

Stochastic Theory for Rate Constants of Chemical Reactions in Liquid Solution

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The stochastic model of irreversible processes is developed in a fashion that yields expressions for the magnitudes and temperature dependences of chemical reaction rate constants. The model is sufficiently abstract to encompass reactions in liquids as well as those in gases. For liquid reactions both the general point of view and one feature of the results (the "frequency factor") are apparently new. For gas reactions the viewpoints and the results are compatible with (though not as detailed as) those of well-established collision theory. An approximation (to the effect that non-reactive but energy-redistributing transitions are much more frequent than reactive ones) may limit the quantitative, though not the schematic, application of this development to reactions in the presence of an excess of inert diluent. The traditional assumption to the effect that reactants are in equilibrium with "activated complexes" (whether or not such exist in the sense of possessing well-defined microstates) is avoided. As in previous discussion of sufficient conditions for an Arrhenius rate law, in which certain complicating features (treated here) of the case of chemical reactions were ignored, the method used here involves taking explicit account of the role of those (rapidly equilibrating via frequent nonreactive transitions) degrees of freedom that serve as the activation-energy-supplying (and temperature defining) "reservoir" by use of an especially detailed form of stochastic master equation. A concise form for the master equation facilitates (1) the appropriate extension of the previously described steady state treatment of the case in which a "transition state" lasts sufficiently long to

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be internally equilibrated and (2) the treatment of the probably more realistic case in which reactants undergo transitions directly to products without a definable intermediate and in which "transition state" can only be defined in terms of an energy threshold in the reaction transition probability. The latter case is a generalization to arbitrary density of that originally treated by Ross and Mazur within the framework of collision theory for bimolecular dilute gas reactions.

The familiar exponential dependence on "free energy of activation" is obtained for both cases, but the physical basis for it is different (in both cases) from that provided by the classical version of transition state theory.

The "frequency factor" is not in either case simply kT/h but rather is dependent on the fundamental couplings within the system. It is also dependent on an effective "number of states" of reactants, products, and reservoir. A brief discussion of the possible significance of this latter feature in both enzymatic catalysis and heterogeneous catalysis is presented.

KEY WORDS: Chemical kinetics; stochastic master equation; transition state theory; liquid solution; catalysis.

1. INTRODUCTION

Recent theoretical progress in the interpretation of the magnitudes and temperature dependences of chemical reaction rate constants has dealt primarily with reactions in (dilute) gases. This is true not only of the modern version of "collision theory"^(1,2) but also of the "phase space trajectory"⁽³⁾ treatment.

Despite their importance in organic, inorganic, and biological chemistry, reactions in liquids have received little recent theoretical attention, a circumstance that has left the interpretation of their kinetics in the hands of a transition state theory that is now almost 40 years old (see, e.g., Ref. 4).

Until relatively recently it seemed permissible to view the classical transition state theory as an abstraction of those features of collision theory that are capable of generalization to the encompassment of reactions in dense media. Indeed the point of view that transition state theory is a generalization of collision theory was supported by identification of putatively corresponding factors in the results of these theories (e.g., "entropy of activation factor" from transition state theory and "steric factor" from collision theory).

That such identifications are not unique shows that the fact that they can be made does not constitute good evidence for close kinship of the theories in question. Indeed, it is clear that modern versions of collision theory cannot be viewed as detailed analyses of a special case of the classical transition state theory. In the first place, modern versions of collision theory

do not make the assumption of an equilibrium between reactants and transition state species ("activated complexes"). Such an assumption was the essential basis for the appearance of exponential dependences of rate constants of "free energies of activation" in the classical transition state theory, whereas modern collision theory can arrive at this result without this assumption.⁽¹⁾ In the second place the assumption of the very existence of a transition state in the sense required by the transition state theory, that is, in the sense of an entity possessing identifiable microstates (e.g., quantum levels), is sometimes avoided⁽¹⁾ in modern gas reaction theory.

