On the Fokker–Planck approach to the stochastic thermodynamics of reactive systems

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ABSTRACT

Stochastic thermodynamics is an extension of classical nonequilibrium thermodynamics that aims at including the effect of fluctuations occurring at small scales. In many cases, the starting point of such approaches is a Fokker–Planck equation for the probability density associated to the underlying stochastic variables. It is known that for chemically reactive systems, the usual equation for entropy production derived in this framework is not consistent with its macroscopic counterpart. It moreover also differs from the expression obtained with the master equation, from which the aforementioned Fokker–Planck equation derives. In the present work, we obtain a Fokker–Planck based alternative formula for entropy production in reactive systems that converges to the correct expression in the thermodynamic limit and is moreover consistent with expressions obtained with the master-equation based approach.

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1. Introduction

The main objective of stochastic thermodynamics is to reassess the laws of classical thermodynamics by including information related to fluctuations, which requires thermodynamic quantities of interest to be expressed in terms of stochastic processes. The early developments of stochastic thermodynamics focused on ensemble-averaged properties of Markovian systems, including those where chemical reactions take place [1–6]. More recently, a growing attention has been paid to extending these concepts to individual trajectories, which has led to expressions connecting thermodynamic quantities and the properties of large deviations [7–14].

In this work, we focus on the stochastic thermodynamics of Markovian reactive systems. The most appropriate way to model these systems is to start from the master equation ruling the probability distribution for the number of particles. The Gibbs–Shannon definition of entropy has been used in combination with such chemical master equations to build a self-consistent stochastic thermodynamics, which can be shown to lead to results compatible with classical thermodynamics [2–5]. In particular, it is possible to deduce in this framework a stochastic entropy production that is always non-negative and converges to the expected expression in the macroscopic limit [3,4].

For moderately small systems, the master equation can be replaced by a Fokker–Planck equation for the associated probability density. In a way similar to what is done with the master equation, the resulting chemical Fokker–Planck equation can be combined with the Gibbs–Shannon definition to give an evolution equation for the stochastic entropy. The identification of entropy production is, however, problematic in this case. A general expression for entropy production

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based on the Fokker–Planck equation has been put forth [7,15–18]. To be consistent with the other approaches, this Fokker–Planck entropy production should be equal to the weak-noise limit of the entropy production obtained with the master equation, and should converge to the classical thermodynamic form in the macroscopic limit. However, previous studies showed that these basic constraints are not respected in the case of reactive systems [19–21]. It has been proposed that this discrepancy arises from the fact that the Fokker–Planck equation is a coarse graining in time of the master equation, and that this situation leads to a loss of information and, thus, of entropy [21]. As a consequence, a stochastic thermodynamics based on the chemical Fokker–Planck equation would be consistent only at or close to equilibrium, where this loss of information becomes negligible.

In the present work, we show that a consistent thermodynamic framework can, in fact, be constructed from the chemical Fokker–Planck equation. The key ingredient to do so resides in the way thermodynamic forces and fluxes, and thus entropy production, are defined. We start by rapidly recalling, in Section 2, how the rate of change of entropy and entropy production are defined in classical macroscopic thermodynamics. In Section 3, we present the master equation-based approach to stochastic thermodynamics. Section 4 contains the main results of this work. We first introduce the general expression for the evolution of the stochastic entropy based on the Fokker–Planck equation. Then, we discuss how to decompose this equation into an entropy production and an entropy flow. Section 5 is devoted to a simple example, with which we compare our approach to previous ones. Conclusions and potential extensions of the present work are presented in Section 6.

2. Macroscopic nonequilibrium thermodynamics

We start with a short presentation of the classical macroscopic approach to nonequilibrium thermodynamics. Consider a reactive system at constant temperature T and volume V. The number of particles of each species k in the system can change due to the occurrence of processes, which can correspond either to a chemical reaction or to an exchange of particles with external reservoirs. The state of the system is defined by the number of particles of each species, $\mathbf{N} = (N_1, N_2, \ldots N_c)$. Each elementary process r induces a change of this state in the form of a jump $\mathbf{N} \to \mathbf{N} + \mathbf{v}_r$, where $\mathbf{v}_r = (v_{1r}, v_{2r}, \ldots v_{cr})$ is a vector of stoichiometric coefficients, which are integers reflecting the process-induced variation in the number of particles. Notice that there corresponds to each process r a backward process $-r$ such that $\mathbf{N} \to \mathbf{N} - \mathbf{v}_r$.

