

Fluctuation theorem for entropy production in a chemical reaction channel

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Fluctuation theorem for entropy production in a mesoscopic chemical reaction network is discussed. When the system size is sufficiently large, it is found that, by defining a kind of coarse-grained dissipation function, the entropy production in a reversible reaction channel can be approximately described by a type of detailed fluctuation theorem. Such a fluctuation relation has been successfully tested by direct simulations in a linear reaction model consisting of two reversible channels and in an oscillatory model wherein only one channel is reversible.

nonequilibrium thermodynamics, chemical reaction network, entropy production, fluctuation theorem

1 Introduction

The study of fluctuation theorem (FT) has attracted considerable attention in recent years. As an important topic in non-equilibrium thermodynamics, FT associates the statistical irreversibility and the time-reversible dynamics and, in particular, it gives a quantitative description of the “second law violation” within a short time for small systems [1–18]. FT was first introduced in N -particle deterministic systems [1–5] described by a Hamiltonian equation or equivalent Liouville equation, and was later extended to general stochastic processes described by master equations or Langevin equations [6–15]. Generally speaking, FT considers the fluctuations of some well-defined dissipation function Σ , which may have physical significance such as the dissipated work and thermodynamic entropy production, or in more general case quantifies the ratio of the probability of finding a forward trajectory to that of finding a time-reversed one. In its integrated form, FT reads $\langle e^{-\Sigma} \rangle = 1$, and if a nonequilibrium stationary state exists, one also has a so-called “de-

tailed FT”, say, $p(\Sigma = A)/p(\Sigma = -A) = e^A$. Although the dissipation function Σ is usually defined as an ensemble property, it is worthy noting that it can also apply to a single stochastic trajectory, as proposed recently by Seifert [16]. Such a “stochastic thermodynamics” description of a single path has been successfully applied experimentally to optically trapped colloidal particles and periodically driven two-level systems [17, 18].

The present paper is concerned with FT in mesoscopic chemical reaction networks. Due to molecular fluctuations, such systems are often described by master equations governing the evolution of probability distribution of some relevant reactant species. There have been several works contributing to this issue. For instance, Gaspard has studied FT in nonequilibrium reactions by investigating the fluctuation property of an action functional $Z(t)$, which relates to the relative probability of finding a forward reaction path relative to that of a time-reversed one. FT was manifested in the form of Lebowitz-Spohn symmetry by $Q(\eta) = Q(1-\eta)$, where $Q(\eta) = \lim_{t \rightarrow \infty} \frac{1}{t} \langle e^{-\eta Z(t)} \rangle$, and it was successfully tested in a bistable model [12] and an oscillation model [13].

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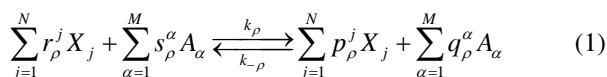
By defining energy and entropy on a stochastic trajectory in a proper way, Seifert established a consistent nonequilibrium thermodynamic description along a single stochastic trajectory of reaction events [16]. The total entropy production ΔS_{tot} along such a single trajectory can be split into a “media” part ΔS_m and a “system” part Δs , wherein ΔS_{tot} satisfies an integrated FT, i.e., $\langle e^{-\Delta S_{\text{tot}}} \rangle = 1$, and a detailed FT in the stationary state, i.e., $p(\Delta S_{\text{tot}} = A)/p(\Delta S_{\text{tot}} = -A) = e^A$. In the long time limit, the system entropy change Δs only contributes a boundary term and ΔS_m dominates overwhelmingly, such that $\Delta S_m \cong \Delta S_{\text{tot}}$ and both types of FT also hold for ΔS_m . One notes that the path-ensemble average of $Z(t)$ and ΔS_m are exactly the same according to their definitions, which demonstrates the agreement between these two author’s works.

