THE FLUCTUATION THEOREM FOR CURRENTS AND NONEQUILIBRIUM THERMODYNAMICS

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ABSTRACT

Recently, remarkable results have been discovered for transport across small open systems in contact with reservoirs at different temperatures and chemical potentials. These results are deduced from the fluctuation theorem for the currents flowing across the system. A direct corollary of the fluctuation theorem is that the entropy production is non negative in agreement with the second law of thermodynamics. The fluctuation theorem has further corollaries, in particular, the Onsager reciprocity relations and the Green-Kubo formulas, as well as their extensions to the nonlinear response regime. These results find applications in physical, chemical, and biological systems at the microscale and the nanoscale. Their implications have been studied in transmembrane ion channels, molecular motors, effusion processes, chemical reactions, quantum electronic transport, among other systems.

1 INTRODUCTION

During the last decades, important advances have been carried out in our understanding of the thermodynamic properties of small nonequilibrium systems. Remarkable relationships, called fluctuation theorems [1; 2; 3; 4], have been established for the fluctuating currents flowing across open systems. These relationships find their origin in the microreversibility of the underlying Hamiltonian classical or quantum dynamics of the atoms and electrons composing matter. Yet, these relationships are associated with nonequilibrium conditions that break the time-reversal symmetry at the statistical level of description and they are in agreement with the second law of thermodynamics, according to which the entropy production is always non negative. These advances allow us to understand with unprecedented clarity the connections between the microscopic mechanical motion of atoms and electrons and the macroscopic thermodynamic properties of the global system. Moreover, the new relationships remain valid far from equilibrium. In this regard, the consequences of microreversibility can be investigated not only close to equilibrium, but also farther away from equilibrium in regimes where nonlinear response properties manifest themselves. In this way, generalizations of the Green-Kubo formulae and the Onsager reciprocity relations have been discovered among the nonlinear response coefficients.

These results apply to small nonequilibrium systems studied in nanosciences, such as transmembrane ion channels, molecular motors, chemical reactions, or mesoscopic electronic devices. The nanoscale starts just above the size of the atoms and smallest molecules that compose matter. Typically, the movement of atoms and molecules – although ruled by Hamiltonian dynamics – is at the origin of thermal and molecular fluctuations, which are inherent to the discrete atomic structure of matter. Therefore, the currents of electrons, atoms, or molecules flowing across nanosystems are fluctuating, which

requires a statistical description in terms of probability theory. Since nanosystems acquire their function if they are driven out of equilibrium, the new results play a central role to understand and characterize quantitatively the properties of their function and, in particular, the thermodynamic efficiency of energy transduction that they can perform.

The purpose of the present paper is to give an overview of these recent advances. Emphasis is given to the fluctuation theorem for currents, which is well founded because the currents are defined at the microscopic mechanical level of description. This fluctuation theorem is shown to imply the non-negativity of the thermodynamic entropy production in accordance with the second law. Further implications about nonlinear response are also presented. Nowadays, the current fluctuation theorem has been applied to several small systems and some of them have been investigated experimentally. Moreover, relations characterizing the nonequilibrium breaking of time-reversal symmetry in path statistics are also reviewed in the perspective they give to understand the thermodynamics of information processing at the molecular scale.

The plan of this paper is the following. The fluctuation theorem for currents and its consequences are presented in Section 2. Its applications are described in Section 3. In Section 4, further results are given about path statistics and the thermodynamics of information in copolymerization processes. Conclusions are drawn in Section 5.

2 THE FLUCTUATION THEOREM FOR CURRENTS AND ITS CONSEQUENCES

2.1 The multivariate fluctuation relation

Currents of particles or energy may flow across an open system in contact with several reservoirs at different temperatures and chemical potentials (see Fig. 1). The system is at equi-
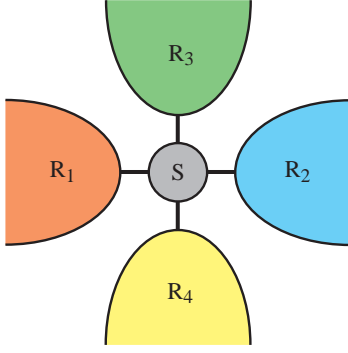
Figure 1. Schematic representation of an open system S in contact with the four reservoirs R_1, R_2, R_3, and R_4.

librium if the temperature and the chemical potentials are uniform in all the reservoirs. Otherwise, the global system is out of equilibrium and a nonequilibrium steady state may establish itself after some transient behavior. At the macroscale, the steady state is characterized by the average values of the currents across the open system. These currents depend on the thermodynamic forces or affinities **A** including

the thermal affinities: $\quad A_{i0} = \dfrac{1}{k_B T_r} - \dfrac{1}{k_B T_i}, \quad$ (1)

the chemical affinities: $\quad A_{ip} = \dfrac{\mu_{ip}}{k_B T_i} - \dfrac{\mu_{rp}}{k_B T_r}, \quad$ (2)

between the reservoirs $i = 1, 2, ..., r - 1$ at the temperatures $\{T_i\}$ and the chemical potentials $\{\mu_{ip}\}$ for the different particle species $p = 1, 2, ..., s$ and the reference reservoir $i = r$ [5; 6; 7]. k_B is Boltzmann's constant. The nonequilibrium conditions are thus fixed by $(r - 1)(s + 1)$ different affinities. All these affinities are vanishing at equilibrium.

