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Recurrence Relations for the Equilibrium Means of Distributions Arising in Chemical Reactions

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علاقات تعاودية لمتوسط توزيع الاحتمالات الإتزاني في حركية التفاعلات الكيميائية

الفضل خليفة الشيخ

خلاصة : نستخلص في هذه الورقة علاقات تعاودية تصف كيفية تغير متوسط عدد جزئيات المادة المتفاعلة عند الإتزان مع كل معلم من المعالم التي تحدد الحالة الإبتدائية للتفاعل وذلك لأربع تفاعلات كيميائية عكسية أساسية . توفر هذه العلاقات في جوهرها طريقة لتعديل المتوسط الإتزاني بعد إضافة أو سحب جزئي من أحد المواد المشتركة في التفاعل وهناك علاقة لكل مادة . وقد تم تعديل العلاقات باستحداث معالم جديدة للتوزيعات بحيث أصبحت توفر طرقا سهلة لحساب المتوسطات والتباينات وبعض العزوم المهمة الأخرى من غير حاجة لحساب توزيعات الاحتمال . ولتبيان الأهمية التطبيقية للعلاقات المعدلة فقد استعملت لاستحداث وتقييم مقادير تقريبية للمتوسطات والتباينات .

ABSTRACT: In this paper we derive recurrence relations that describe how the equilibrium mean of the number of molecules of a reactant varies with each of the parameters defining the initial state for four basic reversible chemical reactions. In essence, the relations provide a rationale for updating the equilibrium mean following the addition (or removal) of a molecule of one of the types involved in the reaction, there being a relation for each type. With a new parametrization introduced for each reaction, the relations provide a convenient means of evaluating the means, variances and other important moments without any need to work out the underlying distributions. As an application, the relations are used to numerically assess approximate expressions for the means and variances.

The stochastic approach to chemical reaction kinetics (cf., e.g. Darvey *et al* (1996), Staff (1967), Oppenheim *et al* (1969), Thakur *et al* (1978), and Formosinho and Miguel (1979)) treats the quantities of the reactants present at any time as random variables and offers a description of the course of the reaction concerned by finding the corresponding probability distributions. Interest is usually focussed on the equilibrium situation. However, the equilibrium distributions of the number of molecules of the reactants are difficult to handle algebraically and computationally. As an example consider the equilibrium distribution for the number of molecules of reactant A in the reaction

$$A + B \underset{K_1}{\overset{K_2}{\leftrightharpoons}} C$$

as given by below (2.7a) below, where α, β, γ are the number of molecules of reactants A, B, C present at the start of the reaction, and K is the ratio of the forward to the backward reaction rates. In the simplest practical situation the support of this distribution may well span all the integers in an interval like $[0, 10^9]$. The equilibrium means cannot be expressed solely in terms of the parameters, and computing it through the definition would entail working out the complete distribution, a massive exercise even for a single set of parameters. The approach adopted in the literature has been to seek normal and other approximations to these distributions and their moments. (See for example Dunstan and Reynolds, 1981 and Hall, 1983. This solves most of the practical situation. However, as will be shown here, the exact solution has more to offer.

In this paper, we look at the equilibrium distribution from a different angle, again referring to (2.7a) as an example. Instead of considering (2.7a) as a single distribution for a given fixed set of parameters, we look at it as a *family* of distributions indexed by the natural space of these parameters, noting that α, β, and γ are non-negative integers. It will be shown that members of this family are tied by simple recurrence relations that are also reflected in their moments. Our main emphasis will be on the means and the variances. If these are known for a given member, they can be *deduced* for other members using the recurrence relations. This should be compared to the direct approach of computing the means and variances, where, for each member(i.e. for each set of parameters), the complete distribution (2.7a) is worked out. In fact, for some members of the family the means will be trivially known, e.g., if $\beta=\gamma=0$, then the mean equals α. This, coupled with the recurrence relations given in *Theorem* 2.1, can be used to generate the mean for any member in the family.

In this paper, we shall be concerned with the four basic reversible chemical reactions $A+B \rightleftharpoons C$, $A+B \rightleftharpoons C+D$, $2A \rightleftharpoons C+D$ and $2A \rightleftharpoons C$ discussed by McQuarrie (1967) in his survey paper on the stochastic approach to chemical kinetics. For each of these reactions, we derive recurrence relations that describe how the equilibrium mean varies with each of the parameters defining the initial state when the other parameters are kept constant. As a byproduct we also obtain expressions for the variances. The relations can be interpreted, in the subject-matter context, as means of updating the equilibrium mean following the addition or removal of a molecule of one of the types involved in the reaction. This is appealing because it gives rise to the discovery of what might be considered *basic chemical laws*, assuming the validity of the stochastic model. It would be interesting if these laws can be justified, independently, by a purely chemical argument. The relations can also be used to derive approximate expressions for the means and variances as will be shown in section 7. In addition, as mentioned above, the relations provide a very effective means of computing the means and variances and this facility has been consolidated by introducing a new parametrization for each reaction. This makes it feasible, perhaps for the first time, to numerically assess the approximate expressions for the equilibrium means and variances over a large set of parameters, as will be done for the reaction $A+B \rightleftharpoons C$ in section 7. Finally, the relations can be used to control the equilibrium mean to desired levels by gauging the initial conditions. The stability of the level might also be controlled by making use of the relations obtained for the variances. This use of the relations is not dealt with here.

