

Irreversible thermodynamics in multiscale stochastic dynamical systems

Moisés Santillán*

*Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Unidad Monterrey,
Parque de Investigación e Innovación Tecnológica, 66600 Apodaca, Nuevo León, Mexico*

Hong Qian†

*Department of Applied Mathematics, University of Washington, Seattle, Washington 98195, USA
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This work extends the results of a recently developed theory of a rather complete thermodynamic formalism for discrete-state, continuous-time Markov processes with and without detailed balance. We investigate whether and in what way the thermodynamic structure is invariant in a multiscale stochastic system, that is, whether the relations between thermodynamic functions of state and process variables remain unchanged when the system is viewed at different time scales and resolutions. Our results show that the dynamics on a fast time scale contribute an entropic term to the internal energy function $u_S(x)$ for the slow dynamics. Based on the conditional free energy $u_S(x)$, we can then treat the slow dynamics as if the fast dynamics is nonexistent. Furthermore, we show that the free energy, which characterizes the spontaneous organization in a system without detailed balance, is invariant with or without the fast dynamics: The fast dynamics is assumed to reach stationarity instantaneously on the slow time scale; it has no effect on the system's free energy. The same cannot be said for the entropy and the internal energy, both of which contain the same contribution from the fast dynamics. We also investigate the consequences of time-scale separation in connection to the concepts of quasi-stationarity and steady adiabaticity introduced in the phenomenological steady-state thermodynamics.

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I. INTRODUCTION

Stochastic dynamics that can be described by a Markov process embody a rich thermodynamic structure. Recently, inspired by the discovery of the fluctuation theorem [1–7], there has been a growing interest in concepts such as the Gibbs entropy and the free energy associated with Markov processes [8–13]. The free energy of a stochastic dynamics is intimately related to the relative entropy, which is of great importance in the general theory of dynamical systems [14–16].

In the very recent paper [10], a rather complete thermodynamics was presented for discrete-state, continuous-time stochastic Markov systems with or without detailed balance. The thermodynamics is characterized by (i) a balance equation for the Gibbs entropy that includes a non-negative entropy production rate σ , (ii) a decreasing free energy $dF/dt \leq 0$, and (iii) a decomposition of σ into $-dF/dt$ and the housekeeping heat Q_{hk} , which are both non-negative.

Assertion (iii) indicates that the total irreversibility has two distinct origins: the spontaneous self-organization into a nonequilibrium steady state and the continuous environmental drive that keeps the system away from its equilibrium. These terms respectively correspond to Boltzmann's thesis and Prigogine's thesis [10]. For systems in a nondriving environment, detailed balance holds. Then $Q_{hk} = 0$, $\sigma = -dF/dt$, and the system relaxes to an equilibrium steady state with $\sigma = 0$. The mathematical theory is an abstraction from an earlier phenomenological study of nonequilibrium steady-state thermodynamics by Oono and Paniconi [17].

For almost all applications of stochastic dynamical theories in physics, chemistry, and biology there will be multiple time

scales, often with a significant separation. Recall that in the Gibbs formalism for equilibrium statistical mechanics the conditional free energy plays a central role in applications: One usually does not work with the pure mechanical energy of a system; rather one works with a conditional free energy from coarse graining and develops a partition function thereafter. This paper focuses on the important issue of whether the thermodynamic structure discussed herein is invariant in a multiscale stochastic dynamical system or, in other words, whether the relation between state and process variables remains unchanged when the system is viewed at different time scales.

We show that the dynamics on a fast time scale contributes an entropic term to the internal energy function $u_S(x)$ for the slow dynamics. The term $u_S(x)$ should be understood as the conditional free energy. Based on $u_S(x)$, one can then treat the dynamics on the slow time scale as if the fast dynamics is nonexistent. Furthermore, we show that the free energy (which characterizes the spontaneous organization in a system) is invariant with or without the fast dynamics. Since the dynamics on the fast time scale reaches its stationarity instantaneously on the slow time scale, it has no effect on the system's free energy. The same cannot be said for the entropy and the internal energy, both of which contain the same entropic contribution from the fast dynamics. Since free energy equals internal energy minus entropy, there is a compensation. Finally, we study how the time-scale separation affects the concepts of stationary and steady-adiabatic processes introduced by Oono and Paniconi [17].

II. ADIABATIC APPROXIMATION

In this section we follow the idea of a quasi-steady-state approximation, or singular perturbation [18–21], in a

*msantillan@cinvestav.mx

†qian@amath.washington.edu

stochastic dynamics to perform an adiabatic treatment in a generic Markovian stochastic process where separation of time scales is possible. We find that the concept of conditional probability provides a natural language in which to perform this multiple-time-scale analysis.

