Asymmetric Pumping of Particles

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Through the analysis of a simple two-level model, we show how and to what extent structures possessing vectorial symmetry act as pumps in the presence of dissipation. The relevance to new separation concepts and protein motor assemblies is discussed.

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Macroscopic average motion of particles result in general from the action of macroscopic external forces or gradients. In this Letter we describe a different mechanism based on the combined action of spatial asymmetry and energy dissipation. Consider a Brownian particle evolving in a structure characterized by a vectorial symmetry (i.e., parity is broken along a direction x) but homogeneous on large scales (for instance periodic or random). Then we know from thermodynamics that the long time motion of the particle is diffusive and symmetric: the sole violation of the $x \to -x$ symmetry is not sufficient to promote a net average velocity. However, if an external action induces energy absorption and dissipation, then the time reversal $t \to -t$ symmetry is also broken, and Curie arguments [1] allow for the existence of a macroscopic velocity. It is important to note that dissipation can be forced on any degree of freedom of the particle, so that motion can result even in the absence of any external force: this defines pumping activity.

The first presentation and quantification of this argument [2,3] concerned the proposition of a new separation (or selective pumping) technique, making use of man-made structures providing spatially asymmetric pinning potentials that could be switched on and off periodically in time. The net current resulting from the permanent oscillation between two transient behaviors (during which dissipation occurs) was calculated and shown to be highly sensitive to the particle diffusion constant when the off time was well chosen. No macroscopic gradient is ever exerted on the particles in this scheme. A more obvious case was subsequently investigated, corresponding to the situation in which an external force is actually applied in the x direction but with zero temporal average value [4,5].

Dissipation can more interestingly be induced on internal degrees of freedom (conformational, electronic, etc.) if the particles are susceptible to undergo a transition under irradiation or take part in chemical reactions [2,3]. This case is very important on at least two grounds: First, it could lead to pumping and separation devices which would have the degree of selectivity of specific chemical reactions (such as antigen-antibody recognition) or that of optical resonances; second, it provides a paradigm for the behavior of motor protein assemblies.

Indeed, there is presently a considerable effort aiming at the analysis and comprehension of the mechanisms involved in the latter biological function [6,7].

The motors (myosin, kinesin, or dynein), under the action of a chemical energy source (ATP, adenosine triphosphate), successively attach to and detach from a substrate of vectorial symmetry (an actin or tubulin filament, which acts essentially as a one dimensional periodic structure). Although "attached" and "detached" correspond to complex and various underlying behaviors, an essential feature for motion generation is the existence of these two "states."

Therefore, we propose a simple model: a particle can exist in two states, and in each of them it experiences a different pinning potential. These two potentials have the same symmetry but may be different in amplitude. The external action (i.e., chemical reaction, optical transition, etc.) simply drives the transition rates between the two states away from their spontaneous values so that Boltzmann equilibrium is perturbed. This forces dissipation and results in an average motion of the particle. Note that such a one-particle treatment does not aim at the description of collective behavior, nicely addressed in Ref. [7].

In this Letter, after defining the model, we show on general grounds how the asymmetry of the spatially periodic pinning potentials results in an effective potential exhibiting a macroscopic gradient, which implies a pumping activity. Then we give analytical and numerical results for the cases of homogeneous or localized external action, which exhibit the utility of a quasidetached state. Eventually we discuss the relevance of our considerations with respect both to possible separation techniques and to the understanding of protein motor assemblies.

