Decomposition of the entropy production rate and nonequilibrium thermodynamics of switching diffusion processes

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A switching diffusion process (SDP) is a widely used stochastic model in physics and biology, especially for molecular motors that exhibit a discrete internal chemical kinetics as well as a continuous external mechanical motion. The nonequilibrium thermodynamics of switching diffusion processes has not been extensively studied yet. In the present paper, we propose the decomposition of the entropy production rate in one-dimensional SDPs, based on the flux decomposition. However, similar decompositions of the housekeeping heat dissipation rate and free energy dissipation rate cannot guarantee the non-negativity of each decomposed component. Hence, we modify this decomposition with the flow of exponential relative information under steady-state fluxes, resulting in another decomposition with all non-negative components. Furthermore, we also provide the nonequilibrium thermodynamics of one-dimensional SDPs under the perspectives of coarse -graining and exchange of information between the chemical kinetics and mechanical motion, resulting in several other decompositions of entropy production rate. Finally, we generalize all the results to high-dimensional SDPs with a more general mathematical treatment.

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I. INTRODUCTION

In the past 25 years, the modeling of molecular motors has drawn a great amount of attention because of the tremendous progress of experimental techniques, which has enabled the monitoring of single biological molecules in aqueous solutions at room temperature [1–8]. Generally, molecular motors are microscopic objects (motor proteins) that unidirectionally move along one-dimensional periodic structures, converting chemical energy to mechanical work [9,10].

The chemical kinetics of an individual molecular motor, i.e., the transition between the different inner chemical (conformational) states, can be modeled by the master equation

$$\frac{dp_i(t)}{dt} = \sum_{j\neq i}[q_{ji}p_j(t) - q_{ij}p_i(t)], \quad i = 1,2,\ldots,N, \qquad (1)$$

where $p_i(t)$ is the probability distribution over chemical states $i = 1,2,\ldots,N$ of the system and q_{ij} is the transition rate from chemical state i to chemical state j. On the other hand, the unidirectional motion of an individual molecular motor can be modeled by the Langevin equation

$$\gamma\dot{x} = -\frac{\partial U(x)}{\partial x} + f + \xi(t),$$

where $\xi(t)$ represents Gaussian white noise with intensity $2\gamma k_BT$, γ is the friction constant, f is the nonconservative force, and we take the mass equal to 1. The probability distribution $p(x,t)$ of the position $x(t)$ is governed by the Fokker-Planck equation (Kolmogorov forward equation)

$$\frac{\partial p(t,x)}{\partial t} = \frac{\partial}{\partial x}\left(\frac{k_BT}{\gamma}\frac{\partial p(t,x)}{\partial x} - \frac{-\frac{\partial U(x)}{\partial x}+f}{\gamma}p(t,x)\right). \qquad (2)$$

However, the internal chemical kinetics and external mechanical dynamics should be combined into one framework in order to model the chemomechanical dynamics of a molecular motor [3]. Mathematically, this combination leads to a switching diffusion process (SDP) [11–26]. An SDP is a two-component process $Y(t) = (X(t),\alpha(t))$ with a continuous component $X(t)$ and a discrete component $\alpha(t)$ [13], where $X(t)$ evolves according to the diffusion process specified by the drift and diffusion coefficients at given discrete state $\alpha(t)$, the alteration of which indicates the switching.

The stochastic theory of nonequilibrium thermodynamics in pure jumping processes (master-equation systems) and pure diffusion processes has been established over the past two decades [27,28]. The second law of thermodynamics is always expressed as the non-negativity of the entropy production rate and it vanishes if and only if the stochastic process is time reversible. Generally, there are two different approaches to studying the nonequilibrium thermodynamics of stochastic processes. One is the fluctuation relation approach, in which the entropy production can be regarded as a Kullback-Leibler divergence between a process and suitable time reversal [29,30]

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and this fact can be used to refine the Clausius inequality by applying the theory of optimal transport [31–33]. The other is the approach focusing on the decomposition of the entropy production rate, resulting also in more refined forms of the second law [34–39].

In the present paper, we follow the second approach. The broad goal with which we are concerned here is to develop the mathematical structure of the nonequilibrium thermodynamics of SDPs, especially focusing on the decomposition of the entropy production rate and the refined second law of thermodynamics. The dynamics of the switching diffusion model already has a very clear decomposition of chemical kinetics and mechanical diffusion. So we wonder whether the corresponding thermodynamics also has such a clear decomposition and whether such a decomposition will lead to more refined second law of thermodynamics.

We answer these questions from two different perspectives. One is the natural decomposition based on the flux decomposition, because in SDPs, the fluxes between different chemical states and those along the mechanical motion are well defined and can be easily addressed separately. However, the decompositions of the housekeeping heat dissipation rate and the free energy dissipation rate based on the flux decomposition cannot give rise to non-negative components. Hence, we modify these decompositions with the flow of the exponential relative information under steady-state fluxes, resulting in another decomposition with only non-negative components.

The other perspective is from analyzing the nonequilibrium thermodynamics of coarse-grained dynamics. Coarse graining is a method that integrates groups of microscopic states together, forming mesoscopic states, through appropriate regulations such as different time scales [40–42] and limitations of the experimental approach [43,44]. Applying the frameworks of nonequilibrium thermodynamics under coarse graining [45], we carefully investigate the nonequilibrium thermodynamics for the cases where only the mechanical motion or chemical kinetics of an SDP can be observed, identical to the approach that has been used in experiments. The entropy production rate then is decomposed into three non-negative terms, one of which is equal to one of the decomposed components obtained using flux decomposition. Finally, we apply the framework of information thermodynamics [46,47] to provide the expressions for the information flow in SDPs.

The structure of this paper is organized as follows. In Sec. II we define the one-dimensional SDP and introduce the flux decomposition. In Sec. III the decomposition of the entropy production rate and several other thermodynamic quantities are investigated in one-dimensional SDP. In Sec. IV the coarse-grained dynamics of one-dimensional SDPs is given and the corresponding decomposition of the entropy production rate and information thermodynamics are studied. Sections V–VII discuss the case of high-dimensional SDPs, in which the results are parallel to the case of one-dimensional SDPs, but with more general and detailed mathematical treatments. The one-dimensional part (Secs. II–IV) is for general readers, emphasizing the physics, and one can skip the high-dimensional part (Secs. V–VII) without losing the physics; in contrast, the high-dimensional part is for experts who are interested in the more general mathematical treatment, which is not completely a straightforward generalization of the one-dimensional part and needs more careful derivations.

II. ONE-DIMENSIONAL SDP AND FLUX DECOMPOSITION

A one-dimensional SDP $Y(t) = (X(t),\alpha(t))$ can be used to model a single-motor protein moving unidirectionally along a filament, converting chemical energy from adenosine triphosphate hydrolysis in an aqueous solution to mechanical work, where the continuous component $X(t)$ is one dimensional and the discrete component $\alpha(t)$ has a finite state space of $M = \{1,2,\dots,N\}$. This SDP satisfies [13,48]

$$dX(t) = b(X(t),\alpha(t))dt + \sigma(X(t),\alpha(t))dw(t), \tag{3}$$

$$\begin{aligned} &P(\alpha(t+\Delta t) = j|\alpha(t) = i, X(s),\alpha(s), s \leqslant t)\\ &\quad = q_{ij}(X(t))\Delta t + o(\Delta t) \quad \text{for } i \neq j, \end{aligned} \tag{4}$$

where $b(x,i)$, $\sigma(x,i)$, and $q_{ij}(x)$ are smooth and bounded on $\mathbb{R}$ and the matrix $Q = q_{ij}(x)$ is conservative for every $x \in \mathbb{R}$, i.e.,

$$q_{ii}(x) = -\sum_{j\neq i} q_{ij}(x) \quad \text{for any } i \in M.$$

Governed by Eq. (3), the continuous component $X(t)$ should evolve as a diffusion process, given a frozen $\alpha(t) = i$, with the drift coefficient $b(X(t),i)$ and the diffusion coefficient $\sigma^2(X(t),i)$. The discrete component $\alpha(t)$, according to Eq. (4), is a jumping process with a random transition-probability rate $q_{ij}(X(t))$ from state i to j, given $X(t)$.

The stochastic integral $\sigma(X(t),\alpha(t))dw(t)$ in (3) is in the anti-Itô form [27,49,50], which is defined through the Fokker-Planck equation satisfied by the joint probability $p(t,x,i)$ of the motor protein with internal state i and external position x at time t [3,13,21],

$$\begin{aligned} \frac{\partial p(t,x,i)}{\partial t} &= \frac{\partial}{\partial x}\left(\frac{1}{2}\sigma^2(x,i)\frac{\partial p(t,x,i)}{\partial x} - b(x,i)p(t,x,i)\right)\\ &\quad + \sum_{j=1}^{N} p(t,x,j)q_{ji}(x) \quad \text{for any } x \in \mathbb{R}, i \in M. \end{aligned} \tag{5}$$

The stationary distribution of $Y(t)$ is a unique probability distribution density $\pi(x,i)$ that cancels the right-hand side of (5), i.e.,

$$\begin{aligned} &\frac{\partial}{\partial x}\left(\frac{1}{2}\sigma^2(x,i)\frac{\partial \pi(x,i)}{\partial x} - b(x,i)\pi(x,i)\right)\\ &\quad + \sum_{j=1}^{N}\pi(x,j)q_{ji}(x) = 0 \quad \text{for any } x \in \mathbb{R}, i \in M. \end{aligned} \tag{6}$$

The state space of SDP $Y(t) = (X(t),\alpha(t))$, namely, $\mathbb{R} \times M$, could be recognized as N parallel lines, $\{\text{state } 1, \text{state } 2, \dots, \text{state } N\}$, indexed by the chemical state i of the motor. Then $Y(t)$ could be understood as N diffusion processes on N different parallel lines [13]. As shown in Fig. 1 for an illustration of the trajectory with $N = 4$, the process is initially at $(X(0),\alpha(0)) = (x,1)$, diffusing along the line

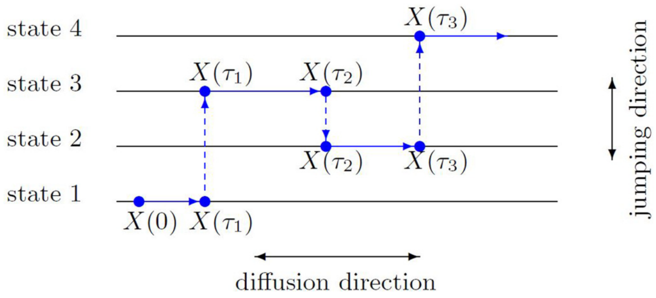

FIG. 1. Sample path of the SDP $Y(t) = (X(t),\alpha(t))$ with $N = 4$.

of state 1 for a random time τ_1, which is the sojourn time in state 1 of the jumping process. Then the state $\alpha(t)$ switches to state 3, with the drift and diffusion coefficients determined by $\alpha(t) = 3$. The process wanders along the line of state 3 until another jumping time τ_2, then switches to state 2, and so on. The illustration makes it clear that the fluxes of $Y(t)$ should have two different directions, moving along the lines due to the subprocess of diffusion (mechanical dynamics) and switching among the chemical states according to the subprocess of jumping (chemical kinetics).

Based on the two different subprocesses, we can define two fluxes accordingly, i.e., $J_i^{\mathrm{mech}}(t,x)$, named the mechanical flux, is the flux due to diffusion and $J_x^{\mathrm{chem}}(t,i)$, named the chemical flux, is the flux due to chemical states jumping. Then the Fokker-Planck equation (5) could be rewritten as

$$\begin{aligned}\frac{\partial p(t,x,i)}{\partial t} &= -\frac{\partial}{\partial x}J_i^{\mathrm{mech}}(t,x) + J_x^{\mathrm{chem}}(t,i)\\ &= -\frac{\partial}{\partial x}J_i^{\mathrm{mech}}(t,x) + \sum_{j\neq i} J_{x,ji}^{\mathrm{chem}}(t)\\ &\qquad \text{for any } x\in\mathbb{R}, i\in M,\end{aligned}\tag{7}$$

in which

$$\begin{aligned}J_i^{\mathrm{mech}}(t,x) &= b(x,i)p(t,x,i) - \frac{1}{2}\sigma^2(x,i)\frac{\partial p(t,x,i)}{\partial x},\\ J_{x,ji}^{\mathrm{chem}}(t) &= p(t,x,j)q_{ji} - p(t,x,i)q_{ij}(x)\\ &\qquad \text{for any } x\in\mathbb{R} \text{ and } i,j\in M,\end{aligned}\tag{8}$$

where $J_{x,ji}^{\mathrm{chem}}(t)$ is the net flux from chemical state j to chemical state i at position x. At the steady state, the stationary fluxes $\mathfrak{J}_i^{\mathrm{mech}}(x) = b(x,i)\pi(x,i) - \frac{1}{2}\sigma^2(x,i)\frac{\partial \pi(x,i)}{\partial x}$ and $\mathfrak{J}_{x,ji}^{\mathrm{chem}} = \pi(x,j)q_{ji} - \pi(x,i)q_{ij}(x)$ would cancel out each other according to Eq. (7),

$$\frac{\partial \mathfrak{J}_i^{\mathrm{mech}}(x)}{\partial x} = \mathfrak{J}_x^{\mathrm{chem}}(i) = \sum_{j\neq i}\mathfrak{J}_{x,ji}^{\mathrm{chem}}.\tag{9}$$

It has been proved that a stationary SDP $Y(t)$ is time reversible if and only if there exists a function $V(x,i)$ such that $\frac{2b(x,i)}{\sigma^2(x,i)} = -\frac{\partial V(x,i)}{\partial x}$, where $V(x,i)$ satisfies [21]

$$\sum_{i=1}^{N}\int_{-\infty}^{+\infty} e^{-V(x,i)}dx < \infty$$

and

$$e^{-V(x,i)}q_{ij}(x) = e^{-V(x,j)}q_{ji}(x) \quad \text{for any } x\in\mathbb{R},\ i,j\in M.$$

In this case, $V(x,i) = -\ln\pi(x,i) + C$, in which C is a constant and

$$\frac{2b(x,i)}{\sigma^2(x,i)} = \frac{\partial \ln\pi(x,i)}{\partial x},\quad \pi(x,i)q_{ij}(x) = \pi(x,j)q_{ji}(x),\tag{10}$$

which is the detailed balance relation of the SDP [21]. The detailed balance (10) is equivalent to the vanishing of all the fluxes at the steady state, i.e.,

$$\mathfrak{J}_i^{\mathrm{mech}}(x) \equiv 0,\quad \mathfrak{J}_{x,ji}^{\mathrm{chem}} \equiv 0\tag{11}$$

for all $x\in\mathbb{R}$ and $i\in M$, which is indeed the equilibrium state.