Consider a Markov system whose state can be represented by a dual vector (x, y) , where variables x and y take discrete values. Let $p(x, y)$ be the probability of state (x, y) and $v(x, y; x', y')$ be the transition probability per unit time from state (x, y) to state (x', y') . We further assume that $v(x, y; x', y') \gg v(x'', y''; x''', y''')$ for all $y \neq y', x'' \neq x'''$, and $(x'', y'') \neq (x''', y''')$, that is, for any given x , the transition $y \rightarrow y'$ is much faster than all transitions involving $x'' \rightarrow x'''$. If the sets of all possible values attained by x and y are finite, the master equation (or forward Kolmogorov equation) for this system can be written as

$$\begin{aligned} \frac{dp(x, y)}{dt} = & \sum_{\forall y'} p(x, y') v(x, y'; x, y) - p(x, y) v(x, y; x, y) \\ & + \sum_{x' \neq x} \sum_{\forall y'} p(x', y') v(x', y'; x, y) \\ & - p(x, y) v(x, y; x', y'). \end{aligned} \quad (1)$$

By adding the above equation over all values of y and taking into consideration that $p(x) = \sum_y p(x, y)$ we obtain

$$\begin{aligned} \frac{dp(x)}{dt} = & \sum_{\forall y, y'} p(x, y') v(x, y'; x, y) - p(x, y) v(x, y; x, y') \\ & + \sum_{x' \neq x} \sum_{\forall y, y'} p(x', y') v(x', y'; x, y) - p(x, y) v(x, y; x', y'). \end{aligned}$$

Note that the first summand on the right-hand side of this equation equals zero because each term in it is added and subtracted once. After some algebra this equation can be rewritten as

$$\frac{dp(x)}{dt} = \sum_{x'} p(x') \Upsilon(x'; x) - p(x) \Upsilon(x; x'), \quad (2)$$

with

$$\Upsilon(x; x') = \sum_{y, y'} p(y|x) v(x, y; x', y'). \quad (3)$$

In Eq. (3) $p(y|x)$ is the conditional probability defined as

$$p(y|x) = p(x, y) / p(x). \quad (4)$$

In order to find the equation governing the dynamics of $p(y|x)$ we differentiate Eq. (4) to obtain the following expression after some algebraic steps:

$$p(x) \frac{dp(y|x)}{dt} = \frac{dp(x, y)}{dt} - p(y|x) \frac{dp(x)}{dt}.$$

Further substitution of Eqs. (1) and (2) into this equation leads to

$$\frac{dp(y|x)}{dt} = \sum_{y'} p(y'|x) v(x, y'; x, y) - p(y|x) v(x, y; x, y'), \quad (5)$$

where we have neglected all terms multiplied by either $v(x, y; x', y')$ [$x \neq x'$ and $(x, y) \neq (x', y')$] or $\Upsilon(x; x')$, based on the fact that they are much smaller than $v(x, y'; x, y)$. Finally, from the same assumed time-scale separation, we can make an adiabatic approximation and suppose that $p(y|x) \approx p^s(y|x)$, where the conditional stationary distribution $p^s(y|x)$ satisfies

$$\sum_{y'} p^s(y'|x) v(x, y'; x, y) - p^s(y|x) v(x, y; x, y') = 0. \quad (6)$$

In summary, after performing the above-described adiabatic approximation, the dynamics of $p(x)$ are governed by Eq. (2), where the effective transition probability from state x to state x' is given by

$$\Upsilon(x; x') = \sum_{y, y'} p^s(y|x) v(x, y; x', y'), \quad (7)$$

while $p^s(y|x)$ is the solution of Eq. (6). Notice that the adiabatic approximation that we have introduced here is equivalent to that introduced by Pigolotti and Vulpiani [20].

III. THERMODYNAMIC STATE FUNCTIONS

A. Internal energy

Consider a molecular system that is irreducible and thus has a unique long-time stationary probability distribution $p^s(x, y)$. Further assume that the system is in contact with an isothermal bath with a potential difference. Thus we can define, following Ge and Qian [10], the energy function associated with state (x, y) via the stationary distribution $p^s(x, y)$ as

$$u(x, y) = -k_B T \ln p^s(x, y), \quad (8)$$

where k_B is the Boltzmann constant and T is the absolute temperature. In systems with detailed balance $p^s(x, y)$ equals the thermodynamic-equilibrium probability distribution $p^e(x, y)$ and Eq. (8) is equivalent to the Gibbs grand canonical ensemble. When detailed balance is not fulfilled, the above definition of internal energy is related to the stochastic potential studied by Kubo *et al.* [22].

From Eq. (8), the mean internal energy of the mesoscopic state $p(x, y)$ can be written as

$$U = \sum_{x, y} p(x, y) u(x, y) = -k_B T \sum_{x, y} p(x, y) \ln p^s(x, y). \quad (9)$$

By substituting Eq. (4) into Eq. (9), Eq. (9) can be rearranged as follows:

$$U = \sum_{x, y} p(x, y) u(x, y) = \sum_x p(x) [u_S(x) + u_F(x)], \quad (10)$$

where

$$u_S(x) = -k_B T \ln p^s(x), \quad (11)$$

$$u_F(x) = -k_B T \sum_y p(y|x) \ln p^s(y|x).$$

Moreover, if we impose the adiabatic approximation stating that $p(y|x) \approx p^s(y|x)$,

$$u_F(x) = -k_B T \sum_y p^s(y|x) \ln p^s(y|x). \quad (12)$$

These results imply that the internal energy can be split in two components ($U = U_S + U_F$) corresponding to the slow [$U_S = \sum_x p(x) u_S(x)$] and fast [$U_F = \sum_x p(x) u_F(x)$] time scales, respectively.