At the mesoscale, the currents are fluctuating and their statistical properties are described by a stationary probability distribution if the system is in a steady state. The random variables of interest are the quantities of matter and energy $\Delta \mathbf{Q} = \{\Delta Q_\alpha\}$ that are transferred between the reservoirs during a time interval $[0, t]$. There are as many such quantities as there are affinities. The fluctuating currents are thus defined as $\mathbf{J} = \Delta \mathbf{Q}/t$. If $P_\mathbf{A}$ denotes the probability distribution describing the steady state corresponding to the affinities **A**, the fluctuation relation for the currents reads

$$\frac{P_\mathbf{A}(\mathbf{J})}{P_\mathbf{A}(-\mathbf{J})} \simeq_{t \to \infty} \exp(\mathbf{A} \cdot \mathbf{J} t). \quad (3)$$

This theorem has been established for Markovian stochastic processes using graph theory [8]. Equation (3) compares the opposite fluctuations of the currents. At equilibrium where $\mathbf{A} = 0$, we recover the principle of detailed balancing, according to which opposite fluctuations are equiprobable. Out of equilibrium, the fluctuation relation (3) shows that opposite fluctuations no longer have equal probabilities. Since the ratio of probabilities is increasing or decreasing with time, one of both fluctuations dominates over the opposite and a directionality appears in the open system. Accordingly, the principle of detailed balance is no longer satisfied by the probability distribution $P_\mathbf{A}$, which breaks the time-reversal symmetry under nonequilibrium conditions $\mathbf{A} \neq 0$. Nevertheless, the fluctuation relation remains

compatible with the time-reversal symmetry because the ratio of the probabilities is inverted if the sign of the affinities or the currents is changed, which expresses the fact that the directionality is reversed together with the nonequilibrium conditions.

2.2 Consequences for the entropy production and the thermodynamic efficiencies

The fluctuation relation (3) implies that the entropy production, which is given by the sum of the affinities multiplied by the average values of the fluctuating currents, is always non negative:

$$\frac{1}{k_B} \frac{d_i S}{dt} = \mathbf{A} \cdot \langle \mathbf{J} \rangle_\mathbf{A} \geq 0. \quad (4)$$

This inequality can be proved by writing

$$\mathbf{A} \cdot \langle \mathbf{J} \rangle_\mathbf{A} = \lim_{t \to \infty} \frac{1}{t} \int d\mathbf{J} \, P_\mathbf{A}(\mathbf{J}) \ln \frac{P_\mathbf{A}(\mathbf{J})}{P_\mathbf{A}(-\mathbf{J})} \geq 0 \quad (5)$$

because the Kullback-Leibler divergence between the distributions $P_\mathbf{A}(\mathbf{J})$ and $P_\mathbf{A}(-\mathbf{J})$ is always non negative. Another way to obtain the non-negativity of the entropy production is by using Jensen's inequality $\langle e^X \rangle \geq e^{\langle X \rangle}$ with $X = -\mathbf{A} \cdot \mathbf{J} t$ and the statistical average $\langle \cdot \rangle_\mathbf{A}$ and by noting that $\langle e^X \rangle \simeq 1$ as the consequence of the fluctuation relation (3) in the long-time limit.

In order to drive a particular current $\langle J_\gamma \rangle_\mathbf{A}$ in the direction opposite to its associated affinity A_γ by using the other currents, energy should be supplied and the second law determines a limit to the efficiency of energy transduction. In this case, $A_\gamma \langle J_\gamma \rangle_\mathbf{A} < 0$ and a thermodynamic efficiency can be defined according to

$$0 \leq \eta \equiv -\frac{A_\gamma \langle J_\gamma \rangle_\mathbf{A}}{\sum_{\alpha(\neq \gamma)} A_\alpha \langle J_\alpha \rangle_\mathbf{A}} \leq 1. \quad (6)$$

Since the fluctuation relation (3) implies the non-negativity of the entropy production (4), it also implies that this efficiency cannot reach values larger than unity.

Since the currents are random, the question arises whether it is possible to guess the direction of the affinities **A** imposed by the reservoirs from the observation of some current fluctuation **J**. Bayesian inference gives the likelihood of the hypotheses that the observed current fluctuation **J** goes either forward $(+)$ or backward $(-)$ with respect to the direction **A** as [9; 10]

$$P(+|\mathbf{J}) = \frac{1}{1 + \frac{P(-)P(\mathbf{J}|-)}{P(+)P(\mathbf{J}|+)}}. \quad (7)$$

Tossing a fair coin on either hypothesis amounts to take $P(+) = P(-) = \frac{1}{2}$, while $P(\mathbf{J}|\pm) = P_\mathbf{A}(\pm\mathbf{J})$. According to the fluctuation relation (3), the likelihood that the observed current fluctuation **J** indeed goes forward with respect to the direction of the affinities **A** is thus given by

$$P(+|\mathbf{J}) \simeq \frac{1}{1 + \exp(-\mathbf{A} \cdot \mathbf{J} t)} \to_{t \to +\infty} \theta(\mathbf{A} \cdot \mathbf{J}) \quad (8)$$

where $\theta(x)$ is Heaviside's function. In the limit of a long positive time, the likelihood reaches the unit probability that

