confined biopolymers such as DNA or even proteins could potentially lead to interesting ways to gain better access to their mid part and its properties.

Let us first consider a polymer of N segments (or monomers) of Kuhn length b and width d confined to a channel of diameter D_c with x being the coordinate along the channel's axis. We will here consider, for simplicity and brevity, that we are in the de Gennes regime with $b < D_c < R_g$, but we remind the reader that the regime landscape for nano-confined polymers is much richer [14–16]. One can then imagine the polymer is composed of a series of N/g blobs of size $D \sim D_c$ containing g segments each. In each blob, the chain size follows the usual bulk statistics. We recall the well known Flory free-energy [17] that we write for a blob here:

$$\beta A_{\rm blob} \cong \frac{D^2}{gb^2} + \frac{gb^2}{D^2} + v\frac{g^2}{D^3} + w\frac{g^3}{D^6}, \qquad (1)$$

where $\beta = 1/k_BT$. The four terms in Eq. 1 are, in order of appearance: the entropic cost of stretching (1) and compression (2), the two particles (3) and three particles (4) EVI terms where $v \approx \frac{T-\theta}{T}b^2d$ and $w \cong (bd)^3$ essentially give their respective strengths. The excluded volume v characterizes the solvent quality, that is the relative strength of the monomer-solvent, monomer-monomer, and solvent-solvent interaction energies [17]. As one raises the temperature across the θ value, solvent-monomer interactions come to dominate, we go from a poor solvent to a good solvent, and the whole polymer experiences a globule to coil transition or in other terms, it swells. When $T \gg \theta$, the chain is in an athermal solvent and $v \cong b^2d$. When $T \ll \theta$ we are dealing with a non-solvent and $v \cong -b^2d$.

Let us establish a stable symmetric temperature gradient $T(x)$ in the system from the middle of the polymer as reported in [5] (if $x = 0$ is the midpoint of the chain, $T(x) = T(-x)$). We choose it to be of the following functional form that fits the true experimental profile:

$$T(x) = T_{\rm room} + T_0 \exp\left[-\left(1 + \frac{c}{2}(x - x_0)^2\right)^{\alpha}\right], \qquad (2)$$

where x_0 is the midpoint, $T_{\rm room}$, the room or reference temperature, and T_0, c, α are tunable parameters. In the experiment that lead to the observed monomer concentration profile of Fig. 7c in [5], the parameters that fit the thermal profile used are: $x_0 = 55.86\mu$m, $T_0 = 37.44$K, $c = 0.987\text{m}^{-2}$, and $\alpha = 0.175$. The chain is then stretched symmetrically and non-uniformly along x by local thermophoretic forces proportional to the temperature gradient $f_T(x) \propto -\nabla T(x)$ acting on all segments. The proportionality constant is equal to $S_T(T)/\beta$ where $S_T(T)$ is the temperature dependent Soret coefficient [8]. Indeed, thermophoresis experiments conducted on colloids show that S_T grows with temperature to an asymptotic limit of S_T^∞ [12]. For many colloids, S_T^∞ is reached close to room or physiological temperatures. Unfortunately, for segments of DNA we do not know if this is the case, but since experiments in [5] were conducted between 300K and 320K, we will assume $S_T \approx S_T^\infty$ such that:

$$f_T(x) \approx -S_T^\infty \frac{\nabla T(x)}{\beta(x)}. \qquad (3)$$

Thermophoretic forces push segments away from the polymer's center where forces are the strongest. One should thus expect the segment density to go up as we go from the middle of the chain to its ends. The experimental monomer concentration profile in Fig. 2 shows exactly this. Let us include thermophoretic forces in Eq. 1 and calculate this profile. It was shown that the action of external forces reduces the size of Pincus blobs [17, 18]. Here we assume that all blobs are of mean size $D \sim D_c$ and that it's the number of segments g per blob that varies. We then assume, by a mean-field type approach, that all g_i segments in the i-th blob whose center is positioned at x_i feel a temperature $T(x_i)$ and are subject to a thermophoretic force $f_T(x_i)$. Each blob is considered to be an entropic spring and the work done by thermophoretic forces on blob i is given by the sum of all f_Ts acting on all segments in the blobs from x_{i+1} to the nearest end of the polymer which is approximately:

$$W_{T,i} \sim DF_{T,i} = -DS_T^\infty \sum_{j=i+1}^{n_b/2} g_j \frac{\nabla T(x_j)}{\beta(x_j)}, \qquad (4)$$

where n_b is the number of blobs in the chain. We can then rewrite the free-energy of a blob now including the thermophoretic work:

$$\beta_i A_i \cong \frac{D^2}{g_i b^2} + \frac{g_i b^2}{D^2} + v\frac{g_i^2}{D^3} + w\frac{g_i^3}{D^6} - \beta_i W_{T,i}. \qquad (5)$$

