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Fluctuation theorem and Onsager reciprocity relations

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The Onsager and higher-order reciprocity relations are derived from a fluctuation theorem for nonequilibrium reactions ruled by the chemical master equation. The fluctuation theorem is obtained for the generating function of the macroscopic fluxes between chemiostats maintaining the system in a nonequilibrium steady state. The macroscopic affinities associated with the fluxes are identified by graph theory. The Yamamoto-Zwanzig formulas for the reaction constants are also derived from the fluctuation theorem.

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I. INTRODUCTION

Out-of-equilibrium systems are characterized by a positive entropy production due to the fluxes of matter and energy generated by the thermodynamic forces also called the affinities. These forces or affinities arise because of inhomogeneities in the chemical potentials, the pressure or the temperature. This is the case for systems driven out of equilibrium at their boundaries by contact with chemiostats. At the statistical-mechanical level of description, the time evolution can be considered as a Markovian stochastic process ruled by a master equation for the probability distribution of the stochastic variables which are the number of molecules of the intermediate species participating to a nonequilibrium reaction network, as proposed by Nicolis and coworkers.[1–7] Such Markovian stochastic processes can describe the molecular fluctuations down to the nanoscale. When driven out of equilibrium by flux boundary conditions, the system may reach a nonequilibrium steady state (NESS) described by a probability distribution which is a stationary solution of the master equation. According to recent work, such a NESS obeys a fluctuation theorem, which is one of the few exact relationships valid arbitrarily far from equilibrium.[8–15] The fluctuation theorem is a general identity based on the microreversibility and the breaking of detailed balance due to the nonequilibrium boundary conditions. As shown elsewhere,[15] the fluctuation theorem also holds for nonequilibrium reactions ruled by the Markovian master equation proposed by Nicolis and coworkers.[1–7]

The purpose of the present paper is to prove that the Onsager reciprocity relations[16] as well as higher-order reciprocity relations can be derived from the fluctuation theorem for nonequilibrium reactions. This derivation requires to generalize the fluctuation theorem[15] to the generating function of the macroscopic fluxes between the chemiostats. Such a generating function can be defined if we can identify the macroscopic affinities in the stochastic description. For this purpose, we have based our method on Schnakenberg's graph analysis of master equation systems.[7] According to this analysis, the macroscopic affinities can be determined by the cycles of the basic graph of the reaction network.[7] This results allows us to derive the Onsager and higher-order reciprocity relations from the fluctuation theorem. Furthermore, we also obtain the corresponding Yamamoto-Zwanzig formulas.[17,18]

The paper is organized as follows. The general framework is formulated in Sec. II. In Sec. III, the generating function of the macroscopic fluxes is obtained by using Schnakenberg's graph analysis and the generalized fluctuation theorem is proved. Onsager reciprocity relations at second and higher orders are derived in Sec. IV together with the corresponding Yamamoto-Zwanzig formulas. The results are applied to simple reactions in Sec. V. Conclusions are drawn in Sec. VI.

II. STOCHASTIC DESCRIPTION OF NONEQUILIBRIUM REACTIONS

A. The master equation and the entropy production

We consider an open homogeneous reactor in contact with chemiostats of reactants and products, which drive the system out of equilibrium. The system is assumed to be isothermal. The reactants and products are denoted by $\{\mathrm{A}^i\}_{i=1}^a$ and the intermediate species in the reactor by $\boldsymbol{X} = \{\mathrm{X}^j\}_{j=1}^c$. The process is described by the following network of reactions $\rho = 1, 2, ..., r$:

$$\sum_{i=1}^{a} \nu^i_{<\rho}\ \mathrm{A}^i + \sum_{j=1}^{c} \nu^j_{<\rho}\ \mathrm{X}^j \underset{k_{-\rho}}{\overset{k_{+\rho}}{\rightleftharpoons}} \sum_{i=1}^{a} \nu^i_{>\rho}\ \mathrm{A}^i + \sum_{j=1}^{c} \nu^j_{>\rho}\ \mathrm{X}^j \tag{1}$$

of stoichiometric coefficients

$$\nu^j_\rho \equiv \nu^j_{>\rho} - \nu^j_{<\rho} \tag{2}$$

$(j = 1, 2, ..., c)$.

At a reacting event of the reaction ρ, the numbers of molecules of the intermediate species change according to:

$$\boldsymbol{X} \xrightarrow{\rho} \boldsymbol{X} + \boldsymbol{\nu}_\rho \tag{3}$$

with the jump vector given by the stoichiometric coefficients $\boldsymbol{\nu}_\rho = \{\nu^j_\rho\}^c_{j=1}$. The probability $P(\boldsymbol{X}; t)$ for the system to be in the state $\boldsymbol{X}$ at time t is ruled by the master equation[1–7]

$$\frac{d}{dt} P(\boldsymbol{X}; t) = \sum_{\rho=\pm 1}^{\pm r} \left[W_\rho(\boldsymbol{X} - \boldsymbol{\nu}_\rho | \boldsymbol{X})\ P(\boldsymbol{X} - \boldsymbol{\nu}_\rho; t) - W_{-\rho}(\boldsymbol{X} | \boldsymbol{X} - \boldsymbol{\nu}_\rho)\ P(\boldsymbol{X}; t) \right] \tag{4}$$

