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(Citation)
Physical Review E,91(5):052814-052814

(Issue Date)
2015-05-26

(Resource Type)
journal article

(Version)
Version of Record

Distinguishing between discreteness effects in stochastic reaction processes

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(Received 5 February 2015; revised manuscript received 7 April 2015; published 26 May 2015)

The effect of discreteness on stochastic dynamics of chemically reacting systems is studied analytically. We apply the scheme bridging the chemical master equation and the chemical Fokker-Planck equation by a parameter representing the degree of discreteness previously proposed by the author for two concrete systems. One is an autocatalytic reaction system, and the other is a branching-annihilation reaction system. It is revealed that the change in characteristic time scales when discreteness is decreased is yielded between the two systems for different reasons. In the former system, it originates from the boundaries where one of the chemical species is zero, whereas in the latter system, it is due to modification of the most probable extinction path caused by discreteness loss.

DOI: 10.1103/PhysRevE.91.052814 PACS number(s): 82.20.−w, 05.40.−a, 02.50.Ey

I. INTRODUCTION

Stochastic dynamics of chemically reacting systems can be described by the chemical master equation (CME) [1,2]. Of particular interest are those involving a small number of molecules because they are found in several scientific disciplines, such as cell biology, population genetics, ecology, and so on. However, in general it is difficult to solve the CME analytically. Hence, in previous work, stochastic dynamics of chemically reacting systems have been typically studied via stochastic numerical simulations [3] or the linear noise approximation [4,5] in which the average behavior predicted by the mean-field deterministic equation is corrected by a fluctuation term around that. In general, the linear noise approximation is effective when the system size is moderately large. Examples include resonant amplification of intrinsic noise leading to a sustainable cycling behavior [6] and correction to the Michaelis-Menten equation in a small subcellular compartment [7], to name but a few.

Two notions should be distinguished with respect to stochastic dynamics of chemically reacting systems. One is intrinsic noise, and the other is discreteness. Intrinsic noise refers to stochasticity originating from the intrinsic randomness of occurrences of reactions. This is in contrast to extrinsic noise resulting from randomness evoked by environment. Discreteness, on the other hand, simply means that state variables are non-negative integers. One might suspect that discreteness may have a great impact on systems with a small number of molecules because the relative change in the number of molecules becomes larger as the system size decreases. If the CME is replaced by an equation with continuous variables (e.g., Fokker-Planck equations), then discreteness disappears while some properties of intrinsic noise can be preserved (see below).

In previous work, the author introduced a general scheme bridging the CME and the chemical Fokker-Planck equation (CFPE) with the discreteness parameter ϵ representing the degree of discreteness [8]. Namely, ϵ is a unit of the change in the number of molecules. $\epsilon = 1$ gives the CME, and the CFPE is obtained as $\epsilon \to 0$. In this scheme, the first and second jump moments of each reaction are preserved up to an adjustment. We can quantitatively evaluate the effect of discreteness distinguished from that of intrinsic noise, which cannot be captured by the CFPE, by applying the scheme to chemically reacting systems.

In this paper, we study two concrete chemically reacting systems in order to demonstrate how the effect of discreteness emerges. The first example is an autocatalytic reaction system [9,10]. We will calculate the correlation time analytically and show that the effect of discreteness on it originates from the boundaries where the number of one molecular species is zero. The second example is a branching-annihilation reaction system [11,12]. In this system, it was shown that extinction to zero occurs with probability one for both the CME and the CFPE. We will show that modification in the most probable extinction path induced by discreteness loss results in an exponential difference in the average extinction time between the CME and the CFPE.

This paper is organized as follows. In Sec. II, the scheme to bridge the CME and the CFPE is reviewed. In Secs. III and IV, the autocatalytic reaction system and the branching-annihilation reaction system are studied, respectively. In Sec. V, concluding remarks are given.

II. BRIDGING THE CME AND THE CFPE

In this section, we review the scheme bridging the CME and the CFPE proposed in Ref. [8].

We consider a chemically reacting system consisting of N molecular species $X_1, \ldots, X_N$ and M chemical reactions $R_1, \ldots, R_M$. The state of the system at time t is specified by a vector $\boldsymbol{X}(t) = [X_1(t), \ldots, X_N(t)]$, where $X_i(t)$ represents the number of X_i molecules in the system at time t $(i = 1, \ldots, N)$. In the following, we use the same symbol to denote both the molecular species and the number of that molecular species because there is no fear of confusion. Let $a_j(\boldsymbol{X})$ be the probability that reaction R_j occurs once per unit time called the propensity function $(j = 1, \ldots, M)$. ν_{ij} denotes the change in the number of X_i molecules when reaction R_j occurs. We set $\boldsymbol{\nu}_j = (\nu_{1j}, \ldots, \nu_{Nj})$ for $j = 1, \ldots, M$. If $P(\boldsymbol{X},t)$ denotes the probability that $\boldsymbol{X}(t) = \boldsymbol{X}$ holds given an initial condition $\boldsymbol{X}(t_0) = \boldsymbol{X}_0$, then the time evolution of $P(\boldsymbol{X},t)$ is governed by

