

Stability and Fluctuation in Chemical Systems

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Fluctuations around the steady state in chemical reactions are discussed. The connection between the two approaches in the literature, the Langevin equation approach and the master equation approach, is shown in terms of a path integral.

KEY WORDS: Fluctuations; chemical reactions; Markovian process; Langevin equation; path integral.

1. INTRODUCTION

Cooperative effects in chemical reactions have been of considerable interest recently; due to feedback mechanisms in reaction networks, instability occurs when some external parameters are set at critical values.⁽¹⁻⁵⁾ This phenomenon is very much analogous to second-order phase transitions. The analogy has been discussed by many authors.^(1,6-10) It has been predicted that the fluctuations of concentrations of chemical species diverge and that relaxation of concentrations to the steady state becomes extremely slow. The latter may be called "the critical slowing down."

The anomaly of the fluctuations and the slowing down of the relaxation are related. Mazo⁽⁶⁾ showed that the variance of fluctuations is related to the sum of two eigenvalues of the relaxation matrix in the linearized chemical kinetic equation. Suppose the relaxation matrix has complex-conjugate eigenvalues. Then the variance is divergent when the real part of one of the

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complex eigenvalues vanishes. The argument of Mazo is based on Lax's treatment⁽¹¹⁾ of nonlinear stochastic processes. Nitzan *et al.*⁽⁷⁾ have shown the same results starting from phenomenological rate equations. They linearized them around the steady state, and assuming that these linearized equations are valid also for describing regression of fluctuations around the steady state, they add random forces to the equations, which excite the fluctuations. Recently Mashiyama *et al.*⁽⁸⁾ analyzed the evolution equations for the most probable values of concentrations and the variances of fluctuations around the most probable values. The evolution equations were derived first by van Kampen⁽¹²⁾ and a systematic derivation and generalization to multi-variable cases were given by Kubo *et al.*⁽¹³⁾ under the assumption that the system size is large. Mashiyama *et al.* expanded the evolution equations in the power of the distance from the critical situations, i.e., in the power of so-called bifurcation parameters.⁽¹⁴⁾ The steady values of variances are found to be divergent as the critical values of parameters are approached.

At this point, it is worthwhile looking into the relations between the approach of Nitzan *et al.* (the so-called Langevin equation approach) and the approach of Mashiyama *et al.* (the so-called master equation approach). The key is to derive a weight of an evolution path of concentrations from the master equation and compare the weight with the Langevin equation, which is also an equation for the evolution path. If we identify the most probable evolution, which maximizes the path weight, with the phenomenological kinetic rate equation, then the random forces play the role of describing the motion of less probable evolutions. Thus we can specify the nature of random forces precisely by the parameters appearing in the master equation. We will find that the critical anomaly of fluctuations is due to the critical slowing down of relaxation, not due to the nature of random forces, which have no anomaly in the critical situations.

2. RELATION BETWEEN THE MASTER EQUATION AND THE LANGEVIN EQUATION

Suppose we have a system of several reacting chemical species. The number of molecules of the i th species is denoted by N_i ($i = 1, 2, \dots, M$). The stochastic processes associated with the reactions among these chemical species are described by the master equation for the probability $P(N_1, \dots, N_M, t)$ of having N_i molecules of the i th species ($i = 1, \dots, M$) at time t :

$$\begin{aligned}
 (\partial/\partial t)P(\mathbf{N}, t) = & - \sum_{\mathbf{r}} W(\mathbf{N} \rightarrow \mathbf{N} + \mathbf{r})P(\mathbf{N}, t) \\
 & + \sum_{\mathbf{r}} W(\mathbf{N} - \mathbf{r} \rightarrow \mathbf{N})P(\mathbf{N} - \mathbf{r}, t)
 \end{aligned}
 \tag{1}$$