III. DECOMPOSITION OF THE ENTROPY PRODUCTION RATE IN A ONE-DIMENSIONAL SDP

A. Decomposition based on flux decomposition

Throughout the present work, $k_B = 1$ and the temperature T is assumed to be a constant. We can define the entropy of the whole system as

$$S(t) = -\sum_{i=1}^{N}\int_{-\infty}^{+\infty} p(t,x,i)\ln p(t,x,i)dx.\tag{12}$$

For a frozen chemical state i, the evolution of the system is a pure diffusion process, so we can define the force along the diffusion direction of the SDP following the definition of force for a pure diffusion process, i.e., $F_i^{\mathrm{mech}}(x) = \frac{2b(x,i)}{\sigma^2(x,i)}$ [27,28]. Similarly, the system follows the master equation at a frozen position x, so we can define the force between the chemical states as $F_{ij}^{\mathrm{chem}}(x) = \ln\frac{q_{ij}(x)}{q_{ji}(x)}$ [27,28]. It is widely known that the change of entropy $dS(t)$ could be decomposed into two different terms [51–54]. So we can derive that

$$\begin{aligned}\frac{dS(t)}{dt} &= -\sum_{i=1}^{N}\int_{-\infty}^{+\infty} J_i^{\mathrm{mech}}(t,x)\frac{\partial \ln p(t,x,i)}{\partial x}dx\\ &\quad + \int_{-\infty}^{+\infty}\frac{1}{2}\sum_{i\neq j}J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)}{p(t,x,j)}dx\\ &= e_p(t) - h_d(t),\end{aligned}\tag{13}$$

where

$$\begin{aligned}e_p(t) &= \sum_{i=1}^{N}\int_{-\infty}^{+\infty}\frac{2\left[J_i^{\mathrm{mech}}(t,x)\right]^2}{\sigma^2(x,i)p(t,x,i)}dx\\ &\quad + \int_{-\infty}^{+\infty}\frac{1}{2}\sum_{i\neq j}J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)q_{ij}(x)}{p(t,x,j)q_{ji}(x)}dx\end{aligned}\tag{14}$$

is the instantaneous entropy production rate at time t [21,55] and

$$\begin{aligned}h_d(t) &= \sum_{i=1}^{N}\int_{-\infty}^{+\infty} J_i^{\mathrm{mech}}(t,x)F_i^{\mathrm{mech}}(x)dx\\ &\quad + \int_{-\infty}^{+\infty}\frac{1}{2}\sum_{i\neq j}J_{x,ij}^{\mathrm{chem}}(t)F_{ij}^{\mathrm{chem}}(x)dx\end{aligned}\tag{15}$$

is due to the exchange of heat with the exterior, called the heat dissipation rate. By convention, we take the sign of the heat to be positive when it flows from the system to the heat bath. The total heat transport with the surroundings is given by $Q_{\mathrm{tot}}(t) = Th_d(t)$.

According to the flux decomposition, the entropy change could be separated into two different contributions in a straightforward manner as

$$\frac{dS(t)}{dt} = \dot{S}^{(1)}(t) + \dot{S}^{(2)}(t),$$

where

$$\dot{S}^{(1)}(t) = -\sum_{i=1}^{N}\int_{-\infty}^{+\infty} J_i^{\mathrm{mech}}(t,x)\frac{\partial \ln p(t,x,i)}{\partial x}dx$$

is the entropy change due to the mechanical flux and

$$\dot{S}^{(2)}(t) = \int_{-\infty}^{+\infty}\frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)}{p(t,x,j)}dx$$

is the entropy change according to the chemical flux. Also $e_p(t)$ can be decomposed into two components according to the flux decomposition

$$e_p(t) = e_p^{\mathrm{mech}}(t) + e_p^{\mathrm{chem}}(t),$$

where

$$e_p^{\mathrm{mech}}(t) = \sum_{i=1}^{N}\int_{-\infty}^{+\infty}\frac{2\left[J_i^{\mathrm{mech}}(t,x)\right]^2}{\sigma^2(x,i)p(t,x,i)}dx \tag{16}$$

is the entropy production arising from the mechanical flux and

$$e_p^{\mathrm{chem}}(t) = \int_{-\infty}^{+\infty}\tfrac{1}{2}\textstyle\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)q_{ij}(x)}{p(t,x,j)q_{ji}(x)}dx \tag{17}$$

is the contribution of the chemical flux. It is easy to see that

$$e_p^{\mathrm{mech}}(t) \geqslant 0,\quad e_p^{\mathrm{chem}}(t) \geqslant 0,\quad e_p(t) \geqslant 0.$$

The equality $e_p(t) = 0$ is equivalent to $e_p^{\mathrm{mech}}(t) = e_p^{\mathrm{chem}}(t) = 0$ and holds if and only if the system, which is at the steady state, satisfies detailed balance (10). Similarly, the flux decomposition also leads to the decomposition of the heat dissipation rate

$$h_d(t) = h_d^{\mathrm{mech}}(t) + h_d^{\mathrm{chem}}(t),$$

where

$$h_d^{\mathrm{mech}}(t) = \sum_{i=1}^{N}\int_{-\infty}^{+\infty} J_i^{\mathrm{mech}}(t,x)F_i^{\mathrm{mech}}(x)dx,$$

$$h_d^{\mathrm{chem}}(t) = \int_{-\infty}^{+\infty}\frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)F_{ij}^{\mathrm{chem}}(x)dx.$$

The above decompositions are consistent with each other, namely,

$$\dot{S}^{(1)}(t) = e_p^{\mathrm{mech}}(t) - h_d^{\mathrm{mech}}(t),$$

$$\dot{S}^{(2)}(t) = e_p^{\mathrm{chem}}(t) - h_d^{\mathrm{chem}}(t),$$

followed by two more detailed Clausius inequalities

$$\begin{aligned} T\dot{S}^{(1)}(t) + Q_{\mathrm{tot}}^{\mathrm{mech}}(t) &= T\dot{S}^{(1)}(t) + Th_d^{\mathrm{mech}}(t)\\ &= Te_p^{\mathrm{mech}}(t) \geqslant 0,\end{aligned}$$

$$\begin{aligned} T\dot{S}^{(2)}(t) + Q_{\mathrm{tot}}^{\mathrm{chem}}(t) &= T\dot{S}^{(2)}(t) + Th_d^{\mathrm{chem}}(t)\\ &= Te_p^{\mathrm{chem}}(t) \geqslant 0.\end{aligned}$$

B. Three faces of the second law

During the past ten years, it has been found that in both master equation and diffusion systems, the entropy production rate can be decomposed into two non-negative terms, which are the housekeeping heat dissipation rate $Q_{hk}(t)$ and the free energy dissipation rate $f_d(t)$ [34–36,56,57]. The non-negativity of $e_p(t)$, $Q_{hk}(t)$, and $f_d(t)$ is called the three faces of the second law [34,57]. We determine that the same decomposition

$$Te_p(t) = Q_{hk}(t) + f_d(t)$$

and the non-negativity of each term also hold in SDPs (see Sec. VI B for the detailed derivation and proof in the case of high dimension), where the housekeeping heat dissipation rate is given by

$$\begin{aligned} Q_{hk}(t) = {} & \sum_{i=1}^{N} T\int_{-\infty}^{+\infty} J_i^{\mathrm{mech}}(t,x)\frac{2\mathfrak{J}_i^{\mathrm{mech}}(x)}{\sigma^2(x,i)\pi(x,i)}dx\\ & + \int_{-\infty}^{+\infty}\frac{T}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)}dx \end{aligned} \tag{18}$$

and the free energy dissipation rate is given by

$$\begin{aligned} f_d(t) = {} & \sum_{i=1}^{N} T\int_{-\infty}^{+\infty} J_i^{\mathrm{mech}}(t,x)\frac{\partial \ln\frac{\pi(x,i)}{p(t,x,i)}}{\partial x}dx\\ & + \int_{-\infty}^{+\infty}\frac{T}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)\pi(x,j)}{p(t,x,j)\pi(x,i)}dx. \end{aligned} \tag{19}$$

The reason why we call $f_d(t)$ the free energy dissipation rate is that $-f_d(t)$ is just the time derivative of the relative entropy, which is a generalization of the free energy, i.e.,

$$\frac{dF(t)}{dt} = -f_d(t), \tag{20}$$

where

$$F(t) = T\sum_{i=1}^{N}\int_{-\infty}^{+\infty} p(t,x,i)\ln\frac{p(t,x,i)}{\pi(x,i)}dx. \tag{21}$$

The housekeeping heat dissipation rate $Q_{hk}(t) = 0$ if and only if the detailed balance relation (10) is satisfied and has nothing to do with the transient distribution $p(t,x,i)$ (see Sec. VI B for the detailed derivation and proof in the case of high dimension). Breaking of the detailed balance relation (10) indeed implies that the system is driven by either the nonconservative force or gradient of chemical potentials [21]. So $Q_{hk}(t)$ implies the nonequilibrium essence of the system. On the other hand, $f_d(t) = 0$ if and only if the system is at the steady state. So the positivity of $f_d(t)$ implies the spontaneous nonstationarity of the system.

We now derive the extended Clausius inequality. Defining $Q_{ex}(t) = Q_{\mathrm{tot}}(t) - Q_{hk}(t)$, we then obtain

$$\begin{aligned} TdS(t) + Q_{ex}(t) &= Te_p(t) - Q_{\mathrm{tot}}(t) + Q_{ex}(t)\\ &= Te_p(t) - Q_{hk}(t) = f_d(t) \geqslant 0. \end{aligned} \tag{22}$$

C. Decomposition of the housekeeping heat dissipation rate and the free energy dissipation rate

Due to the flux decomposition, $Q_{hk}(t)$ could naturally be decomposed into two parts $Q_{hk}^{\text{mech}}(t)$ and $Q_{hk}^{\text{chem}}(t)$:

$$Q_{hk}^{\text{mech}}(t) = \sum_{i=1}^{N} T \int_{-\infty}^{+\infty} J_i^{\text{mech}}(t,x) \frac{2\mathfrak{J}_i^{\text{mech}}(x)}{\sigma^2(x,i)\pi(x,i)} dx, \quad (23)$$

$$Q_{hk}^{\text{chem}}(t) = \int_{-\infty}^{+\infty} \frac{T}{2} \sum_{i\neq j} J_{x,ij}^{\text{chem}}(t) \ln \frac{q_{ij}(x)\pi(x,i)}{q_{ji}(x)\pi(x,j)} dx. \quad (24)$$

However, the non-negativity of $Q_{hk}^{\text{mech}}(t)$ and $Q_{hk}^{\text{chem}}(t)$ cannot be guaranteed. So we would like to search for another decomposition with both non-negative components.

We note that for a pure diffusion process described by $dX(t) = b(x)dt + \sigma(x)dw(t)$, the housekeeping heat dissipation rate can be rewritten as [35]

$$T \int_{-\infty}^{+\infty} \frac{2\left[b(x) - \frac{1}{2}\sigma^2(x)\frac{\partial \ln \pi(x)}{\partial x}\right]^2}{\sigma^2(x,i)} p(t,x) dx,$$

in which $[b(x) - \frac{1}{2}\sigma^2(x)\frac{\partial \ln \pi(x)}{\partial x}]\pi(x)$ is the steady-state flux. Therefore, we can similarly define a modified version of the housekeeping heat dissipation rate along the diffusion component of the SDP system,

$$\tilde{Q}_{hk}^{\text{mech}}(t) = \sum_{i=1}^{N} T \int_{-\infty}^{+\infty} \frac{2\left[\frac{\mathfrak{J}_i^{\text{mech}}(x)}{\pi(x,i)}\right]^2}{\sigma^2(x,i)} p(t,x,i) dx \geqslant 0,$$

and the remainder is the modified housekeeping heat dissipation rate due to jumping between the chemical states, given by

$$\begin{aligned}\tilde{Q}_{hk}^{\text{chem}}(t) &= Q_{hk}(t) - \tilde{Q}_{hk}^{\text{mech}}(t)\\ &= \int_{-\infty}^{+\infty} T \sum_{i,j} p(t,x,i) q_{ij}(x)\\ &\quad \times \left[\ln \frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)} + \frac{\pi(x,j)q_{ji}(x)}{\pi(x,i)q_{ij}(x)}\right] dx,\end{aligned}$$

which is also non-negative (see Sec. VIC for the detailed derivation and proof in the case of high dimension). Here $\tilde{Q}_{hk}^{\text{mech}}(t) = \tilde{Q}_{hk}^{\text{chem}}(t) = 0$ if and only if the system satisfies the detailed balance relation (10). Therefore,

$$Q_{hk}(t) = \tilde{Q}_{hk}^{\text{chem}}(t) + \tilde{Q}_{hk}^{\text{mech}}(t) \quad (25)$$

is exactly the decomposition of housekeeping heat dissipation rate that we are looking for. This is one of the main results in the present paper.

We then turn to studying the difference between $\tilde{Q}_{hk}^{\text{mech}}(t)$ and $Q_{hk}^{\text{mech}}(t)$, i.e.,

$$\begin{aligned}&Q_{hk}^{\text{mech}}(t) - \tilde{Q}_{hk}^{\text{mech}}(t)\\ &= T \sum_{i=1}^{N} \int_{-\infty}^{+\infty} \mathfrak{J}_i^{\text{mech}}(x) \frac{\partial \frac{p(t,x,i)}{\pi(x,i)}}{\partial x} dx\\ &= -\frac{T}{2} \int_{-\infty}^{+\infty} \sum_{i\neq j} \mathfrak{J}_{x,ij}^{\text{chem}} \left[\frac{p(t,x,j)}{\pi(x,j)} - \frac{p(t,x,i)}{\pi(x,i)}\right] dx. \quad (26)\end{aligned}$$

After defining the relative information of each state (x,i) at time t as $I_R(t,x,i) = \ln \frac{p(t,x,i)}{\pi(x,i)}$, the difference between $\tilde{Q}_{hk}^{\text{mech}}(t)$ and $Q_{hk}^{\text{mech}}(t)$ can be regarded as the flow of exponential relative information under steady-state fluxes along the mechanical diffusion or between different chemical states. More precisely, we define the flow of exponential relative information under the steady-state flux along the mechanical diffusion as

$$J_{ERI}^{\text{mech}}(t) = T \sum_{i=1}^{N} \int_{-\infty}^{+\infty} \mathfrak{J}_i^{\text{mech}}(x) \frac{\partial \frac{p(t,x,i)}{\pi(x,i)}}{\partial x} dx$$

and that between different chemical states as

$$J_{ERI}^{\text{chem}}(t) = \frac{T}{2} \int_{-\infty}^{+\infty} \sum_{i,j} \mathfrak{J}_{x,ij}^{\text{chem}} \left[\frac{p(t,x,j)}{\pi(x,j)} - \frac{p(t,x,i)}{\pi(x,i)}\right] dx.$$

According to Eq. (26), we obtain $J_{ERI}^{\text{mech}}(t) = -J_{ERI}^{\text{chem}}(t)$. It is easy to derive that, for a pure diffusion process or master equation dynamics, $J_{ERI}^{\text{mech}}(t)$ and $J_{ERI}^{\text{chem}}(t)$ always vanish for each t. In conclusion, we found two decompositions of $Q_{hk}(t)$,

$$\begin{aligned}Q_{hk}(t) &= Q_{hk}^{\text{mech}}(t) + Q_{hk}^{\text{chem}}(t)\\ &= \tilde{Q}_{hk}^{\text{mech}}(t) + \tilde{Q}_{hk}^{\text{chem}}(t),\end{aligned}$$

in which

$$\begin{aligned}\tilde{Q}_{hk}^{\text{chem}}(t) &= Q_{hk}^{\text{mech}}(t) - J_{ERI}^{\text{mech}}(t) \geqslant 0,\\ \tilde{Q}_{hk}^{\text{chem}}(t) &= Q_{hk}^{\text{chem}}(t) - J_{ERI}^{\text{chem}}(t) \geqslant 0.\end{aligned}$$

Based on the flux decomposition, we can also decompose the free energy dissipation rate $f_d(t)$, i.e., $f_d(t) = f_d^{\text{mech}}(t) + f_d^{\text{chem}}(t)$, where

$$f_d^{\text{mech}}(t) = \sum_{i=1}^{N} T \int_{-\infty}^{+\infty} J_i^{\text{mech}}(t,x) \frac{\partial \ln \frac{\pi(x,i)}{p(t,x,i)}}{\partial x} dx,$$

$$f_d^{\text{chem}}(t) = \int_{-\infty}^{+\infty} \frac{T}{2} \sum_{i\neq j} J_{x,ij}^{\text{chem}}(t) \ln \frac{p(t,x,i)\pi(x,j)}{p(t,x,j)\pi(x,i)} dx.$$

The $f_d^{\text{mech}}(t)$ and $f_d^{\text{chem}}(t)$ are also not always non-negative. However, after modifying them also by the flows of exponential relative information $J_{ERI}^{\text{mech}}(t)$ and $J_{ERI}^{\text{chem}}(t)$, we obtain two non-negative components (see Sec. VIC for the detailed derivation and proof in the case of high dimension)

$$\begin{aligned}\tilde{f}_d^{\text{mech}}(t) &= f_d^{\text{mech}}(t) - J_{ERI}^{\text{mech}}(t)\\ &= \sum_{i=1}^{N} T \int_{-\infty}^{+\infty} \frac{\sigma^2(x,i)}{2} \left[\frac{\partial \ln \frac{\pi(x,i)}{p(t,x,i)}}{\partial x}\right]^2 p(t,x,i) dx\\ &\geqslant 0,\\ \tilde{f}_d^{\text{chem}}(t) &= f_d^{\text{chem}}(t) - J_{ERI}^{\text{chem}}(t)\\ &= \int_{-\infty}^{+\infty} T \sum_{i,j} p(t,x,i) q_{ij}(x)\\ &\quad \times \left[\ln \frac{p(t,x,i)\pi(x,j)}{p(t,x,j)\pi(x,i)} + \frac{p(t,x,j)\pi(x,i)}{p(t,x,i)\pi(x,j)}\right] dx\\ &\geqslant 0,\end{aligned}$$

and $f_d(t) = \tilde{f}_d^{\text{mech}}(t) + \tilde{f}_d^{\text{chem}}(t)$. Here $\tilde{f}_d^{\text{mech}}(t) = \tilde{f}_d^{\text{chem}}(t) = 0$ if and only if the system is at the steady state.

