Fluctuation theorem for the flashing ratchet model of molecular motors

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Molecular motors convert chemical energy derived from the hydrolysis of adenosine triphosphate (ATP) into mechanical energy. A well-studied model of a molecular motor is the flashing ratchet model. We show that this model exhibits a fluctuation relation known as the Gallavotti-Cohen symmetry. Our study highlights the fact that the symmetry is present only if the chemical and mechanical degrees of freedom are both included in the description.

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Molecular motors are subject to intense study both from biological and technological point of view [1,2]. These remarkable nanomachines are enzymes capable of converting chemical energy derived from ATP hydrolysis into mechanical work. They typically operate far from equilibrium, in a regime where the usual thermodynamical laws do not apply. Generically such motors are modeled either in terms of continuous flashing ratchets [3,4] or by a master equation on a discrete space [5,6]. Recently, a general organizing principle for nonequilibrium systems has emerged which is known under the name of fluctuation relations [7,8]. These relations, which hold for nonequilibrium steady states, can be seen as macroscopic consequences of generalized detailed balance conditions, which themselves arise due to the invariance under time reversal of the dynamics at the microscopic scale [9].

An interesting ground to apply these concepts is the field of molecular motors [10–16]. The fluctuation relations impose thermodynamic constraints on the operation of these machines, particularly in regimes arbitrary far from equilibrium. Near equilibrium, they lead to Einstein and Onsager relations. For nonequilibrium steady states, they can be used to quantify deviations from Einstein and Onsager relations as we have shown in Refs. [13,14].

In this paper, we investigate fluctuation relations for continuous ratchet models. We first study a purely mechanical ratchet (model I), which applies to the translocation of a polymer through a pore [17]. We then consider a flashing ratchet (model II), which applies to molecular motors [3]. Using a method inspired by Refs. [7,18], we show that the Gallavotti-Cohen symmetry is always present in model I, but we emphasize that in model II the symmetry exists only if the chemical and mechanical degrees of freedom of the motor are both included in the description.

Let us first consider a random walker in a periodic potential subject to an external force F (model I) [2,19]. The corresponding Fokker-Planck equation is

$$\frac{\partial P}{\partial t} = D_0 \frac{\partial}{\partial x}\left[\frac{\partial P}{\partial x} + \frac{U'(x) - F}{k_B T} P\right], \tag{1}$$

where $U(x)$ is a periodic potential $U(x+a)=U(x)$ and a is the period. This equation describes the stochastic dynamics of a particle in the effective potential $U_{eff}(x)=U(x)-Fx$. By solving Eq. (1) with periodic boundary conditions [17,19], it can be readily proven that the system reaches a stationary state with a uniform current J in the long-time limit. This current is nonvanishing if a nonzero force is applied. When $F=0$, there is no tilt in the potential, $J=0$ and the stationary probability is given by the equilibrium Boltzmann-Gibbs factor.

We call $x(t)$ the position of the ratchet at time t knowing that the ratchet was located at $x(0)=0$ at time $t=0$, which we decompose as $x=(n+\zeta)a$ where n is an integer and $0 \le \zeta < 1$. The stationary current J is related to the average position $x(t)$ by $J=\lim_{t\to\infty}\frac{\langle x(t)\rangle}{t}$, i.e., J is the mean speed of the ratchet in the long-time limit. More generally we are interested in the higher cumulants of $x(t)$ when $t\to\infty$. It is useful to define the generating function

$$F_\lambda(\zeta,t) = \sum_n \exp[\lambda(\zeta+n)]P[(n+\zeta)a,t]. \tag{2}$$

The time evolution of this generating function F_λ is obtained by summing over Eq. (1). This leads to the following equation:

$$\frac{\partial F_\lambda(\zeta,t)}{\partial t} = \mathcal{L}(\lambda)F_\lambda(\zeta,t), \tag{3}$$

where the deformed differential operator $\mathcal{L}(\lambda)$ acts on a periodic function $\Phi(\zeta,t)$ of period 1 as follows:

