

Mobility of a Reptating Polymer

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The reptation model for the dynamics of an entangled polymer is considered for the case where the diffusion is driven by a weak field. If the distance between entanglements is greater than the persistence length, the mobility of long chains is predicted to be independent of their size and *proportional* to the field strength. This difference from previous predictions is due to the fact that fluctuations alter the field dependence of the tube orientation. Implications for the separation of DNA using gel electrophoresis are discussed.

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The driven diffusion of an entangled polymer is a theoretical problem that has received much attention, particularly in the context of the gel electrophoresis of DNA. Discussion has centered on whether the reptation model [1,2], successful for the case of purely Brownian motion, remains an appropriate description when the molecule also experiences a force due to an external field. The "biased reptation model" (BRM) [3-8], which supposes that the polymer is constrained to move in a tube with its diffusion biased by the net force acting along the tube axis, has been shown to be inadequate when the field is strong [9-11]; excursions of loops of the chain laterally out of the tube and longitudinal fluctuations of the molecule within the tube both become significant, leading to more complex dynamical behavior. In this Letter, however, we wish to reconsider the case of gel electrophoresis in a weak field; in this situation the basic premise of the BRM is valid and yet the currently accepted version of the theory is, we believe, incorrect.

In the BRM, the polymer is modeled as a primitive path of N segments. Each segment represents a blob of charge q and linear dimension a , where a is the mean distance between entanglements or the average pore size, and a fluid friction ζ is associated with each blob. In an electric field E , the average curvilinear velocity of the polymer along the tube is [4] (neglecting numerical factors)

$$\langle \dot{s} \rangle = \varepsilon - \frac{\langle |h_x| \rangle a}{Na \tau}, \quad (1)$$

where h_x is the component of the end-to-end vector in the field direction, $\varepsilon = qEa/kT$ is a dimensionless measure of the field strength, and $\tau = \zeta a^2/kT$ is the Brownian time of a blob. Then by writing the mean velocity of the center of mass as $\langle \dot{x} \rangle = \langle \dot{s} h_x \rangle / Na$, one obtains the electrophoretic mobility

$$\mu \equiv \langle \dot{x} \rangle / E = \mu_0 \langle h_x^2 \rangle / (Na)^2, \quad (2)$$

where $\mu_0 = q/\zeta$. So the mobility depends on the average molecular conformation and the problem is to determine what this is. Lumpkin, Dejaridin, and Zimm [5] and

Slater and Noolandi [6] developed different versions of the BRM, but both proposed that when the end segment of the chain emerges from the tube, its orientation θ with respect to the field direction is biased by the field, with a weight governed by the Boltzmann factor $\exp(-\varepsilon \cos\theta)$. Each segment of the tube eventually receives this bias so that its mean orientation is [5]

$$\langle \cos\theta \rangle = \mathcal{L}(\varepsilon) \equiv \coth(\varepsilon) - \varepsilon^{-1}, \quad \sim \varepsilon \text{ for } \varepsilon \ll 1. \quad (3)$$

In weak fields ($\varepsilon \ll 1$), the orientation per segment is slight so that short chains remain approximately Gaussian; long chains, on the other hand, are aligned along the field with a mean end-to-end distance proportional to the field strength. Thus this theory for the orientation predicted that the mobility should vary as [5]

$$\mu/\mu_0 \sim \begin{cases} N^{-1}, & N \ll N^*, \\ \varepsilon^2, & N \gg N^*, \quad \varepsilon \ll 1, \end{cases} \quad (4a)$$

$$(4b)$$

$$N^* \sim \varepsilon^{-2}. \quad (5)$$

The most immediate success was the prediction that, above a certain size limit N^* , molecules of different lengths travel at the same speed and cannot be distinguished from each other. This is only too well known to occur in practice, where it severely restricts the usefulness of continuous-field gel electrophoresis as a method of separating and analyzing DNA. A second achievement was that, by including the diffusional fluctuations of the drift velocity in the theory [6-8] so that either end of the molecule may lead alternately, the existence of "band inversion" was predicted and experimentally confirmed: In certain experimental conditions the mobility varies non-monotonically with molecular weight. Perhaps these successes have tended to obscure the fact that the agreement between the predicted field dependence of the mobility (4b) and the experimental data is rather poor, for little attention has been paid to the discrepancy since it was first noticed [5]. Nevertheless, an understanding of this point is highly desirable, since the field strength is the most readily tunable experimental parameter.

The question of chain orientation is a rather delicate one and demands, in our opinion, a more considered approach. The argument of Refs. [5,6] is an equilibrium one, since it assumes that the terminal segment of the chain attempts to minimize its potential energy. Is this justified? A quasiequilibrium approach to a dynamical problem will be valid only if it has internal consistency: One must ask *on what length scale* the chain has the opportunity to equilibrate.