In classical nonequilibrium thermodynamics, the evolution equations for state functions are obtained by assuming that their dependence on the state variables under nonequilibrium conditions is the same as in equilibrium [22,23]. Consequently, the time evolution for the entropy density $s = S/V$ of a system with the above-mentioned constraints is given by

$$\frac{ds}{dt} = \sum_k \left(\frac{\partial s}{\partial n_k} \right)_{T,V,n_{l \neq k}} \frac{dn_k}{dt}, \tag{1}$$

where we introduced the number densities $n_k = N_k/V$, whose rate of change is given by

$$\frac{dn_k}{dt} = \sum_r v_{kr}\, v_r. \tag{2}$$

In the above expression, v_r is the macroscopic rate of process r and v_{kr} are the stoichiometric coefficients. Introducing (2) in (1), the evolution law for s can be split into two distinct contributions (see [22,23] for details):

$$\frac{ds}{dt} = \phi + \sigma. \tag{3}$$

The first part is the entropy flow,

$$\phi = \frac{1}{T} \sum_{k,r} v_{kr} \left(\frac{\partial u}{\partial n_k} \right)_{T,V,n_{l \neq k}} v_r, \tag{4}$$

where u is the density of internal energy. This contribution represents the variation of entropy due to exchange of mass and heat with the environment. The second part, on which we focus here, is the entropy production and is a measure of the dissipation due to the various processes:

$$\sigma = \sum_r \mathcal{A}_r\, v_r = \frac{1}{2} \sum_r \mathcal{A}_r\, (v_r - v_{-r}), \tag{5}$$

where we introduced the affinity of reaction,

$$\mathcal{A}_r = -\frac{1}{T} \sum_k v_{kr}\, \mu_k, \tag{6}$$

in which $\mu_k = (\partial u/\partial n_k)_{T,V,n_{l \neq k}} - T\,(\partial s/\partial n_k)_{T,V,n_{l \neq k}}$ is the chemical potential of species k. Note that we set Boltzmann's constant $k_B = 1$ throughout the text for readability. For elementary chemical processes the affinity can be shown to be

the logarithm of the ratio of forward and reverse rates [24],

$$A_r = \ln \frac{v_r}{v_{-r}}. \tag{7}$$

The second law of thermodynamics stipulates that $\sigma \geq 0$ for any spontaneously occurring macroscopic process, with the equality holding only at equilibrium. Eq. (5) indeed respects these constraints, since it can be rewritten as (see Eq. (7))

$$\sigma = \frac{1}{2} \sum_r \ln \frac{v_r}{v_{-r}} \, (v_r - v_{-r}) . \tag{8}$$

This quantity is always non-negative because of Jensen's inequality, $(a-b) \ln(a/b) \geq 0$. It vanishes only whenever detailed balance ($v_r = v_{-r}$) holds for all reactions, which defines the chemical equilibrium state.

3. Stochastic thermodynamics based on the chemical master equation

We wish to extend Eq. (5) to systems where spontaneous fluctuations of composition take place. The effect of fluctuations on the dynamics can be accounted for by considering the chemical master equation, which is an evolution equation for the probability $P(\mathbf{N}, t)$ to find the system in a state $\mathbf{N}$ at time t:

$$\frac{dP(\mathbf{N}, t)}{dt} = V \sum_r \left[w_r(\mathbf{N}|\mathbf{N}') P(\mathbf{N}', t) - w_{-r}(\mathbf{N}'|\mathbf{N}) P(\mathbf{N}, t) \right]$$

$$\equiv V \sum_r \left[\Phi_r(\mathbf{N}', t) - \Phi_{-r}(\mathbf{N}, t) \right] \tag{9}$$

In this equation, w_r and w_{-r} are the transition probabilities per unit time and per unit volume of the process r and of the reverse process $-r$, respectively. Consequently, the quantities Φ_r and Φ_{-r} are probability fluxes associated to the corresponding reactions.

To find an expression for entropy production based on the above equation, a definition of the stochastic entropy is required. Typically, the Gibbs–Shannon formula is used:

$$\tilde{S}(t) = \sum_{\mathbf{N}} \left[S^0(\mathbf{N}) - \ln P(\mathbf{N}, t) \right] P(\mathbf{N}, t) \equiv \sum_{\mathbf{N}} S^*(\mathbf{N}, t) \, P(\mathbf{N}, t). \tag{10}$$

$S^* = S^0 - \ln P$ plays the role of a statewise entropy and consists of two contributions: a part S^0 representing the entropy density of a system with a fixed number of particles, and a logarithmic part accounting for the variability of the system through the probability distribution of the particles. The evolution equation for the stochastic entropy per unit volume $\tilde{s} = \tilde{S}/V$ can be obtained by combining Eqs. (10) and (9):

$$\frac{d\tilde{s}}{dt} = \frac{1}{V} \sum_{\mathbf{N}} S^*(\mathbf{N}, t) \, \frac{dP(\mathbf{N}, t)}{dt}. \tag{11}$$

This equation is then usually split into two contributions:

$$\frac{d\tilde{s}}{dt} = \tilde{\phi} + \tilde{\sigma} \tag{12}$$

where the stochastic entropy production is given by [2,3]

$$\tilde{\sigma} = \frac{1}{2} \sum_{\mathbf{N},r} \tilde{A}_r \left[\Phi_r(\mathbf{N}', t) - \Phi_{-r}(\mathbf{N}, t) \right]. \tag{13}$$

In this expression, the *mesoscopic affinity* is defined by

$$\tilde{A}_r = \ln \frac{\Phi_r(\mathbf{N}', t)}{\Phi_{-r}(\mathbf{N}, t)}. \tag{14}$$

The stochastic entropy production (13) is always non-negative. Moreover, it becomes zero if and only if a stochastic detailed balance holds for every reaction, i.e., whenever $\Phi_r(\mathbf{N}', t) = \Phi_{-r}(\mathbf{N}, t)$ for all r. This condition can be seen as a stochastic extension of the macroscopic detailed balance and thus defines the equilibrium state in this framework. Eq. (13) can also be shown to lead to the macroscopic expression (5) in the limit of infinite V, under the condition that $\lim_{V \to \infty} w_r = v_r$. These properties suggest that Eq. (13) is a legitimate extension of entropy production to fluctuating systems.