In dilute systems, the transition rates of the reaction ρ are given by the mass-action law according to[1–7]

$$W_\rho(\boldsymbol{X} | \boldsymbol{X} + \boldsymbol{\nu}_\rho) = \Omega\ k_\rho\ \prod_{i=1}^{a} [\mathrm{A}^i]^{\nu^i_{<\rho}} \prod_{j=1}^{c} \frac{X^j}{\Omega} \frac{X^j - 1}{\Omega} \frac{X^j - 2}{\Omega} \cdots \frac{X^j - \nu^j_{<\rho} + 1}{\Omega} \tag{5}$$

where Ω is an extensivity parameter, k_ρ is the reaction constant, and the brackets denote concentrations. The entropy production of the process is given by[6,7]

$$\frac{d_{\mathrm{i}} S}{dt} = \sum_{\rho=1}^{r} \sum_{\boldsymbol{X}} J_\rho(\boldsymbol{X}; t)\ A_\rho(\boldsymbol{X}; t) \geq 0 \tag{6}$$

in terms of the reaction rates or mesoscopic fluxes:

$$J_\rho(\boldsymbol{X}; t) \equiv W_\rho(\boldsymbol{X} - \boldsymbol{\nu}_\rho | \boldsymbol{X})\ P(\boldsymbol{X} - \boldsymbol{\nu}_\rho; t) - W_{-\rho}(\boldsymbol{X} | \boldsymbol{X} - \boldsymbol{\nu}_\rho)\ P(\boldsymbol{X}; t) \tag{7}$$

and the reaction affinities or mesoscopic affinities

$$A_\rho(\boldsymbol{X}; t) \equiv \ln \frac{W_\rho(\boldsymbol{X} - \boldsymbol{\nu}_\rho | \boldsymbol{X})\ P(\boldsymbol{X} - \boldsymbol{\nu}_\rho; t)}{W_{-\rho}(\boldsymbol{X} | \boldsymbol{X} - \boldsymbol{\nu}_\rho)\ P(\boldsymbol{X}; t)} \tag{8}$$

We take units where the Boltzmann constant is equal to one.

B. The fluctuation theorem and the entropy production

In the stochastic description, the reactive process is a succession of random jumps occurring at successive times $0 < t_1 < t_2 < \cdots < t_n < t$ and forming a *history* or *path*:

$$\mathcal{X}(t) = \boldsymbol{X}_0 \xrightarrow{\rho_1} \boldsymbol{X}_1 \xrightarrow{\rho_2} \boldsymbol{X}_2 \xrightarrow{\rho_3} \cdots \xrightarrow{\rho_n} \boldsymbol{X}_n \tag{9}$$

During this path, the loss of detailed balance due to the openess of the nonequilibrium system can be investigated by considering the quantity:

$$Z(t) \equiv \ln \frac{W_{\rho_1}(\boldsymbol{X}_0 | \boldsymbol{X}_1)\ W_{\rho_2}(\boldsymbol{X}_1 | \boldsymbol{X}_2)\ \cdots\ W_{\rho_n}(\boldsymbol{X}_{n-1} | \boldsymbol{X}_n)}{W_{-\rho_1}(\boldsymbol{X}_1 | \boldsymbol{X}_0)\ W_{-\rho_2}(\boldsymbol{X}_2 | \boldsymbol{X}_1)\ \cdots\ W_{-\rho_n}(\boldsymbol{X}_n | \boldsymbol{X}_{n-1})} \tag{10}$$

This quantity can be rewritten in the form of the time integral:

$$Z(t) = \int_0^t \sum_k z_k(t') dt' \tag{11}$$

where

$$z_k(t) = \delta(t-t_k)\ \ln \frac{W_{\rho_k}(\boldsymbol{X}_{k-1}|\boldsymbol{X}_k)}{W_{-\rho_k}(\boldsymbol{X}_k|\boldsymbol{X}_{k-1})} \tag{12}$$

The generating function of the quantity (10) is defined by

$$Q(\eta) \equiv \lim_{t\to\infty} -\frac{1}{t} \ln\langle e^{-\eta Z(t)}\rangle \tag{13}$$

where $\langle\cdot\rangle$ denotes the statistical average with respect to the stationary probability distribution of the NESS. It can be obtained as the maximal eigenvalue, $\hat{L}_\eta G(\boldsymbol{X}) = -Q(\eta) G(\boldsymbol{X})$, of the operator

$$\hat{L}_\eta G(\boldsymbol{X}) \equiv \sum_{\rho=\pm1}^{\pm r} \left[W_\rho(\boldsymbol{X}-\boldsymbol{\nu}_\rho|\boldsymbol{X})^\eta\ W_{-\rho}(\boldsymbol{X}|\boldsymbol{X}-\boldsymbol{\nu}_\rho)^{1-\eta}\ G(\boldsymbol{X}-\boldsymbol{\nu}_\rho) - W_{-\rho}(\boldsymbol{X}|\boldsymbol{X}-\boldsymbol{\nu}_\rho)\ G(\boldsymbol{X})\right] \tag{14}$$

as shown by Lebowitz and Spohn.[13]

The generating function (13) obeys the fluctuation theorem

$$Q(\eta) = Q(1-\eta) \tag{15}$$

as a consequence of the microreversibility.[15] It identically vanishes $Q(\eta) = 0$ at thermodynamic equilibrium where the conditions of detailed balance are satisfied. A further property is that the mean entropy production (6) of the reaction in the NESS is given by

$$\left.\overline{\frac{d_{\rm i}S}{dt}}\right|_{\rm st} = \frac{dQ}{d\eta}(0) = \lim_{t\to\infty} \frac{1}{t}\langle Z(t)\rangle_{\rm st} \geq 0 \tag{16}$$

This fundamental result can be proved by transforming the quantity (10) by multiplying the numerator and the denominator by the same product of the stationary probabilities as

$$Z(t) = \ln \frac{P(\boldsymbol{X}_0)\ W_{\rho_1}(\boldsymbol{X}_0|\boldsymbol{X}_1)\ P(\boldsymbol{X}_1)\ W_{\rho_2}(\boldsymbol{X}_1|\boldsymbol{X}_2)\ \cdots\ P(\boldsymbol{X}_{n-1})\ W_{\rho_n}(\boldsymbol{X}_{n-1}|\boldsymbol{X}_n)}{P(\boldsymbol{X}_1)\ W_{-\rho_1}(\boldsymbol{X}_1|\boldsymbol{X}_0)\ P(\boldsymbol{X}_2)\ W_{-\rho_2}(\boldsymbol{X}_2|\boldsymbol{X}_1)\ \cdots\ P(\boldsymbol{X}_n)\ W_{-\rho_n}(\boldsymbol{X}_n|\boldsymbol{X}_{n-1})} - \ln\frac{P(\boldsymbol{X}_0)}{P(\boldsymbol{X}_n)} \tag{17}$$

