



Stretch dependency of the electrophoretic mobility of DNA

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Abstract

We develop a theory on DNA electrophoresis that shows stretch-dependent electrophoretic mobility in agreement with an experiment observation. In our theory, a DNA molecule is modeled as a freely-jointed-chain, each of whose segments consists of a collinear series of charged spheres, which we call a “shish-kebab” segment. First, by calculating the interaction between charged spheres in an electric field, we show that the electrophoretic mobility of a shish-kebab segment is dependent on the orientation relative to its direction of the electric field. Then, the electrophoretic mobility of the whole DNA chain is evaluated by taking an ensemble average over the orientation of the shish-kebab segments in the chain. The result shows an enhancement of the magnitude of the electrophoretic mobility under the stretch of the DNA molecule.

Introduction

The electrophoretic velocity of an insulating charged particle of arbitrary shape in a uniform electric field E is given by $v = \mu^{EP} E = (\epsilon \zeta / \eta) E$, where μ^{EP} is the electrophoretic mobility of the particle, ϵ the fluid permittivity, ζ the zeta potential of the particle, and η the fluid viscosity, when it is assumed that the radius of curvature of the particle surface is much larger than the thickness of the electric double layer on the particle [1]. However, it is not clear if this is also relevant for an electrophoresis of a DNA molecule since the radius of the DNA cross-section is as small as the typical thickness of the electric double layer. Recent experiments show that the electrophoretic mobility of a DNA molecule under deformation is dependent on the molecular conformation (Fig. 3). The DNA deformation was induced by an electric field gradient imposed by a converging channel; see Fig. 2(b). In this study, we develop a theory on DNA electrophoresis that shows stretch-dependent electrophoretic mobility in agreement with the experiment observation.

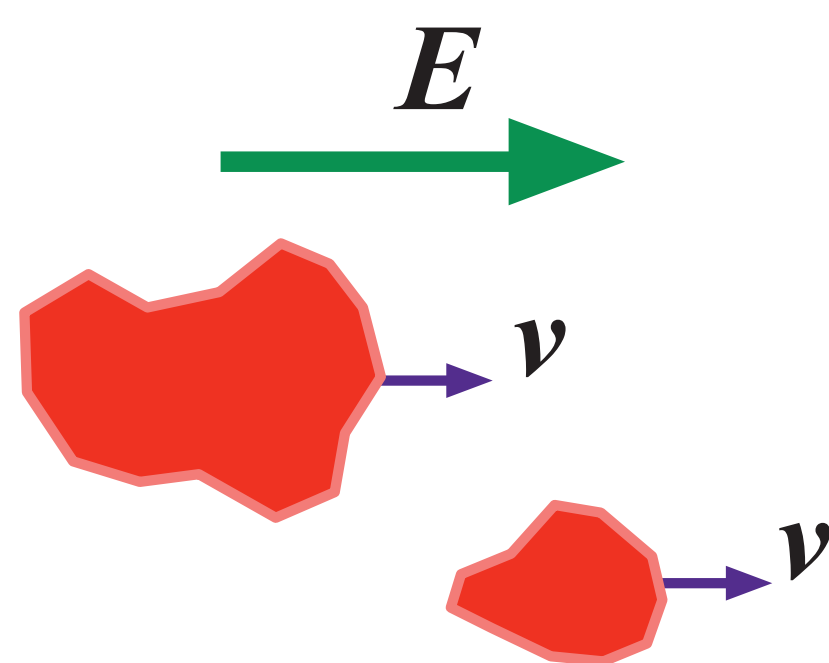


Figure 1. The electrophoretic velocity of an insulating charged particle of arbitrary shape in a uniform electric field E is given by $v = \mu^{EP} E = (\epsilon \zeta / \eta) E$ and independent of the shape and the size of the particle.