The main purpose of the present paper is to investigate the entropy production and related FT in a single reaction channel. Generally, a chemical reaction network consists of many channels which are not independent of each other. A stochastic reaction trajectory is made up of successive reaction events via different channels ρ , and the media entropy change ΔS_m can be split into those of different channels $\Delta S_{m,\rho}$, i.e., $\Delta S_m = \sum_{\rho} \Delta S_{m,\rho}$. Due to the correlation between different channels, one would not expect FT to hold for $\Delta S_{m,\rho}$ separately [6]. Herein, we prove that in the large system volume limit and for a trajectory that is not too long, FT can indeed hold approximately for $\Delta S_{m,\rho}$ of a single reaction channel given that it is reversible. The physical basis of this relation is that the propensity function of each reaction channel remains nearly unchanged along the trajectory if the system size is large enough and the path is not too long. It is interesting to note that this relation holds even when only one reaction channel is reversible in the whole network, which may lead to more applications than FT of ΔS_m or $Z(t)$ that requires that all the reaction channels are reversible. We have also tested this kind of FT for $\Delta S_{m,\rho}$ by exact stochastic simulations via Gillespie’s algorithm, in a linear reaction model consisting of two reversible channels and in an oscillatory model wherein only one channel is reversible.

2 Model

2.1 Chemical master equation

We consider the general chemical reaction network



where $1 \leq \rho \leq N_r$ labels the single reactions. The X_j ($j=1, \dots, N$) molecules are those intermediate species whose number $\mathbf{X} = (X_1, \dots, X_N)$ can be measured along a chain of reaction events and can be used to characterize the state of the system, while A_{α} ($\alpha=1, \dots, M$) molecules correspond to those

species that contact particle reservoirs and whose concentration are controlled externally. We consider the case that $\{A_{\alpha}\}$ concentrations are kept at constant values. Assuming a dilute solution, the transition probabilities per unit time for the N_r reactions in (1) take the textbook form [19]:

$$w_{\rho}(\mathbf{X}) = k_{\rho} \prod_{\alpha} A_{\alpha}^{s_{\rho}^{\alpha}} \prod_j \frac{X_j!}{(X_j - r_{\rho}^j)!} \quad (2a)$$

$$w_{-\rho}(\mathbf{X}) = k_{-\rho} \prod_{\alpha} A_{\alpha}^{q_{\rho}^{\alpha}} \prod_j \frac{X_j!}{(X_j + p_{\rho}^j)!} \quad (2b)$$

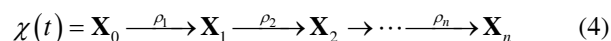
At the mesoscopic level, molecular fluctuations are considerable, such that the chemical reaction is described as a birth–death process of the intermediate species [20], and the dynamics of the system is governed by a master equation for the probability $p(\mathbf{X}; t)$

$$\begin{aligned} \partial_t p(\mathbf{X}; t) &= \sum_{\rho=\pm 1}^{\pm N_r} [w_{\rho}(\mathbf{X} - \mathbf{v}_{\rho}) p(\mathbf{X} - \mathbf{v}_{\rho}; t) - w_{-\rho}(\mathbf{X}) p(\mathbf{X}; t)] \\ &\equiv \sum_{\rho} J_{\rho}(\mathbf{X}; t) \end{aligned} \quad (3)$$

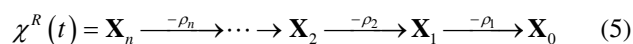
where \mathbf{v}_{ρ} is the vector of the stoichiometric coefficients, $\mathbf{v}_{\rho} = \{v_{\rho}^j \equiv p_{\rho}^j - r_{\rho}^j\}_{j=1}^N$, and $J_{\rho}(\mathbf{X}; t) \equiv w_{\rho}(\mathbf{X} - \mathbf{v}_{\rho}) \times p(\mathbf{X} - \mathbf{v}_{\rho}; t) - w_{-\rho}(\mathbf{X}) p(\mathbf{X}; t)$ is the stochastic reaction flux for reaction ρ . Generally eq. (3) admits a stationary solution $p_s(\mathbf{X})$ such that $\partial_t p_s(\mathbf{X}) = 0$.