B. Entropy

The Gibbs entropy is defined as usual:

$$S = -k_B \sum_{x,y} p(x,y) \ln p(x,y). \quad (13)$$

Substitution of Eq. (4) into Eq. (13) leads to

$$S = -k_B \sum_x p(x) \ln p(x) - k_B \times \sum_x p(x) \sum_y p(y|x) \ln p(y|x). \quad (14)$$

Again we see that the entropy can be separated into slow and fast components ($S = S_S + S_F$) defined, respectively, as

$$S_S = -k_B \sum_x p(x) \ln p(x), \quad (15)$$

$$S_F = -k_B \sum_x p(x) \sum_y p(y|x) \ln p(y|x).$$

If we enforce the adiabatic approximation $p(y|x) = p^s(y|x)$, the fast component becomes $S_F = \sum_x p(x) s_F(x)$, with

$$s_F(x) = -k_B \sum_y p^s(y|x) \ln p^s(y|x). \quad (16)$$

By comparing Eqs. (12) and (16) we note that $u_F(x) = T s_F(x)$ due to the adiabatic approximation.

C. Free energy

From its definition, $F = U - TS$, and Eqs. (9) and (13), the Helmholtz free energy is given by [10]

$$\begin{aligned} F &= k_B T \sum_{x,y} p(x,y) \ln \left(\frac{p(x,y)}{p^s(x,y)} \right) \\ &= k_B T \sum_x p(x) \ln \frac{p(x)}{p^s(x)} + k_B T \\ &\quad \times \sum_x p(x) \sum_y p(y|x) \ln \frac{p(y|x)}{p^s(y|x)}. \end{aligned} \quad (17)$$

In this case it is also possible to identify slow (F_S) and fast [$F_F = \sum_x p(x) f_F(x)$] components for the free energy, where

$$\begin{aligned} F_S &= k_B T \sum_x p(x) \ln \frac{p(x)}{p^s(x)}, \\ f_F(x) &= k_B T \sum_y p(y|x) \ln \frac{p(y|x)}{p^s(y|x)}. \end{aligned}$$

However, the imposition of the adiabatic approximation implies that $f_F(x) = 0 \forall x$ and thus $F_F = \sum_x p(x) f_F(x) = 0$. This is in agreement with the fact that enforcing the adiabatic approximation is equivalent to assuming that the fast-time-scale distribution $p(y|x)$ equilibrates instantaneously with the slow one $p(x)$ for every given x . Therefore, the system's free energy is invariant whether one considers or neglects the faster dynamics, as long as there is a reasonable separation of time scales.

D. Slow-dynamics perspective and whole-system-level interpretation

First we note from Eqs. (12) and (16) that, once the adiabatic approximation has been made, $s_F(x) = u_F(x)/T$. This term should be regarded as the entropy of state x due to the fast dynamics of variable y within the given x . Then Eq. (10) indicates that the energy of the slow time scale obeys

$$u_S(x) = \left(\sum_y p^s(y|x) u(x,y) \right) - T s_F(x) = \tilde{u}(x) - T s_F(x), \quad (18)$$

where the first term on the right-hand side, $\tilde{u}(x)$, is the mean internal energy of state x . Finally, in terms of $\tilde{u}(x)$, one has the canonical form of the thermodynamics for the slow variable

$$F_S = F = \sum_x p(x) \tilde{u}_S(x) + k_B T \sum_x p(x) \ln p(x). \quad (19)$$

To gain more insight into the physical meaning of $u_S(x)$ we shall discuss another feasible interpretation for this quantity when x is a continuous variable. In such a case, $u_S(x)$ takes the form of a potential of mean force. In fact, noting that $p^s(x) = \sum_y p^s(x,y)$, together with the definitions for $u(x,y)$ [Eq. (8)] and $u_S(x)$ [Eq. (11)], one has

$$u_S(x) = -k_B T \ln \sum_y \exp[-u(x,y)/k_B T], \quad (20)$$

while

$$\frac{d}{dx} u_S(x) = \frac{\sum_y \exp[-u(x,y)/k_B T] \partial u(x,y)/\partial x}{\sum_y \exp[-u(x,y)/k_B T]}, \quad (21)$$

which corresponds to the usual potential of mean force definition [23].

IV. TIME EVOLUTION AND THERMODYNAMIC FUNCTIONS

A. Time derivative of the thermodynamic functions

Following Ge and Qian [10], we shall differentiate the expressions for U , S , and F [Eqs. (10), (14), and (17)] and write the corresponding rates of change in terms of energy

and entropy fluxes since understanding these fluxes under different conditions provides valuable information regarding the system's dynamic and thermodynamic behavior. In particular, we are interested in investigating how the slow- and fast-dynamics subspaces contribute to the energy and entropy fluxes and whether their structures remain invariant from the slow-dynamics perspective.

