Stochastic thermodynamics of reactive systems: An extended local equilibrium approach

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The recently developed extended local equilibrium approach to stochastic thermodynamics is applied to reactive systems. The properties of the fluctuating entropy and entropy production are analyzed for general linear and for prototypical nonlinear kinetic processes. It is shown that nonlinear kinetics typically induces deviations of the mean entropy production from its value in the deterministic (mean-field) limit. The probability distributions around the mean are derived and shown to qualitatively differ in thermodynamic equilibrium, under nonequilibrium conditions and in the vicinity of criticalities associated to the onset of multistability. In each case large deviation-type properties are shown to hold. The results are compared with those of alternative approaches developed in the literature.

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I. INTRODUCTION

Classical thermodynamics is built on the existence of an extensive state function, the entropy S, which evolves in time due to exchanges between a system and its environment and to internal processes occurring spontaneously within the system [1],

$$\frac{dS}{dt} = \frac{d_e S}{dt} + \frac{d_i S}{dt}. \tag{1}$$

The second law of thermodynamics stipulates that spontaneous transformations yield a positive entropy production, i.e., $d_i S/dt \geqslant 0$, with the equality holding only for transformations involving equilibrium states. This fundamental property provides a universal constraint on the macroscopic variables and on the parameters describing a system.

In their original setting the laws of thermodynamics are concerned with macroscopic (large-size) systems. In recent years there has been a growing interest in how these laws are to be extended—or amended—when dealing with small-size systems, where fluctuations of the state variables can play an essential role. Different approaches, referred to as stochastic thermodynamics, have been reported [2–10]. An important issue arising in this context is how to define a stochastic extension of entropy. The Gibbs-Shannon definition of entropy has been used for this purpose and shown to lead to results compatible with classical thermodynamics in the macroscopic limit [2–4]. However, while this definition accounts for global (ensemble-averaged) properties, it cannot address properties pertaining to individual trajectories. Attempts to circumvent this limitation have been proposed [5,8–10]. They lead to expressions of the entropy production satisfying large deviation equalities linking the probabilities of increase of the stochastic entropy production along a direct path and of a corresponding decrease associated to the reverse path.

Despite their interest, these latter approaches are, to a large extent, definition dependent and their link to phenomenological thermodynamics is not firmly established. Recently, two of the present authors have introduced an alternative definition of entropy and entropy production incorporating the effect of fluctuations, which gives access to both global and individual trajectory-related properties while being firmly related to the observables of phenomenological thermodynamics [11]. The approach is based on an extended local equilibrium hypothesis, whereby entropy remains a function(al) of the state variables having the same form as in classical thermodynamics but with the additional feature that these variables are undergoing transformations governed by stochastic rather than deterministic processes. A generalized balance equation for entropy has been derived which allows for the identification of a fluctuating entropy production and a fluctuating entropy flux and brings out the important role played by the nonlinearities in the properties of these quantities.

In the present paper this formalism is applied to reactive processes. In addition to their fundamental role in chemistry and related fields, the interest of this class of processes is also to generate a variety of complex phenomena, from bistability and oscillations to chaos, under conditions of constant temperature, spatial homogeneity, and absence of external forces. Furthermore, the relevant state variables incorporating the effect of the fluctuations are here discrete positive numbers. Because of this, reactive systems constitute an ideal ground for testing various hypotheses and for carrying out analyses that would become considerably more involved for other types of systems like, e.g., fluids under stress.

In Sec. II, a short reminder of our formulation of the extended local equilibrium approach is given. Section III is devoted to an analysis of entropy production around stable steady states. We consider chemical reactions under both equilibrium and nonequilibrium conditions. We analyze how fluctuations affect the mean entropy production and derive simple analytical expressions for the probability distribution of this quantity in one-variable systems. We show in particular that fluctuation-type theorems can be obtained. In Sec. IV, we address the problem of entropy production at bifurcation points, where fluctuations display critical behavior. A comparison of these results with those obtained with alternative definitions of entropy production is carried out in Sec. V. Section VI is devoted to an extension of the results to the case of multivariate systems. The main conclusions are summarized in Sec. VII.

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II. GENERAL FORMULATION

We focus on spatially uniform reactive systems of constant volume, with no bulk velocity and in the absence of external forces. We, moreover, assume that the temperature T is maintained constant through contact with an external heat reservoir. The stochastic variables of interest are thus the concentrations (moles per unit volume) $\boldsymbol{c} \equiv \{c_i\}$, $i = (1, \ldots, n)$ of the n different species involved, the time evolution of which is given by a balance equation of the form [12,13]

$$\frac{dc_i}{dt} = \Phi_i + \sigma_i. \tag{2}$$

In the above expression, Φ_i denotes the exchange of matter with the environment while σ_i accounts for the rate of change of species i due to internal processes which, in our setting, are the chemical reactions.

We incorporate the spontaneous fluctuations of composition by expressing the exchange and the production terms as the superposition of a systematic and a fluctuating part:

$$\Phi_i = J_i(\boldsymbol{c}) + j_i(t), \tag{3a}$$

$$\sigma_i = \sum_\rho \nu_{i\rho}\,[W_\rho(\boldsymbol{c}) + w_\rho(t)] \equiv \sum_\rho \nu_{i\rho}\, v_\rho. \tag{3b}$$

Here J_i is the rate of exchange of mass as used in macroscopic nonequilibrium thermodynamics, in which, however, the state variables are now stochastic quantities. W_ρ denotes the rates of the different elementary reaction steps and incorporates, again, fluctuating variables. $\nu_{i\rho}$ are the stoichiometric coefficients of species i in the reactive process ρ. The quantities j_i and w_ρ stand for the contributions of random forces accounting for the effect of microscopic processes. We will here assume that they can be adequately modeled as independent zero-mean Gaussian white noises. More specifically, we will consider that the intensity of the noise related to internal processes is given by the fluctuation-dissipation relation

$$\overline{w_\rho(t)\, w_{\rho'}(t')} = \frac{W_\rho^m}{\Omega}\, \delta^{Kr}_{\rho,\rho'}\, \delta(t - t'), \tag{4}$$

where Ω is an extensivity parameter and where the superscript m indicates that the rate function takes its mean-field (deterministic) value $W_\rho[\boldsymbol{c}^m(t)]$, in which $c_i^m(t)$ is the solution of Eq. (2) in the absence of fluctuations. Note that in this formulation a random force w_ρ is associated to each elementary step ρ. This accounts automatically for the fact that since the different chemical species react with each other, their concentrations cannot be considered as independent stochastic processes.

Our main objective in this work is to determine the statistical properties of the entropy production associated to such systems. We will do so be relying on a stochastic extension of the local equilibrium hypothesis which, in phenomenological nonequilibrium thermodynamics, stipulates that state functions depend on the state variables through the same relations as in equilibrium. It can be shown that this assumption holds true as long as the constraints acting on a system vary over time and space scales that are significantly larger than those associated with microscopic-scale processes [14]. This encompasses a wide range of phenomena, from the linear to the fully nonlinear range of irreversible processes. In the extended local equilibrium approach that we propose, the thermodynamic state functions will be taken to depend on the *fluctuating* state variables through similar relations [11]. The rationale behind this extension is that as long as heat release due to chemical reactions is moderate, microscopic variables like velocity distributions are decoupled from the statistics of composition variables and are thus expected to be described by equilibrium distributions [13,14]. This decoupling is also at the basis of the chemical master equation.

In view of the foregoing, the rate of change of the entropy per unit volume s is given by

$$\frac{ds}{dt} = \frac{1}{T}\frac{du}{dt} - \sum_i \frac{\mu_i}{T}\frac{dc_i}{dt}, \tag{5}$$

where u is the internal energy per unit volume and $\mu_i = -T\,(\partial s/\partial c_i)_{u,V,c_{j\neq i}}$ is the chemical potential of species i. Utilizing the first law of thermodynamics and using the assumptions adopted in this work, the time evolution of u can be written as

$$\frac{du}{dt} = \Phi_u = \frac{dq'}{dt}, \tag{6}$$

where dq'/dt is the generalized heat flux per unit volume. This flux can be decomposed into a term dq/dt representing the transfer of heat due to temperature gradients and a term taking into account heat transfer arising from the exchange of mass [13]:

$$\begin{aligned}\frac{dq'}{dt} &= \frac{dq}{dt} + \sum_i \left(\frac{\partial u}{\partial c_i}\right)_{T,V,c_{j\neq i}} \Phi_i \\ &= \frac{dq}{dt} + \sum_i h_i\, \Phi_i,\end{aligned} \tag{7}$$

where we used $u = h - p$, performed a change of variable, and used Maxwell's relations, and in which $h_i = (\partial h/\partial c_i)_{T,p,c_{j\neq i}}$ is the partial specific enthalpy of species i. Note that because of our assumption of thermal equilibrium, the temperature in the system is at all times exactly equal to that of the environment, so $dq/dt = 0$ and only the exchange of matter contributes to the flow of internal energy.

The rate of change of entropy can thus be written as [12]

$$\frac{ds}{dt} = \Phi + \sigma, \tag{8}$$

in which the exchange of entropy Φ reads

$$\Phi = \sum_i s_i\, \Phi_i, \tag{9}$$

$s_i = (h_i - \mu_i)/T$ being the partial specific entropy of component i. Utilizing (3b), one may define the entropy production as

$$\sigma = -\sum_i \frac{\mu_i}{T}\sigma_i = \sum_\rho \frac{\mathcal{A}_\rho}{T}\, v_\rho, \tag{10}$$

where we have introduced the affinity of reaction ρ,

$$\mathcal{A}_\rho = -\sum_i \nu_{i\rho}\, \mu_i. \tag{11}$$

We observe that both the exchange and the production of entropy contain systematic and fluctuating parts. By virtue of the second law of thermodynamics, the systematic part of the entropy production is expected to respect a strict constraint of positivity,

$$\sigma_{\rm I} \equiv \sum_\rho \frac{\mathcal{A}_\rho}{T}\, W_\rho \geqslant 0, \tag{12}$$

while nothing can be said *a priori* concerning the entropy flow or the contribution of fluctuations to the entropy production

$$\sigma_{\rm II} \equiv \sum_\rho \frac{\mathcal{A}_\rho}{T}\, w_\rho(t), \tag{13}$$

since the random forces w_ρ need not be aligned with the macroscopically imposed thermodynamic forces $\mathcal{A}_\rho$.