$$\frac{a^2}{D_0}\mathcal{L}(\lambda)\Phi = \frac{\partial^2 \Phi}{\partial \zeta^2} + \frac{\partial}{\partial \zeta}(\tilde{U}'_{eff}\Phi) - 2\lambda\frac{\partial \Phi}{\partial \zeta} - \lambda \tilde{U}'_{eff}\Phi + \lambda^2\Phi, \tag{4}$$

where $\tilde{U}'_{eff}=a\partial_x U_{eff}/k_B T$ and the left-hand side of Eq. (4) is proportional to the inverse of the characteristic time $\tau=a^2/D_0$. A similar procedure exists in solid-state physics, where periodic functions are expanded in eigenfunctions of Bloch form, which are eigenfunctions of an operator similar to $\mathcal{L}(\lambda)$ [17].

The operator $\mathcal{L}(\lambda)$ has the following fundamental conjugation property:

$$e^{U(x)/k_BT}\mathcal{L}(\lambda)(e^{-U(x)/k_BT}\Phi) = \mathcal{L}^\dagger(-f-\lambda)\Phi, \tag{5}$$

with $f=Fa/k_BT$ the normalized force. This property implies that operators $\mathcal{L}(\lambda)$ and $\mathcal{L}^\dagger(-f-\lambda)$ are adjoint to each other, and thus have the same spectrum. If we call $\Theta(\lambda)$ the largest

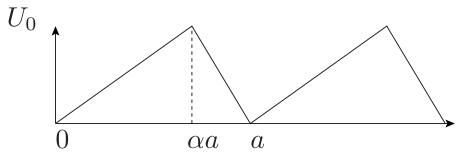

FIG. 1. Sketch of the sawtooth potential $U(x)$. The potential has period a, αa is the distance from a minimum to the next maximum on the right, and U_0 is the maximum of the potential.

eigenvalue of $\mathcal{L}(\lambda)$, we obtain from Eq. (5) that $\Theta(\lambda)$ satisfies the Gallavotti-Cohen symmetry

$$\Theta(\lambda) = \Theta(-f-\lambda). \tag{6}$$

In fact, this symmetry holds for all eigenvalues. For the special case $f=0$, the conjugation relation (5) reduces to the *detailed balance* property [18]. Finally, it is important to note that $\Theta(\lambda)$ is the generating function for the cumulants of $x(t)$.

We have calculated numerically the function $\Theta(\lambda)$ for the case of the sawtooth potential shown in Fig. 1, with a barrier height U_0 on order of several k_BT [17]. This function was obtained by first discretizing the operator $\mathcal{L}(\lambda)$ and then calculating its largest eigenvalue using the Ritz variational method. This method does not require finding a basis specific to the chosen potential, in contrast to what was done in Ref. [20]. for the cosine potential. Our numerical method can handle any shape of the potential.

The form of $\Theta(f\eta)$ with $\eta=\lambda/f$ is shown in Fig. 2 for different values of the normalized force f. The symmetry of all the curves with respect to $\eta=1/2$ corresponds to the symmetry of Eq. (6). At weak force, $\Theta(f\eta)$ has a parabolic shape associated with Gaussian fluctuations, whereas at higher forces a flattening occurs associated with non-Gaussian fluctuations [10,14,20]. By numerically taking derivatives of $\Theta(\lambda)$ with respect to λ near $\lambda=0$, we recover the velocity obtained by directly solving Eq. (1) [17,19].

We now come to the derivation of the Gallavotti-Cohen symmetry for the flashing ratchet model (model II). In this model [3,21,22], the motor has two internal states $i=1,2$, which are described by two time-independent potentials $U_i(x)$. We assume that these potentials are periodic with a common period a. The probability density for the motor to