Again we can minimize the free-energy with respect to D to find the equilibrium configuration which leads to the following polynomial:

$$c_0 g_i^4 + c_1 g_i^3 + c_2 g_i^2 + c_3 g_i + c_4 = 0, \qquad (6)$$

where $c_0 = 6w/D^7$, $c_1 = 3|v|/D^4$, $c_2 = 2b^2/D^3$, $c_3 = -\beta_i S_T^\infty \sum_j g_j \nabla T(x_j)/\beta(x_j)$, and $c_4 = -2D/b^2$. This polynomial can be solved numerically and recursively starting from the ends of the polymer where $g = 0$ and iterating over the blobs until the center of the chain is reached. Thermophoretic forces contribute to blob segregation. Therefore our model should be able to predict the segment concentration profile close to the middle part of the chain even in conditions where blob overlap is expected near the ends, as in the case of an ideal chain. In

fact, as long as the thermophoretic work done on a particular blob is more important than thermal agitation around that position ($W_{T,i} > k_BT(x_i)$), the number of segments in that blob should be correctly estimated. If the chain is in an athermal solvent, strong EVI naturally segregate blobs and the model is expected to correctly predict the full extent of the segment concentration profile in quality if not in quantity.

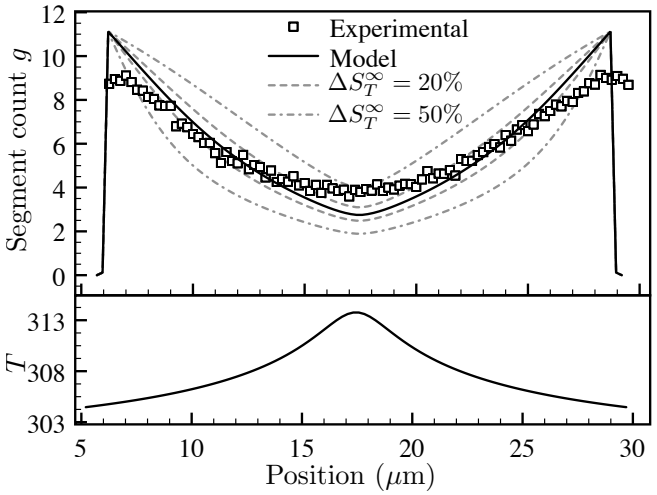

FIG. 2. Top panel: fit of our model of thermophoretic stretch to data of experiments on DNA taken from Fig. 7c in the paper by Thamdrup *et al.* [5]. Bottom panel: the temperature profile used. All parameters are specified in the text.

In Thamdrup *et al.* paper [5], they inserted and then thermophoretically stretched YOYO dyed T4 dsDNA strands of 166 kbp (contour length $L_c \approx 70\mu$m, Kuhn length $b \approx 124$nm, number of Kuhn segments $N_K \cong 564$, and width $d \approx 2$nm [19]) confined to a square nanochannel of side $D = 250$nm and under the thermal gradient defined previously. Fig. 7c in the paper shows a fluorescence intensity time trace of the experiment. We processed the image and extracted the segment concentration profile plotted in Fig. 2 where it has been renormalized using the known total number of Kuhn segments and assuming the blobs are the size of the channel's side of length D. We then fitted our model considering an athermal solvent. Clearly, we can reproduce the shape of the profile well. However, divergences are present which can be attributed to two main factors: first, the data from [5] used was preliminary, and data with better statistics could be expected in the future; second, the blobs contain very few monomers, especially those in the central region, where the limits of our Flory free-energy based model are stretched. As a result of fitting the data, we found the Soret coefficient for a DNA Kuhn segment $S_T^\infty = 0.068 \pm 0.006\text{K}^{-1}$ sensitive to variations beyond 10% (see Fig. 2). This compares favourably to a value of roughly 0.1K^{-1} found for DNA filaments of length $L_c \sim b$ in Fig. 4c of [13]. Other factors which might influence the Soret coefficient here are the collective effects, that is the segments of DNA are connected to each other, and the strong confinement the DNA chain is under. Thamdrup *et al.* report a value of 50fN for the entropic recoil force of the T4 DNA fragments [5]. A thermophoretic force of comparable strength is needed to strongly stretch the central part as is the case here. Using our value of S_T^∞ we found $F_{T,0} \approx 52$fN as required.