IV. ONE-DIMENSIONAL SDP UNDER COARSE GRAINING AND INFORMATION THERMODYNAMICS

A. Coarse-grained dynamics

Applying the framework of nonequilibrium thermodynamics under coarse graining [45], we are interested in the nonequilibrium thermodynamics in terms of only the dynamics of the transitions among the chemical states or unidirectional mechanical diffusion. The probability of the system at position x is given by

$$p(t,x) = \sum_{i=1}^{N} p(t,x,i). \tag{27}$$

Summing Eq. (5) over i, we obtain the Fokker-Planck equation for the dynamics of the mechanical motion only

$$\frac{\partial p(t,x)}{\partial t} = \frac{\partial}{\partial x}\left(\frac{1}{2}\tilde{A}(t,x)\frac{\partial p(t,x)}{\partial x} - \tilde{b}(t.x)p(t,x)\right), \tag{28}$$

where

$$\tilde{A}(t,x) = \sum_{i=1}^{N} \mathbb{P}(t,i|x)\sigma^2(x,i),$$

$$\tilde{b}(t,x) = \sum_{i=1}^{N}\left(b(x,i)\mathbb{P}(t,i|x) - \frac{1}{2}\sigma^2(x,i)\frac{\partial \mathbb{P}(t,i|x)}{\partial x}\right),$$

and

$$\mathbb{P}(t,i|x) = \frac{p(t,x,i)}{p(t,x)}$$

is the probability of being in chemical state i conditioned on position x. On the other hand, the probability of the system in chemical state i is given by

$$p_i(t) = \int_{-\infty}^{+\infty} p(t,x,i)dx, \tag{29}$$

followed by the dynamics of transitions among chemical states only given by

$$\frac{dp_i(t)}{dt} = \sum_{j=1}^{N} \tilde{q}_{ji}(t)p_j(t), \tag{30}$$

in which

$$\tilde{q}_{ji}(t) = \int_{-\infty}^{+\infty} \mathbb{P}(t,x|j)q_{ji}(x)dx, \tag{31}$$

where

$$\mathbb{P}(t,x|i) = \frac{p(t,x,i)}{p_i(t)} \tag{32}$$

is the probability of being at position x conditioned on chemical state i.

B. Nonequilibrium thermodynamics of the continuous mechanical diffusion only

The total dynamics of an SDP is decomposed into three different contributions: mesostate dynamics described by $p(t,x)$ under coarse graining, microstate dynamics for every fixed mesostate x according to $\mathbb{P}(t,i|x)$, and the remaining dynamics that characterizes the difference of mechanical diffusions under different chemical states. We use the subscripts meso, micro, and rem to represent the three different dynamics components.

For the dynamics of the mesostates, the entropy is given by

$$S_{\text{meso}}^{\text{mech}}(t) = -\int_{-\infty}^{+\infty} p(t,x)\ln p(t,x)dx. \tag{33}$$

The microscopic entropy of a mesostate x is defined as

$$\mathbb{S}(t,x) = -\sum_{i=1}^{N} \mathbb{P}(t,i|x)\ln \mathbb{P}(t,i|x). \tag{34}$$

We then obtain the total microstate entropy of the system as

$$\begin{aligned} S_{\text{micro}}^{\text{mech}}(t) &= \int_{-\infty}^{+\infty} \mathbb{S}(t,x)p(t,x)dx \\ &= -\int_{-\infty}^{+\infty}\sum_{i=1}^{N} p(t,x,i)\ln \mathbb{P}(t,i|x)dx. \end{aligned} \tag{35}$$

It turns out that the remaining dynamics has no contribution to the total entropy of the system which is given by

$$S(t) = S_{\text{meso}}^{\text{mech}}(t) + S_{\text{micro}}^{\text{mech}}(t). \tag{36}$$

By making use of the evolution of the dynamics of the mesostates (28) and the dynamics of the original SDP (7), we can decompose the evolution of the total entropy into three contributions according to three dynamics components (see Sec. VII B for the detailed derivation in the case of high dimension)

$$\frac{dS(t)}{dt} = \dot{S}^{(1,\text{mech})}(t) + \dot{S}^{(2,\text{mech})}(t) + \dot{S}^{(3,\text{mech})}(t). \tag{37}$$

The first term $\dot{S}^{(1,\text{mech})}(t)$ denotes the entropy change due to the coarse-grained mesostate dynamics and it is just the time evolution of the coarse-grained mesostate dynamics $S_{\text{meso}}^{\text{mech}}(t)$, i.e.,

$$\dot{S}^{(1,\text{mech})}(t) = -\int_{-\infty}^{+\infty}\frac{\partial p(t,x)}{\partial t}\ln p(t,x)dx = \frac{dS_{\text{meso}}^{\text{mech}}(t)}{dt}. \tag{38}$$

The second one $\dot{S}^{(2,\text{mech})}(t)$ is the entropy change of microstate dynamics and is evaluated as the ensemble average of the microstates entropy change within each mesostate,

$$\dot{S}^{(2,\mathrm{mech})}(t) = \int_{-\infty}^{+\infty} p(t,x)\left[\sum_{i\neq j}\mathbb{P}(t,i|x)q_{ij}(x)\ln\frac{\mathbb{P}(t,i|x)}{\mathbb{P}(t,j|x)}\right]dx.$$

It is easy to derive that the entropy change of the microstate dynamics is just the entropy change arising from the chemical flux in Sec. III A, i.e.,

$$\dot{S}^{(2,\mathrm{mech})}(t) = \dot{S}^{(2)}(t).$$

The third contribution $\dot{S}^{(3,\mathrm{mech})}(t)$ is the entropy change due to the remaining dynamics

$$\dot{S}^{(3,\mathrm{mech})}(t) = -\int_{-\infty}^{+\infty} p(t,x) \times\left(\sum_{i=1}^{N}\mathbb{J}(t,i|x)\frac{\partial\ln\mathbb{P}(t,i|x)}{\partial x}\right)dx,$$

where

$$\mathbb{J}(t,i|x) = b(x,i)\mathbb{P}(t,i|x) - \frac{1}{2}\sigma^2(x,i)\frac{\partial\mathbb{P}(t,i|x)}{\partial x}$$

is the diffusion flux according to the conditional probability $\mathbb{P}(t,i|x)$. It is very clear that both the second and third contributions arise from the transitions between the microstates, i.e.,

$$\dot{S}^{(2,\mathrm{mech})}(t) + \dot{S}^{(3,\mathrm{mech})}(t) = \frac{dS^{\mathrm{mech}}_{\mathrm{micro}}(t)}{dt}, \tag{39}$$

which together contain all the information of entropy change that we lose under coarse graining.

We can also decompose the entropy production rate into three contributions according to the mesostate, microstate, and remaining subsystems (see Sec. VII B for the detailed derivation in the case of high dimension)

$$e_p(t) = e^{\mathrm{mech}}_{p,\mathrm{meso}}(t) + e^{\mathrm{mech}}_{p,\mathrm{micro}}(t) + e^{\mathrm{mech}}_{p,\mathrm{rem}}(t), \tag{40}$$

in which

$$e^{\mathrm{mech}}_{p,\mathrm{meso}}(t) = \int_{-\infty}^{+\infty}\frac{2\left[J^{\mathrm{mech}}_{\mathrm{meso}}(t,x)\right]^2}{\tilde{A}(t,x)p(t,x)}dx, \tag{41}$$

where $J^{\mathrm{mech}}_{\mathrm{meso}}(t,x) = \tilde{b}(t.x)p(t,x) - \frac{1}{2}\tilde{A}(t,x)\frac{\partial p(t,x)}{\partial x}$ is the diffusion flux of the coarse-grained dynamics of the mesostates,

$$e^{\mathrm{mech}}_{p,\mathrm{micro}}(t) = \int_{-\infty}^{+\infty} p(t,x) \times\left[\sum_{i\neq j}\mathbb{P}(t,i|x)q_{ij}(x)\ln\frac{\mathbb{P}(t,i|x)q_{ij}(x)}{\mathbb{P}(t,j|x)q_{ji}(x)}\right]dx$$

is equal to $e^{\mathrm{chem}}_p(t)$, and

$$\begin{aligned} e^{\mathrm{mech}}_{p,\mathrm{rem}}(t) &= e^{\mathrm{mech}}_p(t) - e^{\mathrm{mech}}_{p,\mathrm{meso}}(t) \\ &= \int_{-\infty}^{+\infty} 2\left[\sum_{i=1}^{N}\frac{(\mathbb{J}(t,i|x))^2}{\mathbb{P}(t,i|x)\sigma^2(x,i)} - \frac{\tilde{b}^2(t,x)}{\tilde{A}(t,x)}\right] \\ &\quad\times p(t,x)dx \end{aligned}$$

arises from the difference between the diffusion processes caused by the transition between chemical states [57]. We can prove that $e^{\mathrm{mech}}_{p,\mathrm{rem}}(t) \geqslant 0$ (see Sec. VII B for the detailed derivation in the case of high dimension). Therefore, the three contributions of the total entropy production rate are all non-negative, i.e.,

$$e^{\mathrm{mech}}_{p,\mathrm{meso}}(t) \geqslant 0, \quad e^{\mathrm{mech}}_{p,\mathrm{micro}}(t) \geqslant 0, \quad e^{\mathrm{mech}}_{p,\mathrm{rem}}(t) \geqslant 0. \tag{42}$$

Since $e^{\mathrm{mech}}_{p,\mathrm{micro}}(t) + e^{\mathrm{mech}}_{p,\mathrm{rem}}(t) \geqslant 0$, we would underestimate the entropy production rate of the total system after coarse graining.

The heat dissipation rate can also be decomposed into three terms

$$h_d(t) = h^{\mathrm{mech}}_{d,\mathrm{meso}}(t) + h^{\mathrm{mech}}_{d,\mathrm{micro}}(t) + h^{\mathrm{mech}}_{d,\mathrm{rem}}(t), \tag{43}$$

where

$$\begin{aligned} h^{\mathrm{mech}}_{d,\mathrm{meso}}(t) &= \int_{-\infty}^{+\infty} J^{\mathrm{mech}}_{\mathrm{meso}}(t,x)F^{\mathrm{mech}}_{\mathrm{meso}}(t,x)dx, \\ h^{\mathrm{mech}}_{d,\mathrm{micro}}(t) &= \int_{-\infty}^{+\infty} p(t,x)\left[\frac{1}{2}\sum_{i\neq j}(\mathbb{P}(t,i|x)q_{ij}(x)\right. \\ &\quad\left. - \mathbb{P}(t,j|x)q_{ji}(x))\ln\frac{q_{ij}(x)}{q_{ji}(x)}\right]dx \\ &= h^{\mathrm{chem}}_d(t), \\ h^{\mathrm{mech}}_{d,\mathrm{rem}}(t) &= h^{\mathrm{mech}}_d(t) - h^{\mathrm{mech}}_{d,\mathrm{meso}}(t) \\ &= \int_{-\infty}^{+\infty}\left[\sum_{i=1}^{N} J^{\mathrm{mech}}_i(t,x)F^{\mathrm{mech}}_i(t,x)\right. \\ &\quad\left. - J^{\mathrm{mech}}_{\mathrm{meso}}(t,x)F^{\mathrm{mech}}_{\mathrm{meso}}(t,x)\right]dx, \end{aligned}$$

where $F^{\mathrm{mech}}_{\mathrm{meso}}(t,x) = \frac{2\tilde{b}(t,x)}{\tilde{A}(t,x)}$ is the force along the coarse-grained diffusion system. The above decompositions are consistent with each other, i.e.,

$$\begin{aligned} \dot{S}^{(1,\mathrm{mech})}(t) &= e^{\mathrm{mech}}_{p,\mathrm{meso}}(t) - h^{\mathrm{mech}}_{d,\mathrm{meso}}(t), \\ \dot{S}^{(2,\mathrm{mech})}(t) &= e^{\mathrm{mech}}_{p,\mathrm{micro}}(t) - h^{\mathrm{mech}}_{d,\mathrm{micro}}(t), \\ \dot{S}^{(3,\mathrm{mech})}(t) &= e^{\mathrm{mech}}_{p,\mathrm{rem}}(t) - h^{\mathrm{mech}}_{d,\mathrm{rem}}(t), \end{aligned} \tag{44}$$

followed by the more detailed Clausius inequalities

$$\begin{aligned} T\dot{S}^{(1,\mathrm{mech})}(t) + Q^{\mathrm{mech}}_{\mathrm{tot,meso}}(t) &= Te^{\mathrm{mech}}_{p,\mathrm{meso}}(t) \geqslant 0, \\ T\dot{S}^{(2,\mathrm{mech})}(t) + Q^{\mathrm{mech}}_{\mathrm{tot,micro}}(t) &= Te^{\mathrm{mech}}_{p,\mathrm{micro}}(t) \geqslant 0, \\ T\dot{S}^{(3,\mathrm{mech})}(t) + Q^{\mathrm{mech}}_{\mathrm{tot,rem}}(t) &= Te^{\mathrm{mech}}_{p,\mathrm{rem}}(t) \geqslant 0. \end{aligned}$$