2.2 Stochastic trajectory and entropy production

Generally, the master equation cannot be solved analytically, but it provides the basis for stochastic simulations, as proposed by Gillespie [21, 22], which randomly determine what the next reaction channel is and when it will happen. A stochastic reaction trajectory χ can be generated by simulation as



where reaction ρ_k occurs at time t_k leading to the state change $\mathbf{X}_{k-1} \rightarrow \mathbf{X}_{k-1} + \mathbf{v}_{\rho_k}$, and $0 < t_1 < t_2 < \dots < t_n = \tau$. Accordingly, the time–reversed trajectory reads



According to Seifert [16], one may define entropy along the stochastic trajectory (4) as $s(t) \equiv -\ln p_{\chi(t)}(t)$, where $p_{\chi(t)}(t)$ is the solution of the master eq. (3) for a given initial distribution taken along the specific path $\chi(t)$. As mentioned above, the total entropy change along such a trajectory can be split into a “system” part Δs and a “medium” part ΔS_m , where the latter takes the explicit form,

$$\Delta S_m = \sum_k \ln \frac{w_{\rho_k}(\mathbf{X}_{k-1})}{w_{-\rho_k}(\mathbf{X}_k)} \quad (6)$$

In a stationary state, ΔS_m can be approximately thought of as the logarithm of the ratio between the probabilities of the forward and backward paths given by eqs. (4) and (5), i.e.,

$$\Delta S_m \approx \ln \frac{p_{st}(\chi)}{p_{st}(\chi^R)} \quad (7)$$

Actually, ΔS_m is exactly the same as the fluctuation quantity $Z(t)$ introduced by Gaspard [12]. In the stationary state, the statistical average of this quantity can be interpreted as the entropy irreversibly generated inside the system along the path. Note however that an additional degeneracy factor should be included and first-law balance be considered when one tries to interpret ΔS_m as an exchanged heat [11].

The entropy change defined in eq. (6) contains the contribution of different reaction channels. One may then define media entropy change $\Delta S_{m,\rho}$ for a specific channel ρ along the trajectory as

$$\Delta S_{m,\rho} = \sum_k \delta_{\rho|\rho_k} \ln \frac{w_{\rho_k}(\mathbf{X}_{k-1})}{w_{-\rho_k}(\mathbf{X}_k)} \quad (8)$$

where δ_{ij} is the Kronecker delta function. Clearly,

$$\Delta S_m = \sum_{\rho=1}^{N_r} \Delta S_{m,\rho} \quad (9)$$

3 Fluctuation theorem for a single channel

3.1 The fluctuation theorem for all channels

Strictly speaking, it is the total entropy change along the path, $\Delta S_{\text{tot}} = \Delta s + \Delta S_m$, that satisfies both the integrated FT and detailed FT. However, since ΔS_m increases almost linearly with time and Δs is simply a bounded term, FT also holds—actually in a quite accurate way—for ΔS_m [12, 16]. Written in an explicit form, one has a detailed FT such as

$$p(\Delta S_m = A) / p(\Delta S_m = -A) \cong e^A \quad (10)$$

when the system remains in a stationary state.

Using eq. (7), one can generalize eq. (10) to a stronger form. Denoting $p(\{\Delta S_{m,\rho} = A_\rho\})$ as the joint probability that the media entropy change for reaction channel ρ takes the specific values A_ρ in the stationary state we can obtain,

$$p(\{\Delta S_{m,\rho} = A_\rho\}) / p(\{\Delta S_{m,\rho} = -A_\rho\}) \cong e^{\sum_{\rho=1}^{N_r} A_\rho} \quad (11)$$

The proof of this relation is straightforward,

$$\begin{aligned} & p(\{\Delta S_{m,\rho} = A_\rho\}) \\ &= \sum_{\chi} p_{st}(\chi) \Big|_{\{\Delta S_{m,\rho} = A_\rho\}} \approx \sum_{\chi} e^{\sum_{\rho=1}^{N_r} A_\rho} p_{st}(\chi^R) \Big|_{\{\Delta S_{m,\rho} = A_\rho\}} \end{aligned}$$

$$\begin{aligned} &= e^{\sum_{\rho=1}^{N_r} A_\rho} \sum_{\chi} p_{st}(\chi^R) \Big|_{\{\Delta S_{m,\rho} = A_\rho\}} \\ &= e^{\sum_{\rho=1}^{N_r} A_\rho} \sum_{\chi^R} p_{st}(\chi) \Big|_{\{\Delta S_{m,\rho} = -A_\rho\}} \\ &= e^{\sum_{\rho=1}^{N_r} A_\rho} p(\{\Delta S_{m,\rho} = -A_\rho\}), \end{aligned} \quad (12)$$

where the second equality holds because of eq. (7), the final equality uses the fact that summing over χ^R is the same as summing over χ since both sums cover all possible paths, and the fourth equality holds because all $\Delta S_{m,\rho}$ change to $-\Delta S_{m,\rho}$ when we replace χ by the corresponding χ^R .