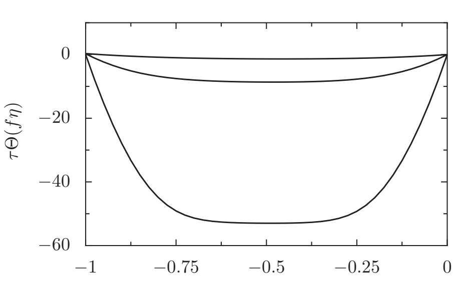

FIG. 2. Normalized eigenvalue $\tau\Theta(f\eta)$ (with $\tau=a^2/D_0$) as function of η for different values of the normalized force f; from top to bottom, $f=5$, $f=10$, and $f=20$. The parameters of the potential are $\alpha=0.7$, $U_0/k_BT=5$. The symmetry of all the curves with respect to $\eta=-1/2$ is Gallavotti-Cohen symmetry expected for model I.

be at position x at time t and in state i is $P_i(x,t)$. The dynamics of the model is described by

$$\frac{\partial P_1}{\partial t} + \frac{\partial J_1}{\partial x} = -\omega_1(x)P_1 + \omega_2(x)P_2$$

$$\frac{\partial P_2}{\partial t} + \frac{\partial J_2}{\partial x} = \omega_1(x)P_1 - \omega_2(x)P_2, \tag{7}$$

where $\omega_1(x)$ and $\omega_2(x)$ are space dependent transition rates, and the local currents J_i are defined by

$$J_i = -D_0\left[\frac{\partial P_i}{\partial x} + \frac{1}{k_BT}\left(\frac{\partial U_i}{\partial x} - F\right)P_i\right], \tag{8}$$

with D_0 the diffusion coefficient of the motor and F a nonconservative force acting on the motor. The transition rates can be modeled using standard kinetics for the different chemical pathways between the two states of the motor [21]

$$\omega_1(x) = [\omega(x) + \psi(x)e^{\Delta\mu}]e^{(U_1(x)-fx)/k_BT},$$

$$\omega_2(x) = [\omega(x) + \psi(x)]e^{(U_2(x)-fx)/k_BT}, \tag{9}$$

where $\Delta\mu=\Delta\tilde{\mu}/k_BT$ is the normalized chemical potential and $\Delta\tilde{\mu}$ the chemical potential associated with ATP hydrolysis. Terms proportional to $\omega(x)$ are associated with thermal transitions, while terms proportional to $\psi(x)$ correspond to transitions induced by ATP hydrolysis. One could easily introduce more chemical pathways than the ones considered here [21] but this extension is not essential for the present argument. Note that the way the force enters the rates is unambiguous in such a continuous model [5,14].

Note that Eq. (7) can be rewritten as a matrix $\mathcal{L}$ of operators

$$\frac{\partial}{\partial t}\begin{pmatrix} P_1 \\ P_2 \end{pmatrix} = \mathcal{L}\begin{pmatrix} P_1 \\ P_2 \end{pmatrix} = \begin{pmatrix} \mathcal{L}_1 - \omega_1 & \omega_2 \\ \omega_1 & \mathcal{L}_2 - \omega_2 \end{pmatrix}\begin{pmatrix} P_1 \\ P_2 \end{pmatrix}, \tag{10}$$

where the action of the operator $\mathcal{L}_i$ on a function $\Phi(x,t)$ is given by

$$\mathcal{L}_i\Phi = D_0\frac{\partial^2\Phi}{\partial x^2} + D_0\frac{\partial}{\partial x}\left(\frac{U_i' - F}{k_BT}\Phi\right). \tag{11}$$

When $F=0$ and $\Delta\mu=0$, the system is at equilibrium and

$$\frac{\omega_2(x)}{\omega_1(x)} = \exp\left(\frac{U_2 - U_1}{k_BT}\right). \tag{12}$$

In this case, the stationary solution of the system (7) is the Boltzmann distribution for P_1 and P_2, the currents J_1 and J_2 vanish and there is no global displacement of the motor. If both F and $\Delta\mu$ do not vanish, then the system is out of equilibrium and nonvanishing currents can appear.

