Molecular Transitions and Chemical Reaction Rates

The stochastic model relates the rate of a chemical reaction to the underlying transition probabilities.

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A chemical reaction is the result of a complex sequence of elementary molecular processes. Each molecule in a reaction mixture undergoes continual changes in its state—in its energy, geometry, and so on—most of these changes, perhaps, being minute and scarcely noticeable, others being sudden and violent as the result of extremely disruptive collisions. The processes are apparently aimless, each molecule being excited and de-excited with no obvious regularity. But when we view the reaction mixture as a macroscopic system the molecular turmoil is invisible, and what we see instead is a seemingly purposeful drive to equilibrium, rapid at first, then slower, until finally equilibrium is achieved and the chemical reaction is at an end. At the molecular level, however, the reaction is *not* at an end, the interactions, the transitions from state to state, and the violent disruptions being just as frequent and as confused as ever.

The connection between the macroscopic approach to chemical equilibrium and the elementary molecular processes which underlie it is devious and subtle. Much of what we have learned about it in recent years has come from a study of "stochastic" models of chemical reaction (*1*), and my purpose here is to describe these models and to make clear what their implications are.

A Stochastic Model

We may isolate the essential problem from all extraneous difficulties and technicalities by supposing that the reaction mixture contains only a single kind of molecule undergoing transitions, by whatever mechanism and however chaotically. Now imagine that each of these molecules is always in some well-defined state, though passing irregularly from state to state by instantaneous transitions as time goes on. To fix our ideas and to allow a pictorial representation, let us take the possible states to be discrete and represent them by discrete points in a plane (Fig. 1). The transitions from state to state which each molecule continually undergoes may now be represented by sudden jumps from one to another of these points. Imagine, further, that the states fall into two groups (separated by the solid boundary in Fig. 1); then, according to the group of states to which the instantaneous state of one of our molecules belongs, let us call it a molecule of chemical substance A or of chemical substance B. Whenever a molecule undergoes a transition from one of the A states to one of the B states it is contributing to the chemical reaction A → B, whereas if the jump across the boundary occurs in the opposite direction then the transition contributes to the reaction B → A.

We now make the model stochastic, or probabilistic, by specifying that a transition from any state i to any second state j, whether they be on the same or opposite sides of the A–B boundary, is determined by a transition probability per unit time, p_{ij}, which depends only on the states i and j and not on the number of molecules which happen to be in either. Thus, if at some instant t the number of molecules in state i is $n_i(t)$ and the number in state j is $n_j(t)$, then $p_{ij}n_i$ is the rate (in number of molecules per unit time) at which molecules are making transitions from state i to state j, while $p_{ji}n_j$ is the rate at which the reverse transitions are occurring. Therefore, at the time t, the population in each state i is changing at the rate

$$\mathrm{d}n_i/\mathrm{d}t = \sum_j (p_{ji}n_j - p_{ij}n_i), \qquad (1)$$

where the summation is over *all* the states j. This expresses the net rate of change as the difference between the rate at which state i is being *populated* by transitions *from* all other states j and the rate at which it is being *depopulated* by transitions *to* all other states j.

Equation 1 is a whole set of equations, one for each state i, and together they determine the detailed evolution of the system. The equations are coupled, the rate of change $\mathrm{d}n_i/\mathrm{d}t$ of population in any one state i being expressed in terms of the instantaneous value not only of that n_i but of every other n_j as well. The solution to such a set of coupled differential equations has been known for 200 years. It is essentially the same problem as that arising with coupled oscillators, which is solved by transformation to independent normal modes of vibration, each of which has associated with it a single characteristic frequency. I shall digress for a moment to recall the major features of such a resolution into normal modes.

Normal Modes of Vibration

Figure 2 is a very familiar illustration, showing two diagrams (*a* and *b*) each representing two identical masses (the outer ones) and a third mass (the inner one) which may be different. The three masses are connected by two identical springs, and all are confined to a line.

If initially the two springs are distended or compressed by identical amounts (as in Fig. 2*a*) and then released, the inner mass will remain stationary while the two outer masses will move alternately toward and away from each other, the configuration always remaining symmetrical, and the coordinates and velocities of the masses will vary periodically with a single definite frequency ν_1.