4. Stochastic thermodynamics based on a chemical Fokker–Planck equation

An important property of the master equation is that it leads, in the limit of large V, to a Fokker–Planck equation for the probability density $\rho(\boldsymbol{n}, t) \equiv V^c P(\boldsymbol{N}, t)$ that the concentrations $\boldsymbol{n}$ take a given value at time t. Consider, to show this, the case of a 1-variable system (a more general derivation is given in Appendix A). Since the configuration N' leading to a final state N after a reactive event r is given by $N' = N - \nu_r$, the fluxes in Eq. (9) can be expanded to the leading order in V^{-1} as [25]

$$\Phi_r(V\,\boldsymbol{n}', t) = \frac{1}{V}\left[w_r\,\rho - \frac{\nu_r}{V}\left(\frac{\partial\,w_r\,\rho}{\partial n}\right) + \frac{\nu_r^2}{2\,V^2}\left(\frac{\partial^2\,w_r\,\rho}{\partial n^2}\right) + \cdots \right]. \tag{15}$$

We will not note the dependences in n and t anymore, for clarity. Eq. (9) thus yields to the dominant order in V^{-1} an equation of the form

$$\frac{\partial\rho}{\partial t} = -\sum_r \nu_r \frac{\partial J_r}{\partial n}, \tag{16}$$

in which

$$J_r = w_r\,\rho - \frac{\nu_r}{2\,V}\left(\frac{\partial\,w_r\,\rho}{\partial n}\right) \tag{17}$$

is a probability flux associated to process r. An evolution equation such as (16) corresponds to multiple diffusion processes in state space, with

$$\frac{\nu_r\,w_r}{2\,V} \equiv D_r \tag{18}$$

playing the role of a diffusion coefficient associated to each reaction r. We will refer to Eq. (16) as the chemical Fokker–Planck equation, since it includes explicitly the contributions of various reaction channels.

Formulations of stochastic thermodynamics relying on the Fokker–Planck equation have been put forth, based on the continuous Gibbs–Shannon entropy per unit volume

$$\tilde{s} = \int d\boldsymbol{n}\left[s^0 - \frac{1}{V}\ln\frac{\rho}{V} \right]\rho \equiv \int d\boldsymbol{n}\,s^*\,\rho, \tag{19}$$

where $s^0 = S^0/V$. An evolution equation for $\tilde{s}$ can easily be computed from the Fokker–Planck equation, in a way similar to what is done for the master equation. However, the way it is decomposed into an entropy flow and an entropy production differs. In most cases, the evolution law for entropy is rearranged in the following way:

$$\begin{aligned}
\frac{d\tilde{s}}{dt} &= \int dn\,s^*\left(\frac{\partial\rho}{\partial t}\right) \\
&= \int dn \sum_r \nu_r \left(\frac{\partial s^*}{\partial n}\right) J_r \\
&= \frac{1}{2}\int dn \sum_r \nu_r \left(\frac{\partial s^*}{\partial n}\right)(J_r - J_{-r}) \\
&= \frac{1}{2\,V}\int dn \sum_r \nu_r \left[V\left(\frac{\partial s^0}{\partial n}\right) - \frac{w_r - w_{-r}}{D_r - D_{-r}} + \frac{1}{Dr - D_{-r}}\left(\frac{\partial(D_r + D_{-r})}{\partial n}\right) \right](J_r - J_{-r}) \\
&\quad + \frac{1}{2\,V}\int dn \sum_r \nu_r \frac{(J_r - J_{-r})^2}{\rho\,(D_r - D_{-r})}.
\end{aligned} \tag{20}$$

With this decomposition, the mean stochastic entropy production is defined by

$$\tilde{\sigma}_{FP} = \frac{1}{2\,V}\int dn \sum_r \nu_r \frac{(J_r - J_{-r})^2}{\rho\,(D_r - D_{-r})} = \int dn \sum_r \frac{(J_r - J_{-r})^2}{\rho\,(w_r + w_{-r})} \geq 0. \tag{21}$$

Expressions of this type have been used to analyze the stochastic thermodynamics of various problems, including Brownian motion, mass transport in the presence of multiple reservoirs, electrical circuits, etc. Despite its apparent universality, this formula is inappropriate in the case of reactive systems. The entropy production (21) is zero at equilibrium because of detailed balance (since then $J_r = J_{-r}$) and is non-negative out of equilibrium, but its form is not compatible with the macroscopic formula (8) and the master-equation expressions (13)–(14). This is obvious from the fact that Eq. (21) lacks the logarithmic terms found in the macroscopic and in the master-equation based equations. Note that this issue had been pointed out by other authors before (see, for example, [21]), and was interpreted as a loss of information related to the transition from a master equation to a Fokker–Planck equation. Our objective in this work is

to show that a correct expression for the stochastic entropy production can nevertheless be obtained, based on quantities entering the chemical Fokker–Planck equation (16).