where we use the notations $\mathbf{N} = (N_1, \dots, N_M)$ for the populations and $\mathbf{r} = (r_1, \dots, r_M)$ for jumps of the populations. We assume the transition probability $W(\mathbf{N} \rightarrow \mathbf{N} + \mathbf{r})$ takes the form

$$W(\mathbf{N} \rightarrow \mathbf{N} + \mathbf{r}) = \Omega w(\mathbf{x}; \mathbf{r}) \tag{2}$$

where $\mathbf{x} = (x_1, \dots, x_M)$ are the concentrations, $x_i = N_i/\Omega$, and Ω is the volume of the system. It was shown in a previous publication⁽¹³⁾ that the fundamental solution of Eq. (1) is given in terms of the path integral; if we define the fundamental solution $G(\mathbf{x}, t | \mathbf{x}_0, t_0)$ by

$$P(\mathbf{x}, t) = \int d\mathbf{x}_0 G(\mathbf{x}, t | \mathbf{x}_0, t_0) P(\mathbf{x}_0, t_0) \tag{3}$$

then the asymptotic form of the fundamental solution for large Ω is given in the form of a path integral,

$$G(\mathbf{x}, t | \mathbf{x}_0, t_0) = \int \mathcal{D}(\sigma) \exp \left[\Omega \int_{t_0}^t ds L(\mathbf{x}(s; \sigma), \dot{\mathbf{x}}(s; \sigma)) \right] \tag{4}$$

where the summation is over all paths $\mathbf{x}(s; \sigma)$, $t_0 \leq s \leq t$, which are parametrized by σ and satisfy the initial and the final conditions $\mathbf{x}(t_0) = \mathbf{x}_0$, $\mathbf{x}(t) = \mathbf{x}$. The Lagrangian $L(\mathbf{x}(s), \dot{\mathbf{x}}(s))$ is approximately written as

$$L(\mathbf{x}, \dot{\mathbf{x}}) \simeq -\frac{1}{2} \sum_{i,j} \{C_i(\mathbf{x}) - \dot{x}_i\} (D^{-1})_{ij} \{C_j(\mathbf{x}) - \dot{x}_j\} \tag{5}$$

where

$$C_i(\mathbf{x}) = \sum_{\mathbf{r}} r_i w(\mathbf{x}; \mathbf{r}) \tag{6}$$

and $(D^{-1})_{ij}$ is the inverse matrix of D , which is defined by

$$D_{ij} = \sum_{\mathbf{r}} r_i r_j w(\mathbf{x}; \mathbf{r}) \tag{7}$$

By the definition, the matrix D is positive definite and so is the matrix D^{-1} . Therefore the rhs of Eq. (5) is negative,

$$L^0(\mathbf{x}, \dot{\mathbf{x}}) = -\frac{1}{2} \sum_{ij} \{C_i(\mathbf{x}) - \dot{x}_i\} (D^{-1})_{ij} \{C_j(\mathbf{x}) - \dot{x}_j\} \leq 0 \tag{8}$$

In the path integral (4), the functional of a path

$$\mathcal{D}(\sigma) = \exp \left[\Omega \int_{t_0}^t ds L^0(\mathbf{x}(s; \sigma), \dot{\mathbf{x}}(s; \sigma)) \right] \tag{9}$$

can be interpreted as a weight of the path σ and Eqs. (5) and (8) show that the path σ_0 that satisfies the equation

$$\sigma_0: \dot{x}_j - C_j(\mathbf{x}) = 0 \tag{10}$$

maximizes the weight $\mathcal{P}(\sigma)$. The most probable path (10) can be identified with the macroscopic phenomenological equation. Paths other than the most probable path σ_0 can be described by introducing an additional term $f_j(t; \sigma)$,

$$\dot{x}_j(t; \sigma) - C_j(\mathbf{x}(t; \sigma)) = f_j(t; \sigma) \quad (11)$$