where $P(\boldsymbol{X}) = P_{\rm st}(\boldsymbol{X})$ denotes the probability distribution of the stationary state. Therefore, we find that the quantity (10) is the sum of the affinities of all the reactive events occurring in the interval $[0,t]$

$$Z(t) = \sum_{k=1}^{n} A_{\rho_k}(\boldsymbol{X}_k) - \ln\frac{P(\boldsymbol{X}_0)}{P(\boldsymbol{X}_n)} \tag{18}$$

with the mesoscopic affinities

$$A_{\rho_k}(\boldsymbol{X}_k) = \ln\frac{P(\boldsymbol{X}_{k-1})W_{\rho_k}(\boldsymbol{X}_{k-1}|\boldsymbol{X}_k)}{P(\boldsymbol{X}_k)W_{-\rho_k}(\boldsymbol{X}_k|\boldsymbol{X}_{k-1})} \tag{19}$$

Since the reactive events of the reaction ρ occur with a frequency given by the reaction rate (7) in the stationary state, we find that

$$\langle Z(t)\rangle \simeq t\sum_{\rho=1}^{r}\sum_{\boldsymbol{X}} J_\rho(\boldsymbol{X})A_\rho(\boldsymbol{X})\Big|_{\rm st} = t\left.\overline{\frac{d_{\rm i}S}{dt}}\right|_{\rm st} \tag{20}$$

Hence the relationship (16) between the quantity $Z(t)$, the derivative of its generating function $Q(\eta)$, and the mean entropy production.

III. THE FLUCTUATION THEOREM IN TERMS OF THE MACROSCOPIC AFFINITIES

The Onsager reciprocity relations concern the macroscopic fluxes between the chemiostats. These fluxes are induced by the differences between the chemical potentials or, equivalently, by the corresponding macroscopic affinities. To derive the Onsager reciprocity relations, we thus have to identify the macroscopic affinities and fluxes instead of the mesoscopic affinities (8) and fluxes (7). Indeed, these latter are associated with each mesoscopic internal state $\boldsymbol{X}$ and may differ from the macroscopic ones. For the purpose of identifying the macroscopic affinities in the stochastic description,we use Schnakenberg's network theory for master equation systems.[7]

A. Graph analysis and the macroscopic affinities

For each system governed by such an equation, a graph G is associated in which each state $\boldsymbol{X}$ constitutes a vertex while the edges represent the transitions allowed by the reactions $\rho = 1, 2, ..., r$ between two states $\boldsymbol{X}$ and $\boldsymbol{X}' = \boldsymbol{X} + \boldsymbol{\nu}_\rho$. Accordingly, two states can be connected by several edges if several reactions allow transitions between them. The macroscopic affinities are incorporated in the transition rates $W_\rho(\boldsymbol{X}|\boldsymbol{X}')$ of reactions involving the species $\{\mathrm{A}^i\}_{i=1}^a$ of the chemiostats. The relation between the macroscopic affinities and the transition rates is made by the following observation by Schnakenberg.[7] The ratio of the products of the transition rates along the two possible directions of a single cycle $\vec{C}_l$ between two connected states is independent of the current numbers of molecules and only depends on the chemical potentials of the chemiostats. Indeed, according to Eq. (5), we observe that the ratio

$$\prod_{\rho\in\vec{C}_l} \frac{W_\rho(\boldsymbol{X}|\boldsymbol{X}+\boldsymbol{\nu}_\rho)}{W_{-\rho}(\boldsymbol{X}+\boldsymbol{\nu}_\rho|\boldsymbol{X})} = \prod_{\rho\in\vec{C}_l} \frac{k_\rho \prod_{i=1}^a [\mathrm{A}^i]^{\nu^i_{<\rho}}}{k_{-\rho} \prod_{i=1}^a [\mathrm{A}^i]^{\nu^i_{>\rho}}} = e^{\frac{\Delta\mu(\vec{C}_l)}{T}} = e^{\mathcal{A}(\vec{C}_l)} \tag{21}$$

only depends on the difference of chemical potentials

$$\Delta\mu(\vec{C}_l) = \sum_{i=1}^a \nu^i(\vec{C}_l)\, \mu_{\mathrm{A}^i} \tag{22}$$

with the stoichiometric coefficients

$$\nu^i(\vec{C}_l) = \sum_{\rho\in\vec{C}_l} \left(\nu^i_{>\rho} - \nu^i_{<\rho}\right) \tag{23}$$

of the species A^i of the chemiostats in the overall reaction corresponding to the cycle $\vec{C}_l$:

$$\sum_{\rho\in\vec{C}_l}\sum_{i=1}^a \nu^i_{<\rho}\, \mathrm{A}^i \rightleftharpoons \sum_{\rho\in\vec{C}_l}\sum_{i=1}^a \nu^i_{>\rho}\, \mathrm{A}^i \tag{24}$$

In Eq. (21), T denotes the temperature. The chemical potential (22) defines an affinity $\mathcal{A}(\vec{C}_l)$ associated with the cycle $\vec{C}_l$ and which only depends on the properties of the chemiostats.

Moreover, since the reaction network takes place between a finite number a of chemiostats, there is a finite number $a-1$ of independent overall reactions (24) Therefore, the differences of chemical potentials $\Delta\mu(\vec{C}_l)$ associated with the infinitely many cycles $\vec{C}_l$ of the graph G only take $a-1$ possible values:

$$\Delta\mu(\vec{C}_l) = \Delta\mu_\gamma \tag{25}$$

with $\gamma = 1, 2, ..., a-1$. These differences of chemical potentials are the Gibbs free energy differences associated with the $a-1$ independent overall reactions between the chemiostats.[19] The macroscopic affinities can thus be defined as

$$\mathcal{A}_\gamma = \frac{\Delta\mu_\gamma}{T} \qquad \text{with} \quad \gamma = 1, 2, ..., a-1 \tag{26}$$

The macroscopic affinities are dimensionless in consistency with the definition (8) of the mesoscopic affinities. We here define affinities as thermodynamic forces following the terminology used by Callen,[20] which explains the extra factor T^{-1} with respect to the original definition.[19]

The property (21) is verified for numerous systems[21] and the work of Schnakenberg[7] was to justify this conclusion. Schnakenberg has provided a method to determine all the cycles $\vec{C}_l$ in a graph G. The method is based on the definition of a maximal tree $T(G)$ of the graph G, which should satisfy the following properties:

(1) $T(G)$ is a covering subgraph of G, i.e., $T(G)$ contains all the vertices of G and all the edges of $T(G)$ are edges of G;

(2) $T(G)$ is connected;

(3) $T(G)$ contains no circuit (i.e., no cyclic sequence of edges).