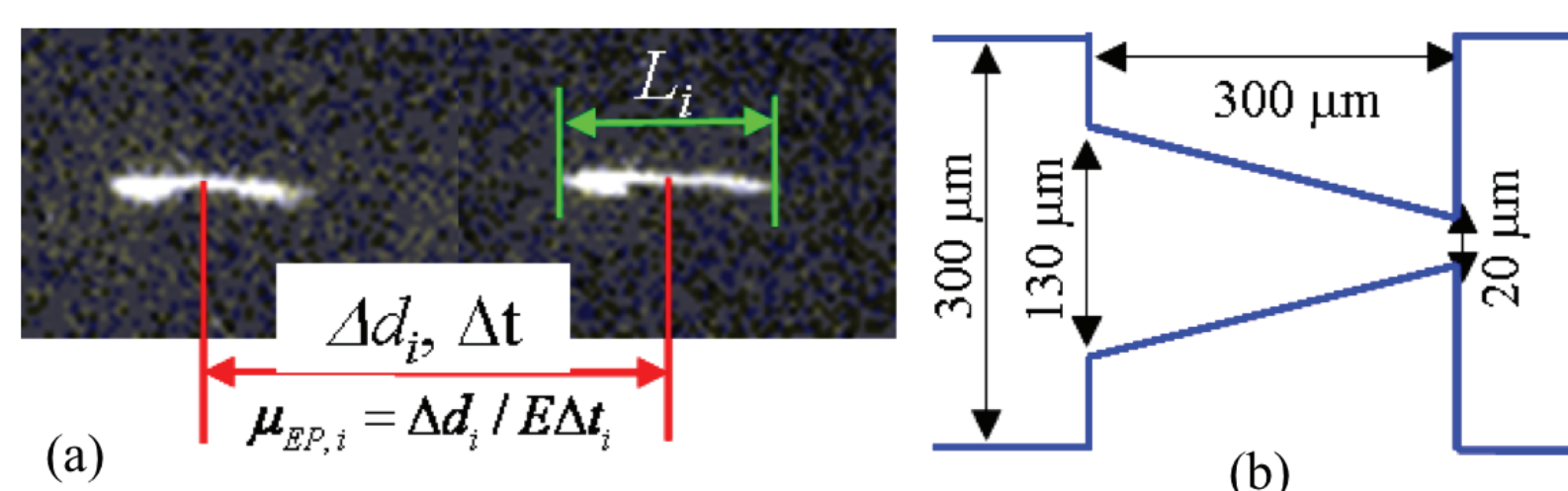


Figure 2. (a) The measurement of instantaneous electrophoretic mobility, where E is the magnitude of the local electric field; (b) dimensions of a converging microchannel used in experiments.