We shall consider first the case of a polymer that is flexible on the scale of the gel pores (Kuhn length $b < a$). Its reptative motion is a net consequence of longitudinal fluctuations of the chain density in the tube, which are governed by one-dimensional Rouse dynamics. The tube length does not remain constant, as assumed in the BRM, but rapidly fluctuates so that the terminal section of the chain is continually retracting and reextending, thereby exploring new pathways in the gel. After a time t , the number n_{fluc} of tube segments that have been modified by the length fluctuations is [2,12]

$$n_{\text{fluc}} \sim \begin{cases} (t/\tau)^{1/4}, & t/\tau < N^2, \\ N^{1/2}, & t/\tau > N^2. \end{cases} \quad (6a)$$

$$(6b)$$

Concurrently, the chain has been drifting along the tube so that it has advanced a distance of n_{drift} pores along the axis, where

$$n_{\text{drift}} = \langle \dot{s} \rangle t/a. \quad (7)$$

We propose that the condition

$$n = n_{\text{drift}} = n_{\text{fluc}} \quad (8)$$

determines the size n of the terminal section of the chain that has time to equilibrate (see also Ref. [13]).

The effect of length fluctuations may then be treated by imagining the n end segments of the primitive path (labeled $i=1$ to n) to swiftly sample alternative routes through the gel, while the "permanent" part of the tube starts only at the $(n+1)$ th segment (Fig. 1). The terminal section of the chain behaves as though it is anchored at the mouth of the permanent tube, but is otherwise free to minimize its potential energy. Then the orientation of the i th segment depends on the total force exerted on the preceding segments: $\langle \cos\theta_i \rangle = \mathcal{L}(i\varepsilon)$ [14]. As the chain

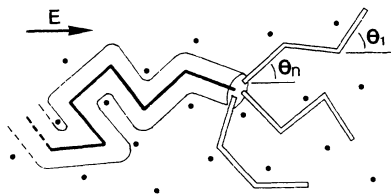


FIG. 1. Primitive path representation of a flexible polymer migrating through a gel. In black: the part of the molecule inhabiting a permanent tube. In white: alternative conformations of the rapidly fluctuating end section of the chain (consisting of n segments).

advances, the permanent tube assumes the orientation of the n th segment so that the tube orientation is

$$\langle \cos\theta \rangle = \mathcal{L}(n\varepsilon), \quad \sim n\varepsilon \text{ for } \varepsilon \ll 1. \quad (9)$$

Equations (6)–(9) together with (1) provide a closed set of equations for the mean orientation of a tube segment. In the long-chain limit, the Gaussian component of the end-to-end vector is negligible so that $\langle h_x \rangle = Na \times \langle \cos\theta \rangle$. Then for weak fields ($\varepsilon \ll 1$), one obtains $n \sim \varepsilon^{-1/2}$ and

$$\langle \cos\theta \rangle \sim \varepsilon^{1/2}. \quad (10)$$

Compared with the BRM result (3), the inclusion of tube fluctuations not only enhances the orientation, but also alters its field dependence. As the chain size is reduced, a crossover will be reached at $N = N^*$ when either (i) the size of the equilibrated fluctuation reaches its limiting value (6b), or (ii) the Gaussian component of the end-to-end vector becomes equal in magnitude to the contribution due to the orientation. In fact, both conditions are attained simultaneously at $N^* \sim \varepsilon^{-1}$. Thus, for flexible polymers, Eqs. (4) and (5) for the mobility should be replaced by

$$\mu/\mu_0 \sim \begin{cases} N^{-1}, & N \ll N^*, \\ \varepsilon, & N \gg N^*, \quad \varepsilon \ll 1, \end{cases} \quad (11a)$$

$$(11b)$$

$$N^* \sim \varepsilon^{-1}. \quad (12)$$

The mobility of long chains varies *linearly*, and the size limit above which no separation is achievable *inverse linearly*, with the field strength.

In this analysis we have neglected the diffusional component of the motion of the polymer in the tube. By analogy with Refs. [7,8] we should expect that its inclusion would lead to a small degree of band inversion, with molecules of size in the region of N^* having the minimum mobility. Thus the field dependence of band inversion should differ, too, from previous predictions.

Our main result (10)–(12) is corroborated by a second approach which requires no quasiequilibrium assumption for it is based on a purely dynamical argument. The mean orientation of the molecule may be determined by calculating the probability that a new primitive path segment, created with orientation θ by a length fluctuation, is not subsequently removed, but survives to become part of the permanent tube. We require a description of the dynamics of the chain end, which we obtain by exploiting the connection between tube length fluctuations and tracer diffusion of impenetrable particles on a line [15,16]. The latter problem may be approximated, in turn, by the closely related one of a random walk on a random walk [17].

