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The Poisson Representation. I. A New Technique for Chemical Master Equations

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We introduce a new technique for handling chemical master equations, based on an expansion of the probability distribution in Poisson distributions. This enables chemical master equations to be transformed into Fokker–Planck and stochastic differential equations and yields very simple descriptions of chemical equilibrium states. Certain nonequilibrium systems are investigated and the results are compared with those obtained previously. The Gaussian approximation is investigated and is found to be valid almost always, except near critical points. The stochastic differential equations derived have a few novel features, such as the possibility of pure imaginary noise terms and the possibility of higher order noise, which do not seem to have been previously studied by physicists. These features are allowable because the transform of the probability distribution is a quasiprobability, which may be negative or even complex.

KEY WORDS: Chemical reactions; correlations; fluctuations; instabilities; stochastic differential equations; master equations; reaction diffusion systems; statistical mechanics.

1. INTRODUCTION

The investigation of fluctuation phenomena in chemical reactions is a subject which has been studied through two main formulations, the Langevin equation approach, espoused by Nitzan *et al.*⁽¹⁾ and Keizer,⁽²⁾ and the stochastic master equation approach used by Gardiner *et al.*,⁽³⁾ van Kampen,⁽⁴,⁵⁾ and Prigogine, Nicolis, and co-workers.⁽⁶⁻¹⁰⁾ At the basis of the former approach is the concept of concentration fluctuations in chemical reactions as Gaussian, a concept whose validity is assumed to be assured by the central limit theorem. The precise magnitude of the fluctuations is, in thermodynamic equilibrium, computable from fluctuation dissipation theorems, most clearly

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enunciated by Grossman.(11) Gardiner has recently emphasized(12) that the extension of these Langevin equations to nonequilibrium systems requires some information of the mechanisms involved, such as a master equation as discussed in the next paragraph. Indeed, Kurtz's(13) central limit theorem for master equations can be used to give a Gaussian approximation that is equivalent to Keizer's(2) Langevin equations.

The stochastic master equation methods are more precisely defined, since they have as their starting point a simple kinetic picture of reactions being induced by collisions between molecules which move about in space by diffusion. The master equations that arise from such considerations have a rather simple appearance, but are by no means easy to solve in any systematic way, particularly when there are many variables, as when diffusion is included. Various methods exist; e.g., van Kampen's system size expansion(4) generating function methods,(14) the cumulant expansion methods,(15,16) and the recent work of Görtz and Walls.(17) None of these is easy to use in practice, though van Kampen's method(4,18) is capable of yielding a systematic method of approximation.

Any method for transforming stochastic master equations into Langevin equations would obviously be very useful, and we have been able to do this by means of a simple technical device. We expand the probability distribution for the numbers of molecules of chemical species as a superposition of Poisson distributions, and thus introduce a quasiprobability distribution[2] which obeys a generalized Fokker–Planck equation. If only bimolecular steps are involved, which is in realistic cases almost always true, this Fokker–Planck equation involves no more than the usual first derivative (drift) and second derivative (diffusion) terms. In general cases, derivatives of no more than finite order occur. This Fokker–Planck equation is totally different from that which arises from the system-size-expansion method, which is only an approximate consequence of the master equation, whereas ours follows exactly from the master equation.

The quasiprobability introduced has one major difference from a genuine probability distribution: It need not be positive and indeed the range of the transformed stochastic variable is in some cases a curve in the complex plane. Nevertheless, the moments of the quasiprobability are equal to the factorial moments of the probability distribution in numbers of molecules, and the quasiprobability provides all the information one normally requires, simply and directly.

The reader with some familiarity with quantum optics will recognize a certain qualitative resemblance to the Glauber–Sudarshan *P*-representation for the photon density matrix in terms of coherent states, which give Poisson

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[2] This method was introduced in Ref. 19.

distributions in the photon number.(20,21) Although we were motivated by the success of the *P*-representation, we must emphasize that this Poisson representation is quite different from it.

In the case of a single-variable system, we may solve for the steady state of the generalized Fokker–Planck equation by direct integration as for any Fokker–Planck equation. It is now possible to obtain from the quasiprobability an asymptotic expansion of moments in inverse powers of the system volume. The lowest order terms are the same as those obtained by making any of the more conventional approximations mentioned above. For multivariate systems, or time-dependent systems, the solution of the Fokker–Planck equation is no longer readily accessible in general, and it is best to go over to the stochastic differential equation method by means of the well-known equivalence between Fokker–Planck equations (diffusion processes) and Langevin equations, or more precisely, stochastic differential equations.(22,24) This equivalence is rigorous and the stochastic differential equation that thus arises is a mathematically well-defined object, which can be solved iteratively to an arbitrary accuracy, to give an expansion in inverse powers of the system volume, which is applicable in multivariable and time-dependent situations. In the case of systems with spatial diffusion, the system must be divided up into cells of volume ΔV and the expansion will be in inverse powers of this volume.

Our paper is divided rather naturally into three parts. In Sections 2, 3, and 6, we introduce our Poisson representation, and apply it to systems whose steady state is thermodynamic equilibrium. We show that, by always using the grand canonical ensemble and ideal gas or solution theory, steady states in thermodynamic equilibrium may always be chosen to be Poissonian. To emphasize this fact, we derive this Poisson result purely from statistical mechanical considerations. In a Poisson representation, such distributions are very simply treated.

Sections 4 and 5 are technical in nature. Section 4 reviews the formalism of stochastic differential equations, and Section 5 extends these techniques heuristically to define higher order noise, which is necessary for higher order Fokker–Planck equations. This appears to be a new theory, applicable only to quasiprobabilities, since in general higher order noise generates negative probabilities.

Sections 7 and 8 treat various systems whose steady state is not thermodynamic equilibrium, omitting spatial dependence in Section 7, and including it in Section 8.

Our conclusions are given in Section 9, and the appendices contain various technical points.

This is the first of two papers, the second of which will treat two-time correlation functions.

2. THE POISSON DISTRIBUTION AND ITS RELATION TO STATISTICAL MECHANICAL SYSTEMS DESCRIBED BY CHEMICAL MASTER EQUATIONS

2.1. The Grand Canonical and Canonical Ensembles in Thermodynamic Equilibrium

Although we shall base most of this paper on the use of chemical master equations, it is necessary to establish firmly that under conditions of ideal reacting gas or solution theory, and using only the techniques of statistical mechanics, distribution functions may be chosen as Poissonian. If we consider a system composed of chemically reacting components A, B, C,..., the distribution function in the grand canonical ensemble is given by

$$P(I) = \exp\left\{\beta\left[\Omega + \sum_a \mu_a n_a(I) - E(I)\right]\right\} \tag{1}$$

where I is an index describing the microscopic state of the system, $n_a(I)$ is the number of molecules of A in the state I, $E(I)$ is the energy of the state, μ_a is the chemical potential of component A, Ω is a normalization factor, and

$$\beta = 1/kT \tag{2}$$

The fact that the components can react requires certain relations between the chemical potentials to be satisfied, since a state I can be transformed into a state J only if

$$\sum_a \nu_a{}^A n_a(I) = \sum_a \nu_a{}^A n_a(J), \qquad A = 1, 2, 3, \ldots \tag{3}$$

where the $\nu_a{}^A$ are certain integers. The relations (3) are the stoichiometric constraints.

The canonical ensemble for a reacting system is defined by requiring

$$\sum_a \nu_a{}^A n_a(I) = \tau^A \tag{4}$$

whereas the grand canonical ensemble is defined by requiring

$$\sum_I P(I) \sum_a \nu_a{}^A n_a(I) \equiv \sum_a \nu_a{}^A \langle n_a \rangle = \tau^A \tag{5}$$

Maximization of entropy subject to the constraint (5) (and the usual constraints of fixed total probability and mean energy) gives the grand canonical form (1), in which the chemical potentials also satisfy the relation

$$\mu_a = \sum_A \kappa_A \nu_a{}^A \tag{6}$$

When one takes the ideal solution or ideal gas limit, in which interaction energies (but not kinetic or internal energies) are neglected, there is no difference between the distribution function for an ideal reacting system and an ideal nonreacting system, apart from the requirement that the chemical potentials be expressible in the form (6).

The canonical ensemble is not so simple, since the constraints (3) must appear explicitly as a factor of the form

$$\prod_A \delta\left(\sum_a \nu_a{}^A n_a(I),\ \tau^A\right) \tag{7}$$

and the distribution function is qualitatively different for every kind of reacting system (including a nonreacting system as a special case).

The distribution in total numbers n_a of molecules of reacting components in the grand canonical ensemble of an ideal reacting system is easily evaluated; namely

$$P(\{n_a\}) = \exp\left\{\beta\left[\Omega + \sum_a \mu_a n_a\right]\right\} \sum_I \prod_a \delta(n_a(I), n_a) \exp[-\beta E(I)] \tag{8}$$

The sum over states is the same as that for the canonical ensemble of an ideal nonreacting mixture, so that

$$P(\{n_a\}) = \exp\left\{\beta\left[\Omega + \sum_a \mu_a n_a\right]\right\} \prod_a \frac{1}{n_a!}\left\{\sum_k \exp\left[-\beta E_k(a)\right]\right\}^{n_a} \tag{9}$$

where $E_k(a)$ are the energy eigenstates of a single molecule of the substance A. This result is a multivariate Poisson with mean numbers given by

$$\log[\langle n_a\rangle] = \beta\mu_a - \log\left(\sum_k e^{-\beta E_k(a)}\right) \tag{10}$$

which, as is well known, when combined with the requirement (6) gives the law of mass action.

The canonical ensemble is obtained by maximizing entropy subject to the stronger constraint (4), which implies the weak constraint (5). Thus, the distribution function in total numbers for the canonical ensemble will simply be given by

$$P(\{n_a\}) \propto \left[\prod_a \frac{1}{n_a!}\left(\sum_k e^{-\beta E_k(a)}\right)^{n_a}\right] \prod_A \delta\left(\sum_a \nu_a{}^A n_a,\ \tau^A\right) \tag{11}$$

2.2. Appropriateness of the Grand Canonical Ensemble and Poisson Distributions

It is usual to state that it is quite unimportant for physical purposes which ensemble is used, and we agree with this. However, what is unfortunately also true is that many stochastic master equations describe quite unphysical quantities, and in these cases, there may be very large differences between the two ensembles. This is no fault of the master equations—rather, it is a fault of the investigator in choosing to study unmeasurable quantities. Consider, for example, the system

$$\mathrm{X} \underset{k_1}{\overset{k_2}{\leftrightharpoons}} \mathrm{Y} \tag{12}$$

in which we use the symbols X and Y to denote the numbers of molecules of X and Y in the system, which consists of a macroscopic vessel, e.g., a test tube. Then the grand canonical ensemble gives for variances and correlations

$$\sigma_X{}^2 = \langle X \rangle, \qquad \sigma_Y{}^2 = \langle Y \rangle, \qquad \sigma_{XY} = 0 \tag{13}$$

while the canonical ensemble gives

$$\sigma_X{}^2 = \sigma_Y{}^2 = \sigma_{XY} = \langle X \rangle \langle Y \rangle / (\langle X \rangle + \langle Y \rangle) \tag{14}$$

From the point of view of fluctuations, there is a world of difference between the two ensembles. In practice, as is well known, it is quite impossible to measure these quantities for a macroscopic system, and the choice of which ensemble to use is purely a matter of taste, as both results are equally irrelevant to physics.

What are of interest, though, are locally fluctuating quantities. In such a case one divides the system into cells labeled i and introduces local numbers X_i and Y_i. Since transport can occur between cells, all stoichiometric relations will include summation over all cells, i.e., (4) becomes

$$\sum_a \nu_a{}^A \sum_i n_{a,i} = \tau^A \tag{15}$$

and one obtains for the grand canonical distribution

$$P(\{n_{a,i}\}) = \exp\left\{\beta\left[\Omega + \sum_{a,i} \mu_a n_{a\cdot i}\right]\right\} \prod_{a,i} \frac{1}{n_{a,i}!} \left\{\sum_k \exp[-\beta E_k(a)]\right\}^{n_{a,i}} \tag{16}$$

and for the canonical distribution

$$P(\{n_{a\cdot i}\}) \propto \prod_A \delta\left(\sum_{a,i} \nu_a{}^A n_{a,i}, \tau^A\right) \left\{\prod_{a,i} \frac{1}{n_{a,i}!} \left(\sum_k e^{-\beta E_k(a)}\right)^{n_{a,i}}\right\} \tag{17}$$

In Appendix A we show that for all *local calculations*, these distributions are equivalent—the canonical distribution gives locally Poissonian uncorrelated results in the large-volume limit, as indeed ought to be the case. The grand canonical result for the thermodynamic equilibrium is so much simpler to use that we shall use it almost exclusively in the rest of this paper.

3. THE POISSON REPRESENTATION

3.1. Generalized Fokker–Planck Equations

A natural procedure which arises from the multi-Poissonian nature of ideal system distributions in the grand canonical ensemble is to expand all distributions as linear combinations of the Poissonian result. In this section we shall illustrate the method of the Poisson representation through a few examples of chemical reactions whose steady state is thermodynamic equilibrium. We shall show that both canonical and grand canonical ensembles can be treated, but the method is clearly adapted to the grand canonical ensemble.

3.1.1. A Linear Reaction. Consider a two-component linear reaction(3,4)

$$X \underset{k_2}{\overset{k_1}{\rightleftharpoons}} Y \tag{18}$$

described by the master equation

$$\begin{aligned} dP(X, Y, t)/dt = {} & k_1[(X+1)P(X+1, Y-1, t) - XP(X, Y, t)] \\ & + k_2[(Y+1)P(X-1, Y+1, t) - YP(X, Y, t)] \end{aligned} \tag{19}$$

We expand $P(X, Y, t)$ in Poisson distributions thus

$$P(X, Y, t) = C \int d\alpha_X \, d\alpha_Y \, e^{-\alpha_X} \frac{\alpha_X{}^X}{X!} e^{-\alpha_Y} \frac{\alpha_Y{}^Y}{Y!} f(\alpha_X, \alpha_Y, t) \tag{20}$$

where C is the normalization factor. (The region of integration is as yet unspecified.) A major advantage of the Poisson representation is the relation between factorial moments of X and Y and the moments of α_X and α_Y, i.e.,

$$\begin{aligned} & \sum_{X,Y} X(X-1) \cdots (X-r+1) Y(Y-1) \cdots (Y-s+1) P(X, Y, t) \\ & \qquad = C \int d\alpha_X \, d\alpha_Y \, \alpha_X{}^r \alpha_Y{}^s f(\alpha_X, \alpha_Y, t) \end{aligned} \tag{21}$$

This simple relation is valid only for equal time correlation functions; we treat two-time correlation functions in a separate paper.