Eqs. (10) and (11) raise an interesting question as to whether FT holds for a single reaction channel. In the following part, we show that this can be approximately true when the system volume V is sufficient large and the path is not long.

3.2 Fluctuation theorem for a single channel

The main result we want to address is

$$p(\Delta S_{m,\rho} = A_\rho) / p(\Delta S_{m,\rho} = -A_\rho) \cong e^{A_\rho} \quad (13)$$

for any single channel ρ that is reversible. Since the reactions via this channel along the path χ are generally not connected, and we do not have information about the dissipation in other channels, a direct derivation such as that presented in eq. (12) is not available for eq. (13). Here we find a sufficient (but maybe not necessary) condition for eq. (13), our argument is constructed in two steps. Firstly, we find a detailed FT for a coarse-grained dissipation function R defined for a channel ρ along the path χ , and then we argue that $\Delta S_{m,\rho}$ converges to this dissipation function under the proposed condition.

When the system volume V is sufficient large, there always exist a “macro-infinitesimal” time scale τ_0 during which the transition probability $w_\rho(\mathbf{X})(\propto V)$ of each channel does not change significantly and each reaction channel can occur many times, which is known as the “leap” condition as proposed by Gillespie [23, 24]. We now consider a short time path $\chi(t)$ defined in eq. (4) where $\tau \leq \tau_0$. Under these conditions ($V \gg 1$, $\tau \leq \tau_0$), the transition probability $w_\rho(\mathbf{X}_k)$ defined along χ remains nearly unchanged, i.e.,

$$w_\rho(\mathbf{X}_k) / w_\rho(\mathbf{X}_0) = 1 + O(V^{-1}) \quad (14)$$

It is also known that N_ρ , the number of reaction events in channel ρ during this small time interval $(0, \tau)$, satisfies a Poissonian distribution [23, 24] of the form

$$p_\rho(N_\rho) = e^{-\lambda_\rho} \lambda_\rho^{N_\rho} / N_\rho! \quad (15)$$

where $\lambda_\rho = w_\rho(\mathbf{X}_0)\tau$.

Particular attention must be paid to reactions in a certain

channel l along the path, in both forward and backward directions. We denote $P(n, m, \mathbf{X}_0)$ as the probability that $N_l = n$ and $N_{-l} = m$ events happen respectively in the forward and backward direction given the initial state \mathbf{X}_0 selected from an initial distribution $p(\mathbf{X}_0)$, and it reads

$$P(n, m, \mathbf{X}_0) = p(\mathbf{X}_0) p_l(n) p_{-l}(m) \quad (16)$$

where $p_l(n)$ and $p_{-l}(m)$ are given by eq. (15). We now introduce a coarse-grained fluctuation quantity R as

$$R(n, m, \mathbf{X}_0) \equiv \ln \frac{P(n, m, \mathbf{X}_0)}{P(m, n, \mathbf{X}_0)} \quad (17)$$

Using eqs. (15) and (16), we obtain

$$R(n, m, \mathbf{X}_0) = (n - m) \ln \frac{w_l(\mathbf{X}_0)}{w_{-l}(\mathbf{X}_0)} \quad (18)$$

A detailed FT for R can then be obtained as follows:

$$\begin{aligned} p(R = A) &= \sum_{n, m, \mathbf{X}_0} P(n, m, \mathbf{X}_0) |_{R(n, m, \mathbf{X}_0) = A} \\ &= \sum_{n, m, \mathbf{X}_0} e^A P(m, n, \mathbf{X}_0) |_{R(n, m, \mathbf{X}_0) = A} \\ &= e^A \sum_{n, m, \mathbf{X}_0} P(n, m, \mathbf{X}_0) |_{R(n, m, \mathbf{X}_0) = -A} = e^A p(R = -A) \end{aligned} \quad (19)$$

where eq. (17) is used to obtain the second equality, and $R(n, m, \mathbf{X}_0) = -R(m, n, \mathbf{X}_0)$ is used for the third equality.