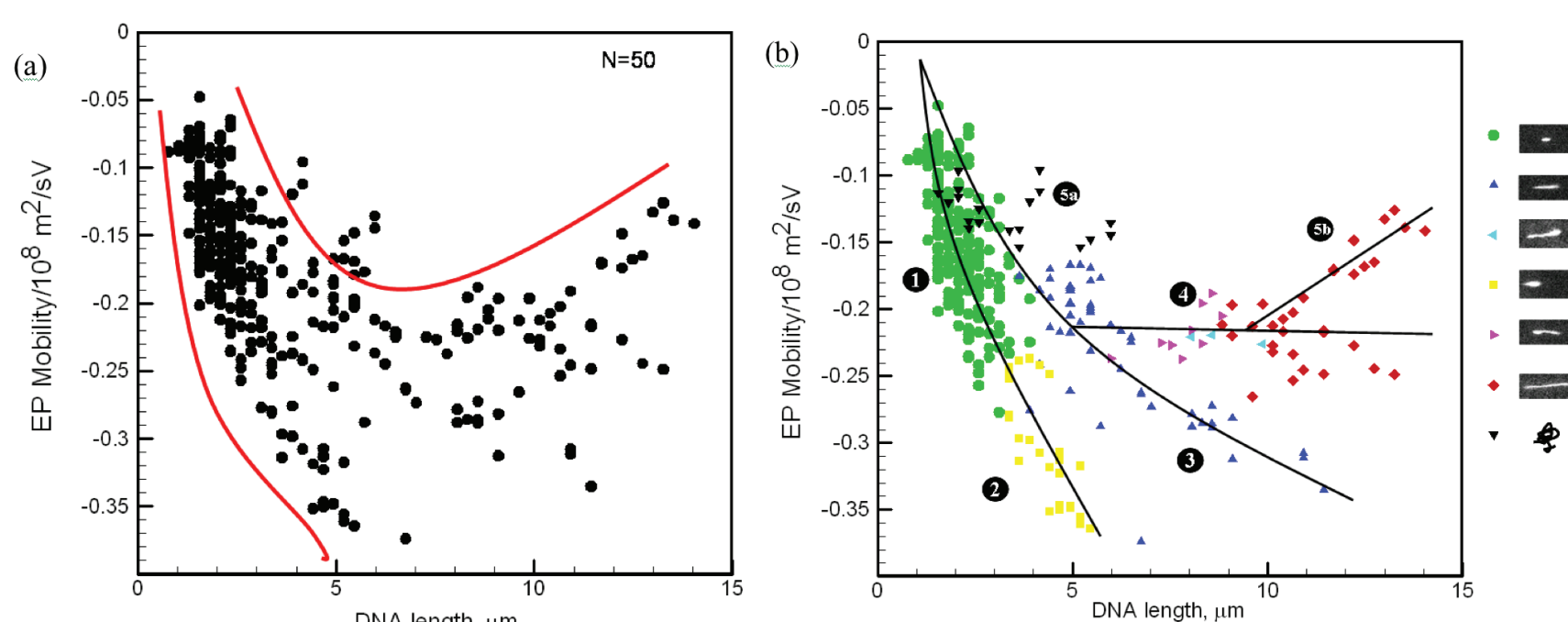


Figure 3. Instantaneous electrophoretic mobility data for 50 λ -DNA molecules (a) as a function of DNA length and (b) as a function of DNA configuration and its configuration dynamics.

[1] F.A. Morrison, *Journal of Colloid and Interface Science*, **34**, 210-214 (1970)

Shish-kebab model

The electrophoretic mobility of a charged spherical particle is determined by its radius a , the charge Q , the Debye length κ^{-1} and the viscosity of the solvent η . In the limit of a thin electric double layer, theoretical studies suggest that electrophoresis of a charged spherical particle induces a flow perturbation around it, which decays with distance r from the particle as $\sim r^{-3}$. The velocity perturbation at position r_j induced by the electrophoretic motion of a charged particle at r_j in a uniform electric field E is given by [2],

$$v^{EPH}(r_i) = S_{ij}(r_{ij}) \cdot Q_j E,$$

$$S_{ij}(r_{ij}) = \frac{1}{4\pi\eta\kappa^2 r_{ij}^3} \left(I - 3 \frac{r_{ij} r_{ij}}{r_{ij}^2} \right).$$

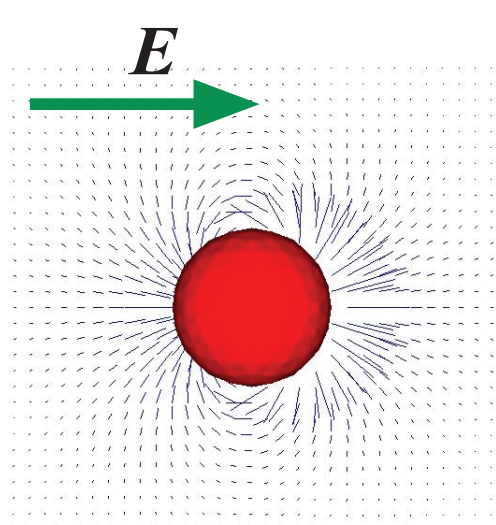


Figure 4. The flow perturbation induced by electrophoresis of a charged spherical particle, which decays with distance r from the particle as $\sim r^{-3}$.

To create a simple model of a charged rigid polymer, we connect charged spherical particles with rods on a straight line to create a “shish-kebab” model; see Fig. 5. Suppose that each particle has charge Q and radius a , and the distance between two adjacent particles is b . Then, the center-of-mass migration velocity of a shish-kebab with N beads in electric field $E = (E, 0, 0)^T$ can be written as,

$$v^{SK} = \mu^{EP}(a, Q, \kappa, \eta) E + \frac{1}{N} \sum_{i=1}^N \sum_{j \neq i} v^{EPH}(r_{ij}),$$

$$= \mu^{EP}(a, Q, \kappa, \eta) E + \frac{1}{N} \sum_{i=1}^N \sum_{j \neq i} \frac{QE}{2\pi\eta\kappa^2 (b|i-j|)^3} \begin{pmatrix} 3 \cos^2 \theta - 1 \\ 3 \cos \theta \sin \theta \cos \phi \\ 3 \cos \theta \sin \theta \sin \phi \end{pmatrix}$$

$$= \mu^{EP}(a, Q, \kappa, \eta) E + \frac{2QE}{\pi\eta\kappa^2 b^3} \begin{pmatrix} 3 \cos^2 \theta - 1 \\ 3 \cos \theta \sin \theta \cos \phi \\ 3 \cos \theta \sin \theta \sin \phi \end{pmatrix}$$

