Biasing Brownian Motion in Different Directions in a 3-State Fluctuating Potential and an Application for the Separation of Small Particles

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We consider diffusive motion on a periodic, anisotropic potential. Multiplicative three-state noise can bring about net flow. As the speed of this noise varies, the direction of the flux can change. We explain the flux reversals and discuss a possible application for the construction of a device for the separation of small particles. [S0031-9007(96)00105-6]

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Nonequilibrium fluctuations acting on a particle on an anisotropic periodic potential $U(x)$ can cause transport [1–3]. Thermal noise can complicate the situation and is sometimes necessary to get any flow at all. The study of such systems has been motivated in part by recent advances in the experimental study of motor proteins, i.e., proteins that convert the energy of ATP hydrolysis into motion along a biopolymer [4]. These tiny engines may work by using the nonequilibrium fluctuations, brought about by the ATP turnover, to make a Brownian step in one direction more likely than in the opposite direction. This biasing of Brownian motion is an operating principle that is fundamentally different from that of macroscopic engines. Furthermore, nanotechnological devices have been constructed where the same principles are employed to drive microscopic ($<10\ \mu$m) particles. In this Letter we go one step further. We fluctuate a potential in such a way that the direction of the biasing depends on the coefficient of friction of the particle. We thus have a possible tool for the separation of such particles.

The setup is summarized by the following Langevin equation:

$$\beta\frac{dx}{dt} = -\frac{\partial}{\partial x}[g(t)U(x)] + f(t) + (\beta\sqrt{2D})\xi(t)\,,$$

where β is the coefficient of viscous friction, $\xi(t)$ is the function representing zero average, normalized white noise [5], and D controls the amplitude of this noise. The fluctuation-dissipation theorem $D = kT/\beta$ relates the coefficient of friction and the amplitude of thermal noise. The functions $f(t)$ and $g(t)$ describe the "nonthermal" additive and multiplicative noise, respectively. When $g(t)$ does not vary in time and $f(t) = 0$ no transport can occur. Transport occurring with $f(t) = 0$ and constant $g(t)$ means that thermal fluctuations are converted into work and implies a violation of the second law of thermodynamics [6]. A great many investigations have focused on additive fluctuations [1,7–9] or oscillations [10]. In this Letter we focus on multiplicative noise, i.e., a $g(t)$ that varies in time while $f(t) = 0$, which means that the periodic potential changes shape but no net macroscopic force ever occurs. The study of multiplicative noise has already led to the construction of a device to drive and possibly separate small particles or macromolecules [11]. Multiplicative noise is also more likely to be the operating principle for motor proteins. The binding of ATP, the subsequent hydrolysis, and the release of ADP do not cause a macroscopic force along a biopolymer, but simply change the distribution of charges in the motor protein and thus the energy profile that the motor protein "feels" on the periodic biopolymer. The fluctuations of this profile can account for the observed speeds and stopping forces of real motors [2,12].

The models for which fluctuation induced flow has been studied have generally been as simple as possible. A piecewise linear potential with two pieces per period and a two-state additive or multiplicative Markovian fluctuation allows for analytic evaluation and why flux occurs and how it changes when parameter values are changed can be understood easily [1–3]. But when only slight complications are added the behavior of the system can become surprisingly rich [7–9,13] and flux can actually change its direction more than once when a certain parameter is varied. Doering studied a two piece piecewise linear potential and observed how in the fast noise limit of an added fluctuation the direction of the induced flow depends on a characteristic of the noise [8]. Bier considered a similar system with a three-state fluctuating force and observed and explained the many flux reversals as noise characteristics were varied [7]. Chauwin, Ajdari, and Prost investigated a three piece piecewise linear periodic potential. When transition rates between such a potential and a flat potential are changed a reversal of flow occurs [13].

