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Nonequilibrium steady-state circulation and heat dissipation functional

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A nonequilibrium steady-state (NESS), different from an equilibrium, is sustained by circular balance rather than detailed balance. The circular fluxes are driven by energy input and heat dissipation, accompanied by a positive entropy production. Based on a Master equation formalism for NESS, we show the circulation is intimately related to the recently studied Gallavotti-Cohen symmetry of heat dissipation functional, which in turn suggests a Boltzmann's formulalike relation between rate constants and energy in NESS. Expanding this unifying view on NESS to diffusion is discussed.

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The master equation is a widely used stochastic model for single-molecule conformational kinetics. In a thermal equilibrium, the probability ratio between any two states is related to the rate constants between them, which in turn is related to energy according to the Boltzmann formula

$$p_i/p_j = q(j,i)/q(i,j), \quad q(j,i)/q(i,j) = e^{\Delta E}, \tag{1}$$

where ΔE is the energy difference, in k_BT, between states i and j or, equivalently, the heat dissipated in the jump from j to i. These relations, consequences of detailed balance, are fundamental to chemical equilibrium. In recent years, master-equation models have also been applied to motor protein kinetics [1]. The novel feature of this class of models is that a system reaches its stationarity via *circular balance* rather than detailed balance [2,3]. In a nonequilibrium steady-state (NESS), there is also a relation between rate constants and certain probabilities. The relation was extensively studied in Refs. [4,5], but it has not been widely recognized in statistical mechanics. Here we try to develop the recent stochastic theory of Gallavotti-Cohen symmetry [6] from the circulation approach, and thus unify the two theories for far-from-equilibrium statistical mechanics. Both approaches yield the Onsager reciprocity [2] in the linear regime [4,7]. Reference [4] also provided the Onsager's coefficients with a probabilistic interpretation.

Figure 1(a) gives an example. It is easy to compute the steady-state flux $J = \mu_1 q(1,2) - \mu_2 q(2,1) = \mu_2 q(2,3) - \mu_3 q(3,2) = \mu_3 q(3,1) - \mu_1 q(1,3)$, which in general is nonzero. The μ_i are the steady-state distributions, which can be easily obtained from the master equation $d\mu_i/dt = \Sigma_j \mu_j q(j,i) - \mu_i q(i,j) = 0$. It was shown in Ref. [4] that J can be uniquely decomposed into two *one-way-cycle fluxes*: $J = J_+ - J_-$ such that $J_+/J_- = q(1,2)q(2,3)q(3,1)/q(2,1)q(3,2)q(1,3)$. Furthermore, if one follows the trajectory of the Markov jump process X_s $(0 \leqslant s \leqslant t)$, which visits in succession the states $x_1, x_2, \ldots, x_k, \ldots, x_n$, $(x_k \in \{1,2,3\})$, and denotes N_+ (or N_-) the number of times X_s completes the cycle 1231 (or 1321), then $\lim_{t\to\infty}[N_+(t)/t] = J_+$ and $\lim_{n\to\infty}[N_-(t)/t] = J_-$. Thus, J_+ and J_- have strong probabilistic meaning. Figure 1(b) shows how to compute J_+ and J_-. See Refs. [4,5] for for details.

It is important to point out that the stochastic approach to NESS of macromolecules in aqueous solution at constant temperature, based on either master equations or diffusion, is more than a phenomenological theory. Recent work on stochastic macromolecular mechanics [8,9] of motor proteins and other biomolecules have shown that a complete set of thermodynamic laws can be obtained from the formalism. Thus, it is an approach in parallel and complementary to Boltzmann's approach to irreversibility for gases and liquids. Both approaches are rooted in Newtonian mechanics, both invoke a stochastic element *a priori* in dealing with collisions [10], and both give the second law of thermodynamics as an inequality: $\dot{H} \geqslant 0$ [10] and $\dot{\Psi} \leqslant 0$ [9] with H and Ψ being nonequilibrium generalizations of entropy and Helmholtz free energy for microcanonical and canonical ensembles, respectively.