In general a given graph G has several maximal tree $T(G)$.

The edges s_l of G which do not belong to $T(G)$ are called the chords of $T(G)$. If we add to $T(G)$ one of its chords s_l, the resulting subgraph $T(G) + s_l$ contains exactly one circuit, C_l, which is obtained from $T(G) + s_l$ by removing all the edges which are not part of the circuit. The set of circuits $\{C_1, C_2, ..., C_l, ...\}$ is called a fundamental set. An arbitrary orientation can be assigned to each circuit C_l to define a cycle $\vec{C}_l$. A maximal tree $T(G)$ together with its associated fundamental set of cycles $\{\vec{C}_1, \vec{C}_2, ..., \vec{C}_l, ...\}$ provides a decomposition of the graph G. We notice that the maximal tree $T(G)$ can be chosen arbitrarily because each cycle $\vec{C}_l$ can be redefined by linear combinations of the cycles of the fundamental set.

A further result is that, in a NESS, the mean entropy production can be defined in terms of the fluxes and affinities on the cycles $\vec{C}_l$ of a fundamental set:

$$\overline{\frac{d_{\rm i}S}{dt}}\bigg|_{\rm st} = \sum_l J(\vec{C}_l)\mathcal{A}(\vec{C}_l) \tag{27}$$

as a consequence of Kirchhoff current law according to which the sum of all currents converging to a vertex must be zero for each vertex in a steady state.[7] This means that, on average, only the cycles contributes to the mean entropy production because each edge either belongs to a cycle either the average current traversing it is zero by Kirchhoff current law. Defining the macroscopic flux

$$\mathcal{J}_\gamma \equiv \sum_{\vec{C}_l \in \gamma} J(\vec{C}_l) \tag{28}$$

associated with the overall reaction γ, the mean entropy production (27) is thus given by

$$\overline{\frac{d_{\rm i}S}{dt}}\bigg|_{\rm st} = \sum_\gamma \mathcal{J}_\gamma \mathcal{A}_\gamma \tag{29}$$

B. The generating function of the macrofluxes and its fluctuation theorem

Thanks to these results, a given history or path (9) of the stochastic process can be decomposed into subsets of reactive events taking place on the cycles $\vec{C}_l$. We can thus separate the quantity (10) into a sum of terms associated with the different cycles $\vec{C}_l$ of a fundamental set constructed from an arbitrary maximal tree $T(G)$:

$$Z(t) = \sum_l \int_0^t z_l(t')dt' + \int_0^t z_e(t')dt' \tag{30}$$

with

$$z_l(t) = \sum_{\rho_k \in \vec{C}_l} z_k(t) \tag{31}$$

There is an excess contribution $z_e(t)$ because a history or path is not necessarily composed of basic cycles. We notice that this excess contribution becomes negligible on average in a stationary state in the limit $t \to \infty$ because of the result (27). We can further regroup all the contributions from the cycles corresponding to the same overall reaction γ between the chemiostats as:

$$Z(t) = \sum_\gamma \int_0^t z_\gamma(t')dt' + \int_0^t z_e(t')dt' \tag{32}$$

with

$$z_\gamma(t) = \sum_{\vec{C}_l \in \gamma} z_l(t) \tag{33}$$

We now introduce the parameters $\{\eta_\gamma\}_{\gamma=1}^{a-1}$ associated with the overall reactions γ and a parameter η_e associated with the excess contribution in order to define the generalized quantity

$$\tilde{Z}(t) \equiv \sum_\gamma \eta_\gamma \int_0^t z_\gamma(t')dt' + \eta_e \int_0^t z_e(t')dt' \tag{34}$$

The quantities $z_\gamma(t)$ associated with the overall reactions γ can be expressed in terms of the macroscopic affinities $\mathcal{A}_\gamma$ multiplied by the instantaneous fluxes of the overall reactions:

$$z_\gamma(t) = \mathcal{A}_\gamma j_\gamma(t) \tag{35}$$

These instantaneous fluxes are given by a sum of deltas at each random time $\{t_{\gamma,m}\}$ when a cycle $\vec{C}_l \in \gamma$ is closed by the path. The average over time of the instantaneous fluxes gives the macroscopic fluxes

$$\mathcal{J}_\gamma = \lim_{t\to\infty} \frac{1}{t} \int_0^t j_\gamma(t')dt' \tag{36}$$

in the NESS. Since the affinities of the basic cycles are independent of the instantaneous state $\boldsymbol{X}(t)$ of the system according to Eq. (21) and thus time independent, they can exit the time integrals and the quantity (34) can be rewritten as

$$\tilde{Z}(t) = \sum_\gamma \eta_\gamma \mathcal{A}_\gamma \int_0^t j_\gamma(t')dt' + \eta_e \int_0^t z_e(t')dt' \tag{37}$$

which is the crucial step in our demonstration.

