Bidirectional Transport of Polyelectrolytes Using Self-Modulating Entropic Ratchets

Gary W. Slater,* Hong L. Guo, and Grant I. Nixon
Department of Physics, University of Ottawa, 150 Louis-Pasteur, Ottawa, Ontario, Canada K1N 6N5

(Received 27 June 1996)

Asymmetric cavities are shown to induce net transport, for random walkers and polyelectrolytes, upon the application of zero-mean, time-symmetric, fluctuating external fields (and similarly for zero-mean, temporally *asymmetric* fluctuating fields with *symmetric* cavities). Entropic trapping is shown to enhance the ratchet effect for polyelectrolytes. Time biasing an ac field can even cause different polymers to migrate in opposite directions. Entropic trapping can thus convert simple steric ratchets into self-modulating ratchets capable of size fractionating polyelectrolytes such as DNA. [S0031-9007(97)02379-X]

PACS numbers: 82.45.+z, 05.40.+j, 83.10.Nn, 87.15.He

Recently, Magnasco [1] demonstrated that *ratchet potentials* (i.e., potentials spatially asymmetric with respect to their maxima) can rectify zero-mean, correlated fluctuations and generate net motion (hence the name "correlation ratchet"). Chialvo and Millonas also demonstrated that temporally asymmetric, zero-mean fluctuations can operate a correlation ratchet even when the potential is *spatially symmetric* [2]. This idea was actually exploited earlier in a process called zero-integrated field gel electrophoresis (ZIFE) which uses unbiased pulsed electric fields to separate chromosomal DNA [3]. According to the pioneering work of Curie [4], spatially asymmetric, periodic structures may act as ratchets for Brownian particles in the presence of dissipation or other sources of time-reversal symmetry breaking. Ajdari and Prost put Curie's symmetry principle to the test in showing how a simple microstructure could act, in principle, as a ratchet [5]. However, as Leibler remarked [6], the success of future applications for correlation ratchets is still somewhat dubious, especially when compared with well-established separation techniques such as gel electrophoresis. Here, we investigate the possibility of exploiting a new ratchet-like system for DNA electrophoresis. In particular, we show that the internal entropy of long polyelectrolytes (which can be thought of as a series of charged tethered Brownian particles) magnifies the ratchet effect for small steric asymmetries. An efficient ratchet system can thus be built *without* using an external asymmetric electrostatic potential. Finally, we offer a rough estimate of the specifications for such a ratchet separation device constructed using microlithographic techniques.

When the velocity V is a nonlinear function of the applied force (spatially or temporally), asymmetric systems may exhibit net drift velocities even though the time-averaged force is zero. Consider Magnasco's example of a pointlike particle in a sawtoothed one-dimensional potential with different uphill slopes on each side of the extrema [1]. Since the critical forces $E_{\pm}$ allowing the ratchet to move in the ± directions are different, one can obtain net transport by applying an unbiased ac force made of, e.g., square pulses of amplitude $E_{-} < E < E_{+}$ and duration T_E. Here, the pulse durations T_E are assumed to be much longer than the thermally activated jumping times (i.e., we are not dealing with stochastic resonance [7]). For symmetric potentials ($E_{+} = E_{-}$), a net drift can be obtained with alternating (square) pulses of intensity E_1 and $-E_2$ and duration T_{E1} and T_{E2}, respectively, with $E_1 T_{E1} = E_2 T_{E2}$ (i.e., zero mean) and $E_2 < E_{\pm} < E_1$ [2,3].

We first demonstrate that it is possible, in principle, to build a ratchet system using *only steric interactions.* Our toy model consists of biased random walkers migrating through a 2D channel with "rough" walls (Fig. 1). We use a square lattice with diagonal periodic boundary conditions. The walkers are $n \times n$ lattice plaquettes. The (dimensionless) scaled field E is directed along the diagonal, i.e., $E_x = E_y = E/\sqrt{2}$. For each step of duration $\Delta t = \tanh(E_x)/E_x$, a walker must jump along the $\pm x$ or $\pm y$ directions with probabilities $p_{\pm} = [1 + \exp(\mp 2E_x)]^{-1}/2$ [8]. Jumps that make the particle