Our starting point is that we interpret the inadequacy of Eq. (21) as a sign that this definition of the stochastic entropy production incorrectly identifies the thermodynamic forces in the case of chemical reactions. Indeed, we expect a general expression for the stochastic entropy production to read

$$\tilde{\sigma}_{FP} = \frac{1}{2} \int dn \sum_r \tilde{\mathcal{A}}_r^{FP} (J_r - J_{-r}),$$ (22)

where $\tilde{\mathcal{A}}_r^{FP}$ would be the Fokker–Planck thermodynamic force associated to each process r. Using Eq. (21) amounts to assuming that the affinity of each reaction is proportional to its associated flux, $\tilde{\mathcal{A}}_r^{FP} \propto (J_r - J_{-r})$, which corresponds to the *linear* regime of nonequilibrium thermodynamics. It is well known that in a macroscopic description, the validity of the linear regime for chemical reactions is restricted to systems that are very close to equilibrium, because of the essentially exponential dependence of the macroscopic reaction rates on the corresponding affinities. It is thus, retrospectively, not surprising that equations such as Eq. (21) were observed to provide a self-consistent thermodynamic framework only in the close vicinity of chemical equilibrium [21]. What we must be looking for now is thus a *nonlinear* relation connecting the probability fluxes of the Fokker–Planck equation to affinities.

We adopt to this hand an approach based on the observation that although they are distinctly different quantities, J_r/ρ plays in the Fokker–Planck formulation a role analogous to the rates v_r in the macroscopic approach. This equivalence appears more clearly by comparing the macroscopic evolution equation for entropy,

$$\frac{ds}{dt} = \left(\frac{\partial s}{\partial n}\right) \frac{dn}{dt} = \sum_r v_r \left(\frac{\partial s}{\partial n}\right) v_r,$$ (23)

to its Fokker–Planck counterpart,

$$\frac{d\tilde{s}}{dt} = \int dn \sum_r v_r \left(\frac{\partial s^*}{\partial n}\right) J_r$$
$$= \int dn \left[\sum_r v_r \left(\frac{\partial s^*}{\partial n}\right) \frac{J_r}{\rho}\right] \rho$$ (24)

Indeed, Eq. (24) can be seen as the mean of a state-dependent rate of change (the terms under bracket), which has the same structure as the macroscopic rate itself, provided that J_r/ρ represents a stochastic extension of v_r. This idea is further supported by the fact that in the macroscopic limit, J_r tends to $w_r \rho$ and the equivalence with the macroscopic rate is ensured since $\lim_{V \to \infty} w_r = v_r$ in order for the master equation to predict the correct macroscopic kinetics. Building on this analogy, and remembering that the macroscopic affinity is given by Eq. (7), we are led to propose the following expression for the stochastic affinity in the Fokker–Planck approach:

$$\tilde{\mathcal{A}}_r^{FP} = \ln \frac{J_r}{J_{-r}}$$ (25)

The evolution equation for $\tilde{s}$ can thus be reorganized as follows:

$$\frac{d\tilde{s}}{dt} = \int dn \sum_r v_r \left(\frac{\partial s^*}{\partial n}\right) J_r$$
$$= \int dn \sum_r \left[v_r \left(\frac{\partial s^*}{\partial n}\right) - \ln \frac{J_r}{J_{-r}}\right] J_r$$ (26)
$$+ \int dn \sum_r \ln \frac{J_r}{J_{-r}} J_r,$$ (27)

in which we now define the stochastic entropy production as

$$\tilde{\sigma}_{FP} = \int dn \sum_r \ln \frac{J_r}{J_{-r}} J_r = \frac{1}{2} \int dn \sum_r \ln \frac{J_r}{J_{-r}} (J_r - J_{-r}).$$ (28)

The generalization to multiple variables is straightforward (see Appendix A).