If the switching between the two potentials occurs only by thermal transitions, i.e., when $\Delta\mu=0$, the rates satisfy the detailed balance condition of Eq. (12), even in the presence of a nonzero force F. The Gallavotti-Cohen symmetry follows by considering a 2×2 diagonal matrix of operators $\mathcal{L}_i(\lambda)$ of the form (4). The symmetry is indeed present as shown in the solid curves of Fig. 3. In the general case how-

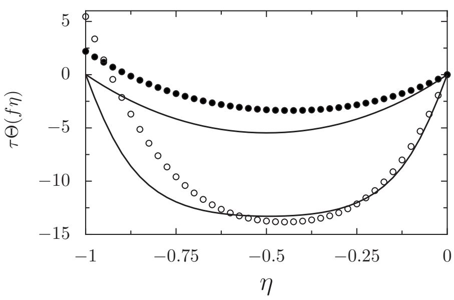

FIG. 3. Normalized eigenvalue $\tau\Theta(f\eta)$ as function of η for a normalized force $f=5$ (top two curves) and $f=10$ (bottom two curves) for the flashing ratchet (model II). The solid curves correspond to the case where the switching rates satisfy detailed balance which leads to the Gallavotti-Cohen symmetry. The curves with filled symbols ($f=5$) and empty symbols ($f=10$) correspond to cases where detailed balance is broken with constant switching rates $\omega_1(x)=\omega_2(x)=10\tau^{-1}$ and with the same potentials. The lack of symmetry in these curves with respect to $\eta=-1/2$ is apparent especially near $\eta=-1$.

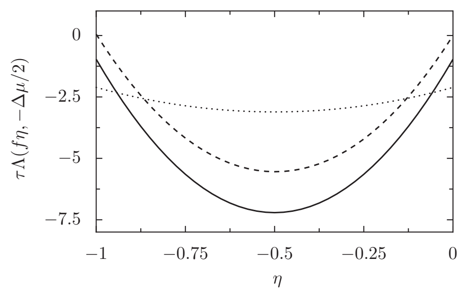

FIG. 4. For model II, the normalized eigenvalue $\tau\Lambda(f\eta,-\Delta\mu/2)$ is shown as function of η. The dashed curve corresponds to $f=5$ and $\Delta\mu=0$, the solid curve corresponds to $f=5$ and $\Delta\mu=10$, and the dotted curve corresponds to $f=2$ and $\Delta\mu=10$. The symmetry is recovered in all cases in this description which includes both the mechanical and chemical degrees of freedom.

ever, where the normalized force f and chemical-potential $\Delta\mu$ are both nonzero, the relation (12) is no more satisfied and the Gallavotti-Cohen relation (6) is not valid. This is shown in the curves with symbols in Fig. 3 where for simplicity we took constant switching rates $\omega_1=\omega_2=10\tau^{-1}$. For all the curves of this figure, we took a sawtooth potential U_1 with the same parameters as in Fig. 2, and a potential U_2 constant in space. The breaking of the symmetry of Eq. (6) can be interpreted as a result of the existence of internal degrees of freedom, similarly to the violations discussed in Ref. [23].

To establish a fluctuation relation for the flashing ratchet model, one must consider both the mechanical and chemical currents present [13,16].

Let us introduce the probability density $P_i(x,q;t)$ associated with the probability that at time t the ratchet is in the internal state i, at position x and that q chemical units of ATP have been consumed. The evolution equations for this probability density is obtained by modifying Eq. (7) after taking into account the dynamics of the discrete variable q. We have

$$\frac{\partial P_1(x,q,t)}{\partial t}=[\mathcal{L}_1-\omega_1(x)]P_1(x,q,t)+\omega_2^{-1}(x)P_2(x,q+1,t)+\omega_2^0(x)P_2(x,q,t) \quad (13)$$

$$\frac{\partial P_2(x,q,t)}{\partial t}=[\mathcal{L}_2-\omega_2(x)]P_2(x,q,t)+\omega_1^0(x)P_1(x,q,t)+\omega_1^1(x)P_1(x,q-1,t). \quad (14)$$

We use a notation similar to that of Ref. [14], where $\omega_i^l(x)$ denotes the transition rate at position x from the internal state i with $l=-1,0,1$ ATP molecules consumed. This leads to $\omega_1^0=\omega e^{(U_1-fx)/k_BT}$, $\omega_2^0=\omega e^{(U_2-fx)/k_BT}$, $\omega_1^1=\psi e^{(U_1-fx)/k_BT+\Delta\mu}$, and $\omega_2^{-1}=\psi e^{(U_2-fx)/k_BT}$, with $\omega_1(x)=\omega_1^0(x)+\omega_1^1(x)$ and $\omega_2(x)=\omega_2^0(x)+\omega_2^{-1}(x)$.