Furthermore, the representation (20) always exists, at least in the sense of a generalized function, since

$$\delta_{X,X'} = \int d\alpha \, e^{-\alpha} \frac{\alpha^X}{X!} [\delta^{X'}(-\alpha) e^{\alpha}] \tag{22}$$

and any distribution in X can be realized as linear combinations of $\delta_{X,X'}$ for different X'.

Then if $f(\alpha_X, \alpha_Y, t)$ (henceforth referred to as the quasiprobability distribution) vanishes at the boundary of the region of integration, substitution of (19) in (18) and integration by parts yields the Fokker–Planck equation

$$\frac{\partial f(\alpha_X, \alpha_Y, t)}{\partial t} = \left(-\frac{\partial}{\partial \alpha_X} + \frac{\partial}{\partial \alpha_Y}\right)[(k_1\alpha_X - k_2\alpha_Y)f(\alpha_X, \alpha_Y, t)] \tag{23}$$

Note that the diffusion coefficient in the above Fokker–Planck equation is zero. This is a characteristic feature of linear reactions, which indicates that all the noise arises from Poissonian fluctuations.

The region of integration in (20) is obtained by solving (23) and finding the region in the (α_X, α_Y) plane on the boundary of which $f(\alpha_X, \alpha_Y)$ vanishes.

A general steady-state solution of (23) that satisfies the boundary condition that f vanishes at the limits of the region of integration is

$$f(\alpha_X, \alpha_Y) = \delta(k_1\alpha_X - k_2\alpha_Y)\phi(\alpha_X, \alpha_Y) \tag{24}$$

where $\phi(\alpha_X, \alpha_Y)$ is any arbitrary function of α_X and α_Y.[3] If ϕ is chosen to be $\delta(\alpha_X - \bar{X})$, the corresponding steady-state distribution $P(X, Y)$ is

$$P(X, Y) = C\int d\alpha_X\, d\alpha_Y\, e^{-\alpha_X}\frac{\alpha_X{}^X}{X!}\, e^{-\alpha_Y}\frac{\alpha_Y{}^Y}{Y!}\,\delta(k_1\alpha_X - k_2\alpha_Y)\,\delta(\alpha_X - \bar{X}) \tag{25}$$

The region of integration in (25) is any region in the (α_X, α_Y) plane that contains the point where the arguments of the two delta functions vanish.

From (25) we get

$$P(X, Y) = [\exp(-\bar{X} - \bar{Y})]\frac{(\bar{X})^X}{X!}\frac{(\bar{Y})^Y}{Y!} \tag{26}$$

a Poisson distribution in X and Y, $\bar{X}$ and $\bar{Y}$ being related by the deterministic equation

$$k_1\bar{X} - k_2\bar{Y} = 0 \tag{27}$$

If, however, we set

$$\phi(\alpha_X, \alpha_Y) = (-1)^N\,\delta^N(\alpha_Y)e^{\alpha_X + \alpha_Y} \tag{28}$$

where $\delta^N(\alpha_Y)$ is the Nth derivative of $\delta(\alpha_Y)$ with respect to α_Y, then we obtain

$$P(X, Y) = C'\frac{1}{X!}\frac{1}{Y!}(\bar{X})^X(\bar{Y})^Y\,\delta(X + Y - N) \tag{29}$$

with

$$k_1\bar{X} = k_2\bar{Y} = [k_1k_2/(k_1 + k_2)]N \tag{30}$$

a binomial distribution, corresponding to the canonical ensemble.

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[3] There is also the possibility $f(\alpha_X, \alpha_Y) = g(\alpha_X + \alpha_Y)/(k_1\alpha_X - k_2\alpha_Y)$, which is actually equivalent as a generalized function to (24), provided integrations are chosen in the complex plane. With the choice of integration region along the real axis, the form (24) is unique.

3.1.2. A General Reaction. Let us consider a reaction of the form

$$lW + mX \underset{k_2}{\overset{k_1}{\rightleftharpoons}} pY + qZ \tag{31}$$

described by the master equation

$$\begin{aligned}\frac{dP(W,X,Y,Z,t)}{dt} &= k_1\left[\frac{(W+l)!}{W!}\frac{(X+m)!}{X!}P(W+l, X+m, Y-P, Z-q, t)\right.\\ &\quad \left. - \frac{W!}{(W-l)!}\frac{X!}{(X-m)!}P(W,X,Y,Z,t)\right]\\ &\quad + k_2\left[\frac{(Y+p)!}{p!}\frac{(Z+q)!}{q!}P(W-l, X-m, Y+p, Z+q, t)\right.\\ &\quad \left. - \frac{Y!}{(Y-p)!}\frac{Z!}{(Z-q)!}P(W,X,Y,Z,t)\right]\end{aligned} \tag{32}$$

We thus define by the choice of master equation (32) "combinatorial kinetics," in which the probability per unit time of a given reaction is given by the number of ways of assembling the relevant initial states, multiplied by a certain rate constant, which gives a generalized Fokker–Planck equation,

$$\begin{aligned}&\frac{\partial f(\alpha_W, \alpha_X, \alpha_Y, \alpha_Z, t)}{\partial t}\\ &= \left[\left(-\frac{\partial}{\partial\alpha_W}+1\right)^l\left(-\frac{\partial}{\partial\alpha_X}+1\right)^m - \left(-\frac{\partial}{\partial\alpha_Y}+1\right)^p\left(-\frac{\partial}{\partial\alpha_Z}+1\right)^q\right]\\ &\quad\times [(k_2\alpha_Y{}^p\alpha_Z{}^q - k_1\alpha_W{}^l\alpha_X{}^m)f(\alpha_W, \alpha_X, \alpha_Y, \alpha_Z, t)]\end{aligned} \tag{33}$$

the steady-state solution of which is of the form

$$\delta(k_1\alpha_W{}^l\alpha_X{}^m - k_2\alpha_Y{}^p\alpha_Z{}^q)\phi(\alpha_W, \alpha_X, \alpha_Y, \alpha_Z) \tag{34}$$

(We have again made the requirement that f vanishes on the boundaries of the range of the variables.) Different forms for $\phi(\alpha_W, \alpha_X, \alpha_Y, \alpha_Z)$ give different distributions for $P(W, X, Y, Z)$. By choosing

$$\phi(\alpha_W, \alpha_X, \alpha_Y, \alpha_Z) = \delta(\alpha_W - \hat{W})\,\delta(\alpha_X - \hat{X})\,\delta(\alpha_Y - \hat{Y})\,\theta(\alpha_Z) \tag{35}$$

where

$$\begin{aligned}\theta(\alpha_Z) &= 0, \qquad \alpha_Z < 0\\ &= 1, \qquad \alpha_Z \geqslant 0\end{aligned} \tag{36}$$

we obtain a multi-Poisson solution for $P(W, X, Y, Z)$. The alternative

$$\begin{aligned}&\delta(k_1\alpha_W{}^l\alpha_X{}^m - k_2\alpha_Y{}^p\alpha_Z{}^q)\phi(\alpha_W, \alpha_X, \alpha_Y, \alpha_Z)\\ &= e^{\alpha_W+\alpha_X+\alpha_Y+\alpha_Z}\,\delta^K(-\alpha_W)\,\delta^M(-\alpha_X)\,\delta^N(-\alpha_Y)\,\delta\left[\alpha_Z - \left(\frac{k_1\alpha_W{}^l\alpha_X{}^m}{k_2\alpha_Y{}^p}\right)^{1/q}\right]\end{aligned} \tag{37}$$

(which is not normalized) gives the solution

$$P(W, X, Y, Z) = \frac{K!\, M!\, N!}{W!\, X!\, Y!\, Z!} \delta_{K,W+Zl/q}\, \delta_{M,X+Zm/q}\, \delta_{N,Y-pZ/q} \left(\frac{k_1}{k_2}\right)^{Z/q} \tag{38}$$

By defining

$$k_1 \hat{W}^l \hat{X}^m = k_2 \hat{Y}^p \hat{Z}^q \tag{39}$$

we can rewrite this as

$$P(W, X, Y, Z) \propto \frac{\hat{W}^W \hat{X}^X \hat{Y}^Y \hat{Z}^Z}{W!\, X!\, Y!\, Z!} \delta_{K,W+Zl/q}\, \delta_{M,X+Zm/q}\, \delta_{N,Y-pZ/q} \tag{40}$$

This corresponds to a canonical distribution. The conserved quantities for the reaction (31) are

$$A = mW - lX, \qquad B = qY - pZ, \qquad C = pq(mW + lX) + ml(qY + pZ) \tag{41}$$

and the product of Kronecker deltas in (38) can be written

$$\delta_{A,mK-lM}\delta_{B,qN}\delta_{C,mlqN+pqlM+pqmK} \tag{42}$$

Thus we find that the probability distribution that arises from the form (37) for $\phi(\alpha_W, \alpha_X, \alpha_Y, \alpha_Z)$ is a multivariate Poisson, multiplied by Kronecker deltas which fix the values of the conserved quantities. Van Kampen(23) has shown that a general chemical master equation admits solutions of the form (11), of which (40) is a special case.

It is clear that not all possible distributions of the canonical form are obtained by the choice (37), in which α_Z is integrated first, but by selecting α_W, α_Y, and α_X in turn, we can get every possibility.

3.2. General Solutions

The functions ϕ in the last two reactions are arbitrary, and the most general solution corresponds to an arbitrary distribution over all values of the conserved quantities. However, these give, from the thermodynamic point of view, distributions that one does not normally consider. In order to keep close contact with thermodynamics, we have considered only canonical and grand canonical solutions.

3.3. Reactions Including Spatial Diffusion

Any realistic description of a chemical reaction system must incorporate diffusion of particles from one region to another. This may be achieved by dividing the system into n cells and viewing the process of diffusion as an exchange of one particle at a time between cells. The master equation for reaction-diffusion systems has been treated thoroughly in Refs. 3 and 4.

Using the notation of Ref. 3, we write the master equation for an arbitrary chemical reaction including diffusion of two species as

$$\begin{aligned}\frac{\partial P(\mathbf{X}, \mathbf{Y}, t)}{\partial t} = \sum_{ij} [&d_{ij}^{X}(X_i + 1)\, P(X_i + 1, X_j - 1, \hat{\mathbf{X}}, \mathbf{Y}, t) - d_{ij}^{X} X_j\, P(\mathbf{X}, \mathbf{Y}, t) \\ &+ d_{ij}^{Y}(Y_i + 1)\, P(\mathbf{X}, Y_i + 1, Y_j - 1, \hat{\mathbf{Y}}, t) - d_{ij}^{Y} Y_j\, P(\mathbf{X}, \mathbf{Y}, t)] \\ &+ \sum_i \left(\frac{\partial P}{\partial t}\right)_{i,\mathrm{Chem}} \end{aligned} \tag{43}$$

The chemical part for each cell is determined from the appropriate reaction. The corresponding Fokker–Planck equation is

$$\begin{aligned}\frac{\partial f(\boldsymbol{\alpha}_X, \boldsymbol{\alpha}_Y, t)}{\partial t} = &\sum_i \frac{\partial}{\partial \alpha_{X,i}} \left[\sum_j d_{ij}^{X}(\alpha_{X,j} - \alpha_{X,i})\, f(\boldsymbol{\alpha}_X, \boldsymbol{\alpha}_Y, t)\right] \\ &- \sum_i \frac{\partial}{\partial \alpha_{Y,i}} \left[\sum_j d_{ij}^{Y}(\alpha_{Y,j} - \alpha_{Y,i})\, f(\boldsymbol{\alpha}_X, \boldsymbol{\alpha}_Y, t)\right] + \sum_i \left(\frac{\partial f}{\partial t}\right)_{i,\mathrm{Chem}}\end{aligned} \tag{44}$$

The noise in this Fokker–Planck equation arises only from the chemical term, and is entirely independent of the spatial diffusion, which is a linear process. This considerably simplifies the treatment of such systems.

The steady-state solution of (44) for the reaction

$$l\mathrm{X} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} m\mathrm{Y} \tag{45}$$

is

$$f(\alpha_X, \boldsymbol{\alpha}_Y) = \prod_{i=1}^{n-1} \delta(\alpha_{X,i} - \alpha_{X,i+1}) \prod_{i=1}^{n} \delta(k_1 \alpha_{X,i}^{l} - k_2 \alpha_{Y,i}^{m})\, \delta(\alpha_{X,n} - \hat{X}) \tag{46}$$

and gives a multi-Poisson distribution for $P(X, Y)$. The alternative canonical form arises from

$$f(\alpha_X, \alpha_Y) = \prod_{i=1}^{n-1} \delta(\alpha_{X,i} - \alpha_{X,i+1}) \prod_{i=1}^{n} \delta(k_1 \alpha_{X,i}^{l} - k_2 \alpha_{Y,i}^{m})(-1)^N\, \delta^N(\alpha_{X,n}) \tag{47}$$

which gives

$$P(\mathbf{X}, \mathbf{Y}) = \prod_{i=1}^{n} \frac{(\hat{X})^{X_i}}{X_i!} \frac{(\hat{Y})^{Y_i}}{Y_i!}\, \delta\left[\sum_{i=1}^{n} (lX_i + mY_i) - N\right] \tag{48}$$

3.4. The Poisson Representation and Its Relation to the Generating Function Method

A well-known procedure for solving chemical master equations is the generating function method discussed extensively in Refs. 3 and 14. The generating function $G(\mathbf{s}, t)$ defined as

$$G(\mathbf{s}, t) = \sum_{\{X_i\}} s_1^{X_1} \cdots s_N^{X_N} P(\mathbf{X}, t) \tag{49}$$

enables one to convert the master equation into a partial differential equation in the variables $s_1, \ldots, s_{N,t}$.