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the CME,

$$\partial_t P(\boldsymbol{X},t) = \sum_{j=1}^{M} [a_j(\boldsymbol{X} - \boldsymbol{\nu}_j)P(\boldsymbol{X} - \boldsymbol{\nu}_j,t) - a_j(\boldsymbol{X})P(\boldsymbol{X},t)]. \tag{1}$$

The CFPE is obtained by formally truncating the Kramers-Moyal expansion of the CME up to the second order [13],

$$\partial_t P(\boldsymbol{X},t) = -\sum_{i=1}^{N} \partial_{X_i}[A_i(\boldsymbol{X})P(\boldsymbol{X},t)] + \frac{1}{2}\sum_{i,i'=1}^{N} \partial_{X_i}\partial_{X_{i'}}[B_{ii'}(\boldsymbol{X})P(\boldsymbol{X},t)], \tag{2}$$

where

$$A_i(\boldsymbol{X}) = \sum_{j=1}^{M} \nu_{ij} a_j(\boldsymbol{X}), \tag{3}$$

$$B_{ii'}(\boldsymbol{X}) = \sum_{j=1}^{M} \nu_{ij}\nu_{i'j} a_j(\boldsymbol{X}) \tag{4}$$

for $i,i' = 1,\ldots,N$. Note that X_i $(i = 1,\ldots,N)$ are non-negative real numbers in the CFPE.

The CFPE can be derived as an approximation of the CME under an appropriate condition [14]. However, our interest in this paper is the effect of discreteness. Here, we do not regard the CFPE as an approximation of the CME but as a reference to quantify the effect of discreteness.

It is known that a Fokker-Planck equation can be approximated by a sequence of master equations parametrized by the parameter ϵ which represents jump width [13]. In the case of the CFPE, there is a sequence of master equations $\{M_\epsilon\}_{0<\epsilon\leqslant 1}$ such that the CFPE is recovered as $\epsilon \to 0$ and $\epsilon = 1$ is identical to the CME [8]. ϵ is a unit of the change in the number of molecules and thus represents the degree of discreteness.

The master equation M_ϵ for each $0 < \epsilon \leqslant 1$ is defined as follows. For each reaction R_j in a given chemically reacting system, we introduce two reactions R_j^+ and R_j^- whose propensity functions are

$$a_{j,\epsilon}^+(\boldsymbol{X}) = \frac{a_{j,\epsilon}(\boldsymbol{X})}{2\epsilon} + \frac{a_{j,\epsilon}(\boldsymbol{X})}{2\epsilon^2}, \tag{5}$$

$$a_{j,\epsilon}^-(\boldsymbol{X}) = -\frac{a_{j,\epsilon}(\boldsymbol{X})}{2\epsilon} + \frac{a_{j,\epsilon}(\boldsymbol{X})}{2\epsilon^2}, \tag{6}$$

and state change vectors are $+\epsilon\boldsymbol{\nu}_j$ and $-\epsilon\boldsymbol{\nu}_j$, respectively. Here, $a_{j,\epsilon}(\boldsymbol{X})$ is defined by declaring the unit of change in the number of molecules as ϵ. For example, let us assume that reactions follow the mass action kinetics. Namely, for a reaction R_j of the form

$$n_1 X_{i_1} + \cdots + n_k X_{i_k} \to \cdots,$$

we specify

$$a_j(\boldsymbol{X}) = c_j \prod_{l=1}^{k} \binom{X_{i_l}}{n_l} \tag{7}$$

for a non-negative constant c_j. $a_{j,\epsilon}(\boldsymbol{X})$ is obtained by replacing $(X_{i_l} - m)$ by $(X_{i_l} - m\epsilon)$ in the binomial coefficients in Eq. (7).

The transition probability from state $\boldsymbol{X}$ to $\boldsymbol{X'}$ per unit time is given by

$$W_\epsilon(\boldsymbol{X}'|\boldsymbol{X}) = \sum_{j=1}^{M} \{a_{j,\epsilon}^+(\boldsymbol{X})\delta[\boldsymbol{X}' - (\boldsymbol{X} + \epsilon\boldsymbol{\nu}_j)] + a_{j,\epsilon}^-(\boldsymbol{X})\delta[\boldsymbol{X}' - (\boldsymbol{X} - \epsilon\boldsymbol{\nu}_j)]\}, \tag{8}$$

where δ is the Dirac δ function. Thus, the master equation M_ϵ is

$$\partial_t P(\boldsymbol{X},t) = \int d\boldsymbol{X}' [W_\epsilon(\boldsymbol{X}|\boldsymbol{X}')P(\boldsymbol{X}',t) - W_\epsilon(\boldsymbol{X}'|\boldsymbol{X})P(\boldsymbol{X},t)]. \tag{9}$$

Since $a_{j,1}^+(\boldsymbol{X}) = a_j(\boldsymbol{X})$, $a_{j,1}^-(\boldsymbol{X}) = 0$, M_1 is identical to the original CME.