NONEQUILIBRIUM STEADY-STATE

We now consider a N-state Markov jump process X_s, $(0 \leqslant s \leqslant t)$ with transition rates $q(i,j)$. Again, we assume X_s visits in succession the states $x_1, x_2, \ldots, x_k, \ldots, x_n$. We introduce a function of the trajectory $\{X_s\}$:

$$W(t) = \log\left(\frac{q(x_1,x_2)q(x_2,x_3)\ldots q(x_{n-1},x_n)}{q(x_2,x_1)q(x_3,x_2)\ldots q(x_n,x_{n-1})}\right). \tag{2}$$

Note $k_BT \log[q(i,j)/q(j,i)]$ is the energy difference between

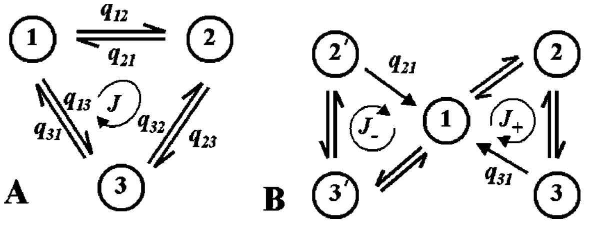

FIG. 1. (a) A simple model of conformational transitions with three states. If the system is closed without pumping, then $q_{12}q_{23}q_{31} = q_{21}q_{32}q_{13}$ and the stationary state is detail balanced. For a pumped system, the equality does not hold, and the stationary state is a NESS with circular flux $J \neq 0$. The J can be further decomposed into probabilistically meaningful J_+ and J_- such that $J = J_+ - J_-$ and $J_+/J_- = q_{12}q_{23}q_{31}/q_{21}q_{32}q_{13}$. J_+ and J_- can be computed from the scheme in (b) in which the clockwise (cw) and counter clockwise (ccw) one-way-cycle fluxes are shown. See Ref. [4] for computing one-way-cycle fluxes in more complex systems.

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states i and j. Hence Eq. (2) is the heat dissipation associated with the jumps $x_1 \rightarrow x_2 \ldots \rightarrow x_n$ in k_BT unit. We shall therefore call it an *instantaneous heat dissipation functional*, which is a more informative name than the *action functional* [6]. In terms of $W(t)$, a cycle completed by X_s is particularly important in NESS: The system returns to its original state after a cycle but a finite amount of heat has been dissipated due to the irreversible jumps: $x_i \rightarrow x_j$ when $\mu_i q(i,j) \neq \mu_j q(j,i)$. To sustain the stationarity, an equal amount of energy has to be ''pumped'' into the system to compensate the heat loss. Recent work on the ''fluctuation theorem'' focuses on the statistical properties of $W(t)$ [6]. By identifying W with heat energy, a Boltzmann formulalike relation exists in NESS: $J_+/J_- = e^{\Delta W}$, where ΔW is the heat dissipation for completing a cycle. As we shall show, the Gallavotti-Cohen symmetry of $W(t)$ is a consequence of this important relation.

Since the total number of states is finite, the X_s continuously completes cycles. Let $\mathcal{C}$ be the set of all possible cycles. This immediately provides us a method to compute the limit of $W(t)$:

$$\lim_{t\rightarrow\infty}\frac{W(t)}{t} = \sum_{\nu\in\mathcal{C}} \frac{N_+^\nu(t)}{t}\log\left(\frac{J_+^\nu}{J_-^\nu}\right) + \frac{N_-^\nu(t)}{t}\log\left(\frac{J_-^\nu}{J_+^\nu}\right)$$
$$= \sum_{\nu\in\mathcal{C}} (J_+^\nu - J_-^\nu)\log\left(\frac{J_+^\nu}{J_-^\nu}\right) \qquad (3)$$

in which $N_+^\nu(t)$ $[N_-^\nu(t)]$ is the number of times the cycle ν is completed clockwise, cw (counterclockwise, ccw) up to time t. Equation (3) turns out to be the entropy production rate (EPR)! In an isothermal NESS, the EPR equals the mean heat dissipation rate (HDR). The right-hand side of Eq. (3) can be rewritten as [4,5,11]

$$\mathrm{EPR} = \xi = \sum_{ij} [\mu_i q(i,j) - \mu_j q(j,i)]\log\left(\frac{\mu_i q(i,j)}{\mu_j q(j,i)}\right), \qquad (4)$$

where μ_k is the steady-state distribution. It is clear that $\xi \geqslant 0$ and the equality holds if and only if the Markov process is detail balanced: $\mu_i q(i,j) = \mu_j q(j,i)$.