Likewise, if (as in Fig. 2*b*) one spring is initially compressed while the other is distended to the same degree that the first is compressed, and they

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are then released, the system will vibrate, with the two outer masses moving in one direction and the inner mass in the other (the distance between the outer masses remaining fixed at its equilibrium value), and the coordinates and velocities of the masses will vary periodically with a single definite frequency, ν_2.

These very special vibrations are the two normal modes of the system. A general displacement of the masses corresponds not to either one alone but to a combination of the two. Any initial conditions other than those I have described lead to the simultaneous excitation of both normal modes, and in such a general vibration the coordinates and velocities of the masses are not periodic functions with a definite frequency ν_1 or ν_2; instead, the displacements of the masses from their equilibrium positions are combinations of such periodic functions,

$$A_1\cos(2\pi\nu_1 t + \theta_1) + A_2\cos(2\pi\nu_2 t + \theta_2),$$

with certain constant amplitudes A_1 and A_2 and phase angles θ_1 and θ_2.

More complicated systems may be similarly analyzed, and lead to as many normal modes, each with its characteristic frequency, as there are vibrational coordinates in the system.

Normal Modes of Relaxation

Now let us return to our model chemical system, the evolution of which is governed by the coupled Eqs. 1. As time goes on, the population $n_i(t)$ of each state i approaches a unique, constant equilibrium population, $n_i(\infty)$. This approach to the equilibrium population, as determined by Eqs. 1, is resolvable into normal modes of relaxation, each of which has associated with it a characteristic time constant, its relaxation time, which is the reciprocal of what we may call a relaxation rate. While normal modes of *vibration* vary periodically in the time, normal modes of *relaxation* decay monotonically. From the point of view of the theory of vibrations, a relaxation is a vibration with an imaginary frequency, whereas, from the point of view of the theory of relaxation, a vibration is a relaxation with an imaginary relaxation rate.

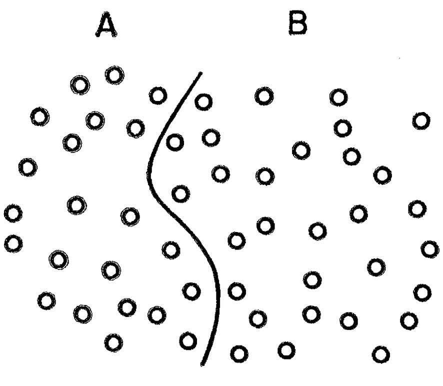

Fig. 1. The states of a molecule represented by discrete points in a plane. The boundary separates the states of substance A from those of substance B.

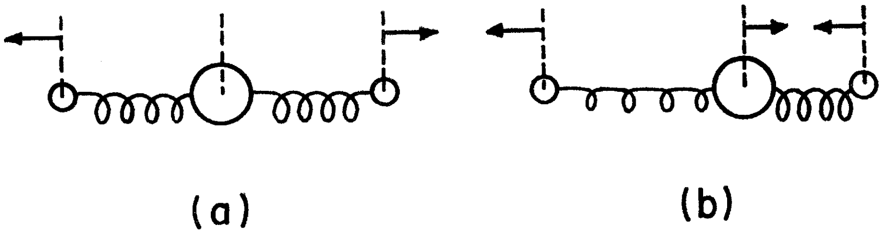

Fig. 2. The symmetric (*a*) and antisymmetric (*b*) normal modes of vibration of two identical, coupled oscillators.

In mathematical terms, the solution to Eqs. 1 is

$$n_i = n_i(\infty) + \sum_l c_{il}\exp(-\lambda_l t). \qquad (2)$$

The normal modes of relaxation are indexed by l, and λ_l is the relaxation rate (reciprocal of the relaxation time) associated with the lth mode. Pursuing the analogy with vibration theory, we see that the population n_i of state i is a "coordinate," the displacement of which from equilibrium is being expressed as a combination of normal modes; the "amplitude" of the lth normal mode in the displacement of the coordinate i is a constant, c_{il}, which depends not only on the transition probabilities p_{ij} but also on all the initial displacements $n_j(0)-n_j(\infty)$. With the appropriate choice of initial displacements it is possible to achieve a condition in which all the c_{il} vanish except those corresponding to a single l. In such a case only a single normal mode has been "excited," and the population of every state i relaxes to equilibrium with the same relaxation rate λ_l, via this single mode of relaxation. With arbitrary initial displacements, however, all the modes are excited, and each displacement $n_i(t)-n_i(\infty)$ is a combination of all the exponentials $\exp(-\lambda_l t)$. Nevertheless, while the question of which normal modes are excited, and with what amplitudes, depends on the initial populations, the relaxation rates λ_l do not—they are functions *only* of the transition probabilities p_{ij}. In the language of vibration theory, the frequencies of the normal modes do not depend on the initial displacements from equilibrium but depend only on the masses and force constants of the coupled oscillators.