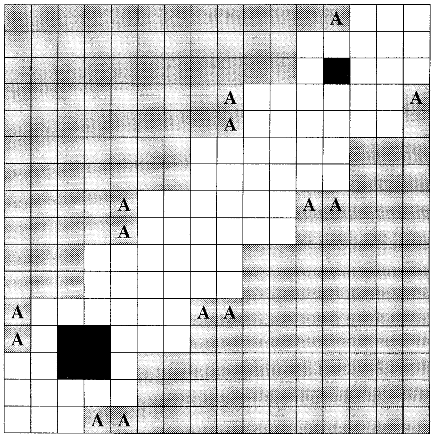

FIG. 1. Our toy model: 1 × 1 and 2 × 2 plaquettes (black) perform biased random walks on the square lattice between the symmetric rough walls (gray). An asymmetric channel can be created if those wall plaquettes denoted with A's are removed.

overlap with a wall structure are rejected. The exact dc mobility $\mu = V/E$ of 1×1 and 2×2 walkers (*for the same given charge*) has been calculated as a function of E following a method first used to study gel electrophoresis [8]. For a pathway with symmetrically alternating narrow and wide passages (Fig. 1), the mobilities are even functions of E_x; e.g., we find that

$$\mu_{1\times1} = \frac{16 + 12\,\mathrm{sech}(2E_x)}{39 + 32\,\mathrm{sech}(2E_x) + \mathrm{sech}^2(2E_x)}, \tag{1}$$

$$\mu_{2\times2} = \frac{4}{11 + \mathrm{sech}(2E_x)}. \tag{2}$$

For 1×1 plaquettes, the asymptotic mobilities for $E \to 0$ and $E \to \infty$ are thus $\mu_0 = \frac{7}{18}$ and $\mu_\infty = \frac{16}{39}$, respectively, while the critical field $E_\pm$, which we define as that value of E for which $\mu = (\mu_0 + \mu_\infty)/2$, is $E_\pm = 1.04421$. For 2×2 plaquettes, we find $\mu_0 = \frac{1}{3}$, $\mu_\infty = \frac{4}{11}$, and $E_\pm = 0.967\,267$. Using ac square pulses of intensities $+E$ and $-E/R$, with $E \approx E_\pm$, and (arbitrarily long) durations T_+ and $T_- = RT_+$, respectively, we can obtain net motion in the "positive" north-east (NE) direction (i.e., if $R > 1$) even though the mean field is zero. Figure 2 depicts the net velocity of these particles vs E for a ratio $R = 2$. The ratchet velocities are a maximum for $E \approx 2.4$.

For a channel with a broken spatial symmetry (same as Fig. 1 after removal of the "A" squares), motion in the negative direction is now easier. Exact solutions for this case have also been obtained but are too unwieldy to be given here. For a 1×1 particle, we have $\mu_0 = 4594/11781$ and $\mu_\infty = 256/609$ (for *both* the $+$ and $-$ direction); the critical fields are given by $E_+ = 0.822\,858$ and $E_- = 0.731\,974$. Since $E_+ \neq E_-$, we have an asymmetric ratchet potential similar to one studied by Magnasco [1], except that the potential is purely due to steric interactions. Figure 3 shows that we indeed obtain a net velocity for an unbiased ac field made of long square pulses. Similarly, for a 2×2 particle, we find that $\mu_0 = \frac{56}{165}$, $\mu_\infty = \frac{32}{83}$, $E_+ = 0.731\,964$, and $E_- = 0.655\,653$. Again, a net drift ensues (Fig. 3). Maximum ratchet velocities occur for the fields $E = 0.648\,113$ and $E = 0.769\,662$ for the 2×2 and 1×1 particles, respectively, which correspond roughly to the lower critical fields for these particles. The inset of Fig. 3 shows the effect of a time bias $\Delta = (T_+ - T_-)/(T_+ + T_-)$, where T_+ and T_- are the pulse durations in the two directions, with $E = 0.518\,038$. When $\Delta \in [0.00\,272\,707, 0.00\,438\,592]$, the 2×2 particle moves in the negative direction while the 1×1 particle moves in the positive direction. This is a remarkable result since the two particles have the *same* charge. In principle, this simple idea may be exploited for the construction of a separation process. However, the range of Δ's over which the effect exists is quite narrow. This is so because steric ratchet barriers are very inefficient for hard objects. However, as we will demonstrate below, such steric barriers are quite efficient for polymers because *the internal configurational entropy of a polymer directly modulates the height and the degree of asymmetry of the steric barriers.*