C. Nonequilibrium thermodynamics of the discrete chemical kinetics only

Similar to the preceding section, we can write

$$S(t) = S^{\mathrm{chem}}_{\mathrm{meso}}(t) + S^{\mathrm{chem}}_{\mathrm{micro}}(t), \tag{45}$$

where

$$S_{\text{meso}}^{\text{chem}}(t) = -\sum_{i=1}^{N} p_i(t) \ln p_i(t) \tag{46}$$

is the entropy due to the dynamics of mesostates and

$$S_{\text{micro}}^{\text{chem}}(t) = \sum_{i=1}^{N} \mathbb{S}(t,i) p_i(t) \tag{47}$$

is the ensemble average of the entropy within each mesostate

$$\mathbb{S}(t,i) = -\int_{-\infty}^{+\infty} \mathbb{P}(t,x|i) \ln \mathbb{P}(t,x|i) dx. \tag{48}$$

Then (see Sec. VII C for the detailed derivation in the case of high dimension)

$$\frac{dS(t)}{dt} = \dot{S}^{(1,\text{chem})}(t) + \dot{S}^{(2,\text{chem})}(t) + \dot{S}^{(3,\text{chem})}(t), \tag{49}$$

in which

$$\begin{aligned} \dot{S}^{(1,\text{chem})}(t) &= \frac{1}{2}\sum_{i\neq j}[p_i(t)\tilde{q}_{ij}(t) - p_j(t)\tilde{q}_{ji}(t)] \ln \frac{p_i(t)}{p_j(t)} \\ &= \frac{dS_{\text{meso}}^{\text{chem}}(t)}{dt}, \end{aligned} \tag{50}$$

$$\begin{aligned} \dot{S}^{(2,\text{chem})}(t) &= \sum_{i=1}^{N} p_i(t) \int_{-\infty}^{+\infty} -\mathbb{J}_i(t,x)\frac{\partial \ln \mathbb{P}(t,x|i)}{\partial x} dx \\ &= \dot{S}^{(1)}(t), \end{aligned} \tag{51}$$

where $\mathbb{J}_i(t,x) = b(x,i)\mathbb{P}(t,x|i) - \frac{1}{2}\sigma^2(x,i)\frac{\partial \mathbb{P}(t,x|i)}{\partial x}$, and

$$\begin{aligned} \dot{S}^{(3,\text{chem})}(t) &= \frac{dS_{\text{micro}}^{\text{chem}}(t)}{dt} - \dot{S}^{(2,\text{chem})}(t) \\ &= \sum_{i\neq j} p_i(t) \int_{-\infty}^{+\infty} \mathbb{P}(t,x|i) q_{ij}(x) \\ &\quad \times \ln \frac{\mathbb{P}(t,x|i)}{\mathbb{P}(t,x|j)} dx. \end{aligned} \tag{52}$$

The entropy production rate $e_p(t)$ can also be decomposed into three contributions (see Sec. VII C for the detailed derivation in the case of high dimension)

$$e_p(t) = e_{p,\text{meso}}^{\text{chem}}(t) + e_{p,\text{micro}}^{\text{chem}}(t) + e_{p,\text{rem}}^{\text{chem}}(t), \tag{53}$$

in which

$$e_{p,\text{meso}}^{\text{chem}}(t) = \frac{1}{2}\sum_{i\neq j}[p_i(t)\tilde{q}_{ij}(t) - p_j(t)\tilde{q}_{ji}(t)] \ln \frac{p_i(t)\tilde{q}_{ij}(t)}{p_j(t)\tilde{q}_{ji}(t)}, \tag{54}$$

$$\begin{aligned} e_{p,\text{micro}}^{\text{chem}}(t) &= \sum_{i=1}^{N} p_i(t) \int_{-\infty}^{+\infty} \frac{2(\mathbb{J}_i(t,x))^2}{\sigma^2(x,i)\mathbb{P}(t,x|i)} dx \\ &= e_p^{\text{mech}}(t), \end{aligned} \tag{55}$$

and

$$e_{p,\text{rem}}^{\text{chem}}(t) = \sum_{i\neq j} p_i(t)\tilde{q}_{ij}(t)\mathbb{D}_{ij}(t), \tag{56}$$

where

$$\mathbb{D}_{ij}(t) = \int_{-\infty}^{+\infty} f_{ij}(t,x) \ln \frac{f_{ij}(t,x)}{f_{ji}(t,x)} dx,$$

$$f_{ij}(t,x) = \frac{\mathbb{P}(t,x|i)q_{ij}(x)}{\tilde{q}_{ij}(t)}.$$

We can prove that (see Sec. VII C for the detailed proof in the case of high dimension)

$$\mathbb{D}_{ij}(t) \geqslant 0;$$

therefore,

$$e_{p,\text{meso}}^{\text{chem}}(t) \geqslant 0, \quad e_{p,\text{micro}}^{\text{chem}}(t) \geqslant 0, \quad e_{p,\text{rem}}^{\text{chem}}(t) \geqslant 0.$$

Finally, we give the corresponding decomposition of the heat dissipation rate

$$h_d(t) = h_{d,\text{meso}}^{\text{chem}}(t) + h_{d,\text{micro}}^{\text{chem}}(t) + h_{d,\text{rem}}^{\text{chem}}(t), \tag{57}$$

where

$$h_{d,\text{meso}}^{\text{chem}}(t) = \frac{1}{2}\sum_{i,j}[p_i(t)\tilde{q}_{ij}(t) - p_j(t)\tilde{q}_{ji}(t)] \ln \frac{\tilde{q}_{ij}(t)}{\tilde{q}_{ji}(t)}, \tag{58}$$

$$\begin{aligned} h_{d,\text{micro}}^{\text{chem}}(t) &= \sum_{i=1}^{N} p_i(t) \int_{-\infty}^{+\infty} \mathbb{J}_i(t,x) F_i^{\text{mech}}(x) dx \\ &= h_d^{\text{mech}}(t), \end{aligned} \tag{59}$$

$$\begin{aligned} h_{d,\text{rem}}^{\text{chem}}(t) &= \sum_{i\neq j} p_i(t)\tilde{q}_{ij}(t) \int_{-\infty}^{+\infty} f_{ij}(t,x) \\ &\quad \times \ln \frac{f_{ij}(t,x)\mathbb{P}(t,x|j)}{f_{ji}(t,x)\mathbb{P}(t,x|i)} dx, \end{aligned} \tag{60}$$

followed by

$$\begin{aligned} \dot{S}^{(1,\text{chem})}(t) &= e_{p,\text{meso}}^{\text{chem}}(t) - h_{d,\text{meso}}^{\text{chem}}(t), \\ \dot{S}^{(2,\text{chem})}(t) &= e_{p,\text{micro}}^{\text{chem}}(t) - h_{d,\text{micro}}^{\text{chem}}(t), \\ \dot{S}^{(3,\text{chem})}(t) &= e_{p,\text{rem}}^{\text{chem}}(t) - h_{d,\text{rem}}^{\text{chem}}(t). \end{aligned}$$

D. Information thermodynamics of a one-dimensional SDP

Applying the framework of information thermodynamics in [46],

$$S_{\text{meso}}^{\text{mech}}(t) + S_{\text{meso}}^{\text{chem}}(t) - S(t) = I(t), \tag{61}$$

in which $I(t)$ denotes the mutual information [46]

$$I(t) = \sum_{i=1}^{N} \int_{-\infty}^{+\infty} p(t,x,i) \ln \frac{p(t,x,i)}{p(t,x)p_i(t)} dx, \tag{62}$$

which measures the correlations that quantify how much one subsystem "knows" about the other. It should be noted that

$$I(t) \geqslant 0,$$

where $I(t) = 0$ if and only if the two subsystems are statistically independent.

The evolution of $I(t)$ describes a flow of information and can be decomposed into two parts

$$\frac{dI(t)}{dt} = \sum_{i=1}^{N}\int_{-\infty}^{+\infty} J_i^{\text{mech}}(t,x)\frac{\partial \ln \mathbb{P}(t,i|x)}{\partial x}dx - \int_{-\infty}^{+\infty}\frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\text{chem}}(t)\ln\frac{\mathbb{P}(t,x|i)}{\mathbb{P}(t,x|j)}dx.$$

We denote the two parts of information flow by $\dot{I}^{\text{mech}}(t)$ and $\dot{I}^{\text{chem}}(t)$, i.e.,

$$\frac{dI(t)}{dt} = \dot{I}^{\text{mech}}(t) + \dot{I}^{\text{chem}}(t), \tag{63}$$

where

$$\begin{aligned}\dot{I}^{\text{mech}}(t) &= \sum_{i=1}^{N}\int_{-\infty}^{+\infty} J_i^{\text{mech}}(t,x)\frac{\partial \ln \mathbb{P}(t,i|x)}{\partial x}dx\\ &= -\dot{S}^{(3,\text{mech})}(t),\end{aligned} \tag{64}$$

$$\begin{aligned}\dot{I}^{\text{chem}}(t) &= -\int_{-\infty}^{+\infty}\frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\text{chem}}(t)\ln\frac{\mathbb{P}(t,x|i)}{\mathbb{P}(t,x|j)}dx\\ &= -\dot{S}^{(3,\text{chem})}(t).\end{aligned} \tag{65}$$

Taking the derivative of $S_{\text{meso}}^{\text{mech}}(t) + S_{\text{meso}}^{\text{chem}}(t) - S(t) = I(t)$, we have

$$e_p^{\text{mech}}(t) = \frac{dS_{\text{meso}}^{\text{mech}}(t)}{dt} + h_d^{\text{mech}}(t) - \dot{I}^{\text{mech}}(t), \tag{66}$$

$$e_p^{\text{chem}}(t) = \frac{dS_{\text{meso}}^{\text{chem}}(t)}{dt} + h_d^{\text{chem}}(t) - \dot{I}^{\text{chem}}(t). \tag{67}$$

At the steady state, the entropy change and total information flow would vanish

$$\frac{dS(t)}{dt} = 0, \quad \frac{dS_{\text{meso}}^{\text{mech}}(t)}{dt} = 0, \quad \frac{dS_{\text{meso}}^{\text{chem}}(t)}{dt} = 0,$$

and

$$\dot{I}^{\text{mech}} + \dot{I}^{\text{chem}} = \frac{dI(t)}{dt} = 0.$$

Defining $\dot{I} = \dot{I}^{\text{chem}}$, we have $\dot{I}^{\text{mech}} = -\dot{I}$; then Eqs. (66) and (67) can be rewritten as

$$e_p^{\text{mech}} = h_d^{\text{mech}} + \dot{I} \geqslant 0, \tag{68}$$

$$e_p^{\text{chem}} = h_d^{\text{chem}} - \dot{I} \geqslant 0, \tag{69}$$

followed by $h_d^{\text{mech}} + h_d^{\text{chem}} = e_p^{\text{mech}} + e_p^{\text{chem}} = e_p$, which is the first law of thermodynamics.

It is well known that a molecular motor transforms the chemical energy h_d^{chem} to the mechanical energy h_d^{mech}, which implies that $h_d^{\text{chem}} > 0$ and $h_d^{\text{mech}} < 0$, but $h_d^{\text{chem}} - (-h_d^{\text{mech}}) > 0$. Once $\dot{I} > 0$, according to (69), the chemical energy takes the information flow $\dot{I}$ as its lower bound $h_d^{\text{chem}} \geqslant \dot{I}$ and the extracted mechanical energy $-h_d^{\text{mech}}$ has an upper bound $\dot{I}$, i.e., $-h_d^{\text{mech}} \leqslant \dot{I}$ according to (68).

V. HIGH-DIMENSIONAL SDP AND FLUX DECOMPOSITION

In this section, we consider a d-dimensional SDP, i.e., $X(t)$ has a state space of $\mathbb{R}^d$. The SDP $(X(t),\alpha(t))$ satisfies [13]

$$dX(t) = b(X(t),\alpha(t))dt + \sigma(X(t),\alpha(t))dW(t), \tag{70}$$

$$\begin{aligned}P(\alpha(t+\Delta t) = j|\alpha(t) = i, X(s),\alpha(s), s \leqslant t)&\\ = q_{ij}(X(t))\Delta t + o(\Delta t) \quad \text{for } i \neq j,&\end{aligned} \tag{71}$$

where $b(\cdot,\cdot):\mathbb{R}^d\times M\to\mathbb{R}^d$ is smooth; $\sigma(\cdot,\cdot):\mathbb{R}^d\times M\to\mathbb{R}^d\times\mathbb{R}^d$ is smooth, nonsingular, and bounded matrix for any $x\in\mathbb{R}^d$ and $i\in M$; and $W(t)$ is an $\mathbb{R}^d$-valued standard Brownian motion. Mathematically, we also need the diffusion coefficients $A(x,i) = \sigma(x,i)\sigma^T(x,i)$ satisfying [21] the following conditions: (i) $A(x,i)$ is positive definite and bounded for any $x\in\mathbb{R}^d$ and $i\in M$ and (ii) for the local ellipse condition, for any $x\in\mathbb{R}^d$ and $i\in M$, there exists $r(x,i) > 0$ such that

$$\sum_{k,l=1}^{d} a_{kl}(x,i)\xi_k\xi_l \geqslant r(x,i)\sum_{k=1}^{d}\xi_k^2, \quad (\xi_1,\xi_2,\ldots,\xi_d)\in\mathbb{R}^d.$$

The stochastic integral $\sigma(X(t),\alpha(t))dW(t)$ is in the anti-Itô form [27,49,50], which is defined through the corresponding Fokker-Planck equation [21]

$$\frac{\partial p(t,x,i)}{\partial t} = \nabla\cdot\left[\frac{1}{2}A(x,i)\nabla p(t,x,i) - b(x,i)p(t,x,i)\right] + \sum_{j=1}^{N} p(t,x,j)q_{ji}(x) \quad \text{for any } x\in\mathbb{R}^d,\ i\in M. \tag{72}$$

Note that this anti-Itô form is neither Stratonovich nor a postpoint stochastic integral in the high-dimensional case, although it matches the postpoint integral in the one-dimensional case. Its justification comes from the convergence theorem from the underdamped second-order dynamics to the corresponding overdamped limit [49,50]. Physically, it comes also from the local fluctuation-dissipation relation.

In the high-dimensional case, an SDP could be described as N different diffusion processes sitting on N parallel d-dimensional planes. We can define the mechanical flux $J_i^{\text{mech}}(t,x)$ and chemical flux $J_x^{\text{chem}}(t,i)$, as we have done for one-dimensional case, such that

$$\frac{\partial p(t,x,i)}{\partial t} = -\nabla\cdot J_i^{\text{mech}}(t,x) + J_x^{\text{chem}}(t,i), \tag{73}$$

where

$$J_i^{\text{mech}}(t,x) = b(x,i)p(t,x,i) - \tfrac{1}{2}A(x,i)\nabla p(t,x,i), \tag{74}$$

$$J_x^{\text{chem}}(t,i) = \sum_{j=1}^{N} J_{x,ji}^{\text{chem}}(t), \tag{75}$$

$$J_{x,ji}^{\text{chem}}(t) = p(t,x,j)q_{ji}(x) - p(t,x,i)q_{ij}(x). \tag{76}$$

At the steady state, the unique stationary distribution of the SDP $\{\pi(x,i)\}$ satisfies

$$\nabla \cdot \mathfrak{J}_i^{\mathrm{mech}}(x) = \mathfrak{J}_x^{\mathrm{chem}}(i) = \sum_{j\neq i} \mathfrak{J}_{x,ji}^{\mathrm{chem}}, \tag{77}$$

where $\mathfrak{J}_i^{\mathrm{mech}}(x)$ and $\mathfrak{J}_{x,ji}^{\mathrm{chem}}$ are the stationary fluxes given by the diffusion component and the transition between the chemical states, i.e.,

$$\mathfrak{J}_i^{\mathrm{mech}}(x) = b(x,i)\pi(x,i) - \tfrac{1}{2}A(x,i)\nabla\pi(x,i),$$
$$\mathfrak{J}_{x,ji}^{\mathrm{chem}} = \pi(x,j)q_{ji}(x) - \pi(x,i)q_{ij}(x).$$

The detailed balance condition in the high-dimensional case is

$$\begin{aligned} 2A^{-1}(x,i)b(x,i) &= \nabla \ln \pi(x,i), \\ \pi(x,i)q_{ij}(x) &= \pi(x,j)q_{ji}(x), \end{aligned} \tag{78}$$

which is equivalent to

$$\mathfrak{J}_i^{\mathrm{mech}}(x) \equiv 0, \quad \mathfrak{J}_{x,ij}^{\mathrm{chem}} \equiv 0 \tag{79}$$

for any $x \in \mathbb{R}^d$ and $i,j \in M$.