Let us consider the one dimensional motion along a direction x of a particle which can be in either of two states 1 and 2. The probability distribution functions of the particle in states 1 and 2, $P_1(x,t)$ and $P_2(x,t)$, obey the following coupled Fokker-Planck equations:

$$\begin{aligned} \partial_t P_1 + \partial_x J_1 = s = -\omega_1(x)P_1 + \omega_2(x)P_2 , \\ \partial_t P_2 + \partial_x J_2 = -s = -\omega_1(x)P_1 - \omega_2(x)P_2 , \end{aligned} \tag{1}$$

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in which the fluxes J_1 and J_2 read

$$J_1 = -D_1[P_1(x)\partial_x(W_1/kT)+\partial_x P_1],$$
$$J_2 = -D_2[P_2(x)\partial_x(W_2/kT)+\partial_x P_2]. \quad (2)$$

$W_1(x)$ and $W_2(x)$ are the potentials experienced by the particle in states 1 and 2, respectively, which we take periodic of period p, whereas $\omega_1(x)$ and $\omega_2(x)$ are the transition rates between states 1 and 2. Expression (2) insures that the Boltzmann distribution is an equilibrium solution for each state separately. Under no external action it is a global equilibrium solution so that $\omega_1(x)/\omega_2(x)=\exp\{[W_1(x)-W_2(x)]/kT\}$, and as stated in the introduction there is no macroscopic current: $\mathcal{J}=J_1+J_2=0$ [since $J_1(x)=J_2(x)=0$].

What happens if $\omega_1(x)/\omega_2(x)\neq\exp\{[W_1(x)-W_2(x)]/kT\}$? The transition rate from state 1 to state 2 (or vice versa) may for instance be modified by irradiating the particles with an electromagnetic wave of appropriate frequency; in such a case the source s of the Fokker-Planck equations is modified by the addition of the new term $-\kappa I P_1$ in which κ is the quantum yield of the photon absorption process, and I the wave intensity (for simplicity we omit the stimulated emission term, which is quite admissible in most cases). Note that, since κ depends on the energy difference between states 1 and 2, it will also in general depend on the spatial coordinate x. It is important to understand that the photon source is external to the system, and the photon population is not allowed to reach thermal equilibrium. Under these circumstances $\omega_1=\omega_1^0+\kappa I$, where ω_1^0 is the bare transition rate which satisfies detailed balance, and κI is a direct measure of detailed balance breaking. Similarly a compound like ATP which biases the rate of change from one state to the other, through a hydrolysis process, will also drive ω_1/ω_2 out of detailed balance, as long as its concentration does not relax to equilibrium, which is the case in practice. In the following, we consider steady state situations so that a local relation between the probability distributions in the two states exist: $P_1(x)=\lambda_1(x)\mathcal{P}(x)$, $P_2(x)=\lambda_2(x)\mathcal{P}(x)$, where $P_1(x)+P_2(x)=\mathcal{P}(x)$. It is then straightforward to show that the total probability distribution $\mathcal{P}$ obeys an effective Fokker-Planck equation with a current:

$$\mathcal{J}=J_1+J_2=-\mathcal{D}[\mathcal{P}\partial_x(\mathcal{W}/kT)+\partial_x\mathcal{P}], \quad (3)$$

where the effective diffusion coefficient is $\mathcal{D}=\lambda_1 D_1+\lambda_2 D_2$ and the effective potential $\mathcal{W}$ can be written

$$\mathcal{W}(x)-\mathcal{W}(0)=\int_0^x dx\frac{D_1\lambda_1\partial_x W_1+D_2\lambda_2\partial_x W_2}{D_1\lambda_1+D_2\lambda_2}+kT[\ln(\mathcal{D})]_0^x, \quad (4)$$

where it is understood that $\lambda_1,\lambda_2,W_1,W_2$ are functions of position. Indeed λ_1 and λ_2 have to be calculated from a proper elimination of $\mathcal{P}$ in Eqs. (1) and (2); the result clearly depends on the boundary conditions.