We also fitted our model to the results of MD simulations. This was done in part to better evaluate its accuracy and in part to explore the effects of temperature dependent EVI. A bead-spring chain of N beads was placed in a cylindrical channel of radius R_c. Interactions in the system are those found in [20]: beads can interact through a Lennard-Jones (LJ) inspired potential $U_{\text{LJ}}(r) = \epsilon\left[(\sigma/r)^{12} - 2(\sigma/r)^6\right]$ and springs are modelled with harmonic potentials of the form $U_{\text{H}}(r) = k_s(r-\sigma)^2$ where $k_s = 16.67\epsilon/\sigma^2$. Thus, the MD chain is akin to single-stranded DNA (ssDNA) and not dsDNA. We set the unit of energy $\epsilon = 1$ ($k_B = 1$), the unit of length $\sigma = 1$, the unit of mass $m = 1$, and the unit of time $\tau = 1$. All observables from this point on are considered to be in the appropriate MD units. If the LJ potential is truncated at $r_{\text{cut}} = 2.5$, the chain thus simulated exhibits a globule-coil transition around $\theta = 2.18$ which allows the study of solvent quality effects. One can also truncate at $r_{\text{cut}} = 1$ to recuperate the behavior of a chain in an athermal solvent using purely repulsive interactions or avoid using the LJ potential altogether to simulate an ideal chain. Each segment of the chain has a length equal to its width $b = d = 1$ such that the volume is $b^3 = 1$. We modified the Langevin thermostat in the ESPREsSo package [21] to accommodate for a temperature profile as given by Eq. 2 and an explicit thermophoretic force of magnitude $-k_BTS_T^\infty\nabla T$ acting on all particles in the system where S_T^∞ can be tuned and is in units of k_B/ϵ. The middle bead was anchored with a soft harmonic spring in the middle of the channel where the temperature is set to be the highest to prevent longitudinal diffusion and improve the acquisition of the segment concentration profile. The confinement parameter $D = 2(R_c - \sigma)$, as the monomers always interact with the channel wall via the repulsive part of the LJ potential.

Fig. 3 shows the data from MD simulations in various solvent conditions (variable T_{room}) and the corresponding best fits of our model. The values for the thermal profile were: $T_0 = 5.5$, $c = 0.987$, and $\alpha = 0.175$. The chains considered here are long compared to the width of the thermal profile ($L_c = 201$ vs $2\Delta_{T_{\max}/2} = 12.8$). The Soret coefficient was set to $S_T^\infty = 2.5$. In good solvent conditions (Fig. 3), the maximum temperature is $T_{\max} \approx 6$ which leads to $S_T^\infty T_{\max} \approx 15$. For comparison, the same operation using experimental values also gives ~ 15. Clearly our model reproduces well the shape of the monomer concentration profile no matter the range of temperature explored and the solvent quality. Such

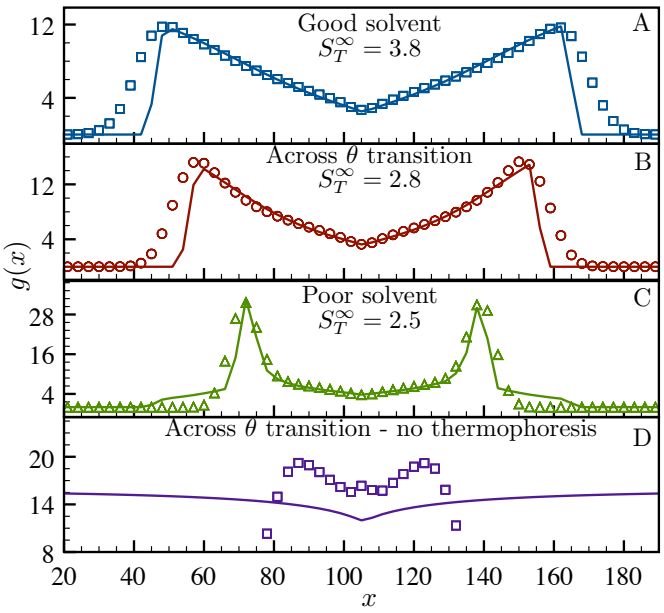

FIG. 3. Monomer concentration profiles for a MD simulation of nano-confined polymer in a symmetric temperature gradient in various solvent conditions: A) good solvent, $T_{\text{room}} = 4.0$; B) across the θ-transition, $T_{\text{room}} = 2.0$; C) poor to θ solvent, $T_{\text{room}} = 1.0$; D) across the θ-transition, no explicit thermophoretic force. The symbols represent the data from simulations and the solid lines, the best fits. The confinement $D = 4.75$ and the Soret coefficient $S_T^\infty = 2.5$, while $N = 201$ and $b = 1$.

agreement for our simple model is impressive. From the fits, we obtained Soret coefficients that do not exactly match the one imposed to the systems, although they are certainly of the same order of magnitude and are all comparable. The chains are quite extended in their mid part for strong enough thermophoretic forces and thus the effects of EVI should be negligible which means all densities should coincide. Although we do not explicitly show this in Fig. 3, both the data and our model adhere to this conclusion. Therefore, for experiments conducted with polymers that have contour lengths close to the width of this central region corresponding to a faster changing temperature gradient, the effects of EVI can be neglected.