Below we consider a two piece piecewise linear potential, but the imposed fluctuation is multiplicative and three state. Recently Mielke gave a very general treatment of multiplicative fluctuations acting on a periodic potential [14]. Here we consider a specific case for which analytic solution is possible and where flux reversals can be intuitively understood. Our setup is depicted in Fig. 1. $V_+(x)$ is a two piece piecewise linear potential with an energy difference between minimum and maximum of E. $V_0(x)$ is a flat potential and by multiplying $V_+(x)$ with -1, which

is equivalent to turning it upside down, we obtain $V_-(x)$. The arrows indicate how the transitions occur. The transition rates are such that equal amounts of time are spent in $V_+(x)$ and $V_-(x)$, leaving three parameters, γ, μ, and λ, to vary. The value of γ varies the speed of the noise. The parameter μ governs the separation of time scales for the $V_+ \leftrightarrow V_0$ fluctuation relative to the $V_0 \leftrightarrow V_-$ fluctuation; μ times as many transitions are made into V_+ as into V_- but the dwelling time in V_+ is μ times as small as the one in V_- so the fractions of time in V_+ and V_- end up to be the same. Obviously, for $\mu = 1$ the system is effectively isotropic and no flux can occur. With λ we can regulate the time spent in V_0 relative to V_+ and V_-. For $\lambda \to \infty$ the fluctuation becomes dichotomous between V_+ and V_- and for $\lambda \to 0$ all time is spent in V_0. A commonly used variable is the "flatness." When we identify the V_+ state with $g = 1$, the V_- state with $g = -1$, and the V_0 state with $g = 0$, the flatness is defined as $\varphi = \langle g^4 \rangle / \langle g^2 \rangle^2$ and as such is a good measure for how close to zero the value of g stays on the average. For our case the flatness can be derived to be $\varphi = 1 + 1/(2\lambda)$ (see also [7]).

To make the resulting formulas as concise as possible we absorb the coefficient of friction of the Brownian particle β into the time scale, take energy in units of kT and take L as the unit of distance. The Fokker-Planck equations for the probability distribution in the stationary state are the following:

$$\begin{bmatrix} F_i^+ - \mu\gamma & \mu\lambda\gamma & 0 \\ \mu\gamma & F_i^0 - (\mu + 1)\lambda\gamma & \gamma \\ 0 & \lambda\gamma & F_i^- - \gamma \end{bmatrix} \begin{bmatrix} P_i^+ \\ P_i^0 \\ P_i^- \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix},$$

where $i = 1$ represents the system on the interval $(0, \alpha)$ and $i = 2$ represents the system on the interval $(\alpha, 1)$. $P^+(x)$, $P^0(x)$, and $P^-(x)$ are the joint probability densities for the particle to be at x and the potential to be in the V_+, V_0, or V_- configuration, respectively. The terms F_i^+, F_i^0, F_i^- are the respective Fokker-Planck operators: $F_i^+ = \partial_{xx} P_i^+ - f_i^+ \partial_x P_i^+$ and likewise for F_i^0 and F_i^-, where f_i^+, f_i^0, and f_i^- represent the forces $-\partial_x V_i^+$, $-\partial_x V_i^0$, and $-\partial_x V_i^-$. Because of the piecewise linearity these forces are independent of x. In the matrix the terms μ, λ, and γ parametrize the flow of probability from one potential to another. $(f_i^+ - \partial_x) P_i^+$ is the flow J_i^+ along the x axis in the + state; likewise we have $J_i^0 = (f_i^0 - \partial_x) P_i^0$ and $J_i^- = (f_i^- - \partial_x) P_i^-$. The net flow at any point x is $J = J_i^+ + J_i^0 + J_i^-$ and in the stationary state this quantity must be the same at any point x. The above matrix equation can be viewed as a way of saying $\partial_x J = 0$ in terms of forces, transition rates, and probability densities. There are boundary conditions at $x = \alpha$ and $x = 0$ (which must coincide with $x = 1$), where the probability densities P_i^+, P_i^0, and P_i^- and the flows J_i^+, J_i^0, and J_i^- must be identical for $i = 1$ and $i = 2$.