The idea behind the fluctuation theorem was to obtain further statistical details about $W(t)$. This can be accomplished by computing its logarithmic moment generating function [6]: $Q(\lambda) = -(1/T)\log E[e^{-\lambda W(T)}]$, where $E[\cdot]$ stands for expectation. Note that $W(t)$ is not stationary in general; it is stationary only when the X_s satisfies detailed balance. We can express the expectation in terms of the circulations as [12]

$$E[e^{-\lambda W(t)}] = \sum_{n=0}^{\infty} P_{N(t)}(n) \sum_{N_+^\nu, N_-^\nu} P(\{N_+^\nu, N_-^\nu\}|N(t)=n)$$
$$\times \prod_{\nu\in\mathcal{C}} \left(\frac{J_+^\nu}{J_-^\nu}\right)^{-\lambda N_+^\nu} \left(\frac{J_-^\nu}{J_+^\nu}\right)^{-\lambda N_-^\nu}$$
$$\approx \sum_{n=0}^{\infty} P_{N(t)}(n) \left\{ \sum_{\nu\in\mathcal{C}} p_-^\nu \left[\left(\frac{J_+^\nu}{J_-^\nu}\right)^{1-\lambda} \right.\right.$$
$$\left.\left. + \left(\frac{J_+^\nu}{J_-^\nu}\right)^{\lambda} - \left(\frac{J_+^\nu}{J_-^\nu} + 1\right) \right] \right\}^n, \qquad (5)$$

where $P_{N(t)}$ is the probability for the number of returns, cw and ccw, as well as the noncircular reversed path, up to time t; $P(\{N_+^\nu, N_-^\nu\}|N(t))$ is assumed to be multinomial with $p_\pm^\nu$ being the stationary probabilities for $\nu_\pm$ and $p_+^\nu/p_-^\nu = J_+^\nu/J_-^\nu$. The symmetry $Q(1-\lambda) = Q(\lambda)$ is evident.

What does this symmetry tell us about the random process $W(t)$? The symmetry indicates that $W(t)$ has a probability density function in the form of $f_{W(t)}(w) = e^{w/2}g(w^2,t)$. It reflects a natural symmetry in $\mathcal{C}$ with each ν divided into cw and ccw. The instantaneous heat dissipation $W(t)$ is a stochastic process increasing linearly, on average, with rate $\xi > 0$. There is a small tail of probability of being negative [13]. Note that the logarithmic moment generating function for a Brownian motion with diffusion constant D and drift rate V is $-V\lambda + D\lambda^2$. Only when $D = V = \alpha$, $(1/\sqrt{4\pi\alpha t})\exp[-(w-\alpha t)^2/4\alpha t]$ has the symmetry $Q(\lambda) = -\alpha\lambda(1-\lambda)$. Therefore, the symmetric $Q(\lambda)$ suggests a certain relationship between the rate (V) and fluctuation (D) of the heat dissipation $W(t)$ in a NESS.