The ideas involved in deriving the recurrence relations for the four reactions are essentially the same. To avoid repetition we give proofs only for reaction $A+B \rightleftharpoons C$, dealt with in section 2. In sections 3, 4 and 5 we give the corresponding relations for the other three reactions. Each relation is verified using a simple example. In section 6 we derive recurrence relations involving the factorial moments. Finally, in section 7, as a demonstration of the usefulness of the recurrence relations, we introduce and numerically assess approximate expressions for the equilibrium mean and variance for reaction (2.1).

The reaction $A + B \rightleftharpoons C$

Consider the reversible reaction

$$A + B \underset{K_1}{\overset{K_2}{\rightleftharpoons}} C \,, \tag{2.1}$$

where K_1 and K_2 are the forward and backward reaction rates. Assume initially we have α , β and γ molecules of types A, B and C respectively. Let

$$K = K_1/K_2 \tag{2.2}$$

The number of molecules of types A, B, and C at time t will be denoted by $N_A(t)$, $N_B(t)$, and $N_C(t)$, respectively. The conservation equations

$$\alpha - N_A(t) = \beta - N_B(t) = N_C(t) - \gamma \tag{2.3}$$

imply that the course of the reaction can be described by one random variable. We choose N_A. The usual assumptions for modeling the reaction as a stochastic process are as follows: In any small interval of time $(t, t+h)$,

(i) the probability of a single AB association is

$$K_1 N_A(t) N_B(t) h + o(h) \,,$$

(ii) the probability of a dissociation of a molecule of C is

$$K_2 N_C(t) h + o(h) \,,$$

and

(iii) the probability of the occurrence of more than one event is $o(h)$, where

$$\lim_{h \to 0} \frac{o(h)}{h} = 0 \,.$$

Let

$$p_r(t) = P(N_A(t) = r) \tag{2.4}$$

be the probability distribution of $N_A(t)$. Using the standard procedure of representing $p_r(t+h)$ as a difference equation in $p_r(t)$, it is easy to show that $p_r(t)$ satisfies the following differential difference equation

$$\frac{dp_r(t)}{dt} = K_2(\alpha+\gamma-r+1)p_{r-1}(t) + K_1(r+1)(\beta-\alpha+r+1) p_{r+1}(t) - (K_2(\alpha+\gamma-r) + K_1 r(\beta-\alpha+r))p_r(t) \tag{2.5}$$

where r can take any integer value provided $p_r(t)$ is defined as 0 for r outside the range $\max(0, \alpha-\beta) \le r \le \alpha+\gamma$. The equilibrium solution is obtained by putting the derivative in (2.5) equal to zero and solving for $p_r = p_r(\infty)$. It can easily be verified that p_r satisfies the recurrence relation

$$K(r+1)(\beta-\alpha+r+1)p_{r+1} = (\alpha+\gamma-r)p_r \tag{2.6}$$

with solution

$$p_r = \frac{(\alpha+\gamma)!\,(\beta-\alpha)!}{K^r r!\,(\alpha+\gamma-r)!\,(\beta-\alpha+r)!}\,p_o \tag{2.7a}$$

for $\max(0, \alpha-\beta) \le r \le \alpha+\gamma$, where p_r is taken as 0 outside this range. The equilibrium solution of N_C can be obtained similarly as

$$p_r^C = \frac{K^r(\alpha+\gamma)!\,(\beta+\gamma)!}{r!\,(\alpha+\gamma-r)!\,(\beta+\gamma-r)!}\,p_o^C\,, \tag{2.7b}$$

for $0 \le r \le \min(\alpha+\gamma, \beta+\gamma)$, where p_r^C is taken as 0 outside this range.

Summing (2.6) over all r and simplifying gives

$$K\mu(\beta-\alpha+\mu) + K\sigma^2 = \alpha+\gamma-\mu\,, \tag{2.8}$$

where μ and σ^2 are the mean and variance of the equilibrium distribution of N_A. It is customary to put σ^2 equal to 0 in order to approximately express μ solely in terms of the parameters of the reaction. This is equivalent to using the deterministic value. Here, we take the approach of first deriving an expression for σ^2 and then plugging it in (2.8) to get an *exact* relation in means free of variances. As mentioned in the introduction, such a relation can have several applications.