VI. DECOMPOSITION OF THE ENTROPY PRODUCTION RATE IN A HIGH-DIMENSIONAL SDP

A. Decomposition based on flux decomposition

The entropy of the system is defined as

$$S(t) = -\sum_{i=1}^{N} \int_{\mathbb{R}^d} p(t,x,i)\ln p(t,x,i)dx. \tag{80}$$

Then, by using the Fokker-Planck equation (72), we can derive

$$\frac{dS(t)}{dt} = e_p(t) - h_d(t), \tag{81}$$

where

$$\begin{aligned} e_p(t) = &\sum_{i=1}^{N} \int_{\mathbb{R}^d} \frac{J_i^{\mathrm{mech}}(t,x)\cdot \left\{[2A^{-1}(x,i)]J_i^{\mathrm{mech}}(t,x)\right\}}{p(t,x,i)}dx \\ &+ \int_{\mathbb{R}^d} \frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)q_{ij}(x)}{p(t,x,j)q_{ji}(x)}dx \end{aligned} \tag{82}$$

is the instantaneous entropy production rate [21], and noting that $F_i^{\mathrm{mech}}(x) = 2A^{-1}(x,i)b(x,i)$ and $F_{ij}^{\mathrm{chem}}(x) = \ln\frac{q_{ij}(x)}{q_{ji}(x)}$ are the force along the diffusion and the force between chemical states [27,28], we obtain

$$\begin{aligned} h_d(t) = &\sum_{i=1}^{N} \int_{\mathbb{R}^d} J_i^{\mathrm{mech}}(t,x)\cdot F_i^{\mathrm{mech}}(x)dx \\ &+ \int_{\mathbb{R}^d} \frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)F_{ij}^{\mathrm{chem}}(x)dx, \end{aligned} \tag{83}$$

which is due to the exchange of heat with the exterior and is called the heat dissipation rate [52]. The total heat $Q_{\mathrm{tot}}(t)$ conducting with the surroundings is equivalent to the heat dissipation rate $h_d(t)$:

$$Q_{\mathrm{tot}}(t) = Th_d(t). \tag{84}$$

The change of entropy $dS(t)$ can be separated into the mechanical and chemical components due to the decomposition of the flux

$$\frac{dS(t)}{dt} = \dot{S}^{(1)}(t) + \dot{S}^{(2)}(t),$$

where

$$\dot{S}^{(1)}(t) = -\sum_{i=1}^{N} \int_{\mathbb{R}^d} J_i^{\mathrm{mech}}(t,x)\cdot \nabla \ln p(t,x,i)dx,$$
$$\dot{S}^{(2)}(t) = \int_{\mathbb{R}^d} \frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)}{p(t,x,j)}dx.$$

Similar to the one-dimensional case, we can derive that

$$e_p(t) = e_p^{\mathrm{mech}}(t) + e_p^{\mathrm{chem}}(t),$$

where

$$\begin{aligned} e_p^{\mathrm{mech}}(t) = &\sum_{i=1}^{N} \int_{\mathbb{R}^d} J_i^{\mathrm{mech}}(t,x)\cdot \left\{[2A^{-1}(x,i)]J_i^{\mathrm{mech}}(t,x)\right\} \\ &\times \frac{1}{p(t,x,i)}dx, \end{aligned} \tag{85}$$

$$e_p^{\mathrm{chem}}(t) = \int_{\mathbb{R}^d} \frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)q_{ij}(x)}{p(t,x,j)q_{ji}(x)}dx, \tag{86}$$

and

$$h_d(t) = h_d^{\mathrm{mech}}(t) + h_d^{\mathrm{chem}}(t),$$

with

$$h_d^{\mathrm{mech}}(t) = \sum_{i=1}^{N} \int_{\mathbb{R}^d} J_i^{\mathrm{mech}}(t,x)\cdot F_i^{\mathrm{mech}}(x)dx,$$
$$h_d^{\mathrm{chem}}(t) = \int_{\mathbb{R}^d} \frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)F_{ij}^{\mathrm{chem}}(x)dx.$$

It is easy to see that

$$e_p^{\mathrm{mech}}(t) \geqslant 0, \quad e_p^{\mathrm{chem}}(t) \geqslant 0, \quad e_p(t) \geqslant 0 \tag{87}$$

and the equalities hold if and only if the system satisfies the detailed balance relation (78) and is at the steady state. Based on these decompositions, the following more detailed Clausius inequalities are satisfied:

$$T\dot{S}^{(1)}(t) + Q_{\mathrm{tot}}^{\mathrm{mech}}(t) = Te_p^{\mathrm{mech}}(t) \geqslant 0,$$
$$T\dot{S}^{(2)}(t) + Q_{\mathrm{tot}}^{\mathrm{chem}}(t) = Te_p^{\mathrm{chem}}(t) \geqslant 0.$$

B. Three faces of the second law

For a high-dimensional SDP system, we first give the expressions of housekeeping heat dissipation rate $Q_{hk}(t)$ and free energy dissipation rate $f_d(t)$:

$$\begin{aligned} Q_{hk}(t) = &\sum_{i=1}^{N} T\int_{\mathbb{R}^d} \frac{J_i^{\mathrm{mech}}(t,x)\cdot \left\{[2A^{-1}(x,i)]\mathbf{J}_i^{\mathrm{mech}}(x)\right\}}{\pi(x,i)}dx \\ &+ \int_{\mathbb{R}^d} \frac{T}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)}dx, \end{aligned} \tag{88}$$

$$f_d(t) = \sum_{i=1}^{N} T \int_{\mathbb{R}^d} J_i^{\mathrm{mech}}(t,x) \cdot \left(\nabla \ln \frac{\pi(x,i)}{p(t,x,i)}\right) dx + \int_{\mathbb{R}^d} \frac{T}{2} \sum_{i,j} J_{x,ij}^{\mathrm{chem}}(t) \ln \frac{p(t,x,i)\pi(x,j)}{p(t,x,j)\pi(x,i)} dx. \tag{89}$$

The entropy production rate of the SDP system can be decomposed as $Te_p(t) = Q_{hk}(t) + f_d(t)$ and the non-negativity of each term holds, which is called three faces of the second law together with the non-negativity of $e_p(t)$ [34,57].

We give the derivation and proof as follows:

$$\begin{aligned}
Q_{hk}(t) + f_d(t) &= \sum_{i=1}^{N} T \int_{\mathbb{R}^d} \frac{J_i^{\mathrm{mech}}(t,x) \cdot \{[2A^{-1}(x,i)]\mathfrak{J}_i^{\mathrm{mech}}(x)\}}{\pi(x,i)} dx + \int_{\mathbb{R}^d} \frac{T}{2} \sum_{i \neq j} J_{x,ij}^{\mathrm{chem}}(t) \ln \frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)} dx \\
&\quad + \sum_{i=1}^{N} T \int_{\mathbb{R}^d} J_i^{\mathrm{mech}}(t,x) \cdot \left(\nabla \ln \frac{\pi(x,i)}{p(t,x,i)}\right) dx + \int_{\mathbb{R}^d} \frac{T}{2} \sum_{i \neq j} J_{x,ij}^{\mathrm{chem}}(t) \ln \frac{p(t,x,i)\pi(x,j)}{p(t,x,j)\pi(x,i)} dx \\
&= \sum_{i=1}^{N} T \int_{\mathbb{R}^d} J_i^{\mathrm{mech}}(t,x) \cdot \left[2A^{-1}(x,i) \frac{\mathfrak{J}_i^{\mathrm{mech}}(x)}{\pi(x,i)} + \nabla \ln \frac{\pi(x,i)}{p(t,x,i)}\right] dx \\
&\quad + \int_{\mathbb{R}^d} \frac{T}{2} \sum_{i \neq j} J_{x,ij}^{\mathrm{chem}}(t) \left[\ln \frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)} + \ln \frac{p(t,x,i)\pi(x,j)}{p(t,x,j)\pi(x,i)}\right] dx \\
&= \sum_{i=1}^{N} T \int_{\mathbb{R}^d} \frac{J_i^{\mathrm{mech}}(t,x) \cdot \{[2A^{-1}(x,t)]J_i^{\mathrm{mech}}(t,x)\}}{p(t,x,i)} dx + \int_{\mathbb{R}^d} \frac{T}{2} \sum_{i \neq j} J_{x,ij}^{\mathrm{chem}}(t) \ln \frac{p(t,x,i)q_{ij}(x)}{p(t,x,j)q_{ji}(x)} dx \\
&= Te_p(t).
\end{aligned}$$

Next we can prove the non-negativity of $Q_{hk}(t)$ and $f_d(t)$,

$$\begin{aligned}
Q_{hk}(t) &= \sum_{i=1}^{N} T \int_{\mathbb{R}^d} \frac{J_i^{\mathrm{mech}}(t,x) \cdot \{[2A^{-1}(x,i)]\mathfrak{J}_i^{\mathrm{mech}}(x)\}}{\pi(x,i)} dx + \int_{\mathbb{R}^d} \frac{T}{2} \sum_{i \neq j} J_{x,ij}^{\mathrm{chem}}(t) \ln \frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)} dx \\
&= \sum_{i=1}^{N} T \int_{\mathbb{R}^d} \frac{J_i^{\mathrm{mech}}(t,x) \cdot \{[2A^{-1}(x,i)]\mathfrak{J}_i^{\mathrm{mech}}(x)\}}{\pi(x,i)} dx - \sum_{i=1}^{N} T \int_{\mathbb{R}^d} \nabla \cdot \mathfrak{J}_i^{\mathrm{mech}}(x) \frac{p(t,x,i)}{\pi(x,i)} dx \\
&\quad + \int_{\mathbb{R}^d} \frac{T}{2} \sum_{i \neq j} J_{x,ij}^{\mathrm{chem}}(t) \ln \frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)} dx + \sum_{i=1}^{N} T \int_{\mathbb{R}^d} \sum_{j=1}^{N} \mathfrak{J}_{x,ji}^{\mathrm{chem}} \frac{p(t,x,i)}{\pi(x,i)} dx \\
&= \sum_{i=1}^{N} T \int_{\mathbb{R}^d} \frac{J_i^{\mathrm{mech}}(t,x) \cdot \{[2A^{-1}(x,i)]\mathfrak{J}_i^{\mathrm{mech}}(x)\}}{\pi(x,i)} dx + \sum_{i=1}^{N} T \int_{\mathbb{R}^d} \mathfrak{J}_i^{\mathrm{mech}}(x) \cdot \nabla \frac{p(t,x,i)}{\pi(x,i)} dx \\
&\quad + \int_{\mathbb{R}^d} \frac{T}{2} \sum_{i \neq j} J_{x,ij}^{\mathrm{chem}}(t) \ln \frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)} dx + \int_{\mathbb{R}^d} \frac{T}{2} \sum_{i \neq j} J_{x,ij}^{\mathrm{chem}}(t) \frac{\pi(x,j)q_{ji}(x)}{\pi(x,i)q_{ij}(x)} dx \\
&= \sum_{i=1}^{N} T \int_{\mathbb{R}^d} \mathfrak{J}_i^{\mathrm{mech}}(x) \cdot \{[2A^{-1}(x,i)]\mathfrak{J}_i^{\mathrm{mech}}(x)\} \frac{p(t,x,i)}{\pi^2(x,i)} dx + \int_{\mathbb{R}^d} T \sum_{i \neq j} p(t,x,i)q_{ij}(x) \left[\ln \frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)} + \frac{\pi(x,j)q_{ji}(x)}{\pi(x,i)q_{ij}(x)}\right] dx \\
&\geqslant 0,
\end{aligned}$$

where the second equality is due to

$$\nabla \cdot \mathfrak{J}_i^{\mathrm{mech}}(x) = \mathfrak{J}_x^{\mathrm{chem}}(i) = \sum_{j=1}^{N} \mathfrak{J}_{x,ji}^{\mathrm{chem}} \tag{90}$$

under the stationary distribution $\pi(x,i)$, the third equality is obtained by using integration by parts, and the last inequality is obtained according to the non-negativity of the integrant and by making use of the inequality $\ln x \leqslant x - 1$ for $x > 0$. Hence, the equality $Q_{hk}(t) = 0$ holds if and only if the system satisfies the detailed balance relation (78) and has nothing to do with the transient distribution $p(t,x,i)$, which implies the nonequilibrium essence of the system. On the other hand, since

$$T \sum_{i=1}^{N} \int_{\mathbb{R}^d} \left[-\nabla \cdot \mathfrak{J}_i^{\mathrm{mech}}(x) + \sum_{j=1}^{N} \mathfrak{J}_{x,ji}^{\mathrm{chem}}\right] \frac{p(t,x,i)}{\pi(x,i)} dx = 0,$$

then

$$
\begin{aligned}
f_d(t) &= T\sum_{i=1}^{N}\int_{\mathbb{R}^d} J_i^{\mathrm{mech}}(t,x)\cdot\left(\nabla\ln\frac{\pi(x,i)}{p(t,x,i)}\right)dx - T\sum_{i=1}^{N}\int_{\mathbb{R}^d}\nabla\cdot\mathfrak{J}_i^{\mathrm{mech}}(x)\frac{p(t,x,i)}{\pi(x,i)}dx\\
&\quad + T\int_{\mathbb{R}^d}\frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)\pi(x,j)}{p(t,x,j)\pi(x,i)}dx + T\sum_{i=1}^{N}\int_{\mathbb{R}^d}\sum_{j=1}^{N}\mathfrak{J}_{x,ji}^{\mathrm{chem}}\frac{p(t,x,i)}{\pi(x,i)}dx\\
&= T\sum_{i=1}^{N}\int_{\mathbb{R}^d}\left[\left(\nabla\ln\frac{\pi(x,i)}{p(t,x,i)}\right)^T\frac{A(x,i)}{2}\left(\nabla\ln\frac{\pi(x,i)}{p(t,x,i)}\right)\right]p(t,x,i)dx\\
&\quad + T\int_{\mathbb{R}^d}\sum_{i,j}p(t,x,i)q_{ij}(x)\left[\ln\frac{p(t,x,i)\pi(x,j)}{p(t,x,j)\pi(x,i)} + \frac{p(t,x,j)\pi(x,i)}{p(t,x,i)\pi(x,j)}\right]dx\\
&\geqslant 0.
\end{aligned}
$$

Here $f_d(t) = 0$ if and only if the system is at the steady state. So the positivity of $f_d(t)$ implies the spontaneous nonstationarity of the system. We define the excess heat of the system $Q_{ex}(t) = Q_{\mathrm{tot}}(t) - Q_{hk}(t)$ and we obtain

$$
\begin{aligned}
T\,dS(t) + Q_{ex}(t) &= Te_p(t) - Q_{\mathrm{tot}}(t) + Q_{ex}(t)\\
&= Te_p(t) - Q_{hk}(t) = f_d(t) \geqslant 0,
\end{aligned}
$$

which is the extended Clausius inequality.