$\mathbf{A} \cdot \mathbf{J} \geq 0$, if the system is out of equilibrium with $\mathbf{A} \neq 0$. If the affinities vanish $\mathbf{A} = 0$, the likelihood remains at the value $P(+|\mathbf{J}) \simeq \frac{1}{2}$, which confirms the absence of directionality at equilibrium. The reasoning is compatible with the overall time-reversal symmetry because a similar result holds in the limit $t \rightarrow -\infty$ for $\mathbf{A} \cdot \mathbf{J}$ replaced by $-\mathbf{A} \cdot \mathbf{J}$. A further remark is that the characteristic time taken by the likelihood (8) to approach asymptotically the unit probability is estimated as the inverse of the entropy production in units of Boltzmann's constant: $\Delta t = (\mathbf{A} \cdot \langle \mathbf{J} \rangle_{\mathbf{A}})^{-1} = \left(\frac{1}{k_B} \frac{d_i S}{dt} \right)^{-1}$. This characteristic time becomes tiny if the system is macroscopic and driven far from equilibrium by increasing the affinities $\mathbf{A}$. We also notice that the observation of the current fluctuation $\mathbf{J}$ in the frame defined by the reservoirs together with the knowledge of their affinities $\mathbf{A}$ provides the answer to the question without having to guess it [11; 12].

2.3 Consequences for the response properties

An alternative expression of the fluctuation relation (3) can be obtained in terms of the generating function of the statistical cumulants defined as

$$Q_{\mathbf{A}}(\boldsymbol{\lambda}) \equiv \lim_{t \to \infty} -\frac{1}{t} \ln \int P_{\mathbf{A}}(\mathbf{J}) e^{-\boldsymbol{\lambda} \cdot \mathbf{J} t} \, d\mathbf{J} \qquad (9)$$

where $\boldsymbol{\lambda}$ are the so-called counting parameters. The average values of the currents, their diffusivities, as well as their higher cumulants are given by taking the successive derivatives of this generating function with respect to the counting parameters:

$$\langle J_\alpha \rangle_{\mathbf{A}} = \left. \frac{\partial Q_{\mathbf{A}}}{\partial \lambda_\alpha} \right|_{\boldsymbol{\lambda}=0}, \qquad (10)$$

$$D_{\alpha\beta}(\mathbf{A}) = -\frac{1}{2} \left. \frac{\partial^2 Q_{\mathbf{A}}}{\partial \lambda_\alpha \partial \lambda_\beta} \right|_{\boldsymbol{\lambda}=0}, \qquad (11)$$

$$C_{\alpha\beta\gamma}(\mathbf{A}) = \left. \frac{\partial^3 Q_{\mathbf{A}}}{\partial \lambda_\alpha \partial \lambda_\beta \partial \lambda_\gamma} \right|_{\boldsymbol{\lambda}=0}, \qquad (12)$$

$$B_{\alpha\beta\gamma\delta}(\mathbf{A}) = -\frac{1}{2} \left. \frac{\partial^4 Q}{\partial \lambda_\alpha \partial \lambda_\beta \partial \lambda_\gamma \partial \lambda_\delta} \right|_{\boldsymbol{\lambda}=0}, \qquad (13)$$

$$\vdots$$

On the other hand, the average value of a current can be expanded in powers of the affinities as

$$\langle J_\alpha \rangle_{\mathbf{A}} = \sum_\beta L_{\alpha,\beta} A_\beta + \frac{1}{2} \sum_{\beta,\gamma} M_{\alpha,\beta\gamma} A_\beta A_\gamma + \frac{1}{6} \sum_{\beta,\gamma,\delta} N_{\alpha,\beta\gamma\delta} A_\beta A_\gamma A_\delta + \cdots \qquad (14)$$

which defines the linear and nonlinear response coefficients:

$$L_{\alpha,\beta} = \left. \frac{\partial^2 Q_{\mathbf{A}}}{\partial \lambda_\alpha \partial A_\beta} \right|_{\boldsymbol{\lambda}=\mathbf{A}=0}, \qquad (15)$$

$$M_{\alpha,\beta\gamma} = \left. \frac{\partial^3 Q_{\mathbf{A}}}{\partial \lambda_\alpha \partial A_\beta \partial A_\gamma} \right|_{\boldsymbol{\lambda}=\mathbf{A}=0}, \qquad (16)$$

$$N_{\alpha,\beta\gamma\delta} = \left. \frac{\partial^4 Q_{\mathbf{A}}}{\partial \lambda_\alpha \partial A_\beta \partial A_\gamma \partial A_\delta} \right|_{\boldsymbol{\lambda}=\mathbf{A}=0}, \qquad (17)$$

$$\vdots$$

Remarkably, these properties are interrelated as the consequences of the fluctuation theorem (3), as the following reasoning shows. Inserting the fluctuation relation (3) in the definition (9) of the cumulant generating function yields the symmetry relation

$$Q_{\mathbf{A}}(\boldsymbol{\lambda}) = Q_{\mathbf{A}}(\mathbf{A} - \boldsymbol{\lambda}). \qquad (18)$$

Taking successive derivatives of this relation with respect to the counting parameters and the affinities, the cumulants (11), (12), (13), ... and the response coefficients (15), (16), (17), ... are found to be interrelated.