I shall now illustrate these ideas with an example which is the direct analog, in relaxation theory, of the symmetrical coupled oscillator system I discussed above. Let there be only three states, numbered 1, 2, 3; let the transition probability per unit time for the $2 \rightarrow 1$ and $3 \rightarrow 1$ transitions be μ, and that for the $1 \rightarrow 2$ and $1 \rightarrow 3$ transitions be ν; and let the transition probability per unit time for the transitions $2 \rightarrow 3$ and $3 \rightarrow 2$ be zero, so that the states 2 and 3 are not accessible, one from the other, by direct transition, but only indirectly through state 1. Schematically, we express this as follows:

$$2 \underset{\nu}{\overset{\mu}{\rightleftarrows}} 1 \underset{\nu}{\overset{\mu}{\leftrightarrows}} 3.$$

If, initially, state 1 has the same population that it is destined to have at equilibrium but states 2 and 3 do not, then state 1 will maintain a constant population during the entire relaxation process, and there will be a unidirectional flow of molecules *through* state 1 tending to equalize the populations in states 2 and 3, this being the final equilibrium condition. This is a single, pure mode of relaxation, the analog of the asymmetric mode of vibration of Fig. 2*b*. During the course of this relaxation the deviations from the equilibrium populations in states 2 and 3 vanish proportionally to $\exp(-\mu t)$, so that the relaxation rate in this mode is μ. (Here is an intriguing puzzle: Why is the relaxation rate in this mode independent of ν?)

If, on the other hand, the populations in states 2 and 3 are initially equal but are not at the level that corresponds to equilibrium, there will be a flow of molecules to or from state 1 such that the populations of states 2 and 3 remain equal to each other while, together, they come to equilibrium with state 1. This is the second normal mode of relaxation, the analog of the symmetric mode of vibration in Fig. 2*a*. During the course of this relaxation the deviations from the equilibrium populations in all three states vanish proportionally to $\exp[-(\mu + 2\nu)t]$, so that the relaxation rate in this mode is $\mu + 2\nu$.

Generally, however, the initial conditions will be neither of these very special ones, so that both modes of relaxation will be simultaneously operative and the deviation from equilibrium in each of the three states will be a combination of $\exp(-\mu t)$ and $\exp[-(\mu + 2\nu)t]$.

An even simpler example, and one to which I later have occasion to refer, is that in which there are only two states ($i = 1, 2$). Equations 1 are in this case simply

$$-\,dn_1/dt = dn_2/dt = p_{12}n_1 - p_{21}n_2. \quad (3)$$

There is now only a single relaxation rate, related to the two transition probabilities by

$$\lambda = p_{12} + p_{21}. \quad (4)$$

The equilibrium condition toward which the system strives is that which causes the vanishing of the time derivatives in Eq. 3,

$$n_2(\infty)/n_1(\infty) = p_{12}/p_{21}, \quad (5)$$

for only when the populations are in this ratio does the number of molecules making the transition 1 → 2 per unit time, $p_{12}n_1$, equal the number making the transition 2 → 1 per unit time, $p_{21}n_2$, and therefore only then is there no longer a net transfer of molecules from one state to the other.

It is the relaxation rates λ_l which determine directly the rate of approach to equilibrium, and therefore, in particular, the speed of the chemical reaction A → B or B → A. Ultimately, of course, it is the transition probabilities per unit time, p_{ij}, which govern, but they do so only by way of the λ_l, which are in general rather intricate functions of the p_{ij}. The number of λ_l is always less by one than the number of states (which, in turn, is usually infinite!), and the relations between the λ_l and the p_{ij} become increasingly complex as the number of states increases (*2*).