C. Decomposition of the housekeeping heat dissipation rate and the free energy dissipation rate

As we have done in Sec. III C, we first give the natural decomposition of $Q_{hk}(t)$ according to flux decomposition, i.e.,

$$
Q_{hk}(t) = Q_{hk}^{\mathrm{mech}}(t) + Q_{hk}^{\mathrm{chem}}(t),
$$

in which

$$
\begin{aligned}
Q_{hk}^{\mathrm{mech}}(t) &= \sum_{i=1}^{N}T\int_{\mathbb{R}^d}\frac{J_i^{\mathrm{mech}}(t,x)\cdot\left\{[2A^{-1}(x,i)]\mathfrak{J}_i^{\mathrm{mech}}(x)\right\}}{\pi(x,i)}dx,\\
Q_{hk}^{\mathrm{chem}}(t) &= \int_{\mathbb{R}^d}\frac{T}{2}\sum_{i\neq j}J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)}dx.
\end{aligned}
$$

The two parts $Q_{hk}^{\mathrm{mech}}(t)$ and $Q_{hk}^{\mathrm{chem}}(t)$ would not always be non-negative. So we must modify the decomposition. First, we define the relative information of state (x,i) at time t as $I_R(t,x,i) = \ln\frac{p(t,x,i)}{\pi(x,i)}$ and express the flows of the exponential relative information along diffusion and between different chemical states under steady-state fluxes as

$$
\begin{aligned}
J_{ERI}^{\mathrm{mech}}(t) &= T\sum_{i=1}^{N}\int_{\mathbb{R}^d}\mathfrak{J}_i^{\mathrm{mech}}(x)\cdot\nabla e^{I_R(t,x,i)}dx\\
&= T\sum_{i=1}^{N}\int_{\mathbb{R}^d}\mathfrak{J}_i^{\mathrm{mech}}(x)\cdot\nabla\frac{p(t,x,i)}{\pi(x,i)}dx,\\
J_{ERI}^{\mathrm{chem}}(t) &= \frac{T}{2}\int_{\mathbb{R}^d}\sum_{i\neq j}\mathfrak{J}_{x,ij}^{\mathrm{mech}}[e^{I_R(t,x,j)} - e^{I_R(t,x,i)}]dx\\
&= \frac{T}{2}\int_{\mathbb{R}^d}\sum_{i\neq j}\mathfrak{J}_{x,ij}^{\mathrm{mech}}\left[\frac{p(t,x,j)}{\pi(x,j)} - \frac{p(t,x,i)}{\pi(x,i)}\right]dx.
\end{aligned}
$$

It can be easily derived that $J_{ERI}^{\mathrm{mech}}(t) + J_{ERI}^{\mathrm{chem}}(t) = 0$. Then we modify $Q_{hk}^{\mathrm{mech}}(t)$ and $Q_{hk}^{\mathrm{chem}}(t)$ with the flow of exponential relative information, i.e.,

$$
\begin{aligned}
\tilde{Q}_{hk}^{\mathrm{mech}}(t) &= Q_{hk}^{\mathrm{mech}}(t) - J_{ERI}^{\mathrm{mech}}(t)\\
&= \sum_{i=1}^{N}T\int_{\mathbb{R}^d}\mathfrak{J}_i^{\mathrm{mech}}(x)\cdot\left\{[2A^{-1}(x,i)]\mathfrak{J}_i^{\mathrm{mech}}(x)\right\}\\
&\quad\times\frac{p(t,x,i)}{\pi^2(x,i)}dx,\\
\tilde{Q}_{hk}^{\mathrm{chem}}(t) &= Q_{hk}^{\mathrm{chem}}(t) - J_{ERI}^{\mathrm{chem}}(t)\\
&= \int_{\mathbb{R}^d}T\sum_{i,j}p(t,x,i)q_{ij}(x)\\
&\quad\times\left[\ln\frac{\pi(x,i)q_{ij}(x)}{\pi(x,j)q_{ji}(x)} + \frac{\pi(x,j)q_{ji}(x)}{\pi(x,i)q_{ij}(x)}\right]dx
\end{aligned}
$$

such that

$$
Q_{hk}(t) = \tilde{Q}_{hk}^{\mathrm{mech}}(t) + \tilde{Q}_{hk}^{\mathrm{chem}}(t).
$$

We can derive that $\tilde{Q}_{hk}^{\mathrm{mech}}(t) \geqslant 0$ and $\tilde{Q}_{hk}^{\mathrm{chem}}(t) \geqslant 0$ due to the positive definiteness of $A^{-1}(x,i)$ and by using the inequality $\ln x \leqslant x - 1$ for $x > 0$, respectively. In addition, we note that $\tilde{Q}_{hk}^{\mathrm{mech}}(t) = \tilde{Q}_{hk}^{\mathrm{chem}}(t) = 0$ if and only if the detailed balance (78) is satisfied. Similarly, we give the natural decomposition of $f_d(t)$ according to the flux decomposition as

$$
f_d(t) = f_d^{\mathrm{mech}}(t) + f_d^{\mathrm{chem}}(t), \tag{91}
$$

where

$$
\begin{aligned}
f_d^{\mathrm{mech}}(t) &= \sum_{i=1}^{N}T\int_{\mathbb{R}^d}J_i^{\mathrm{mech}}(t,x)\cdot\left(\nabla\ln\frac{\pi(x,i)}{p(t,x,i)}\right)dx,\\
f_d^{\mathrm{chem}}(t) &= \int_{\mathbb{R}^d}\frac{T}{2}\sum_{i,j}J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)\pi(x,j)}{p(t,x,j)\pi(x,i)}dx.
\end{aligned}
$$

However, the non-negativity of $f_d^{\mathrm{mech}}(t)$ and $f_d^{\mathrm{chem}}(t)$ cannot be guaranteed. So we should also modify the decomposition of free energy dissipation rate $f_d(t)$ by the flow of exponential relative information, i.e.,

$$\begin{aligned}\tilde{f}_d^{\text{mech}}(t) &= f_d^{\text{mech}}(t) - J_{ERI}^{\text{mech}}(t)\\ &= \sum_{i=1}^{N} T \int_{\mathbb{R}^d} \left(\nabla \ln \frac{\pi(x,i)}{p(t,x,i)}\right)^T\\ &\quad \times \frac{A(x,i)}{2}\left(\nabla \ln \frac{\pi(x,i)}{p(t,x,i)}\right) p(t,x,i)dx,\\ \tilde{f}_d^{\text{chem}}(t) &= f_d^{\text{chem}}(t) - J_{ERI}^{\text{chem}}(t)\\ &= \int_{\mathbb{R}^d} T \sum_{i,j} p(t,x,i) q_{ij}(x)\\ &\quad \times \left[\ln \frac{p(t,x,i)\pi(x,j)}{p(t,x,j)\pi(x,i)} + \frac{p(t,x,j)\pi(x,i)}{p(t,x,i)\pi(x,j)}\right] dx,\end{aligned}$$

such that

$$f_d(t) = \tilde{f}_d^{\text{mech}}(t) + \tilde{f}_d^{\text{chem}}(t).$$

The positive definiteness of $A(x,i)$ implies that $\tilde{f}_d^{\text{mech}}(t) \geqslant 0$, and by using the inequality $\ln x \leqslant x - 1$ for $x > 0$, we obtain that $\tilde{f}_d^{\text{chem}}(t) \geqslant 0$. Furthermore, $\tilde{f}_d^{\text{mech}}(t) = \tilde{f}_d^{\text{chem}}(t) = 0$ if and only if the system is at the steady state.

VII. HIGH-DIMENSIONAL SDP UNDER COARSE GRAINING AND INFORMATION THERMODYNAMICS

A. Coarse-grained dynamics

By using the method of coarse graining [45], we can get two different mesostate coarse-grained systems. First, by integration of discrete chemical states, we obtain the marginal distribution $p(t,x) = \sum_{i=1}^{N} p(t,x,i)$, which satisfies

$$\frac{\partial p(t,x)}{\partial t} = \nabla \cdot \left[\frac{1}{2}\tilde{A}(t,x)\nabla p(t,x) - \tilde{b}(t.x)p(t,x)\right], \tag{92}$$

where

$$\begin{aligned}\tilde{A}(t,x) &= \sum_{i=1}^{N} \mathbb{P}(t,i|x)A(x,i),\\ \tilde{b}(t,x) &= \sum_{i=1}^{N} \mathbb{J}(t,i|x),\\ \mathbb{J}(t,i|x) &= b(x,i)\mathbb{P}(t,i|x) - \frac{1}{2}A(x,i)\nabla \mathbb{P}(t,i|x),\end{aligned}$$

and

$$\mathbb{P}(t,i|x) = \frac{p(t,x,i)}{p(t,x)}.$$

Second, integrating continuous microstates, we get a mesostate system governed by the distribution of i,

$$p_i(t) = \int_{\mathbb{R}^d} p(t,x,i)dx,$$

which satisfies

$$\frac{dp_i(t)}{dt} = \sum_{j=1}^{N} \tilde{q}_{ji}(t)p_j(t), \tag{93}$$

where

$$\tilde{q}_{ji}(t) = \int_{\mathbb{R}^d} \mathbb{P}(t,x|j)q_{ji}(x)dx, \tag{94}$$

with

$$\mathbb{P}(t,x|i) = \frac{p(t,x,i)}{p_i(t)}. \tag{95}$$

Just like what we have done in Secs. IV B and IV C, the SDP system could be distinguished into three different subdynamics: the first one, the mesostate subdynamics, arising from coarse graining; the second one, the microstate subdynamics, describing the dynamics within each mesostate; and the last one, the remaining subdynamics, arising from the difference of diffusion processes (or jumping processes) under different discrete components (or continuous components). We use the subscripts meso, micro, and rem to represent the three different subsystems.

B. Nonequilibrium thermodynamics of the continuous mechanical diffusion only

For the dynamics of the mesostates, the entropy is defined as

$$S_{\text{meso}}^{\text{mech}}(t) = -\int_{\mathbb{R}^d} p(t,x)\ln p(t,x)dx \tag{96}$$

and the microscopic entropy of each mesostate x is given by

$$\mathbb{S}(t,x) = -\sum_{i=1}^{N} \mathbb{P}(t,i|x)\ln \mathbb{P}(t,i|x), \tag{97}$$

followed by

$$\begin{aligned}S_{\text{micro}}^{\text{mech}}(t) &= \int_{\mathbb{R}^d} \mathbb{S}(t,x)p(t,x)dx\\ &= -\int_{\mathbb{R}^d}\sum_{i=1}^{N} p(t,x,i)\ln \mathbb{P}(t,i|x)dx.\end{aligned} \tag{98}$$

It turns out that

$$S(t) = S_{\text{meso}}^{\text{mech}}(t) + S_{\text{micro}}^{\text{mech}}(t). \tag{99}$$

Then we can decompose the entropy change of the SDP system into three parts according to the three different dynamics of the system

$$\frac{dS(t)}{dt} = \dot{S}^{(1,\text{mech})}(t) + \dot{S}^{(2,\text{mech})}(t) + \dot{S}^{(3,\text{mech})}(t). \tag{100}$$

By taking the derivative of Eq. (99), we get

$$\frac{dS(t)}{dt} = \frac{dS_{\text{meso}}^{\text{mech}}(t)}{dt} + \frac{dS_{\text{micro}}^{\text{mech}}(t)}{dt} \tag{101}$$

$$\begin{aligned}&= \dot{S}^{(1,\text{mech})}(t)\\ &\quad + \int_{\mathbb{R}^d}\sum_{i=1}^{N} -\frac{\partial p(t,x,i)}{\partial t}\ln \mathbb{P}(t,i|x)dx\\ &\quad + \int_{\mathbb{R}^d}\sum_{i=1}^{N} -p(t,x,i)\frac{\partial \ln \mathbb{P}(t,i|x)}{\partial t}dx,\end{aligned} \tag{102}$$

where

$$\begin{aligned}\dot{S}^{(1,\mathrm{mech})}(t) &= \frac{dS_{\mathrm{meso}}^{\mathrm{mech}}(t)}{dt}\\ &= -\int_{\mathbb{R}^d} J_{\mathrm{meso}}^{\mathrm{mech}}(t,x)\cdot\nabla\ln p(t,x)dx\end{aligned}$$

is the entropy change of the coarse-grained system,

$$J_{\mathrm{meso}}^{\mathrm{mech}}(t,x) = \tilde{b}(t,x)p(t,x) - \tfrac{1}{2}\tilde{A}(t,x)\nabla\ln p(t,x)$$

is the diffusion flux of the coarse-grained mechanical dynamics, and the expression (102) vanishes due to the conservation of $\mathbb{P}(t,i|x)$, i.e.,

$$\begin{aligned}\int_{\mathbb{R}^d}\sum_{i=1}^{N} -p(t,x,i)\frac{\partial\ln\mathbb{P}(t,i|x)}{\partial t}dx &= \int_{\mathbb{R}^d}\sum_{i=1}^{N} -p(t,x,i)\frac{1}{\mathbb{P}(t,i|x)}\frac{\partial\mathbb{P}(t,i|x)}{\partial t}dx\\ &= \int_{\mathbb{R}^d} -p(t,x)\left[\sum_{i=1}^{N}\frac{\partial\ln\mathbb{P}(t,i|x)}{\partial t}\right]dx = 0.\end{aligned}$$

According to the Fokker-Planck equation (72), we can divide the second term on the right-hand side of (102) into two parts

$$\begin{aligned}\int_{\mathbb{R}^d}\sum_{i=1}^{N} -\frac{\partial p(t,x,i)}{\partial t}\ln\mathbb{P}(t,i|x)dx &= \int_{\mathbb{R}^d}\sum_{i=1}^{N} -\nabla\cdot\left[\frac{1}{2}A(x,i)\nabla p(t,x,i) - b(x,i)p(t,x,i)\right]\ln\mathbb{P}(t,i|x)dx\\ &\quad -\int_{\mathbb{R}^d}\sum_{i=1}^{N}\left[-\sum_{j=1}^{N} p(t,x,j)q_{ji}(x)\ln\mathbb{P}(t,i|x)\right]dx\\ &= \int_{\mathbb{R}^d} p(t,x)\frac{1}{2}\sum_{i\neq j}[\mathbb{P}(t,i|x)q_{ij}(x) - \mathbb{P}(t,j|x)q_{ji}(x)]\ln\frac{\mathbb{P}(t,i|x)}{\mathbb{P}(t,j|x)}dx\\ &\quad +\int_{\mathbb{R}^d}\sum_{i=1}^{N}\left[\frac{1}{2}A(x,i)\nabla p(t,x,i) - b(x,i)p(t,x,i)\right]\cdot\nabla\ln\mathbb{P}(t,i|x)dx\\ &= \int_{\mathbb{R}^d} p(t,x)\frac{1}{2}\sum_{i\neq j}[\mathbb{P}(t,i|x)q_{ij}(x) - \mathbb{P}(t,j|x)q_{ji}(x)]\ln\frac{\mathbb{P}(t,i|x)}{\mathbb{P}(t,j|x)}dx\\ &\quad +\int_{\mathbb{R}^d} p(t,x)\sum_{i=1}^{N}\left[\frac{A(x,i)}{2}\nabla\mathbb{P}(t,i,|x) - b(x,i)\mathbb{P}(t,i|x)\right]\cdot\nabla\ln\mathbb{P}(t,i|x)dx\\ &= \dot{S}^{(2,\mathrm{mech})}(t) + \dot{S}^{(3,\mathrm{mech})}(t),\end{aligned}$$

where

$$\dot{S}^{(2,\mathrm{mech})}(t) = \int_{\mathbb{R}^d} p(t,x)\sum_{i\neq j}\mathbb{P}(t,i|x)q_{ij}(x)\ln\frac{\mathbb{P}(t,i|x)}{\mathbb{P}(t,j|x)}dx$$

is the ensemble average of entropy change according to the microstates within a mesostate and

$$\begin{aligned}\dot{S}^{(3,\mathrm{mech})}(t) &= \int_{\mathbb{R}^d} p(t,x)\sum_{i=1}^{N}\left[\frac{A(x,i)}{2}\nabla\mathbb{P}(t,i|x) - b(x,i)\mathbb{P}(t,i|x)\right]\cdot\nabla\ln\mathbb{P}(t,i|x)dx\\ &= -\int_{\mathbb{R}^d} p(t,x)\left[\sum_{i=1}^{N}\mathbb{J}(t,i|x)\cdot\nabla\ln\mathbb{P}(t,i|x)\right]dx\end{aligned}$$

is the entropy change according to the difference of the diffusion processes arising from the transition between the chemical states, and recall that

$$\mathbb{J}(t,i|x) = b(x,i)\mathbb{P}(t,i|x) - \tfrac{1}{2}A(x,i)\mathbb{P}(t,i|x).$$