NOTE ON NOTATION: As seen from (2.7a), the distribution p_r and its moments are functions of α, β, γ, and K. However, when considering the variation of p_r or its moments with some of these parameters, keeping the others fixed, only the arguments that are varied will be shown explicitly. Thus, for example, $\mu(\alpha)$ will be used to denote μ as a function of α for fixed β, γ, and K, whereas $\mu(\alpha, \beta)$ will be used to denote μ as a function α and β for fixed γ and K. Similarly for $\mu(\alpha,\beta,\gamma)$. This convenient notation is followed throughout starting from (2.9a) below.

Considering the dependence of p_r on γ, for fixed α, β and K, we have by replacing γ by $\gamma-1$ on both sides of (2.7a)

$$(\alpha+\gamma)p_r(\gamma-1) = (\alpha+\gamma-r)p_r(\gamma)\,\frac{p_o(\gamma-1)}{p_o(\gamma)}\,. \tag{2.9a}$$

This relation is true for all r. By construction, it is true over the support of $p_r(\gamma-1)$, namely, $\max(0,\alpha-\beta) \le r \le \alpha+\gamma-1$. It is true for $r=\alpha+\gamma$ by direct substitution and noting that this value is outside the support of $p_r(\gamma-1)$. Finally, it is trivially true for all other values of r as these are outside the supports of both $p_r(\gamma-1)$ and $p_r(\gamma)$.

In a similar way, we can also obtain the following relation from (2.7a)

$$(\alpha+\gamma)p_r^C(\alpha-1) = (\alpha+\gamma-r)p_r^C(\alpha)\,\frac{p_o^C(\alpha-1)}{p_o^C(\alpha)} \tag{2.9b}$$

It can be shown that this relation is also true for all r.

Now, summing (2.9a) over all r we get

$$\frac{p_o(\gamma-1)}{p_o(\gamma)} = \frac{\alpha+\gamma}{\alpha+\gamma-\mu(\gamma)}\,. \tag{2.10}$$

Multiplying (2.9a) by r and summing over all r leads to the expression

$$(\alpha+\gamma)\,\mu(\gamma-1) = [(\alpha+\gamma)\,\mu(\gamma) - \mu^2(\gamma) - \sigma^2(\gamma)]\,\frac{p_o(\gamma-1)}{p_o(\gamma)} \tag{2.11}$$

It follows from (2.10) and (2.11) that

$$\sigma^2(\gamma) = (\alpha+\gamma-\mu(\gamma))[\mu(\gamma)-\mu(\gamma-1)]\,. \tag{2.12}$$

It follows similarly from (2.9b) that

$$\sigma_C^2(\alpha) = (\alpha+\gamma-\mu_C(\alpha))[\mu_C(\alpha)-\mu_C(\alpha-1)] \tag{2.12b}$$

where σ_C^2 and μ_C are the variance and mean of N_C. But as seen from (2.3) we have

$$\alpha - \beta + \mu_B = \alpha + \gamma - \mu_C = \mu_A = \mu, \ \sigma^2 = \sigma_A{}^2 = \sigma_B{}^2 = \sigma_C{}^2 \tag{2.13}$$

Hence, substituting in (2.12b) we get

$$\sigma^2(\alpha) = \mu(\alpha)[\mu(\alpha - 1) - \mu(\alpha) + 1] \tag{2.14}$$

Finally, interchanging α and β and $\mu(=\mu_A)$ and μ_B, we see from (2.14), by symmetry, that

$$\sigma^2(\beta) = \sigma_B{}^2(\beta) = \mu_B(\beta)[\mu_B(\beta - 1) - \mu_B(\beta) + 1] \tag{2.15}$$

Hence, substituting from (2.13) in (2.15), we get

$$\sigma^2(\beta) = [\beta - \alpha + \mu(\beta)][\mu(\beta - 1) - \mu(\beta)] \tag{2.16}$$

Substituting (2.12), (2.14) and (2.16), in turn, into (2.8) and simplifying the resulting expressions we arrive at the following theorem.