The generating function of this quantity is now defined as

$$Q(\{\eta_\gamma\}; \{\mathcal{A}_\gamma\}) \equiv \lim_{t\to\infty} -\frac{1}{t} \ln\langle e^{-\tilde{Z}(t)}\rangle \tag{38}$$

where the statistical average $\langle\cdot\rangle$ is taken with respect to the probability distribution $P_{\rm st}$ of the NESS. By the same argument as the one given elsewhere,[15] the generating function (38) obeys the fluctuation theorem

$$Q(\{\eta_\gamma\}; \{\mathcal{A}_\gamma\}) = Q(\{1-\eta_\gamma\}; \{\mathcal{A}_\gamma\}) \tag{39}$$

According to Kirchhoff current law in the NESS, we have the property that

$$\frac{\partial Q}{\partial \eta_e} = 0 \tag{40}$$

for any value of the driving force, which means that the parameter η_e does not appear in the generating function (38). Equation (38) can thus be rewritten in the form

$$Q(\{\eta_\gamma\}; \{\mathcal{A}_\gamma\}) = \lim_{t\to\infty} -\frac{1}{t} \ln\langle e^{-\sum_\gamma \eta_\gamma \mathcal{A}_\gamma \int_0^t j_\gamma(t')dt'}\rangle \tag{41}$$

If we define

$$\lambda_\gamma \equiv \mathcal{A}_\gamma \eta_\gamma \tag{42}$$

the generating function (41) becomes

$$q(\{\lambda_\gamma\}; \{\mathcal{A}_\gamma\}) \equiv Q(\{\lambda_\gamma/\mathcal{A}_\gamma\}; \{\mathcal{A}_\gamma\}) = \lim_{t\to\infty} -\frac{1}{t} \ln\langle e^{-\sum_\gamma \lambda_\gamma \int_0^t j_\gamma(t')dt'}\rangle \tag{43}$$

which shows that this function generates the statistical moments of the fluxes (36). In the NESS, the mean flux or rate of the overall reaction γ is given by

$$\mathcal{J}_\gamma = \frac{\partial q}{\partial \lambda_\gamma}\Big|_{\lambda_\gamma=0} \tag{44}$$

which justifies to call the function (43) the generating function of the macroscopic fluxes. Equation (44) is a consequence of

$$\frac{\partial q}{\partial \lambda_\gamma}\Big|_{\lambda_\gamma=0} = \lim_{t\to\infty} \frac{\langle \int_0^t j_\gamma(t')dt' e^{-\tilde{Z}(t)}\rangle}{t\,\langle e^{-\tilde{Z}(t)}\rangle}\Big|_{\lambda_\gamma=0} = \mathcal{J}_\gamma \tag{45}$$

and of Eq. (36).

Finally, the generating function (43) obeys the fluctuation theorem

$$q(\{\lambda_\gamma\}; \{\mathcal{A}_\gamma\}) = q(\{\mathcal{A}_\gamma - \lambda_\gamma\}; \{\mathcal{A}_\gamma\}) \tag{46}$$

as a consequence of Eq. (39).

IV. RECIPROCITY RELATIONS

In this section, we prove reciprocity relations from the fluctuation theorem (46) and the macroscopic fluxes (44) in the NESS. In general, the macroscopic fluxes can be expanded as a Taylor series of the macroscopic affinities

$$\mathcal{J}_\alpha = \sum_\beta L_{\alpha\beta}\mathcal{A}_\beta + \frac{1}{2}\sum_{\beta,\gamma} M_{\alpha\beta\gamma}\mathcal{A}_\beta\mathcal{A}_\gamma + \frac{1}{6}\sum_{\beta,\gamma,\delta} N_{\alpha\beta\gamma\delta}\mathcal{A}_\beta\mathcal{A}_\gamma\mathcal{A}_\delta + \cdots \tag{47}$$

The linear response of the fluxes $\mathcal{J}_\alpha$ to a small perturbation in the macroscopic affinities $\mathcal{A}_\beta$ is characterized by the Onsager coefficients $L_{\alpha\beta}$, and the nonlinear response by the higher-order coefficients $M_{\alpha\beta\gamma}$, $N_{\alpha\beta\gamma\delta}$,...

A. Onsager reciprocity relations

The Onsager coefficients are defined close to the equilibrium in terms of the generating function (43) by

$$L_{\alpha\beta} = \frac{\partial \mathcal{J}_\alpha}{\partial \mathcal{A}_\beta}\bigg|_{\mathcal{A}_\gamma=0} = \frac{\partial^2 q}{\partial\lambda_\alpha\partial\mathcal{A}_\beta}(0;0) \tag{48}$$

If we differentiate the expression (46) of the fluctuation theorem with respect to λ_α and $\mathcal{A}_\beta$ we find that

$$\frac{\partial^2 q}{\partial\lambda_\alpha\partial\mathcal{A}_\beta}(\{\lambda_\gamma\};\{\mathcal{A}_\gamma\}) = -\frac{\partial^2 q}{\partial\lambda_\alpha\partial\lambda_\beta}(\{\mathcal{A}_\gamma-\lambda_\gamma\};\{\mathcal{A}_\gamma\}) - \frac{\partial^2 q}{\partial\lambda_\alpha\partial\mathcal{A}_\beta}(\{\mathcal{A}_\gamma-\lambda_\gamma\};\{\mathcal{A}_\gamma\}) \tag{49}$$

Setting $\{\lambda_\gamma=0\}$ and $\{\mathcal{A}_\gamma=0\}$, we obtain the relation

$$2\frac{\partial^2 q}{\partial\lambda_\alpha\partial\mathcal{A}_\beta}(0;0) = -\frac{\partial^2 q}{\partial\lambda_\alpha\partial\lambda_\beta}(0;0) \tag{50}$$

or

$$L_{\alpha\beta} = -\frac{1}{2}\frac{\partial^2 q}{\partial\lambda_\alpha\partial\lambda_\beta}(0;0) \tag{51}$$

Hence the Onsager reciprocity relations

$$L_{\alpha\beta} = L_{\beta\alpha} \tag{52}$$

B. Yamamoto-Zwanzig formulas

If we differentiate twice the generating function (43) according to Eq. (51), we obtain the Onsager coefficients in terms of the time correlation functions of the instantaneous fluxes

$$L_{\alpha\beta} = \frac{1}{2}\int_{-\infty}^{+\infty}\langle[j_\alpha(t)-\langle j_\alpha\rangle]\,[j_\beta(0)-\langle j_\beta\rangle]\rangle_{\text{eq}}\,dt \tag{53}$$

where the statistical average is carried out with respect to the state of thermodynamic equilibrium. The formulas (53) give the reaction constants close to equilibrium and are known as the Yamamoto-Zwanzig formulas.[17,18]