The time derivatives for U , S , and F are calculated in the Appendix. After imposing the adiabatic approximation $p(y|x) \approx p^s(y|x)$ on the corresponding expressions we obtain

$$\begin{aligned} \dot{U} = & -\frac{k_B T}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \ln \frac{p^s(x)}{p^s(x')} \\ & - \frac{k_B T}{2} \sum_x p(x) \sum_{y,y'} [p^s(y'|x)v(x,y';x,y) \\ & - p^s(y|x)v(x,y;x,y')] \ln \frac{p^s(y|x)}{p^s(y'|x)}, \end{aligned} \quad (22)$$

$$\begin{aligned} \dot{F} = & -\frac{k_B T}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \\ & \times \ln \frac{p(x')p^s(x)}{p(x)p^s(x')}, \end{aligned} \quad (23)$$

$$\begin{aligned} \dot{S} = & \frac{k_B}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \\ & \times \left(\ln \frac{p(x')\Upsilon(x';x)}{p(x)\Upsilon(x;x')} - \ln \frac{\Upsilon(x';x)}{\Upsilon(x;x')} \right) \\ & + \frac{k_B}{2} \sum_x p(x) \sum_{y,y'} [p^s(y'|x)v(x,y';x,y) \\ & - p^s(y|x)v(x,y;x,y')] \left(\ln \frac{p^s(y'|x)v(x,y';x,y)}{p^s(y|x)v(x,y;x,y')} \right. \\ & \left. - \ln \frac{v(x,y';x,y)}{v(x,y;x,y')} \right). \end{aligned} \quad (24)$$

Before proceeding any further, notice that the formulas for \dot{U} and \dot{S} possess terms corresponding to the slow- and fast-dynamics subspaces. Moreover, the slow- and fast-dynamics terms in each equation have the same general structure. The same is true when each (slow- or fast-dynamics) term is compared with that on the right-hand side of the corresponding equation in Ref. [10]. Finally, because of the adiabatic approximation, the fast-dynamics terms in \dot{U} and \dot{S} are equal, except for the multiplicative factor T . Hence they cancel in $U - TS$ and, as a result, the time derivative for the free energy (\dot{F}) is the same whether or not a fast time scale exists [24].

B. Detailed balance

So far we have obtained all of our results without making use of the detailed balance condition. When the environment of a stochastic system is not driving it out of equilibrium, the system ultimately reaches an equilibrium steady state, which is characterized by the fulfillment of detailed balance:

$$p^e(x,y)v(x,y;x',y') = p^e(x',y')v(x',y';x,y). \quad (25)$$

Throughout the present section we denote the stationary distribution by $p^e(x,y)$, rather than $p^s(x,y)$, to emphasize that it obeys detailed balance and thus corresponds to thermodynamic equilibrium.

We consider the effective transition probability defined in Eq. (3) and make use of Eq. (4) to arrive at the following expression:

$$p(x)\Upsilon(x;x') = \sum_{y,y'} p(x,y)v(x,y;x',y').$$

We assume now that the system is in equilibrium and substitute Eq. (25) into the preceding equation to obtain

$$p^e(x)\Upsilon(x;x') = p^e(x')\Upsilon(x';x), \quad (26)$$

that is, Eq. (26) is the form of the detailed balance condition for the variable with slow dynamics, with the probability distribution $p^e(x) = \sum_y p^e(x,y)$. On the other hand, for the fast-dynamics variable, it follows from Eq. (4) that detailed balance implies that

$$p^e(y|x)v(x,y;x,y') = p^e(y'|x)v(x,y';x,y). \quad (27)$$

By employing the preceding results and following the procedure introduced by Ge and Qian [10], we can decompose \dot{U} , \dot{S} , and \dot{F} as follows:

$$\dot{U} = -Q_d, \quad \dot{F} = -T\sigma, \quad \dot{S} = \sigma - \frac{Q_d}{T}, \quad (28)$$

with

$$\begin{aligned} Q_d = -\dot{U} = & \frac{k_B T}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) \\ & - p(x)\Upsilon(x;x')] \ln \frac{\Upsilon(x';x)}{\Upsilon(x;x')}, \end{aligned} \quad (29)$$

$$\begin{aligned} \sigma = & \frac{k_B}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) \\ & - p(x)\Upsilon(x;x')] \ln \frac{p(x')\Upsilon(x';x)}{p(x)\Upsilon(x;x')}. \end{aligned} \quad (30)$$

A comparison of Eqs. (28) and (30) with the equations defining the dissipation heat and the entropy production rate in Ref. [10], respectively, reveals that Q_d and σ possess the same mathematical structure as, and thus can be identified with, those quantities.

When the system is in equilibrium with detailed balance, $\dot{U} = \dot{F} = \dot{S} = 0$. Furthermore, it is straightforward to verify that $Q_d = \sigma = 0$ as well. We thus conclude from these results that the thermodynamic equilibrium state is characterized not only by the constancy in time of the thermodynamic state functions U , F , and S , but also by the nonexistence of both energy flow and entropy production.