Theorem 2.1. The equilibrium mean μ satisfies each of the following recurrence relations:

$$[K(\beta + \gamma) + 1 + K\mu(\alpha, \beta, \gamma - 1)]\mu(\alpha, \beta, \gamma) = \alpha + \gamma + K(\alpha + \gamma)\mu(\alpha, \beta, \gamma - 1), \tag{2.17}$$

$$[1 + K\mu(\alpha, \beta - 1, \gamma)]\mu(\alpha, \beta, \gamma) = \alpha + \gamma - K(\beta - \alpha)\mu(\alpha, \beta - 1, \gamma) \tag{2.18}$$

$$[K(\beta - \alpha + 1 + \mu(\alpha - 1, \beta, \gamma)) + 1]\ \mu(\alpha, \beta, \gamma) = \alpha + \gamma \tag{2.19}$$

with initial values

$$\mu(0, \beta, 0) = 0 \quad \text{and} \quad \mu(\alpha, 0, 0) = \alpha \tag{2.20}$$

Note that if the reaction starts with no molecules of types A and C, then the number of molecules of type A will remain zero irrespective of the number of molecules of type B. This explains the first initial value given in (2.20). The same logic is followed throughout in determining initial values.

The relations in *Theorem* 2.1 clearly describe how the equilibrium mean varies following the addition or removal of a molecule of one of the types involved in the reaction. They can be looked upon as *basic chemical laws*, assuming the validity of the model. One interesting application of the relations is in the evaluation of the means and variances.

The equilibrium mean can be evaluated using recurrence relation (2.17) and either of relations (2.18) or (2.19) with the appropriate starting values. Thus, for example, one can put γ = 0 in (2.18) and set β = 1, 2, etc ... to express μ(α, β, 0) in terms of μ(α,0,0), making use of the second initial value in (2.20). One can now use (2.17) with μ(α, β, 0) as a starting value to evaluate μ(α,β,γ). It is possible, however, to evaluate μ using a single recurrence relation. For this we introduce the parameters *N* and *M* defined by

$$N = \alpha + \gamma, \quad M = \beta + \gamma \tag{2.21}$$

This parametrization is the natural one in some applications. For example, in the study of the behaviour of ion-channels, reaction (2.1) corresponds to the so-called classical theory of drug action, where A is the molecule of the agonist drug, B is the free (closed) channel and C is the open channel (see, for example, Colquhoun & Hawkes, 1977, 1981). In that formulation *M* is the total number of molecules of the agonist drug and *N* is the total number of channels.

Noting the correspondences (α-1,β,γ) ↔ (*N*-1, M), (α, β-1,γ) ↔ (*N*, M-1), and (α,β,γ-1) ↔ (*N*-1, M-1), we can now rephrase and arrange *Theorem* 2.1 and the expressions for the variance in (2.12), (2.14) and (2.16) in the following theorem.

Theorem 2.2. (i) The equilibrium mean satisfies each of the relations:

$$[K(M - N + 1) + K\mu(N - 1, M) + 1]\mu(N, M) = N, \quad \mu(0, M) = 0 \tag{2.22}$$

$$[1 + K\mu(N, M - 1)]\mu(N, M) = N - K(M - N)\mu(N, M - 1), \quad \mu(N, 0) = N, \tag{2.23}$$

$$[KM + 1 + K\mu(N - 1, M - 1)]\mu(N, M) = N[1 + K\mu(N - 1, M - 1)], \ \mu(N, 0) = N, \ \mu(0, M) = 0 \tag{2.24}$$

(ii) The corresponding expressions for the variance are:

$$\sigma^2(N, M) = \mu(N, M)\,[\mu(N-1, M) - \mu(N, M) + 1]\,, \tag{2.25}$$

$$\sigma^2(N, M) = [N - M + \mu(N, M)][\mu(N, M-1) - \mu(N, M)]\,, \tag{2.26}$$

$$\sigma^2(N, M) = [N - \mu(N, M)][\mu(N, M) - \mu(N-1, M-1)]\,, \tag{2.27}$$

It should be noted that any two of the relations (2.22), (2.23), and (2.24) lead to the third.

The use of *Theorem* 2.2 to evaluate μ and σ^2 is best illustrated by an example.

Example: Let $\alpha=2$, $\beta=3$, $\gamma=1$ and $K=1$. Thus $N=3$ and $M=4$. Using (2.6) or (2.7a) it is easy to see that the equilibrium distribution is given as

r	0	1	2	3
p_r	24/73	36/73	12/73	1/73

Direct computation gives

$\mu = \mu(3, 4) = 63/73$ and $\sigma^2 = \sigma^2(3, 4) = 2820/5329$.

From relation (2.22), the most feasible in the number of steps needed to obtain the mean in this case, we have: $\mu(1, 4) = 1/5$, $\mu(2, 4) = 10/21$, and $\mu(3, 4) = 63/73$, as required. Note the ease with which these three means are generated without reference to the underlying distributions, as compared to the direct approach where we need first to work out those distributions. Now, from (2.24)

$\sigma^2(3, 4) = \mu(3, 4)[\mu(2, 4) - \mu(3, 4) + 1] = 2820/5329$.