If $W(x)$ is periodic, the system acts as a passive effective medium, with periodically distributed pinning sites. On the contrary, if $\mathcal{W}(x+p)\neq\mathcal{W}(x)$, the effective potential develops a macroscopic bias, and the system acts as a pump equivalent to that produced by an average external force $\mathcal{F}=-[\mathcal{W}(x+p)-\mathcal{W}(x)]/p$. Depending on boundary conditions the system develops either a chemical potential gradient and no net current (blocked situation) or a current with a constant average probability distribution ("free end" case) or any intermediate situation. Note that even if the increment over a period $\mathcal{W}(x+p)-\mathcal{W}(x)$ is very small compared to kT (in case of rather "bad" pumping conditions), the accumulation of N elements (typically 10^3 to 10^4 in a separation device) can lead to an overall significant chemical potential difference in the blocked case: $N[\mathcal{W}(x+p)-\mathcal{W}(x)]\gg kT$. Note also that since λ_1 and λ_2 depend on boundary conditions, the effective potential may be different for blocked and free end situations.

From now on, we specialize to free boundary conditions, in the sense that the probability densities (and consequently λ_1 and λ_2) are taken p periodic, and we look for the current $\mathcal{J}$. A simple inspection of the integral part of the right hand side of (4) shows that for symmetric pinning potentials W_1 and W_2, and (consequently if the excitation is homogeneous) symmetric rates ω_1 and ω_2, the integrand is asymmetric and the effective potential $\mathcal{W}$ is periodic. As expected no pumping activity can be achieved: spatial symmetry breaking is a clear requirement. Similarly, if no dissipation takes place (no exterior action), the rates ω_1 and ω_2 must satisfy detailed balance:

$$\omega_1(x)=\omega(x)\exp(-W_2/kT)$$

and

$$\omega_2(x)=\omega(x)\exp(-W_1/kT).$$

Then the integrand is the derivative of

$$-kT\ln[D_1\exp(-W_1/kT)+D_2\exp(-W_2/kT)]$$

and $\mathcal{W}$ is periodic. The absence of dissipation forbids any pumping activity.

A quantitative use of Eq. (4) requires solving differential equations which do not admit analytic solutions for arbitrary potentials W_1,W_2. We have thus focused our attention on two approaches: (i) An analytic one, concerning the "sawtooth" potential of Fig. 1, under "homogeneous strong excitation" conditions: the lifetime $1/\omega_2$ of the particle in the "excited" state 2 is taken constant, whereas its lifetime in the "fundamental" state 1 is inversely proportional to the amplitude Ω of the external action taken constant in space, so that $\omega_1=\Omega$. (ii) A computer simulation, based on a Monte Carlo algorithm to solve the Langevin equations associated with Eqs. (1) and (2), which allows us to analyze different potential shapes and excitations. To complete (1) and (2) we generically chose to set the "relaxation rate" ω_2 to a constant "spontaneous" value, while the excitation rate con-

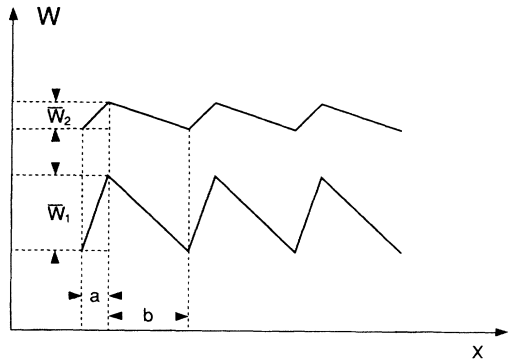

FIG. 1. Three periods of the sawtooth potentials W_1, W_2.

sists of a spontaneous part satisfying Boltzmann law and the induced part Ω:

$$\omega_1 = \omega_2 \exp\{[W_1(x) - W_2(x)]/kT\} + \Omega(x) .$$

With the sawtooth potential of Fig. 1 and the homogeneous strong excitation conditions, Eqs. (1) and (2) are piecewise linear with constant coefficients, and can thus be solved in a straightforward way. In view of the awkwardness of the resulting expressions we postpone their derivation and presentation to a further article [8]. We will here rather display a few curves corresponding to a given choice of parameters: the asymmetry ratio $a/b = 1/9$ (or $a = p/10$, $b = 9p/10$) common to the two potentials (see Fig. 1), and the height of the barriers in the fundamental state somewhat larger than the thermal energy $\overline{W}_1 = 10kT$. The diffusion constants are for simplicity taken equal $D_1 = D_2 = D$. A few points corresponding to numerical simulations are also displayed exhibiting quantitative agreement with the analytical calculations.