C. State functions for systems without detailed balance

We now return to Eqs. (22)–(24). We see by following the procedure in Ref. [10] that, when detailed balance is not fulfilled, the entropy rate of change can still be decomposed as

$$\dot{S} = \sigma - \frac{Q_d}{T}, \quad (31)$$

where the entropy production rate is now given by

$$\begin{aligned} \sigma = & \frac{k_B}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \ln \frac{p(x')\Upsilon(x';x)}{p(x)\Upsilon(x;x')} \\ & + \frac{k_B}{2} \sum_x p(x) \sum_{y,y'} [p^s(y'|x)v(x,y';x,y) \\ & - p^s(y|x)v(x,y;x,y')] \ln \frac{p^s(y'|x)v(x,y';x,y)}{p^s(y|x)v(x,y;x,y')}, \end{aligned}$$

while the dissipated heat rate is

$$\begin{aligned} Q_d = & \frac{k_B T}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \ln \frac{\Upsilon(x';x)}{\Upsilon(x;x')} \\ & + \frac{k_B T}{2} \sum_x p(x) \sum_{y,y'} [p^s(y'|x)v(x,y';x,y) \\ & - p^s(y|x)v(x,y;x,y')] \ln \frac{v(x,y';x,y)}{v(x,y;x,y')}. \end{aligned} \quad (32)$$

Observe that both σ and Q_d can be decomposed into two different terms with the same structure, each one corresponding to the slow- and fast-dynamics subspaces.

Equation (31) is one of the fundamental postulates of phenomenological irreversible thermodynamics [25]. By using these definitions we can also rewrite \dot{U} and \dot{F} as

$$\dot{U} = Q_{hk} - Q_d, \quad \dot{F} = Q_{hk} - T\sigma, \quad (33)$$

where

$$\begin{aligned} Q_{hk} = & \frac{k_B T}{2} \sum_{x,x'} (p(x')\Upsilon[x';x] - p(x)\Upsilon(x;x')) \\ & \times \ln \frac{p^s(x')\Upsilon(x';x)}{p^s(x)\Upsilon(x;x')} + \frac{k_B T}{2} \sum_x p(x) \\ & \times \sum_{y,y'} [p^s(y'|x)v(x,y';x,y) - p^s(y|x)v(x,y;x,y')] \\ & \times \ln \frac{p^s(y'|x)v(x,y';x,y)}{p^s(y|x)v(x,y;x,y')}. \end{aligned}$$

This expression for Q_{hk} can again be decomposed into two terms corresponding to the slow- and fast-dynamics subspaces. Observe that both terms have the same mathematical structure as the definition for the housekeeping heat in Ref. [10]. Hence we can identify Q_{hk} with this quantity, originally introduced by Oono and Paniconi [10,17] and interpreted as the energy flow that has to be administered to the system to keep the stationary state out of equilibrium.

By defining

$$\begin{aligned} A(x,y',y) &= p^s(y'|x)v(x,y';x,y) - p^s(y|x)v(x,y;x,y'), \\ B(x,y) &= \ln p^s(y|x), \end{aligned}$$

it is straightforward to verify that A is antisymmetric in y and y' : $A(x,y',y) = -A(x,y,y')$. Moreover, since $p^s(y|x)$ is by definition the stationary conditional probability distribution for variable y (conditioned to the value of x), it follows from Eq. (5) that $\sum_{y'} A(x,y',y) = 0 \forall x,y$. Furthermore, as a function of y and y' , A is an antisymmetric matrix with all its rows, and all columns, summing to zero. Then for any real vector B with component $B(\cdot,y)$,

$$\begin{aligned} & \sum_{y,y'} A(x,y,y')[B(x,y) - B(x,y')] \\ &= \sum_y B(x,y) \left(\sum_{y'} A(x,y,y') \right) \\ & - \sum_{y'} B(x,y') \left(\sum_y A(x,y,y') \right) = 0. \end{aligned} \quad (34)$$

This result further implies that

$$\begin{aligned} Q_{hk} = & \frac{k_B T}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \\ & \times \ln \frac{p^s(x')\Upsilon(x';x)}{p^s(x)\Upsilon(x;x')} + \frac{k_B T}{2} \sum_x p(x) \\ & \times \sum_{y,y'} [p^s(y'|x)v(x,y';x,y) - p^s(y|x)v(x,y;x,y')] \\ & \times \ln \frac{v(x,y';x,y)}{v(x,y;x,y')}, \end{aligned} \quad (35)$$

$$\begin{aligned} \sigma = & \frac{k_B}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \\ & \times \ln \frac{p(x')\Upsilon(x';x)}{p(x)\Upsilon(x;x')} \\ & + \frac{k_B}{2} \sum_x p(x) \sum_{y,y'} [p^s(y'|x)v(x,y';x,y) \\ & - p^s(y|x)v(x,y;x,y')] \ln \frac{v(x,y';x,y)}{v(x,y;x,y')}. \end{aligned} \quad (36)$$

Finally, the expressions for \dot{U} and \dot{S} transform into

$$\dot{U} = -\frac{k_B T}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \ln \frac{p^s(x)}{p^s(x')}, \quad (37)$$

$$\begin{aligned} \dot{S} = & \frac{k_B}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \\ & \times \left(\ln \frac{p(x')\Upsilon(x';x)}{p(x)\Upsilon(x;x')} - \ln \frac{\Upsilon(x';x)}{\Upsilon(x;x')} \right), \end{aligned} \quad (38)$$

while \dot{F} remains the same as in Eq. (23).