The variance can also be obtained from (2.7). Relations (2.22) and (2.23) lead to the same answers.

The reaction $A + B \rightleftharpoons C + D$

For the reaction

$$A + B \underset{K_1}{\overset{K_2}{\rightleftharpoons}} C + D\,, \tag{3.1}$$

we assume initially we have α, β, γ and δ molecules of types A, B, C and D respectively. The equilibrium distribution of N_A satisfies the recurrence relation

$$K(r+1)(\beta-\alpha+r+1)p_{r+1} = (\alpha+\beta-r)(\alpha+\delta-r)p_r\,, \tag{3.2}$$

with solution

$$p_r = \frac{(\alpha+\gamma)!\,(\alpha+\delta)!\,(\beta-\alpha)!}{K^r r!\,(\alpha+\gamma-r)!\,(\alpha+\delta-r)!\,(\beta-\alpha+r)!}\,p_o\,. \tag{3.3}$$

From (3.2) it follows that

$$K\mu(\beta-\alpha+\mu) + K\sigma^2 = (\alpha+\gamma-\mu)(\alpha+\delta-\mu) + \sigma^2\,. \tag{3.4}$$

Note that when $K=1$, we have

$$\mu = \frac{(\alpha+\gamma)(\alpha+\delta)}{\alpha+\beta+\gamma+\delta} \tag{3.5}$$

Proceeding in exactly the same way as we did for reaction (2.1) it is easy to see that the expressions (2.12), (2.14) and (2.16) for σ^2 are still valid (but now σ^2 is a function of α, β, γ and δ). The variation of σ^2 with δ is governed by the relation

$$\sigma^2(\delta) = [\alpha+\delta-\mu(\delta)][\mu(\delta)-\mu(\delta-1)]\,. \tag{3.6}$$

Eliminating σ^2 between each of these expressions and equation (3.4) we obtain the following theorem.

Theorem 3.1. Keeping the other parameters fixed, the mean varies with the argument according to the following relations

$$[K(\beta-\alpha+1) + 2\alpha + \gamma + \delta - 1 + (K-1)\,\mu(\alpha-1)]\,\mu(\alpha) = (\alpha+\gamma)(\alpha+\delta), \tag{3.7}$$

$$[\alpha+\beta+\gamma+\delta+(K-1)\mu(\beta-1)]\,\mu(\beta) = (\alpha+\gamma)(\alpha+\delta) - (K-1)(\beta-\alpha)\mu(\beta-1) \tag{3.8}$$

$$[K(\beta+\gamma)+\alpha+\delta+(K-1)\,\mu(\gamma-1)]\,\mu(\gamma) = (\alpha+\gamma)(\alpha+\delta) + (K-1)(\alpha+\gamma)\mu(\gamma-1) \tag{3.9}$$

$$[K(\beta+\delta)+\alpha+\gamma+(K-1)\,\mu(\delta-1)]\mu(\delta) = (\alpha+\gamma)(\alpha+\delta)$$

$$+(K-1)(\alpha+\delta)\,\mu(\delta-1) \quad (3.10)$$

Note that when K=1 then, in each case, μ reduces to the expression in (3.5) as it should.

For the easy computation of μ we introduce the new parameters defined by

$$N=\alpha+\gamma\,,\ M=\beta+\gamma\,,\ S=\alpha+\delta\,,\ R=\beta+\delta\,. \quad (3.11)$$

With this parametrization *Theorem* 3.1 can now be rephrased in the following:

Theorem 3.2. Keeping all parameters fixed except those shown in the argument of μ we have the following relations

$$[S+M+(K-1)\mu(M-1))\mu(M)=SN-(K-1)(M-N)\,\mu(M-1),$$

$$\mu(0)=N, \quad (3.12)$$

$$[K(M-N+S)+N+(K-1)\mu(S-1]\mu(S)=S[N+(K-1)\mu(S-1)],$$

$$\mu(0)=0, \quad (3.13)$$

$$[N+R+(K-1)\mu(R-1)]\mu(R)=NS-(K-1)(R-S)\mu(R-1),$$

$$\mu(0)=S, \quad (3.14)$$

$$[K(M-N+1)+S+(K-1)\mu(N-1)]\mu(N)=N[S-\mu(N-1)],$$

$$\mu(0)=0. \quad (3.15)$$

It should be mentioned that relation (3.15) is not an immediate consequence of *Theorem* 3.1. It follows after a process of elimination using the other relations.
We illustrate the use of *Theorem* 3.2. by the following example:

Example: Take α=2, ß=3, γ=1, δ=2, K=1/2. Thus N=3, M=4, S=4, R=5. The equilibrium distribution is given by

r	0	1	2	3
p_r	1/45	12/45	24/45	8/45

Thus μ = 28/15 and σ^2 = 116/225. To economize on the number of steps needed to obtain μ we choose the relation involving N, the smallest of the 4 parameters. Direct computation leads to μ(1)= 2/3, μ(2)= 40/31, μ(3) = 28/15, as it should. The other three relations lead to the same conclusion. The variance can now be obtained from (3.4).