The first and second jump moments of M_ϵ are given by

$$\int d\boldsymbol{X}'(X_i' - X_i)W_\epsilon(\boldsymbol{X}'|\boldsymbol{X}) = \sum_{j=1}^{M} \nu_{ij} a_{j,\epsilon}(\boldsymbol{X}), \tag{10}$$

$$\int d\boldsymbol{X}'(X_i' - X_i)(X_{i'}' - X_{i'})W_\epsilon(\boldsymbol{X}'|\boldsymbol{X}) = \sum_{j=1}^{M} \nu_{ij}\nu_{i'j} a_{j,\epsilon}(\boldsymbol{X}), \tag{11}$$

respectively. The fact that the CFPE is derived in the limit of $\epsilon \to 0$ follows from Eqs. (10) and (11). Equations (10) and (11) also show that the first and second jump moments are preserved up to the adjustment resulting from the change in the unit of the change in the number of molecules.

It is clear that the term in $a_{j,\epsilon}^+(\boldsymbol{X})$ reciprocal to ϵ and that the reciprocal to ϵ^2 correspond to the drift and the diffusion terms in the CFPE, respectively. These two terms balance each other in the CME $[a_{j,\epsilon}^-(\boldsymbol{X}) = 0]$. However, as ϵ approaches 0, the discrepancy between the two terms becomes large.

III. AUTOCATALYTIC REACTION SYSTEM

Let us consider the following autocatalytic reaction system:

$$\begin{aligned}
R_1&: X \to Y, \quad a_1(X,Y) = kX, \quad \boldsymbol{\nu}_1 = (-1,+1),\\
R_2&: Y \to X, \quad a_2(X,Y) = kY, \quad \boldsymbol{\nu}_2 = (+1,-1),\\
R_3&: X + Y \to 2X, \quad a_3(X,Y) = sXY, \quad \boldsymbol{\nu}_3 = (+1,-1),\\
R_4&: X + Y \to 2Y, \quad a_4(X,Y) = sXY, \quad \boldsymbol{\nu}_4 = (-1,+1).
\end{aligned}$$

This system undergoes a transition from a unimodal to a bimodal stationary probability distribution due to the multiplicative nature of intrinsic noise [9]. This phenomenon was found by numerical simulation in a similar system consisting of four molecular species [15]. Recently, the mean switching time between the two peaks in the bimodal regime has received attention [10,16]. The time-dependent analytic solution has been also obtained [17].

Since the total number of molecules $N := X + Y$ is preserved in every reaction, this autocatalytic reaction system can be treated as a one-variable system. In the following, we focus on X.

Let $P^s(X)$ be the stationary probability distribution for the number of X molecules. The CME and the CFPE have the same transition condition from unimodality to bimodality [9]: $k = s$. When $k > s$, $P^s(X)$ has a unique maximum at $X = N/2$. If $k < s$, then it has two peaks at the boundaries $X = 0, N$. It can be shown that this also holds for every M_ϵ. Thus, the qualitative feature of the stationary probability distribution (unimodal or bimodal) is independent of the degree of discreteness. However, we can expect that the characteristic time scale of the stochastic dynamics is dependent on the degree of discreteness because it was shown that the CFPE fails to predict the mean switching time in the bimodal regime [10,16].

Here, we calculate the correlation time (which is easier to calculate than the mean switching time in the CME and has more generality because it is applicable for systems that do not necessarily exhibit switching behavior) for M_ϵ in order to reveal how it is dependent on the degree of discreteness.

M_ϵ is given by

$$\begin{aligned}\partial_t P(X,t) = {} & t_\epsilon^+(X-\epsilon)P(X-\epsilon,t) \\ & + t_\epsilon^-(X+\epsilon)P(X+\epsilon,t) \\ & - [t_\epsilon^+(X) + t_\epsilon^-(X)]P(X,t), \end{aligned} \tag{12}$$

where

$$t_\epsilon^+(X) = \begin{cases} k_+ N + (N-k_0)X - X^2, & \text{if } 0 \leqslant X < N, \\ 0, & \text{otherwise,} \end{cases}$$

$$t_\epsilon^-(X) = \begin{cases} k_- N + (N+k_0)X - X^2, & \text{if } 0 < X \leqslant N, \\ 0, & \text{otherwise,} \end{cases}$$

$k_0 = \epsilon \frac{k}{s}$, $k_+ = \frac{1+\epsilon}{2}\frac{k}{s}$, and $k_- = \frac{1-\epsilon}{2}\frac{k}{s}$. We perform the time scale transformation $t \to t(\epsilon^{-2}s)$ and write the time after this rescaling again as t.