Substituting the Poisson representation for $P(\mathbf{X}, t)$ in (49), we get

$$G(\mathbf{s}, t) = \int_C d\boldsymbol{\alpha} \left\{ \exp\left[\sum_i \alpha_i (s_i - 1) \right] \right\} f(\boldsymbol{\alpha}, t) \tag{50}$$

which corresponds to the expansion of $G(\mathbf{s}, t)$ in terms of the generating functions for the Poisson distribution.

Substituting (50) in the generating function equation and integrating by parts, one obtains the generalized Fokker–Planck equation provided that the contour C is chosen such that the boundary terms vanish. In general, there are several such contours, and to each of these there corresponds, by use of (50), a different solution of the generating function differential equation. However, only one of these solutions, and thus one of the contours, corresponds to an admissible probability distribution.

Now from (49) it follows that if $P(\mathbf{X}, t)$ and all its moments exist, then $G(\mathbf{s}, t)$ must be analytic in and on the boundary of the region $|s_i| \leqslant 1$, $i = 1, \ldots, N$, in the manifold of complex variables $s_1, \ldots, s_N$. In particular, $G(\mathbf{s}, t)$ and all its derivatives must be finite at $s_i = \pm 1$. This criterion enables one to eliminate physically inadmissible contours; we shall illustrate its use by specific examples in Appendix C.

Here we wish to emphasize that the requirement that $G(\mathbf{s}, t)$ be analytic for $|s_i| \leqslant 1$ is valid only if all the moments of $P(\mathbf{X}, t)$ exist. This is usually the case with the chemical master equations with combinatorial kinetics. However, in general, by an appropriate choice of the transition probabilities it is possible to write a master equation such that all the moments of $P(\mathbf{X}, t)$ higher than, say, the rth moment diverge, in which case the criterion stated above would not be valid.

An example is given in Appendix C.

4. STOCHASTIC DIFFERENTIAL EQUATION METHODS

The Fokker–Planck equations derived above are not easily solved directly, except in the case of the steady-state solutions, and even in this case, no easy method of solution exists in multivariable situations, in particular, when the molecules diffuse in space.

A Fokker–Planck equation that involves no higher than second-order derivatives is, under certain conditions, equivalent to a stochastic differential equation, and from such stochastic differential equations iterative methods of solution can be developed.

There are two formalisms available, that of Itô and that of Stratonovich. The two methods yield different stochastic differential equations (SDEs) corresponding to the same Fokker–Planck equation and have different integration rules, so that the solutions of the different stochastic differential equation forms are the same.[4] We choose the formalism developed in Ref. 22, where Itô rules are used. (SDEs are developed in a physical context in Refs. 24 and 25, where Stratonovich rules are used.) We choose the Itô form in this work because of its greater simplicity and elegance as well as the fact that in iterative procedures, it guarantees the vanishing of a large number of terms.

The rule for associating a stochastic differential equation with a Fokker–Planck equation is as follows: for the multivariate system in which the variables are the vector $\mathbf{y} = \{y_i\}$,

$$\frac{\partial P}{\partial t} = \sum_i \frac{\partial}{\partial y_i}\left\{-v_i(\mathbf{y})P + \frac{1}{2}\sum_j \frac{\partial}{\partial y_j}[b_{ij}(\mathbf{y})P]\right\} \tag{51}$$

the corresponding (Itô) stochastic differential equation is

$$dy_i = v_i(\mathbf{y})\,dt + \sum_j g_{ij}(\mathbf{y})\,dW_j(t) \tag{52}$$

where

$$b_{ij} = \sum_k g_{ik}g_{jk} \tag{53}$$

The $dW_j(t)$ are the increments of a Gaussian stochastic process, and satisfy the following:

(i) $dW_j(t) = W_j(t+dt) - W_j(t)$ (54)

(ii) $\langle dW_j(t)\rangle = 0$ (55)

(iii) $dW_i(t)\,dW_j(t) = \langle dW_i(t)\,dW_j(t)\rangle = \delta_{ij}\,dt$ (56)

---

[4] The physical problem of which formalism corresponds to the physical process of adding a noise source to a nonstochastic differential equation is not one which we wish to discuss here, except to say that the Stratonovich procedure is generally the most realistic. This is well discussed in Refs. 22 and 26. This difficulty does not arise here, since we know our Fokker–Planck equation, and may make our own choice of correspondence with complete mathematical and physical equivalence.

(iv) The distribution of $dW_j(t)$ is *Gaussian*, and, from (iii) and (ii), has mean zero and variance dt.

(v) $dW_j(t)$ is statistically independent of $W_i(t) - W_i(0)$, where

$$W_i(t) - W_i(0) = \int_{t_0}^{t} dW_i(t) \tag{57}$$

In particular,

$$\langle [dW_j(t)][W_i(t) - W_i(t_0)] \rangle = 0 \tag{58}$$

for $t \geqslant t_0$, but the postulate of statistical independence means that the joint probability distribution of the $\mathbf{W}(t_n)$ for a set of increasing times t_n satisfies

$$\begin{aligned} &P[\mathbf{W}(t_1), \mathbf{W}(t_2), \mathbf{W}(t_3), \ldots, \mathbf{W}(t_n)] \\ &\quad = P[\mathbf{W}(t_1)]P[\mathbf{W}(t_2) - \mathbf{W}(t_1)]P[\mathbf{W}(t_3) - \mathbf{W}(t_2)] \cdots P[\mathbf{W}(t_n) - \mathbf{W}(t_{N-1})] \end{aligned} \tag{59}$$

It is this aspect of *independent increments*—the increment being statistically independent of all $W(t')$ for $t' < t$—that characterizes the Itô method and yields simple formulas.

The connection with the physicists' way of writing a stochastic differential equation is obtained by setting

$$\xi_i(t)\,dt = dW_i(t) \tag{60}$$

From (22), (23), and (25) we obtain

$$\langle \xi_i(t)\xi_j(t') \rangle = \delta_{ij}\,\delta(t - t') \tag{61}$$

If we now check (25), we find that

$$\langle [dW_i(t)][W_i(t) - W_i(t_0)] \rangle = \int_{t_0}^{t} dt'\,\delta(t - t') \tag{62}$$

The Itô prescription requires us to set (62) equal to zero, that is, we give zero weight to a delta-function singularity that occurs at the upper limit of a time integral. Thus, Itô rules say

$$\int_{t_0}^{t} dt'\,\delta(t - t') = 0, \qquad \int_{t_0}^{t} dt'\,\delta(t_0 - t') = 1 \tag{63}$$

The Stratonovich rules make the choice

$$dW_j(t) = \tfrac{1}{2}[W_j(t + dt) - W_j(t - dt)] \tag{64}$$

and thus both integrals (63) become equal to $\frac{1}{2}$. The statistical independence of $dW_j(t)$ and $W_i(t) - W_i(0)$ is thus abandoned.

We make this point here because in the evaluation of results in an iterative procedure, integrals with delta-function singularities at the upper limit occur frequently. It will be apparent that the Itô choice, which makes these all vanish, will yield a much simpler procedure.

5. STOCHASTIC DIFFERENTIAL EQUATION METHODS FOR HIGHER ORDER FOKKER–PLANCK EQUATIONS

The relationship between Fokker–Planck equations and the above stochastic differential equations is valid only for the case when the Fokker–Planck equation is of no more than second order. Our techniques can yield Fokker–Planck equations that are of higher but always finite order, and it is appropriate to devise stochastic differential equation methods for Fokker–Planck equations of higher order. We have found no evidence that this has ever been done before. This is not really surprising, since it appears likely that higher order Fokker–Planck equations give probabilities whose positivity cannot be guaranteed. Since we deal with quasiprobabilities, this is not a problem, and we have been able to generalize the methods of Section 4 to arbitrary orders of the Fokker–Planck equation. We now show how this can be done for a third-order Fokker–Planck equation.

Introduce the stochastic variable $V(t)$ whose probability distribution $P(V, t)$ obeys the third-order partial differential equation

$$\partial P(V, t)/\partial t = -\tfrac{1}{6}\, \partial^3 P(V, t)/\partial V^3 \tag{65}$$

We then know that the solution of (65), subject to the boundary condition

$$P(V, t_0) = \delta(V - V_0) \tag{66}$$

is given, by Fourier transform methods, as the conditional probability,

$$P(V, t\,|\,V_0, t_0) = (1/2\pi) \int_{-\infty}^{\infty} dq \exp\{i[q(V - V_0) + \tfrac{1}{6}q^3(t - t_0)]\} \tag{67}$$

The moments of V can be calculated, after a partial integration, to be

$$\begin{aligned} \langle [V(t) - V_0]^n \rangle &= 0,\ n \text{ not a multiple of } 3 \\ \langle [V(t) - V_0]^{3m} \rangle &= (\tfrac{1}{6})^m (3m!/m!)(t - t_0)^m \end{aligned} \tag{68}$$

Further, since the process (65) is a generalized Markov process, the joint probability distribution that V has the value V_1 at time t_1 *and* the value V_2 at the later time t_2 is given by

$$P(V_2 t_2 : V_1 t_1) = P(V_2 t_2 | V_1 t_1) P(V_1, t_1) \tag{69}$$

and from (67) we see that the first factor is a function of only $V_2 - V_1$ and $t_2 - t_1$, so that the variable $V(t_2) - V(t_1)$ is statistically independent of $V(t_1)$, so that this process is a *process with independent increments*: thus $dV(t)$ will be independent of $V(t)$.

The rigorous definition of stochastic integration with respect to $V(t)$ is a task that we shall not attempt at this stage. We can show, however, that a stochastic differential equation of the form

$$dy(t) = a(y)\,dt + b(y)\,dW(t) + c(y)\,dV(t) \tag{70}$$

[with $W(t)$ and $V(t)$ independent processes] is equivalent to a third-order Fokker–Planck equation. It is clear that because $W(t)$ and $V(t)$ are Markov processes, $y(t)$ is a Markov process. We then calculate

$$\lim_{t\to t_0} \frac{\langle [y(t) - y(t_0)]^n \rangle}{t - t_0} = \lim_{dt_0 \to 0} \frac{\langle [dy(t_0)]^n \rangle}{dt_0} \tag{71}$$

where $y(t_0)$ is a numerical initial value, not a stochastic variable. From (70), it is clear that $y(t)$ depends on $W(t')$ and $V(t')$ for only $t' \leqslant t$ and, since $dW(t)$ and $dV(t)$ are independent of $y(t)$, we find

$$\begin{aligned}\langle dy(t_0)\rangle &= \langle a[y(t_0)]\rangle\,dt_0 + \langle b[y(t_0)]\rangle\langle dW(t_0)\rangle + \langle c[y(t_0)]\rangle\langle dV(t_0)\rangle \\ &= \langle a[y(t_0)]\rangle\,dt_0 = a[y(t_0)]\,dt_0 \end{aligned}\tag{72}$$

because $y(t_0)$ is a numerical initial value. Similarly,

$$\begin{aligned}\langle dy(t_0)^2\rangle &= a[y(t_0)]^2\,dt_0{}^2 + b[y(t_0)]^2\langle dW(t_0)^2\rangle \\ &= a[y(t_0)]^2\,dt_0{}^2 + b[y(t_0)]^2\,dt_0 \end{aligned}\tag{73}$$

$$\begin{aligned}\langle dy(t_0)^3\rangle &= a[y(t_0)]^3\,dt_0{}^3 + c[y(t_0)]^3\langle dV(t_0)^3\rangle \\ &= a[y(t_0)]^3\,dt_0{}^3 + c[y(t_0)]^3\,dt_0 \end{aligned}\tag{74}$$

Thus we find

$$\begin{aligned}\lim_{t\to t_0}[\langle y(t) - y(t_0)\rangle/(t - t_0)] &= a[y(t_0)] \\ \lim_{t\to t_0}[\langle [y(t) - y(t_0)]^2\rangle/(t - t_0)] &= b[y(t_0)]^2 \\ \lim_{t\to t_0}[\langle [y(t) - y(t_0)]^3\rangle/(t - t_0)] &= c[y(t_0)]^3 \end{aligned}\tag{75}$$

and all higher powers give a zero result. This is sufficient(22,24,25) to show that $y(t)$ is a generalized diffusion process, whose generalized Fokker–Planck equation is

$$\frac{\partial P(y, t)}{\partial t} = -\frac{\partial}{\partial y}\left(a(y)P - \frac{\partial}{\partial t}\left\{\frac{1}{2}\,b(y)^2P + \frac{\partial}{\partial y}\left[\frac{1}{6}\,c(y)^3P\right]\right\}\right) \tag{76}$$

We define a noise source $\xi(t)$ by

$$dV(t) = \zeta(t)\,dt \tag{77}$$

where

$$\langle \zeta(t)\rangle = \langle \zeta(t)\zeta(t')\rangle = 0 \tag{78}$$

$$\langle \zeta(t)\zeta(t')\zeta(t'')\rangle = \delta(t - t')\,\delta(t' - t'') \tag{79}$$

and higher moments can be readily calculated from the moments of $dV(t)$. The independence of increments means that, as in the previous case, integrals that have a delta-function singularity at their upper limit are to be taken as zero.