Then we can also divide the entropy production rate into three terms according to different subsystems, i.e.,

$$e_p(t) = e^{\text{mech}}_{p,\text{meso}}(t) + e^{\text{mech}}_{p,\text{micro}}(t) + e^{\text{mech}}_{p,\text{rem}}(t). \tag{103}$$

First, according to the Fokker-Planck equation of the coarse-grained system (92), the entropy production rate of mesostates dynamics can be defined as

$$e^{\text{mech}}_{p,\text{meso}}(t) = \int_{\mathbb{R}^d} \frac{J^{\text{mech}}_{\text{meso}}(t,x)\cdot\left\{[2\tilde{A}^{-1}(t,x)]J^{\text{mech}}_{\text{meso}}(t,x)\right\}}{p(t,x)}dx.$$

Noting that for any $x \in \mathbb{R}^d$ and $i \in M$, $A(x,i)$ is positive definite and the coarse-grained diffusion coefficient $\tilde{A}(t,x)$ is also positive definite because it is the average of $A(x,i)$ according to the conditional probability distribution $\mathbb{P}(t,i|x)$. Then $e^{\text{mech}}_{p,\text{meso}}(t) \geqslant 0$ due to the positive-definite property of $\tilde{A}^{-1}(t,x)$.

Next, for a fixed mesostate x, the microstate dynamics in the mesostate are governed by $\mathbb{P}(t,i|x)$ as a jumping process. Therefore, the entropy production rate within a mesostate x is given as

$$\sum_{i\neq j}\mathbb{P}(t,i|x)q_{ij}(x)\ln\frac{\mathbb{P}(t,i|x)q_{ij}(x)}{\mathbb{P}(t,j|x)q_{ji}(x)}. \tag{104}$$

Then the ensemble average over the mesostates of (104) is the total microstate entropy production rate, which is the second part of our decomposition. Meanwhile, we can derive that the total microstates entropy production rate is just the entropy production rate of chemical flux according to flux decomposition, i.e.,

$$\begin{aligned}
e^{\text{mech}}_{p,\text{micro}}(t) = &\int_{\mathbb{R}^d} p(t,x)\\
&\times\left[\sum_{i\neq j}\mathbb{P}(t,i|x)q_{ij}(x)\ln\frac{\mathbb{P}(t,i|x)q_{ij}(x)}{\mathbb{P}(t,j|x)q_{ji}(x)}\right]dx\\
= &\, e^{\text{chem}}_p(t).
\end{aligned}$$

Then

$$\begin{aligned}
e^{\text{mech}}_{p,\text{rem}}(t) &= e_p(t) - e^{\text{mech}}_{p,\text{meso}}(t) - e^{\text{mech}}_{p,\text{micro}}(t)\\
&= e^{\text{mech}}_p(t) - e^{\text{mech}}_{p,\text{meso}}(t)\\
&= \sum_{i=1}^N\int_{\mathbb{R}^d}\frac{J^{\text{mech}}_i(t,x)\cdot\left\{[2A^{-1}(x,i)]J^{\text{mech}}_i(t,x)\right\}}{p(t,x,i)}dx\\
&\quad - \int_{\mathbb{R}^d}\frac{J^{\text{meso}}(t,x)\cdot\{[2\tilde{A}^{-1}(t,x)]J^{\text{meso}}(t,x)\}}{p(t,x)}dx\\
&= 2\int_{\mathbb{R}^d}\left\{\sum_{i=1}^N\frac{\mathbb{J}(t,i|x)\cdot\{[A^{-1}(x,i)]\mathbb{J}(t,i|x)\}}{\mathbb{P}(t,i|x)}\right.\\
&\quad\left. - \tilde{b}(t,x)\cdot[\tilde{A}^{-1}(t,x)\tilde{b}(t,x)]\right\}p(t,x)dx
\end{aligned}$$

is the entropy production rate according to the remaining dynamics. Here $e^{\text{mech}}_{p,\text{micro}}(t)$ is obviously non-negative and we can prove that $e^{\text{mech}}_{p,\text{rem}}(t) \geqslant 0$ by making use of the inequality

$$\sum_{i=1}^N X_i\cdot\left(A_i^{-1}X_i\right) \geqslant \sum_{i=1}^N X_i\cdot\left[\left(\sum_{i=1}^N A_i\right)^{-1}\sum_{i=1}^N X_i\right] \tag{105}$$

for the positive-definite A_i and by setting $X_i = \mathbb{J}(t,i|x)$ and $A_i = A(x,i)\mathbb{P}(t,i|x)$. Therefore, the three contributions to the entropy production are all non-negative,

$$e^{\text{mech}}_{p,\text{meso}}(t) \geqslant 0,\quad e^{\text{mech}}_{p,\text{micro}}(t) \geqslant 0,\quad e^{\text{mech}}_{p,\text{rem}}(t) \geqslant 0.$$

The heat dissipation rate can also be decomposed as

$$h_d(t) = h^{\text{mech}}_{d,\text{meso}}(t) + h^{\text{mech}}_{d,\text{micro}}(t) + h^{\text{mech}}_{d,\text{rem}}(t),$$

where

$$\begin{aligned}
h^{\text{mech}}_{d,\text{meso}}(t) &= \int_{\mathbb{R}^d} J^{\text{mech}}_{\text{meso}}(t,x)\cdot F^{\text{mech}}_{\text{meso}}(t,x)dx,\\
h^{\text{mech}}_{d,\text{micro}}(t) &= \int_{\mathbb{R}^d} p(t,x)\left[\frac{1}{2}\sum_{i\neq j}[\mathbb{P}(t,i|x)q_{ij}(x)\right.\\
&\quad\left. - \mathbb{P}(t,j|x)q_{ji}(x)]F^{\text{chem}}_{ij}(x)\right]dx\\
&= h^{\text{chem}}_d(t),
\end{aligned}$$

and

$$\begin{aligned}
h^{\text{mech}}_{d,\text{rem}}(t) &= h^{\text{mech}}_d(t) - h^{\text{mech}}_{d,\text{meso}}(t)\\
&= \int_{\mathbb{R}^d}\left[\sum_{i=1}^N J^{\text{mech}}_i(t,x)\cdot F^{\text{mech}}_i(x)\right.\\
&\quad\left. - J^{\text{mech}}_{\text{meso}}(t,x)\cdot F^{\text{mech}}_{\text{meso}}(t,x)\right]dx,
\end{aligned}$$

where $F^{\text{mech}}_{\text{meso}}(t,x) = 2\tilde{A}^{-1}(t,x)\tilde{b}(t,x)$ is the force of the mesostate system, followed by the equations of entropy balance

$$\begin{aligned}
\dot{S}^{(1,\text{mech})}(t) &= e^{\text{mech}}_{p,\text{meso}}(t) - h^{\text{mech}}_{d,\text{meso}}(t),\\
\dot{S}^{(2,\text{mech})}(t) &= e^{\text{mech}}_{p,\text{micro}}(t) - h^{\text{mech}}_{d,\text{micro}}(t),\\
\dot{S}^{(3,\text{mech})}(t) &= e^{\text{mech}}_{p,\text{rem}}(t) - h^{\text{mech}}_{d,\text{rem}}(t)
\end{aligned} \tag{106}$$

and the Clausius inequalities

$$\begin{aligned}
T\dot{S}^{(1,\text{mech})}(t) + Q^{\text{mech}}_{\text{tot,meso}}(t) &= Te^{\text{mech}}_{p,\text{meso}}(t) \geqslant 0,\\
T\dot{S}^{(2,\text{mech})}(t) + Q^{\text{mech}}_{\text{tot,micro}}(t) &= Te^{\text{mech}}_{p,\text{micro}}(t) \geqslant 0,\\
T\dot{S}^{(3,\text{mech})}(t) + Q^{\text{mech}}_{\text{tot,rem}}(t) &= Te^{\text{mech}}_{p,\text{rem}}(t) \geqslant 0.
\end{aligned}$$

C. Nonequilibrium thermodynamics of the discrete chemical kinetics only

The entropy of the coarse-grained subsystem is given by

$$S^{\text{chem}}_{\text{meso}}(t) = -\sum_{i=1}^N p_i(t)\ln p_i(t) \tag{107}$$

and the entropy due to the transformation of microstates is

$$S_{\text{micro}}^{\text{chem}}(t) = \sum_{i=1}^{N} \mathbb{S}(t,i)p_i(t), \tag{108}$$

where

$$\mathbb{S}(t,i) = -\int_{\mathbb{R}^d} \mathbb{P}(t,x|i)\ln \mathbb{P}(t,x|i)dx. \tag{109}$$

Then the total entropy of the system is given by

$$S(t) = S_{\text{meso}}^{\text{chem}}(t) + S_{\text{micro}}^{\text{chem}}(t). \tag{110}$$

The entropy change of the system can be decomposed into three contributions

$$\frac{dS(t)}{dt} = \dot{S}^{(1,\text{chem})}(t) + \dot{S}^{(2,\text{chem})}(t) + \dot{S}^{(3,\text{chem})}(t). \tag{111}$$

As we have done in the preceding section, taking the derivative of Eq. (110), we obtain

$$\begin{aligned}\frac{dS(t)}{dt} &= \frac{dS_{\text{meso}}^{\text{chem}}(t)}{dt} + \frac{dS_{\text{micro}}^{\text{chem}}(t)}{dt} &(112)\\ &= \dot{S}^{(1,\text{chem})}(t) - \sum_{i=1}^{N}\int_{\mathbb{R}^d}\frac{\partial p(t,x,i)}{\partial t}\ln \mathbb{P}(t,x|i)dx\\ &\quad - \sum_{i=1}^{N}\int_{\mathbb{R}^d} p(t,x,i)\frac{\partial \ln \mathbb{P}(t,x|i)}{\partial t}dx, &(113)\end{aligned}$$

in which

$$\begin{aligned}\dot{S}^{(1,\text{chem})}(t) &= \frac{dS_{\text{meso}}^{\text{chem}}(t)}{dt}\\ &= \frac{1}{2}\sum_{i\neq j}[p_i(t)\tilde{q}_{ij}(t) - p_j(t)\tilde{q}_{ji}(t)]\ln\frac{p_i(t)}{p_j(t)}\end{aligned}$$

is the entropy change due to the mesostate subsystem and

$$\begin{aligned}&\sum_{i=1}^{N}\int_{\mathbb{R}^d} p(t,x,i)\frac{\partial \ln \mathbb{P}(t,x|i)}{\partial t}dx\\ &\quad= \sum_{i=1}^{N}\int_{\mathbb{R}^d} p(t,x,i)\frac{1}{\mathbb{P}(t,x|i)}\frac{\partial \mathbb{P}(t,x|i)}{\partial t}dx\\ &\quad= \sum_{i=1}^{N} p_i(t)\left[\int_{\mathbb{R}^d}\frac{\partial \mathbb{P}(t,x|i)}{\partial t}dx\right]\\ &\quad= 0.\end{aligned}$$

Based on the Fokker-Planck equation (72), we can decompose the second term on the right-hand side of (113) into

$$\begin{aligned}&-\sum_{i=1}^{N}\int_{\mathbb{R}^d}\frac{\partial p(t,x,i)}{\partial t}\ln \mathbb{P}(t,x|i)dx\\ &\quad= \sum_{i=1}^{N}\int_{\mathbb{R}^d} -J_i^{\text{mech}}(x)\cdot\nabla\ln \mathbb{P}(t,x|i)dx\\ &\qquad+ \int_{\mathbb{R}^d}\sum_{i\neq j}^{N} J_{x,ij}^{\text{chem}}(t)\ln\frac{\mathbb{P}(t,x|i)}{\mathbb{P}(t,x|j)}dx\\ &\quad= \sum_{i=1}^{N} p_i(t)\int_{\mathbb{R}^d} -\mathbb{J}_i(t,x)\cdot\nabla\ln \mathbb{P}(t,x|i)dx\\ &\qquad+ \sum_{i\neq j} p_i(t)\int_{\mathbb{R}^d}\mathbb{P}(t,x|i)q_{ij}(x)\ln\frac{\mathbb{P}(t,x|i)}{\mathbb{P}(t,x|j)}dx\\ &\quad= \dot{S}^{(2,\text{chem})}(t) + \dot{S}^{(3,\text{chem})}(t),\end{aligned}$$

where

$$\dot{S}^{(2,\text{chem})}(t) = \sum_{i=1}^{N} p_i(t)\int_{\mathbb{R}^d} -\mathbb{J}_i(t,x)\cdot\nabla\ln \mathbb{P}(t,x|i)dx$$

is the contribution of entropy change according to the microstate subsystem,

$$\dot{S}^{(3,\text{chem})}(t) = \sum_{i\neq j} p_i(t)\int_{\mathbb{R}^d}\mathbb{P}(t,x|i)q_{ij}(x)\ln\frac{\mathbb{P}(t,x|i)}{\mathbb{P}(t,x|j)}dx$$

is the entropy change arising from the difference of the jumping processes due to different positions, and

$$\mathbb{J}_i(t,x) = b(x,i)\mathbb{P}(t,x|i) - \tfrac{1}{2}A(x,i)\nabla\mathbb{P}(t,x|i)$$

is the flux due to the conditional probability distribution $\mathbb{P}(t,x|i)$. Furthermore, we notice that

$$\dot{S}^{(2,\text{chem})}(t) = \dot{S}^{(1)}(t).$$

Also, we can derive the decomposition of the entropy production rate $e_p(t)$ of the SDP system

$$e_p(t) = e_{p,\text{meso}}^{\text{chem}}(t) + e_{p,\text{micro}}^{\text{chem}}(t) + e_{p,\text{rem}}^{\text{chem}}(t). \tag{114}$$

First, according to the mesostate dynamics, we can define the corresponding entropy production rate of this dynamics as

$$e_{p,\text{meso}}^{\text{chem}}(t) = \frac{1}{2}\sum_{i\neq j}[p_i(t)\tilde{q}_{ij}(t) - p_j(t)\tilde{q}_{ji}(t)]\ln\frac{p_i(t)\tilde{q}_{ij}(t)}{p_j(t)\tilde{q}_{ji}(t)}.$$