Let us introduce the probability generating function by

$$G(q,t) = \sum_{n=0}^{N/\epsilon} q^n P(\epsilon n, t). \tag{13}$$

The generating function equation corresponding to M_ϵ is

$$\partial_t G(q,t) + H(\partial_q, q)G(q,t) = b(q,t), \tag{14}$$

where $H(p,q) = f_2(q)p^2 + f_1(q)p + f_0(q)$, $b(q,t) = b_0(q)P(0,t) + b_N(q)P(N,t)$, $f_2(q) = \epsilon^2 q(1-q)^2$, $f_1(q) = \epsilon(1-q)[(N-k_0-\epsilon)q - (N+k_0-\epsilon)]$, $f_0(q) = N(1-q)(k_+ - k_- q^{-1})$, $b_0(q) = k_- N(1-q^{-1})$, and $b_N(q) = k_- N(q^{N/\epsilon} - q^{N/\epsilon+1})$. We assume that ϵ is taken such that N/ϵ is an integer.

Note that $b(q,t) = 0$ for $\epsilon = 1$. However, it is not necessarily so for $\epsilon < 1$. As one can see from the above definition, the term $b(q,t)$ originates from the boundaries $X = 0, N$. Inequality $b(q,t) \neq 0$ represents the imbalance between the "drift part" and the "diffusion part" of the propensity functions at the boundaries $X = 0, N$.

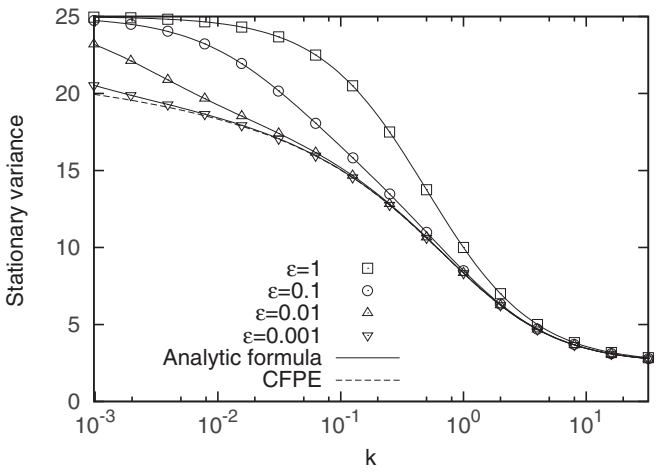

FIG. 1. Stationary variance in X in the autocatalytic reaction system with $N = 10$ and $s = 1$ for different values of ϵ and the CFPE. Marks represent numerically calculated stationary variance from the stationary distribution ($\epsilon = 1$: square; $\epsilon = 0.1$: circle; $\epsilon = 0.01$: upper triangle; $\epsilon = 0.001$: lower triangle). The solid lines are Eq. (17). The dashed line is Eq. (18).

The CFPE obtained in the limit of $\epsilon \to 0$ (before the time rescaling) is

$$\partial_t P(X,t) = -\partial_X[A(X)P(X,t)] + \tfrac{1}{2}\partial_X^2[B(X)P(X,t)], \tag{15}$$

with $A(X) = k(N-2X)$ and $B(X) = kN + 2sX(N-X)$.

In the following subsections, we denote the stationary probability distribution of X for M_ϵ by $P_\epsilon^s(X)$ and that for the CFPE by $P_0^s(X)$. First, we calculate the stationary variance because we need it to obtain the correlation time. Then, we proceed to the calculation of the correlation time.

A. Stationary variance

Let $G^s(q)$ be the generating function of $P_\epsilon^s(X)$ and $b^s(q) = b_0(q)P_\epsilon^s(0) + b_N(q)P_\epsilon^s(N)$. From Eq. (14), we have

$$H(\partial_q, q)G^s(q) = b^s(q). \tag{16}$$

By appealing to the formula $\partial_q^k G^s|_{q=1} = \langle n(n-1)\cdots(n-k+1)\rangle$, where $\langle\cdots\rangle$ is the stationary average, we obtain

$$\begin{aligned}\langle X^2\rangle - \langle X\rangle^2 = {} & \frac{N(sN+2k)}{4(s+2k)} \\ & - \frac{(1-\epsilon)kN(N+\epsilon)}{2(s+2k)} P_\epsilon^s(0)\epsilon^{-1}, \end{aligned} \tag{17}$$

where we make use of the fact that $P_\epsilon^s(0) = P_\epsilon^s(N)$.