The dynamics of an irreversible process can be viewed as a process stochastically completing dissipative cycles in succession [5]. Again, considering Fig. 1(a), and assuming $q(1,2) = q(2,3) = q(3,1) = q_+$, and $q(2,1) = q(3,2) = q(1,3) = q_-$, the motion can be mapped to a continuous-time biased random walk with q_+ and q_-. For large t, $W(t) \approx \{\sqrt{q_+ + q_-}B_t + (q_+ - q_-)t\}\log(q_+/q_-)$, where B_t is the standard Brownian motion. Clearly $E[W(t)]/t = (q_+ - q_-)\log(q_+/q_-)$. The Brownian motion approximation for the random walk, however, is not sufficiently accurate for computing the symmetric $Q(\lambda)$ for $W(t)$: $Q^{RW}(\lambda) = q_+(q_+/q_-)^\lambda + q_-(q_-/q_+)^\lambda - (q_+ + q_-)$ but $Q^{BM}(\lambda) = -\lambda(q_+ - q_-)\ln(q_+/q_-) + \lambda^2(q_+ + q_-)[\ln(q_+/q_-)]^2/2$. The latter, the Taylor expansion of the former at $\lambda = 0$, destroys the symmetry. Since the Brownian motion approximation preserves the expectation and the variance of the $W(t)$, the symmetry in this case must reflect higher-order statistics of $W(t)$: $\langle(\Delta W)^3\rangle = tQ'''(0) = t(q_+ - q_-)[\ln(q_+/q_-)]^3$ while the Browian motion approximation gives 0. Note $W(t)$ is always positively skewed; the fluctuations in $W(t)$ are not symmetrical in the conventional sense. However, there are two ''symmetric'' characteristics associated with the $W(t)$.

(1) With respect to time, for each X_s there is a corresponding time-reversible process $\tilde{X}_s$; their respective HDF's $W(t)$ and $\tilde{W}(t)$ are the same.

(2) With respect to the probability distribution for W, the cornerstones for the symmetry are the two relations $q_+/q_- = J_+/J_-$ and $J_+/J_- = e^{\Delta W}$. They are to be compared with Eq. (1). The latter relation resembles and generalizes the Boltzmann formula to NESS: the ratio of the rates going cw and ccw on a cycle is related to the heat dissipation of the cycle via a ''Boltzmann factor.'' In an equilibrium, $\Delta W = 0 \Leftrightarrow J_+ = J_-$ on a cycle.

DIFFUSION PROCESSES

Motor proteins have also been modeled in terms of a Brownian motion in an energy landscape [14,8]. The above analyses can be generalized to the diffusion process with Smoluchowski equation

$$\partial P(\boldsymbol{x},t)/\partial t = D\nabla P(\boldsymbol{x},t) - (1/\eta)\nabla\cdot(\boldsymbol{F}P) \tag{6}$$

in which a conservative $\boldsymbol{F}$ leads to a reversible diffusion process $\boldsymbol{X}_t$ with corresponding stationary equilibrium. The relation between equilibrium probability and force $\boldsymbol{F}$ is the Boltzmann's formula $P_{eq}(\boldsymbol{x}) \propto \exp^{[-U(\boldsymbol{x})/k_BT]}$, where $k_BT = \eta D$ and $-\nabla U = \boldsymbol{F}$. Nonconservative $\boldsymbol{F}$ necessarily leads to NESS [15,8], in which the stationary probability distribution satisfies $-D\nabla P_{ss}(\boldsymbol{x}) + (1/\eta)\boldsymbol{F}P_{ss}(\boldsymbol{x}) = \boldsymbol{J}$, where $\boldsymbol{J}$ is the stationary probability flux and $\nabla\cdot\boldsymbol{J}=0$. It is possible to generalize the one-way-cycle fluxes to continuous space [15–17], known as Watanabe formula:

$$\frac{(\text{Prob. of } \boldsymbol{X}_t \text{ cycling cw along } \Gamma)}{(\text{Prob. of } \boldsymbol{X}_t \text{ cycling ccw along } \Gamma)} = \exp\left\{\frac{1}{k_BT}\oint_\Gamma \boldsymbol{F}\cdot dl\right\} \tag{7}$$

for an arbitrary simple closed curve Γ [18]. The right-hand side is known as the thermodynamic *cycle force* along the Γ [4,8]. More importantly, one defines the heat dissipation functional (force×displacement):

$$W(t) = \int_0^t \boldsymbol{F}(\boldsymbol{X}_s)\circ d\boldsymbol{X}_s$$

$$= \int_0^t \boldsymbol{F}(\boldsymbol{X}_s)\cdot d\boldsymbol{X}_s + \frac{1}{2}\int_0^t d\boldsymbol{X}_s\cdot(\nabla\boldsymbol{F}\, d\boldsymbol{X}_s), \tag{8}$$