In view of the foregoing, we expect the entropy exchange (9) and the entropy production (10) to deviate from the deterministic expressions

$$\Phi^m = \sum_i s_i^m\, J_i^m, \tag{14a}$$

$$\sigma^m = \sum_\rho \frac{\mathcal{A}_\rho^m}{T}\, W_\rho^m. \tag{14b}$$

In order to assess the extent to which fluctuations can affect these quantities, we introduce deviations from the solutions in the mean-field limit as

$$c_i = c_i^m + \Delta c_i, \tag{15a}$$

$$J_i = J_i^m + \Delta J_i; \quad s_i = s_i^m + \Delta s_i, \tag{15b}$$

$$W_\rho = W_\rho^m + \Delta W_\rho; \quad \mathcal{A}_\rho = \mathcal{A}_\rho^m + \Delta \mathcal{A}_\rho. \tag{15c}$$

and, accordingly,

$$\Delta\Phi = \Phi - \Phi^m = \sum_i \left(s_i^m\, \Delta J_i + \Delta s_i\, J_i^m + s_i^m\, j_i\right) + \sum_i \Delta s_i\, \Delta J_i + \sum_i \Delta s_i\, j_i, \tag{16a}$$

$$\Delta\sigma = \sigma - \sigma^m = \frac{1}{T}\sum_\rho \left(\mathcal{A}_\rho^m\, \Delta W_\rho + \Delta\mathcal{A}_\rho\, W_\rho^m + \mathcal{A}_\rho^m\, w_\rho\right) + \frac{1}{T}\sum_\rho \Delta\mathcal{A}_\rho\, \Delta W_\rho + \frac{1}{T}\sum_\rho \Delta\mathcal{A}_\rho\, w_\rho. \tag{16b}$$

We will refer to $\Delta\Phi$ and $\Delta\sigma$ as the entropy flux and the entropy production of the fluctuations, respectively. Similar expressions can be written for the deviations from the ensemble averages, $\delta\Phi = \Phi - \overline{\Phi}$ and $\delta\sigma = \sigma - \overline{\sigma}$, the difference being that the subscript "m" is replaced by averaging and that the deviations ΔJ_i, etc., are replaced by the corresponding fluctuations δJ_i.

In the sequel, the properties of representative stochastic thermodynamic quantities will be analyzed for typical cases of nonequilibrium reactive systems. We will consider situations where the distance from equilibrium can be controlled by maintaining the concentration of some of the chemical species, $p = (1, \ldots, \gamma)$ with $\gamma < n$, constant in time thanks to a rapid exchange of matter with the environment. We will refer to such components as the *pool species*. The remaining reactants $r = (1, \ldots, n-\gamma)$ are supposed to be contained in the reactive volume and will thus be referred to as the *internal species*. With this distinction, $\Phi_p = -\sigma_p$ at all times for the pool species, while the time evolution of the internal reactants contains only a source term. Our analysis will focus on the statistical properties of the entropy production associated to such systems. More specifically, we will consider the time-averaged quantity

$$\Sigma_t \equiv \frac{1}{t}\int_0^t \sigma(t')\, dt' \tag{17}$$

in order to avoid the singular contributions coming from the random forces. We will also be interested in the cumulative entropy production, that is, the entropy produced along a given path

$$\Delta_i S = \Omega \int_0^t \sigma(t')\, dt' = \Omega\, \Sigma_t\, t, \tag{18}$$

to allow for a comparison with results obtained previously with the Gibbs-Shannon-like definition of the trajectory-wise entropy production (as in Refs. [5,8–10]).

III. SYSTEMS INVOLVING ONE INTERNAL VARIABLE

As a first step we analyze the effect of fluctuations on the entropy production for reactive systems characterized by a single fluctuating concentration, limiting ourselves to the behavior around stable steady states. Mean values as well as the probability distribution of this quantity will be deduced. The case of entropy production at a critical point will be addressed in Sec. IV.

A. Mean entropy production of fluctuations

Utilizing Eq. (10), one can express the ensemble average of the deviation of entropy production from the mean-field value as

$$T\, \overline{\Delta\sigma} = -\sum_i \overline{\Delta(\mu_i\, \sigma_i)}. \tag{19}$$

According to Eq. (16b) this expression involves an intricate combination of the reaction rates and concentrations of all the species participating in the reactions. A fairly simple expression can, however, be obtained by noting that at a steady state, $\overline{\Phi} + \overline{\sigma}$ and $\Phi^m + \sigma^m$ are both equal to zero, so $\overline{\Delta\sigma} = -\overline{\Delta\Phi}$. Furthermore, in view of our separation of reactants into pool and internal species, only the pool reactants enter Eqs. (9) and (14a) so

$$\overline{\Delta\sigma} = \sum_p \left(s_p^m\, J_p^m - \overline{s_p\, \Phi_p}\right). \tag{20}$$

Adding to the right-hand side of Eq. (20), the expression

$$\frac{1}{T}\frac{d(\overline{u} - u^m)}{dt} = \frac{1}{T}\sum_p \left(\overline{h_p\, \Phi_p} - h_p^m\, J_p^m\right) = 0 \tag{21}$$

leads to our final result:

$$T\, \overline{\Delta\sigma} = \sum_p \overline{\Delta\,(\mu_p\, \Phi_p)} = -\sum_p \overline{\Delta\,(\mu_p\, \sigma_p)}, \tag{22}$$

where we also made use of the fact that for the pool variables, $\Phi_p = -\sigma_p$ at all times.

In short, the rates of change of internal species do not contribute explicitly to the mean entropy production of fluctuations. The deviations of the entropy production from its deterministic value are thus solely determined by the dynamics of the species that are exchanged with the environment and by the distance from equilibrium, through the values taken by their chemical potentials, suggesting that general conclusions on the role played by fluctuations can be obtained whatever the dynamics of the internal variables might be. Consider as an example the case of reactions taking place in a system where the chemical potentials of the pool species are kept constant thanks to the exchanges with the environment. In such conditions, Eq. (22) further simplifies to

$$T\,\overline{\Delta\sigma} = -\sum_p \mu_p\,\overline{\Delta\,\sigma_p}. \tag{23}$$

The correction term is here a weighted sum of the deviations of the mean production rates of the pool variables with respect to their deterministic values. Consequently, the mean entropy of fluctuations will be zero for all systems comprising only linear processes. Nonlinearities thus play an essential role in the deviations from the mean-field entropy production.

The role of nonlinearities is especially transparent in the case of systems involving a single fluctuating concentration. Consider as an illustration the classical Schlögl model [15]

$$\mathrm{A} + 2\,\mathrm{X} \rightleftharpoons 3\,\mathrm{X}, \tag{24}$$

$$\mathrm{X} \rightleftharpoons \mathrm{B}, \tag{25}$$

where X is the internal species and A, B the pool species. Note that two such species are needed to allow for the realization of nonequilibrium states. The evolution of the fluctuating concentration c of the internal species is ruled by

$$\begin{aligned}\frac{dc}{dt} &= v_1 - v_{-1} + v_{-2} - v_2\\ &= k_1\,c_A\,c^2 - k_{-1}\,c^3 + k_{-2}\,c_B - k_2\,c\\ &\quad + w_1(t) - w_{-1}(t) + w_{-2}(t) - w_2(t),\end{aligned} \tag{26}$$

while for the pool variables c_A,c_B associated to species A and B, one has

$$\frac{dc_A}{dt} = \phi_A + v_{-1} - v_1 = 0, \tag{27}$$

$$\frac{dc_B}{dt} = \phi_B + v_2 - v_{-2} = 0. \tag{28}$$

The corresponding stochastic entropy production reads

$$\begin{aligned}\sigma &= \frac{\mathcal{A}_1}{T}\,(v_1 - v_{-1}) + \frac{\mathcal{A}_2}{T}\,(v_2 - v_{-2})\\ &= k_B\left[k_1\,c_A\,c^2 - k_{-1}\,c^3 + w_1(t) - w_{-1}(t)\right]\ln\left(\frac{k_1\,c_A}{k_{-1}\,c}\right)\\ &\quad + k_B\left[k_2\,c - k_{-2}\,c_B + w_2(t) - w_{-2}(t)\right]\ln\left(\frac{k_2\,c}{k_{-2}\,c_B}\right).\end{aligned} \tag{29}$$

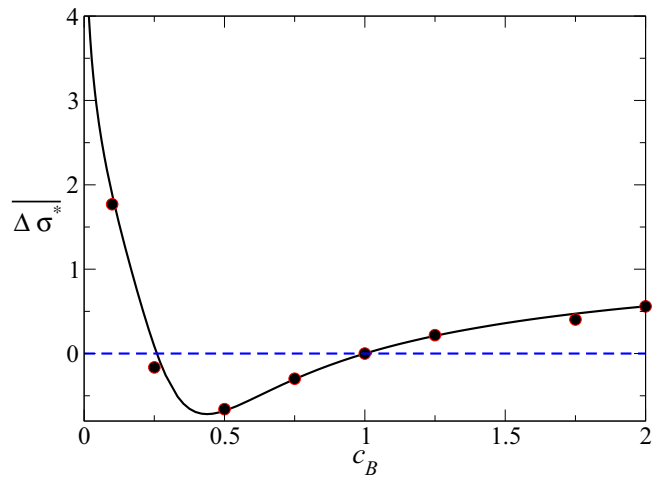

FIG. 1. Mean normalized entropy production of fluctuations $\overline{\Delta\sigma^*}$ (see text) for the model (24) and (25), as a function of the control parameter c_B. The other kinetic parameters are all set to 1 and $\Omega = 1000$. The dots correspond to the outcome of numerical integrations (total time = 10, the Stratonovich interpretation was used) averaged over 10 000 realizations of the corresponding stochastic differential equation, with $dt = 1.0 \times 10^{-5}$. The plain curve is the analytical prediction as obtained from (30). The dashed line is used to highlight states of zero entropy production of fluctuations.