Here, as a first approximation, we assume that the chain has been stretched by a weakly non-uniform electric field, but we neglect this non-uniformity in computing the mobility of the deformed chain. From the second term, the electrophoretic velocity of the center-of-mass in the direction of the electric field is enhanced most at $\theta = n\pi$ ($n = \dots, 0, \pm 1, \pm 2, \dots$). Moreover, a migration perpendicular to the electric field is induced when $\theta \neq n\pi/2$. These results qualitatively agree with theoretical and experimental studies on the electrophoresis of spheroidal particles [3] and polymers under deformation in a Poiseuille flow [4].

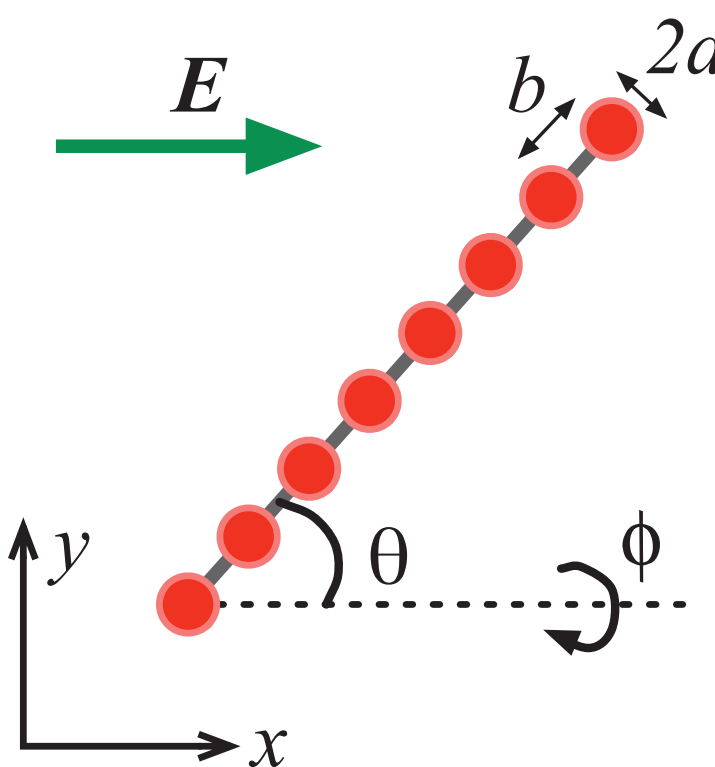


Figure 5. The “shish-kebab” model of a rigid charged polymer.

Model for a flexible molecule

In order to estimate the electrophoretic velocity of a charged polymer, we connect together shish-kebabs, each of length equal to a single Kuhn step length of the polymer molecule, to assemble a flexible polymer, in the same way as rods are connected together to form a freely-jointed-chain.

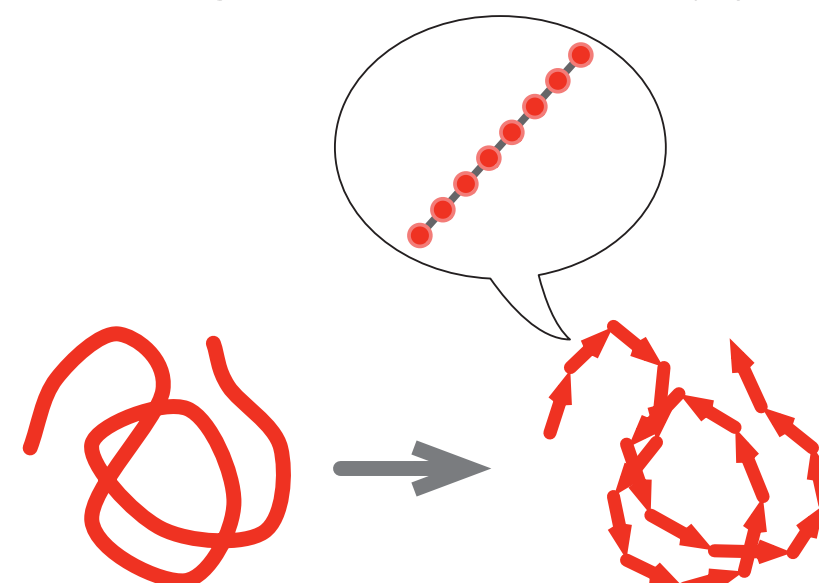


Figure 6. A freely-jointed-chain consisting of charged “shish-kebab” segments.