Using second derivatives, the symmetry relation (18) implies the Green-Kubo formulas and the Onsager reciprocity relations for the linear response coefficients:

$$L_{\alpha,\beta} = D_{\alpha\beta}(0), \qquad (19)$$

$$L_{\alpha,\beta} = L_{\beta,\alpha}. \qquad (20)$$

With higher derivatives, generalizations of these relations to the higher cumulants and the nonlinear response coefficients can be deduced [13; 14; 15]. In particular, the nonlinear response coefficients (16) are related to the diffusivities (11) according to

$$M_{\alpha,\beta\gamma} = \left(\frac{\partial D_{\alpha\beta}}{\partial A_\gamma} + \frac{\partial D_{\alpha\gamma}}{\partial A_\beta} \right)_{\mathbf{A}=0}, \qquad (21)$$

$$N_{\alpha,\beta\gamma\delta} = \left(\frac{\partial^2 D_{\alpha\beta}}{\partial A_\gamma \partial A_\delta} + \frac{\partial^2 D_{\alpha\gamma}}{\partial A_\beta \partial A_\delta} + \frac{\partial^2 D_{\alpha\delta}}{\partial A_\beta \partial A_\gamma} - \frac{1}{2} B_{\alpha\beta\gamma\delta} \right)_{\mathbf{A}=0}, \qquad (22)$$

$$\vdots$$

which are generalizations of the Green-Kubo formulas. A generalization of Onsager reciprocity relations is given by the total symmetry of the following fourth-order tensor:

$$N_{\alpha,\beta\gamma\delta} - \left(\frac{\partial^2 D_{\alpha\beta}}{\partial A_\gamma \partial A_\delta} + \frac{\partial^2 D_{\alpha\gamma}}{\partial A_\beta \partial A_\delta} + \frac{\partial^2 D_{\alpha\delta}}{\partial A_\beta \partial A_\gamma} \right)_{\mathbf{A}=0}, \qquad (23)$$

which is the consequence of Eq. (22) and the total symmetry of the fourth-cumulant tensor (13) [13; 14; 15]. The derivative of the third-cumulant tensor (12) with respect to an affinity is also totally symmetric

$$\left(\frac{\partial C_{\alpha\beta\gamma}}{\partial A_\delta} \right)_{\mathbf{A}=0} = B_{\alpha\beta\gamma\delta}(0). \qquad (24)$$

Similar relations exist at higher orders as well [15]. They are the consequences of the underlying microreversibility.

Similar results generalizing the Casimir-Onsager reciprocity relations have been obtained for open quantum systems in an external magnetic field [16].

2.4 From multivariate to univariate fluctuation relations

In general, the fluctuation relation (3) holds for all the currents flowing across an open system and it does not imply the

validity of similar relations for a subset of currents. Let us consider a system with two currents, in which case the fluctuation relation (3) is bivariate and reads

$$\frac{P_{A_1,A_2}(J_1,J_2)}{P_{A_1,A_2}(-J_1,-J_2)} \simeq_{t\to\infty} e^{(A_1 J_1 + A_2 J_2)t}. \tag{25}$$

We may wonder [17] if there exist specific conditions under which the univariate fluctuation relation

$$\frac{P_{A_1,A_2}(J_1)}{P_{A_1,A_2}(-J_1)} \simeq_{t\to\infty} e^{\tilde{A}_1 J_1 t} \tag{26}$$

is satisfied for the marginal distribution of the current J_1 defined as

$$P_{A_1,A_2}(J_1) \equiv \int dJ_2 \, P_{A_1,A_2}(J_1,J_2). \tag{27}$$

It turns out that the univariate fluctuation relation indeed holds under the following specific conditions.

Tight coupling between the currents. This condition is defined by requiring that both currents remain proportional to each other during their random time evolution:

$$J_2 = \sigma J_1, \tag{28}$$

which is only possible under special circumstances encountered for instance in molecular motors. Inserting the condition (28) in the bivariate fluctuation relation (25), we get the univariate fluctuation relation (26) with the affinity $\tilde{A}_1 \equiv A_1 + \sigma A_2$ associated with the coupled currents. In this case, the entropy production (4) reduces to

$$\frac{1}{k_B}\frac{d_i S}{dt} = \tilde{A}_1 \langle J_1 \rangle \geq 0 \tag{29}$$

so that the sole affinity $\tilde{A}_1$ drives the system out of equilibrium. Under the tight-coupling condition (28), the thermodynamic efficiency is directly determined by the affinities:

$$\eta \equiv -\frac{A_1 \langle J_1 \rangle}{A_2 \langle J_2 \rangle} = -\frac{A_1}{\sigma A_2} = \frac{1}{1 - \tilde{A}_1/A_1}. \tag{30}$$

Separation of time scales. In other circumstances, the transition rates for one current may be much higher than for the other current, e.g. $|\langle J_2 \rangle| \gg |\langle J_1 \rangle|$, and it is assumed that

$$\int dJ_2 \, e^{-A_2 J_2 t} P_{A_1,A_2}(J_1,J_2) \simeq P_{A_1,A_2}(J_1) e^{-\Delta A_1 J_1 t} \tag{31}$$

holds for some $\Delta A_1(A_1, A_2)$ in the long-time limit. Inserting the bivariate fluctuation relation (25) in the assumption (31), we get the univariate fluctuation relation (26) for the marginal (27) and the effective affinity $\tilde{A}_1 = A_1 + \Delta A_1 = \tilde{A}_1(A_1, A_2)$, which depends on both affinities A_1 and A_2.