We now estimate the mean entropy production of fluctuations. We start by noting that since, at steady state, $\overline{v_1 - v_{-1}} = \overline{v_2 - v_{-2}}$ and $v_1^m - v_{-1}^m = v_2^m - v_{-2}^m$,

$$\begin{aligned}T\,\overline{\Delta\sigma} &= \mu_A\,\overline{\Delta\,(v_1 - v_{-1})} - \mu_B\,\overline{\Delta\,(v_2 - v_{-2})}\\ &= (\mu_A - \mu_B)\,\overline{\Delta\,(v_2 - v_{-2})} = (\mu_A - \mu_B)\,k_2\,\overline{\Delta c},\end{aligned} \tag{30}$$

in which $\overline{\Delta c} = \overline{c} - c^m$. This deviation can be estimated by averaging Eq. (26) over the noise, which at the steady state leads to

$$k_1\,c_A\,\overline{c^2} - k_{-1}\,\overline{c^3} - k_2\,\overline{c} + k_{-2}\,c_B = 0. \tag{31}$$

Expanding the moments of c in powers of $\delta c = c - \overline{c}$ in the above equation, and subsequently developing $\overline{c}$ around c^m, leads to the leading order

$$\overline{\Delta c} = -\left[\frac{3\,k_{-1}\,c^m - k_1\,c_A}{2\,k_1\,c_A\,c^m - 3\,k_{-1}\,(c^m)^2 - k_2}\right]\overline{\delta c^2}. \tag{32}$$

We observe that the value taken by $\overline{\Delta\sigma}$ depends both on a "thermodynamic" quantity, the affinity of the overall reaction

$$A \rightleftharpoons B, \tag{33}$$

and on kinetic parameters through Eq. (32). Figure 1 plots $\overline{\Delta\sigma^*} = \overline{\Delta\sigma}/(k_B\,\overline{\delta c^2})$ as a function of the concentration c_B for a specific choice of parameters. The dots in this figure denote an evaluation of the entropy of fluctuations from numerical integrations of the full Eq. (26) with the Euler-Maruyama algorithm. The agreement with the analytic estimate is excellent. We observe that the entropy production of fluctuations is zero at equilibrium, as expected (here, at $c_B = 1$), but also in the nonequilibrium state $c^m = k_1\,c_A/(3\,k_{-1})$. For other values of the control parameter, the mean entropy production can be either larger or smaller than the mean-field value: Contrary to

what intuition might suggest, fluctuations do not always lead to more dissipation in the sense of more entropy production.

B. Probability distribution of the entropy production

We now go one step further and derive the probability distribution of entropy production. Since we consider here systems having a single fluctuating concentration c, the entropy production can be expanded in powers of the deviation of this variable from its ensemble average:

$$\delta\sigma = \sigma - \overline{\sigma} = \sigma_I'(\overline{c})\,\delta c + \frac{\sigma_I''(\overline{c})}{2}\,\delta c^2 + \sum_\rho \frac{\mathcal{A}_\rho(\overline{c})}{T}\,w_\rho + \sum_\rho \frac{\mathcal{A}_\rho'(\overline{c})}{T}\,w_\rho\,\delta c + \ldots, \quad (34)$$

where the primes stand for derivation with respect to c. We will refer to $\delta\sigma$ as the excess of entropy production. The stochastic evolution Eq. (2) ruling the temporal evolution of c can be expanded in a similar fashion, which, to the leading order, reads

$$\frac{d\,\delta c}{dt} \approx \sum_\rho \nu_\rho\, W_\rho'(\overline{c})\,\delta c + \sum_\rho \nu_\rho\, w_\rho \equiv -\lambda\,\delta c + R(t), \quad (35)$$

where $\lambda > 0$ since we are considering fluctuations around a stable steady state, and where the intensity of the noise is given by

$$\overline{R(t)\,R(t')} = \frac{q^2}{\Omega} = \frac{1}{\Omega}\sum_\rho \nu_\rho^2\, W_\rho^m\,\delta(t-t'). \quad (36)$$

In the weak noise limit one expects that an appropriate expression for the probability distribution of $\delta\sigma$ can be obtained by considering likewise only the dominant contributions of the development in (34) which, generally speaking, would consist in keeping the first and the third terms of the sum. At equilibrium, however, both σ_I' and $\mathcal{A}_\rho$ are zero by definition and such an approximation cannot hold anymore. The statistical properties of entropy production will thus qualitatively differ depending on the state of the system with respect to equilibrium.

1. Nonequilibrium stable steady states

As stated previously, for generic nonequilibrium situations and in the weak noise limit, the sum in (34) can be reduced to its dominant part given by the first and the third terms. We emphasize that this as well as the analogous assumption leading to Eq. (35) do not limit the analysis to the linear range of irreversible processes but remain compatible with far-from-equilibrium situations.

Summarizing, the time-averaged excess of entropy production is given to the dominant order by

$$\delta\Sigma_t = \frac{\sigma_I'(\overline{c})}{t}\int_0^t \delta c(t')\,dt' + \sum_\rho \frac{\mathcal{A}_\rho(\overline{c})}{t\,T}\int_0^t w_\rho(t')\,dt' \equiv Z_t + V_t. \quad (37)$$

The mean $\overline{Z_t}$ of the process Z_t is zero since by definition $\overline{\delta c} = 0$, while its variance reads

$$\overline{\delta Z_t^2} = \frac{q^2\,\sigma_I'(\overline{c})^2}{\lambda^2\,\Omega\,t}. \quad (38)$$

Moreover, since on the grounds of Eq. (35) this quantity is obtained as the time integral of an Ornstein-Ulhenbeck process, it can be assumed to be distributed in a Gaussian way in view of the central limit theorem. As for process V_t, it is a Wiener process of zero mean and of variance $Q^2/(\Omega t)$ with

$$Q^2 = \sum_\rho \frac{\mathcal{A}_\rho^2(\overline{c})\,W_\rho^m}{T^2}. \quad (39)$$

The distribution of $\delta\Sigma_t$ thus takes the form (see also Ref. [11])

$$P(\delta\Sigma_t) \approx \sqrt{\frac{\Omega\,t}{2\,\pi\,\Delta_0}}\,\exp\left(-\frac{\Omega\,t}{2\,\Delta_0}\,\delta\Sigma_t^2\right), \quad (40)$$

where

$$\Delta_0 = \frac{q^2\,\sigma_I'(\overline{c})^2}{\lambda^2} + Q^2. \quad (41)$$

We observe that this distribution is Gaussian and contains contributions which are specific to the details of the kinetics. The variance of $\delta\Sigma_t$ is thus process dependent:

$$\mathrm{Var}(\delta\Sigma_t) = \frac{\Delta_0}{\Omega\,t}. \quad (42)$$

Note that it decreases as the size of the system or time increase.

For similar reasons, the distribution of the cumulative excess entropy production $\Delta_i S$ is also Gaussian with process-dependent coefficients,

$$P(\Delta_i S) \approx \frac{1}{\sqrt{2\,\pi\,\Delta_0\,\Omega\,t}}\,\exp\left[-\frac{(\Delta_i S - \overline{\Delta_i S})^2}{2\,\Delta_0\,\Omega\,t}\right], \quad (43)$$

where $\overline{\Delta_i S} = \overline{\sigma}\,\Omega\,t$ is the mean entropy produced at the steady state during a time t. In Fig. 2 we plot the probability distribution of $\Delta_i S$ for the Schlögl model as obtained numerically using the full expression of $\delta\sigma$ in Eq. (34) incorporating all contributions in δc. Despite the relatively small size of the system considered, $\Delta_i S$ closely follows the Gaussian form in Eq. (43), thereby confirming the validity of the procedure where $\delta\sigma$ was limited to its dominant terms. Small deviations from the Gaussian curve could exist in the tails of the numerically obtained histograms, i.e., for large values of the cumulative entropy production.

We note finally that Eq. (43) gives rise to a fluctuation-type theorem of the form

$$\frac{P(\Delta_i S)}{P(-\Delta_i S)} = \exp\left(\frac{2\,\overline{\sigma}}{\Delta_0}\,\Delta_i S\right). \quad (44)$$

The exponential dependence in (44) and the value of the coefficient in this exponential are confirmed numerically (see Fig. 3). The extensivity of $\Delta_i S$ has the consequence that the probability to observe a negative entropy production decreases rapidly with the size of the system or, equivalently, with the sampling time. Notice that the range of validity of Eq. (44) is more limited compared to the classic fluctuation theorem of Gallavotti and Cohen [16], since large deviations incorporated

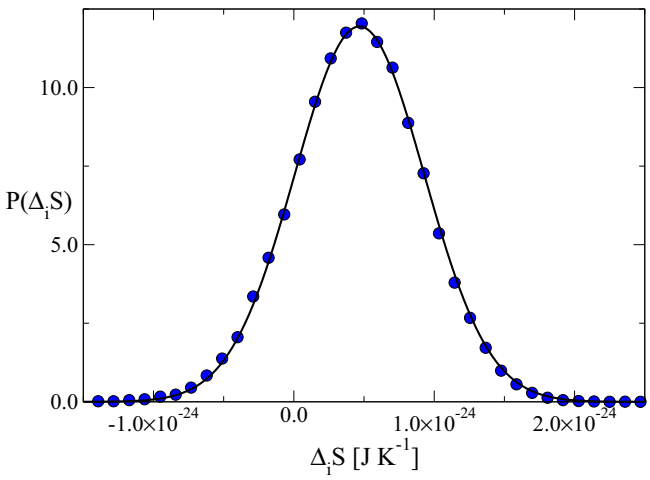

FIG. 2. Probability distribution of the cumulative entropy production $\Delta_i S$ for the Schlögl model (24) and (25). All constants are set to 1 as before, except for $c_B = 1.1$. The size of the system is $\Omega = 50$ and the total integration time is 10. The plain curve is a Gaussian fitting, while the dots mark the statistics extracted from 50 000 numerical realizations of the stochastic model.

in this theorem are not fully accounted for in our Gaussian approximation. Nevertheless, in view of Fig. 2, one can expect that their effect is limited under the conditions adopted for the system size and the time window.