C. Third-order reciprocity relations

If we differentiate the identity (49) with respect to $\mathcal{A}_\gamma$ and set $\{\lambda_\gamma=0\}$ and $\{\mathcal{A}_\gamma=0\}$, we obtain the third-order response coefficients as

$$M_{\alpha\beta\gamma} = -\frac{1}{2}\frac{\partial^3 q}{\partial\lambda_\alpha\partial\lambda_\beta\partial\lambda_\gamma}(0;0) - \frac{1}{2}\frac{\partial^3 q}{\partial\lambda_\alpha\partial\lambda_\beta\partial\mathcal{A}_\gamma}(0;0) - \frac{1}{2}\frac{\partial^3 q}{\partial\lambda_\alpha\partial\lambda_\gamma\partial\mathcal{A}_\beta}(0;0) \tag{54}$$

If we define the sensitivity of the integrals of the time correlation functions of the fluxes with respect to the macroscopic affinities as

$$R_{\alpha\beta,\gamma} = \frac{\partial}{\partial \mathcal{A}_\gamma} \int_{-\infty}^{+\infty} \langle [j_\alpha(t) - \langle j_\alpha \rangle]\, [j_\beta(0) - \langle j_\beta \rangle] \rangle_{\rm st}\, dt \Big\vert_{\{\mathcal{A}_\delta = 0\}} = -\frac{\partial^3 q}{\partial\lambda_\alpha \partial\lambda_\beta \partial\mathcal{A}_\gamma}(0;0) \tag{55}$$

we find the third-order reciprocity relation that the tensor

$$2M_{\alpha\beta\gamma} - R_{\alpha\beta,\gamma} - R_{\alpha\gamma,\beta} \tag{56}$$

must be totally symmetric.

D. Fourth-order reciprocity relations

A similar reasoning can be carried out for the fourth-order response coefficients, which are given by

$$N_{\alpha\beta\gamma\delta} = -\frac{1}{2}\frac{\partial^4 q}{\partial\lambda_\alpha \partial\lambda_\beta \partial\lambda_\gamma \partial\lambda_\delta}(0;0) - \frac{1}{2}\left(S_{\alpha\beta\gamma,\delta} + S_{\alpha\beta\delta,\gamma} + S_{\alpha\gamma\delta,\beta} + T_{\alpha\beta,\gamma\delta} + T_{\alpha\gamma,\beta\delta} + T_{\alpha\delta,\beta\gamma}\right) \tag{57}$$

with

$$S_{\alpha\beta\gamma,\delta} = \frac{\partial^4 q}{\partial\lambda_\alpha \partial\lambda_\beta \partial\lambda_\gamma \partial\mathcal{A}_\delta}(0;0) \tag{58}$$

and

$$T_{\alpha\beta,\gamma\delta} = \frac{\partial^4 q}{\partial\lambda_\alpha \partial\lambda_\beta \partial\mathcal{A}_\gamma \partial\mathcal{A}_\delta}(0;0) \tag{59}$$

We thus obtain the fourth-order reciprocity relation that the tensor

$$2N_{\alpha\beta\gamma\delta} + S_{\alpha\beta\gamma,\delta} + S_{\alpha\beta\delta,\gamma} + S_{\alpha\gamma\delta,\beta} + T_{\alpha\beta,\gamma\delta} + T_{\alpha\gamma,\beta\delta} + T_{\alpha\delta,\beta\gamma} \tag{60}$$

must be totally symmetric.

V. APPLICATION TO SIMPLE REACTION NETWORKS

In this section, the previous results are applied to a simple reaction network which involves a single intermediate species X transforming into several possible chemiostatic species.

A. Reactions between several chemiostats

We consider the following reaction network:

$$\mathrm{A}^1 \underset{k_{-1}}{\overset{k_{+1}}{\rightleftharpoons}} \mathrm{X}\,, \quad \mathrm{A}^2 \underset{k_{-2}}{\overset{k_{+2}}{\rightleftharpoons}} \mathrm{X}\,, \quad \cdots \mathrm{A}^a \underset{k_{-a}}{\overset{k_{+a}}{\rightleftharpoons}} \mathrm{X} \tag{61}$$

The stationary state of the master equation (4) is the Poisson distribution:

$$P_{\rm st}(X) = e^{-\langle X \rangle_{\rm st}}\, \frac{\langle X \rangle_{\rm st}^X}{X!} \tag{62}$$

with the mean value

$$\langle X \rangle_{\rm st} = \frac{\sum_{i=1}^a k_{+i} \langle A^i \rangle}{\sum_{i=1}^a k_{-i}} \tag{63}$$

The operator (14) at the basis of the fluctuation theorem (15) is here given by

$$\begin{aligned}\hat{L}_\eta G(X) &= \left\{\sum_{i=1}^{a}(k_{+i}\langle A^i\rangle)^\eta \;(k_{-i}X)^{1-\eta}\right\} G(X-1)\\ &+\left\{\sum_{i=1}^{a}(k_{+i}\langle A^i\rangle)^{1-\eta} \;[k_{-i}(X+1)]^\eta\right\} G(X+1)\\ &-\left\{\sum_{i=1}^{a}\left[k_{+i}\langle A^i\rangle + k_{-i}X\right]\right\} G(X) \qquad (64)\end{aligned}$$

The solution of the eigenvalue problem $\hat{L}_\eta G(X) = -Q(\eta)G(X)$ has the form

$$G(X) = C\,\frac{\alpha(\eta)^X}{(X!)^\eta} \qquad (65)$$

with

$$\alpha(\eta) = \frac{\sum_{i=1}^{a}(k_{+i}\langle A^i\rangle)^\eta \;(k_{-i})^{1-\eta}}{\sum_{i=1}^{a} k_{-i}} \qquad (66)$$

We notice that the solution (65) consistently reduces to the stationary probability distribution (62) for $\eta = 1$ because $\langle X\rangle_{\rm st} = \alpha(1)$.