Consider first the field-free case. The position of the end of the tube at time t may be described as $s(\xi(t))$, where $\xi(t)$ is a random walk on a base walk $s(\xi)$ (see Fig. 2):

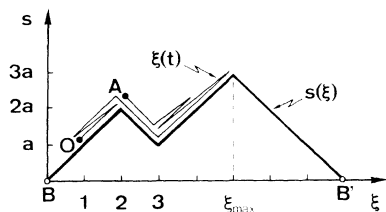


FIG. 2. Motion of the chain end, represented as a random walk $\xi(t)$ on a base walk $s(\xi)$. The walk started at O and, after time t , has reached A . The arrival of the walk at either B or B' corresponds to the removal of the part of the tube that housed the end segment of the chain at $t=0$.

$$\xi(t+\tau) = \xi(t) \pm 1, \quad s(\xi+1) = s(\xi) \pm a.$$

Suppose that at time $t=0$ a fluctuation has just caused the chain end to move from $s=0$ to $s=a$, thereby creating a new primitive path segment. Then we have

$$\xi(0) = 1, \quad s(0) = 0, \quad s(1) = a.$$

The new segment will not have been removed at time t if the chain end has never returned to $s=0$ in the time interval. For it to survive, then, two conditions must be satisfied. First, the walk must remain in the region $\xi > 0$. The probability of this is given by the expression [18] for the weight of a one-dimensional walk of t/τ steps that does not return to the origin: $P_1(t) \sim (t/\tau)^{-1/2}$. Second, the base walk must stay in the region $s > 0$. Now, if ξ has not returned to $\xi=0$ at time t , it will have attained a maximum value which scales as $\xi_{\max} \sim (t/\tau)^{1/2}$, so the probability that the second condition is satisfied is $P_2(t) \sim \xi_{\max}^{-1/2} \sim (t/\tau)^{-1/4}$. Thus, we obtain

$$P(t) = P_1 P_2 \sim (t/\tau)^{-3/4}. \quad (13)$$

To discuss the modification of this expression when there is a field present, it is convenient to consider the probability $p(t)$ that the segment is removed at time t :

$$p(t) = -dP/dt \sim (t/\tau)^{-7/4}. \quad (14)$$

When the chain end has a nonzero curvilinear drift velocity \dot{s} , the position of the end of the chain is approximately Gaussian distributed: $\phi(s) \sim \exp[-(s-\dot{s}t)^2/a^2(t/\tau)^{1/2}]$. Since the removal of the segment always takes place at $s=0$, this introduces an extra factor $\phi(0)$ compared to the field-free case so that (14) is modified to

$$p(t) \sim (t/\tau)^{-7/4} \exp[-(\dot{s}\tau/a)^2(t/\tau)^{3/2}] \quad (15)$$

and (13) is changed to $P(t) = 1 - \int^t p(t') dt'$. The exponential in Eq. (15) acts as a cutoff in the integral at

$$t_{\text{cut}}/\tau \sim (\dot{s}\tau/a)^{-4/3}, \quad (16)$$

so that $P(\infty)$ varies as $(t/\tau)^{-3/4}$ evaluated at the cutoff. Thus

$$P(\infty) \sim \dot{s}\tau/a \quad (17)$$

and we obtain the result that the probability that a new primitive path segment becomes permanent is simply proportional to the drift velocity \dot{s} .

Different orientations θ of the segment perturb the velocity of the chain end from its mean value $\langle \dot{s} \rangle$ by different amounts $\Delta \dot{s}(\theta)$, thereby leading to different probabilities of retention of the segment. The relevant velocity in Eqs. (16) and (17) is the drift velocity of the section of the chain adjacent to the end whose Rouse time is equal to t_{cut} (recall footnote [12]). The length of this section is $m = (t_{\text{cut}}/\tau)^{1/2}$ segments. If we make the mean-field approximation that, apart from the new segment, the rest of the Rouse section has the mean tube orientation $\langle \cos\theta \rangle$, then $\dot{s} = \langle \dot{s} \rangle + \Delta \dot{s}$ where [from Eq. (1), and keeping only first-order terms]

$$\Delta \dot{s}(\theta)/\langle \dot{s} \rangle = \cos\theta/m\langle \cos\theta \rangle. \quad (18)$$

Combining Eqs. (16)–(18), one obtains the perturbation to the probability (17)

$$\Delta P(\infty, \theta)/P(\infty) \sim (\dot{s}\tau/a)^{2/3} \cos\theta/\langle \cos\theta \rangle.$$

Assuming that a newly created primitive path segment is *randomly oriented*, the probability that a permanent tube segment has orientation θ is proportional to $\sin\theta\{1 + \Delta P(\infty, \theta)/P(\infty)\}$, so performing the average of $\cos\theta$ one obtains

$$\langle \cos\theta \rangle \sim (\dot{s}\tau/a)^{2/3}/\langle \cos\theta \rangle. \quad (19)$$

Equations (19) and (1) yield the result $\langle \cos\theta \rangle \sim \varepsilon^{1/2}$ for the long-chain limit in which the molecule is oriented. So the result (10) is recovered.