2. *Fluctuations around equilibrium*

In equilibrium, the first and the third terms in (34) are identically zero and the dominant part of the excess of entropy production is now

$$\delta\sigma \approx \frac{\sigma_I''(\overline{c})}{2}\,\delta c^2 + \sum_\rho \frac{\mathcal{A}_\rho'(\overline{c})}{T}\,w_\rho\,\delta c. \tag{45}$$

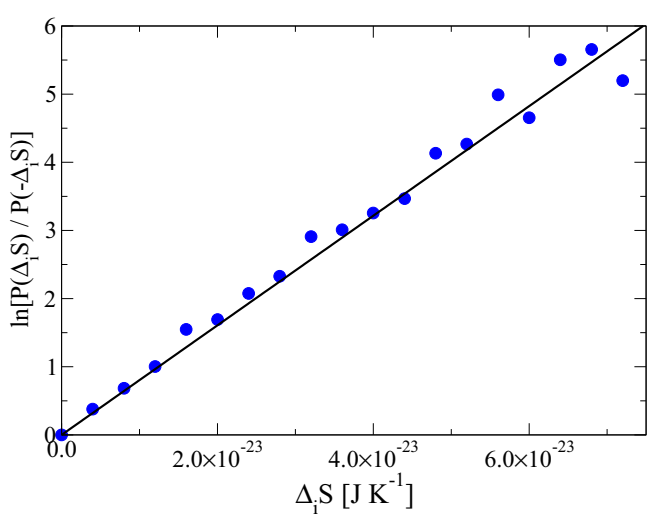

FIG. 3. Verification of the fluctuation theorem (44) for the Schlögl model (24) and (25). All constants and parameters are the same as in Fig. 2. The plain straight line is the analytical prediction and the dots represent numerical estimates.

The coefficient appearing in front of the δc^2 contribution reduces to

$$\frac{\sigma_I''(\overline{c})}{2} = \sum_\rho \frac{\mathcal{A}_\rho'(\overline{c})}{T}\,W_\rho'(\overline{c}) = \lambda\,\frac{\mu'(\overline{c})}{T} \tag{46}$$

since the affinities and the reaction rates vanish at equilibrium and the chemical potential of the other (pool) variables is assumed constant. Using the same properties as well as Eq. (35), the second contribution becomes

$$\sum_\rho \frac{\mathcal{A}_\rho'(\overline{c})}{T}\,w_\rho\,\delta c = -\frac{\mu'(\overline{c})}{T}\,\delta c\,R(t), \tag{47}$$

so

$$\delta\sigma \approx -\frac{\mu'(\overline{c})}{T}\,\delta c\,\frac{d\,\delta c}{dt} = -\frac{\mu'(\overline{c})}{2\,T}\left(\frac{d}{dt}\,\delta c^2\right). \tag{48}$$

We thus arrive at the conclusion that the dominant part of the time-averaged excess of entropy production is given by

$$\delta\Sigma_t \approx \frac{\mu'(\overline{c})}{2\,T}\,\frac{\left(\delta c_0^2 - \delta c_t^2\right)}{t}, \tag{49}$$

where the subscripts indicate the time at which the fluctuation is measured.

The probability distribution of $\delta\Sigma_t$ can be obtained explicitly in the limit of long times, for which we expect δc_t and δc_0 to be independent in first approximation. Using the convolution of distributions, and inasmuch as the initial condition is sampled over the invariant distribution of the process, we obtain

$$\begin{aligned} P(\delta\Sigma_t) &= \int_0^\infty d\left(\delta c_0^2\right)\int_0^\infty d\left(\delta c_t^2\right)P\left(\delta c_0^2\right)P\left(\delta c_t^2\right)\delta_D \\ &\quad\times\left[\delta\Sigma_t - \frac{\mu'}{2\,T\,t}\left(\delta c_0^2 - \delta c_t^2\right)\right] \\ &= 4\int_0^\infty d(\delta c_0)\int_0^\infty d(\delta c_t)\,P(\delta c_0)\,P(\delta c_t)\,\delta_D \\ &\quad\times\left[\delta\Sigma_t - \frac{\mu'}{2\,T\,t}\left(\delta c_0^2 - \delta c_t^2\right)\right], \end{aligned} \tag{50}$$

where δ_D stands for a Dirac δ. To obtain the second expression, we performed a change of variable remembering that, in view of Eq. (35), δc is an Ornstein-Uhlenbeck process of variance $q^2/(2\,\Omega\,\lambda)$ and hence that $P(\delta c)$ is symmetric around 0. Using, in addition, the properties of Dirac δs, one arrives at the conclusion that[1] (see also Ref. [11])

$$P(\delta\Sigma_t) = \frac{2\,T\,\lambda\,\Omega\,t}{\pi\,\mu'(\overline{c})\,q^2}\,K_0\left(\left|\frac{2\,T\,\lambda\,\Omega\,\delta\Sigma_t\,t}{\mu'(\overline{c})\,q^2}\right|\right), \tag{51}$$

in which K_0 is the modified Bessel function of the second kind. A more transparent expression can be obtained for sufficiently large values of $\Omega\,\delta\Sigma_t\,t$, for which an asymptotic expansion leads to

$$P(\delta\Sigma_t) \approx \sqrt{\frac{\Omega\,t}{4\,\pi\,k_B\,|\delta\Sigma_t|}}\,\exp\left(-\frac{\Omega\,t}{k_B}\,|\delta\Sigma_t|\right), \tag{52}$$

[1]Note that the situations where $\delta\Sigma_t > 0$ and $\delta\Sigma_t < 0$ need to be considered separately.

which is valid for long times and/or large systems. Note that we used the fact that at equilibrium one has the fluctuation-dissipation relation

$$q^2/(2\lambda) = k_B\, T/\mu'. \tag{53}$$

The equilibrium distribution of $\delta\Sigma_t$ as given by Eq. (52) has a zero mean, is symmetric around (and singular in) $\delta\,\Sigma_t = 0$ where it tends to infinity, and rapidly decreases to zero for nonzero values of the excess of the time-averaged entropy production. Negative and positive entropy productions are thus possible and equally probable, but most of the probability mass is concentrated around the macroscopic value $\delta\Sigma_t = \Sigma_t = 0$, a feature which is also reflected in the expression for the variance [as obtained from Eq. (51)]

$$\mathrm{Var}(\delta\Sigma_t) = \left(\frac{k_B}{\Omega\, t}\right)^2. \tag{54}$$

We observe that the variance decreases as the size of the system or time increase, but more rapidly (i.e., as Ω^{-2} and t^{-2}) than it does in regular out-of-equilibrium cases (for which the variance goes like $\Omega^{-1}\, t^{-1}$). Finally, and more surprisingly, the distribution of Σ_t is independent of the type of process taking place in the system and of the thermodynamic properties of the species involved. It depends only on fundamental constants, on the size of the system, and on the time of sampling.

This universality appears even more clearly in the probability distribution of the cumulative excess entropy production $\Delta_i S$, which takes the form

$$P(\Delta_i S) = \frac{1}{\pi\, k_B}\, K_0\!\left(\frac{|\Delta_i S|}{k_B}\right), \tag{55}$$

$$\approx \sqrt{\frac{1}{4\,\pi\, k_B\, |\Delta_i S|}}\, \exp\left(-\frac{|\Delta_i S|}{k_B}\right). \tag{56}$$

Figure 4 shows the equilibrium distribution of the cumulative entropy production as obtained for the Schlögl model (24) and (25). These results are in full agreement with Eq. (56) and confirm that the same distribution is obtained for different system sizes and sampling times. Contrary to the trajectory-wise entropy production defined in earlier work (see Introduction), $\Delta_i S$ is here a distributed quantity. This major difference will be discussed in Sec. V.

In short, at equilibrium not only do all reactive systems of the type considered here produce zero entropy on average, but the distribution of the fluctuations of entropy production around that mean is universal with a standard deviation equal to k_B. This reinforces the role of entropy production as a universal indicator of the equilibrium state.

IV. CRITICAL BEHAVIOR

So far, we assumed that the concentration of the single internal species was fluctuating around a mean value corresponding to a stable steady state. Far from equilibrium, however, the stability of states can be compromised as the system crosses a bifurcation point. This has important repercussions at the level of the probability distributions. In particular, it has been established that the distributions of the dynamical variables at a bifurcation point are no longer described adequately by a Gaussian distribution, even in the limit of large systems. In this section, we analyze how such changes can affect the statistical properties of entropy production. We will investigate in particular if and how the scaling of fluctuations with respect to the extensivity parameter Ω changes at critical points.