The reaction $2A \rightleftharpoons C+D$

For the reaction

$$2A \overset{K_2}{\underset{K_1}{\rightleftharpoons}} C+D\,, \quad (4.1)$$

the equilibrium distribution of N_A satisfies the recurrence relation

$$K(r+1)(r+2)p_{r+2}=(\alpha+2\gamma-r)(\alpha+2\delta-r)p_r \quad (4.2)$$

The equilibrium mean thus satisfies

$$2K\mu(\mu-1)+2K\sigma^2=(\alpha+2\gamma-\mu)(\alpha+2\delta-\mu)+\sigma^2 \quad (4.3)$$

Manipulations similar to those employed in reaction (2.1) lead to the following expressions for σ^2:

$$\sigma^2(\alpha)=\mu(\alpha)[\mu(\alpha-1)-\mu(\alpha)+1]\,, \quad (4.4)$$

$$\sigma^2(\gamma)=[\alpha+2\gamma-\mu(\gamma)][\mu(\gamma)-\mu(\gamma-1)]\,, \quad (4.5)$$

$$\sigma^2(\delta)=[\alpha+2\delta-\mu(\delta)][\mu(\delta)-\mu(\delta-1)] \quad (4.6)$$

Eliminating σ^2 between each of these expressions and equation (4.3) we arrive at the following theorem.

Theorem 4.1. The equilibrium mean μ varies with each of α, γ, δ, keeping the other two fixed, according to the following relations:

$$[2(\alpha+\gamma+\delta)-1+(2K-1)\mu(\alpha-1)]\mu(\alpha)=(\alpha+2\gamma)(\alpha+2\delta), \quad (4.7)$$

$$(\alpha + 2\delta + 2K(\alpha + 2\gamma - 1) + (2K - 1)\,\mu(\gamma - 1))\,\mu(\gamma) = (\alpha + 2\gamma)\,[\alpha + 2\delta + (2K - 1)\,\mu(\gamma - 1)], \tag{4.8}$$

$$[\alpha + 2\gamma + 2K(\alpha + 2\delta - 1) + (2K - 1)\,\mu(\delta - 1)]\,\mu(\delta) = (\alpha + 2\delta)\,[\alpha + 2\gamma + (2K - 1)\,\mu(\delta - 1)]. \tag{4.9}$$

We introduce the new parameters defined by

$$\alpha + 2\gamma = N, \quad \alpha + 2\delta = M. \tag{4.10}$$

Note that $\alpha + 2\gamma = 0$ implies that $\alpha = 0$ and $\gamma = 0$. Also $\alpha + 2\gamma = 1$ implies that $\alpha = 1$ and $\gamma = 0$ and hence $\mu = 1$. This explains the starting values that hold when expressing *Theorem* (4.1) in the following theorem.

Theorem 4.2. The equilibrium mean μ varies with N and M, according to the following relations

$$[M + 2K(N - 1) + (2K - 1)\,\mu(N - 2)]\,\mu(N) = N[(M + (2K - 1)\,\mu(N - 2)], \quad \mu(0) = 0,\ \mu(1) = 1, \tag{4.11}$$

$$[(N + 2K(M - 1) + (2K - 1)\mu(M - 2)]\mu(M) = M[N + (2K - 1)\,\mu(M - 2)], \quad \mu(0) = 0,\ \mu(1) = 1. \tag{4.12}$$

Example: Take $N=4$, $M=6$, $K=1$. The equilibrium distribution is given by

r	0	2	4
p_r	1/9	6/9	2/9

Hence $\mu = 20/9$ and $\sigma^2 = 104/81$. Using (4.11) we have $\mu(0) = 0$, $\mu(2) = 3/2$, $\mu(4) = 20/9$. The other relations lead to the same answers. Had N been odd, one would have started with $\mu(1) = 1$.