Mathematically the problem reduces to two sets of three coupled ordinary differential equations that are connected at the boundaries $x = \alpha$ and $x = 0$. The two linear systems are sixth order and have constant coefficients. Because of the symmetry of the system the zero eigenvalue turns out to be degenerate, so the solution is the sum of a constant, a linear term, and four exponentials. The coefficients are determined by the connections at $x = \alpha$ and $x = 0$. Because $J = J_i^+ + J_i^0 + J_i^-$ is valid at both $x = \alpha$ and $x = 0$ there is one redundancy, and this leaves room for the normalization of the total probability over one period. A computer algebra system like MATHEMATICA can solve the system and determine the induced flow within seconds. Figure 2 shows the induced flow J as a function of $\log \gamma$ for three different values of λ with $\mu = 1000$. There are two extrema and a flux reversal. Maximum and minimum flow have about the same magnitude (they were different by several orders of magnitude in the setup studied by Chauwin, Ajdari, and Prost [13]). Next we will explain flux reversals in terms that are more intuitive and directly comprehensible than the large body of algebra solved by MATHEMATICA.

We call $-3 < \log \gamma < 0$ the low frequency domain. In this domain the sojourns into the minus state are too rare to be of significance, but the flipping between V_+ and V_0 is sufficiently frequent to bring about a pumping effect. An important notion is the adiabatic adjustment time. The adiabatic adjustment time on each of the two slopes is the characteristic time for a probability distribution to

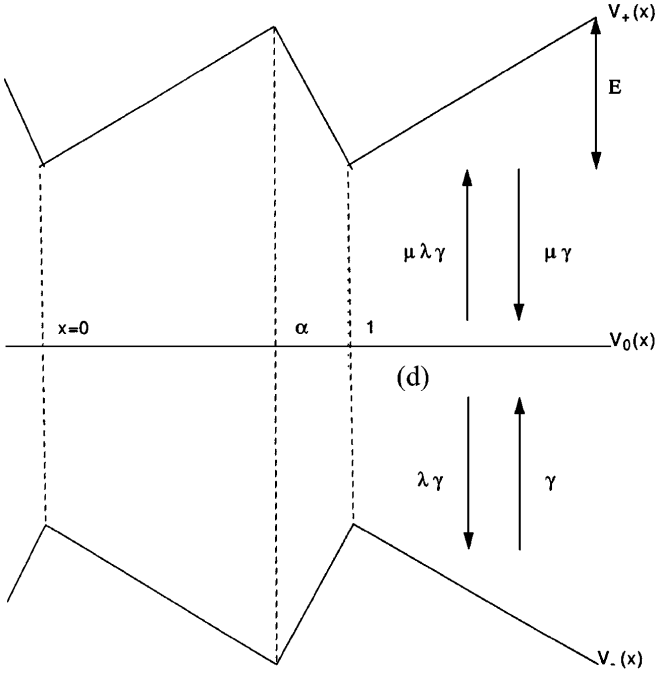


FIG. 1. The setup for the system. We study diffusive motion along the x axis as the potential is flipping in a Markovian fashion between $V_+(x)$, $V_0(x)$, and $V_-(x)$ with the indicated transition rates. We have $V_-(x) = -V_+(x)$ and the transition rates are such that equal amounts of time are spent in $V_+(x)$ and $V_-(x)$.