In Fig. 2(a) the average velocity V induced by a given homogeneous external action Ω (here $\Omega = 1.85\omega_2$, the value 1.85 is chosen close to optimal conditions discussed below) is plotted as a function of the period p of the structure, for a flat excited state $\overline{W}_2 = 0$. Figure 2(b) displays plots of the average induced velocity V as a function of the amplitude of the external action Ω, for different excited state potential W_2 modulations. Two observations can be made: (i) Increasing the potential modulation in the excited states reduces the average motion in a way compatible with a Kramers type of exponential decrease [$\cong \exp(-\overline{W}_2/kT)$], indicating the pinning of the particles by W_2. In fact the behavior is more subtle when $\overline{W}_2$ is of order kT since the optimum pumping conditions (V maximum) correspond to a slightly negative value of $\overline{W}_2/kT$ rather than a flat potential $\overline{W}_2 = 0$. (ii) In both curves a clear maximum is observed.

A simple picture of the corresponding optimum conditions is a particle in state 1 slides downhill toward the corresponding well of the fundamental potential; as it arrives in its proximity it is kicked up to the excited state without loss of time, it then diffuses almost isotropically

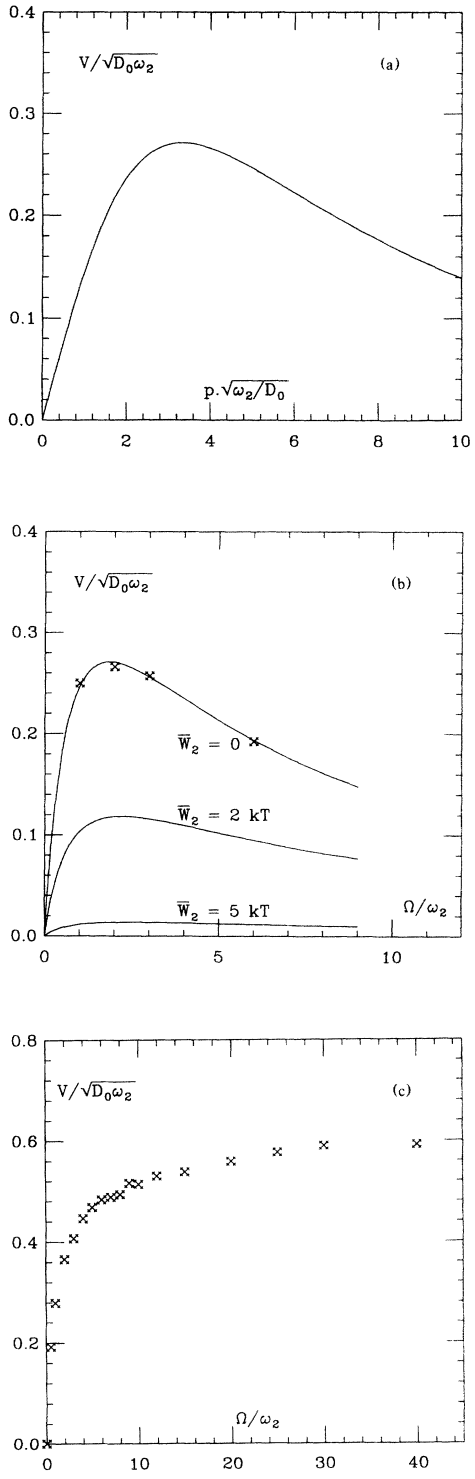

FIG. 2. Lines: analytical calculations (strong external action regime); crosses: Monte Carlo simulations, obtained by averaging over 1000 runs of at least 50 "1 → 2 → 1 cycles." (a) Average velocity V as a function of period p; $\overline{W}_2 = 0$. (b) Average velocity V as a function of excitation amplitude Ω (homogeneous case), for different values of $\overline{W}_2$. (c) Average velocity V as a function of excitation amplitude Ω (localized case); $\overline{W}_2 = 0$.