Expression (28) has the properties expected from a stochastic extension of entropy production. First, it is always non-negative because of Jensen's inequality. Second, it becomes zero if and only if the probability flux associated to each reaction channel vanishes ($J_r = J_{-r}$ for all r). It thus acts as a measure of the distance from chemical equilibrium, just like its macroscopic counterpart and the master equation expression. Finally, $\tilde{\sigma}_{FP}$ can be shown to be the weak-noise limit of the entropy production obtained in the master equation framework, Eq. (13). Comparing Eqs. (17) and (15), we note indeed that the fluxes J_r and Φ_r are related to the dominant order in V^{-1} by

$$\Phi_r(N', t) = \frac{1}{V} \left[J_r - \frac{v_r}{2V} \left(\frac{\partial w_r \rho}{\partial n}\right) + \dots\right].$$

Inserting this relation into Eq. (13) and switching to continuous coordinates yields (see Appendix B for details)

$$
\begin{aligned}
\tilde{\sigma} &= \frac{1}{2} \int dn \sum_r \left[J_r - J_{-r} - \frac{v_r}{2V} \left(\frac{\partial w_r \rho}{\partial n} \right) - \frac{v_{-r}}{2V} \left(\frac{\partial w_{-r} \rho}{\partial n} \right) \right] \\
&\quad \times \ln \frac{J_r - \frac{v_r}{2V} \left(\frac{\partial w_r \rho}{\partial n} \right)}{J_{-r} + \frac{v_{-r}}{2V} \left(\frac{\partial w_{-r} \rho}{\partial n} \right)} \\
&= \frac{1}{2} \int dn \sum_r \ln \frac{J_r}{J_{-r}} (J_r - J_{-r}) + o(V^{-1}).
\end{aligned}
\tag{29}
$$

We thus reach the conclusion that to the dominant order in V^{-1}, $\tilde{\sigma} = \tilde{\sigma}_{FP}$, inasmuch as the rates w_r appearing in both approaches are the same. Since $\tilde{\sigma}$ converges to the correct macroscopic expression, the entropy production (28) based on the fluxes appearing in the Fokker–Planck equation is thus consistent with both the master equation and the macroscopic expressions. Note that this result can be extended to the case of multiple variables (see Appendix B).

To summarize, we just showed that it is possible to define an entropy production from the chemical Fokker–Planck equation in a way that is consistent with other thermodynamic frameworks. The important step here was to realize that the stochastic affinity should be expressed as a nonlinear function of fluxes, just like in macroscopic thermodynamics. We now illustrate these results on a simple example.

5. Example: A nonequilibrium linear reaction scheme

To illustrate the properties of the expression hereby proposed, let us consider a simple, yet representative example of chemical reaction,

$$
A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} B.
\tag{30}
$$

In this scheme A and B are pool species whose concentrations a and b are kept constant and X is a variable intermediate. For isothermal ideal systems, the mean-field rate equation for n is

$$
\begin{aligned}
\frac{dn}{dt} &= (v_1 - v_{-1}) - (v_2 - v_{-2}) \\
&= (k_1 a - k_{-1} n) - (k_2 n - k_{-2} b).
\end{aligned}
\tag{31a}
$$

The deterministic entropy production associated with this scheme reads

$$
\begin{aligned}
\sigma &= (v_1 - v_{-1}) \ln \frac{v_1}{v_{-1}} + (v_2 - v_{-2}) \ln \frac{v_2}{v_{-2}} \\
&= (k_1 a - k_{-1} n) \ln \frac{k_1 a}{k_{-1} n} + (k_2 n - k_{-2} b) \ln \frac{k_2 n}{k_{-2} b}
\end{aligned}
\tag{31b}
$$

As expected, σ vanishes when the two fluxes vanish separately, which occurs under the zero overall affinity (equilibrium) condition $k_1 k_2 a = k_{-1} k_{-2} b$.

Since the reaction rates are linear in the composition of the system, one has $w_i = v_i$ in the master equation (9). The linearity of this system also has the consequence that the probability distribution $P(N, t)$ is Poissonian. Consequently, it can be shown [3] that the stochastic entropy production of the master equation approach and the macroscopic entropy production coincide at the steady state: $\tilde{\sigma} = \sigma$. Our expression (28) reads

$$
\tilde{\sigma}_{FP} = \int dn \left[(J_1 - J_{-1}) \ln \frac{J_1}{J_{-1}} + (J_2 - J_{-2}) \ln \frac{J_2}{J_{-2}} \right].
\tag{32}
$$

In order to calculate this entropy production explicitly, both the reaction rates and the probability density ρ are required. This is in general a difficult task, but evaluating these quantities at steady state is much simpler if one limits oneself to corrections of the order of V^{-1}. Indeed, it can easily be shown (in a manner similar to what was done in [4]) that in such case the entropy production can be approximated by

$$
\tilde{\sigma}_{FP} = \left(\ln \frac{v_1}{v_{-1}} \right)_{n_s} \int dn \, (J_1 - J_{-1}) + \left(\ln \frac{v_2}{v_{-2}} \right)_{n_s} \int dn \, (J_2 - J_{-2}),
$$