The stationary variance for the CFPE directly calculated from Eq. (15) is

$$\langle X^2\rangle - \langle X\rangle^2 = \frac{N(sN+2k)}{4(s+2k)} - \frac{kN^2}{2(s+2k)} P_0^s(0). \tag{18}$$

It is clear that the right hand side of Eq. (17) converges to that of Eq. (18) as $\epsilon \to 0$.

Figure 1 shows the stationary variance for several values of ϵ and that for the CFPE. Here, $N = 10$ and $s = 1$. k is varied for several orders of magnitude. The difference between these

curves is noticeable in the bimodal regime of the stationary distribution ($k < s = 1$).

The second term on the right hand side of Eq. (17) originates from $b^s(q)$. Thus, the effect of discreteness loss to the stationary variance only comes from the broken balance between the drift and the diffusion parts in the propensity functions at the boundaries $X = 0, N$. Since this term is strictly negative when $\epsilon < 1$, the stationary variance for $\epsilon < 1$ has smaller values than that for the CME.

However, it should be emphasized that the difference in the stationary variance vanishes for the small k limit. Indeed, we have $P_0^s(0) = B(0)^{k/s-1}/\int_0^N B(X)^{k/s-1}dX \sim s(k\ln k^{-1})^{-1}$. Thus, the second term on the right hand side of Eq. (18) becomes 0 as $k \to 0$, implying that $\langle X^2\rangle - \langle X\rangle^2 \to N^2/4$ in both Eqs. (17) and (18).

B. Correlation time

In this subsection, we calculate the correlation time,

$$\tau = \int_0^\infty C(t)dt/C(0), \tag{19}$$

where $C(t) = \langle X(t)X(0)\rangle - \langle X\rangle^2$ is the stationary autocorrelation function before the time rescaling $t \to (\epsilon^{-2}s)t$. For the calculation of τ, we appeal to the large deviation theory for stationary processes [18]: Let W be the transition matrix for M_ϵ (12). Then, we have

$$\int_{-\infty}^\infty C(t)dt = \epsilon^2 s^{-1}\frac{d^2}{dr^2}\phi(0), \tag{20}$$

where $\phi(r)$ is the largest eigenvalue of the matrix $W + rU$, U is a diagonal matrix whose (i,j) element is $U_{ij} = \epsilon i\delta_{ij}$, and δ_{ij} is the Kronecker δ function.

In order to calculate $\frac{d^2}{dr^2}\phi(0)$, we add the term $r\epsilon n P(\epsilon n,t)$ to the right hand side of M_ϵ. Let $P_r(\epsilon n,t)$ be a solution of this new equation. The corresponding generating function $G_r(q,t)$ satisfies

$$\partial_t G_r(q,t) + H_r(\partial_q,q)G_r(q,t) = b_r(q,t), \tag{21}$$

where $H_r(p,q) = f_2(q)p^2 + f_{r,1}(q)p + f_0(q)$, $f_{r,1}(q) = f_1(q) - r\epsilon q$, and $b_r(q,t) = b_0(q)P_r(0,t) + b_N(q)P_r(N,t)$.

Let $\boldsymbol{P}_{\phi(r)} = [P_{\phi(r)}(0), P_{\phi(r)}(\epsilon), \ldots]$ be the unique eigenvector of the maximum eigenvalue $\phi(r)$ normalized by the inner product $\langle \boldsymbol{Q},\boldsymbol{R}\rangle = \sum_n Q(\epsilon n)R(\epsilon n)/P^s(\epsilon n)$. Now, we take the following solution:

$$P_r(\epsilon n,t) = e^{\phi(r)t}P_{\phi(r)}(\epsilon n). \tag{22}$$

The generating function for this solution is $G_r(q,t) = e^{\phi(r)t}F_r(q)$ where $F_r(q) = \sum_n P_{\phi(r)}(\epsilon n)q^n$. Substituting this into Eq. (21), we obtain

$$\phi F + f_2\partial_q^2 F + f_1\partial_q F + f_0 F = b_0 P_\phi(0) + b_N P_\phi(N), \tag{23}$$

where we omit variables q and r for simplicity.

Equation (23) holds in the neighborhood of $(q,r) = (1,0)$. Hence, we can take an arbitrary curve $q = q(r)$ which passes through $(q,r) = (1,0)$ and differentiate Eq. (23) with respect to r at $r = 0$. Here, we consider the Hamiltonian system [19],

$$\dot q = \partial_p H_r(p,q), \tag{24}$$

$$\dot p = -\partial_q H_r(p,q) \tag{25}$$

and take the family of equilibrium solutions $\{(p(r),q(r))\}_r$ such that $q(0) = 1$. From $\dot q = \dot p = 0$, we obtain $q' = s/(2k\epsilon)$ and $q'' = s^2(k-s)/(4k^3\epsilon^2)$ after some algebra, where $'$ denotes differentiation with respect to r at $r = 0$.