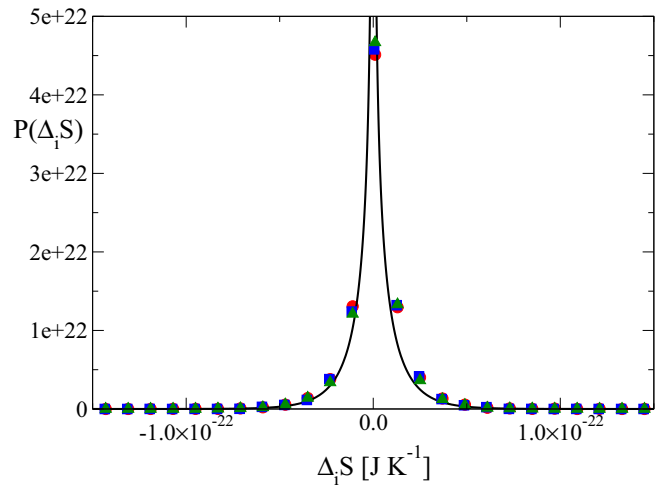

FIG. 4. Equilibrium probability distribution $P(\Delta_i S)$ for the model (24) and (25), with all constants set to 1. The plain curves correspond to the asymptotic analytical expression (56). The different marks stand for the distributions of $\Delta_i S$ obtained from 10 000 realizations of the stochastic differential equation (26) (the numerical method and the time step being the same as in Fig. 2). The circles correspond to a system of size $\Omega = 1000$ and a total integration time $t = 50$, the squares are for $\Omega = 10\,000$ and $t = 50$, while for triangles, $\Omega = 1000$ and $t = 10$.

Since we are considering far-from-equilibrium systems, the time-averaged excess of entropy production can be estimated as the sum of the two stochastic processes Z_t and V_t introduced in (37). The process V_t is insensitive to the presence of a critical point and is thus characterized as before by a Gaussian distribution having the same variance and mean. On the other hand, Z_t is now proportional to the time integral of a process that is not of the Ornstein-Uhlenbeck type anymore since at a bifurcation point, the first derivative of the deterministic rate equation (here equal to λ) vanishes. $\delta c(t)$ will thus be the solution of a stochastic differential equation of the form

$$\frac{d\,\delta c}{dt} \approx -\lambda_k\, \delta c^k + R(t), \tag{57}$$

in which λ_k stands for (minus) the first nonzero value of the kth derivative of the deterministic evolution law evaluated at the steady state. As a consequence, the stationary probability distribution of δc is non-Gaussian. It is given instead by [17]

$$P(\delta c) = \mathcal{N}\, \exp\left[-2\,\frac{\lambda_k\,\Omega}{q^2}\,\frac{\delta c^{k+1}}{(k+1)!}\right], \tag{58}$$

where the factor $\mathcal{N}$ can be determined by normalization. This expression leads to a variance

$$\overline{\delta c^2} = \left[\frac{q^2}{2\,\lambda_k\,\Omega}\,(k+1)!\right]^{2/(k+1)} \frac{\Gamma\!\left(\frac{3}{k+1}\right)}{\Gamma\!\left(\frac{1}{k+1}\right)}, \tag{59}$$

in which Γ is Euler's gamma function. Note that we recover a Gaussian distribution with the expected variance for $k = 1$.

Since δc is not distributed in a Gaussian way, the probability distribution $P(Z_t)$ cannot be expressed analytically in the most general case. We can, however, use the central limit theorem to conjecture that, for long-enough times, Z_t can be seen as a normally distributed quantity with

$$\overline{Z_t} \propto \sigma_I'(\overline{c})\,\overline{\delta c} = 0, \tag{60}$$

$$\overline{\delta Z_t^2} \propto \frac{\sigma_I'(\overline{c})^2}{t}\,\overline{\delta c^2}. \tag{61}$$

This leads us to conclude that the probability distribution of the time-averaged entropy production should be

$$P(\delta\Sigma_t) \approx \sqrt{\frac{\Omega\, t}{2\,\pi\,\Delta_1}}\,\exp\left(-\frac{\Omega\, t}{2\,\Delta_1}\,\delta\Sigma_t^2\right), \tag{62}$$

where

$$\Delta_1 = \Omega\, t\,\overline{\delta Z_t^2} + Q^2. \tag{63}$$

We observe that the variance of $\delta\Sigma_t$ still decreases linearly with time, but that because of (61) the way it scales with the size of the system depends explicitly on k. More specifically, it will contain a term in Ω^{-1} associated with the white noise and a term in $\Omega^{-2/(k+1)}$ arising from the stochastic process δc. For regular out-of-equilibrium cases, $k = 1$ and the usual scaling law is found. However, since $k > 1$ at criticality, we expect the second contribution to dominate for large enough systems. The variance of the time-averaged entropy production thus presents a scaling with Ω that is specific to the type of bifurcation considered.

The cumulative entropy production also follows a Gaussian distribution,

$$P(\Delta_i S) \approx \frac{1}{\sqrt{2\,\pi\,\Delta_1\,\Omega\, t}}\,\exp\left[-\frac{\left(\Delta_i S - \overline{\Delta_i S}\right)^2}{2\,\Delta_1\,\Omega\, t}\right], \tag{64}$$

with a variance given by

$$\mathrm{Var}(\Delta_i S) = \Delta_1\,\Omega\, t. \tag{65}$$

Consequently, the fluctuation-type theorem for this quantity retains its exponential character,

$$\frac{P(\Delta_i S)}{P(-\Delta_i S)} = \exp\left(\frac{2\,\overline{\sigma}}{\Delta_1}\,\Delta_i S\right), \tag{66}$$

with the coefficient in front of $\Delta_i S$ having the same form as before. We note, however, that contrary to the case of noncritical steady states, this coefficient is in general size-dependent since it scales as $\Omega^{-(k-1)/(k+1)}$ [cf. (63) in combination with (61) and (59)]. Since at a bifurcation point $k > 1$, the ratio between the probabilities to have positive and negative entropy production increases slower with the size of the system than it does for stable steady states. The probability to observe "antithermodynamic" behaviors, consequently, is greater at bifurcation points than for regular, nonequilibrium situations.

We illustrate some of these properties on the Schlögl model introduced earlier (Fig. 5). An appropriate rescaling of the variables and time leads to the following deterministic evolution law [17]:

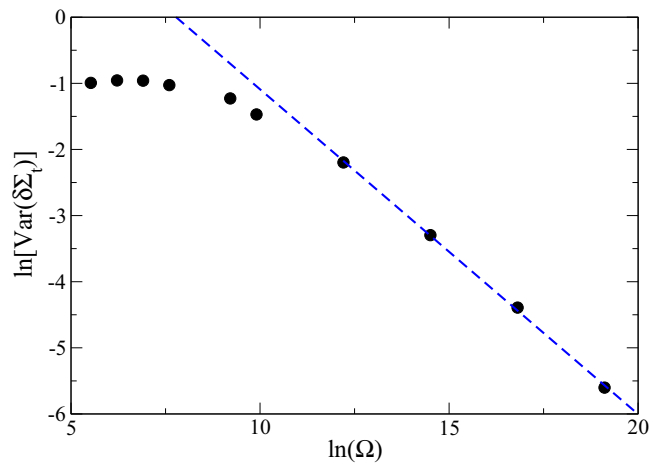

FIG. 5. Dependence of the variance of the (rescaled) excess entropy production $\delta\Sigma_t/k_B$ on the size of the system for the rescaled Schlögl model (67) at criticality. The dots correspond to results obtained by numerical integrations of the corresponding stochastic evolution law. The line is a linear fitting done on the last four points.

$$\frac{dc^m}{dt} = 3\,(c^m)^2 - (c^m)^3 + (1+\delta') - (3+\delta)\,c^m, \tag{67}$$

while the intensity of the noise term in the corresponding stochastic equation now reads

$$q^2 = 3\,(c^m)^2 + (c^m)^3 + (1+\delta') + (3+\delta)\,c^m. \tag{68}$$

This system admits a critical point for $\delta' = \delta = 0$, for which the first and second derivatives of the evolution law are zero since the stationary solution is given by $c^m = 1$. The first nonzero derivative is the third one ($k = 3$, $\lambda_3 = 6$), so the variance of the time-averaged excess of entropy production $\delta\Sigma_t$ is expected to scale as $\Omega^{-1/2}$ in the macroscopic limit. We verified this prediction with a numerical integration of the stochastic evolution law, the results of which are shown in Fig. 5, which plots $\ln[\mathrm{Var}(\delta\Sigma_t)]$ as a function of $\ln(\Omega)$. We see that the variance is almost independent of the size of the system for small Ωs but that it subsequently follows a power law. A linear fitting of this latter stage gives an exponent of -0.49 ± 0.01. For systems that are not at the critical point, the variance scales as Ω^{-1}, in full agreement with the analytical predictions. In all cases, the distribution of entropy production is very well approximated by a Gaussian distribution (not shown here).

V. COMPARISON WITH OTHER DEFINITIONS OF ENTROPY PRODUCTION

In this section, we compare the results of our extended local equilibrium approach for the probability distribution of entropy production with those using a Gibbs-Shannon-inspired definition of entropy. In these latter approaches an entropy production term associated to single trajectories is introduced

in the form

$$\Delta_i S = k_B \ln \frac{\mathbf{P}(\boldsymbol{\xi})}{\tilde{\mathbf{P}}(\tilde{\boldsymbol{\xi}})}, \tag{69}$$

in which $\mathbf{P}(\boldsymbol{\xi})$ is the probability to have a succession of states $\boldsymbol{\xi} = (c_0,t_0;c_1,t_1,\ldots,c_f,t_f)$ and $\tilde{\mathbf{P}}(\tilde{\boldsymbol{\xi}})$ is the probability to observe the "reverse" trajectory starting from the final state c_f and performing a time reversal.

We first consider nonequilibrium systems subjected to time-independent constraints so $\tilde{\mathbf{P}}(\tilde{\boldsymbol{\xi}}) = \mathbf{P}(\tilde{\boldsymbol{\xi}})$. The Langevin equation ruling the temporal evolution of the concentration takes the general form

$$\frac{dc}{dt} = F(c) + R(t), \tag{70}$$

where $F(c)$ refers to the systematic part of the evolution law and $R(t)$ is, as before, the random force having an intensity q^2/Ω. To illustrate the differences with our approach, we focus on the simplest case where $F(c)$ is a linear function of c, $F(c) = \beta - \lambda\, c$. This can correspond either to the dominant terms of an expansion of $F(c)$ around the stationary mean $\bar{c}$ or to the rate equation associated with a simple chain of linear processes like

$$\mathrm{A} \rightleftharpoons \mathrm{X} \rightleftharpoons \mathrm{B}. \tag{71}$$

We emphasize that in both cases the systems considered can be in equilibrium, near equilibrium as well as arbitrarily far-from-equilibrium states.