Actually, we find that R is related to the entropy change of the specific channel l . Recalling that $w_\rho(\mathbf{X})$ does not change significantly along the path (4), and that we may use $w_\rho(\mathbf{X}_0)$ to approximate $w_\rho(\mathbf{X}_k)$ when V is large and τ is small, the media entropy change $\Delta S_{m,l}$ can thus be well approximated by $\Delta S_{m,l} = \sum_{\rho_k = \pm l} \ln \frac{w_{\rho_k}(\mathbf{X}_{k-1})}{w_{-\rho_k}(\mathbf{X}_k)} \approx (n - m) \ln \frac{w_l(\mathbf{X}_0)}{w_{-l}(\mathbf{X}_0)}$

which is equal to $R(n, m, \mathbf{X}_0)$. This argument finally leads to eq. (13) as expected.

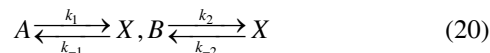
The argument above indicates that $(V \gg 1, \tau \leq \tau_0)$ is a sufficient condition for eq. (13) to hold. However, whether it is necessary or not is not known to us. Of course the proof shown in eqs. (17) to (19) requires that these two conditions be fulfilled, but one may also have other ways to prove eq. (13) such that $(V \gg 1, \tau \leq \tau_0)$ is not necessary. Indeed, as we will show numerically in the following section, a type of FT in the form of Lebowitz-Spohn symmetry may also hold approximately in the long time limit if the system is near equilibrium. We notice that eq. (13) even holds when the system is not in the stationary state, and is actually true for any "short time" trajectory when V is large. Furthermore, eq. (13) only requires that the specific channel of interest is reversible, irrespective of whether other channels are reversible or not. Therefore, even for chemical reaction networks that contain irreversible channels—in which case the total entropy production diverges—one also has a kind of

FT for those reversible channels. In the following section, we will test such a result by exact stochastic simulations.

4 Applications

4.1 A model with two reversible reactions

First we consider a simple linear reaction model with two reversible channels:



where X is the intermediate species. The concentration of species A and B are denoted by a and b respectively. Here b is the control parameter, and the other parameters are fixed as $k_1 = k_{-1} = k_2 = k_{-2} = 1$, $a = 1$. From the condition that the macroscopic flux of each reaction channel is zero, i.e. $k_1 a = k_{-1} x_e$ and $k_2 b = k_{-2} x_e$, one can find that the equilibrium state is located at $b = 1$ and the equilibrium concentration of X is $x_e = 1$.

We use Gillespie's algorithm to generate stochastic trajectories, and calculate the media entropy change of a single

channel as $\Delta S_{m,\rho}(t) = \sum_{\rho_k = \pm \rho} \ln \frac{w_{\rho_k}(\mathbf{X}_{k-1})}{w_{-\rho_k}(\mathbf{X}_k)}$ ($\rho = 1, 2$). The

total media entropy change is then $\Delta S_{m,t} = \Delta S_{m,1} + \Delta S_{m,2}$. As an example, we take $b = 2$ and the system volume $V = 10^3$. A total of 10^5 stationary trajectories with length $t = 0.02$ are generated to obtain the distributions of $\Delta S_{m,1}$, $\Delta S_{m,2}$ and $\Delta S_{m,t}$, which are shown in Figure 1(a). Note that for such short trajectories, negative $\Delta S_{m,\alpha}$ ($\alpha = 1, 2, t$) could be observed which seems to violate the second law, but since $\langle \Delta S_{m,\alpha} \rangle > 0$ it is actually in accordance with the second law. The probability that $\Delta S_{m,\alpha}$ takes a certain value A , $p(\Delta S_{m,\alpha} = A)$, denoted simply as $p(A)$, can be drawn from Figure 1(a), and the dependence of $\ln[p(A)/p(-A)]$ as a function of A is presented in Figure 1(b), which is a straight line with unit slope, i.e. $\ln[p(A)/p(-A)] = A$, as expected from eqs. (10) and (13). Hence FT holds for the entropy change of all channels as well as for that of a single channel.