Let's consider a polymer of length M and radius of gyration $R_g(M)$ in linear channels having a periodically

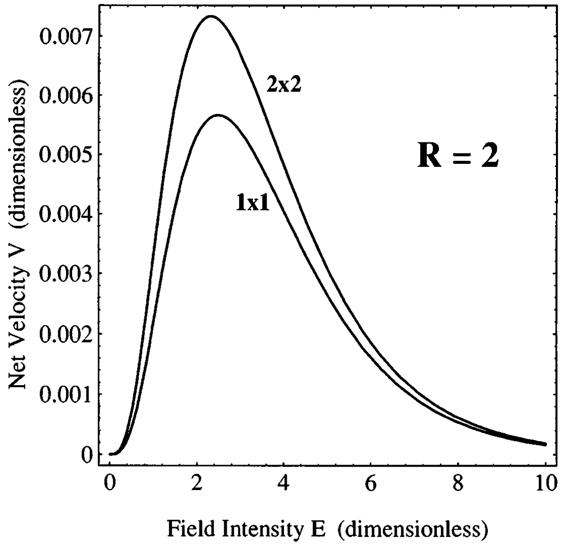

FIG. 2. Net velocity vs applied field E for 1×1 and 2×2 plaquettes in the symmetric tube shown in Fig. 1. Square pulses of intensity $+E$ and duration T_+ alternate with pulses of intensity $-E/R$ and duration $T_- = RT_+$ where $R = 2$. Although the mean field is zero, the ac field is temporally asymmetric.

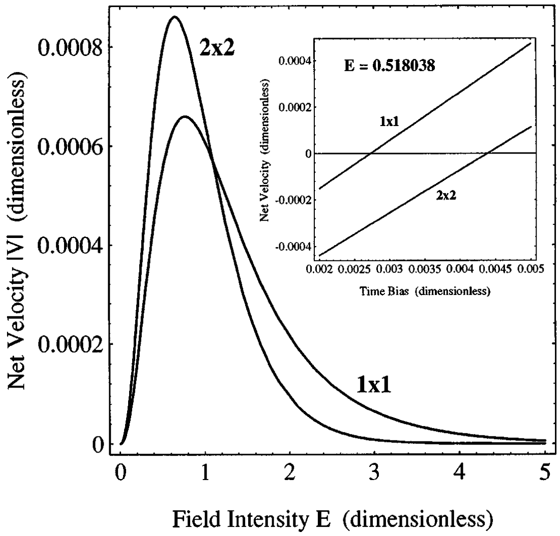

FIG. 3. Absolute value of net velocity vs the applied field E for 1×1 and 2×2 plaquettes in the asymmetric tube shown in Fig. 1 upon removal of the gray squares labeled A. Unbiased ac square pulses of amplitude E and arbitrarily long durations are applied. Inset: Net velocity of the two particles vs the time bias Δ of the square ac pulses of amplitude $E = 0.518\,038$.

varying bore radius R_T [with $(R_T)_{\min} < R_f < (R_T)_{\max}$] and a spatially asymmetric profile (Fig. 4) along the tube axis (x). In those stricture regions where $R_T(x) < R_g(M)$, the polymer's entropy decreases like $\Delta S \sim k_B(R_g/R_T)^{1/\nu}$, where ν is Flory's exponent [9–12]. Therefore, the internal entropy of the polymer is a function of the local tube radius, $S = S(R_T(x))$, and the polymer experiences an entropic force $F_S(x) \sim -T(dS/dx) = -(\partial S/\partial R_T) \times (\partial R_T/\partial x)$ wherever the tube radius $R_T(x)$ varies; the strictures thus act like potential barriers. Since the conformational entropy is an extensive variable ($S \sim M$), the entropic force $F_S = F_S(M)$ at any given stricture corresponds to different potential barriers for different polymer sizes M. In other words, the internal configurational entropy of the polymer modulates the nature of the potential barrier.