Let us define

$$Q_{\text{fast}} = \frac{k_B T}{2} \sum_x p(x) \sum_{y, y'} [p^s(y'|x) v(x, y'; x, y) - p^s(y|x) v(x, y; x, y')] \ln \frac{v(x, y'; x, y)}{v(x, y; x, y')}. \quad (39)$$

We can see from this definition that Q_{fast} is an energy flux related to a fast time scale. Observe that Q_{fast} appears as a summand in the expressions for Q_d [Eq. (32)] and Q_{hk} [Eq. (35)], while Q_{fast}/T appears in the expression for σ [Eq. (36)], that is, the fast-dynamics contributions to the dissipated heat, the housekeeping heat, and the entropy production rate are identical (except for a factor T in the case of σ) in all three cases. Furthermore, Q_{fast} cancels when Q_d , Q_{hk} , and $T\sigma$ are subtracted, which explains why such a term does not appear in the expressions for \dot{U} , \dot{S} , and \dot{F} .

D. Partial detailed balance with rapid pre-equilibrium

We assume that detailed balance is fulfilled by the fast-dynamics distribution $p(y|x)$, but not necessarily by $p(x)$. Then there is a rapid pre-equilibrium $p(y|x) \approx p^e(y|x)$, with $p^e(y|x)$ satisfying Eq. (27). If this is the case, then $Q_{\text{fast}} = 0$. Interestingly, the expressions for \dot{U} , \dot{S} , and \dot{F} do not change. They are the same as in Eqs. (23), (37), and (38), except that $p^s(y|x)$ is replaced by $p^e(y|x)$ whenever the former term appears. This means that having or not having detailed balance in the fast-dynamics space makes a difference for the energy flows Q_d and Q_{hk} , as well as for the entropy production rate σ (all of them are smaller in the first case because the contribution due to fast dynamics vanishes); however, the existence or nonexistence of a fast dynamics space makes no difference for the rate of change of all thermodynamic state functions (U , S , and F).

E. Stationary distribution without detailed balance

To analyze the behavior of the process variables when the system is at a steady state without detailed balance we define

$$\begin{aligned} \mathcal{A}(x, x') &= p^s(x) \Upsilon(x; x') - p^s(x') \Upsilon(x'; x), \\ \mathcal{B}(x) &= \ln p^s(x), \\ \mathcal{C}(x) &= u^s(x)/k_B T. \end{aligned}$$

Clearly, $\mathcal{A}(x, x')$ is antisymmetric [$\mathcal{A}(x, x') = -\mathcal{A}(x', x)$]. Moreover, since $p^s(x)$ is the stationary probability distribution for variable x , it follows from Eq. (2) that $\sum_{x'} \mathcal{A}(x', x) = 0$. Hence, similar to the result in Eq. (34), we have

$$\sum_{x, x'} \mathcal{A}(x', x) [\mathcal{B}(x') - \mathcal{B}(x)] = \sum_{x, x'} \mathcal{A}(x', x) [\mathcal{C}(x') - \mathcal{C}(x)] = 0.$$

This equation, together with Eqs. (23), (37), and (38), further implies that

$$\begin{aligned} T\sigma = Q_d = Q_{hk} &= \frac{k_B T}{2} \sum_{x, x'} [p^s(x') \Upsilon(x'; x) \\ &- p^s(x) \Upsilon(x; x')] \ln \frac{\Upsilon(x'; x)}{\Upsilon(x; x')} + Q_{\text{fast}} \end{aligned} \quad (40)$$

when $p(x) = p^s(x)$ and $p(y|x) = p^s(y|x)$. Finally, from Eq. (40) we obtain the result $\dot{U} = \dot{S} = \dot{F} = 0$ in the stationary state. Indeed, we can see from Eq. (17) that $F = 0$ in such a case.

The results in the preceding paragraph corroborate the following: Once the system reaches the steady-state distribution, all the thermodynamic state functions (internal energy, free energy, and entropy) will remain constant. However, contrary to an equilibrium steady state in which detailed balance is fulfilled, a nonequilibrium steady state has nonzero fluxes, given by Eq. (40). The equalities between the fluxes reflect both the energy conservation and the isothermal Clausius equality: On the one hand, to keep the system out of equilibrium, energy has to be supplied to the system (Q_{hk}), which is then dissipated as heat (Q_d), while, on the other hand, entropy is produced in the process of the conversion of useful energy to heat ($\sigma = Q_d/T$).