where n_s is the deterministic steady state value obtained by setting (31a) equal to 0. Moreover, since in the weak-noise limit ρ is a Gaussian centered on the macroscopic solution, all the contributions proportional to the diffusion coefficients in the fluxes J_r will be zero upon averaging. One thus finds that the stochastic entropy production is in this case equal to Eq. (31b), and thus also to the master equation expression, as required.
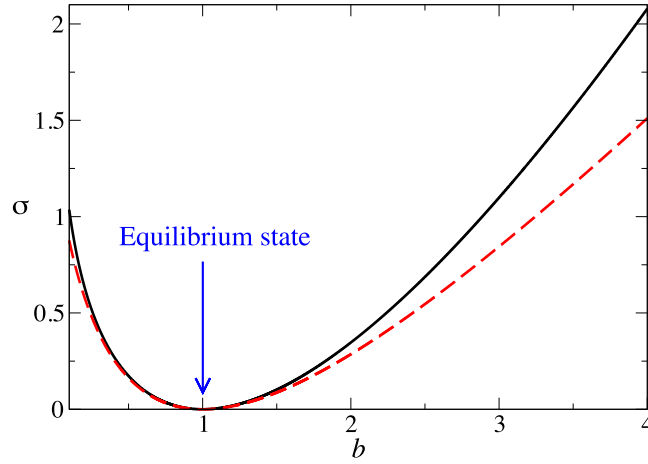
Fig. 1. Steady-state entropy production associated with the reactive system (30). The black line is given by our definition for the stochastic entropy based on the Fokker–Planck equation, Eq. (32), which is here equal to the macroscopic expression (31b). The red dashed curve is the formerly used expression for entropy production, Eq. (34). Parameter values are: $k_1 a = k_{-1} = k_2 = k_{-2} = 1$, so that the steady-state value for n is $n_s = (b+1)/2$.

For comparison purposes, note that the "classical" Fokker–Planck expression (21) reads here

$$\tilde{\sigma}_{FP} = 2 \int dn \, \frac{(J_1 - J_{-1})^2}{\rho(k_1 a + k_{-1} n)} + 2 \int dn \, \frac{(J_2 - J_{-2})^2}{\rho(k_2 n + k_{-2} b)}. \tag{33}$$

In the macroscopic limit, this expression becomes at steady-state

$$\tilde{\sigma}_{FP} = 2 \, \frac{(k_1 a - k_{-1} n_s)^2}{k_1 a + k_{-1} n_s} + 2 \, \frac{(k_2 n_s - k_{-2} b)^2}{k_2 n_s + k_{-2} b}. \tag{34}$$

As mentioned earlier, this expression will be zero at equilibrium and non-zero for nonequilibrium states as expected, but is in general not compatible with the macroscopic equation for entropy production. We note, however, that close to equilibrium where $v_1 \approx v_{-1}$ one can expand

$$\ln \frac{v_1}{v_{-1}} \approx \frac{v_1 - v_{-1}}{v_{-1}} \approx 2 \, \frac{v_1 - v_{-1}}{v_1 + v_{-1}}. \tag{35}$$

Inserting this (and a similar equation for the other term in the entropy production) into (31b) leads to Eq. (34), which is thus correct only in the direct vicinity of the equilibrium state. This is illustrated in Fig. 1.

6. Conclusions

For moderately small systems, the master equation on which the stochastic kinetics of reactive systems usually rests can be approximated by a Fokker–Planck equation. Previous attempts at developing a thermodynamic framework based on such Fokker–Planck equations were shown to lead to inconsistencies in the case of chemically active systems. These discrepancies were explained in terms of errors induced by the temporal coarse-graining procedure used to derive the Fokker–Planck equation from the master equation (see [21]).

In the present work, we propose an alternative explanation. Our starting point was to note that the expression for the ensemble-averaged entropy production that is typically used in stochastic thermodynamics based on the Fokker-Planck equation implies that the thermodynamic fluxes (the rates of the processes) are simply proportional to the corresponding thermodynamic forces. While this is a reasonable assumption for mass or heat diffusion, the rates of chemical reactions are known to depend exponentially on the affinities, at least at the macroscopic scale.

We thus proposed a new definition in which the stochastic affinities are logarithms of the ratio of the forward and reverse stochastic fluxes associated with a given reaction. We showed that this new definition is consistent with the weak-noise limit of the master-equation formulation as well as with the classical expression of macroscopic nonequilibrium thermodynamics. The expression that we derived can be used as a reliable basis for studies on the effect of fluctuations on the thermodynamics of mesoscopic reactive systems.

A natural next step would be to try and generalize this approach to pathwise quantities. It is known that Fokker–Planck equations make large errors in the probability of time-reversed paths. It would be interesting to see if the present approach can lead to thermodynamically consistent results in such cases, or if better approximations of the master equation (for example, stochastic differential equations with Poissonian noise) are needed.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Multivariate expression for entropy production

We show here how to derive the multivariate expression for entropy production. The expansion of the probability fluxes of the master equation reads, for multivariate systems (c is the total number of species),

$$\Phi_r(V\,\boldsymbol{n}', t) = V^c \left[w_r\, \rho - \sum_k \frac{v_{kr}}{V} \left(\frac{\partial\, w_r\, \rho}{\partial n_k} \right) + \sum_{k,l} \frac{v_{kr}\, v_{lr}}{2\, V^2} \left(\frac{\partial^2\, w_r\, \rho}{\partial n_k\, \partial n_l} \right) + \cdots \right]. \tag{A.1}$$