Let us index the relaxation rates in such a way that the smallest is called λ_1, the next smallest λ_2, and so on. Then when the elapsed time t has become so great that

$$(\lambda_2 - \lambda_1)t >> 1,$$

every term beyond the one with $l = 1$ in Eq. 2 has become negligible compared to the term with $l = 1$, and for all times thereafter the deviation from equilibrium vanishes by way of this slowest mode of relaxation alone. When this condition has been reached —that is, when the elapsed time has been so great that the transient faster modes of relaxation are no longer making a significant contribution to the evolution of the system—the population in each state i varies with time simply as

$$n_i = n_i(\infty) + c_{i1}\exp(-\,\lambda_1 t),$$

so that

$$-dn_i/dt = \lambda_1[n_i - n_i(\infty)]. \quad (6)$$

Thus, after a sufficiently long time has elapsed, the population of each state approaches its equilibrium value at a rate which is proportional to its deviation from equilibrium at that instant, the constant of proportionality being λ_1, the smallest of the relaxation rates.

The Chemical Reaction

Now recall that the states i have been divided into two groups, as in Fig. 1, those belonging to one group being called states of substance A, those belonging to the other, states of substance B. The sum of $n_i(t)$ over all the A states is the total number, $N_A(t)$, of molecules of substance A present at the time t, while the sum of $n_i(t)$ over all the B states is the total number, $N_B(t)$, of molecules of substance B. Therefore, after the elapse of the transient period, when Eq. 6 holds, the total numbers of A and B molecules vary according to

$$\begin{aligned}-dN_A/dt &= \lambda_1[N_A - N_A(\infty)]\\ -dN_B/dt &= \lambda_1[N_B - N_B(\infty)]. \quad (7)\end{aligned}$$

A most important observation was made at this point by Snider, in a recent incisive analysis of the stochastic model (*3*). Because the total number of molecules in A and B states together is constant, Eqs. 7 are equivalent to

$$-dN_A/dt = dN_B/dt = kN_A - k'N_B \quad (8)$$

where k and k' are two constants the sum of which is

$$k + k' = \lambda_1 \quad (9)$$

and the ratio of which is

$$k/k' = N_B(\infty)/N_A(\infty). \quad (10)$$

In other words, after the elapse of the transient period—that is, after times which are long compared to $1/(\lambda_2 - \lambda_1)$ —the total population in all the A states together and the total population in all the B states together behave formally as though they were the individual populations in a two-state system. Equation 8 is analogous to Eq. 3, with k and k' taking the place of the transition probabilities p_{12} and p_{21}, while Eqs. 9 and 10 are the analogs of Eqs. 4 and 5.

The importance of Eq. 8 lies in the fact that it is of a form frequently found to hold experimentally as one of a class of chemical reaction-rate laws (*4*). The stochastic model, therefore, accounts for one of the phenomenological laws of chemistry. To be sure, the theory qualifies the validity of Eq. 8 by restricting its application to times that are long compared with $1/(\lambda_2 - \lambda_1)$, but, as a practical matter, the transient period during which modes of relaxation other than the very slowest are significant is over almost instantaneously. Typically, the relaxation times $1/\lambda_2$, $1/\lambda_3$, $1/\lambda_4$, . . . are less than a microsecond, while the relaxation time $1/\lambda_1$ may be of the order of seconds, or years, or millennia. It is $1/\lambda_1$ which sets the characteristic time scale of the chemical reaction once the transients have decayed, and on *that* time scale the time during which the transients have *not* decayed is infinitesimal. Practically from the initial instant, therefore, the rate of the chemical reaction is determined by Eq. 8, with constants k and k' that depend on the transition probabilities per unit time and on the choice of the A–B boundary in Fig. 1, but on nothing else.

Notice that these conclusions are entirely independent of which states we have chosen to call states of substance A and which we have chosen to call states of substance B. This is fortunate, because the position of the A–B boundary is in principle quite arbitrary. Suppose two experimenters make this decision in different ways and then proceed to measure the constants k and k' in Eq. 8. They do not agree on what N_A and N_B are at any time; they do not agree on the value of the ratio $N_B(\infty)/N_A(\infty)$ (called the *equilibrium constant* for the reaction A → B); and they do not agree on the values of the rate constants k and k'. Yet each one finds *his* rate-constant ratio k/k' equal to *his* equilibrium constant. Further, and most significantly, the two experimenters are in complete agreement on the value of the sum of the two rate constants, $k + k'$; for this is λ_1, the slowest relaxation rate in the system, and the relaxation rates depend on the transition probabilities alone and have nothing whatever to do with the division of the states into two groups.