The maximal eigenvalue (13) of the operator (64) is therefore

$$Q(\eta) = \sum_{i=1}^{a} k_{+i}\langle A^i\rangle - \left(\sum_{i=1}^{a} k_{-i}\right)\;\alpha(\eta)\;\alpha(1-\eta) \qquad (67)$$

This function clearly satisfies the symmetry $Q(\eta) = Q(1-\eta)$ of the fluctuation theorem (15). Moreover, $Q(\eta) = 0$ in the case of thermodynamic equilibrium where detailed balance implies that $k_{+i}\langle A^i\rangle/k_{-i} = \langle X\rangle_{\rm eq}$ holds independently of $i = 1, 2, ..., a$. The mean entropy production is given by

$$\overline{\frac{d_{\rm i}S}{dt}}\Big|_{\rm st} = \frac{dQ}{d\eta}(0) = \sum_{i=1}^{a}\left(k_{+i}\langle A^i\rangle - k_{-i}\langle X\rangle_{\rm st}\right)\ln\frac{k_{+i}\langle A^i\rangle}{k_{-i}\langle X\rangle_{\rm st}} \geq 0 \qquad (68)$$

which is exactly the same as the macroscopic entropy production in the steady state (63).

B. Reactions between two chemiostats

The simplest reaction network sustaining a nonequilibrium steady state in the family (61) is the case of an intermediate species X between $a = 2$ chemiostats:

$$\mathrm{A} \underset{k_{-1}}{\overset{k_{+1}}{\rightleftharpoons}} \mathrm{X} \underset{k_{+2}}{\overset{k_{-2}}{\rightleftharpoons}} \mathrm{B} \qquad (69)$$

There is here only one macroscopic affinity and one macroflux. The graph G of this reaction network is depicted in Fig. 1. Between the states X and $X+1$, there is one circuit and one cycle if the orientation is chosen as in Fig. 1. Therefore, the cycles $\vec{C}_X$ of the graph G are labeled by the state $X = l$.

The transition rates are

$$\begin{aligned}W_{+1}(X|X+1) &= k_{+1}\langle A\rangle\\ W_{-1}(X|X-1) &= k_{-1}X\\ W_{+2}(X|X+1) &= k_{+2}\langle B\rangle\\ W_{-2}(X|X-1) &= k_{-2}X \qquad (70)\end{aligned}$$

and the ratio of the products of the transition rates along the two possible directions of the cycle $\vec{C}_X$

$$\frac{W_{+1}(X|X+1)W_{-2}(X+1|X)}{W_{-1}(X+1|X)W_{+2}(X|X+1)} = \frac{k_{+1}k_{-2}\langle A\rangle}{k_{-1}k_{+2}\langle B\rangle} = e^{\frac{\Delta\mu}{T}} = e^{\mathcal{A}} \qquad (71)$$

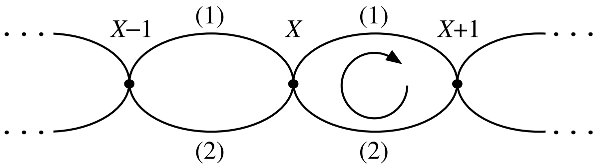

FIG. 1: Graph of the reaction network (69) with two reactions and two chemiostats.

is independent of the state X and define the single macroscopic affinity $\mathcal{A}$ of this reaction network in terms of the Gibbs free energy difference of the reaction $\Delta\mu = \mu_{\rm A} - \mu_{\rm B}$.

The generating function (13) of this reaction network is exactly given by Eq. (67) with (66) and it obeys the fluctuation theorem (15). The entropy production can be deduced from the generating function according to Eq. (68). Since we here have a single macroscopic affinity, the mean flux in a NESS is thus given by

$$\mathcal{J} = \frac{1}{\mathcal{A}}\frac{\partial Q}{\partial \eta}(0) = \frac{1}{\mathcal{A}}\overline{\frac{d_{\rm i}S}{dt}}\Big|_{\rm st} \tag{72}$$

according to Eq. (44). We thus obtain

$$\mathcal{J} = \frac{k_{+1}k_{-2}\langle A\rangle - k_{-1}k_{+2}\langle B\rangle}{k_{-1}+k_{-2}} \tag{73}$$

or, equivalently, in terms of the Gibbs free energy as

$$\mathcal{J} = \frac{k_{-1}k_{+2}\langle B\rangle}{k_{-1}+k_{-2}}\left(e^{\frac{\Delta\mu}{T}}-1\right) \tag{74}$$

The flux or current saturates at a constant negative value $-\mathcal{J}_0$ for $\Delta\mu \to -\infty$. This behavior is reminiscent of the electric current in a diode. The value $\mathcal{J}_0$ is also the Onsager coefficient close to equilibrium where the macroflux can be expanded in powers of the affinity as

$$\mathcal{J} = L\mathcal{A} + M\mathcal{A}^2 + N\mathcal{A}^3 + \cdots \tag{75}$$

with $L = \mathcal{J}_0$, $M = \mathcal{J}_0/2$, $N = \mathcal{J}_0/6$,... The Onsager coefficient is given by the Yamamoto-Zwanzig formula (53) as the integral of the time autocorrelation function of the instantaneous flux of the overall reaction between both chemiostats.

C. Reactions between three chemiostats

The simplest reaction network showing a nontrivial Onsager reciprocity relations in the family (61) is the case of an intermediate species X between $a = 3$ chemiostats:

$$\mathrm{A} \underset{k_{-1}}{\overset{k_{+1}}{\rightleftharpoons}} \mathrm{X}\,, \quad \mathrm{B} \underset{k_{-2}}{\overset{k_{+2}}{\rightleftharpoons}} \mathrm{X}\,, \quad \mathrm{C} \underset{k_{-3}}{\overset{k_{+3}}{\rightleftharpoons}} \mathrm{X} \tag{76}$$

In this case, there are two macroscopic affinities and fluxes. We choose the macrofluxes from the chemiostat of species C to either A or B. This reaction network is the chemical analogue of a transistor. The graph G of the reaction network (76) is depicted in Fig. 2. Between the states X and $X+1$, there are now two circuits and cycles as seen in Fig. 2. Here, the cycles $\vec{C}_{X,\gamma}$ of the graph G are labeled not only by the state X but also by the overall reaction $\gamma = 1, 2$.