This leads to a Fokker–Planck equation of the type

$$\frac{\partial \rho}{\partial t} = -\sum_k \left(\frac{\partial J_k}{\partial n_k} \right) \tag{A.2}$$

where the probability flux per species J_k reads

$$J_k = \sum_r v_{kr}\, w_r\, \rho - \sum_{r,l} \frac{v_{kr}\, v_{lr}}{2\, V} \left(\frac{\partial\, w_r\, \rho}{\partial n_l} \right). \tag{A.3}$$

In a way similar to what was done in the main text, each of these fluxes can be decomposed as a sum over processes, $J_k = \sum_r v_{kr} J_r$, where

$$J_r = w_r\, \rho - \sum_l \frac{v_{lr}}{2\, V} \left(\frac{\partial\, w_r\, \rho}{\partial n_l} \right). \tag{A.4}$$

The evolution law for the stochastic entropy now reads

$$\frac{d\bar{s}}{dt} = \frac{1}{2} \int d\boldsymbol{n} \sum_{k,r} v_{kr} \left(\frac{\partial s^*}{\partial n_k} \right) (J_r - J_{-r}). \tag{A.5}$$

Introducing the quantity

$$\tilde{\mathcal{A}}_r^{FP} = \ln \frac{J_r}{J_{-r}} \tag{A.6}$$

and rewriting (A.5) as

$$\frac{d\bar{s}}{dt} = \frac{1}{2} \int d\boldsymbol{n} \sum_{k,r} \left[v_{kr} \left(\frac{\partial s^*}{\partial n_k} \right) - \mathcal{A}_r^{FP} \right] (J_r - J_{-r}) + \frac{1}{2} \int d\boldsymbol{n} \sum_r \mathcal{A}_r (J_r - J_{-r}), \tag{A.7}$$

we obtain our final expression for the stochastic entropy production in the Fokker–Planck framework:

$$\tilde{\sigma}_{FP} = \frac{1}{2} \int d\boldsymbol{n} \sum_r \mathcal{A}_r^{FP} (J_r - J_{-r}). \tag{A.8}$$

Appendix B. Equivalence with the master equation approach

We give here details concerning the equivalence between our formulation and the master equation approach. The master equation takes the form (see Eq. (7) in the main text for the definition of the various quantities entering this equation)

$$\frac{dP(\boldsymbol{N}, t)}{dt} = V \sum_r \left[\Phi_r(\boldsymbol{N}', t) - \Phi_{-r}(\boldsymbol{N}, t) \right]. \tag{B.1}$$

The stochastic entropy in this setting is usually taken to be the Gibbs–Shannon entropy,

$$\tilde{S} = \sum_{\boldsymbol{N}} \left[S^0(\boldsymbol{N}) - \ln P(\boldsymbol{N}, t) \right] P(\boldsymbol{N}, t). \tag{B.2}$$

The evolution equation for the density of stochastic entropy $\tilde{s}$ obtained by differentiating (B.2) with respect to time and then dividing by V can again be split into two contributions [3,4]:

$$\frac{d\tilde{s}}{dt} = \tilde{\phi} + \tilde{\sigma}. \tag{B.3}$$

We are interested here in the production term, which reads

$$\tilde{\sigma} = \frac{1}{2} \sum_{\boldsymbol{N},r} \left[\varPhi_r(\boldsymbol{N}',t) - \varPhi_{-r}(\boldsymbol{N},t) \right] \ln \frac{\varPhi_r(\boldsymbol{N}',t)}{\varPhi_{-r}(\boldsymbol{N},t)}. \tag{B.4}$$

We now consider the weak-noise limit of the systems under consideration. We start by noting that the configuration $\boldsymbol{N}'$ leading to a final state $\boldsymbol{N}$ after a reactive event r is given by $\boldsymbol{N}' = \boldsymbol{N} - \boldsymbol{v}_r$, where $\boldsymbol{v}_r$ is the vector of stoichiometric coefficients (see main text). Introducing the probability density, the product $w_r P$ can be expanded as (remember that c stands for the total number of species)

$$\varPhi_r(\boldsymbol{N}',t) = w_r(\boldsymbol{N}')P(\boldsymbol{N}',t) = V^{-c} \left[w_r \left(\boldsymbol{n} - \frac{\boldsymbol{v}_r}{V} \right) \rho \left(\boldsymbol{n} - \frac{\boldsymbol{v}_r}{V}, t \right) \right]$$

$$= V^{-c} \left[w_r \rho - \sum_k \frac{v_{kr}}{V} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right) + \cdots \right] \tag{B.5}$$

Switching to continuous variables and introducing (B.5) into (B.4) yields

$$\tilde{\sigma} = \frac{1}{2} \int d\boldsymbol{n} \sum_r \left[w_r \rho - w_{-r} \rho - \sum_k \frac{v_{kr}}{V} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right) \right] \ln \frac{w_r \rho - \sum_k \frac{v_{kr}}{V} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right)}{w_{-r} \rho}. \tag{B.6}$$