Then obviously for the most probable path σ_0 , $f_j(t; \sigma_0)$ vanishes. The weight of the realization of functions $f_j(t; \sigma)$, $j = 1, \dots, M$, is given by expanding the Lagrangian around the most probable path σ_0 and the resulting expression is

$$\mathcal{P}(\sigma) \simeq \exp \left[-(\Omega/2) \int_{t_0}^t ds f_i(s; \sigma) (D^{-1}(\mathbf{x}(s; \sigma_0)))_{ij} f_j(s; \sigma) \right] \quad (12)$$

Thus one gets

$$\langle f_i(s; \sigma) f_j(s'; \sigma) \rangle = (1/\Omega) D_{ij}(\mathbf{x}(s; \sigma_0)) \delta(s - s') \quad (13)$$

and

$$\langle f_i(s; \sigma) \rangle \simeq O(1/\Omega) \quad (14)$$

Note that the rhs of Eq. (13) contains the time explicitly through the motion of the most probable path σ_0 . Equation (11) can be identified with the Langevin equation and its average behavior is the macroscopic evolution; in fact, if we put $x_i = \langle x_i \rangle + \delta x_i$ in the Langevin equation,

$$\dot{x}_i = C_i(\mathbf{x}) + f_i(t) \quad (15)$$

and take the average, we obtain

$$d\langle x_i \rangle / dt = C_i(\langle \mathbf{x} \rangle) + \frac{1}{2} \sum_{jk} [\partial^2 C_i(\langle \mathbf{x} \rangle) / \partial x_j \partial x_k] \langle \delta x_j \delta x_k \rangle + \langle f_i(t) \rangle \quad (16)$$

The variance $\langle \delta x_j \delta x_k \rangle$ is estimated to be of order $1/\Omega$ in the Gaussian approximation. Therefore if $\langle f_i \rangle$ is also of order $1/\Omega$, we obtain the macroscopic equation

$$d\langle x_i \rangle / dt = C_i(\langle \mathbf{x} \rangle) + O(1/\Omega) \quad (17)$$

which is identical to the equation for the most probable path. Therefore we can identify $f_i(t)$ as the random force in the Langevin equation. From Eq. (13) the variance of the random force is found to be proportional to the second moment \mathbf{D} , which is a function of the most probable path σ_0 . In general the random force is not white noise. When the macroscopic state described by Eq. (10) or (17) reaches the steady state \mathbf{x}^{st} , the process of the random force is white noise,

$$\langle f_i(s; \sigma) f_j(s'; \sigma) \rangle = (1/\Omega) D_{ij}(\mathbf{x}^{\text{st}}) \delta(s - s') \quad (18)$$

Using Eqs. (11) and (18), we can evaluate the fluctuation around the macroscopic steady state \mathbf{x}^{st} by putting $x_i(t) = x_i^{\text{st}} + \delta x_i(t)$,

$$d[\delta x_i(t)]/dt = \sum_j [\partial C_i(\mathbf{x}^{\text{st}})/\partial x_j] \delta x_j(t) + f_i(t) \tag{19}$$

Writing

$$\partial C_i(\mathbf{x}^{\text{st}})/\partial x_j = -\Lambda_{ij} \tag{20}$$

we obtain the time correlation function as

$$\langle \delta x_i(t) \delta x_j(0) \rangle = (2\pi\Omega)^{-1} \int_{-\infty}^{\infty} d\omega e^{i\omega t} (i\omega + \Lambda)^{-1} \mathbf{D} (-i\omega + \tilde{\Lambda})^{-1} \tag{21}$$

where $\tilde{\Lambda}$ denotes the transposed matrix of Λ . Thus the fluctuation around the steady state is

$$\langle \delta x_i \delta x_j \rangle = (2\pi\Omega)^{-1} \int_{-\infty}^{\infty} d\omega (i\omega + \Lambda)^{-1} \mathbf{D} (-i\omega + \tilde{\Lambda})^{-1} \tag{22}$$