The avoidance, as in contemporary gas reaction theory, of these assumptions is a feature that one would wish to embody in any attempt to formulate a theory that is sufficiently general to encompass reactions in liquids. Such a feature would be desirable not only to allow the possibility of obtaining a theory that would be consistent with collision theory in the low-density limit, but also to admit into such a theory the possibility of a full measure of internal self-consistency. That the assumption of equilibrium between reactants and transition state species prevents the latter can be seen by the following argument. A theory for rate constants can obviously impose no restriction on the relative amounts of "reactants" and "products" with which one may choose to start a chemical reaction. Since these concentrations are fully as important as the rate constants in determining the direction in which the given reaction will proceed, the theory has no basis for specifying which reaction is to be considered the "forward" reaction and which the "backward" one. Therefore, in its formal aspects, the theory must treat the reaction one chooses to call "backward" on the same basis as that one calls "forward." It follows that any assumption of equilibrium between transition state and what one chooses to call "reactants" must, strictly speaking, be accompanied by an assumption of equilibrium between transition state and what one calls "products." Since species in equilibrium with a common species are in equilibrium with each other, it is clear that the conventional formulation of transition state theory cannot be fully self-consistent except when reactants are in equilibrium with products.

One line of approach to liquid reaction kinetics that avoids these troublesome assumptions is the stochastic line initiated by Kramers⁽⁵⁾ in 1940. His particular treatment of (Brownian) diffusion over a barrier is relevant to reactions that proceed in increments each of which involves only small momentum and energy transfers. More recently Montroll and Shuler⁽⁶⁾ and Montroll⁽⁷⁾ have given a quantum mechanical counterpart of the Kramers theory in which the restriction to reaction in a series of small steps is represented by the use of Landau-Teller selection rules. In this paper we will avoid this restriction, but will invoke a different one.

We utilize here the classical assumption (common to both transition

state theory and most versions of collision theory) of internal equilibration of individual molecular species. This assumption must not be confused with the assumption that any one species or set of species (e.g., reactants) is equilibrated with any other (e.g., activated complexes). Although less drastic than the latter, the assumption of internal equilibration will limit the precise, if not the schematic, applicability of this analysis to reactions carried out in the presence of an excess of inert solvent (see below).

Widom⁽⁸⁾ has extensively applied stochastic methods to the question of existence and interpretation of chemical rate constants. His work has pointed out the danger inherent in various types of assumptions concerning populations of some molecular quantum states. Indeed, he has shown that the assumption of internal equilibration must be discarded for precise analysis of reactions proceeding in the absence of inert diluent.

McQuarrie⁽⁹⁾ has applied stochastic methods to the analysis of complicated reactions in terms of elementary steps. In this work he was not primarily concerned with interpretation of the rate constants of the elementary steps, the focus of our concern here.

In an article by Gibbs,⁽¹⁰⁾ hereinafter designated as I, an especially detailed form of stochastic "master" (Pauli) equation was used to demonstrate a set of sufficient conditions for an Arrhenius temperature dependence in an idealized simple process possessing little more than those features that constitute the essence of a thermally activated process (potential barrier to be traversed, auxiliary degrees of freedom that equilibrate among themselves sufficiently rapidly to define a temperature, etc.). In this detailed form of master equation, specific formal account was taken not only of transitions in the "system" undergoing the process (e.g., chemical reaction), but also of the requisite accompanying transitions in what was called in I the "reservoir." This "reservoir" is simply the aggregate of those degrees of freedom whose downward (in energy) transitions supply the "activation energy" for activating transitions in the degrees of freedom associated with the "system." In the case, for example, of a nuclear spin-lattice relaxation this "reservoir" would be the "lattice." In the case of a chemical reaction in solution this reservoir would be composed of all translational, rotational, and vibrational degrees of freedom of inert solvent, as well as of many such degrees of freedom of the reacting molecules.

When these auxiliary degrees of freedom, which serve as the reservoir are, in the aggregate, present in large excess relative to the degree of freedom associated with the reaction (i.e., that along the so-called "reaction coordinate") or when they exchange energy nonreactively among themselves sufficiently rapidly, then they suffer no significant departure from equilibrium ratios of the populations of their microstates and consequently provide the requisite definition of "temperature."