Comparing the ends of profiles A and C in Fig 3, we can clearly see collective effects: in a good solvent (A), end monomers appear thermophobic, whereas in a poor solvent (C), they appear thermophilic when in fact the clumping is due to the dominating monomer-monomer attractive interactions. The number of monomers per blob in good solvent conditions without any thermal gradient ($T(x) = 4.0$) is $g \approx 12$ and the full extent of the confined chain is $R_\parallel \approx 71$. In the cases studied here, no matter the solvent quality, the extension of the chain is enhanced by thermophoresis and more importantly, the backbone is better exposed in the central region.

Fig. 3D shows that variable EVI alone do produce the characteristic shape of the concentration profile although they do not enhance stretch as much as with additional thermophoresis (see Fig. 3B). If our prediction falls short of the MD results quantitatively, it is because blobs are not clearly segregated close to the θ transition.

We have demonstrated that a simple model based on blobs and the Flory free-energy can reproduce the monomer concentration profile observed in both experiments and simulations of the thermophoretic stretch of nano-confined polymers such as DNA. The approach we have taken could be applied to other problems where a non-uniform field acts on a confined polymer. Moreover, we have shown that EVI can be decoupled from other contributions to thermophoresis in the specific system studied here, which allowed us to expose collective effects. Temperature dependent EVI alone could partly explain the concentration profiles. The effects of variable EVI should definitely be further explored in the future. We would like to extend this study taking into account the effects of variable electrostatics along the length of the chain confined in the nano-channel since this could prove useful to correctly predict the shape of confined DNA under thermophoresis as presented in [5].

We acknowledge financial support from NSERC and Jonas N. Pedersen for useful discussions.

* bjoos@uottawa.ca

[1] K. Neuman and A. Nagy, Nat. Methods, **5**, 491 (2008).
[2] R. Larson, T. Perkins, D. Smith, and S. Chu, Phys. Rev. E, **55**, 1794 (1997).
[3] S. Smith and A. Bendich, Biopolymers, **29**, 1167 (1990).
[4] J. Tegenfeldt, C. Prinz, H. Cao, S. Chou, W. Reisner, R. Riehn, Y. Wang, E. Cox, J. Sturm, P. Silberzan, *et al.*, Proc. Natl. Acad. Sci. U.S.A., **101**, 10979 (2004).
[5] L. Thamdrup, N. Larsen, and A. Kristensen, Nano Lett., **10**, 826 (2010).
[6] M. Ichikawa, H. Ichikawa, K. Yoshikawa, and Y. Kimura, Phys. Rev. Lett., **99**, 148104 (2007).
[7] H. Jiang and M. Sano, Appl. Phys. Lett., **91**, 154104 (2007).
[8] R. Piazza and A. Parola, J. Phys. Condens. Matter, **20**, 153102 (2008).
[9] P. Epstein, Z. Physik, **54**, 537 (1929).
[10] R. Piazza and A. Guarino, Phys. Rev. Lett., **88**, 208302 (2002).
[11] S. Putnam and D. Cahill, Langmuir, **21**, 5317 (2005).
[12] S. Iacopini, R. Rusconi, and R. Piazza, Eur. Phys. J. E, **19**, 59 (2006).
[13] S. Duhr and D. Braun, Proc. Natl. Acad. Sci. U.S.A., **103**, 19678 (2006).
[14] W. Reisner, K. Morton, R. Riehn, Y. Wang, Z. Yu, M. Rosen, J. Sturm, S. Chou, E. Frey, and R. Austin, Phys. Rev. Lett., **94**, 196101 (2005).
[15] T. Odijk, Phys. Rev. E, **77**, 060901 (2008).
[16] Y. Wang, D. Tree, and K. Dorfman, Macromolecules (2011).

[17] M. Rubinstein and R. Colby, *Polymer physics* (Oxford University Press, USA, 2003).
[18] S. Jun, D. Thirumalai, and B. Ha, Phys. Rev. Lett., **101**, 138101 (2008).
[19] L. Thamdrup, A. Klukowska, and A. Kristensen, Nanotechnology, **19**, 125301 (2008).
[20] M. Ciesla, J. Pawlowicz, and L. Longa, Acta Phys. Pol. B, **38**, 1727 (2007).
[21] H.-J. Limbach, A. Arnold, B. A. Mann, and C. Holm, Comput. Phys. Commun., **174**, 704 (2006).