The ratio of the products of the transition rates along the two possible directions of the cycle $\vec{C}_{X,1}$ is given by

$$\frac{W_{-1}(X+1|X)W_{+3}(X|X+1)}{W_{+1}(X|X+1)W_{-3}(X+1|X)} = \frac{k_{-1}k_{+3}\langle C\rangle}{k_{+1}k_{-3}\langle A\rangle} = e^{\frac{\mu_{\rm C}-\mu_{\rm A}}{T}} = e^{\mathcal{A}_1} \tag{77}$$

and, for the cycle $\vec{C}_{X,2}$ by

$$\frac{W_{-2}(X+1|X)W_{+3}(X|X+1)}{W_{+2}(X|X+1)W_{-3}(X+1|X)} = \frac{k_{-2}k_{+3}\langle C\rangle}{k_{+2}k_{-3}\langle B\rangle} = e^{\frac{\mu_{\rm C}-\mu_{\rm B}}{T}} = e^{\mathcal{A}_2} \tag{78}$$

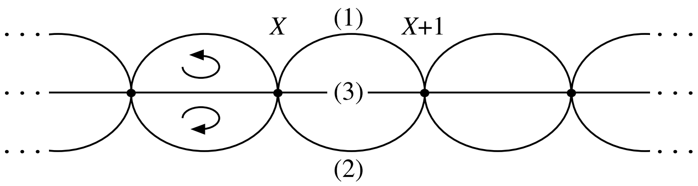

FIG. 2: Graph of the reaction network (76) with three reactions and three chemiostats.

Both ratios (77) and (78) are independent of the state X as expected.

From Eq. (68), the mean entropy production in a stationary state is given in terms of the macroscopic fluxes and affinities as

$$\overline{\frac{d_{\rm i}S}{dt}}\Big|_{\rm st} = \underbrace{\mathcal{J}_{\rm C\to A}}_{\mathcal{J}_1} \underbrace{\frac{\mu_{\rm C}-\mu_{\rm A}}{T}}_{\mathcal{A}_1} + \underbrace{\mathcal{J}_{\rm C\to B}}_{\mathcal{J}_2} \underbrace{\frac{\mu_{\rm C}-\mu_{\rm B}}{T}}_{\mathcal{A}_2} \tag{79}$$

where the macrofluxes are

$$\mathcal{J}_1 = \frac{k_{-1}k_{+3}\langle C\rangle}{k_{-3}(k_{-1}+k_{-2}+k_{-3})}\left[k_{-3}-(k_{-2}+k_{-3})e^{-\mathcal{A}_1}+k_{-2}e^{-\mathcal{A}_2}\right] \tag{80}$$

$$\mathcal{J}_2 = \frac{k_{-2}k_{+3}\langle C\rangle}{k_{-3}(k_{-1}+k_{-2}+k_{-3})}\left[k_{-3}+k_{-1}e^{-\mathcal{A}_1}-(k_{-1}+k_{-3})e^{-\mathcal{A}_2}\right] \tag{81}$$

Expanding in powers of the affinities, we obtain the Onsager coefficients

$$L_{11} = \frac{k_{-1}k_{+3}(k_{-2}+k_{-3})\langle C\rangle}{k_{-3}(k_{-1}+k_{-2}+k_{-3})}\ , \quad L_{22} = \frac{k_{-2}k_{+3}(k_{-1}+k_{-3})\langle C\rangle}{k_{-3}(k_{-1}+k_{-2}+k_{-3})}\ , \quad L_{12}=L_{21}=-\frac{k_{-1}k_{-2}k_{+3}\langle C\rangle}{k_{-3}(k_{-1}+k_{-2}+k_{-3})} \tag{82}$$

which satisfy the Onsager reciprocity relation. The higher-order response coefficients can be calculated as well.

VI. CONCLUSIONS

In this paper, we have derived the Onsager reciprocity relations[16] as well as higher-order reciprocity relations from a generalized fluctuation theorem. Our derivation is based on Schnakenberg's graph analysis[7] which allows one to identify the macroscopic affinities and fluxes of the independent overall reactions between the chemiostats. This observation leads to the definition of the generating function of the macrofluxes and to the associated fluctuation theorem. This fluctuation theorem is valid arbitrarily far from the thermodynamic equilibrium. For this reason, our method allows us to obtain not only the Onsager reciprocity relations but also higher-order reciprocity relations which deal with nonequilibrium properties further away from the thermodynamic equilibrium than the Onsager second-order reciprocity relations do.

Furthermore, our method based on the fluctuation theorem also provides expressions for the Onsager linear response coefficients and the higher-order response coefficients in terms of the time correlation functions of the microscopic fluxes. These expressions are known as the Yamamoto-Zwanzig formulas for the reaction constants.[17,18] (For the transport coefficients, they are called the Green-Kubo formulas.) Similar formulas can be obtained for the higher-order response coefficients from the generating function of the macrofluxes obtained in the present paper. These considerations have been applied to simple reaction networks which can be solved analytically. The present results can be extended to nonequilibrium processes other than reactions, under the condition that the process is described by a master equation similar to Eq. (4) with macroscopic affinities given by relations such as Eqs. (21), as will be reported in a forthcoming publication.[22]

In conclusion, it is possible to formulate the response theory of nonequilibrium reactions from the fluctuation theorem which expresses a symmetry of the generating function of the macrofluxes. This symmetry, which is a consequence of the microreversibility, holds not only close to the thermodynamic equilibrium but also in far-from-equilibrium regimes.

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