[2] D. Long and A. Ajdari, *European Physical Journal E*, **4**, 29-32 (2001).

[3] B. J. Yoon and S. Kim, *Journal of Colloid and Interface Science*, **128**, 275-288 (1970)

[4] J. Zheng and E. S. Yeung, *Analytical Chemistry*, **74**, 4536-4547 (2002)

Results

If we take an ensemble average over the angles (θ, ϕ) of each shish-kebab, the center-of-mass migration velocity of a single shish-kebab can be written as,

$$\langle v^{\text{chain}} \rangle = \frac{1}{N_K} \sum_{n=1}^{N_K} \langle v_n^{\text{SK}} \rangle$$

$$= \mu^{EP}(a, Q, \kappa, \eta) E + \frac{2QE}{\pi\eta\kappa^2 b^3} \begin{pmatrix} 3(\cos^2 \theta) - 1 \\ 3(\cos \theta \sin \theta \cos \phi) \\ 3(\cos \theta \sin \theta \sin \phi) \end{pmatrix}$$

$$= \mu^{EP}(a, Q, \kappa, \eta) E + \frac{2QE}{\pi\eta\kappa^2 b^3} \begin{pmatrix} 3(\cos^2 \theta) - 1 \\ 0 \\ 0 \end{pmatrix}$$

$$\text{where } \langle A \rangle = \int \int P(\theta, \phi) A \sin \theta d\theta d\phi$$

Let us now assume that the polymer as a whole has been stretched to a stretch ratio s/L (L : the maximum stretch) in the x -direction by a stretching force $F^{\text{str}}(s)$ in the x direction. We can then calculate the ensemble average of shish-kebab angles from a Boltzmann distribution:

$$P(\theta, \phi) = \frac{1}{Z} \exp \{ F^{\text{str}}(s) L_K \cos \theta / k_B T \}$$

where L_K is the Kuhn length. For DNA, we employ the worm-like chain (WLC) spring law for the stretching force:

$$F^{\text{str}}(s) = \frac{k_B T}{L_K} \left\{ \left(1 - \frac{s}{L} \right)^{-2} - 1 + 4 \frac{s}{L} \right\}$$

The ensemble-averaged center-of-mass migration rate can then be evaluated as:

$$\langle v^{\text{chain}} \rangle = \mu^{EP}(a, Q, \kappa, \eta) E + \frac{2QE}{\pi\eta\kappa^2 b^3} \begin{pmatrix} 3(\cos^2 \theta) - 1 \\ 0 \\ 0 \end{pmatrix}$$

$$= \mu^{EP}(a, Q, \kappa, \eta) E + \frac{2QE}{\pi\eta\kappa^2 b^3} \begin{pmatrix} g \{ F^{\text{str}}(s) L_K / k_B T \} \\ 0 \\ 0 \end{pmatrix}$$

$$= \left[\mu^{EP}(a, Q, \kappa, \eta) + \frac{2Q}{\pi\eta\kappa^2 b^3} g \{ F^{\text{str}}(s) L_K / k_B T \} \right] E$$

$$\text{where } g(x) = \frac{3}{x} \left\{ \frac{1}{x} - \coth(x) \right\} + 1$$

As shown in Fig. 7, we find from this that the electrophoretic mobility is enhanced as the polymer is stretched.

In this calculation, we took all shish-kebab segments to have the same ensemble average orientation. Therefore, this result doesn't predict the electrophoretic velocity of biased conformations such as dumbbell, half dumbbell and folded states. For example, if the polymer is folded at the center (U-shaped), the maximum stretch will be $L/2$ and the electrophoretic velocity deviates from that for a uniformly stretched conformation, as shown in Fig. 7.