To evaluate the entropy production, we split (69) as

$$\Delta_i S = k_B \ln \frac{P(c_0)}{P(c_t)} + k_B \ln \frac{\mathbf{P}(\boldsymbol{\xi}|c_0)}{\mathbf{P}(\tilde{\boldsymbol{\xi}}|c_t)}. \tag{72}$$

We consider systems for which the initial conditions are sampled from the stationary distribution. $P(c_0)$ is thus a Gaussian of the form

$$P(c_0) = \frac{1}{\sqrt{2\pi\,\Delta_{c_0}}} \exp\left[-\frac{(c_0-\bar{c})^2}{2\,\Delta_{c_0}}\right], \tag{73}$$

where Δ_{c_0} is the variance of c_0 and similarly for $P(c_t)$. Consequently,

$$k_B \ln \frac{P(c_0)}{P(c_t)} = k_b \frac{\delta c_t^2 - \delta c_0^2}{2\,\Delta_c}, \tag{74}$$

where $\Delta_c = q^2/(2\,\Omega\,\lambda)$ is the variance at steady state. Concerning the second contribution to Eq. (72), we note that since the trajectories are generated by a linear Fokker-Planck equation [18],

$$\frac{\mathbf{P}(\boldsymbol{\xi}|c_0)}{\mathbf{P}(\tilde{\boldsymbol{\xi}}|c_t)} = \exp\left[-2\,A(\boldsymbol{\xi}|c_0))\right], \tag{75}$$

where A is the "action" of the trajectory,

$$A(\boldsymbol{\xi}|c_0)) = -\int_0^t \frac{F(c_{t'})}{R^2(t')}\left(\frac{dc}{dt'}\right) dt'. \tag{76}$$

Consequently,

$$\begin{aligned} k_B \ln \frac{\mathbf{P}(\boldsymbol{\xi}|c_0)}{\mathbf{P}(\tilde{\boldsymbol{\xi}}|c_t)} &= k_B \int_0^t \frac{2\,\Omega\,F(c_{t'})}{q^2}\left(\frac{dc}{dt'}\right) dt' \\ &= -\frac{2\,k_B\,\Omega\,\lambda}{q^2}\int_0^t \delta c_{t'}\left(\frac{d\,\delta c}{dt'}\right) dt' \\ &= -k_b\,\frac{\delta c_t^2 - \delta c_0^2}{2\,\Delta_c}, \end{aligned} \tag{77}$$

where we used the fact that $\delta c = c - \bar{c}$ and that

$$F(c) = F(\bar{c}) - \lambda\,\delta c = -\lambda\,\delta c,$$

by definition of a steady state. Combining (74) and (77), one arrives at the conclusion that the entropy production defined by (69) is zero at the level of each trajectory, not only in equilibrium but also in a nonequilibrium steady state, the difference between the two states being merely in the value of parameter λ. This conclusion is at odds with the properties of entropy production as introduced in classical nonequilibrium thermodynamics. One could argue that the above definition of $\Delta_i S$ actually refers to an excess of entropy production with respect to a stationary value. This would mean that for linear processes, there would be no fluctuation of entropy production at all around steady states. The physical reasons why $\Delta_i S$ would behave in such a way have not been discussed convincingly in the literature so far.

We now consider more specifically reactive systems at equilibrium. The trajectory-wise entropy production defined by (69) is then exactly zero at all times and for all systems, because of detailed balance [8]. As a corollary, although at equilibrium all state variables and state functions fluctuate, the fluctuations of entropy production due to, say, changes in the number of particles would always be strictly zero. Since the total entropy change is bound to fluctuate, there will be a substantial difference between the statistical properties of the entropy production and of the entropy flux (see, e.g., Ref. [19]).

The view developed in our approach differs as entropy production, even if zero on average, is allowed to fluctuate. A similar property applies to the entropy flux as well, i.e., these two parts of the total entropy change are here on an equal footing. As a by-product, the entropy production associated with a fluctuation of concentration δc under the condition that the system was kept initially in macroscopic equilibrium is [cf. Eq. (49)]

$$\Delta_i S = -\frac{\mu'\,\Omega}{2\,T}\,\delta c^2. \tag{78}$$

This expression generates in turn the correct equilibrium distribution of fluctuations of concentration through the Einstein formula [20]

$$P(\delta c, eq) \propto \exp\left[\frac{\Delta_i S}{k_B}\right]. \tag{79}$$

Eventually a decisive test of adequacy of the Gibbs-Shannon-like definition of pathwise entropy production would be the compatibility with entropy production of phenomenological thermodynamics. In the approach followed in the present work this compatibility is secured from the outset.

VI. MULTIVARIATE SYSTEMS

In this section we apply the extended local equilibrium hypothesis to representative classes of multivariate systems,

focusing on the properties of the ensemble averaged entropy production and on its probability distribution.

A. Mean entropy production

We have seen in Sec. IIIA that extensive information can be obtained in the univariate case on the mean entropy production of the fluctuations, $\overline{\Delta\sigma}$, by expressing it in terms of the pool variables. Since no assumption has been made on the number of variables to reach equations (22) and (23), these expressions can be used as such to assess the role of nonlinearities in more general situations. Consider, for example, cases for which an external species A can enter a system in which it undergoes a sequential series of decompositions and transformations to give a final product B:

$$\nu_A\,\mathrm{A} \rightleftharpoons \{\mathrm{X}_1 \rightleftharpoons \mathrm{X}_2 \cdots \rightleftharpoons \mathrm{X}_{n-2}\} \rightleftharpoons \nu_B\,\mathrm{B}. \tag{80}$$

We can associate a fluctuating rate of reaction $\tilde{v}_\rho = v_\rho - v_{-\rho}$, $\rho = (1,2,\ldots,n-1)$, be it linear or not, to each of the $n-1$ reactions of this scheme. The dynamics is ruled by the following set of stochastic differential equations:

$$\begin{aligned}
\frac{dc_A}{dt} &= \phi_A - \nu_A\,\tilde{v}_1\\
\frac{dc_{\rho-1}}{dt} &= \overrightarrow{\nu}_{\rho-1}\,\tilde{v}_{\rho-1} - \overleftarrow{\nu}_{\rho-1}\,\tilde{v}_\rho \quad (\rho = 2,\ldots,n-1)\\
\frac{dc_B}{dt} &= \phi_B + \nu_B\,\tilde{v}_{n-1}.
\end{aligned} \tag{81}$$

A and B are kept constant in time (they act as pool species) while the concentrations of intermediates (the internal species) can change and fluctuate. The steady-state entropy production of fluctuations (23) takes the simple form:

$$T\,\overline{\Delta\sigma} = -\mu_A\,\overline{\Delta\sigma_A} - \mu_B\,\overline{\Delta\sigma_B} = \nu_A\,\mu_A\,\overline{\Delta\,\tilde{v}_1} - \nu_B\,\mu_B\,\overline{\Delta\,\tilde{v}_{n-1}}. \tag{82}$$

Since we place ourselves on the steady state, $\overline{\Delta\,\tilde{v}_1}$ and $\overline{\Delta\,\tilde{v}_{n-1}}$ are not independent. Indeed, it can easily be shown that

$$\frac{\overline{\tilde{v}_1}}{\overline{\tilde{v}_{n-1}}} = \frac{\tilde{v}_1^m}{\tilde{v}_{n-1}^m} = \frac{\prod_\rho \overleftarrow{v_\rho}}{\prod_\rho \overrightarrow{v_\rho}} \equiv \alpha. \tag{83}$$

The entropy production (82) thus becomes

$$T\,\overline{\Delta\sigma} = (\alpha\,\nu_A\,\mu_A - \nu_B\,\mu_B)\,\overline{\Delta\,\tilde{v}_{n-1}}. \tag{84}$$

We notice the presence of the affinity $\mathcal{A} = \alpha\,\nu_A\,\mu_A - \nu_B\,\mu_B$ of the overall reaction

$$\alpha\,\nu_A\,\mathrm{A} \rightleftharpoons \nu_B\,\mathrm{B}. \tag{85}$$

This quantity is constant and is controlled externally.

As in the univariate situation, the magnitude and the sign of the steady-state entropy of fluctuations are thus given by a combination of thermodynamic and kinetic ingredients. On the one hand, they are directly related to the macroscopically controlled distance of the reaction (85) from its equilibrium position, through the overall affinity. This has the consequence that $\overline{\Delta\sigma} = 0$ when the global reaction (85) is at equilibrium. On the other hand the excess entropy is also related to the deviation of the rate of production of B (or A) from its deterministic value, which we expect to depend on the details of the microscopic mechanisms and on their rates. As a consequence, $\overline{\Delta\sigma}$ can be positive, negative, or even zero for nonequilibrium systems, depending on the reaction scheme. However, in the special case where all the processes are linear, the stationary mean reaction rates are always equal to their macroscopic value and $\overline{\Delta\sigma}$ is always equal to zero. We thus reach the conclusion that for multivariate systems as well, nonlinearities play an essential role in the value taken by the entropy of fluctuations. It would be interesting to check whether a similar conclusion holds for more complex network topologies as well.