V. QUASISTATIONARY AND STEADY-ADIABATIC PROCESSES

The concepts of quasistationary and adiabatic processes are central to thermodynamics. In systems where the stationary state satisfies detailed balance, a quasistationary process can be defined as a succession of states where $\sigma = 0$, while an adiabatic process is a succession of states satisfying $Q_d = 0$.

Oono and Paniconi [17] generalized these concepts for systems with a nonequilibrium steady state (NESS) by defining the excess heat and the free-energy dissipation rate as

$$Q_{\text{ex}} = Q_d - Q_{hk}, \quad (41)$$

$$\theta = T\sigma - Q_{hk} \quad (42)$$

and noting that, in terms of these variables, the rates \dot{S} , \dot{U} , and \dot{F} can be rewritten as [see Eqs. (31) and (33)]

$$\dot{S} = \frac{\theta - Q_{\text{ex}}}{T}, \quad \dot{U} = -Q_{\text{ex}}, \quad \dot{F} = -\theta. \quad (43)$$

A comparison of Eqs. (28) and (43) reveals that Q_d and σ in systems where the stationary state satisfies detailed balance can be respectively identified with Q_{ex} and θ/T in NESS systems. Based on this identification, Oono and Paniconi [17] generalized the concepts of quasistationary and steady-adiabatic processes for NESS systems as follows: A quasistationary process is a succession of states satisfying $\theta = 0$, while a steady-adiabatic process is a succession of states complying with $Q_{\text{ex}} = 0$. After introducing these concepts, Oono and Paniconi [17] made extensive use of them in the development of their phenomenological steady-state thermodynamics. Here we investigate how a time-scale separation affects these processes.

After substituting Eqs. (32), (35), and (36) into Eqs. (41) and (42) we obtain

$$Q_{\text{ex}} = \frac{k_B T}{2} \sum_{x, x'} [p(x') \Upsilon(x'; x) - p(x) \Upsilon(x; x')] \ln \frac{p^s(x)}{p^s(x')}, \quad (44)$$

$$\theta = \frac{k_B}{2} \sum_{x, x'} [p(x') \Upsilon(x'; x) - p(x) \Upsilon(x; x')] \ln \frac{p(x') p^s(x)}{p(x) p^s(x')}. \quad (45)$$

Recall that the energy flux related to the fast time scale Q_{fast} [see Eq. (39)] appears as a summand in Q_d , Q_{hk} , and σ . Hence it cancels out when subtracting these quantities and so it does not show in either Q_{ex} or θ . Consequently, θ has no contribution whatsoever from the fast-dynamics subspace.

The fact that θ depends only on the slow-dynamics subspace x means that the fast-dynamics subspace y does not influence whether or not a given process is quasistationary. This result is in agreement with the adiabatic approximation we have made to reduce the system's master equation, which is equivalent to assuming that the fast-dynamics subspace immediately equilibrates with the slow-dynamics state x .

Regarding steady-adiabatic processes for NESS systems, we see that, since Q_{ex} depends on the fast dynamics through $s_F(x)$ [see Eqs. (16) and (44)], the fast dynamics cannot be ignored while determining the adiabaticity of a given process. This can be more clearly appreciated by noticing that the following generalized Clausius equality is satisfied in a quasistationary process:

$$\dot{S} = -\frac{Q_{\text{ex}}}{T}.$$

VI. CONCLUSION

In this work we have extended the results of a recent paper [10] where a rather complete thermodynamic formalism was introduced for discrete-state, continuous-time Markov processes with and without detailed balance. Our main objective was to investigate whether the thermodynamic structure is invariant in a multiscale stochastic system. By invariance we mean that the relation between state and process variables remains unchanged when the system is viewed at different time scales.

We proceeded as follows. First we assumed that the states of a system can be classified according to the propensities of the transitions among them. More precisely, we supposed that every state can be represented by a dual vector (x, y) and that transitions involving changes in y alone are much more probable than those involving changes in x or in both x and y . Then we imposed an adiabatic approximation to deduce a reduced master equation for the slower time scale. Finally we analyzed the implications of this adiabatic approximation on the thermodynamic formalism introduced by Ge and Qian [10].

It was revealed that all thermodynamic variables and their time derivatives can be separated in a very natural way into contributions from the slow and fast time scales. The only exceptions were the Helmholtz free energy and its time derivatives, which only involve terms due to the slower time scale. In other words, the Helmholtz free energy (which characterizes the system spontaneous organization) is invariant with and without a fast time scale. This happens because, having reached its stationarity, the fast-time-scale probability distribution does not contribute to the free energy. The same cannot be said about the entropy and the internal energy, both of which have fast-dynamics contributions.