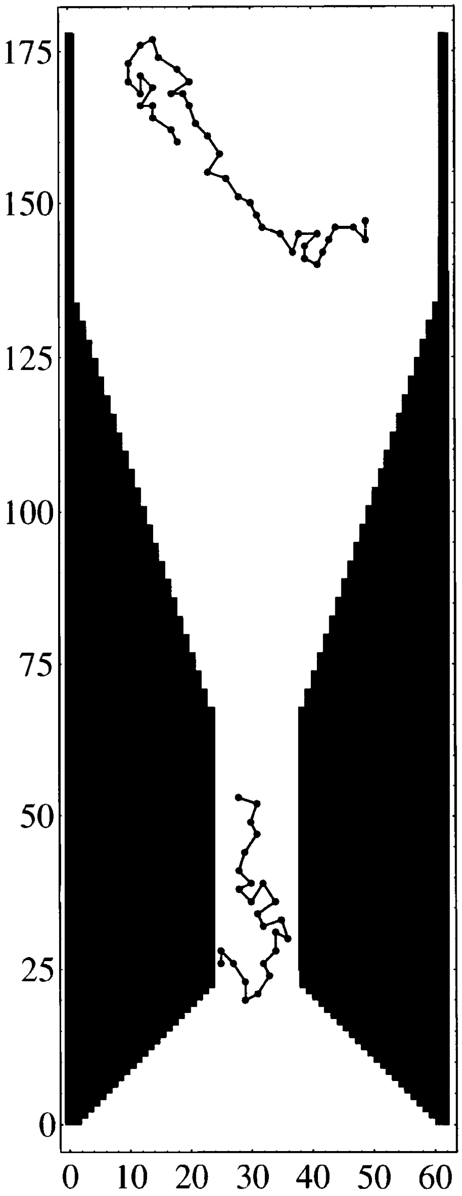

FIG. 4. Two polymers moving in a channel with asymmetric strictures. The smaller one has $M = 25$ monomers and must lose entropy in order to cross the narrow passage channel. The larger $M = 40$ polymer maximizes its internal entropy in the widest part of the channel.

A previous study of the electrophoretic dynamics of long polyelectrolytes in a tube with symmetric strictures [13] has demonstrated that strictures indeed act as entropic potential barriers. When those strictures are spatially asymmetric, however, the entropic force F_S is dependent on the direction of motion (because we have two different slopes $\partial R_T/\partial x$), and thus, in this sense, the system is similar to Magnasco's [1]. In Fig. 4, the two slopes differ by a factor of 3, thus rendering our steric ratchet potential very asymmetric. However, unlike previous ratchet potentials, which were modulated via an externally applied field, it is the conformational entropy of the polymer itself which determines the height (and the degree of asymmetry) of our ratchet potential. We call such a system an *entropic ratchet* (an expression used in a different context in Ref. [14]).

Our computer simulations of this polymer system use the bond-fluctuation algorithm on a square lattice [15]. The field biases the monomer jumps in the field direction according to a Metropolis probability. A polymer molecule is made of M charged monomers which are 1×1 plaquettes. The scaled field intensity being set at $E = 0.003$, the mean Metropolis rejection probability is about 0.3%. The narrow channels are of length 45 and radius $(R_T)_{\min} = 7$, the maximum radius of the channel is $(R_T)_{\max} = 30$, and the periodicity of the system is 182.

One expects only small entropic effects when $R_g(M) < (R_T)_{\min}$. In contrast, larger molecules (Fig. 4) lose a lot of entropy in the narrow channels. Note, however, that very large molecules can occupy the narrow channel and both adjacent "pores" simultaneously; such qualitatively different scenarios are not treated here. The longer funnel tapers in the negative direction, and the dc mobility is substantially larger for motion in that direction. Figure 5 depicts the net mobility $\mu = V/E$ vs size M for an applied ac field made up of unbiased long square pulses of amplitude $E = 0.003$. The vertical line indicates where $R_g(M) = (R_T)_{\min} = 7$. Large mobilities are indeed observed only for large molecules $[R_g(M) > 7]$ which suffer important entropic losses in the narrow channel. This clearly demonstrates a large amplification of the ratchet effect due to conformational entropy (and thus molecular size). Note also that the direction of net transport would remain unchanged under a sign reversal of the molecular charges. The inset of Fig. 5 depicts a case where we have temporally biased the ratchet with longer positive pulses. The three positively charge molecules exhibit very distinctive behaviors. The small one ($M = 8$) migrates in the positive direction since its net drift simply follows the net bias of the applied field. The largest ($M = 30$) molecule, which exhibits very strong ratchet motion for