As a practical matter, however, if the A–B boundary is chosen so as to have a real chemical significance, then there will be very little arbitrariness in k and k'. If the substances A and B are chemically distinguishable, then they transform into each other at a rate slow enough to be observed. Therefore, there is likely to be an energy barrier between them—that is, there is likely to be, somewhere in Fig. 1, a *band* containing states of high energy only. Each of the two experimenters would then surely choose his A–B boundary somewhere in this band, even if they do not agree on precisely where in the band it should lie. But all the states in the band, being states of high energy, are destined to have very low equilibrium populations, and so to make negligible contributions to the equilibrium constant $N_B(\infty)/N_A(\infty)$. Therefore, though there may remain considerable arbitrariness in the position of the boundary, so long as the boundary is chosen somewhere in the high-energy band this arbitrariness does not significantly affect the ratio k/k'. Then with the sum $k + k'$ unique, and the ratio k/k' practically unique, k and k' separately are practically unique.

Reaction Rate Coefficients

Because of the structure of Eq. 8, and its analogy with Eq. 3, where p_{12} and p_{21} are transition probabilities per unit time, it is almost irresistibly tempting to interpret the rate constants k and k' as being also transition probabilities per unit time. The unwary would surely suppose that kN_A is the number of A molecules making the transition $A \rightarrow B$ per unit time, that $k'N_B$ is the number of B molecules making the transition $B \rightarrow A$ per unit time, and that Eq. 8 is simply expressing the net $A \rightarrow B$ flux, $-dN_A/dt$, as the difference between two opposing fluxes. This is certainly the correct interpretation of Eq. 3; is it even possible to conceive of its not being also the correct interpretation of the strikingly analogous Eq. 8?

The answer, forcefully argued by Rice (*5*) and subsequently confirmed by Snider (*3*), is shattering: The rate constants k and k' are *not* the probabilities per unit time of an A molecule making an $A \rightarrow B$ transition and a B molecule making a $B \rightarrow A$ transition; kN_A and $k'N_B$ are *not* the separate $A \rightarrow B$ and $B \rightarrow A$ fluxes. Let us symbolize the equilibrium constant $N_B(\infty)/N_A(\infty)$ by K; it then follows from Eqs. 9 and 10 that

$$k = \frac{K}{1+K}\,\lambda_1, \quad k' = \frac{1}{1+K}\,\lambda_1 \tag{11}$$

That is, k and k' are certain simple fractions of the same relaxation rate, λ_1, which, in turn, depends on *all* the transition probabilities per unit time p_{ij}. Thus, k is not just some average rate of $A \rightarrow B$ transitions but is, rather, a complex of $A \rightarrow B$, $B \rightarrow A$, $A \rightarrow A$, and $B \rightarrow B$ transition rates; and so is k'.

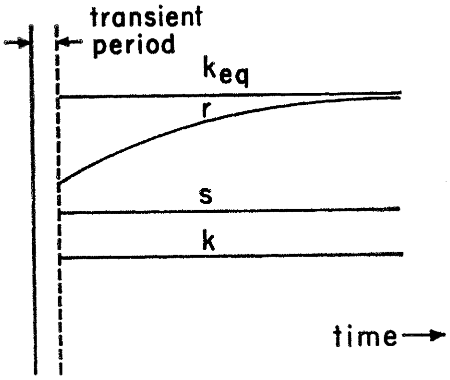

Fig. 3. Four different reaction rate coefficients. The duration of the transient period is highly exaggerated here, being actually too short to be visible on this scale. The whole interval of time covered in the diagram is of the order of magnitude of the longest relaxation time, $1/\lambda_1$, of the system.

In an ordinary measurement of a chemical reaction rate, where the concentrations of the relevant substances in a reaction mixture are measured as functions of the time, it is just k and k' which are determined. On the other hand, rate coefficients which, unlike k and k', do refer to the separate $A \rightarrow B$ and $B \rightarrow A$ fluxes, are easily found in the stochastic model, and are valuable theoretical constructs (*6, 7*). In Fig. 3 are shown three such rate coefficients, k_{eq}, r, and s, in addition to the phenomenological rate constant k. (There are also corresponding k'_{eq}, r', and s' in addition to k'.) Each of these three has, at one time or another in the history of reaction rate theory, been either confused with, or used to approximate, the rate constant k.