6. APPLICATION OF STOCHASTIC DIFFERENTIAL EQUATION METHODS TO SIMPLE REACTIONS

6.1. Introduction

A simple reaction is one with only one basic pathway, like

$$\mathrm{X} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{Y} \tag{80a}$$

$$\mathrm{X} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 2\mathrm{Y} \tag{80b}$$

for which the Fokker–Planck equations have been previously derived. The stochastic differential equations corresponding to these are

$$d\alpha_X/dt = -k_1\alpha_X + k_2\alpha_Y, \qquad d\alpha_Y/dt = k_1\alpha_X - k_2\alpha_Y \tag{81a}$$

and

$$\begin{aligned} d\alpha_X/dt &= -k_1\alpha_X + k_2{\alpha_Y}^2 \\ d\alpha_Y/dt &= 2(k_1\alpha_X - k_2{\alpha_Y}^2) + [2(k_1\alpha_X - k_2{\alpha_Y}^2)]^{1/2}\xi(t) \end{aligned} \tag{81b}$$

In the linear reactions, such as (80a), one finds that there is in fact no noise term, as in (81a), and the equations are ordinary nonstochastic differential equations. Thus, if the initial conditions are fixed numerical values, the solutions to (81a) are deterministic numerical values, which are the mean value parameters of bivariate Poissons. Thus the linear system possesses time-dependent Poisson distribution solutions, whose mean values satisfy the deterministic equations. In contrast, (81b) does have a noise term, and thus the solutions are in general stochastic quantities, indicating that the probability distribution is non-Poissonian. However, at the steady state, when $k_1\alpha_X = k_2{\alpha_Y}^2$, the noise term vanishes, so there are steady states characterized by

$${\alpha_Y}^{\pm} = \pm(k_1\alpha_X/k_2)^{1/2} \tag{82}$$

Notice that both the positive and the negative roots have meaning, a general probability distribution being

$$P(X,Y) = \exp(-\alpha_X)\frac{{\alpha_X}^X}{X!}\left[\lambda\frac{\exp(-{\alpha_Y}^+)}{Y!}({\alpha_Y}^+)^Y + (1-\lambda)\frac{\exp(-{\alpha_Y}^-)}{Y!}({\alpha_Y}^-)^Y\right] \tag{83}$$

which is positive under certain conditions on λ, namely

$$\frac{1}{1+\exp(-2\alpha_Y{}^+)} \leqslant \lambda \leqslant \frac{1}{1-\exp(-2\alpha_Y{}^+)}$$

The lower and upper extreme values give probability distributions allowing, respectively, only odd and even values of Y.

The existence of the noise term shows that a time-dependent Poisson is not a solution for this system, even if the values of α_X and α_Y are fixed initially (i.e., a Poissonian initial condition), the time evolution will cause a spreading of the probability distribution, which eventually, however, in the steady state becomes Poissonian.

Notice also that the coefficient of $\xi(t)$ is not a real number if $k_2\alpha_Y{}^2 > k_1\alpha_X$ and the noise is thus purely imaginary in this region. From a mathematical point of view, this is equivalent to the fact that the solution to the Cauchy problem for a diffusion equation with negative diffusion coefficient requires integration along the imaginary axis, i.e., the Markovian property

$$P(y'', t''|y, t) = \int dy'\, P(y,'' t''|y', t')P(y', t'|y, t) \tag{84}$$

for a P satisfying

$$\partial P(y, t)/\partial t = \tfrac{1}{2}\,\partial^2 P(y, t)/\partial y^2 \tag{85}$$

holds as long as the integral is taken along some *imaginary* axis. This complication causes no difficulty in any practical solution of these equations. All moments are real, and the basic effect is to reduce the variance below the Poissonian value.

6.2. Inclusion of Spatial Diffusion

The diffusion master equations introduced in Section 3 give rise to stochastic differential equations for (80b)

$$\begin{aligned} d\alpha_{X,i}/dt &= \sum_j D_{ij}\alpha_{X,j} - k_1\alpha_{X,i} + k_2\alpha_{Y,i}^2 \\ d\alpha_{Y,i}/dt &= \sum_j D_{ij}\alpha_{Y,j} + 2k_1\alpha_{X,i} - 2k_2\alpha_{Y,i}^2 + [2(k_1\alpha_{X,i} - k_2\alpha_{Y,i}^2)]^{1/2}\xi_i(t) \end{aligned} \tag{86}$$

where we have defined

$$D_{ij} = d_{ij} - \left(\sum_k d_{ik}\right)\delta_{ij} \tag{87}$$

and the $\xi_i(t)$ are independent stochastic sources. Thus, the diffusion, being linear, *does not contribute* to the noise terms and this is a general result. This is to be strongly contrasted with conventional chemical Langevin equations, where there is a noise contribution from chemical and diffusion terms.

The steady-state solution is given by

$$k_1\alpha_{X,i} = k_1\alpha^2_{Y,i} \tag{88}$$

with $\alpha_{X,i}$ and $\alpha_{Y,i}$ spatially constant. As before, the noise term vanishes and the steady state is thus Poissonian.

6.3. Conditions Under Which a Poissonian Steady State Is Achieved

In any *reversible* reaction with only one pathway we will always find that the noise term and the drift terms vanish simultaneously; thus a Poissonian steady state results. Further, in any linear system there is no noise term, so Poissonian steady states again result. If we have a pair of reactions, say

$$\mathrm{X} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 2\mathrm{Z}, \qquad \mathrm{Z} \underset{k_4}{\overset{k_3}{\rightleftharpoons}} 2\mathrm{Y} \tag{89}$$

the stochastic differential equations are

$$\begin{aligned} d\alpha_X/dt &= k_2{\alpha_Z}^2 - k_1\alpha_X \\ d\alpha_Z/dt &= 2(k_1\alpha_X - k_2{\alpha_Z}^2) + (k_4{\alpha_Y}^2 - k_3\alpha_Z) + [2(k_1\alpha_X - k_2{\alpha_Z}^2)]^{1/2}\xi_Z(t) \\ d\alpha_Y/dt &= 2(k_3\alpha_Z - k_4{\alpha_Y}^2) + [2(k_3\alpha_Z - k_4{\alpha_Y}^2)]^{1/2}\xi_Y(t) \end{aligned} \tag{90}$$

and in this case we find the solution in the steady state is given by

$$k_1\alpha_X = k_2{\alpha_Z}^2, \qquad k_3\alpha_Z = k_4{\alpha_Y}^2 \tag{91}$$

and again both noise terms vanish. The result is a reflection of the fact that the steady state of the reactions satisfies detailed balance, so that each drift term and hence each noise term separately vanishes at equilibrium.

This is not to be confused with the conditions often called detailed balance for a master equation in which transitions between all pairs of states cancel in the steady state. By detailed balance here we mean that such transitions for every distinct reaction will cancel. Thus, for example, the reaction

$$\mathrm{A} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{X}, \qquad 2\mathrm{X} \underset{k_4}{\overset{k_3}{\rightleftharpoons}} \mathrm{B}$$

with A and B held fixed, will give a steady-state solution in which the transitions between states cancel in the steady state, but this steady state only satisfies detailed balance when transitions from each pathway separately balance, and the steady state is then thermodynamic equilibrium.

Thus any system obeying combinatorial kinetics whose steady state satisfies detailed balance has a Poissonian steady state. In particular, we recover the Poissonian nature of the grand canonical thermodynamic equilibrium distribution function.

However, there are situations that do not have detailed balance in the steady state, and yet have a Poissonian steady state, for example, the steady state of

$$\mathrm{A} \underset{k_2}{\overset{k_1}{\leftrightharpoons}} n\mathrm{X} \underset{k_4}{\overset{k_3}{\leftrightharpoons}} \mathrm{B}$$

(with A and B held fixed) is always Poissonian, though a net flow from A to B may exist.

7. APPLICATIONS TO NONLINEAR EQUILIBRIUM SYSTEMS (NO DIFFUSION)

In this section we shall apply the techniques developed previously to derived generalized Fokker–Planck equations and the corresponding stochastic differential equations for some interesting examples of nonequilibrium chemical reactions.

All of these reactions have been investigated quite thoroughly by various authors, whose works are noted. Our aim here is basically to illustrate our techniques and show how they apply to well-understood systems.

7.1. Single-Variable Chemical Reactions Involving at Most Bimolecular Steps: The Second-Order Phase Transition

Consider the chemical process(3,19,27,28)

$$\mathrm{A} + \mathrm{X} \underset{k_4}{\overset{k_2}{\rightleftharpoons}} 2\mathrm{X}, \qquad \mathrm{B} + \mathrm{X} \underset{k_3}{\overset{k_1}{\rightleftharpoons}} \mathrm{C} \tag{92}$$

described by the master equation

$$\begin{aligned} dP(X, t)/dt = {} & k_1B(X + 1)P(X + 1, t) + k_3CP(X - 1, t) \\ & + k_2A(X - 1)P(X - 1, t) + k_4(X + 1)XP(X + 1, t) \\ & - [k_1BX + k_3C + k_2AX + k_4X(X - 1)]P(X, t) \end{aligned} \tag{93}$$

On expanding $P(X, t)$ in Poisson distributions, one obtains the Fokker–Planck equation for the quasiprobability

$$\frac{\partial f(\alpha, t)}{\partial t} = -\frac{\partial}{\partial \alpha}\left\{[\kappa_3 V + (\kappa_2 - \kappa_1)\alpha - \kappa_4 V^{-1}\alpha^2] f(\alpha, t) \right.$$
$$\left. + \frac{1}{2}\frac{\partial}{\partial \alpha}[2(\kappa_2 \alpha - \kappa_4 V^{-1}\alpha^2) f(\alpha, t)]\right\} \tag{94}$$

where we have defined

$$k_3 C = \kappa_3 V, \qquad k_2 A = \kappa_2, \qquad k_1 B = \kappa_1, \qquad k_4 = \kappa_4 V^{-1}$$

and thereby exhibited the volume dependence of the various parameters involved.

For $\kappa_4 = 0$, (94) may be solved exactly. The solution is given in Appendix C.

For $\kappa_4 \neq 0$ (we shall set it equal to 1) the exact solution of (94) in terms of known functions is not possible.

In order to obtain a complete asymptotic expansion for the various moments, it is most convenient to deal with the stochastic differential equation equivalent to the Fokker–Planck equation, which for (94) is, after defining $\alpha = \eta V$,

$$d\eta/dt = \kappa_3 + (\kappa_2 - \kappa_1)\eta - \eta^2 + \epsilon[2(\kappa_2 \eta - \eta^2)]^{1/2}\xi(t) \tag{95}$$

where $\epsilon = V^{-1/2}$.

Equation (95) suggests an obvious procedure for its iterative solution. Expanding η in powers of ϵ,

$$\eta = \eta_0 + \epsilon\eta_1 + \epsilon^2\eta_2 + \cdots \tag{96}$$

and equating like powers of ϵ on both sides of (96), we get

$$\frac{d\eta_0}{dt} = \kappa_3 + (\kappa_2 - \kappa_1)\eta_0 - \eta_0^2 \tag{97a}$$

$$\frac{d\eta_1}{dt} = (\kappa_2 - \kappa_1 - 2\eta_0)\eta_1 + [2(\kappa_2\eta_0 - \eta_0^2)]^{1/2}\xi(t) \tag{97b}$$

$$\frac{d\eta_2}{dt} = (\kappa_2 - \kappa_1 - 2\eta_0)\eta_2 - \eta_1^2 + \frac{(\kappa_2 - 2\eta_0)\eta_1}{[2(\kappa_2\eta_0 - \eta_0^2)]^{1/2}}\xi(t) \tag{97c}$$

$$\frac{d\eta_3}{dt} = (\kappa_2 - \kappa_1 - 2\eta_0)\eta_3 - 2\eta_1\eta_2 + \frac{(\kappa_2 - 2\eta_0)\eta_2}{[2(\kappa_2\eta_0 - \eta_0^2)]^{1/2}}\xi(t)$$
$$- \frac{\kappa_2^2\eta_1^2}{2[2(\kappa_2\eta_0 - \eta_0^2)]^{3/2}}\xi(t) \tag{97d}$$

For $\kappa_3 = 0$ and $\kappa_2 > \kappa_1$, $\eta_0 = \kappa_2 - \kappa_1$ is a solution of (97a). Substituting this in (97b) and solving the resulting equations, we get

$$\eta_1(t) = (2\kappa_1\eta_0)^{1/2}\int_0^t dt'\,\{\exp[-\eta_0(t-t')]\}\xi(t') \tag{98a}$$

$$\eta_2(t) = -\int_0^t dt'\,\{\exp[-\eta_0(t-t')]\}\eta_1^2(t') + \frac{2\kappa_1-\kappa_2}{(2\kappa_1\eta_0)^{1/2}}\int_0^t dt'\,\{\exp[-\eta_0(t-t')]\}\eta_1(t')\xi(t') \tag{98b}$$

$$\eta_3(t) = -2\int_0^t dt'\,\{\exp[-\eta_0(t-t')]\}\eta_1(t')\eta_2(t') + \frac{2\kappa_1-\kappa_2}{(2\kappa_1\eta_0)^{1/2}}\int_0^t dt'\,\{\exp[-\eta_0(t-t')]\}\eta_2(t')\xi(t') - \frac{\kappa_2^{\,2}}{2(2\kappa_1\eta_0)^{3/2}}\int_0^t dt'\,\{\exp[-\eta_0(t-t')]\}\eta_1^2(t')\xi(t') \tag{98c}$$

The mean and variance are related to η_i by the following equations:

$$\langle X\rangle = \langle\alpha\rangle = V\eta_0 + \langle\eta_2\rangle + \cdots$$
$$\langle X^2\rangle - \langle X\rangle^2 = V[\eta_0 + \langle\eta_1^2\rangle] + [2\langle\eta_1\eta_3\rangle + \langle\eta_2^2\rangle - \langle\eta_2^2\rangle + \langle\eta_2\rangle] + \cdots \tag{99}$$

where we have used the fact that $\langle\eta_1\rangle = \langle\eta_1\eta_2\rangle = \langle\eta_3\rangle = 0$, as they involve odd factors of $\xi(t)$. The various averages that appear on the rhs may be calculated using (98a)–(98c).