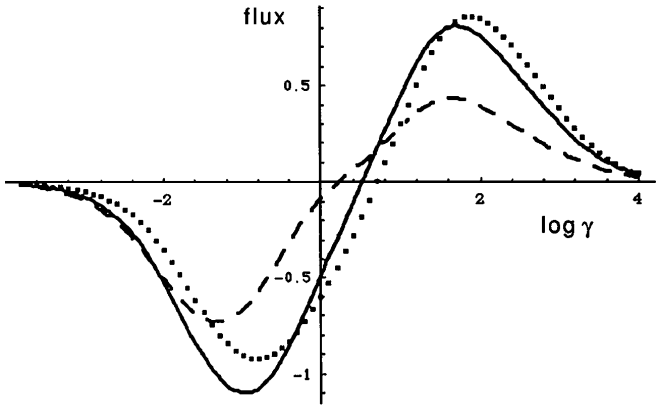
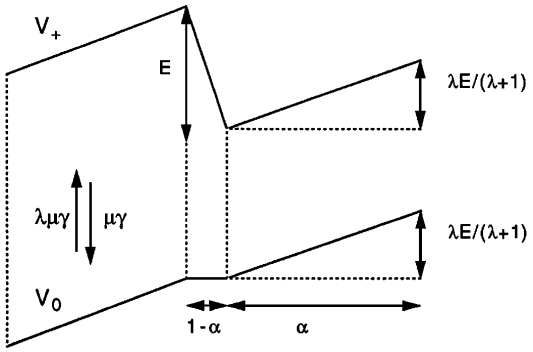


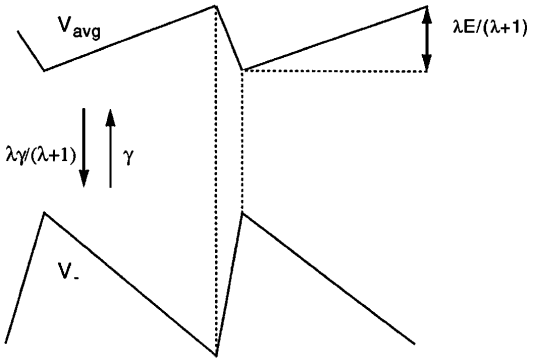
FIG. 2. A graph of the induced flow along the x axis vs $\log\gamma$, a variable that controls the speed of the fluctuations. The parameter values are $E = 10$, $\alpha = 10/11$, and $\mu = 1000$. The variable λ controls how much time is spent in $V_0(x)$ vs the other two states. Curves are drawn for three values of λ : $\lambda = 1/3$ (dotted), $\lambda = 1$ (solid), and $\lambda = 3$ (dashed).

adjust to the shape of the potential $V(x)$ on that slope and we take this time to be equal to the characteristic time for diffusion over the width of that slope if it were a flat potential [15]. The adiabatic adjustment time on the slope $(0, \alpha)$ thus equals $\alpha^2/2$ and the adiabatic adjustment time on the short slope $(\alpha, 1)$ equals $(1 - \alpha)^2/2$. In [2] we have shown and explained in the context of a two-state model how no significant flux occurs when the dwelling time in each state is much shorter than the time for adiabatic adjustment on each of the slopes. In this case the probability distribution is simply the distribution on the average potential. Maximal flux occurs when the dwelling times are in between the adiabatic adjustment times on the long and the short slope. So at maximal flux in the low frequency domain we can think of the system as being adiabatic at all times and with a short slope that flips between 0 and E/α and a stationary long slope with the average height of $\lambda E/(\lambda + 1)$, i.e.,

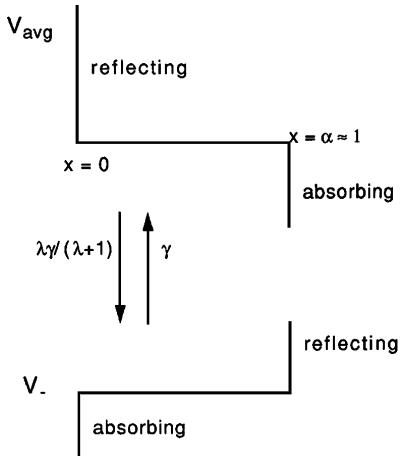


Note that in the V_+ state the slopes have opposite signs and that this is not the case in V_0. For the purpose of a rough approximation we can assume that no flux occurs in the V_+ state and that the negative flux happens because of the sliding down in the V_0 state. For the values we took ($E \approx 10$ and $\alpha \approx 10/11$) the time $(1 - \alpha)^2/2$ to diffuse over the flat part of the V_0 state is negligible in comparison to the time α^2/E that it takes to slide down the long slope. Taking α^2 to be one and multiplying by the fraction of time spent in the 0 state we derive $J_{\text{low fr}} = \lambda E/(2\lambda + 1)(\lambda + 1)$, or in terms of the flatness $J_{\text{low fr}} = \lambda E/(\varphi - 1)E/\varphi(2\varphi - 1)$.