Rate Coefficients r, k_{eq}, s

The quantity r is the probability per unit time that a molecule in an A state will make a transition to some B state—that is, it is precisely the quantity that k, surprisingly, proved *not* to be. Many of the interesting properties of this rate coefficient were discovered by Pyun and Ross (*6*). It and its partner r' are such that

$$-dN_A/dt = dN_B/dt = rN_A - r'N_B,$$

where now rN_A and $r'N_B$, unlike kN_A and $k'N_B$, are indeed the $A \rightarrow B$ and $B \rightarrow A$ fluxes. The *difference* $rN_A - r'N_B$ equals the *difference* $kN_A - k'N_B$. The rate coefficient r, however, depends both on the time (as indicated schematically in Fig. 3) and on the initial condition of the system—that is, on the initial deviation from equilibrium $n_i(0) - n_i(\infty)$ in each state i. As the system approaches equilibrium, r gradually levels off at the constant value k_{eq}.

This limiting value k_{eq} is an interesting quantity in its own right. When every state of the system has its equilibrium population there is no longer a net flow $A \rightarrow B$ or $B \rightarrow A$, but only because the separate, opposing flows rN_A and $r'N_B$ have become equal, not because they have ceased. The probability per unit time that an A molecule will make a transition to some B state, when the system is at equilibrium, is k_{eq}. But it is still k, and not k_{eq}, which is the phenomenological rate constant, *however close the system may be to equilibrium* (*3, 5*). In spite of this distinction, however, k_{eq} and k'_{eq} share with k and k' the property that their ratio is the equilibrium constant; for at equilibrium the fluxes rN_A and $r'N_B$ are equal, while r, r' have become k_{eq}, k'_{eq} and N_A, N_B have become $N_A(\infty)$, $N_B(\infty)$.

If, initially, the reaction mixture contains only substance A, but no B, then according to Eq. 8 the rate of the reaction is simply kN_A, and this remains true until the amount of B produced by the reaction is large enough for $k'N_B$ to be significant compared to kN_A. But the coefficient of N_A is the same k, even in this early stage of the reaction, as it is later; indeed, k is a constant; so it is still a complex of all the transition probabilities, including those of $B \rightarrow A$ transitions, even when no perceptible amount of substance B is present. The point is that the early stage of the reaction, defined by $k'N_B$

$<< kN_A$ when no B is present initially, is still late compared to the transient period. During the transient period an imperceptibly small number of B molecules appears in very highly reactive states, too small a number to make $k'N_B$ appreciable, but quite large enough, in states of sufficiently high reactivity, to affect significantly the net rate of the A → B reaction. Thus, the B → A flux, $r'N_B$, is not negligible compared to the A → B flux, rN_A, even when the term $k'N_B$ in the phenomenological rate equation is negligible compared to kN_A. There is no way, in an ordinary reaction mixture, of eliminating the influence of B → A transitions so as to measure the rate of A → B transitions alone (*8*).

This can, however, be accomplished *theoretically* by considering the hypothetical circumstance in which molecules in B states are removed from the system the instant they appear. Then molecules in A states react, and instantaneously disappear, in accordance with a rate law of the form

$$-dN_A/dt = sN_A. \qquad (12)$$

This defines the last rate coefficient, s, in Fig. 3. After the elapse of a transient period which is of the order of magnitude of, but not identical with, the transient period $1/(\lambda_2 - \lambda_1)$, the coefficient s assumes a constant value. This constant s provides a logical bridge between the rate constant k and the reaction probability r, and illuminates both.

Because, in the situation to which s refers, no B molecules are ever present, sN_A is unambiguously interpretable as an A → B flux. In this respect s is, like r, the probability per unit time that an A molecule will make a transition to some B state. But what these reaction probabilities are, at any moment, depends on the instantaneous populations of the A states, being large or small according as the most highly reactive of the A states are populated to a greater or lesser extent. The existence of a B → A flux affects the populations of the A states and, therefore, affects also the A → B reaction probability r; whereas, when molecules in B states are removed from the system as soon as they are formed, there is no B → A flux influencing the populations of the A states. The reaction probability r, in this idealized circumstance, is s.