Now we shall turn to the case of a polymer in a tight gel ($a < b$). Here the molecule is stiff on the scale of the gel pores so that the orientation of the primitive path is persistent over a number of consecutive segments (it changes by the mean-square amount $\langle \Delta\theta^2 \rangle \sim a/b$ per segment). Although the relative rigidity of the chain suppresses fluctuations within the tube [the size of the fluctuation associated with a length of chain containing m segments is $n_{\text{fluc}} = m^{1/2}(a/b)$; cf. [12]], they remain important enough to modify previously derived results [19]. Following the same quasiequilibrium or dynamical arguments outlined above, we find that short chains, $N < N^*$, remain approximately Gaussian with $\langle h_x^2 \rangle = Nab$, but long molecules are oriented, so that the mobility varies as

$$\mu/\mu_0 \sim \begin{cases} N^{-1}(b/a), & N \ll N^*, \\ \varepsilon(b/a)^{1/2}, & N \gg N^*, \quad \varepsilon \ll (a/b)^{7/2}, \\ \varepsilon^{2/5}(a/b)^{8/5}, & N \gg N^*, \quad (a/b)^{7/2} \ll \varepsilon \ll a/b, \\ \varepsilon^2, & N \gg N^*, \quad a/b \ll \varepsilon \ll 1, \end{cases} \quad \begin{matrix} (20a) \\ (20b) \\ (20c) \\ (20d) \end{matrix}$$

$$N^* \sim \begin{cases} \varepsilon^{-1}(b/a)^{1/2}, & \varepsilon \ll (a/b)^{7/2}, & (21a) \\ \varepsilon^{-2/5}(b/a)^{13/5}, & (a/b)^{7/2} \ll \varepsilon \ll a/b, & (21b) \\ \varepsilon^{-2}(b/a), & a/b \ll \varepsilon \ll 1. & (21c) \end{cases}$$

The different regimes arise because the degree of orientation depends on whether the fluctuating terminal section of the chain should be regarded as flexible or stiff. Equation (20b) corresponds to the case where the fluctuation is longer than the Kuhn length, while Eq. (20c) corresponds to the converse situation. Notice that if the field is not too weak (20d), the effect of tube length fluctuations becomes negligible and the quadratic dependence of the mobility on the field strength (4b), predicted by previous models, is recovered.

What are the implications of our results for the electrophoretic separation of DNA using continuous fields? As one example, let us discuss how to minimize the separation time of molecules in a given size range. Writing the contour length of the DNA as S and the charge per Kuhn length as q_0 , then for large pores ($a > b$) each blob in our representation of the chain is Gaussian and $S/b = N(a/b)^2$, while for small pores ($a < b$) each blob is linear and $S/b = N(a/b)$. Thus, from Eqs. (12) and (21a) we obtain the limit of resolution:

$$S^*/b \sim \begin{cases} \varepsilon_0^{-1}(b/a), & a > b, & (22a) \\ \varepsilon_0^{-1}(b/a)^{3/2}, & a < b, & (22b) \end{cases}$$

with $\varepsilon_0 = q_0 E b / kT$. From Eqs. (11a) and (20a), the mobility in the window of resolution varies as

$$\mu/\mu_0 \sim \begin{cases} (S/b)^{-1}(a/b)^2, & a > b, & (23a) \\ (S/b)^{-1}, & a < b. & (23b) \end{cases}$$

A given range of separation S^* may be obtained using different combinations of pore size and field strength. The combination which provides the most rapid separation is that which maximizes the migration speed $\langle \dot{x} \rangle = \mu E$ of molecules of size S^* . By comparing the dependence on the field strength and on the pore size of Eqs. (22) and (23) we conclude that for the regime $a > b$, more efficient separations within a given size range are obtained by using the combination of larger gel pores and weaker fields; by contrast, for the regime $a < b$, it is more advantageous to choose smaller pores and stronger fields. We remark that the agarose gels used to separate double-stranded DNA, which have a pore size close to the Kuhn length, appear to be a poor choice in this respect [20]. An experimental evaluation of the persistence length of single-stranded DNA would allow discussion of the case of sequencing gels using polyacrylamide.

In conclusion, we have shown that molecular fluctuations play a vital role in determining the orientation and

the weak-field mobility of reptating polymers. One consequence is that the interpretation of gel electrophoresis experiments by the biased reptation model requires revision. Our analysis is also of relevance to other situations such as the sedimentation of macromolecules in gels and the motion of polymers in inhomogeneous melts.

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