Using Jensen's inequality $\langle e^X \rangle \geq e^{\langle X \rangle}$ here with $X = \tilde{A}_1 J_1 t - (A_1 J_1 + A_2 J_2)t$ and noting that $\langle e^X \rangle \simeq 1$ as the consequence of

the assumption (31), we find that the entropy production has the following lower bound:

$$\frac{1}{k_B}\frac{d_i S}{dt} = A_1 \langle J_1 \rangle + A_2 \langle J_2 \rangle \geq \tilde{A}_1 \langle J_1 \rangle \geq 0 \tag{32}$$

in terms of the effective affinity $\tilde{A}_1$ of the univariate fluctuation relation (26). Accordingly, the thermodynamic efficiency is here limited to a value lower than unity:

$$\eta \equiv -\frac{A_1 \langle J_1 \rangle}{A_2 \langle J_2 \rangle} \leq \frac{1}{1 - \tilde{A}_1/A_1} < 1 \quad \text{if} \quad \tilde{A}_1/A_1 < 0. \tag{33}$$

This situation is encountered in mesoscopic electronic devices where the current J_1 in quantum dots is driven by the Coulomb drag of a large current J_2 in a quantum point contact capacitively coupled to the quantum dots [18; 19]. We notice that the bound (33) is attained for the tight-coupling condition, which is thus stronger.

3 APPLICATIONS

3.1 Transmembrane ion channels

Biological cell membranes separate electrolyte solutions at different ionic concentrations maintained out of equilibrium by the metabolism. Membranes are known to host different kinds of proteins responsible for the active or passive transmembrane transport of ions. While transmembrane active transport is powered for instance by ATP hydrolysis, the passive but highly selective transport of small ions such as Na^+, K^+, or Cl^- proceeds in proteins forming a narrow ion channel [20]. In ion channels, the ionic current is driven by the combined effects of the different ionic concentrations and electric voltage across the membrane.

In the simplest models, the channel is supposed to contain a single ion moving along successive sites $i = 1, 2, ..., L-1$ [21; 22]. Transport is described as a continuous-time Markovian jump process with L states including the empty state $i = L$. The master equation writes

$$\frac{d}{dt}P_t(i) = \sum_j [W(j|i)P_t(j) - W(i|j)P_t(i)] \tag{34}$$

where $P_t(i)$ denotes the probability to find the channel in the ith state at the time t and $W(i|j)$ is the rate of the transition $i \to j$. They are given by

$$W(i|i+1) = k_i e^\phi \quad \text{for} \quad i = 1,2,3,...,L-1, \tag{35}$$
$$W(i+1|i) = k_i e^{-\phi} \quad \text{for} \quad i = L,1,2,...,L-2, \tag{36}$$
$$W(L|1) = c k_L e^\phi, \tag{37}$$
$$W(L|L-1) = c' k_L e^{-\phi}, \tag{38}$$

where c and c' are the ionic concentrations on both sides of the membrane and $\phi = zeF\Delta/(2Lk_B T)$ is a dimensionless parameter giving the strength of the applied electric field F in terms of the membrane thickness Δ, the ionic valency z, and the electronic charge e. The graph associated with this Markovian process is composed of a single cycle [21; 22]. The affinity is identified by considering the ratio of the products of transition rates

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forward and backward along the cycle:

$$A = \ln \prod_{i=1}^{L} \frac{W(i|i+1)}{W(i+1|i)} = \ln \frac{c}{c'} + \frac{zeF\Delta}{k_{\mathrm{B}}T} \qquad (39)$$

with $L + 1 \equiv 1$. We notice that the affinity vanishes at equilibrium where $c' = c \exp(2L\phi)$. The remarkable result is that the condition (39) implies the fluctuation theorem (3) for the ion current J in the direction $i = 1 \to L - 1$ through the ion channel for any values of the rate constants $\{k_i\}_{i=1}^{L}$ [14].

The fluctuation theorem also holds for models based on the Nernst-Planck-Poisson equations [23] and for semi-Markovian models of ion channels [24].

3.2 Molecular motors

Energy transduction is possible in molecular motors where mechanical motion is powered by chemical energy from ATP hydrolysis [21]. In molecular motors, two currents – a mechanical and a chemical one – are thus coupled and driven by the chemical affinity

$$A_{\mathrm{c}} = \frac{\Delta\mu}{k_{\mathrm{B}}T} = \frac{\Delta\mu^0}{k_{\mathrm{B}}T} + \ln \frac{[\mathrm{ATP}]}{[\mathrm{ADP}][\mathrm{P_i}]} \qquad (40)$$

of ATP hydrolysis into ADP and inorganic phosphate $\mathrm{P_i}$, and the mechanical affinity

$$A_{\mathrm{m}} = \frac{F}{k_{\mathrm{B}}T} \quad \text{or} \quad \frac{\tau}{k_{\mathrm{B}}T} \qquad (41)$$

due to an external force F or torque τ. The chemical current J_{c} is the rate of ATP consumption, while the mechanical current J_{m} is the velocity in linear motors moving along filaments such as myosin-actin or kinesin-microtubule, or the angular velocity in rotary motors such as $\mathrm{F_1}$-ATPase.

In such systems, the bivariate fluctuation theorem (25) holds, which predicts constraints on the chemomechanical coupling between both currents including the Onsager reciprocity relation and its generalization to the nonlinear response properties. Under physiological conditions, the nonlinear properties turn out to be essential because the Michaelis-Menten kinetics known for molecular motors has the consequence that the average currents have a highly nonlinear dependence on the affinities, as recent studies have pointed out [25; 26; 27].