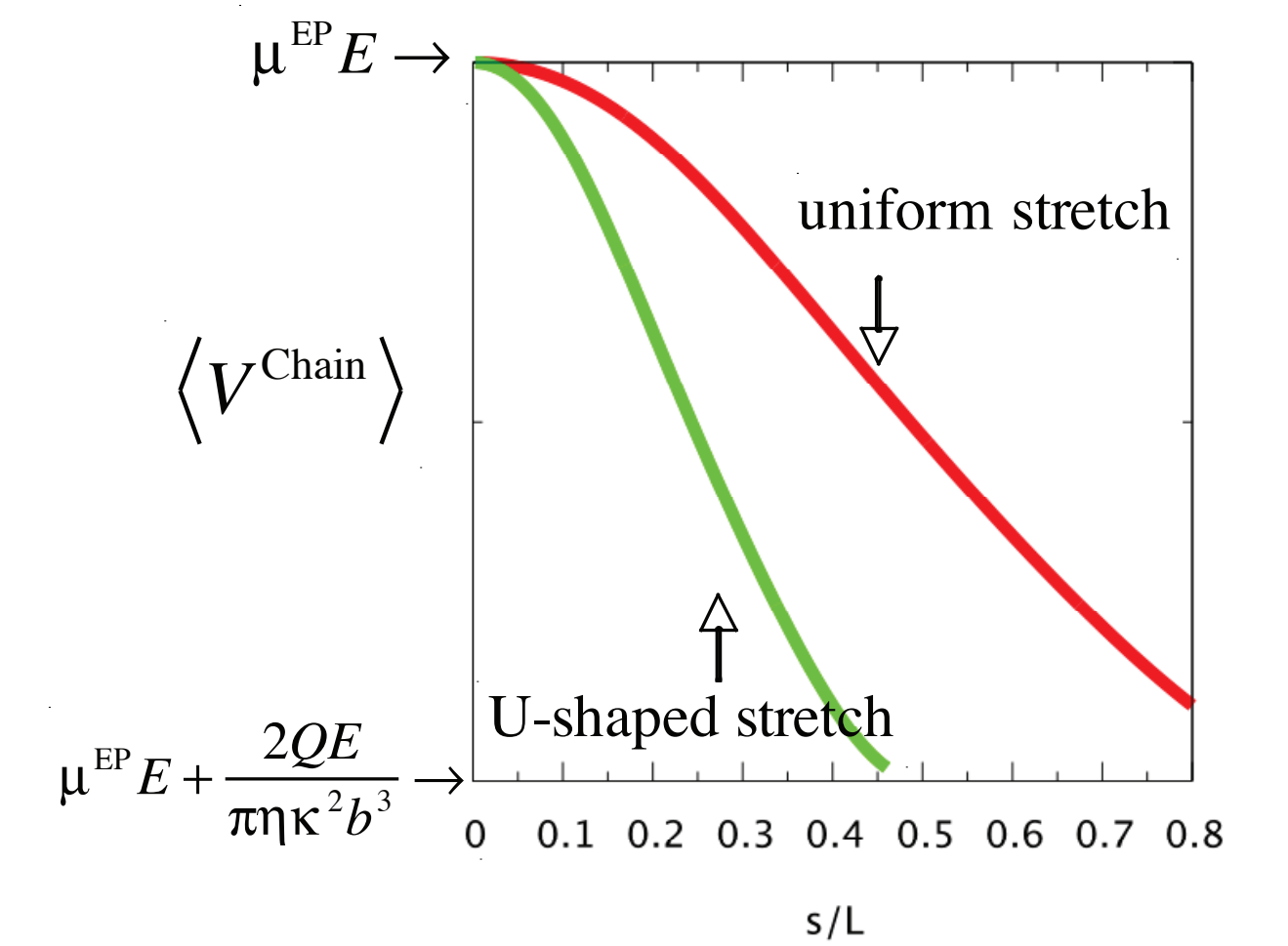


Figure 7. The stretch dependency of the electrophoretic velocity for a negatively charged polymer ($Q < 0$).

Discussion

Experimental results show that in an electric field gradient, DNA molecules are not always uniformly stretched; some are coiled, dumbbell-shaped, half-dumbbell-shaped, or folded. This diversity of DNA conformations results in variability of the electrophoretic mobility, since the orientation distribution of the DNA segments relative to the electric field affects the magnitude of the enhancement in the electrophoretic mobility according to our model. However, since a molecule tends to stretch in the direction of the electric field because of the gradient of the field magnitude, the electrophoretic mobility is always enhanced (or amplified) with stretching regardless of the particular DNA conformation.