B. Probability distribution

1. Nonequilibrium systems

We first consider systems at a nonequilibrium steady state. The time-averaged excess of entropy production is given by [cf. Eqs. (12), (13), and (17)]

$$\delta\Sigma_t = \frac{1}{t}\sum_i \left(\frac{\partial\sigma_I}{\partial c_i}\right)_{\mathrm{eq}} \int_0^t \delta c_i(t')\,dt' + \sum_\rho \frac{\mathcal{A}_\rho(\overline{c})}{t\,T} \times \int_0^t w_\rho(t')\,dt' = Z_t + V_t. \tag{86}$$

Since the w_ρs are, by definition, independent from each other, V_t is expected to be a normally distributed quantity like before. Z_t is, on the other hand, the sum of coupled stochastic processes so $P(Z_t)$ could, in principle, deviate substantially from a normal distribution. However, we note that in the limit of small fluctuations, $\delta c_i(t)$ is a multivariate Ornstein-Uhlenbeck process satisfying a set of equations of the form [cf. Eq. (35)]

$$\frac{d}{dt}\,\delta c_i = -\sum_j \lambda_{ij}\,\delta c_j + R_i(t), \tag{87}$$

where

$$R_i(t) = \sum_\rho \nu_{i\rho}\,w_\rho(t) \tag{88}$$

so

$$\overline{R_i(t)} = 0, \tag{89}$$

$$\overline{R_i(t)\,R_j(t')} = \sum_{\rho,i,j} \nu_{i\rho}\,\nu_{j\rho}\,\frac{W_\rho^m}{\Omega}\,\delta(t-t'). \tag{90}$$

Since the variance of the noise term is just a constant, a change of coordinates obtained by switching to the eigenmodes of the linear system[2]

$$\mathbf{x} = P^{-1}\,\delta\mathbf{c}, \tag{91}$$

where P is the diagonalization matrix, will generate a system of independent Ornstein-Uhlenbeck processes x_i. As a consequence, Z_t is a linear combination of independent

[2]We do not consider here the specific cases of degenerate or null eigenvalues.

Gaussian processes

$$Z_t = \frac{1}{t}\sum_i \left(\frac{\partial \sigma_I}{\partial c_i}\right)_{\rm eq} \int_0^t \delta c_i(t')\,dt' = \frac{1}{t}\sum_{i,j} \left(\frac{\partial \sigma_I}{\partial c_i}\right)_{\rm eq} P_{ij} \int_0^t \delta x_j(t')\,dt' \tag{92}$$

and is thus expected to be itself a zero-mean Gaussian variable with variance Δ_Z. We note, however, that unlike the case of univariate systems, a simple connection between Δ_Z and the kinetic quantities appearing in the thermodynamic expression of the entropy production cannot be established in general, as the sum in Z_t depends explicitly on the coefficients of the linearization matrix. In any case, since $\delta\Sigma_t$ is a normally distributed random variable, the form of the fluctuation theorem (44) established for univariate systems is expected to hold as well for multivariate systems at a stable steady state.

As an illustration, we carried out numerical integrations of the Brusselator model:

$$\mathrm{A} \rightleftharpoons \mathrm{X}, \tag{93}$$

$$\mathrm{B} + \mathrm{X} \rightleftharpoons \mathrm{D} + \mathrm{Y}, \tag{94}$$

$$2\,\mathrm{X} + \mathrm{Y} \rightleftharpoons 3\,\mathrm{X}, \tag{95}$$

$$\mathrm{X} \rightleftharpoons \mathrm{E}. \tag{96}$$

Since we are considering an ideal system, the stochastic differential equations ruling the temporal evolution of concentrations $c_X(t)$ and $c_Y(t)$ simply read

$$\frac{dc_X}{dt} = k_1\,c_A - k_{-1}\,c_X - k_2\,c_B\,c_X + k_{-2}\,c_D\,c_Y + k_3\,c_X^2\,c_Y - k_{-3}\,c_X^3 - k_4\,c_X + k_{-4}\,c_E + R_X(t), \tag{97}$$

$$\frac{dc_Y}{dt} = k_2\,c_B\,c_X - k_{-2}\,c_D\,c_Y - k_3\,c_X^2\,c_Y + k_{-3}\,c_X^3 + R_Y(t), \tag{98}$$

where $R_X(t) = w_1(t) - w_{-1}(t) - w_2(t) + w_{-2}(t) + w_3(t) - w_{-3}(t) - w_4(t) + w_{-4}(t)$ and $R_Y(t) = w_2(t) - w_{-2}(t) - w_3(t) + w_{-3}(t)$. Note that the concentrations of species A, B, D, and E are considered constant (they are pool variables). The stochastic entropy production is given by

$$\begin{aligned}\frac{\sigma}{k_B} &= \frac{\mathcal{A}_1}{k_B\,T}\,v_1 + \frac{\mathcal{A}_2}{k_B\,T}\,v_2 + \frac{\mathcal{A}_3}{k_B\,T}\,v_3 + \frac{\mathcal{A}_4}{k_B\,T}\,v_4 \\ &= [k_1\,c_A - k_{-1}\,c_X + w_1(t) - w_{-1}(t)]\,\ln\left(\frac{k_1\,c_A}{k_{-1}\,c_X}\right) \\ &\quad + [k_2\,c_B\,c_X - k_{-2}\,c_D\,c_Y + w_2(t) - w_{-2}(t)] \\ &\quad \times \ln\left(\frac{k_2\,c_B\,c_X}{k_{-2}\,c_D\,c_Y}\right) + [k_3\,c_X^2\,c_Y - k_{-3}\,c_X^3 \\ &\quad + w_3(t) - w_{-3}(t)]\,\ln\left(\frac{k_3\,c_Y}{k_{-3}\,c_X}\right) \\ &\quad + [k_4\,c_X - k_{-4}\,c_E + w_4(t) - w_{-4}(t)]\,\ln\left(\frac{k_4\,c_X}{k_{-4}\,c_E}\right).\end{aligned} \tag{99}$$

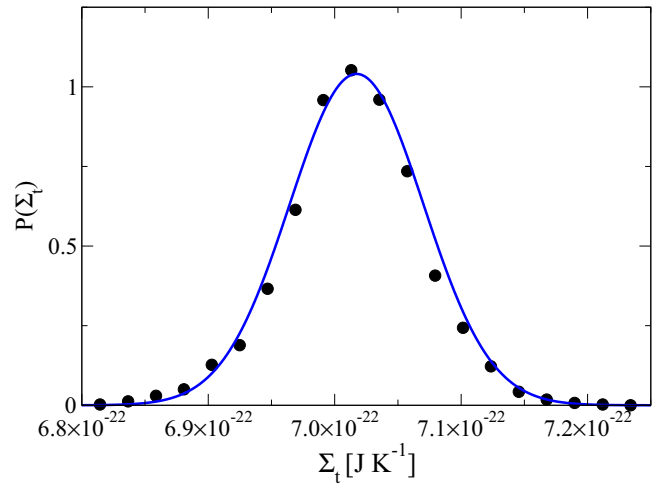

FIG. 6. Steady-state distribution of Σ_t for the Brusselator model with $k_1\,c_A = 0.5$, $k_{-4}\,c_E = 0.25$, $k_{-1} = k_4 = 0.25$, $k_{-2}\,c_D = k_{-3} = 0.25$, $k_2\,c_B = 6$, $k_3 = 1$. The dots correspond to histograms extracted from 10 000 realizations of a system of size $\Omega = 1 \times 10^3$ and a sampling time $t = 200$. The curve is a Gaussian distribution whose mean and variance are those of the numerically obtained data. Note that we use nondimensional time units.

Figure 6 plots the distribution of Σ_t for a choice of parameters for which the system resides at a stable steady state. The agreement between a Gaussian profile constructed with the mean and the variance of the numerical data and the histograms is very good, thereby providing a justification of our procedure. Similar results were also obtained with other reaction schemes, confirming the Gaussian character of the distribution of entropy production in multivariate systems.

2. *Systems at equilibrium*

For multivariate systems at equilibrium, the time-averaged excess of entropy production takes a form very similar to Eq. (49). Indeed, we note that [cf. also (16b)]

$$\delta\sigma = \frac{1}{T}\sum_\rho (\delta W_\rho\,\delta\mathcal{A}_\rho + w_\rho\,\delta\mathcal{A}_\rho) = \frac{1}{T}\sum_{i,\rho} \nu_{i\rho}(\delta W_\rho + w_\rho)\,\delta\mu_i. \tag{100}$$

Using (87) and (3a), this equation reduces to

$$\delta\sigma = \frac{1}{T}\sum_i \delta\mu_i\,\frac{d\delta c_i}{dt} = \frac{1}{T}\sum_{i,j}\left(\frac{\partial\mu_i}{\partial c_j}\right)_{\rm eq}\delta c_j\,\frac{d\delta c_i}{dt} = \frac{1}{2\,T}\,\frac{d}{dt}\sum_{i,j}\left(\frac{\partial\mu_i}{\partial c_j}\right)_{\rm eq}\delta c_i\,\delta c_j, \tag{101}$$

where we also used the symmetry of the cross derivatives of the chemical potentials at equilibrium. Consequently,

$$\delta\Sigma_t = \frac{1}{2\,T}\sum_{i,j}\left(\frac{\partial\mu_i}{\partial c_j}\right)_{\rm eq}\frac{\delta c_{i,0}\,\delta c_{j,0} - \delta c_{i,t}\,\delta c_{j,t}}{t}. \tag{102}$$

We note that, as in the case of univariate systems, this quantity has a zero mean as long as initial conditions are sampled from the equilibrium distribution. Generally speaking, the shape of the probability distribution $P(\Sigma_t)$ will depend on thermodynamic details through the dependence of the chemical potentials on the different concentrations. In what follows we limit ourselves to ideal systems. This will lead to a simple and transparent expression for the probability.