In the case of the rotary motor $\mathrm{F_1}$-ATPase, experimental observations have revealed that the dynamics proceeds by steps and substeps [28]. A full revolution is performed with the hydrolysis of three ATP molecules. The random rotational motion of $\mathrm{F_1}$-ATPase can be described by different kinds of models [26; 27]. The simplest is by a Markovian master equation such as Eq. (34) with six internal states corresponding to the six observed steps and substeps. In such a model, the mechanical current is tightly coupled to the chemical one and the condition (28) is thus satisfied. Accordingly, the bivariate function relation (25) reduces to the univariate relation (26) [25] and the average currents are both proportional to the mean angular velocity

$$\langle V \rangle = V_{\max} \frac{[\mathrm{ATP}] - K_{\mathrm{eq}}[\mathrm{ADP}][\mathrm{P_i}]}{[\mathrm{ATP}] + K_{\mathrm{M}} + K_{\mathrm{P}}[\mathrm{ADP}][\mathrm{P_i}]} \qquad (42)$$
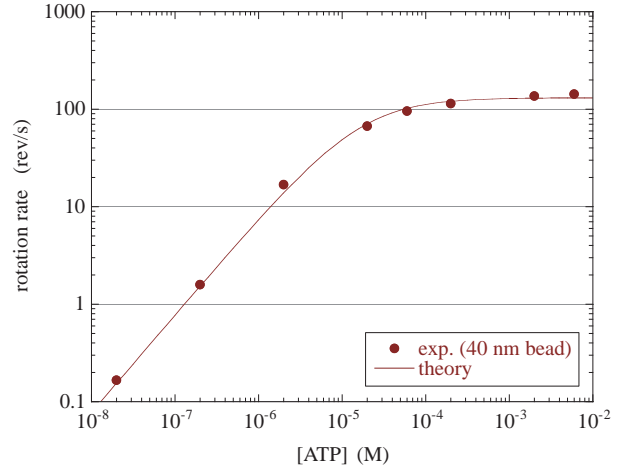

Figure 2. Mean angular velocity of the γ-shaft of $\mathrm{F_1}$-ATPase in revolutions per second, versus the ATP concentration $[\mathrm{ATP}]$ in mole per liter for $[\mathrm{ADP}][\mathrm{P_i}] = 0$. The diameter of the bead attached to the axis of the motor is $d = 40$ nm, the temperature is of 23 degrees Celsius, and the external torque is zero. The circles are the experimental data of Ref. [28]. The solid line is the result of numerical simulation of the discrete-state model. Adapted from Ref. [27].

where $V_{\max}$ is the maximum possible velocity of about 10^2 rev/s determined by the rate constant of ATP binding to a catalytic site, K_{eq} is the equilibrium constant of ATP hydrolysis, K_{M} is the Michaelis-Menten constant characterizing the release of ATP or hydrolytic products from a catalytic site, and K_{P} is the constant characterizing the reverse of the release of hydrolytic products [27]. Figure 2 shows the Michaelis-Menten dependence of the mean angular velocity as a function of ATP concentration with the crossover between the regime where rotation is limited by low concentration and the high-concentration regime with saturation at the maximum velocity $V_{\max}$. Now, Eq. (42) can be expressed in terms of the chemomechanical affinity resulting from the tight-coupling condition (28):

$$A = \underbrace{\frac{\Delta\mu}{k_{\mathrm{B}}T}}_{\text{chemistry}} + \underbrace{\frac{2\pi}{3}\frac{\tau}{k_{\mathrm{B}}T}}_{\text{mechanics}} \qquad (43)$$

because one ATP molecule is consumed for a third of revolution. For given concentrations of ADP and $\mathrm{P_i}$, the chemomechanical affinity determines the ATP concentration according to

$$[\mathrm{ATP}] = K_{\mathrm{eq}}[\mathrm{ADP}][\mathrm{P_i}]\,\mathrm{e}^A . \qquad (44)$$

Therefore, the mean velocity (42) has the alternative expression:

$$\langle V \rangle = V_{\max} \frac{\mathrm{e}^A - 1}{\mathrm{e}^A - 1 + \frac{3V_{\max}}{L}} \qquad (45)$$

with some coefficient L depending on the given concentrations [ADP] and $[\mathrm{P_i}]$. This coefficient controls the linear response of the motor because $\langle V \rangle \simeq LA/3$ for $A \ll 1$. However, the mean velocity depends on the affinity A in a highly nonlinear way, as shown in Fig. 3. The linear regime extends around the thermodynamic equilibrium point at $A = 0$ where the velocity is essentially flat because the linear-response coefficient takes the very

small value $L \simeq 10^{-5}\,\mathrm{s}^{-1}$. Under physiological conditions, the affinity is about $A \simeq 21.4$ and the angular velocity would take the extremely low value $LA/3 \simeq 6.5$ rev/day if the motor was functioning in the linear regime. Thanks to the highly nonlinear dependence on the affinity A, the velocity can reach the maximum value $V_{\mathrm{max}} \simeq 10^2$ rev/s under physiological conditions.
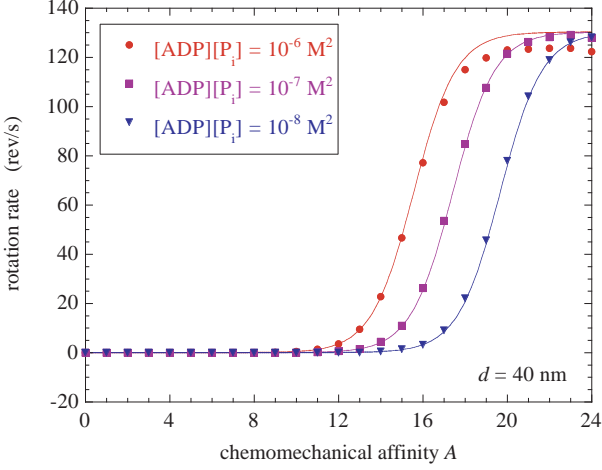