On the other hand, the Ω expansion^(12,13) of the master equation gives an evolution equation for the variance,

$$\langle \delta x_i \delta x_j \rangle_t = (1/\Omega) \sigma_{ij}(t) \tag{23}$$

$$\dot{\sigma}(t) = -\Lambda \sigma(t) - \sigma(t) \tilde{\Lambda} + \mathbf{D} \tag{24}$$

and the solution is

$$\begin{aligned} \sigma(t) &= [\exp(-\Lambda t)] \sigma(0) \exp(-\tilde{\Lambda} t) \\ &+ \int_0^t dt' \{ \exp[-\Lambda(t-t')] \} \mathbf{D} \exp[-\tilde{\Lambda}(t-t')] \end{aligned} \tag{25}$$

Thus the steady solution is given by

$$\sigma_{\text{st}} = \int_0^{\infty} d\tau [\exp(-\Lambda \tau)] \mathbf{D} \exp(-\tilde{\Lambda} \tau) \tag{26}$$

since the initial condition $\sigma(0)$ will be forgotten as $t \rightarrow \infty$. It can be easily shown that Eq. (26) is equivalent to Eq. (22) by using the formula $\exp(-\Lambda t) = \int_{-\infty}^{\infty} d\omega e^{i\omega t} (i\omega + \Lambda)^{-1}$. Thus the Langevin equation and the master equation give the same form for the variance of fluctuations around the steady state. It should be noted that the two matrices Λ and $\tilde{\Lambda}$ have the same eigenvalues η_i , $i = 1, \dots, M$, so the variance is written as a sum of terms such as $1/(\eta_i + \eta_j)$, $i, j = 1, \dots, M$. Therefore the variance diverges in the following two cases. (i) All the eigenvalues of Λ are real and at least one of them vanishes; (ii) some of the eigenvalues of Λ are complex and the real part of a complex eigenvalue vanishes. In any case, the divergence of the variance is

related to the instability of the steady states of the phenomenological equations (10) and not to the random forces. The variance D of the random forces is not necessarily divergent at the onset of instability. The vanishing of the restoring force [i.e., $\text{Re}(\Lambda) \rightarrow 0$] gives rise to an accumulation of fluctuations excited by the random forces $f_i(t)$. In the appendix we give some examples.

3. CONCLUDING REMARKS

Throughout this paper, we assumed that the chemical process under discussion was given in terms of the concentrations. However, as pointed out by Nicolis,⁽¹⁵⁾ what really happens in a chemical reaction is that there are transitions among the internal states of the molecules as well as changes in the population of each component. If these internal degrees of freedom are taken into account, then the change in the populations of the chemical components should obey a non-Markovian process. Therefore, the present analysis is valid only when the relaxation of the internal states is very rapid in comparison with the change in populations of the species.

APPENDIX. EXAMPLES

In the linear rate equation for the concentration X of a species,

$$dX/dt = -kX + I \quad (\text{A.1})$$

the first term stands for the spontaneous decay of the species and I is the constant input. Correspondingly, we can construct a master equation for the number of particles of the species with the following transition probability^(16,17):

$$W(N \rightarrow N + r) = \begin{cases} kN, & r = +1 \\ I, & r = -1 \end{cases} \quad (\text{A.2})$$

or in terms of the concentration $x = N/\Omega$, we may write the transition probability as

$$w(x; r) = \begin{cases} kx, & r = +1 \\ I, & r = -1 \end{cases} \quad (\text{A.3})$$