To illustrate the use of Itô rules in the context of our iterative procedure, we shall calculate $\langle\eta_2\rangle$, which contributes to the terms of $O(1)$ in the expansion for $\langle X(t)\rangle$. Now

$$\langle\eta_2(t)\rangle = -\int_0^t dt'\,\{\exp[-\eta_0(t-t')]\}\langle\eta_1^2(t')\rangle + \frac{2\kappa_1-\kappa_2}{(2\kappa_1\eta_0)^{1/2}}\int_0^t dt'\,\{\exp[-\eta_0(t-t')]\}\langle\eta_1(t')\xi(t')\rangle \tag{100}$$

Now if we calculate $\langle\eta_1(t')\xi(t')\rangle$, we get

$$\langle\eta_1(t')\xi(t')\rangle = (2\kappa_1\eta_0)^{1/2}\int_0^{t'} dt''\,\{\exp[-\eta_0(t'-t'')]\}\,\delta(t'-t'') \tag{101}$$

which, therefore, as was noted in Section 4, must be set equal to zero, since the argument of the delta function vanishes at the upper limit of the integration. Hence

$$\langle\eta_2(t)\rangle = -\int_0^t dt' \{\exp[-\eta_0(t-t')]\}\langle\eta_1^2(t')\rangle \tag{102}$$

Now

$$\langle\eta_1^2(t)\rangle = 2\kappa_1\eta_0 \tag{103}$$

which gives

$$\langle\eta_2(t)\rangle = -(\kappa_1/\eta_0)(1-e^{-2\eta_0 t}) \tag{104}$$

Similarly, keeping in mind the rule that

$$\int_0^t dt' \, g(t,t')\,\delta(t-t') = 0$$

we can calculate all the terms on the rhs of (99). Taking the limit $t \to \infty$, we obtain the expressions for the mean and the variance in the steady state as

$$\begin{aligned} \langle X\rangle &= V(\kappa_2-\kappa_1) - [\kappa_1/(\kappa_2-\kappa_1)] \\ \langle X^2\rangle - \langle X\rangle^2 &= V\kappa_2 + [\kappa_1\kappa_2/(\kappa_2-\kappa_1)^2] \end{aligned} \tag{105}$$

As a check on the above results, we shall calculate the mean and the variance directly from the steady-state solution of the Fokker–Planck equation (94).

The steady-state solution of the Fokker–Planck equation (94) is obtained by setting equal to zero the terms inside the curly bracket. This can be demonstrated generally in one-variable systems as follows: Suppose

$$\frac{\partial f(\alpha,t)}{\partial t} = -\frac{\partial}{\partial\alpha}\left\{a(\alpha)f(\alpha,t) + \frac{\partial}{\partial\alpha}[b(\alpha)f(\alpha,t)]\right\} \tag{106}$$

and suppose the range of the variable is $[c,d]$. Our boundary conditions required to derive the equation require that $f(\alpha)$ and its derivatives vanish at c and d. Hence, in the steady state, integrating from c to α,

$$0 = \left[a(\alpha)f(\alpha) + \frac{\partial}{\partial\alpha}[b(\alpha)f(\alpha)]\right]_{\alpha=c} - \left[a(\alpha)f(\alpha) + \frac{\partial}{\partial\alpha}[b(\alpha)f(\alpha)]\right] \tag{107}$$

and the first term vanishes, from the boundary condition.

Thus the steady-state solution of (94) becomes

$$f(\alpha) = e^{\alpha}(\kappa_2 V - \alpha)^{V(\kappa_1-\kappa_3/\kappa_2)-1}\alpha^{(\kappa_3 V/\kappa_2 - 1)} \tag{108}$$

and the range of α integration is $(0, \kappa_2)$.

There are other possible choices of the integration contour that satisfy the condition necessary for the equivalence of (93) and (94), but do not lead to an admissible probability distribution. We shall discuss this together with related matters in Appendix C.

Remember from Section 3 that the factorial moments of $P(X, t)$ are equal to the moments of $f(\alpha, t)$. We find, defining $\alpha = \eta V$,

$$\begin{aligned}\langle X^r\rangle_f = V^r\Bigg[\int_0^{\kappa_2} d\eta\,\Bigg(\exp\Bigg\{V\Bigg[\eta + \left(\kappa_1 - \frac{\kappa_3}{\kappa_2}\right)\ln(\kappa_2 - \eta)\\ + \frac{\kappa_3}{\kappa_2}\ln\eta\Bigg]\Bigg\}\Bigg)(\kappa_2 - \eta)^{-1}\eta^{r-1}\Bigg]\\ \times\Bigg[\int_0^{\kappa_2} d\eta\,\Bigg(\exp\Bigg\{V\Bigg[\eta + \left(\kappa_1 - \frac{\kappa_3}{\kappa_2}\right)\ln(\kappa_2 - \eta)\\ + \frac{\kappa_3}{\kappa_2}\ln\eta\Bigg]\Bigg\}\Bigg)(\kappa_2 - \eta)^{-1}\eta^{-1}\Bigg]^{-1} \qquad (109)\end{aligned}$$

By noting that the integrals in (109) are integral representations of the confluent hypergeometric function, we can derive the exact result of McNeil and Walls.(28) From (109) one may obtain a complete asymptotic expansion for the moments in the inverse powers of V using methods outlined in Ref. 29. We have calculated the first two terms in the asymptotic expansion of the mean and the variance in the limit $\kappa_3 \to 0$. The results are identical to those given in (105).

In (105) terms of $O(V)$ are exactly the same as given by cumulant methods or by making the following approximation:

$$\langle X^3\rangle_f = 3[\langle X^2\rangle_f - \langle X\rangle^2]\langle X\rangle + \langle X\rangle^3 \qquad (110)$$

in order to close the hierarchy of the moment equations derived from the master equation. In our formulation these approximations correspond precisely to approximating $f(\alpha)$ by a Gaussian.

7.2. A Reaction That Gives $f(\alpha)$ with Negative Variance

Another interesting example is provided by the following reaction mechanism(6,30,31)

$$\mathrm{B} \xrightarrow{k_1} \mathrm{X}, \qquad 2\mathrm{X} \xrightarrow{k_2} \mathrm{A} \qquad (111)$$

The master equation for this process is

$$\begin{aligned}dP(X, t)/dt &= k_1 B[P(X-1, t) - P(X, t)]\\ &\quad + k_2[(X+2)(X+1)P(X+2, t) - X(X-1)P(X, t)] \qquad (112)\end{aligned}$$

and the corresponding Fokker–Planck equation is

$$\frac{\partial f(\alpha, t)}{\partial t} = -\frac{\partial}{\partial\alpha}\left\{(\kappa_1 V - 2\kappa_2 V^{-1}\alpha^2)f(\alpha, t) + \frac{\partial}{\partial\alpha}[(\kappa_2 V^{-1}\alpha^2)f(\alpha, t)]\right\} \qquad (113)$$

where $\kappa_1 V = k_1 B$, $\kappa_2 V^{-1} = k_2$. Note that the diffusion coefficient in the above Fokker–Planck equation is negative.

The steady-state solution of (113) is

$$f(\alpha) = \alpha^{-2} \exp(2\alpha + aV^2/\alpha) \tag{114}$$

with $a = 2\kappa_1/\kappa_2$ and the α integration is to be performed along a closed contour encircling the origin. In this case, since the contour of integration is closed, the argument that led to (108) is not applicable. However, the most general steady-state solution turns out here not to be single-valued—(114) is the unique single-valued steady-state solution. Here again there is another possible choice of the α contour, but it does not lead to an admissible probability distribution, as we show in Appendix C.

Thus, by putting $\alpha = \eta V$, we get

$$\langle X^r \rangle_f = \frac{V^r \oint d\eta \, e^{V(2\eta + a/\eta)} \eta^{r-2}}{\oint d\eta \, e^{V(2\eta + a/\eta)} \eta^{-2}} \tag{115}$$

Unlike the previous example, the function $(2\eta + a/\eta)$ does not have a maximum at the deterministic steady state. In fact, it has a minimum at the deterministic steady state $\eta = +(a/2)^{1/2}$. However, in the complex η plane this point is a saddle point and provides the dominant contribution to the integral.

Thus, the negative diffusion coefficient in (113) reflects itself by giving rise to a saddle point at the deterministic steady state, which results in the variance in X being less than $\langle X \rangle$.

From (115) all the steady states moments can be calculated exactly. The results are

$$\langle X^r \rangle_f = \left[V \left(\frac{a}{2} \right)^{1/2} \right]^r \frac{I_r[2(2a)^{1/2} V]}{I_1[2(2a)^{1/2} V]} \tag{116}$$

where $I_r[2(2a)^{1/2} V]$ are the modified Bessel functions.

Using the large-argument expansion for $I_r[2(2a)^{1/2} V]$, we get

$$\begin{aligned} \langle X \rangle &= V(a/2)^{1/2} + \tfrac{1}{8} + O(1/V) \\ \langle X^2 \rangle - \langle X \rangle^2 &= \tfrac{3}{4} V(a/2)^{1/2} - \tfrac{1}{16} + O(1/V) \end{aligned} \tag{117}$$

which agrees with the results of Refs. 6, 30, and 31.

The stochastic differential equation corresponding to (113) is

$$d\eta/dt = \kappa_1 - 2\kappa_2 \eta^2 + i\epsilon(2\kappa_2)^{1/2} \eta(t) \xi(t) \tag{118}$$

where as before $\alpha = \eta V$.

Proceeding exactly as before, we have calculated the first two terms in the asymptotic expansion for the mean and the variance, which in the steady state are identical to those given by (118).

7.3. A Single-Variable Chemical Reaction Involving a Trimolecular Step(27,32,33)

Consider the chemical process

$$\mathrm{A} + 2\mathrm{X} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 3\mathrm{X}, \qquad \mathrm{A} \underset{k_4}{\overset{k_3}{\rightleftharpoons}} \mathrm{X} \tag{119}$$

The master equation for (119) is

$$\begin{aligned} dP(X,t)/dt = {} & k_1A(X-1)(X-2)P(X-1,t) + k_2(X+1)X(X-1)P(X+1,t) \\ & + k_3AP(X-1,t) + k_4(X+1)P(X+1,t) \\ & - [k_1AX(X-1) + k_2X(X-1)(X-2) + k_3A + k_4X]P(X,t) \end{aligned} \tag{120}$$

and the corresponding Fokker–Planck equation is

$$\begin{aligned} \frac{\partial f(\alpha,t)}{\partial t} = {} & -\frac{\partial}{\partial\alpha}[(\kappa_1V^{-1}\alpha^2 - \kappa_2V^{-2}\alpha^3 + \kappa_3V - \kappa_4\alpha)f(\alpha,t)] \\ & +\frac{1}{2}\frac{\partial^2}{\partial\alpha^2}[4(\kappa_1V^{-1}\alpha^2 - \kappa_2V^{-2}\alpha^3)f(\alpha,t)] \\ & -\frac{1}{3!}\frac{\partial^3}{\partial\alpha^3}[6(\kappa_1V^{-1}\alpha^2 - \kappa_2V^{-2}\alpha^3)f(\alpha,t)] \end{aligned} \tag{121}$$

where $\kappa_1V^{-1} = k_1A$, $\kappa_2V^{-2} = k_2$, $\kappa_3V = k_3$, $\kappa_4 = k_4$.

In the steady state (121) reduces to a linear second-order differential equation, which may be solved in terms of hypergeometric functions, and an asymptotic expansion for the various moments can be obtained using methods outlined previously. This procedure, although possible in principle, is not very practicable. It is in such cases that the method of stochastic differential equations proves to be very useful in its ease of application.

Following Section 5, the stochastic differential equation equivalent to (121) is

$$\begin{aligned} d\eta(t)/dt = {} & \kappa_1\eta(t)^2 - \kappa_2\eta(t)^3 + \kappa_3 - \kappa_4\eta(t) \\ & + \mu^3\{4[\kappa_1\eta(t)^2 - \kappa_2\eta(t)^3]\}^{1/2}\xi(t) \\ & + \mu^4\{6[\kappa_1\eta(t)^2 - \kappa_2\eta(t)^3]\}^{1/3}\zeta(t) \end{aligned} \tag{122}$$

where $\alpha = \eta V$, $\mu = V^{-1/6}$, and the noise source $\zeta(t)$, henceforth referred to as the "third-order noise," has been defined in Section 5.

Equation (122) may be solved iteratively by expanding $\eta(t)$,

$$\eta(t) = \eta_0(t) + \mu^3\eta_3(t) + \mu^4\eta_4(t) + \mu^6\eta_6(t) + \mu^8\eta_8(t) + \mu^9\eta_9(t) + \cdots \tag{123}$$

which, when substituted in (122), yields the deterministic equation in the lowest order and linear stochastic differential equations in the higher orders, which may be solved as before.

In the steady state the results are

$$
\begin{aligned}
\langle X\rangle &= V\eta_0 + \langle\eta_6\rangle = V\eta_0 + \frac{2ab}{c^2} \\
\langle X^2\rangle - \langle X\rangle^2 &= V\langle{\eta_3}^2\rangle + [2\langle\eta_9\eta_3\rangle + 2\langle\eta_8\eta_4\rangle + \langle{\eta_6}^2\rangle - \langle\eta_6\rangle^2 + \langle\eta_6\rangle] + \cdots \\
&= V\left(\frac{2a}{c}\right) + \left(\frac{28}{3}\,\frac{a^2b^2}{c^4} + \frac{8ab^2\eta_0}{c^3} - \frac{36\kappa_2 a^2}{c^3} + \frac{8ab}{c^2}\right) + \cdots \\
\langle(X - \langle X\rangle)^3\rangle &= V[\langle{\eta_4}^3\rangle - 3\langle{\eta_3}^2\rangle\langle\eta_6\rangle + 3\langle{\eta_3}^2\rangle + \eta_0] \\
&= V\left(\frac{8a}{c} - \frac{12a^2b}{c^3} + \eta_0\right) \qquad (124)
\end{aligned}
$$

where $a = \kappa_1{\eta_0}^2 - \kappa_2{\eta_0}^3$, $b = 2\kappa_1 - 3\kappa_2\eta_0$, $c = \kappa_4 - 2\kappa_1\eta_0 + 3\kappa_2{\eta_0}^2$, and η_0 is the solution of the steady-state deterministic equation

$$\kappa_1{\eta_0}^2 - \kappa_2{\eta_0}^3 + \kappa_3 - \kappa_4\eta_0 = 0 \qquad (125)$$

Here a few remarks are in order. The "third-order noise" $\zeta(t)$ contributes to $O(V^{-1})$ to the mean, to $O(1)$ to the variance, but contributes to $O(V)$ to the skewness coefficient. To $O(V)$ the results for the mean and the variance are identical to those given by the cumulant method and in fact if one is only interested in calculating the mean and the variance to $O(V)$, the third-order noise may be dropped from (122) and the expansion carried out in the powers of ϵ. Also note that as $c \to 0$ the variance and the higher order corrections become divergent. This, of course, is due to the fact that in this limit, the reaction system exhibits a first-order phase-transition type behavior, as has been discussed in Refs. 27, 32, and 33.