where $\circ$ is integration in the Stratonovich sense, and $\cdot$ is integration in the Ito sense [17,6]. The second set of terms on the right-hand side of Eq. (8) is due to fluctuations while the first term is due to ''hydrodynamic'' movement [19]. It can be shown that in a NESS, $E[W(t)/t]$ equals

$$\int \boldsymbol{F}\cdot\boldsymbol{J}\, d\boldsymbol{x} = \eta\int \boldsymbol{J}^2 P_{ss}^{-1} d\boldsymbol{x} = \int (\nabla\times\boldsymbol{A})\cdot(\nabla\times\boldsymbol{\gamma})\, d\boldsymbol{x}, \tag{9}$$

where $\boldsymbol{\gamma}$ is the curl part of $\boldsymbol{F} = -\nabla\phi + \nabla\times\boldsymbol{\gamma}$ by Helmholtz-Hodge decomposition [8,17]. All these expressions, in terms of the stationary solution to Eq. (6), have been used in literature as EPR of NESS. When near an equilibrium, the P_{ss} in the above expressions can be approximately replaced by the P_{eq}, which possesses certain symmetry due to detailed balance [4,8].

We again consider a simple example to gain insight. Let X_t be a one-dimensional diffusion, with diffusion coefficient D and constant drift rate V, on a circle. The HDF in Eq. (8), in unit k_BT, is $W(t) = (1/k_BT)\int_0^t F\cdot dX_s = (V/D)\int_0^t dX_s = (V/D)X_t = \sqrt{2V^2/D}B_t + (V^2/D)t$, where $F = \eta V = k_BTV/D$ according to the Einstein relation. The second term in Eq. (8) is zero, since F is constant. It is very important to note that for arbitrary D and V, the corresponding $W(t)$ is also a Brownian motion with a drift. However, the ''diffusion coefficient'' and ''drift rate'' for $W(t)$ are the same, $\alpha = V^2/D$! [20] This relation is essential for the symmetry of the logarithmic generating function: $Q(\lambda) = -\alpha\lambda(1-\lambda)$. It suggests that the rate of heat dissipation and the fluctuations in the dissipation have a relationship in NESS.

One can learn more about the properties of $W(t)$ from this simple example. Let us define $W_m = 1/(m\Delta t)\Sigma_{k=0}^m W(k\Delta t)$ as the ''mean heat dissipation rate.'' Then it is easy to show that W_m has a normal distribution with $E[W_m] = (m+1)\alpha\Delta t/2$ and $VAR[W_m] = (m+1)(m+2)\alpha\Delta t/3$. Therefore, the ratio between probabilities of $W_m = w$ and $W_m = -w$: $P_{W_m}(w)/P_{W_m}(-w) = \exp[-3w/(2m+4)]$. This is the Gallavotti-Cohen fluctuation formula (see p. 182, Eq. (13.43) of Ref. [10]).

A connection with Onsager's principle of least dissipation (PLD) can also be established by considering a nonconservative $\boldsymbol{F} = -\nabla\phi + \epsilon\boldsymbol{f}_{irr}$ using the perturbation method. The precise meaning of a NESS near equilibrium is small ϵ with $\nabla\cdot\boldsymbol{f}_{irr} = 0$. Since Gibbs entropy $S[P] = -\int P(\boldsymbol{x},t)\ln P(\boldsymbol{x},t)d\boldsymbol{x}$, its time derivative $\dot{S} = \text{EPR-HDR}$ [21]. This equation should be compared with Eq. (5.10) in Ref. [22]. Onsager introduced $\text{EPR} = \eta\int \boldsymbol{J}^2 P^{-1}\, d\boldsymbol{x}$ and asserted that $\delta(\text{EPR}) = 0$ for linear irreversibility. Expanding $P(\boldsymbol{x}) = \exp[-\phi/k_BT] + \epsilon\psi(\boldsymbol{x})$ the perturbation analysis yields a linear approximation of $\text{EPR} = \epsilon^2\int e^{\phi}(k_BT\nabla\psi + \psi\nabla\phi - e^{-\phi}\boldsymbol{f}_{irr})^2\, d\boldsymbol{x} + O(\epsilon^3)$, which is quadratic in ϵ as expected. The Euler-Lagrange equation for variational principle $\delta(\text{EPR}) = 0$ is