In an ideal system the chemical potential of a species i depends solely on its own concentration. Equation (102), consequently, reduces to

$$\delta\Sigma_t = \frac{1}{2\,T}\sum_i \left(\frac{\partial\mu_i}{\partial c_i}\right)_{\rm eq} \frac{\delta c_{i,0}^2 - \delta c_{i,t}^2}{t}. \tag{103}$$

Since the derivatives of the chemical potentials are related to the variance of the fluctuating concentrations through relations of the type (53), the above equation can be rewritten as

$$\delta\Sigma_t = \frac{k_B}{2\,\Omega\,t}\sum_i \left(\frac{\delta c_{i,0}^2}{\overline{\delta c_{i,0}^2}} - \frac{\delta c_{i,t}^2}{\overline{\delta c_{i,t}^2}}\right). \tag{104}$$

Remembering that the excess concentrations are (Gaussian-distributed) Ornstein-Uhlenbeck processes, we see from (104) that $\delta\Sigma_t$ is the difference between two χ^2 random variables whose number of degrees of freedom is equal to the number of fluctuating concentrations, $\eta = n - \gamma$ (see Sec. II). In the limit of large sampling times, these two random variables can be assumed to be independent so $\delta\Sigma_t$ follows a generalized Laplace distribution of the type (see the Appendix)

$$P(\delta\Sigma_t) \approx \left(\frac{k_B}{\Omega t}\right)^{-\frac{\eta+1}{2}} \frac{|\delta\Sigma_t|^{\frac{\eta-1}{2}}}{2^{\frac{\eta-1}{2}}\sqrt{\pi}\,\Gamma(\frac{\eta}{2})}\, K_{\frac{\eta-1}{2}}\left(\frac{\Omega\,t}{k_B}\,|\delta\Sigma_t|\right), \tag{105}$$

where Γ and K stand for Euler's gamma function and for the modified Bessel function of the second kind, respectively. This distribution predicts that the excess of entropy production has a zero mean, while its variance is simply given by

$$\mathrm{Var}(\delta\Sigma_t) = \eta\left(\frac{k_B}{\Omega\,t}\right)^2. \tag{106}$$

We thus reach the conclusion that, for ideal systems, the variance of the cumulative entropy production around equilibrium is a multiple of k_B^2:

$$\mathrm{Var}(\Delta_i S) = \eta\,k_B^2, \tag{107}$$

which is a simple extension of the result obtained for univariate systems. Moreover, using the asymptotic expansion of K for large $\Delta_i S/k_B$, one gets a simple form for the distribution of $\Delta_i S$,

$$P(\Delta_i S) \approx \frac{|\Delta_i S|^{\frac{\eta}{2}-1}}{2\,\Gamma\left(\frac{\eta}{2}\right)(k_B)^{\frac{\eta}{2}}}\,\exp\left(-\frac{|\Delta_i S|}{k_B}\right). \tag{108}$$

This expression reduces to (55) for the special case $\eta = 1$, as expected. For two-variable systems, like the Brusselator considered in the previous section, we predict the probability distribution to be simply exponential,

$$P(\Delta_i S) \approx \frac{e^{-\frac{|\Delta_i S|}{k_B}}}{2\,k_B}. \tag{109}$$

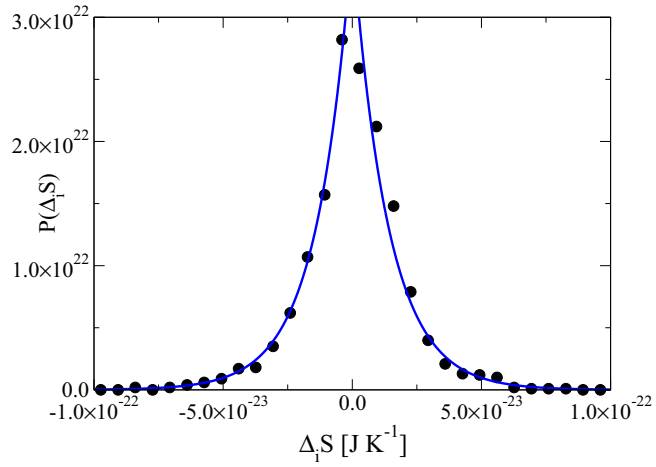

FIG. 7. Equilibrium distribution of $\delta\Sigma_t$ for the Brusselator model. The parameter values are the same as in Fig. 6, except for $k_2\,c_B = 0.0625$. The marks were obtained from 5000 realizations of a system of size $\Omega = 1\times10^3$ and a sampling time $t = 100$. The plain curve corresponds to Eq. (109).

This expression is in full agreement with the results of numerical integrations as given in Fig. 7 for the Brusselator model. In summary, the probability distribution of the entropy production in equilibrium is independent of kinetic parameters and takes a universal form which depends solely on the number of degrees of freedom, here the number of fluctuating concentrations.

VII. CONCLUSIONS

Starting with a recently proposed extension of the local equilibrium formulation of classical irreversible thermodynamics, we analyzed in this work the properties of stochastic entropy production in isothermal reactive systems. The main idea behind our approach is that entropy remains a state functional of the state variables, but these variables obey stochastic differential equations reflecting the presence of fluctuations around mean-field solutions. We showed that fluctuations can affect the steady-state mean value of entropy produced only when non-linear reactions are present, in full accordance with the conclusions reached with approaches based on the master equation. We, moreover, showed how to estimate these deviations explicitly for systems consisting of reactions in series transforming a reactant A in a single product B. It would be interesting to generalize the approach to cases with multiple end products, in which branching reactions would occur. More generally, it would be desirable to connect the properties of entropy production and of the deviations from its deterministic value to the topology of the underlying reactive network.

We also investigated the distribution of entropy production around its mean. At equilibrium, and for univariate systems and ideal multivariate systems, this probability distribution has the form of a modified Bessel function with process-independent coefficients. As a consequence, the distribution

and the moments of entropy production take a universal form at equilibrium, at least to the leading order of deviations of the state variables from their equilibrium value. Our investigations also revealed that the equilibrium fluctuations of entropy production follow an "equipartition" law, in the sense that each degree of freedom gives an equal contribution of k_{B^2} to the variance of the cumulative entropy production. Further investigations are needed to establish whether similar conclusions hold in the case of nonideal multivariate systems.

For nonequilibrium steady states, the entropy production is distributed in a Gaussian fashion and satisfies a fluctuationlike theorem taking a generic form in which both the mean and the variance of the entropy production appear explicitly. Contrary to the case of systems at equilibrium, these quantities are process dependent and the universality of the probability distribution is lost. In all cases, however, one can show that the variance of the entropy production scales inversely with the size of the system, with a scaling law differing for equilibrium, for nonequilibrium stable states, and for critical points. As a rule, the variance decreases faster with the size of the system at equilibrium than it does out of equilibrium. At critical points, the decrease is slower than at stable nonequilibrium steady states.

These results were compared to those obtained with the Gibbs-Shannon-like definition of the pathwise entropy production introduced earlier in the literature and some significant differences were pointed out. Further comparison between the two approaches should focus on how they are able to reproduce, in appropriate limits, the results of the well-established formalism of classical irreversible thermodynamics.

The present work and the previously published introduction on the extended local equilibrium assumption [11] have focused on the properties of entropy and, in this sense, on a stochastic extension of the second law of thermodynamics. A similar approach can be used to revisit the first law of thermodynamics, which would amount to analyzing the role played by fluctuations on other relevant quantities such as the internal energy as well as the statistical properties of work and heat. Previous investigations based on the Fokker-Planck equation for a particle trapped in a one-dimensional harmonic potential revealed in particular that the heat [21] and work [22] follow a probability distribution which can be either a Gaussian or a distribution similar to the form we obtained for $\Delta_i S$ in monovariate systems at equilibrium. This suggests the existence of relations between the fluctuations of the different fundamental thermodynamic quantities.

APPENDIX: EVALUATION OF THE PROBABILITY DISTRIBUTION OF $\delta\Sigma_t$ FOR MULTIVARIATE SYSTEMS

We start from Eq. (104):

$$\delta\Sigma_t = \frac{k_B}{2\,\Omega\,t}\sum_i\left(\frac{\delta c_{i,0}^2}{\overline{\delta c_{i,0}^2}} - \frac{\delta c_{i,t}^2}{\overline{\delta c_{i,t}^2}}\right). \tag{A1}$$

We introduce the new variables

$$X = \sum_i \frac{\delta c_{i,0}^2}{\overline{\delta c_{i,0}^2}}, \quad Y = \sum_i \frac{\delta c_{i,t}^2}{\overline{\delta c_{i,t}^2}}, \quad \text{and} \quad Z = \delta\Sigma_t\left(\frac{2\,\Omega\,t}{k_B}\right). \tag{A2}$$

We see that $Z = X - Y$ is the difference between two χ^2 random variables whose mean and variance are respectively equal to η and $2\,\eta$ (η plays here the role of a number of degrees of freedom). For sampling times $t \gg 0$, X and Y can be considered as independent variables since the correlation of Ornstein-Uhlenbeck processes decreases exponentially fast with t. Consequently, the moment-generating function of Z can be factorized as [23]

$$\begin{aligned} M_Z(r) &\equiv \overline{e^{Z\,r}} = M_X(r)\,M_Y(-r) \\ &= (1-2r)^{-\frac{\eta}{2}}\,(1+2r)^{-\frac{\eta}{2}} \quad (2\,r > 1). \end{aligned} \tag{A3}$$

This result can be rewritten as

$$M_Z(r) = \left(\frac{\frac{1}{4}}{\frac{1}{4} - r^2}\right)^{\frac{\eta}{2}}, \tag{A4}$$

which is the moment-generating function of a generalized Laplace (or variance-γ) distribution [24],

$$M_Z(r) = e^{\mu\,r}\left(\frac{\alpha^2 - \beta^2}{\alpha^2 - (\beta + r)^2}\right)^{\lambda}, \tag{A5}$$

for the special case $\mu = \beta = 0$, $\alpha = 1/2$, and $\lambda = \eta/2$. With such parameters, the distribution itself reads

$$P(Z) = \frac{|Z|^{\frac{\eta-1}{2}}}{2^{\eta-1}\sqrt{\pi}\,\Gamma\left(\frac{\eta}{2}\right)}\,K_{\frac{\eta-1}{2}}\left(\frac{|Z|}{2}\right). \tag{A6}$$

The final expression (105) is obtained by switching back to the original variable and by calculating explicitly the corresponding normalization factor.

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