A further point to note is that our simple iterative method expands about a Poisson whose mean is the deterministic mean. In the case, as arises here, that multiple steady states are possible, it gives an asymptotic expansion for the moments of one or another of the possible stable solutions, but tells nothing about relative stability. The unstable solution, however, gives an iterative solution, which, as expected, diverges.

8. NONLINEAR CHEMICAL REACTIONS WITH DIFFUSION[3,4]

The Fokker–Planck equation for a multicell system with diffusion and the chemical reaction (92) is

$$
\begin{aligned}
\frac{\partial f(\boldsymbol{\alpha}, t)}{\partial t} = -\sum_i \frac{\partial}{\partial\alpha_i}\bigg[\bigg(\sum_j D_{ij}\alpha_j + \Delta V\,\kappa_3 + (\kappa_2 - \kappa_1)\alpha_i - (\Delta V)^{-1}{\alpha_i}^2\bigg) f(\boldsymbol{\alpha}, t)\bigg] \\
+\frac{1}{2}\sum_i \frac{\partial^2}{\partial{\alpha_i}^2}\{2[\kappa_2\alpha_i - (\Delta V)^{-1}{\alpha_i}^2] f(\boldsymbol{\alpha}, t)\} \qquad (126)
\end{aligned}
$$

Here ΔV represents the volume of the cell. Defining $\eta_i = \alpha_i/\Delta V$, the stochastic differential equation equivalent to (126) is

$$\frac{d\eta_i}{dt} = \sum_j D_{ij}\eta_j + \kappa_3 + (\kappa_2 - \kappa_1)\eta_i - \eta_i^2 + \frac{1}{(\Delta V)^{1/2}}[2(\kappa_2\eta_i - \eta_i^2)]^{1/2}\xi_i(t) \tag{127}$$

The mean and the correlation function in X_i variables are related to the moments of η_i variables through the following equations:

$$\begin{aligned}\langle X_i(t)\rangle &= \Delta V\langle\eta_i(t)\rangle \\ \langle X_iX_j\rangle - \langle X_i\rangle\langle X_j\rangle &= (\Delta V)^2\left[\langle\eta_i\eta_j\rangle - \langle\eta_i\rangle\langle\eta_j\rangle + \langle\eta_i\rangle\frac{\delta_{ij}}{\Delta V}\right]\end{aligned} \tag{128}$$

In the continuum limit, i.e., $\Delta V \to 0$, (127) and (128) become

$$\begin{aligned}d\eta(\mathbf{r}, t)/dt = {} & (\mathscr{D}\eta)(\mathbf{r}, t) + \kappa_3 + (\kappa_2 - \kappa_1)\eta(\mathbf{r}, t) - \eta^2(\mathbf{r}, t) \\ & + \{2[\kappa_2\eta(\mathbf{r}, t) - \eta^2(\mathbf{r}, t)]\}^{1/2}\xi(\mathbf{r}, t)\end{aligned} \tag{129}$$

and

$$\begin{aligned}&\langle\rho(\mathbf{r}, t)\rangle = \langle\eta(\mathbf{r}, t)\rangle \\ &\langle\rho(\mathbf{r}, t)\rho(\mathbf{r}', t)\rangle - \langle\rho(\mathbf{r}, t)\rangle\langle\rho(\mathbf{r}', t)\rangle \\ &\quad = \langle\eta(\mathbf{r}, t)\eta(\mathbf{r}', t)\rangle - \langle\eta(\mathbf{r}, t)\rangle\langle\eta(\mathbf{r}', t)\rangle + \langle\eta(\mathbf{r}, t)\rangle\,\delta(\mathbf{r} - \mathbf{r}')\end{aligned} \tag{130}$$

where $\mathscr{D}$ is the continuum limit of the matrix D_{ij} defined previously and

$$(\mathscr{D}\eta)(\mathbf{r}, t) = -\int \mathscr{D}(|\mathbf{r} - \mathbf{r}'|)\eta(\mathbf{r}', t)\,d\mathbf{r}'$$

and

$$\rho(\mathbf{r}, t) = X_i(t)/\Delta V, \qquad \xi(\mathbf{r}, t) = \xi_i(t)/(\Delta V)^{1/2} \tag{131}$$

Here $\rho(\mathbf{r}, t)$ corresponds to the concentration variable.

This adoption of a continuum form is a mathematical device, and will require a cutoff in our Fourier transform variable. The factor $1/(\Delta V)^{1/2}$ becomes absorbed into the noise source, and we are left without any obvious expansion parameter. We formally introduce a parameter λ in (129) as

$$\begin{aligned}d\eta(\mathbf{r}, t)/dt = {} & (\mathscr{D}\eta)(\mathbf{r}, t) + \kappa_3 + (\kappa_2 - \kappa_1)\eta(\mathbf{r}, t) - \eta^2(\mathbf{r}, t) \\ & + \lambda\{2[\kappa_2\eta(\mathbf{r}, t) - \eta^2(\mathbf{r}, t)]\}^{1/2}\xi(\mathbf{r}, t)\end{aligned} \tag{132}$$

and expand $\eta(\mathbf{X}, t)$ in powers of λ as

$$\eta(\mathbf{r}, t) = \eta_0(\mathbf{r}, t) + \lambda\eta_1(\mathbf{r}, t) + \lambda^2\eta_2(\mathbf{r}, t) + \cdots \tag{133}$$

and set λ equal to one at the end of the calculation. However, if it is understood that all Fourier variable integrals have a cutoff $(\Delta V)^{-1/3}$, this will still be in fact a $(\Delta V)^{-1}$ expansion.

Substituting (133) in (129), we get

$$\frac{d\eta_0(\mathbf{r}, t)}{dt} = (\mathscr{D}\eta_0)(\mathbf{r}, t) + \kappa_3 + (\kappa_2 - \kappa_1)\eta_0(\mathbf{r}, t) - \eta_0^2(\mathbf{r}, t) \tag{134a}$$

$$\frac{d\eta_1(\mathbf{r}, t)}{dt} = (\mathscr{D}\eta_1)(\mathbf{r}, t) + [\kappa_2 - \kappa_1 - 2\eta_0(\mathbf{r}, t)]\eta_1(\mathbf{r}, t) + \{2[\kappa_2\eta_0(\mathbf{r}, t) - \eta_0{}^2(\mathbf{r}, t)]\}^{1/2}\xi(\mathbf{r}, t) \tag{134b}$$

$$\frac{d\eta_2(\mathbf{r}, t)}{dt} = (\mathscr{D}\eta_2)(\mathbf{r}, t) + [\kappa_2 - \kappa_1 - 2\eta_0(\mathbf{r}, t)]\eta_2(\mathbf{r}, t) - \eta_1{}^2(\mathbf{r}, t) + \frac{[\kappa_2 - 2\eta_0(\mathbf{r}, t)]\eta_1(\mathbf{r}, t)\xi(\mathbf{r}, t)}{\{2[\kappa_2\eta_0(\mathbf{r}, t) - \eta_0{}^2(\mathbf{r}, t)]\}^{1/2}} \tag{134c}$$

$$\begin{aligned}\frac{d\eta_3(\mathbf{r}, t)}{dt} = {}& (\mathscr{D}\eta_3)(\mathbf{r}, t) + [\kappa_2 - \kappa_1 - 2\eta_0(\mathbf{r}, t)]\eta_3(\mathbf{r}, t) - 2\eta_1(\mathbf{r}, t)\eta_2(\mathbf{r}, t) \\ & + \frac{[\kappa_2 - 2\eta_0(\mathbf{r}, t)]\eta_2(\mathbf{r}, t)\xi(\mathbf{r}, t)}{\{2[\kappa_2\eta_0(\mathbf{r}, t) - \eta_0{}^2(\mathbf{r}, t)]\}^{1/2}} \\ & - \frac{\kappa_2{}^2\eta_1{}^2(\mathbf{r}, t)\xi(\mathbf{r}, t)}{2\{2[\kappa_2\eta_0(\mathbf{r}, t) - \eta_0{}^2(\mathbf{r}, t)]\}^{3/2}}\end{aligned} \tag{134d}$$

For $\kappa_3 = 0$, $\kappa_2 - \kappa_1 > 0$, (134a) has a homogeneous steady-state solution

$$\eta_0(\mathbf{r}, t) = \eta_0 = \kappa_2 - \kappa_1 \tag{135}$$

Substituting this in (134b)–(134d) and taking the Fourier transforms, we get

$$\tilde{\eta}_1(\mathbf{q}, t) = (2\kappa_1\eta_0)^{1/2}\int_0^t dt'\,(\exp\{-[\tilde{\mathscr{D}}(q^2) + \eta_0](t - t')\})\tilde{\xi}(\mathbf{q}, t') \tag{136a}$$

$$\begin{aligned}\tilde{\eta}_2(\mathbf{q}, t) = {}& -\int d^3q_1 \int_0^t dt' \\ & \times (\exp\{-[\tilde{\mathscr{D}}(q^2) + \eta_0](t - t')\})\tilde{\eta}_1(\mathbf{q} - \mathbf{q}_1, t')\tilde{\eta}_1(\mathbf{q}_1, t') \\ & + \frac{2\kappa_1 - \kappa_2}{(2\kappa_1\eta_0)^{1/2}}\int d^3q_1 \int_0^t dt' \\ & \times (\exp\{-[\tilde{\mathscr{D}}(q^2) + \eta_0](t - t')\})\tilde{\eta}_1(\mathbf{q} - \mathbf{q}_1, t')\tilde{\xi}(\mathbf{q}_1, t')\end{aligned} \tag{136b}$$

$$\begin{aligned}\tilde{\eta}_3(\mathbf{q}, t) = {}& -2\int d^3q_1 \int_0^t dt' \\ & \times (\exp\{-[\tilde{\mathscr{D}}(q^2) + \eta_0](t - t')\})\tilde{\eta}_2(\mathbf{q}_1, t')\tilde{\eta}_1(\mathbf{q} - \mathbf{q}_1, t) \\ & + \frac{2\kappa_1 - \kappa_2}{(2\kappa_1\eta_0)^{1/2}}\int d^3q_1 \int_0^t dt' \\ & \times (\exp\{-[\tilde{\mathscr{D}}(q^2) + \eta_0](t - t')\})\tilde{\eta}_2(\mathbf{q}_1, t')\tilde{\xi}(\mathbf{q} - \mathbf{q}_1, t') \\ & - \frac{\kappa_2{}^2}{2(2\kappa_1\eta_0)^{3/2}}\int d^3q_1 \int d^3q_2 \int_0^t dt' \\ & \times (\exp\{-[\tilde{\mathscr{D}}(q^2) + \eta_0](t - t')\})\tilde{\eta}_1(\mathbf{q}_1, t)\tilde{\eta}_1(\mathbf{q}_2, t')\tilde{\xi}(\mathbf{q} - \mathbf{q}_1 - \mathbf{q}_2, t')\end{aligned} \tag{136c}$$

where

$$\tilde{\eta}_1(\mathbf{q}, t) = [1/(2\pi)^{3/2}] \int [\exp(-i\mathbf{q}\cdot\mathbf{r})]\eta_1(\mathbf{r}, t)\, d\mathbf{r}$$

etc., and $\tilde{\mathscr{D}}(q^2)$ is the Fourier transform of $\mathscr{D}(|\mathbf{r} - \mathbf{r}'|)$. We have left out the trivial initial value terms in (136a)–(136c).

To the lowest order, the mean concentration and the correlation function are given by

$$\langle \rho(\mathbf{r}, t)\rangle = \eta_0 \tag{137a}$$

$$\begin{aligned}\langle \rho(\mathbf{r}, t)\rho(\mathbf{r}', t)\rangle &- \langle \rho(\mathbf{r}, t)\rangle\langle \rho(\mathbf{r}', t)\rangle \\ &= \eta_0\, \delta(\mathbf{r} - \mathbf{r}') + \langle \eta_1(\mathbf{r}, t)\eta_1(\mathbf{r}', t)\rangle \end{aligned}\tag{137b}$$

Now from (137b) it follows that

$$\langle \tilde{\eta}_1(\mathbf{q}, t)\tilde{\eta}_1(\mathbf{q}', t)\rangle = \frac{\kappa_1\eta_0\delta(\mathbf{q} + \mathbf{q}')}{[\tilde{\mathscr{D}}(q^2) + \eta_0]}(1 - \exp\{-2[\tilde{\mathscr{D}}(q^2) + \eta_0]t\}) \tag{138}$$

Hence the lowest order contributions to the correlation function in the steady state are given by

$$\begin{aligned}\langle \rho(\mathbf{r})\rho(\mathbf{r}')\rangle &- \langle \rho(\mathbf{r})\rangle\langle \rho(\mathbf{r}')\rangle \\ &= \eta_0\, \delta(\mathbf{r} - \mathbf{r}') + \frac{\kappa_1\eta_0}{(2\pi)^3}\int d^3q\, \frac{\exp[i\mathbf{q}\cdot(\mathbf{r} - \mathbf{r}')]}{[\tilde{\mathscr{D}}(q^2) + \eta_0]}\end{aligned} \tag{139}$$

If we assume that

$$(\mathscr{D}\eta)(\mathbf{r}) = D\, \nabla^2\eta(\mathbf{r}) \tag{140}$$

where D is the diffusion coefficient, (139) corresponds exactly to the results given in Ref. 3.