in an essentially flat landscape over a length typically larger than the small distance a, but smaller than the large one b, before spontaneously returning to ground state 1. With an appreciable probability the following sliding step will take place in the neighboring cell on the right (for the asymmetry choice of Fig. 1). Thus, a net average current to the right is obtained. The fastest velocity we get for our choice of $a = p/10$ is about a third of $(D\omega_2)^{1/2}$ and a tenth of $p\omega_2$.

Note that this picture is very close to the one developed in [2,3]. Two adjustments of times (in the scaling form $p^2/D \simeq 1/\omega_2$ and $p^2 kT/D\overline{W}_1 \simeq 1/\Omega$, the prefactors depending on the asymmetry a/p) are needed to reach the optimum conditions, which implies a high selectivity. The resonant activation over a fluctuating barrier of Ref. [9] appears as a particular case (when the barriers are symmetrical) of our present approach.

We consider now the general case where Ω is a function of position. As we have seen, it occurs whenever the transition rate excitation depends on $W_1(x) - W_2(x)$. For instance, in the case of motor proteins, if the 1-2 state difference was conformational, the change could well be accessible only from particular points of the filament building blocks. It could further be forced artificially in the case of separation devices by using spatially modulated intensities. A simple example of such a "localized" external action is $\Omega(x) = \Omega\Theta(x)$, where $\Theta(x) = 1$ when $W_1(x) \leq \overline{W}_1/100$ and $\Theta(x) = 0$ otherwise. Then a plot of the average velocity as a function of the intensity of the external action Ω saturates for large Ω [Fig. 2(c), $\overline{W}_2 = 0$], instead of displaying a maximum as in the case of a homogeneous external action [Fig. 2(b)]. This can be understood simply: To benefit fully from the asymmetry of the potential W_1 the lifetime in the ground state must be long enough for the particle to slide down an appreciable part of the slopes. A homogeneously large $\Omega(x)$ kicks the particle too quickly back to state 2, whereas in the case of a localized $\Omega(x)$ this kicking process occurs only when the particle has already drifted down to the wells, and with a loss of time that reduces as Ω is increased.

This leads to a robust behavior in the sense that V is rather insensitive to variations of Ω. Note that such a saturation behavior seems typical of the plots of velocity as a function of ATP concentration for motor proteins assemblies [6,7].

Let us eventually point out that another interesting situation is obtained when the two potentials, although of the same vectorial symmetry and period, have their maxima shifted with respect to each other. Macroscopic motion can then be obtained without diffusion-controlled steps, leading to efficient pumping when the energetical barriers are high. This situation and more general ones will be described in more detail in a forthcoming paper [9].

To sum up, we have quantified, with the study of a simple two-level system, how vectorial symmetry plus dissipation creates a macroscopic motion, even in the absence of any externally applied gradient. We have shown how dissipation, which can be provided by a chemical reaction or by wave absorption (either electromagnetic or mechanical), gives rise to an effective macroscopic driving potential. We have evidenced essentially two different behaviors: a selective or resonant one, for which optimum pumping conditions exist, a robust one, in which the average velocity is fairly constant over a broad range of external parameters. Note that the sole existence of an energetically flat state is selective in itself.

Separation techniques could take advantage of either of them. Extracting a single component from a complicated mixture could use the resonant scheme, while simultaneous separation of many rather similar species could benefit from the monotonous variations of the velocity in the second scheme. Motor proteins in the one motor regime seem to share features with the robust picture: detachment is described to be fairly localized and saturation of the velocity as a function of ATP concentration seems ubiquitous [6,7]. Our model allows for velocities of a fraction of the substrate period per attachment-detachment cycle, which is compatible with experimental data [6,7].

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