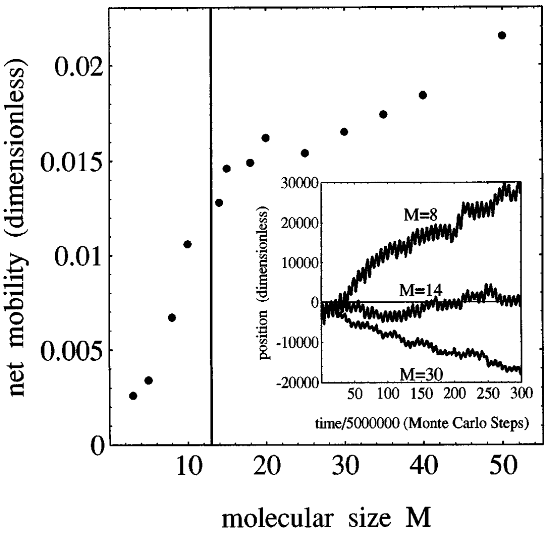

FIG. 5. Net velocity of the polyelectrolyte vs molecular size M for unbiased (zero-mean) ac square pulses of amplitude $E = 0.003$ and arbitrarily long durations. The vertical line at $M = 14$ denotes that molecular size for which $R_g(M) = (R_T)_{\min} = 7$. Inset: Position vs time for molecular sizes $M = 8$, 14, and 30. Square pulses of intensity $E = 0.003$ and duration $4 \times 5\,000\,000$ alternate with square pulses of intensity $E = -0.003$ and duration $2.85 \times 5\,000\,000$.

unbiased pulse conditions, is still characterized by a negative velocity. Finally, the applied time bias exactly cancels the ratchet drift for the intermediate ($M = 14$) molecule. The fact that a very strong temporal bias ($\Delta = 0.167\,88$ compared with $\Delta \approx 0.003$ for the random walkers) is needed indicates that conformational entropy can magnify the effects of steric ratchets by many orders of magnitude. Of course, it is also possible to build a time-asymmetric ratchet using symmetric strictures.

Temporally asymmetric systems have been shown to be useful for the separation of chromosomal DNA [3]. In this paper, we have demonstrated that steric ratchets can be built from spatially asymmetric channels. Moreover, when used with polymers, the height of the potential barriers is *modulated by the internal molecular entropies.* Such steric entropic ratchets do have potential applications in the area of separation science. A system like the one presented in Fig. 4 could be built using, e.g., microlithographic arrays similar to those of Volkmuth and Austin [16]. A channel of maximum diameter 6 μm and minimum diameter 2 μm would be necessary for the electrophoretic separation of double-stranded DNA molecules of sizes 30–200 kbp (whose radii of gyration are in the range 1–3 μm). If the ratchet is to be effective, the total electric force $F_E = QE$ applied to a molecule of charge $Q \sim M$ must be smaller than the entropic forces F_S. Using $F_S \approx TS/d$ where d (≈ 1 μm) is the characteristic length of the strictures, and $S \approx Mk_B$, where M is now the molecular size expressed in Kuhn lengths, we get $E < k_BT/(Q/M)d$. Since the charge per bp is approximately $0.066e$ (with e being the elemental charge of an electron) [17] and the Kuhn length is approximately 100 nm (or about 300 bp), we have $Q/M \approx 20e$. Therefore, we need approximately $E \leq 10$ V/cm, which is typical of electrophoresis systems [3]. An ideal situation would consist of placing a collector at the end of the tube and extracting migrating species of differing molecular weight. For instance, one could use our time-biased steric ratchets (Fig. 5, inset) to make each molecule migrate, one species at a time, towards the exit of the capillary (here in the negative direction). One could first begin with a strong temporal bias and then, by continually decreasing that bias, allow consecutive molecular species to move in succession.

The authors would like to thank André Longtin and Ivan L'Heureux for valuable discussions. All simulations were performed on the Université de Sherbrooke's 16-node IBM SP2 supercomputer. G. W. S. gratefully acknowledges the support of a research grant from the Natural Science and Engineering Research Council of Canada.

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*To whom correspondence should be addressed. E-mail: gary@physics.uottawa.ca

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