The detailed bookkeeping in I permitted specific consideration of the role of energy conservation in limiting the set of allowable composite "reactive" transitions in the system-reservoir combination. With this formal identification of energy-conserving transitions it was also possible to apply the principle of microscopic reversibility to transition probabilities. With these concepts and with use of a steady-state (as contrasted with equilibrium) assumption for overall transition state population, an averaged (with respect to time-dependent microstate populations) Arrhenius-like expression was obtained. When it was additionally assumed that the quantum states of each "system" species (reactant molecule, "activated complex," or product molecule) are internally equilibrated, i.e., that the molecules of a particular species present in the "system" at any given time are distributed among their microstates in the equilibrium ratio (even though the overall concentrations of the various "system" species are changing in time and are not in equilibrium with each other), then a modified version of Eyring's form⁽⁴⁾ for the Arrhenius expression was obtained. Specifically, the exponential dependence on a "free energy of activation"² was recovered, but the expression kT/h for the "frequency factor" was not.

As stated above, the treatment in I dealt exclusively with an idealized, simple process. The disparate complicating features of various individual types of real processes were ignored in I. In the particular case of chemical reactions there are three principal complicating features.

First, there is the fact that the barrier-traversing entities (called "subsystems" in I) of the system are not simply individual particles or individual molecules but rather stoichiometric combinations of molecules. Treatment of this necessitates a generalization of the stochastic master equation of I.

Second, there is the fact that, in the case of reactions proceeding in the absence of a large excess of inert diluent, certain degrees of freedom (translational, rotational, vibrational) of the reactant and product molecules themselves play the role of the activation-energy-supplying "reservoir" and the associated fact that, unless one reactant or product species is present in large excess, the nature of predominant reservoir degrees of freedom changes as the reaction proceeds. In such a case the assumption of internal equilibration of a species among its microstates may no longer be a good one (see below). Nevertheless, this case requires treatment in order that the consistency of the low-density limit of the stochastic approach under discussion with the familiar collision theory for this limit can be seen.

Third, there is the fact that in many cases of chemical reactions the "transition state" may not be sufficiently long-lived to be identified as a well-defined set of microstates (e.g., stationary states of the Hamiltonian).⁽¹⁾

² See Laidler⁽¹¹⁾ for a bibliography of the history of this concept of a "free energy of activation."

This is in contradistinction to the process treated in I, which might be exemplified by a restricted internal rotation in a molecule and for which the transition state could be identified as the set of all microstates with energy sufficiently high to constitute a quasi-free rotation either over or (via tunneling) through the top of the restriction potential barrier. In the case of a chemical reaction, however, the motion defining a "transition state" is that along a "reaction coordinate," and this has been recognized, at least for dilute gas reactions, to be more akin to a portion of a translation than to a contained motion like a rotation or vibration. Unlike a rotation or vibration, a portion (in the neighborhood of a potential barrier) of a translation may be expected to be short-lived; the "transition state" of a chemical reaction in a dilute gas probably decomposes to products (or reactants) very rapidly. While on the one hand, in the case of the internal rotation problem two distinct reactive events could be recognized—namely (1) "activation" to a reasonably well-defined rotator microstate from a librational microstate trapped in an "initial state" potential well and (2) "deactivation" to a liblator state in a "final state" potential well—on the other hand, in a dilute gas chemical reaction a single collisional event may send the reactants rapidly over the barrier and far into the product region; there need be no persistent high-energy oscillation or rotation to and from reactant and product regions, so the transition state will be "short-lived." In the case of a reaction in liquid solution, however, it is conceivable that the so-called solvent "cage" may in some cases constitute containing potential "walls" which provide the transition state with such longer lived oscillatory properties. Therefore both "short-lived" and "long-lived" (in the sense just described) transition states must be considered, though not for the same reaction.