In the high frequency domain, $0 < \log\gamma < 3$, μ is such that $(\mu\gamma)^{-1}$ is shorter than any adiabatic adjustment timescale of the system. This means that we think of the system as flipping between the weighted average of the V_+ and V_0 state, i.e., $V_{\text{avg}} = (\lambda V_+ + V_0)/(\lambda + 1)$, and the V_- state as in the sketch below.



The $1/(\lambda + 1)$ appears in front of the rate of the transition to the $-$ state because, when in the V_{avg} state, $1/(\lambda + 1)$ is the fraction of time spent in the 0 state from where the transition to the V_- state is possible. As in the previous case, we obtain flux when the dwelling times are between the adiabatic adjustment times of the long slope and the short slope. The long slope has a flat average. For high enough E we can think of the short slope as a barrier that fluctuates between being absorbing and reflecting as in the following sketch.



It is obvious that for all λ dwelling time in V_{avg} is longer and therefore we expect positive flux. We obtain this flux by substracting the fraction of time spent in V_- from the fraction spent in V_{avg} and multiplying this difference with the exit rate from the unit interval. For a particle starting

at the reflecting barrier it takes on the average half a unit of time to get to the absorbing barrier. This leads to the following estimate for the flux: $J_{\text{high fr}} = 2/(2 + 1)$, or in terms of the flatness $J_{\text{high fr}} = 2(\varphi - 1)/\varphi$.

Next we compare the approximations $J_{\text{low fr}}$ and $J_{\text{high fr}}$ with the exact evaluations as depicted in Fig. 2. For $\alpha = 10/11$ the adiabatic adjustment times of the two slopes are 2 orders of magnitude apart, their geometric average occurs at $\alpha(1 - \alpha)/2$ and on the $\log\gamma$ axis this corresponds to $\log[2/\alpha(1 - \alpha)] = 1.6$. In the low frequency domain the geometric average of the transition rates between V_+ and V_0 is $\mu\gamma\sqrt{\lambda}$ and in the high frequency domain the geometric average of the transition rates between V_{avg} and V_- is $\gamma\sqrt{\lambda/(\lambda + 1)}$. In Fig. 2 the minima occur at $\mu\gamma\sqrt{\lambda} \approx 2/\alpha(1 - \alpha)$ and the maxima at $\gamma\sqrt{\lambda/(\lambda + 1)} \approx 2/\alpha(1 - \alpha)$ within a factor of 4. The approximations predict that both extrema move left for increasing λ and this is indeed the case in Fig. 2. The estimates $J_{\text{low fr}}$ and $J_{\text{high fr}}$ are within a factor of 2 from the values of the actual extrema of the flux. The formula for $J_{\text{low fr}}$ predicts an extremum at $\lambda = \sqrt{2}/2$. In Fig. 2 we indeed observe that the maximal negative flux is smaller at $\lambda = 1/3$ and $\lambda = 3$ than at $\lambda = 1$. The formula for $J_{\text{high fr}}$ predicts that the positive maximum becomes larger with decreasing λ. This prediction is borne out by the curves in Fig. 2.