Differentiating Eq. (23) with respect to r along $q = q(r)$ at $r = 0$ twice and substituting q' and q'', we finally get

$$\int_{-\infty}^\infty C(t)dt = \frac{N(sN+2k)}{4k(s+2k)} - \frac{(1-\epsilon)N(N+\epsilon)}{2(s+2k)}P_\epsilon^s(0)\epsilon^{-1} + \frac{(1-\epsilon)N}{s}\epsilon\frac{d}{dr}P_{\phi(0)}(0), \tag{26}$$

where we make use of the fact that $P_\epsilon^s(0) = P_\epsilon^s(N)$ and $\frac{d}{dr}P_{\phi(0)}(0) = -\frac{d}{dr}P_{\phi(0)}(N)$, which follows from the following Eqs. (27) and (28). $\frac{d}{dr}\boldsymbol{P}_{\phi(0)}$ is the unique solution of the following linear system of equations:

$$W\frac{d}{dr}\boldsymbol{P}_{\phi(0)} = \left(\frac{d}{dr}\phi(0)I - U\right)\boldsymbol{P}^s, \tag{27}$$

$$0 = \sum_{n=0}^{N/\epsilon}\frac{d}{dr}P_{\phi(0)}(\epsilon n), \tag{28}$$

where I is the identity matrix. Equations (27) and (28) follow by differentiating $(W + rU)\boldsymbol{P}_{\phi(r)} = \phi(r)\boldsymbol{P}_{\phi(r)}$ and the normalization condition $\langle \boldsymbol{P}_{\phi(r)}, \boldsymbol{P}_{\phi(r)}\rangle = 1$ with respect to r at $r = 0$, respectively.

For CFPE (15), we have (by using the method in Sec. S.9 in Ref. [20])

$$\int_{-\infty}^\infty C(t)dt = \frac{N(sN+2k)}{4k(s+2k)} - \frac{N^2}{2(s+2k)}P_0^s(0) - \frac{N}{4k}P_0^s(0)\int_0^N\left[1 - \left(\frac{kN}{B(X)}\right)^{k/s}\right]dX. \tag{29}$$

One can show that the right hand side of Eq. (26) converges to that of Eq. (29) as $\epsilon \to 0$ by considering the continuous limit of Eqs. (27) and (28) before the time rescaling.

Equations (27) and (28) also imply $\frac{d}{dr}P_{\phi(0)}(0) \leqslant 0$. Thus, as in the case of the stationary variance, the effect of discreteness loss originates only from the boundaries $X = 0, N$, and it decreases the value of the integral of the autocorrelation function. Figure 2 shows the correlation time for several values of ϵ and that for the CFPE. One can see that discreteness loss has a negative effect on the values of the correlation time. This tendency is larger in the bimodal regime.

From Fig. 2, one might expect that the divergence of the correlation time for the CFPE as $k \to 0$ is slower than that for the CME. This expectation is correct because of the following reason. As we have noted in the calculation of the stationary variance, we have $P_0^s(0) \sim (k\ln k^{-1})^{-1}$ as $k \to 0$. On the other hand, the rightmost integral in Eq. (29) is $\sim (N/s)k\ln k^{-1}$. Thus, one sees that the last term on the right hand side of Eq. (29) is $\sim N^2/(4k)$. In turn, this term and the first term on the right hand side of Eq. (29) cancel each other. Remembering that the stationary variance $C(0)$ converges to the same value for both the CME and the CFPE as $k \to 0$, we conclude that the correlation time for the CFPE diverges, such as $O[(k\ln k^{-1})^{-1}]$, which is slower than k^{-1} for the CME.

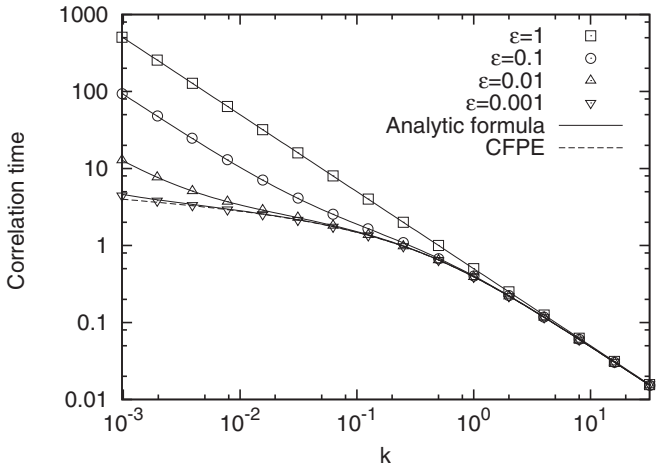

FIG. 2. Correlation time of the autocatalytic reaction system with $N = 10$ and $s = 1$ for different values of ϵ and the CFPE. Marks represent values calculated from the numerical derivative of the numerically obtained maximum eigenvalue $\phi(r)$ ($\epsilon = 1$: square; $\epsilon = 0.1$: circle; $\epsilon = 0.01$: upper triangle; $\epsilon = 0.001$: lower triangle). Solid lines are the combination of Eqs. (17) and (26). The dashed line is the combination of Eqs. (18) and (29).