The reaction $2A \rightleftharpoons C$

For the reaction

$$2A \underset{K_1}{\overset{K_2}{\rightleftharpoons}} C\ , \tag{5.1}$$

we have

$$K(r+1)(r+2)p_{r+2} = (\alpha + 2\gamma - r)p_r\ . \tag{5.2}$$

It follows that

$$K\mu(\mu - 1) + K\sigma^2 = \alpha + 2\gamma - \mu\ . \tag{5.3}$$

Proceeding as for the previous reactions it can easily be shown that

$$\sigma^2(\alpha) = \mu(\alpha)[\mu(\alpha - 1) - \mu(\alpha) + 1]\ , \tag{5.4}$$

$$\sigma^2(\gamma) = [\alpha + 2\gamma - \mu(\gamma)][(\mu(\gamma) - \mu(\gamma - 1)]\ . \tag{5.5}$$

Hence, we have *Theorem 5.1.*

$$[1 + K\mu(\alpha - 1)]\mu(\alpha) = \alpha + 2\gamma \tag{5.6}$$

$$[K(\alpha+2\gamma-1) + 1 + K\mu(\gamma-1)]\mu(\gamma) = (\alpha+2\gamma)(1+K\mu(\gamma-1)) \tag{5.7}$$

We define the new parameter

$$N = \alpha + 2\gamma. \tag{5.8}$$

The following theorem is immediate from *Theorem* 5.1.

Theorem 5.1.

$$[1 + K\mu(N - 1)]\mu(N) = N,\ \mu(0) = 0\ , \tag{5.9}$$

$$[K(N - 1) + 1 + K\,\mu(N - 2)]\,\mu(N) = N(1 + K\,,\ \mu(N - 2)],\ \mu(0) = 0,\ \mu(1) = 1. \tag{5.10}$$

Example: Let $N=5$, $K=1$. Then

r	1	3	5
p_r	15/26	10/26	1/26

Thus $\mu = 25/13$ and $\sigma^2 = 220/169$. Starting with $\mu(1) = 1$ in (5.10) we have $\mu(3) = 3/2$, $\mu(5) = 25/13$.

Evaluating other moments

Factorial moments of the equilibrium distribution of N_A can be evaluated recursively, once the value of the equilibrium mean is provided. The recurrence relations that make this possible are given, for each of the four reactions, in the following theorem.

Theorem 6.1. Let $m_0 = 1$ and

$$m_n = E[N_A(N_A-1)\ldots(N_A-n+1)],\ n=1, 2, 3, \ldots \tag{6.1}$$

The following relations hold for reaction (2.1), (2.2), (2.3) and (2.4), respectively, for each n=0, 1, 2, ...

$$Km_{n+2} = (\alpha+\gamma-n)m_n - [K(\beta-\alpha+1)+n+1]m_{n+1}, \tag{6.2}$$

$$(K-1)m_{n+2} = (\alpha+\gamma-n)(\alpha+\delta-n)m_n - [K(\beta-\alpha+n+1) \\ +2\alpha+\gamma+\delta-2n-1]m_{n+1}, \tag{6.3}$$

$$(2K-1)m_{n+2} = (\alpha+2\gamma-n)(\alpha+2\delta-n)m_n - [2(\alpha+\gamma+\delta)-2n-1]m_{n-1}, \tag{6.4}$$

$$Km_{n+2} = (\alpha+2\gamma-n)m_n - m_{n+1}. \tag{6.5}$$

Proof: We prove relation (6.2). The other relations can be proved similarly. From (2.5), it can easily be shown that

$$(\alpha+\gamma)G(s) - [K(\beta-\alpha+1)+s]\frac{dG}{ds} - Ks\frac{d^2G}{ds^2} = 0, \tag{6.6}$$

where

$$G(s) = E(s^{N_A})$$

is the probability generating function of the equilibrium distribution of N_A. The result follows by differentiating (6.6) n times, using the rule for the n^{th} derivative of a product of two functions, namely,

$$(FG)^{(n)} = \sum_{r=0}^{n} \binom{n}{r} F^{(r)} G^{(n-r)},$$

and then putting $s = 1$.

Assessment of Approximate Formulas for the Mean and Variance

The normal approximation derived by Dunstan and Reynolds (1981) gives approximate expressions for the mean and variance of the distribution in terms of the mode. A direct approximation of the mean, not much different from theirs, can also be justified. Note, for example, that replacing $\mu(N-1, M-1)$ by $\mu(N, M)$ in (2.24) should make little difference for fairly large values of M and N. This amounts to approximating μ from (2.8) by simply putting σ^2 equal to zero. Thus, an approximate expression for the mean number of molecules of type A in reaction (2.1) is given by the positive root of the equation

$$K\mu(M - N + \mu) = N - \mu \tag{7.1}$$

where M and N are as defined in (2.21). It can also be shown, for the same reaction, that μ varies with K according to the relation

$$\frac{d\mu}{dK} = -\frac{\sigma^2}{K}. \tag{7.2}$$

Differentiating (7.1) with respect to K and simplifying leads to

$$[K(M - N + \mu) + K\mu + 1]\sigma^2 = K\mu(M - N + \mu) \tag{7.3}$$

Using (7.1) again we get

$$\frac{1}{\sigma^2} = \frac{1}{\mu} + \frac{1}{N-\mu} + \frac{1}{M-N+\mu}. \tag{7.4}$$

This is the same expression given by Dunstan and Reynolds except that the approximate mode is replaced by the approximate mean. The same expression was also derived by Babiker and Elsheikh (1992) assuming (7.1) and symmetry of the distribution. The other three reactions can be treated similarly.