Upon redimensionalizing the variables a possible application of the above theory comes to mind. To unscale the flipping rates they have to be multiplied with $kT/\beta L^2$, where L is the length of a period of the potential and β represents the coefficient of viscous friction of the diffusing particle. The value of β is specific for each molecule and depends on shape and size. For a given flipping rate, different macromolecules thus find themselves at different locations along the $\log\gamma$ axis in Fig. 2. It is always possible to impose a flipping rate on the system such that a molecule with friction β_1 moves in a direction opposite to the one of a molecule with friction β_2. Devices for the separation of macromolecules usually operate based on the fact that molecules with a larger β move slower in a certain direction when a force is applied in that direction. The device proposed here is actually able to let molecules with different β's move in opposite directions. Thus a device of short length would already be able to separate very efficiently.

In nanotechnology it is now possible to construct grids with a period of about 5 μm. The creation of a field as in Fig. 1 on such a scale is thus feasible. In dilute solutions proteins like hemoglobin have friction coefficients of about 10^{-10} s^{-1} [16]. This translates into a diffusion coefficient of about 50 μm^2/s. So keeping the system in the flat state for a tenth of a second is enough to allow diffusion over about half a period. In terms of our setup this means that the negative minimum occurs when the flipping rate between V_+ and V_0 is about 20 Hz and maximum flow occurs when the flipping rate between V_- and V_0 is about 20 Hz. After redimensionalization the formulas for $J_{\text{low fr}}$ and $J_{\text{high fr}}$ become

$$J_{\min} = \frac{\lambda}{(2\lambda + 1)(\lambda + 1)} \frac{EkT}{\beta L} \quad \text{and}$$

$$J_{\max} = \frac{2}{(2\lambda + 1)} \frac{kT}{\beta L}.$$

When we take $E = 10$ (this is in principle under experimental control with the electrical field strength) we find speeds of about 10 μm/s.

Polystyrene and latex spheres with submicrometer radii are commercially available. The coefficient of friction of such beads is easily evaluated with Stokes' formula $\beta = 6\pi\eta r$, where η is the coefficient of viscosity. A bead with a radius of 0.5 μm thus has a coefficient of friction that is about 100 times as much as that of a hemoglobin molecule. This means that the extrema of the flux are about 0.1 μm/s at characteristic flipping rates of about 0.2 Hz and that separation of particles with radii different by a factor of 2 should be accomplishable in under an hour.

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[1] M. Magnasco, Phys. Rev. Lett. **71**, 1477 (1993).
[2] R. D. Astumian and M. Bier, Phys. Rev. Lett. **72**, 1766 (1994).
[3] J. F. Chauwin, A. Ajdari, and J. Prost, Europhys. Lett. **27**, 421 (1994).
[4] K. Svoboda, C. F. Schmidt, B. J. Schnapp, and S. M. Block, Nature (London) **365**, 721 (1993).
[5] C. W. Gardiner, *Handbook of Stochastic Methods* (Springer, Berlin, 1985), 2nd ed.
[6] R. Feynman, R. B. Leighton, and M. Sands, *The Feynman Lectures on Physics* (Addison-Wesley, Reading, MA, 1966), Vol. 1, Chap. 46.
[7] M. Bier, Phys. Lett. A **211**, 12 (1996).
[8] C. R. Doering, W. Horsthemke, and J. Riordan, Phys. Rev. Lett. **72**, 2984 (1994).
[9] A. Mielke, Ann. Physik (Leipzig) **4**, 476 (1995).
[10] R. Bartussek, P. Hanggi, and J. G. Kissner, Europhys. Lett. **28**, 459 (1994).
[11] J. Rousselet, L. Salome, A. Ajdari, and J. Prost, Nature (London) **370**, 113 (1994).
[12] R. D. Astumian and M. Bier, Biophys. J. **70**, 637 (1996).
[13] J. F. Chauwin, A. Ajdari, and J. Prost, Europhys. Lett. **32**, 373 (1995).
[14] A. Mielke, Ann. Physik (Leipzig) **4**, 721 (1995).
[15] M. Bier and R. D. Astumian, Phys. Rev. Lett. **71**, 1649 (1993).
[16] W. J. Moore, *Physical Chemistry* (Prentice Hall Inc., Englewood Cliffs, NJ, 1972), 5th ed.