From another point of view, however, s has an even more fundamental connection with k than it has with r. The instantaneous removal of B molecules from the system, in the definition of s (or of A molecules in the definition of the corresponding s'), is only one way of insuring that there shall be no opposing flux influencing the distribution of molecules among reactant states, thereby affecting the reaction probability. Another, equally hypothetical, way to insure this is to set equal to zero all the transition probabilities that refer to transitions from B states to A states, leaving the remaining transition probabilities unaltered. This produces a new system, related to the original one by a definite prescription. Because molecules are now incapable of undergoing transitions from B states to A states, the equilibrium condition of the new system is one in which all molecules have accumulated in B states, so that the equilibrium constant $K = N_B(\infty)/N_A(\infty)$ is infinite. The relaxation rate λ_1 in the new system is an altered version of the original λ_1 but is still a finite, positive number. Then from Eq. 11, in the new system $k = \lambda_1$ and $k' = 0$, so that Eq. 8, the phenomenological rate equation, reduces to the form of Eq. 12. Thus, the rate coefficient s associated with the original system is precisely the phenomenological rate constant k of the hypothetically altered system. (The corresponding s' in the original system is the rate constant k' of a still different system—that which is derived from the original one by setting equal to zero each p_{ij} that refers to A → B transitions rather than those that refer to B → A transitions.) Then the rate coefficient s shares with k (as r does not) the fundamental property of being determined by the transition probabilities alone, without reference to the initial condition of the system or to the time which has elapsed in the reaction, while, as we saw before, it shares with r (as k does not) the fundamental property of being a reaction probability per unit time.

Taking again the point of view that s is the probability, per unit time, of an A → B reaction, under circumstances where the products of the chemical reaction are instantaneously removed from the system, it is easy to see why, as shown in Fig. 3, s is less than k_{eq}, which is the A → B reaction probability at equilibrium. When the chemical reaction occurs with instantaneous removal of products, all A states are depleted but the most reactive of the A states are preferentially depleted. When, on the other hand, transitions A → B occur at equilibrium, they again occur preferentially from the most reactive A states, but now there is no depletion because the opposing B → A flux preferentially repopulates just these most reactive states. Thus, at equilibrium, a greater fraction of the A molecules are in highly reactive states than is the case when B molecules are absent, so the probability per unit time that an arbitrarily selected A molecule will react is greater in the former case than in the latter: $k_{eq} > s$. It is also necessarily the case that k_{eq} is greater than the rate constant k. The reason is fundamentally the same, but the argument is more intricate because k is not a simple reaction probability per unit time (*9*).

We have seen that the ratio of the rate constants, k/k', and the ratio of the equilibrium reaction probabilities per unit time, k_{eq}/k'_{eq}, are both equal to the equilibrium constant K—that is, to the ratio of populations, N_B/N_A, in the equilibrium state of the system. On the other hand, r and r', before having attained their limiting values k_{eq} and k'_{eq}, do not have this property (*6*). Likewise, s and s' do not; s, as we have seen, is the k of a hypothetical system which is related to the original system in a certain specified way; s' is the k' of a second hypothetical system, and the ratio of the two bears no simple relation to the equilibrium constant K of the original system. Summarizing these equalities and inequalities, we have

$$k/k' = k_{eq}/k'_{eq} = K$$
$$r/r' \neq K, \quad s/s' \neq K.$$

Summary and Critique

The stochastic model shows clearly how different the behavior of the system may seem according to whether it is viewed at the molecular or the macroscopic level, and in this respect the model closely imitates just those features of the approach to equilibrium which we remarked at the beginning. Though the transition probability per unit time, p_{ij}, introduces a bias which makes some states j more easily accessible from state i than other states j are, any one molecule still appears to jump in an irregular and unpredictable manner from state to state. This does not cease when the system reaches equilibrium, but goes on forever. But if we look only at the total populations of the various states and ignore the identities of the molecules which compose those populations, we see a smooth, efficient, and inexorable drive to a determinate equilibrium condition. If the initial conditions are such that more of the molecules are in A states and fewer are in B states than is the case at equilibrium, what we see at the macroscopic level is the chemical reaction $A \rightarrow B$.

A very serious question which is begged rather than answered by the stochastic model is: What are the real origins of the transition probabilities per unit time? Once we assume them to exist, then Eqs. 1, and the irreversible approach to equilibrium which is implied, are immediate consequences; yet the system is composed of interacting molecules which satisfy time-reversible dynamical laws, so it is far from obvious how there could have arisen the fundamental distinction between past and future which is implied by the approach to equilibrium. While many aspects of this phenomenon are now understood, the general question, in one or another of its guises, is one of the continually recurrent problems of modern science (*10*).