As proved in Section 3, FT in eq. (13) holds for short time trajectories; however, a kind of FT may still exist in the long time condition. As discussed in the literature [25],

the cumulative current $\int_0^t j(t') dt'$ for a single channel in a linear reaction model satisfies a FT in the form of Lebowitz-Spohn symmetry by $Q(\lambda) = Q(K - \lambda)$, where

$$Q(\lambda) \equiv \lim_{t \rightarrow \infty} \frac{1}{-t} \ln \left\langle e^{-\lambda \int_0^t j(t') dt'} \right\rangle$$
 is the generating function of

the current and K is a driving force that is related to the kinetic parameters. As we will show below, a similar FT may hold approximately for the entropy change of a single channel if the system is close to equilibrium. Thanks to the generating function method [12], we can calculate the gen-

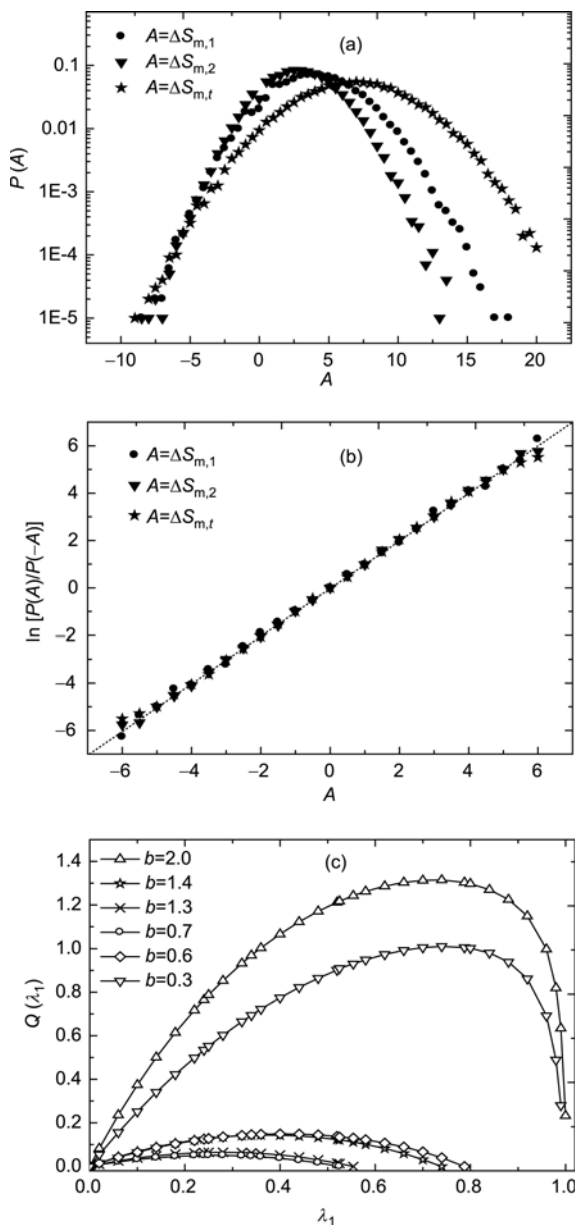


Figure 1 (a) Probability distribution of $\Delta S_{m,1}$ (●), $\Delta S_{m,2}$ (▼) and $\Delta S_{m,t}$ (*), where $b=2, V=10^3$; (b) $\ln[p(A)/p(-A)]$ presented as functions of A in order to test the detailed FT of single reaction channels; (c) the generating function $Q(\lambda_1)$ for channel 1 for different values of parameter b , with $V=20$, where the lines are drawn to guide the eyes.

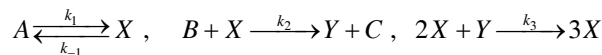
erating function $Q(\lambda_1) \equiv \lim_{t \rightarrow \infty} \frac{1}{-t} \ln \langle e^{-\lambda_1 \Delta S_{m,1}(t)} \rangle$ numerically.