As above we introduce two generating functions $F_{1,\lambda,\gamma}$ and $F_{2,\lambda,\gamma}$, depending on two parameters λ and γ which are conjugate variables to the position of the ratchet and to the ATP counter q. We have for $i=1,2$,

$$F_{i,\lambda,\gamma}(\zeta,t)=\sum_q e^{\gamma q}\sum_n e^{\lambda(\zeta+n)}P_i[a(\zeta+n),q;t]. \quad (15)$$

The evolution equation for these generating functions is obtained from Eq. (15) as

$$\frac{\partial}{\partial t}\begin{pmatrix}F_{1,\lambda,\gamma}\\F_{2,\lambda,\gamma}\end{pmatrix}=\mathcal{L}(\lambda,\gamma)\begin{pmatrix}F_{1,\lambda,\gamma}\\F_{2,\lambda,\gamma}\end{pmatrix}, \quad (16)$$

with the operator $\mathcal{L}(\lambda,\gamma)$ decomposed as

$$\mathcal{L}(\lambda,\gamma)=\mathcal{D}(\lambda)+\mathcal{N}(\gamma), \quad (17)$$

with $\mathcal{D}(\lambda)$ the diagonal matrix diag$[\mathcal{L}_1(\lambda)-\omega_1,\mathcal{L}_2(\lambda)-\omega_2]$, and

$$\mathcal{N}(\gamma)=\begin{pmatrix}0 & \omega_2^0+\omega_2^{-1}e^{-\gamma}\\ \omega_1^0+\omega_1^1e^{\gamma} & 0\end{pmatrix}. \quad (18)$$

Consider now the diagonal matrix Q defined by diag$(e^{-U_1/k_BT},e^{-U_2/k_BT})$. By direct calculation, one can check that $Q^{-1}\mathcal{N}(\gamma)Q=\mathcal{N}^{\dagger}(-\Delta\mu-\gamma)$. From Eq. (5), one obtains $Q^{-1}\mathcal{D}(\gamma)Q=\mathcal{D}^{\dagger}(-\Delta\mu-\gamma)$. By combining these two equations, we conclude that

$$Q^{-1}\mathcal{L}(\lambda,\gamma)Q=\mathcal{L}^{\dagger}(-f-\lambda,-\Delta\mu-\gamma), \quad (19)$$

which leads to the Gallavotti-Cohen symmetry

$$\Lambda(\lambda,\gamma)=\Lambda(-f-\lambda,-\Delta\mu-\gamma), \quad (20)$$

where $\Lambda(\lambda,\gamma)$ is the largest eigenvalue of $\mathcal{L}(\lambda,\gamma)$. If we consider only the mechanical displacement of the ratchet, the relevant eigenvalue $\Theta(\lambda)$ is given by $\Theta(\lambda)=\Lambda(\lambda,0)$, which clearly does not satisfy the fluctuation relation as shown in Fig. 3. In Fig. 4, we have computed $\Lambda(f\eta,-\Delta\mu/2)$ for the same potentials and with rates $\omega_i^l(x)$ of the form given above with $\omega(x)=5\tau^{-1}$ and $\phi(x)=10\tau^{-1}$. We have verified that in all cases the symmetry of Eq. (20) holds.

In this paper, we have shown that the large deviation function of the mechano-chemical currents obeys the Gallavotti-Cohen relation. Another related but different symmetry relation for the entropy production exists under more general conditions [7,10,15,18,20]. We have shown here that the symmetry for the currents is valid for the flashing ratchet model when internal degrees of freedom are taken into account. This raises a fundamental question concerning the validity of fluctuations relations and their applicability to other types of ratchet models [2,4]. Other mechanisms exist which are known to produce deviations from fluctuations relations [23], and it would be interesting to investigate whether fluctuations relations can always be restored by a suitable modification of the dynamics.