Next, within each mesostate i, we express the entropy production rate due to mesostate i as

$$\int_{\mathbb{R}^d}\frac{\mathbb{J}_i(t,x)\cdot\{[2A^{-1}(x,i)]\mathbb{J}_i(t,x)\}}{\mathbb{p}(t,x|i)}dx$$

and the ensemble average for all mesostates is the second contribution of the entropy production rate

$$\begin{aligned}e_{p,\text{micro}}^{\text{chem}}(t) &= \sum_{i=1}^{N} p_i(t)\int_{\mathbb{R}^d}\frac{\mathbb{J}_i(t,x)\cdot\{[2A^{-1}(x,i)]\mathbb{J}_i(t,x)\}}{\mathbb{P}(t,x|i)}dx\\ &= e_p^{\text{mech}}(t).\end{aligned}$$

Finally, the final contribution

$$
\begin{aligned}
e_{p,\mathrm{rem}}^{\mathrm{chem}}(t) &= e_p(t) - e_{p,\mathrm{meso}}^{\mathrm{chem}}(t) - e_{p,\mathrm{micro}}^{\mathrm{chem}}(t)\\
&= \int_{\mathbb{R}^d} \frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{p(t,x,i)q_{ij}(x)}{p(t,x,j)q_{ji}(x)}dx - \frac{1}{2}\sum_{i\neq j}[p_i(t)\tilde{q}_{ij}(t) - p_j(t)\tilde{q}_{ji}(t)]\ln\frac{p_i(t)\tilde{q}_{ij}(t)}{p_j(t)\tilde{q}_{ji}(t)}\\
&= \int_{\mathbb{R}^d} \frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\left[\ln\frac{p(t,x,i)q_{ij}(x)}{p(t,x,j)q_{ji}(x)} - \ln\frac{p_i(t)\tilde{q}_{ij}(t)}{p_j(t)\tilde{q}_{ji}(t)}\right]dx\\
&= \int_{\mathbb{R}^d} \sum_{i\neq j} p(t,x,i)q_{ij}(x)\ln\frac{p(t,x,i)q_{ij}(x)p_j(t)\tilde{q}_{ji}(t)}{p(t,x,j)q_{ji}(x)p_i(t)\tilde{q}_{ij}(t)}dx\\
&= \sum_{i\neq j} p_i(t)\tilde{q}_{ij}(t)\int_{\mathbb{R}^d} \frac{\mathbb{P}(t,x|i)q_{ij}(x)}{\tilde{q}_{ij}(t)}\ln\frac{\frac{\mathbb{P}(t,x|i)q_{ij}(x)}{\tilde{q}_{ij}(t)}}{\frac{\mathbb{P}(t,x|j)q_{ji}(x)}{\tilde{q}_{ji}(t)}}dx.
\end{aligned}
$$

If we define $f_{ij}(t) = \frac{\mathbb{P}(t,x|i)q_{ij}(x)}{\tilde{q}_{ij}(t)}$ and

$$
\mathbb{D}_{ij}(t) = \int_{\mathbb{R}^d} f_{ij}(t,x)\ln\frac{f_{ij}(t,x)}{f_{ji}(t,x)}dx,
$$

$e_{p,\mathrm{rem}}^{\mathrm{chem}}(t)$ can be rewritten as

$$
\sum_{i\neq j} p_i(t)\tilde{q}_{ij}(t)\mathbb{D}_{ij}(t).
$$

Using the inequality $\ln x \leqslant x-1$ for $x>0$ and the normalization of $f_{ij}(t,x)$, $\int_{\mathbb{R}^d} f_{ij}(t,x)dx = 1$, we can derive that

$$
\begin{aligned}
\mathbb{D}_{ij}(t) &\geqslant -\int_{\mathbb{R}^d} f_{ij}(t,x)\left[\frac{f_{ji}(t,x)}{f_{ij}(t,x)} - 1\right]dx\\
&= \int_{\mathbb{R}^d} f_{ij}(t,x)dx - \int_{\mathbb{R}^d} f_{ji}(t,x)dx = 0.
\end{aligned}
$$

Then $e_{p,\mathrm{rem}}^{\mathrm{chem}}(t) \geqslant 0$. In addition, $e_{p,\mathrm{meso}}^{\mathrm{chem}}(t)$ and $e_{p,\mathrm{micro}}^{\mathrm{chem}}(t)$ are obviously non-negative. Therefore,

$$
e_{p,\mathrm{meso}}^{\mathrm{chem}}(t) \geqslant 0,\quad e_{p,\mathrm{micro}}^{\mathrm{chem}}(t) \geqslant 0,\quad e_{p,\mathrm{rem}}^{\mathrm{chem}}(t) \geqslant 0.
$$

Finally, we give the corresponding decomposition of the heat dissipation rate as

$$
h_d(t) = h_{d,\mathrm{meso}}^{\mathrm{chem}}(t) + h_{d,\mathrm{micro}}^{\mathrm{chem}}(t) + h_{d,\mathrm{rem}}^{\mathrm{chem}}(t), \tag{115}
$$

where

$$
h_{d,\mathrm{meso}}^{\mathrm{chem}}(t) = \frac{1}{2}\sum_{i,j}[p_i(t)\tilde{q}_{ij}(t) - p_j(t)\tilde{q}_{ji}(t)]\ln\frac{\tilde{q}_{ij}(t)}{\tilde{q}_{ji}(t)},
$$

$$
\begin{aligned}
h_{d,\mathrm{micro}}^{\mathrm{chem}}(t) &= \sum_{i=1}^{N} p_i(t)\int_{\mathbb{R}^d} \mathbb{J}_i(t,x)\cdot F_i^{\mathrm{mech}}(x)dx\\
&= h_d^{\mathrm{mech}}(t),
\end{aligned}
$$

and

$$
\begin{aligned}
h_{d,\mathrm{rem}}^{\mathrm{chem}}(t) &= h_d(t) - h_{d,\mathrm{meso}}^{\mathrm{chem}}(t) - h_{d,\mathrm{micro}}^{\mathrm{chem}}(t)\\
&= h_d^{\mathrm{chem}}(t) - h_{d,\mathrm{meso}}^{\mathrm{chem}}(t)\\
&= \sum_{i\neq j} p_i(t)\tilde{q}_{ij}(t)\int_{\mathbb{R}^d} f_{ij}(t,x)\\
&\quad\times \ln\frac{f_{ij}(t,x)\mathbb{P}(t,x|j)}{f_{ji}(t,x)\mathbb{P}(t,x|i)}dx,
\end{aligned}
$$

followed by the more detailed entropy balance equations

$$
\begin{aligned}
\dot{S}^{(1,\mathrm{chem})}(t) &= e_{p,\mathrm{meso}}^{\mathrm{chem}}(t) - h_{d,\mathrm{meso}}^{\mathrm{chem}}(t),\\
\dot{S}^{(2,\mathrm{chem})}(t) &= e_{p,\mathrm{micro}}^{\mathrm{chem}}(t) - h_{d,\mathrm{micro}}^{\mathrm{chem}}(t),\\
\dot{S}^{(3,\mathrm{chem})}(t) &= e_{p,\mathrm{rem}}^{\mathrm{chem}}(t) - h_{d,\mathrm{rem}}^{\mathrm{chem}}(t).
\end{aligned}
$$

D. Information thermodynamics of a high-dimensional SDP

To measure the correlation of the two subsystems, we can define the mutual information as [46]

$$
I(t) = \sum_{i=1}^{N}\int_{\mathbb{R}^d} p(t,x,i)\ln\frac{p(t,x,i)}{p(t,x)p_i(t)}dx, \tag{116}
$$

where it is easy to derive that $I(t) \geqslant 0$ and $I(t) = 0$ if and only if the two subsystems are statistically independent, and we can also derive that

$$
I(t) = S_{\mathrm{meso}}^{\mathrm{mech}}(t) + S_{\mathrm{meso}}^{\mathrm{chem}}(t) - S(t).
$$

The time derivative of information $I(t)$ describe the information flow between the subsystems

$$
\begin{aligned}
\frac{dI(t)}{dt} &= \sum_{i=1}^{N}\int_{\mathbb{R}^d} \frac{\partial p(t,x,i)}{\partial t}\ln\frac{p(t,x,i)}{p(t,x)p_i(t)}dx\\
&= \sum_{i=1}^{N}\int_{\mathbb{R}^d} J_i^{\mathrm{mech}}(t,x)\cdot\nabla\ln\mathbb{P}(t,i|x)dx\\
&\quad - \int_{\mathbb{R}^d}\frac{1}{2}\sum_{i\neq j} J_{x,ij}^{\mathrm{chem}}(t)\ln\frac{\mathbb{P}(t,x|i)}{\mathbb{P}(t,x|j)}dx\\
&= \dot{I}^{\mathrm{mech}}(t) + \dot{I}^{\mathrm{chem}}(t),
\end{aligned}
$$

where the decomposition of the information flow is due to the flux of the subsystems and we can find that

$$
\begin{aligned}
\dot{I}^{\mathrm{mech}}(t) &= -\dot{S}^{(3,\mathrm{mech})}(t),\\
\dot{I}^{\mathrm{chem}}(t) &= -\dot{S}^{(3,\mathrm{chem})}(t).
\end{aligned}
$$

TABLE I. Decomposition of the entropy production rate.

$$e_p(t) = e_p^{\text{mech}}(t) + e_p^{\text{chem}}(t),\ e_p^{\text{mech}}(t) \geqslant 0,\ e_p^{\text{chem}}(t) \geqslant 0$$

$$Te_p(t) = Q_{hk}(t) + f_d(t),\ Q_{hk}(t) \geqslant 0,\ f_d(t) \geqslant 0$$

$$Q_{hk}(t) = Q_{hk}^{\text{mech}}(t) + Q_{hk}^{\text{chem}}(t) = \tilde{Q}_{hk}^{\text{mech}}(t) + \tilde{Q}_{hk}^{\text{chem}}(t),\ \tilde{Q}_{hk}^{\text{mech}}(t) \geqslant 0,\ \tilde{Q}_{hk}^{\text{chem}}(t) \geqslant 0$$

$$f_d(t) = f_d^{\text{mech}}(t) + f_d^{\text{chem}}(t) = \tilde{f}_d^{\text{mech}}(t) + \tilde{f}_d^{\text{chem}}(t),\ \tilde{f}_d^{\text{mech}}(t) \geqslant 0,\ \tilde{f}_d^{\text{chem}}(t) \geqslant 0$$

$$e_p(t) = e_{p,\text{meso}}^{\text{mech}}(t) + e_{p,\text{micro}}^{\text{mech}}(t) + e_{p,\text{rem}}^{\text{mech}}(t),\ e_{p,\text{meso}}^{\text{mech}}(t) \geqslant 0,\ e_{p,\text{micro}}^{\text{mech}}(t) = e_p^{\text{chem}}(t) \geqslant 0,\ e_{p,\text{rem}}^{\text{mech}}(t) \geqslant 0$$

$$e_p(t) = e_{p,\text{meso}}^{\text{chem}}(t) + e_{p,\text{micro}}^{\text{chem}}(t) + e_{p,\text{rem}}^{\text{chem}}(t),\ e_{p,\text{meso}}^{\text{chem}}(t) \geqslant 0,\ e_{p,\text{micro}}^{\text{chem}}(t) = e_p^{\text{mech}}(t) \geqslant 0,\ e_{p,\text{rem}}^{\text{chem}}(t) \geqslant 0$$

$$e_p^{\text{mech}}(t) = \frac{dS_{\text{meso}}^{\text{mech}}(t)}{dt} + h_d^{\text{mech}}(t) - \dot{I}^{\text{mech}}(t),\ e_p^{\text{chem}}(t) = \frac{dS_{\text{meso}}^{\text{chem}}(t)}{dt} + h_d^{\text{chem}}(t) - \dot{I}^{\text{chem}}(t)$$

Then we have

$$e_p^{\text{mech}}(t) = \frac{dS_{\text{meso}}^{\text{mech}}(t)}{dt} + h_d^{\text{mech}}(t) - \dot{I}^{\text{mech}}(t), \tag{117}$$

$$e_p^{\text{chem}}(t) = \frac{dS_{\text{meso}}^{\text{chem}}(t)}{dt} + h_d^{\text{chem}}(t) - \dot{I}^{\text{chem}}(t). \tag{118}$$

At the steady state, the entropy change and information flow vanish

$$\frac{dS(t)}{dt} = 0, \quad \frac{dS_{\text{meso}}^{\text{mech}}(t)}{dt} = 0, \quad \frac{dS_{\text{meso}}^{\text{chem}}(t)}{dt} = 0,$$

and

$$\dot{I}^{\text{mech}} + \dot{I}^{\text{chem}} = \frac{dI(t)}{dt} = 0.$$

If we define $\dot{I} = \dot{I}^{\text{chem}}$, then $\dot{I}^{\text{mech}} = -\dot{I}$ and Eqs. (117) and (118) can be rewritten as

$$e_p^{\text{mech}} = h_d^{\text{mech}} + \dot{I} \geqslant 0, \tag{119}$$

$$e_p^{\text{chem}} = h_d^{\text{chem}} - \dot{I} \geqslant 0. \tag{120}$$

VIII. CONCLUSION AND DISCUSSION

As a mathematical model used to describe complex systems, an SDP has become more popular and has drawn increasing attention in the fields of control engineering, manufacturing systems, estimation and filtering, financial engineering, and especially modern biology [3,58–61]. The nonequilibrium thermodynamics of the master-equation model and pure diffusion process have already been established, while that of a switching diffusion process has not been carefully investigated. Here we mainly focused on the decomposition of the entropy production rate and the question of whether the decomposed components are non-negative, which has now been summarized in Table I. We not only developed the framework of the nonequilibrium thermodynamics of an SDP, parallel to the cases of the master-equation model and pure diffusion processes, but also found equalities and inequalities that emerge from the crosstalk between the mechanical motion and chemical kinetics, such as the modification of the decomposition of $Q_{hk}(t)$ and $f_d(t)$ with the exponential relative information flow in order to make each decomposed component non-negative.

We only considered the time-independent SDP systems. In the time-dependent case, the drift vector $b(x,i)$, the diffusion matrix $A(x,i)$, and transition rates $q_{ij}(x)$ all depend on time. The corresponding Fokker-Planck equation is

$$\frac{\partial p(t,x,i)}{\partial t} = \nabla \cdot \left[\frac{1}{2}A(t,x,i)\nabla p(t,x,i) - b(t,x,i)p(t,x,i)\right] + \sum_{j=1}^{N} p(t,x,j)q_{ji}(t,x) \quad \text{for any } x \in \mathbb{R}^d,\ i \in M. \tag{121}$$

The quasistationary distribution at time t, $\pi(t,x,i)$, which vanishes on the right-hand side of Eq. (121), should also be time dependent.

All results remain exactly the same except for the time derivative of the generalized free energy (relative entropy) given by

$$F(t) = T\sum_{i=1}^{N}\int_{\mathbb{R}^d} p(t,x,i)\ln\frac{p(t,x,i)}{\pi(t,x,i)}dx.$$

In the time-dependent case, we have

$$\frac{dF(t)}{dt} = -f_d(t) + W_d(t), \tag{122}$$

in which

$$W_d(t) = -T\sum_{i=1}^{N}\int_{\mathbb{R}^d} p(t,x,i)\frac{\partial \ln \pi(t,x,i)}{\partial t}dx \tag{123}$$

is called dissipative work by Jarzynski and Crooks [35,62–68].

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