The results discussed above are important because they provide a framework in which to study the thermodynamics of complex Markov processes where time-scale separation is possible. A few examples where this framework may be useful are: enzymatic reactions (in which one of the chemical steps is much slower than the rest) or gene regulatory networks (where transcription initiation typically is an infrequent process compared, for instance, with translation initiation and post-translational modification of the resulting proteins). The same results can also be interpreted from a more fundamental thermodynamic perspective. We elaborate on these ideas next. The dynamics on a fast time scale contribute an entropic term to the energy function $u_S(x)$ for the slow dynamics. This allows us to identify $u_S(x)$ as a free energy. Indeed, $u_S(x)$ ends up being the conditional free energy, a concept used extensively in equilibrium thermodynamics as one usually works with a coarse-grained conditional free energy (not a pure mechanical energy) and develops a partition function thereafter. In contrast, entropy-enthalpy compensation has been studied extensively in biochemistry [26,27]. The strong form of this phenomenon occurs when variations in ΔH and ΔS , caused by regular changes in some experimental variable (excluding temperature), exhibit a linear correlation. In this case ΔG will be small relative to the range of values expected from the experiment.

As pointed out by Qian [24], internal energy is the equivalent of enthalpy, while the Helmholtz free energy is the equivalent of the Gibbs free energy in the types of systems studied here. In that respect, entropy-internal energy compensation in these systems is tantamount to entropy-enthalpy compensation in isobaric ones; the effect of entropy-internal energy compensation will be small changes in F . The insight from the present work is that the compensating part of entropy and internal energy is the contribution from fast dynamics, i.e., rapid fluctuations.

The expressions we derived for dU/dt and dS/dt contain terms associated with the slow and fast time scales. However, when the adiabatic approximation is imposed, the contributions from the faster time scale are equal, except for a factor T in dS/dt [see Eqs. (22) and (24)]. As a consequence, the expression for dF/dt includes only a slow-dynamics term [see Eq. (23)], that is, we have entropy-internal energy cancellation for the fast-dynamics contributions. In fact, it is impossible to know whether or not a fast time scale exists from the perspective of the Helmholtz free energy. These results are in complete agreement with previous studies that prove the existence of entropy-enthalpy compensation by considering that, in response to a small perturbation, the free-energy change of a stationary system is independent of the system's thermodynamic environment, while the entropy and the internal energy changes depend on the environmental constraints [26,27]. Recall that the adiabatic approximation is equivalent to assuming that the fast-dynamics distribution $p(y|x)$ reaches its stationary value instantaneously for every state $x(t)$.

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APPENDIX: RATE OF CHANGE OF THE THERMODYNAMIC STATE VARIABLES

After differentiating Eqs. (10), (14), and (17) we obtain the results for the time derivatives of the internal energy,

$$\begin{aligned}\dot{U} &= \sum_x \dot{p}(x)[u_S(x) + u_F(x)] + \sum_x p(x)\dot{u}_F(x) \\ &= -\frac{k_B T}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \ln \frac{p^s(x)}{p^s(x')} \\ &\quad - \frac{k_B T}{2} \sum_x p(x) \sum_{y,y'} [p(y'|x)v(x,y';x,y) \\ &\quad - p(y|x)v(x,y;x,y')] \ln \frac{p^s(y|x)}{p^s(y'|x)},\end{aligned}$$

the free energy,

$$\begin{aligned}\dot{F} &= \sum_x \dot{p}(x) \left(k_B T \ln \frac{p(x)}{p^s(x)} + f_F(x) \right) + \sum_x p(x)\dot{f}_F(x) \\ &= -\frac{k_B T}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \\ &\quad \times \ln \frac{p(x')p^s(x)}{p(x)p^s(x')} - \frac{k_B T}{2} \sum_x p(x) \\ &\quad \times \sum_{y,y'} -[p(y'|x)v(x,y';x,y) - p(y|x)v(x,y;x,y')] \\ &\quad \times \ln \frac{p(y'|x)p^s(y|x)}{p(y|x)p^s(y'|x)},\end{aligned}$$

and the entropy,

$$\begin{aligned}\dot{S} &= \sum_x \dot{p}(x)[k_B \ln p(x) + s_F(x)] + \sum_x p(x)\dot{s}_F(x) \\ &= \frac{k_B}{2} \sum_{x,x'} [p(x')\Upsilon(x';x) - p(x)\Upsilon(x;x')] \\ &\quad \times \left(\ln \frac{p(x')\Upsilon(x';x)}{p(x)\Upsilon(x;x')} - \ln \frac{\Upsilon(x';x)}{\Upsilon(x;x')} \right) \\ &\quad + \frac{k_B T}{2} \sum_x p(x) \sum_{y,y'} [p(y'|x)v(x,y';x,y) \\ &\quad - p(y|x)v(x,y;x,y')] \\ &\quad \times \left(\ln \frac{p(y'|x)v(x,y';x,y)}{p(y|x)v(x,y;x,y')} - \ln \frac{v(x,y';x,y)}{v(x,y;x,y')} \right).\end{aligned}$$

In the derivation of the preceding equations we have taken into consideration that

$$\sum_x \dot{p}(x)u_F(x), \quad \sum_x \dot{p}(x)f_F(x), \quad \sum_x \dot{p}(x)s_F(x) \approx 0.$$

The demonstration of these last relations is straightforward and follows from the fact that $v(x,y,x',y') \approx 0$ for all $x \neq x'$, which is the basic assumption underlying the time-scale separation.

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