On the experimental side, it would be very interesting to investigate fluctuations relations for molecular motors using single molecule experiments, in a way similar to what was achieved in colloidal beads or biopolymers experiments [8]. Using fluorescently labeled ATP molecules, recent experiments with myosin 5*a* and with the F_0-F_1 rotary motor, aim at simultaneous recording of the turnover of single fluorescent ATP molecules and the resulting mechanical steps of the molecular motor [24]. These exciting results indicate that a simultaneous measurement of the values of the mechanical and chemical variable of the motor is achievable, and therefore from the statistics of such measurements it is possible to construct $P(x,q,t)$. With enough statistics of such data, one could thus in principle verify Eq. (20). Such a verification would confirm that the Gallavotti-Cohen symmetry is a thermodynamic constraint that plays an essential role in the mechano-chemical coupling of molecular motors.

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[1] J. Howard, *Mechanics of Motor Proteins and the Cytoskeleton* (Sinauer Associates, Sunderland, MA, 2001).
[2] P. Hänggi and F. Marchesoni, Rev. Mod. Phys. **81**, 387 (2009).
[3] F. Jülicher, A. Ajdari, and J. Prost, Rev. Mod. Phys. **69**, 1269 (1997).
[4] P. Reimann, Phys. Rep. **361**, 57 (2002).
[5] A. Kolomeisky and M. Fisher, Annu. Rev. Phys. Chem. **58**, 675 (2007).
[6] R. Lipowsky, Phys. Rev. Lett. **85**, 4401 (2000).
[7] J. Kurchan, J. Phys. A **31**, 3719 (1998); e-print arXiv:0901.1271.
[8] D. Collin *et al.*, Nature **437**, 231 (2005); V. Blickle, T. Speck, L. Helden, U. Seifert, and C. Bechinger, Phys. Rev. Lett. **96**, 070603 (2006).
[9] B. Derrida, J. Stat. Mech.: Theory Exp. **2007**, P07023 (2007).
[10] P. Gaspard, J. Chem. Phys. **120**, 8898 (2004); D. Andrieux and P. Gaspard, Phys. Rev. E **74**, 011906 (2006).
[11] U. Seifert, EPL **70**, 36 (2005).
[12] R. Lipowsky and S. Liepelt, J. Stat. Phys. **130**, 39 (2008); **135**, 777 (2009).
[13] A. W. C. Lau, D. Lacoste, and K. Mallick, Phys. Rev. Lett. **99**, 158102 (2007).
[14] D. Lacoste, A. W. C. Lau, and K. Mallick, Phys. Rev. E **78**, 011915 (2008).
[15] W. De Roeck and C. Maes, Phys. Rev. E **76**, 051117 (2007).
[16] T. Schmiedl, T. Speck, and U. Seifert, J. Stat. Phys. **128**, 77 (2007).
[17] D. K. Lubensky and D. R. Nelson, Biophys. J. **77**, 1824 (1999).
[18] J. L. Lebowitz and H. Spohn, J. Stat. Phys. **95**, 333 (1999).
[19] H. Risken, *The Fokker-Planck Equation* (Springer, Berlin, 1989).
[20] J. Mehl, T. Speck, and U. Seifert, Phys. Rev. E **78**, 011123 (2008).
[21] A. Parmeggiani, F. Julicher, A. Ajdari, and J. Prost, Phys. Rev. E **60**, 2127 (1999).
[22] H. Wang, C. S. Peskin, and T. C. Elston, J. Theor. Biol. **221**, 491 (2003).
[23] S. Rahav and C. Jarzynski, J. Stat. Mech.: Theory Exp. **2007**, P09012 (2007).
[24] Y. Ishii and T. Yanagida, HFSP J. **1**, 15 (2007); E. M. De la Cruz and A. O. Olivares, HSFP J. **3**, 67 (2009).