The next order correction to the mean concentration is $\langle \eta_2(\mathbf{r}, t)\rangle$. Now from (136b)

$$\begin{aligned}\langle \tilde{\eta}_2(\mathbf{q}, t)\rangle = -\int d^3q_1 \int_0^t dt'\, (\exp\{-[\tilde{\mathscr{D}}(q^2) + \eta_0](t - t')\}) \\ \times \langle \tilde{\eta}_1(\mathbf{q} - \mathbf{q}_1, t')\tilde{\eta}_1(\mathbf{q}_1, t')\rangle\end{aligned} \tag{141}$$

In the steady state (141) gives

$$\langle \tilde{\eta}_2(\mathbf{q})\rangle = -\kappa_1\, \delta(\mathbf{q}) \int \frac{d^3q_1}{[\tilde{\mathscr{D}}(q^2) + \eta_0]} \tag{142}$$

For the choice of $\mathscr{D}$ given by (140), Eq. (142) gives

$$\langle \eta_2\rangle = -\frac{\kappa_1}{(2\pi)^{3/2}}\int \frac{d^3q_1}{[Dq^2 + \eta_0]} \tag{143}$$

which is divergent at the $q \to \infty$ limit. This of course is a consequence of the continuum notation, which should only be regarded as a mathematical artifice to simplify the solutions. There are two ways in which this problem may be rectified. One may either choose a diffusion operator with a built-in upper cutoff on q or one may simply assume that in all the $\mathbf{q}$ integrals $q \leqslant 1/l$, where l is the cell length. We shall adopt the latter alternative because of its simplicity from a calculational point of view and continue to work with the diffusion operator given by (140). In any case the large-q cutoff does not matter as far as the phase transition behavior is concerned.

We have also worked out the higher order corrections, viz.

$$2\langle\eta_1(\mathbf{r})\eta_3(\mathbf{r}')\rangle + \langle\eta_2(\mathbf{r})\eta_2(\mathbf{r}')\rangle - \langle\eta_2(\mathbf{r})\rangle\langle\eta_2(\mathbf{r}')\rangle + \langle\eta_2(\mathbf{r})\rangle\, \delta(\mathbf{r} - \mathbf{r}')$$

to the density correlation function, but we shall omit the details and only give the expressions for the variance because of their relevance to the phase transition aspects of the chemical reaction model under consideration. The results are

$$\begin{aligned}\langle X^2[V]\rangle - \langle X[V]\rangle^2 &= \int d\mathbf{r}\, d\mathbf{r}'\, [\langle\rho(\mathbf{r})\rho(\mathbf{r}')\rangle - \langle\rho(\mathbf{r})\rangle\langle\rho(\mathbf{r}')\rangle] \\ &= \kappa_2 V + V\frac{(\kappa_1{}^2 + 3\kappa_1\eta_0)}{2D^2} I_1 + \frac{2\kappa_1{}^2\eta_0 V}{2D^3} I_2 \end{aligned} \tag{144}$$

where

$$\begin{aligned} I_1 &= \int_0^{1/l} \frac{d^d q}{(q^2 + \eta_0/D)(q^2 + 3\eta_0/2D)} \\ I_2 &= \int_0^{1/l} \frac{d^d q}{(q^2 + \eta_0/D)^2(q^2 + 3\eta_0/D)} \end{aligned} \tag{145}$$

and

$$X[V] = \int_V d\mathbf{r}\, \rho(\mathbf{r})$$

and for later use we have put the number of space dimensions in (145) equal to d.

The first term in (144) is the same as that given by the Gaussian approximation. We shall now examine the behavior of I_1 and I_2 as a function of d near the phase transition point $\kappa_2 - \kappa_1 = 0$. Putting $\gamma = \eta_0/D$ and defining $q = \gamma^{1/2}x$, we get

$$\begin{aligned} I_1 &= \frac{2\pi^{d/2}}{\Gamma(d/2)}\left(\frac{\eta_0}{D}\right)^{(d-4)/2} \int_0^{1/l\sqrt{\gamma}} \frac{x^{d-1}\, dx}{(x^2 + 1)(x^2 + \frac{3}{2})} \\ I_2 &= \frac{2\pi^{d/2}}{\Gamma(d/2)}\left(\frac{\eta_0}{D}\right)^{(d-6)/2} \int_0^{1/l\sqrt{\gamma}} \frac{x^{d-1}\, dx}{(x^2 + 1)^2(x^2 + \frac{3}{2})} \end{aligned} \tag{146}$$

Thus, as $\eta_0 \to 0$,

$$
\begin{aligned}
I_1 &= \frac{2\pi^{d/2}}{\Gamma(d/2)}\left(\frac{\eta_0}{D}\right)^{(d-4)/2}\int_0^\infty \frac{x^{d-1}\,dx}{(x^2+1)(x^2+\frac{3}{2})} \\
I_2 &= \frac{2\pi^{d/2}}{\Gamma(d/2)}\left(\frac{\eta_0}{D}\right)^{(d-6)/2}\int_0^\infty \frac{x^{d-1}\,dx}{(x^2+1)^2(x^2+\frac{3}{2})}
\end{aligned}
\tag{147}
$$

Both of the x integrals are finite for $d < 4$. From (147) and (145) it follows that the correction to the variance diverges like $\eta_0^{(d-4)/2}$ for $d < 4$ and logarithmically for $d = 4$. For $d > 4$ the corrections are finite, but depend on l, the cell size, and go to zero as $l \to \infty$. Thus we conclude that:

(a) For $d > 4$ the Gaussian approximation is valid, even near the critical points, in the limit of large cell size.

(b) For $d < 4$ the Gaussian approximation breaks down in the critical region and the perturbation theory based on the decomposition of η into a "macroscopic part" and "fluctuating parts" is no longer valid, no matter how large the cell.

This result is clearly related to that of Mori and McNeil,(34) who find that the critical dimension for this model is $d = 4$.

8.1. A Critique of the Cell Model

The modeling of diffusion as a stochastic process in which molecules jump from one cell to the next seems at first to be very natural. However, the corrections to the mean and, in particular, the second-order correction given by (142) are divergent as $l \to 0$, while this does not happen in the corrections to the variance, which approach a well-defined value as long as l is less than the correlation length $(D/\eta_0)^{1/2}$.

This is a disturbing feature of this method of attacking reaction-diffusion equations, whose solution is not clear. It is clear that the divergence has its origin in the $\eta^2(\mathbf{r})$ term, which is local, and implies that only pairs of molecules within a cell react with each other. The very size of the molecules indicates that the interaction must be in some sense nonlocal, and that some term of the form

$$\int d\mathbf{r}'\, d\mathbf{r}''\, g(\mathbf{r}, \mathbf{r}', \mathbf{r}'')\eta(\mathbf{r}')\eta(\mathbf{r}'')$$

should be used, and the Fourier transformation of $g(\mathbf{r}, \mathbf{r}', \mathbf{r}'')$ would provide a natural cutoff. In fact the cell model, before the continuum form is taken, is of this form. The evaluation of the function $g(\mathbf{r}, \mathbf{r}', \mathbf{r}'')$ is, however, a trickier task, and requires some more microscopic theory of the reaction-diffusion system.

9. CONCLUSION AND SUMMARY

In this paper, we have developed a powerful and novel technique for handling chemical master equations, by showing their equivalence to certain stochastic differential equations. We have used the techniques to reformulate and extend the theory of equilibrium and nonequilibrium reaction and reaction-diffusion systems. The major developments achieved by means of our techniques are as follows:

(i) The concept of Poissonian states as fundamental: The multivariate factorizable Poisson distribution is shown in Appendix A to be the most natural distribution to use in the case of thermodynamic equilibrium. The expansion in Poissons, as in the case of quantum optical coherent state methods, reduces linear systems to simple deterministic systems, and yields noise effects in nonlinear systems that are the result of nonlinearity only.

(ii) Systematic approximation procedures have been developed, by means of the stochastic differential equation methods, for the chemical master equations. These are useful basically as methods of checking the accuracy of the lowest order terms, though in principle they can be used to high orders if the complexity of the terms can be handled. The rather complicated form of the noise term can make this difficult. However, the stochastic differential equations are available for other methods of treatment.

(iii) Multivariable systems can be handled by these techniques in a simple and readily comprehensible way. Previous methods have found multivariable systems much more difficult than single-variable systems.

(iv) Simple Gaussian approximation methods by linearizing the stochastic differential equations are available for most situations, reserving the full treatment of nonlinearity for critical phenomena. These linearized stochastic differential equations are valid (in this degree of approximation) for the description of nonequilibrium as well as equilibrium phenomena, and, it should be emphasized, the correct noise parameters are specified (i.e., do not require extra postulates).

(v) An understanding of the range of validity of the Gaussian approximation has been reached by the ability to calculate higher corrections by means of the systematic approximation procedure. We have shown that the Gaussian approximation is almost always valid, as long as the volume of the cells is not too small, except near critical points.

(vi) The formulation of third-order and higher order noise: This theory, developed in Section 5, is in principle necessary for the solution of general higher order Fokker–Planck equations, though we have shown that it is generally of negligible effect, except possibly at critical points, as we noted in the treatment of a simple first-order phase transition model in Section 7.3. There may be work for the mathematicians in making rigorous the somewhat heuristic arguments given in Section 5, and in the generalization to stochastic processes in the complex plane.

As a final point, let us note that the Poisson method is clearly applicable to any master equation in which the transitions are between only finitely separated states and the transition probabilities per unit time are polynomials. There are many examples of such models, e.g., the Glauber Ising model master equation, and certain laser master equations.

APPENDIX A. EQUIVALENCE OF CANONICAL AND POISSONIAN DISTRIBUTIONS

The canonical distribution corresponding to the reaction

$$lX \underset{k_2}{\overset{k_1}{\rightleftharpoons}} mY$$

$$P(\mathbf{X}, \mathbf{Y}) = c \prod_{j=1}^{n} \frac{(\hat{X})^{X_j}}{X_j!} \frac{(\hat{Y})^{Y_j}}{Y_j!} \delta\Big(N - \sum_j mX_j - \sum_j lY_j\Big) \tag{A1}$$

Here η is the total number of cells. This may be written as

$$P(\mathbf{X}, \mathbf{Y}) = \frac{c}{2\pi i} \oint dz\, z^{-N-1} \prod_{j=1}^{n} \frac{(\hat{X}z^m)^{X_j}}{X_j!} \frac{(\hat{Y}z^l)^{Y_j}}{Y_j!} \tag{A2}$$

where the contour encircles the origin.

The generating function is

$$G_n(\mathbf{s}, \mathbf{t}) = \sum_{X_i Y_i} P(\mathbf{X}, \mathbf{Y}) \prod_{i=1}^{n} s_i^{X_i} t_i^{Y_i} \tag{A3}$$

$$= \frac{c}{2\pi i} \oint \frac{dz}{z} z^{-N} \exp\Big(\sum_{i=1}^{n} \hat{X}z^m s_i + \hat{Y}z^l t_i\Big) \tag{A4}$$

The generating function for the probability distribution in a finite volume v of r cells is obtained by setting $s_j = t_j = 1$ for all $j \notin v$. Thus

$$G_r(\mathbf{s}, \mathbf{t}) = \frac{c}{2\pi i} \oint \frac{dz}{z} z^{-N} \exp\{n(\hat{X}z^m + \hat{Y}z^l) + \sum_{i \in v} [\hat{X}z^m(s_i - 1) + \hat{Y}z^l(t_i - 1)]\} \tag{A5}$$

Note that since $\hat{X}$ and $\hat{Y}$ are not equal (although proportional) to $\langle X_i \rangle$ and $\langle Y_i \rangle$, one does not necessarily have

$$n(m\hat{X} + l\hat{Y}) = N \tag{A6}$$

However, because of the delta function on the rhs of (A2), we may always scale $\hat{X}$ and $\hat{Y}$ by the transformation

$$\hat{X} \to \lambda^m \hat{X}, \qquad \hat{Y} \to \lambda^l \hat{Y}$$

altering only the normalization in such a way that (A6) is satisfied.

Henceforth we shall assume that $\hat{X}$ and $\hat{Y}$ are chosen to be such that (A6) is satisfied. Now let

$$n\hat{X} = (N/m)\beta, \qquad n\hat{Y} = (N/l)(1-\beta) \tag{A7}$$

Substituting these in (29), we get

$$G_r(\mathbf{s}, \mathbf{t}) = \frac{c}{2\pi i}\oint \frac{dz}{z}\exp\left\{N\left[\frac{z^m}{m}\beta + \frac{z^l}{l}(1-\beta) - \ln z\right] + \sum_{i\in v}[\hat{X}z^m(s_i - 1) + \hat{Y}z^l(t_i - 1)]\right\} \tag{A8}$$

In the limit $N\to\infty$ the integral may be evaluated asymptotically by the saddle point method.

The saddle points are given by

$$\frac{d}{dz}\left[\frac{z^m}{m}\beta + \frac{z^l}{l}(1-\beta) - \ln z\right] = 0 \tag{A9}$$

which gives

$$z^m\beta + z^l(1-\beta) - 1 = 0 \tag{A10}$$

which has a root at $z = 1$. In all the cases we have checked, this is the dominant root, and we conjecture that it is always the dominant root. We have

$$G_r(\boldsymbol{s}, \boldsymbol{t}) \xrightarrow[n/N\ \textit{finite}]{n\to\infty,\, N\to\infty} \exp\left[\sum_{i\in v}\hat{X}(s_i - 1) + \hat{Y}(t_i - 1)\right] \tag{A11}$$

which corresponds to a multivariate factorized Poisson distribution.

Similar considerations apply to the general reaction (31).