$Q(\lambda_1)$ for channel 1 is shown in Figure 1(c). Actually, for values of $b = 1.4, 1.3, 0.7$ and 0.6 , which are not far from the equilibrium parameter $b = 1$, the data can be fitted very well with the parabola functional form $Q(\lambda_1) = c(K - \lambda_1)\lambda_1$ for $0 \leq \lambda_1 \leq K$, and thus the fluctuation relation $Q(\lambda_1) = Q(K - \lambda_1)$ is recovered. From the fitting, we find that $K < 1$ and K becomes smaller as the values of parameter b approaches unity. However, the Lebowitz-Spohn symmetry is lost when

the system is further away from equilibrium as shown in Figure 1(c) for $b=2$ and 0.3 . According to the previous results [13], $Q(\lambda_1) = Q(K - \lambda_1)$ is equivalent to the detailed FT of the form $\lim_{t \rightarrow \infty} p(\Delta S_m = \sigma t) / p(\Delta S_m = -\sigma t) \simeq e^{K\sigma t}$. Therefore, the entropy change of a single channel in the long time limit also approximately satisfies a kind of FT if the system is near equilibrium.

4.2 A model with only one channel reversible

As noted in Section 3, the detailed FT in eq. (13) is also applicable in systems with irreversible reactions. Since the entropy production of a reversible channel is still well defined even if the other reaction channels are irreversible, it is possible to test this FT by direct simulation. Here we consider the Brusselator model with only one reaction channel reversible:



The concentration of species A and B are denoted by a and b respectively, and the parameters used are $k_1 = k_{-1} = k_2 = k_3 = 1, a = 1, b = 2.5$, where the deterministic system locates at the oscillatory region. The system volume is taken

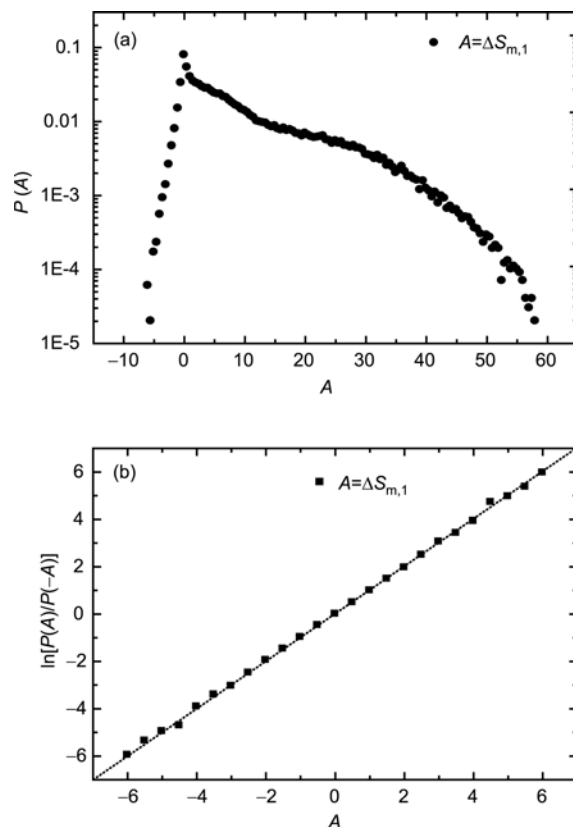


Figure 2 (a) Probability distribution of the medium entropy change in channel 1 in the Brusselator model; (b) test of the detailed FT for a single reversible channel.

as $V = 10^3$, and a total of 10^5 stationary trajectories with length $t = 0.02$ are generated in order to obtain the distribu-

tion of $\Delta S_{m,1} = \sum_{\rho_{k=\pm 1}} \ln \frac{w_{\rho_k}(\mathbf{X}_{k-1})}{w_{-\rho_k}(\mathbf{X}_k)}$ for channel 1, which

is depicted in Figure 2(a). Again, the dependence of $\ln[P(A)/P(-A)]$ as a function of A is a straight line with unit slope as illustrated in Figure 2(b), so that the FT in eq. (13) holds in this irreversible system.

5 Conclusion

Fluctuation theorem can be applied to reaction channels in a mesoscopic chemical reaction network. Generally it is the combination of entropy production of all channels that satisfies a detailed FT when the system reaches a stationary state. However, we find that such a relation may hold approximately for the entropy production of a single reversible channel, defined along a stochastic trajectory, when the system volume is sufficient large and the path is not long. The validity of this fluctuation relation has been discussed and successfully tested by direct simulations in a linear reaction model consisting of two reversible channels and in an oscillatory model wherein only one channel is reversible.

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