$$k_BT\nabla^2\psi + \nabla\cdot(\psi\nabla\phi) = -(\nabla\phi\cdot\boldsymbol{f}_{irr})e^{-\phi}, \tag{10}$$

which is what one obtains from perturbation analysis of Eq. (6). Comparing Eq. (10) with Eq. (6), we immediately have, for linear irreversibility, $\boldsymbol{J} = e^{-\phi}\boldsymbol{f}_{irr}$ [8]. Therefore, the PLD is equivalent to Eq. (6) in the linear regime near an equilibrium! This relationship, however, does not hold, in general, beyond the linear regime [23].

DISCUSSION

In an isothermal NESS there is macroscopic heat dissipation, $\xi t > 0$, which balances the entropy production. Mesoscopically, however, there are fluctuations in the instantaneous heat dissipation $W(t)$. ''Instantaneous'' physically means the time scale is on the order of the correlation time of the white noise in Eq. (6). The symmetry we discussed above indicates that the fluctuations are symmetric with respect to time. When $W(t)/t < \xi$, the system absorbs heat from the surrounding heat bath. This consists of the probability of second law violations [13]. This probability decreases exponentially with increasing t; irreversibility is a macroscopic phenomenon.

We have identified the action functional (W), introduced in Ref. [6], with the heat dissipation in a NESS. We show the concept of cycle and circulation flux (J) is central in the discussion on NESS. In terms of W and J, we discover a relationship $J_+/J_- = e^{\Delta W}$ along each cycle that generalizes the Boltzmann's formula to NESS. The ratio of the rates is again related to an energy, now the dissipated heat in NESS. More importantly, the Gallavotti-Cohen symmetry turns out to be a mathematical consequence of this relationship.

The recent new development in nonequilibrium statistical mechanics, based on a dynamical systems approach and the theory of invariant measures [24], has brought the deterministic and stochastic approach to the subject into a single mathematical framework. The concept of EPR in both approaches can be mathematically defined in terms of the Radon-Nikodym derivatives [25]. The irreversibility of a NESS can be characterized by an instantaneous heat dissipation functional $W(t)$, which is a stochastic process that deserves further investigations, including microscopic experimental measurements.

The main purpose of this paper is to introduce the concept of circulation into the current state of affairs. Systems lacking detail balance have been widely studied but little attention has been paid to the importance of circular balance and the NESS thermodynamics associated with it. Here we have bridged the research on NESS [6], the theory of circulation [5], and Hill's theory for free-energy transduction [4]—the theoretical framework for a large class of biophysical processes [9]. The unified theory also incorporates Japanese and German schools [15,19], both with a long tradition in modeling NESS by diffusion processes. Hill's approach was completely based on master equations that allowed him to obtain many in-depth results [4]. These two approaches are mathematically analogous, though an approach based on diffusion is technically more demanding. On the experimental side, a recent development in motor proteins has provided a concrete experimental system for studying NESS. It is our hope that closer interaction between the theoretical and experimental work in this field will further advance our understanding of statistical mechanics and thermodynamics of living systems far from equilibrium.

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[20] Note also $\alpha = FJ/(k_BT)$, where $F=\eta V$ and $J=V$ are Onsager's force and flux. This is a special case of Eq. (9). This connection to Onsager's work is well-known to T.L. Hill and can be found in his work on biological free energy transduction [4].

[21] If the force $\boldsymbol{F}=-\boldsymbol{\nabla}\phi$ is conservative, then one can also introduce the free energy $\Psi[P]=U[P]-TS[P]$ in which $U[P]=\int\phi(\boldsymbol{x})P(\boldsymbol{x})d\boldsymbol{x}$ is the internal energy and $\dot{U}=-\mathrm{HDR}$. Then $\dot{\Psi}=-\mathrm{EPR}\geqslant 0$ with the equality holds true for the stationary process (equilibrium), the 2nd law for isothermal processes. For nonconservative $\boldsymbol{F}$, the internal energy does not exist; Ψ cannot be defined as a state function but the Gibbs entropy can still be defined.

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