IV. BRANCHING-ANNIHILATION REACTION SYSTEM

In this section, we consider the following chemically reacting systems:

$$R_1: X \to 2X, \quad a_1(X) = \alpha X, \quad \nu_1 = +1,$$
$$R_2: 2X \to \emptyset, \quad a_2(X) = \beta \frac{X(X-1)}{2}, \quad \nu_2 = -2.$$

The deterministic mean-field equation for this system is the logistic equation $\dot{X} = X(\alpha - \beta X)$. It has two equilibrium points: One is repulsive ($X = 0$), and the other is attractive ($X = \alpha/\beta =: N$).

The stochastic dynamics of this system have a qualitatively different feature from that for the deterministic dynamics. It is known that stochastic trajectories from any initial condition falls onto $X = 0$ (extinction) with probability one [11]. This feature is common for both the CME and the CFPE dynamics. The scenario of extinction for $N \gg 1$ is as follows: First, an initial distribution moves to a region close to $X = N$ in time of the order $1/\alpha$, and a quasistationary distribution is formed. Second, the quasistationary distribution is degraded in time of the exponential order of N into the δ peak at $X = 0$. The average time taken in the second process is called the mean extinction time.

However, the mean extinction time for the CFPE has an exponential difference from that for the CME [12,21]. Let us denote the former by $\tau_{\rm CFPE}$ and the latter by $\tau_{\rm CME}$. When $N \gg 1$, it was shown that [11,12,21]

$$\tau_{\rm CME} \approx \frac{2\sqrt{\pi}}{\beta N^{3/2}} \exp[N(2 - 2\ln 2)], \tag{30}$$

$$\tau_{\rm CFPE} \approx \sqrt{\frac{\pi}{3}} \frac{1}{\beta N^{3/2}} \exp\{N[(3/2)\ln 3 - 1]\}. \tag{31}$$

Here, we calculate the mean extinction time for M_ϵ and reveal how discreteness loss gives rise to the exponential difference between $\tau_{\rm CME}$ and $\tau_{\rm CFPE}$.

Mean extinction time

We follow the method developed in Refs. [12,22]. The probability generating function equation corresponding to M_ϵ is

$$\partial_t G(q,t) + H(\partial_q, q) G(q,t) = 0, \tag{32}$$

where $G(q,t) = \sum_{n=0}^{\infty} q^n P(\epsilon n, t)$ and the Hamiltonian $H(p,q)$ is given by

$$H(p,q) = \alpha(1-q)\left(\frac{1+\epsilon^{-1}}{2} q - \frac{-1+\epsilon^{-1}}{2}\right) p + \frac{\beta}{2}(1-q^2)\left(\frac{1-\epsilon}{2} q^2 - \frac{1+\epsilon}{2}\right) p^2. \tag{33}$$

For $t \gg \frac{1}{\alpha}$, assume that $G(q,t) \approx 1 - \phi(q) e^{-Et}$, $P(0,t) \approx 1 - e^{-Et}$, and $P(\epsilon n, t) \approx \pi_n e^{-Et} (n > 0)$, where $\pi_n \geqslant 0$ and $\sum_{n=1}^{\infty} \pi_n = 1$. π_n is called the quasistationary distribution. Since $P(0,t)$ is the probability that X is extinct by time t, the extinction probability density at time t is $p(t) = \frac{dP(0,t)}{dt} \approx E e^{-Et}$. Hence, the mean extinction time is given by [12]

$$\tau = \int_0^\infty t p(t) dt \approx E^{-1}. \tag{34}$$

E can be obtained by substituting $G(q,t) = 1 - \phi(q) e^{-Et}$ into Eq. (32) and solving the following eigenvalue problem:

$$-\frac{\epsilon}{2N}(1-q^2)\left(\frac{-1+\epsilon^{-1}}{2} q^2 - \frac{1+\epsilon^{-1}}{2}\right)\frac{d^2\phi}{dq^2}(q) - (1-q)\left(\frac{1+\epsilon^{-1}}{2} q - \frac{-1+\epsilon^{-1}}{2}\right)\frac{d\phi}{dq}(q) + \frac{E}{\alpha}\phi(q) = 0. \tag{35}$$