Figure 3. Mean angular velocity versus the affinity (43) for the F_1-ATPase molecular motor. The results of the discrete-state model (solid lines) of Ref. [27] are compared with the continuous-angle model (dots) of Ref. [26] for three different values of $[\mathrm{ADP}][P_i]$. The diameter of the bead is $d = 40$ nm, the temperature 23 degrees Celsius, and the external torque zero. Adapted from Ref. [27].
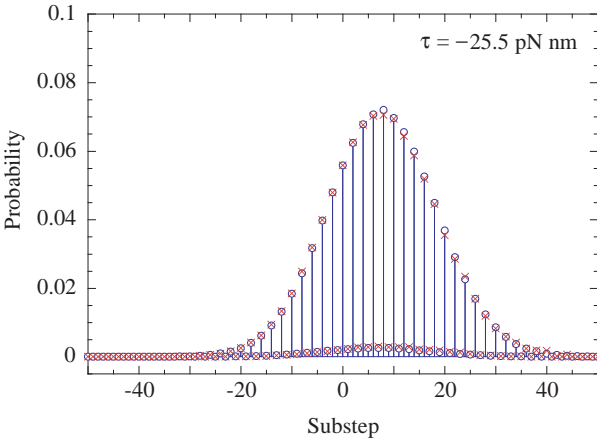

Figure 4. Probability $P(S_t = s)$ (open circles) versus the number $S_t = s$ of substeps of rotation of the F_1-ATPase motor during the time interval $t = 10$ s compared with the prediction $P(S_t = -s)\,\mathrm{e}^{sA/2}$ (crosses) of the univariate fluctuation relation (26), given that the consumption of one ATP molecule may drive two substeps. The concentrations are $[\mathrm{ATP}] = 3 \times 10^{-6}\,\mathrm{M}$, $[\mathrm{ADP}][P_i] = 10^{-6}\mathrm{M}^2$, and the torque $\tau = -25.5\,\mathrm{pN\,nm}$. The diameter of the bead is $d = 80$ nm and the temperature of 23 degrees Celsius. For the given concentrations, the chemomechanical affinity (43) vanishes at the value $\tau_{\mathrm{stall}} = -26.02\,\mathrm{pN\,nm}$ of the torque. The counting statistics is obtained with 10^6 random trajectories simulated for the discrete-state model. Under the present conditions, the catalytic sites are more often empty than occupied, which explains that the probability of an even number of substeps is higher than for an odd number. Adapted from Ref. [27].

Because of thermal and molecular fluctuations, the rotation of such nanometric motors is random with forward and backward movements, which may become equiprobable if the chemomechanical affinity (43) is vanishing. In order to reach this condition, an external torque should be applied to stop the mean forward motion. Close to such a condition, the statistics of forward and backward random steps or substeps can be performed in order to test experimentally the validity of the fluctuation theorem. Figure 4 depicts an example of what would be the result of such a statistics, showing that the univariate fluctuation relation (26) is satisfied. Furthermore, the thermodynamic efficiency (30) has also been studied and it reaches the unit value in the tight-coupling regime if the chemomechanical affinity (43) is vanishing, because $A = A_1 + \sigma A_2 = 0$ if $A_1 = -\sigma A_2$, whereupon $\eta = 1$ [26; 27].

3.3 Mass separation by effusion

In the effusion of a binary gas mixture through a small pore across a thin wall, there are three possible currents: the two currents of particles of different species and the current of kinetic energy. The three corresponding affinities are determined by Eqs. (1)-(2) in terms of the temperatures and chemical potentials of the two reservoirs on both sides of the thin wall. The fluctuation relation (3) holds for the three currents [29; 30] and the formulae (21)-(24) generalizing the Green-Kubo and Onsager reciprocity relations beyond linear response have been verified in detail for this process [30]. A thermodynamic efficiency (6) can be introduced for the separation process, which may be larger in nonlinear regimes than expected with the linear approximation [30].

The fluctuation theorem has also been established for flows of dilute or rarefied gases ruled by the fluctuating Boltzmann equation [31].

3.4 Chemical reactions

At the mesoscopic scale, fluctuations manifest themselves in reacting systems of various kinds, which can be described in terms of stochastic processes ruled by the chemical master equation [32]. Such reactions can be maintained out of equilibrium by supplying the reactants at fixed concentrations and evacuating the products. For such processes, the current fluctuation theorem (3) has been proved as well [13; 33; 34].

3.5 Electron transport in mesoscopic semiconducting devices

The current fluctuation theorem (3) has been extended to electron transport and open quantum systems in the presence of an external magnetic field [3; 14; 16].

Single-electron transfers can be studied at low temperature in semiconducting devices with quantum dots capacitively coupled to quantum point contacts. The large current in the quantum point contact is modulated by the Coulomb repulsion of electrons transiently occupying the quantum dots. Such devices allow the experimental measurement of the full counting statistics for single-electron transfers in the quantum dots. The current fluctuations in the quantum point contact are not observable, but the time scale separation between both currents is such that the univariate fluctuation relation (26) indeed holds with an effective affinity [18; 19], as several experiments have shown [35; 36].

Moreover, the symmetry relations predicted by the fluctuation theorem for the nonlinear-response properties have also been investigated experimentally [37; 38].