The moments of the transition probability are [see Eqs. (6) and (7)]

$$C(x) = \sum_{r=\pm 1} r w(x; r) = -kx + I \quad (\text{A.4})$$

$$D(x) = \sum_{r=\pm 1} r^2 w(x; r) = kx + I \quad (\text{A.5})$$

From Eq. (10), the most probable path is given by

$$\dot{x} = C(x) = -kx + I \quad (\text{A.6})$$

which is identical to the kinetic equation and the solution is obviously

$$x(t) = e^{-kt}[x(0) - (I/k)] + (I/k) \quad (\text{A.7})$$

The correlation function of the random force is obtained from Eq. (14),

$$\langle f(t; \sigma)f(t'; \sigma) \rangle = (1/\Omega) \delta(t - t')\{ke^{-kt}[x(0) - I] + 2I\} \quad (\text{A.8})$$

and in the steady state ($t \rightarrow \infty$),

$$\langle f(t; \sigma)f(t'; \sigma) \rangle = (1/\Omega) \delta(t-t') 2I \quad (\text{A.9})$$

It is noted that the random force in the steady state depends only on the input I .

Another and more complex reaction scheme is a model of a nonlinear chemical oscillation studied by Lefever and Nicolis,⁽¹⁸⁾

$$dx/dt = A + x^2y - Bx - x, \quad dy/dt = Bx - x^2y \quad (\text{A.10})$$

which has a steady state solution

$$x_0 = A, \quad y_0 = B/A \quad (\text{A.11})$$

The eigenvalues of the rate equations linearized about this steady state are

$$\mu_{1,2} = \frac{1}{2}\{B - (A^2 + 1) \pm [B^2 - 2(A^2 + 1)B + (1 - A^2)^2]^{1/2}\} \quad (\text{A.12})$$

and the character of the solution about the steady state changes depending on the value of B , namely: (i) when $B < (1 - A)^2$, the steady state is a stable node, so other solutions tend toward it monotonically; (ii) when $(1 - A) < B < 1 + A^2 = B_c$, the steady state is a stable focus and other solutions tend toward it as damped oscillations; (iii) when $B_c < B < (1 + A)^2$, the steady state is an unstable focus; (iv) when $B > (1 + A)^2$, the steady state is an unstable node. Corresponding to the rate equations, we construct a master equation for the concentrations of particles of species X and Y . The transition probability may be chosen as

$$w(x, y; r_x, r_y) = \begin{cases} A, & r_x = 1, \quad r_y = 0 \\ x^2y, & r_x = 1, \quad r_y = -1 \\ Bx, & r_x = -1, \quad r_y = 1 \\ x, & r_x = -1, \quad r_y = 0 \\ 0, & \text{otherwise} \end{cases}$$

For example, the second expression x^2y corresponds to the process $2X + Y \rightarrow 3X$, i.e., two particles of the species X and one particle of the species Y

react and give three particles of the species X. For this choice of the transition probability, we have

$$\begin{aligned}C_x(x, y) &= A + x^2y - Bx - x \\C_y(x, y) &= Bx - x^2y \\D_{xx}(x, y) &= A + x^2y + Bx + x \\D_{xy}(x, y) &= -x^2y - Bx \\D_{yy}(x, y) &= x^2y + Bx\end{aligned}$$

It is obvious that the equations for the most probable path $\dot{x}_i = C_i(x, y)$, $i = x, y$, are identical to the rate equations (A.10). As B approaches B_c in the case (ii), the real part of the eigenvalues (A.12) vanishes; $\eta_1 + \eta_2 = 2 \operatorname{Re}(\eta_1) \propto |B - B_c| \rightarrow 0$. Thus the covariances of fluctuations of the concentrations diverge as $|B - B_c|^{-1}$. The second moments of the transition probability give the variance of the random forces, especially at the steady state corresponding to the cases (i) and (ii); we have the following expressions.

$$\begin{aligned}\langle f(t; \sigma) f_x(t'; \sigma) \rangle &= (1/\Omega)A(A + B) \delta(t - t') \\ \langle f_x(t; \sigma) f_y(t'; \sigma) \rangle &= (1/\Omega)2AB \delta(t - t') \\ \langle f_y(t; \sigma) f_y(t'; \sigma) \rangle &= (1/\Omega)AB \delta(t - t')\end{aligned}$$

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