To solve Eq. (35), we can directly apply the method in Ref. [22] to it and get

$$\tau_{M_\epsilon} \approx \sqrt{\frac{\pi}{3+\epsilon^2}} \frac{(1+\epsilon)^2}{\beta N^{3/2}} \exp\left[N\left(-\frac{\ln(3+\epsilon^2)}{\epsilon^2} + \frac{1+\epsilon^2}{\epsilon^2\sqrt{1-\epsilon^2}} \ln\left|\frac{(\sqrt{1+\epsilon}+\sqrt{1-\epsilon})[\sqrt{(1+\epsilon)^3}-\sqrt{(1-\epsilon)^3}]}{(\sqrt{1+\epsilon}-\sqrt{1-\epsilon})[\sqrt{(1+\epsilon)^3}+\sqrt{(1-\epsilon)^3}]}\right|\right)\right]. \tag{36}$$

It can be verified that $\tau_{M_\epsilon} \to \tau_{\rm CME}$ as $\epsilon \to 1$ and $\tau_{M_\epsilon} \to \tau_{\rm CFPE}$ as $\epsilon \to 0$.

The origin of the exponential difference between $\tau_{\rm CME}$ and $\tau_{\rm CFPE}$ can be understood from the following geometrical interpretation. Let us consider the Hamiltonian system $\dot{q} = \partial_p H(p,q)$, $\dot{p} = -\partial_q H(p,q)$. On the q-p plane, the area $S(q_0) = \int_{q_0}^1 p(q) dq$ enclosed by three curves $p = 0$, $q = 1$, and $p = p(q) := \frac{2N}{\epsilon} \frac{(1+\epsilon)q - (1-\epsilon)}{(1+q)[(1+\epsilon) - (1-\epsilon)q^2]}$ gives the exponential factor in τ_{M_ϵ} (36), where $q_0 := \frac{1-\epsilon}{1+\epsilon}$ is the q coordinate of

the intersection point between $p = 0$ and $p = p(q)$. The equation $\dot{p} = -\partial_q H(p,q)$, restricted on $q = 1$, corresponds to the deterministic mean-field equation. The p coordinate of the intersection point between $q = 1$ and $p = p(q)$ is N/ϵ. The curve $p = p(q)$ is the most probable extinction path from the metastable state to the extinct state [22]. It moves toward $q = 1$ as $\epsilon \to 0$. This modification of the most probable extinction path causes the change in the area $S(q_0)$, which yields the exponential difference between τ_{CME} and τ_{CFPE}.

V. CONCLUDING REMARKS

In this paper, we investigated the effect of discreteness on the stochastic dynamics of chemically reacting systems. We focused on two concrete systems. One is an autocatalytic reaction system exhibiting an intrinsic noise-induced transition in the stationary probability distribution. The other is a branching-annihilation reaction system in which intrinsic noise gives rise to the extinction of the population of the chemical species.

Discreteness loss yields a change in characteristic time scales in both systems but for different reasons. In the first example, the effect of discreteness loss in the correlation time originates from the imbalance between the drift part and the diffusion part of the propensity functions at the boundaries $X = 0, N$. However, in the second example, the boundary $X = 0$ has nothing to do because there is no term representing the effect at the boundary in the generating function equation. It is revealed that what makes the exponential difference in the mean extinction time when the degree of discreteness decreases is modification of the most probable path to extinction.

It is natural to ask whether the existence of nonzero boundary term $b(q,t)$ always indicates a nontrivial discreteness effect originating from the boundaries. The answer seems to be no because of the following example. Let us consider the reaction system studied in Sec. III with $s = 0$. Namely, now we have no autocatalytic reactions. For this system, we still have a nonzero boundary term $b(q,t)$ in the generating function equation for $\epsilon < 1$. However, first of all, no transition occurs in the stationary probability distribution $P^s(X)$ for the CME as $k \to 0$. Indeed, the stationary probability distribution $P^s(X)$ is the binomial distribution $B(N,1/2)$, which does not depend on k. Furthermore, we have no significant difference in the correlation time between the CME and the CFPE. Indeed, one can see both the stationary variance and the integral of the autocorrelation function for the CFPE have exponentially small deviations from those for the CME as a function of N. Thus, the existence of a nonzero boundary term $b(q,t)$ is only a necessary condition for the boundaries to induce a nontrivial discreteness effect.

In previous work, the CFPE is typically regarded as an approximation of the CME in an appropriate condition [14]. The condition justifying the approximation of the CME by the CFPE is a sufficient condition such that the approximation is effective. Logically, it has nothing to say about what occurs when the approximation is not valid. In contrast, we do not regard that the CFPE is an approximation of the CME but regard that it is a limit of discreteness loss because our aim is to study the effect of discreteness in stochastic dynamics of chemically reacting systems. We hope that the presented approach applied to other chemically reacting systems reveals a variety of quantitative effects of discreteness on the stochastic dynamics of them.

ACKNOWLEDGMENTS

This work was partially supported by the JST PRESTO program. The author expresses his gratitude to the anonymous reviewers for their comments which greatly improved the paper.

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