APPENDIX B. EXACT TIME-DEPENDENT SOLUTION FOR A SIMPLE NONEQUILIBRIUM REACTION

The Fokker–Planck equation for the chemical process$^{(3)}$

$$\mathrm{A} + \mathrm{X} \longrightarrow 2\mathrm{X}, \qquad \mathrm{B} + \mathrm{X} \underset{k_3}{\overset{k_1}{\rightleftharpoons}} \mathrm{C} \tag{B1}$$

is

$$\frac{\partial f(\alpha, t)}{\partial t} = -\frac{\partial}{\partial\alpha}\{[\kappa_3 V + (\kappa_2 - \kappa_1)\alpha]f(\alpha, t)\} + \frac{\partial^2}{\partial\alpha^2}[\kappa_2\alpha f(\alpha, t)] \tag{B2}$$

Substituting

$$f(\alpha, t) = e^{-\lambda t} f(\alpha) g_\lambda(\alpha) \tag{B3}$$

in (B2), where $f(\alpha)$ is the steady-state solution of (B2) given by

$$f(\alpha) = e^{-(\kappa_1-\kappa_2)\alpha/\kappa_2}\,\alpha^{(\kappa_3 V/\kappa_2 - 1)} \tag{B4}$$

we get

$$\kappa_2 \alpha \frac{d^2 g_\lambda}{d\alpha^2} + [\kappa_3 V - (\kappa_1 - \kappa_2)] \frac{d g_\lambda}{d\alpha} + \lambda g_\lambda = 0 \tag{B5}$$

which may be solved to give

$$g_\lambda(\alpha) = M\left(-\frac{\lambda}{\kappa_1 - \kappa_2}, \frac{\kappa_3 V}{\kappa_2}, \frac{\kappa_1 - \kappa_2}{\kappa_2}\alpha\right) \tag{B6}$$

where $M(a, b, z)$ is the confluent hypergeometric function. Thus

$$\begin{aligned} f(\alpha, t) = {} & \left\{\exp(-\lambda t) \exp\left[-\left(\frac{\kappa_1 - \kappa_2}{\kappa_2}\right)\alpha\right]\right\}\alpha^{(\kappa_3 V/\kappa_2 - 1)} \\ & \times M\left(-\frac{\lambda}{\kappa_1 - \kappa_2}, \frac{\kappa_3 V}{\kappa_2}, \frac{\kappa_1 - \kappa_2}{\kappa_2}\alpha\right) \end{aligned} \tag{B7}$$

From the behavior of

$$M\left(-\frac{\lambda}{\kappa_1 - \kappa_2}, \frac{\kappa_3 V}{\kappa_2}, \frac{\kappa_1 - \kappa_2}{\kappa_2}\alpha\right)$$

as $\alpha \to \infty$ it follows that $f(\alpha, t)$ and its first derivative would go to zero as $\alpha \to \infty$ provided that

$$\lambda = m(\kappa_1 - \kappa_2) \tag{B8}$$

where m is any positive integer, in which case the confluent hypergeometric function reduces to Laguerre polynomials. Thus the desired solution of (B2) may be written as

$$f(\alpha, t) = e^{-(\kappa_1-\kappa_2)\alpha}\,\alpha^{\kappa_3 V/\kappa_2 - 1} \sum_m a_m e^{-m(\kappa_1-\kappa_2)t} L_m^{\kappa_3 V/\kappa_2 - 1}\left(\frac{\kappa_1 - \kappa_2}{\kappa_2}\alpha\right) \tag{B9}$$

where the a_m are determined by the initial condition. To obtain $P(X, t)$ corresponding to (B9), the integration has to be carried out along the contour $(0, \infty)$, for $f(\alpha, t)$ and its first derivative vanish at the end points of this contour.

The rhs of (B9) may be simplified if we choose $a_m = 1$, in which case we get

$$f(\alpha, t) = \left(\frac{\alpha}{\phi(t)}\right)^{\kappa_3 V/\kappa_2} \frac{1}{\alpha} \exp\left[-\frac{\kappa_1 - \kappa_2}{\kappa_2}\frac{\alpha}{\phi(t)}\right] \tag{B10}$$

where

$$\phi(t) = 1 - e^{-(\kappa_1 - \kappa_2)t} \tag{B11}$$

It follows from (B10) that the choice $\alpha_m = 1$ corresponds to

$$f(\alpha, 0) = \delta(\alpha) \tag{B12}$$

From (B10), $P(X, t)$ and all its moments may be calculated exactly:

$$\begin{aligned} \langle X^r(t)\rangle_f &= [\phi(t)]^r \left\{ \int_0^\infty \alpha^{(\kappa_3 V/\kappa_2) + r - 1} \exp - \frac{(\kappa_1 - \kappa_2)\alpha}{\kappa_2} \right\} \\ &\quad \times \left[\int_0^\infty \alpha^{\kappa_3 V/\kappa_2 - 1} \exp - \frac{(\kappa_1 - \kappa_2)\alpha}{\kappa_2} \right]^{-1} \\ &= [\phi(t)]^r \left(\frac{\kappa_2}{\kappa_1 - \kappa_2} \right)^r \frac{\Gamma(\kappa_3 V/\kappa_2 + r)}{\Gamma(\kappa_3 V/\kappa_2)} \end{aligned} \tag{B13}$$

corresponding to the initial condition $f(\alpha, 0) = \delta(\alpha)$, which corresponds to

$$P(X, 0) = \delta_{X,0} \tag{B14}$$

APPENDIX C. ON THE CHOICE OF α CONTOURS

The possible choices of the contour of integration for $f(\alpha)$ given by (108) are: (i) contour c_1 extending from 0 to κ_2; (ii) contour c_2 extending from κ_2 to $-\infty$; (iii) contour c_3 extending from 0 to $-\infty$.

The contour c_3 gives a solution which is a linear combination of those given by c_1 and c_2 and hence there are only two independent choices of the contour of integration.

Now for the contour c_2 the generating function corresponding to the probability distribution is

$$G(s) = c \int_{\kappa_2}^{-\infty} e^{\alpha(s-1)} e^{\alpha} (\kappa_2 V - \alpha)^{V(\kappa_1 - \kappa_3/\kappa_2) - 1} \alpha^{\kappa_3 V/\kappa_2 - 1} d\alpha \tag{C1}$$

which is infinite at $s = -1$ and it follows from the argument given in Section 3.4 that it does not lead to an admissible probability distribution. Indeed, in the steady state the generating function equation may be solved directly in terms of the hypergeometric functions and one finds that only one of the two linearly independent solutions is finite at $s = -1$.

Also note that (108) leads to a nontrivial $P(X, t)$ only if the limit $\kappa_3 \to 0$ is taken after the limit $V \to \infty$. If κ_3 is set equal to zero in (108) in the beginning, then the only permissible contour of integration is a closed contour encircling the origin, in which case all the moments of $P(X, t)$ vanish, and

$$P(X)_{ss} = \delta_{X,0} \tag{C2}$$

That this is the exact solution in the case that $\kappa_3 = 0$ is obvious, since, if all molecules of X are lost, there is no mechanism for producing a molecule of

X. However, the $\kappa_3 \to 0$ limit of the larger volume limit is well defined, and does not give the trivial solution (C2).

For $f(\alpha)$ given by (114) the two choices of the contour of integration are (i) a closed contour encircling the origin, (ii) a contour extending from 0^- to $-\infty$.

The generating function for the latter choice is

$$G(s) = \int_{0^-}^{-\infty} \exp[(s-1)\alpha] \exp\left(2\alpha + \frac{aV^2}{\alpha}\right) \frac{d\alpha}{\alpha^2} \tag{C3}$$

which, although finite at $s = -1$, has divergent second and higher order derivatives and therefore does not correspond to an admissible probability distribution.

On the basis of the argument that the difference between the probabilities of having even or odd particles is zero or finite, Mazo[31] and Malek-Mansour and Nicolis[8] have suggested the following boundary condition on the generating function equation:

$$\begin{aligned} &G(-1) = 0 && \text{(Mazo)} \\ &G(-1) = \text{finite} && \text{(Malek-Mansour and Nicolis)} \end{aligned} \tag{C4}$$

Mazo's boundary condition is satisfied by the admissible generating function for the reaction (111) but not by the one for the reaction (92) and is therefore not generally valid, whereas that of Malek-Mansour and Nicolis is satisfied in both cases. However, the inadmissible generating function for (111) is also finite at $s = -1$ and therefore Nicolis' condition is not sufficient and one also has to require the finiteness of all the derivatives of $G(s)$, $s = -1$, if one believes all the moments do exist.

As noted, it is possible to conceive of a master equation that gives divergent moments; for example, consider the system

$$\mathrm{A} + 2\mathrm{X} \to 3\mathrm{X}, \qquad \mathrm{A} + \mathrm{X} \to 2\mathrm{X}, \qquad 2\mathrm{X} \to \mathrm{C}, \qquad \mathrm{X} \to \mathrm{D} \tag{C5}$$

so that

$$\begin{aligned} dP(X,t)/dt = {} & t^+(X-1)P(X-1,t) + t^-(X+1)P(X+1,t) \\ & - [t^+(X) + t^-(X)]P(X,t) \end{aligned} \tag{C6}$$

For suitable values of the concentrations of A, C, and D and the rate constants, we can have

$$t^+(X) = kX^2, \qquad t^-(X) = kX(X+r) \tag{C7}$$

so that

$$P(X)_{ss} = P(0) \prod_{i=1}^{X} \frac{t^+(i-1)}{t^-(i)} = P(0) \frac{r!\,X!}{(X+r)!} \tag{C8}$$

for which all moments $\langle X^n \rangle$ are divergent for $n \geqslant r - 1$.

Thus analyticity of $G(s)$ inside the unit circle, or any condition on $G(s)$ on the unit circle apart from $G(1) = 1$, is impossible, and the correct choice of $G(s)$ can only be made by requiring

$$\sum_{X=0}^{\infty} P(X) = 1 \tag{C9a}$$

$$P(X) \geqslant 0, \qquad \forall x \geqslant 0 \tag{C9b}$$

$$P(X) = 0, \qquad \forall x < 0 \tag{C9c}$$

However, (C9a)–(C9c) do require $G(s)$ to be analytic *inside* the unit circle.

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REFERENCES

1. A. Nitzan, P. Ortoleva, J. Deutch, and J. Ross, *J. Chem. Phys.* **61**:1056 (1974).
2. Joel Keizer, *J. Chem. Phys.* **64**:1679 (1976); **63**:398, 5037 (1975); and preprint to be published in *J. Chem. Phys.*
3. C. W. Gardiner, K. J. McNeil, D. F. Walls, and I. S. Matheson, *J. Stat. Phys.* **14**:307 (1976).
4. N. G. van Kampen, Fluctuations in Continuous Systems, in *Topics in Statistical Mechanics and Biophysics*, R. Picirelli, ed. (American Inst. Physics, 1976).
5. N. G. van Kampen, *Can. J. Phys.* **39**:551 (1961).
6. G. Nicolis and I. Prigogine, *Proc. Nat. Acad. Sci.* (*U.S.*) **68**:2102 (1971).
7. G. Nicolis, M. Malek-Mansour, K. Kitahara, and A. van Nypelseer, *Phys. Lett.* **48A**:217 (1974).
8. M. Malek-Mansour and G. Nicolis, *J. Stat. Phys.* **13**:197 (1975).
9. H. Lemarchand and G. Nicolis, *Physica* **82A**:521 (1976).
10. P. Glansdorff and I. Prigogine, *Thermodynamic Theory of Structure, Stability and Fluctuations* (Wiley–Interscience, New York, 1971).
11. S. Grossman, *J. Chem. Phys.* **65**:2007 (1976).
12. C. W. Gardiner, *J. Stat. Phys.* **15**:451 (1976).
13. T. G. Kurtz, *J. Chem. Phys.* **57**:2976 (1972).
14. D. A. McQuarrie, *J. Appl. Prob.* **4**:413 (1967).
15. R. Kubo, *J. Phys. Soc. Japan* **12**:570 (1962); A. T. Bharucha-Reid, *Elements of the Theory of Markoff Processes and their Applications* (McGraw-Hill, New York, 1960).
16. R. Kubo, K. Matsuo, and K. Kitahara, *J. Stat. Phys.* **9**:51 (1973); K. Kitahara, Thesis, Universite Libre de Bruxelles (1974).
17. R. Görtz and D. F. Walls, Steady State Solutions of Master Equations Without Detailed Balance, to be published in *Z. Physik.*

18. N. G. van Kampen, *Adv. Chem. Phys.* **34**:245 (1976).
19. S. Chaturvedi, C. W. Gardiner, and D. F. Walls, *Phys. Lett.* **57A**:404 (1976).
20. E. C. G. Sudarshan, *Phys. Rev. Lett.* **16**:534 (1966).
21. R. J. Glauber, *Phys. Rev.* **130**:2529 (1963); **131**:2761 (1963).
22. L. Arnold, *Stochastic Differential Equations* (Wiley–Interscience, New York, 1974).
23. N. G. van Kampen, *Phys. Lett.* **59A**:333 (1976).
24. H. Haken, *Rev. Mod. Phys.* **47**:67 (1975).
25. R. Graham, *Springer Tracts in Modern Physics*, Vol. 66, No. 2.
26. Richard E. Mortensen, *J. Stat. Phys.* **1**:271 (1969).
27. F. Schlogl, *Z. Physik* **253**:147 (1972).
28. K. J. McNeil and D. F. Walls, *J. Stat. Phys.* **10**:439 (1974).
29. A. Erdelyi, in *Analytic Methods in Mathematical Physics*, R. P. Gilbert and R. G. Newton, eds. (Gordon and Breach, New York, 1968).
30. G. Nicolis, *J. Stat. Phys.* **6**:195 (1972).
31. R. M. Mazo, *J. Chem. Phys.* **62**:4244 (1975).
32. I. S. Matheson, D. F. Walls, and C. W. Gardiner, *J. Stat. Phys.* **12**:21 (1975).
33. H. K. Janssen, *Z. Physik* **270**:67 (1974).
34. H. Mori and K. J. McNeil, Kyushu University preprint (1976).