4 THERMODYNAMICS OF INFORMATION PROCESSING AT THE MOLECULAR SCALE

4.1 Path statistics and entropy production

The random paths followed by a fluctuating system can be characterized for the temporal disorder they generate. The temporal disorder is defined as the exponential decay rate of the probability to observe a specific path by stroboscopic observation at equal time intervals Δt. If $p_{\boldsymbol{\omega}}$ denotes the probability to observe the path $\boldsymbol{\omega} = \omega_1 \omega_2 \cdots \omega_n$, during which the system has been observed in the coarse-grained states ω_j at the successive instants of time $t_j = j\Delta t$ with $j = 1, 2, ..., n$, the temporal disorder of the process is defined as

$$h(\Delta t) = \lim_{n \to \infty} -\frac{1}{n\Delta t} \sum_{\boldsymbol{\omega}} p_{\boldsymbol{\omega}} \ln p_{\boldsymbol{\omega}} . \qquad (46)$$

To every path $\boldsymbol{\omega}$ corresponds its time reversal $\boldsymbol{\omega}^R = \omega_n \cdots \omega_2 \omega_1$ and we may wonder at which rate its probability decays. In this way, we introduce the average decay rate of the time reversals:

$$h^R(\Delta t) = \lim_{n \to \infty} -\frac{1}{n\Delta t} \sum_{\boldsymbol{\omega}} p_{\boldsymbol{\omega}} \ln p_{\boldsymbol{\omega}^R} . \qquad (47)$$

It turns out that the difference between the quantities (47) and (46) is equal to the thermodynamic entropy production in the limit $\Delta t \to 0$:

$$\frac{1}{k_B} \frac{d_i S}{dt} = \lim_{\Delta t \to 0} \left[h^R(\Delta t) - h(\Delta t) \right] \geq 0 \qquad (48)$$

for the steady states of Markovian processes [39]. In agreement with the second law, this difference is always non negative because it forms a Kullback-Leibler divergence. In this regard, Eq. (48) shows that the thermodynamic entropy production characterizes the time asymmetry of the stochastic process and the breaking of the time-reversal symmetry by nonequilibrium steady states described by the path probability distribution $p_{\boldsymbol{\omega}}$.

To the extend that the decay rates of the path probabilities are the signatures of temporal disorder, the relation (48) shows that the temporal disorder among the typical paths is lower than among their time reversals, i.e., the time reversals are more rare among the typical paths than the typical paths among themselves. In this sense, the relation (48) brings a mathematical expression to the fact that dynamical order manifests itself in nonequilibrium systems [40]. The relation (48) has been tested experimentally in nonequilibrium Brownian motion and electric RC circuits [41; 42].

4.2 Entropy production in copolymerization

The previous result (48) suggests that, if the fluctuations – which evolves in time – can be recorded on a spatial support, they would generate a sequence carrying information on the history followed by the system. Copolymers are natural supports of information coded in the sequence of covalent bonds in the different monomers composing the copolymer. The growth of a single copolymer is a stochastic process taking place at the molecular scale in a solution containing monomers. Their concentrations can be supposed to remain constant if the solution surrounding the copolymer is large enough. Accordingly, the monomer concentrations control the copolymerization and, in particular, its distance from equilibrium where the growth velocity should vanish.

The thermodynamic entropy production of a growing copolymer is given by

$$\frac{1}{k_B} \frac{d_i S}{dt} = v \left(-\frac{g}{k_B T} + D \right) \geq 0 \qquad (49)$$

where v is its growth speed, i.e., the average number of monomers attached to the copolymer per unit time, g is the average free enthalpy per attached monomer, and D is the Shannon disorder per monomer in the copolymer sequence [43; 44]. This result shows that the growth of the copolymer may be powered either by the free enthalpy of attachment if $g < 0$, or by the disorder of the growing sequence if $D > g/(k_B T) > 0$.

The entropy production can also be obtained for copolymerizations on a template as in DNA replication [43; 44]. For such molecular processes, the entropy production depends on the mutual information between the template and the copy, which is a quantity characterizing the fidelity of information transmission from the template to the copy. It turns out that the mutual information takes a positive value under nonequilibrium conditions, but vanishes at equilibrium where information cannot be transmitted.

5 CONCLUSIONS

The present paper gives an overview of recent advances about the fluctuation theorem for currents and other time-reversal symmetry relations in the context of the nonequilibrium thermodynamics of small systems. The fluctuation theorem for currents is a large-deviation property of the currents flowing across a small system in contact with reservoirs at different temperatures and chemical potentials. It finds its origin in the microreversibility of the underlying classical or quantum Hamiltonian dynamics and it is valid far from equilibrium, as well as close to equilibrium. Consequently, the fluctuation theorem for currents leads to results generalizing the Green-Kubo formulae and the Onsager reciprocity relations from the linear to the nonlinear response properties.

Under nonequilibrium conditions, the fluctuation theorem characterizes the breaking of time-reversal symmetry at the statistical level of description and the directionality induced in the system by the affinities of the external reservoirs. At equilibrium, the principle of detailed balancing is recovered.

Interestingly, further symmetry breaking phenomena can also be characterized by relations analogous to the fluctuation relation but in equilibrium systems, such as a magnet in an external magnetic field. The analogy can be developed in detail between time-reversal symmetry breaking out of equilibrium and spin-reversal symmetry breaking at equilibrium [45; 46].

To conclude, the new relationships prove to be fundamental to understand the emergence of macroscopic thermodynamics from the underlying microscopic dynamics ruling the chaotic motion of atoms and the thermal or molecular fluctuations.

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