We now introduce in this expression the stochastic fluxes (A.4),

$$\tilde{\sigma} = \frac{1}{2} \sum_r \int d\boldsymbol{n} \left[J_r - J_{-r} - \sum_k \frac{v_{kr}}{2V} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right) - \sum_k \frac{v_{k-r}}{2V} \left(\frac{\partial \, w_{-r} \rho}{\partial n_k} \right) \right]$$

$$\times \ln \frac{J_r - \sum_k \frac{v_{kr}}{2V} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right)}{J_{-r} + \sum_k \frac{v_{k-r}}{2V} \left(\frac{\partial \, w_{-r} \rho}{\partial n_k} \right)}$$

$$= \frac{1}{2} \sum_r \int d\boldsymbol{n} \, (J_r - J_{-r}) \ln \frac{J_r}{J_{-r}}$$

$$+ \frac{1}{2} \sum_r \int d\boldsymbol{n} \, (J_r - J_{-r}) \left[\ln \left(1 - \sum_k \frac{v_{kr}}{2VJ_r} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right) \right) - \ln \left(1 + \sum_k \frac{v_{k-r}}{2VJ_{-r}} \left(\frac{\partial \, w_{-r} \rho}{\partial n_k} \right) \right) \right]$$

$$- \frac{1}{2} \sum_r \int d\boldsymbol{n} \left[\sum_k \frac{v_{kr}}{2V} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right) - \sum_k \frac{v_{k-r}}{2V} \left(\frac{\partial \, w_{-r} \rho}{\partial n_k} \right) \right] \ln \frac{J_r - \sum_k \frac{v_{kr}}{2V} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right)}{J_{-r} + \sum_k \frac{v_{k-r}}{2V} \left(\frac{\partial \, w_{-r} \rho}{\partial n_k} \right)} \tag{B.7}$$

The first term in the second equality is equal to the Fokker–Planck entropy production that we derived earlier. The second term can be evaluated in the limit of large V by using $\ln(1 + x) \approx x$ for $|x| \ll 1$, which gives

$$- \frac{1}{2} \sum_r \int d\boldsymbol{n} \, [J_r - J_{-r}] \left[\sum_k \frac{v_{kr}}{2VJ_r} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right) + \sum_k \frac{v_{k-r}}{2VJ_{-r}} \left(\frac{\partial w_{-r} \rho}{\partial n_k} \right) \right]$$

$$= - \frac{1}{2} \sum_r \int d\boldsymbol{n} \, [J_{-r} - J_r] \left[\sum_k \frac{v_{k-r}}{2VJ_{-r}} \left(\frac{\partial \, w_{-r} \rho}{\partial n_k} \right) + \sum_k \frac{v_{kr}}{2VJ_r} \left(\frac{\partial w_r \rho}{\partial n_k} \right) \right]$$

$$= \frac{1}{2} \sum_r \int d\boldsymbol{n} \, [J_r - J_{-r}] \left[\sum_k \frac{v_{kr}}{2VJ_r} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right) + \sum_k \frac{v_{k-r}}{2VJ_{-r}} \left(\frac{\partial w_{-r} \rho}{\partial n_k} \right) \right]$$

$$= 0. \tag{B.8}$$

As for the third term, we note that

$$- \frac{1}{2} \sum_r \int d\boldsymbol{n} \left[\sum_k \frac{v_{kr}}{2V} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right) + \sum_k \frac{v_{k-r}}{2V} \left(\frac{\partial \, w_{-r} \rho}{\partial n_k} \right) \right] \ln \frac{J_r - \sum_k \frac{v_{kr}}{2V} \left(\frac{\partial w_r \rho}{\partial n_k} \right)}{J_{-r} + \sum_k \frac{v_{k-r}}{2V} \left(\frac{\partial w_{-r} \rho}{\partial n_k} \right)}$$

$$= - \frac{1}{2} \sum_r \int d\boldsymbol{n} \left[\sum_k \frac{v_{kr}}{2V} \left(\frac{\partial \, w_r \rho}{\partial n_k} \right) + \sum_k \frac{v_{k-r}}{2V} \left(\frac{\partial \, w_{-r} \rho}{\partial n_k} \right) \right] \ln \frac{J_r - \sum_k \frac{v_{kr}}{2V} \left(\frac{\partial w_r \rho}{\partial n_k} \right)}{J_r + \sum_k \frac{v_{kr}}{2V} \left(\frac{\partial w_r \rho}{\partial n_k} \right)}$$

or, using again $\ln(1+x) \approx x$,

$$\approx \quad \frac{1}{2} \sum_r \int d\mathbf{n} \left[\sum_k \frac{v_{kr}}{2V} \left(\frac{\partial w_r \rho}{\partial n_k} \right) + \sum_k \frac{v_{k-r}}{2V} \left(\frac{\partial w_{-r} \rho}{\partial n_k} \right) \right] \left[\sum_k \frac{v_{kr}}{2V J_r} \left(\frac{\partial w_r \rho}{\partial n_k} \right) \right],$$

which is of order V^{-2}. We thus reach the conclusion that to the dominant order in $1/V$,

$$\tilde{\sigma} = \tilde{\sigma}_{FP}, \tag{B.9}$$

inasmuch as the rates appearing in both approaches are the same.

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