References and Notes

1. B. J. Zwolinski and H. Eyring, *J. Am. Chem. Soc.* **69**, 2702 (1947); E. W. Montroll and K. E. Shuler, *Advan. Chem. Phys.* **1**, 361 (1958).
2. In mathematical terms, the rule for constructing the λ_i from the p_{ij} is this: Find the eigenvalues of the matrix of coefficients on the right-hand side of the coupled Eqs. 1; one of these eigenvalues is necessarily 0, and is associated with the constant term $n_i(\infty)$ in Eq. 2; the negatives of the remaining eigenvalues (which are themselves negative) are the (positive) relaxation rates λ_i.
3. N. S. Snider, *J. Chem. Phys.* **42**, 548 (1965).
4. When the reaction rate satisfies Eq. 8, the right-hand member of which is linear with respect to the concentrations of the reacting species, the reaction is said to be of the first order. Reactions of higher order are also of frequent occurrence, but the origin and status of the corresponding nonlinear rate equations are then much more obscure and as yet only imperfectly understood. I accordingly restrict this discussion to first-order reactions.
5. O. K. Rice, *J. Phys. Chem.* **65**, 1972 (1961).
6. C. W. Pyun and J. Ross, *J. Chem. Phys.* **40**, 2572 (1964).
7. B. Widom, *Advan. Chem. Phys.* **5**, 353 (1963).
8. I am most grateful to Professor S. H. Bauer for having raised the questions on which this paragraph was based, and to Dr. N. S. Snider for having provided the illuminating answers. The basic idea is again due to Rice (*5*).
9. Explicit formulas are known (see *3*, *6*, and *7*) for the differences $k_{eq} - k$, $k_{eq} - s$, $k_{eq} - r$. The first two of these differences, in particular, depend on how rapidly reactivity varies from one reactant state to another—more specifically, on the mean square deviation from the mean of the reactivity. As yet, this variation of the reactivity is not well enough known to allow any really quantitative statements to be made about the extent to which the constants k_{eq}, k, and s differ from each other. The best guess at the moment is that they do differ substantially, though all are of the same order of magnitude.
10. A beautiful and lucid account of this problem has been given by G. E. Uhlenbeck, in *Plenarvorträge der Physikertagung Düsseldorf 1964 (im Auftrag der deutschen physikalischen Gesellschaft)*, K. Hecht, Ed. (Univ. of Cologne, Cologne, 1964).

Megaloscience

Because of massive organization and large budgets, scientists are heavily involved with governments.

J. B. Adams

I have chosen the title "Megaloscience" for this discussion of scientific research and its interaction with governments and universities in order to convey the impression of very large-scale scientific research with just a hint of underlying mania.

Scientists who have grown up with this activity and who are still involved in it cannot pretend to be unbiased, but we can try as objectively as possible to analyze the problems which our activities have raised and to find reasonable solutions to them. We must address our minds to these problems now, if only because governments have become very much concerned with scientific research. Partly their concern is due to the rising cost of research and partly it is due to a growing realization in political circles that scientific research and development are the mainspring of our type of civilization. This concern must ultimately lead to decisions being taken by governments, and if we are to take an effective part in the decision-making we must first clear our own minds.

Even if our thinking does no more than dispel that public image of scientific research so well summed up by Academician Artsimovich, "Scientific research is a method of satisfying private curiosity at the public expense," it will not have been in vain.

Limiting Scientific Research Budgets

To the man in the street the impressive thing about megaloscience is its apparently insatiable demand for money. Where it all goes and how it is used is a mystery to most people. What results come out are by and large incomprehensible to almost everybody, including even scientists in other fields of research.

To the astute civil servant a far more ominous characteristic is the growth rate of scientific activity. Ever since the 17th century, we are told, the number of scientists has doubled every 15 years and the cost of scientific research has doubled every 5 years. We should not, of course, accept these statements without some investigation, particularly on such points as the definition of scientist used in the statistics, but during my own professional lifetime these doubling times seem to be about right. Extrapolation of these growth rates gives the fascinating and unlikely result that all the national incomes of our countries will be spent on scientific research in the year 2000 and everybody will be scientists a few decades later. Clearly, between now and the year 2000 something must occur to limit the growth of scientific research, and our problem is to determine what the limit should be and how it can be reached without unstable oscillations.

Such figures as exist show that in countries such as the United States and

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