It should be stated that, differentiating both sides of each of the relations (2.22), (2.23), and (2.24), and making use of (7.2) leads to the following relations:

$$N\sigma^2(N) = \mu(N)[N - \mu(N) - K\mu(N)\sigma^2(N-1)] \tag{7.5}$$

TABLE 1

Compted and Approximate means and variances for reaction(2.1)

N	M	K	mean	approx. Mean	variance	approx. Variance
10^9	10^9	10^4	316.0	316.2	158.1	158.1
10^9	10^8	10^{-4}	311267.0	311267.3	153173.2	153173.2
10^9	10^7	10^{-12}	999990010.1	999990010.1	9979.8	9979.8
10^9	10^5	10^{-9}	999950001.2	999950001.2	24999.4	24999.4
10^7	10^9	10^{-9}	5012499.9	5012499.9	2493718.9	2493718.9
10^7	10^7	10^{-5}	951249.0	951249.2	451873.1	451873.1
10^7	10^5	1.0	9900000.0	9900000.0	0.0	0.0
10^5	10^6	10^{-8}	9091.7	9091.7	8265.0	8265.0
10^5	10^7	10^{-3}	10.1	10.1	10.1	10.1
10^3	10^5	10^{-1}	994.8	995.0	495.0	495.0

$$M\sigma^2(M) = [M - N + \mu(M)][N - \mu(M) - K(M - N + \mu(M)\sigma^2(M-1)] \quad (7.6)$$

$$KMN\sigma^2(N-1,M-1) = [N - \mu(N-1,M-1)^2][1 + K\sigma^2(N-1,M-1)] \quad (7.7)$$

These relations have been used for cross validation in the computational work reported below.

The approximations provided by (7.1) and (7.4) have been investigated for reaction (2.1) using the recurrence relations in *Theorem* 2.2 over a wide range of the values of the parameters. Specifically, values of M, $N \le 10^9$, and $10^{-14} \le K \le 10^4$ have been considered. (Values of $K > 10^4$ are not very interesting for the range of values of M and N considered in that they lead to small values of the mean or variance). It turned out that there is remarkable agreement between the computed and approximate values for both the mean and variance for all values considered. The maximum difference is found to be less than 1 for both the mean and variance. Table 1 provides some of the cases considered.

References

BABIKER, A. A. AND ELSHEIKH, E. K. 1992. An approximation leading to the binomial distribution in the stochastic treatment of a reversible chemical reaction. *Qat. Univ. Sc. J.* **12**, 3-7.

COLQUHOUN, D. AND HAWKES, A. G. 1977. Relaxations and fluctuations of membrane currents that flow through drug-operated channels. *Proc. Roy. Soc. London Ser.* **B 199**, 231-262.

COLQUHOUN, D. AND HAWKES, A. G. 1981. On the stochastic properties of single ion channels. *Proc. Roy. Soc. London Ser.* **B 211**, 205-235.

DARVEY, I. G., NINHAM, B. W. AND STAFF, P. J. 1966. Stochastic models for second-order chemical reaction kinetics. The equilibrium state. *J. Chem. Phys.* **45**, 2145-2155.

DUNSTAN, F. D. J. AND REYNOLDS, J. F. 1981. Normal approximations for distributions arising in the stochastic approach to chemical reaction kinetics. *J. Appl. Prob.* **18** 263-267.

FORMOSINHO, S. J. AND MIGUEL, M. DA G. M. 1979. Markov chains for plotting the course of chemical reactions. *J. Chem. Education* **56**, 582-585.

HALL, A. 1983. On the roles of the Bessel and Poisson distributions in chemical reaction kinetics. *J. Appl. Prob.* **20** 585-599.

McQUARRIE, D. A. 1967. Stochastic approach to chemical kinetics. *J. Appl. Prob.* **4**, 413-478.

OPPENHEIM, I., SHULER, K. E. AND WEISS, G. H. 1969. Stochastic and deterministic formulation of chemical rate equations. *J. Chem. Phys.* **50**, 460-466.

STAFF, P. J. 1967. Approximation method for equilibrium distributions in second-order chemical reaction kinetics. *J. Chem. Phys.* **46**, 2209-2212.

THAKUR, A. K., RESCIGNO, A. AND DE LISI, C. 1978. Stochastic theory of second order chemical reactions. *J. Phys. Chem.* **82**, 552-558.

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