This paper is devoted to expansion of the formulation of I in such a fashion as to allow for these complicating features of chemical reactions. To encompass the features associated with both "short-lived" and "long-lived" "activated complexes," we shall treat two limiting cases, one in which this complex suffers no collisions (other than the one that created it) during its evolution to products and one in which its interactions with other molecules during this period suffice to equilibrate the relative populations of its microstate populations). We shall find that the results for these two cases are remarkably similar and that the physical basis for this is such that one may also expect similar results for intermediate cases.

The stochastic master equation, which provides the point of departure for our analysis, should be at least schematically applicable to reactions in condensed phases as well as to those in the already well-understood gas phase.^(1,2,12)

However, as noted above, the treatment to be given here is not quantitatively applicable to all reactions. It is limited by the fact that we do make the

aforementioned assumption of (approximate) internal equilibration of microstates of each reactant or product species. This approximation is equivalent to the assumption that “nonreactive” events, i.e., ones in which molecules may change their microstates but not their chemical nature, are much more frequent than “reactive” ones. When this is true the system has ample time after each reactive event to reach such a restricted equilibrium, i.e., one subject to the constraint of fixed relative concentrations of the reacting species, before a subsequent reactive event can change these relative concentrations to new values.

One case in which this assumption may be an excellent one is that of a bimolecular reaction in sufficiently dilute solution. For such a reaction nonreactive but energy-redistributing events, which need only involve a single reactant molecule and solvent, are much more frequent than reactive events, which must involve two reactant molecules and (usually) solvent.

One case in which this assumption would be expected to be a poor one is that of dissociation (and recombination) of diatomic molecules in a single component phase. This reaction has been discussed in detail by Donoghue.⁽¹³⁾ Reactive and nonreactive events occur with frequencies that are of the same order of magnitude, so no Boltzmann distribution exists among the levels of reactants until total chemical equilibrium is reached. In particular the error made in the calculation of the associated rate constants with this assumption could be as much as a factor three.

Nevertheless, even for cases in which reactive events are not clearly less frequent than nonreactive ones, the development here should serve the didactic purpose of schematic illustration of the appearance, even without the assumption of equilibrium between reactants and activated complexes,⁽⁴⁾ of the dependence of rate constants on “free energies of activation” in condensed (as well as gaseous) media. More importantly, it shows the dependence of “frequency factors” on “effective numbers of states.” This latter feature should not disappear in a more general treatment, although its quantitative form could be altered. Its effect will often be enormous in comparison with the factor three of error introduced in the least favorable cases by the assumption of internal equilibration.

This assumption is not necessary for the appearance of a generalized version of Arrhenius temperature dependence of rate constants, as was seen in Eq. (7) of I. That equation, involving an Arrhenius exponential factor averaged over time-dependent microstate probabilities, could easily be generalized here. However, neither Eq. (7) of I nor its generalization are very useful, because the average involved cannot be evaluated in general. For a few simple cases, however, the averages can be evaluated and for these Widom⁽⁶⁾ has shown that no equilibrium assumptions, other than those that define the temperature (i.e., those involving the reservoir alone), are necessary

for the appearance of an Arrhenius exponential factor. Evaluation of the average in the general case involves a detailed examination of the full master equation of the system, which contains transition probabilities that involve nonreactive as well as reactive events. The master equation (9) employed here is a particular moment of this full equation, which involves only the reactive events (including the coupled reservoir transitions). When the transition probabilities for nonreactive events greatly exceed those for reactive ones, the internal equilibrium assumption is valid and we need only explicitly consider (9). The general discussion of chemical reactions when the reactive transition probabilities are comparable to nonreactive ones is a problem for further research.

The basic results to be obtained for the model treated here are that (1) although the rate constant proves to depend on a "free energy of activation" in the familiar exponential fashion, it does so for a physical reason different from that assigned to it by classical transition state theory, (2) the rate constant carries a preexponential factor that depends on the fundamental couplings involved in the reaction and is thus not simply kT/h , and (3) a dependence on an "effective number of states" is identifiable in this preexponential factor. The recognition of the existence of this dependence on "number of states" and of the physical basis for it may have important implications for interpretation of a possibly important feature of certain types of catalysis (specifically heterogeneous catalysis and catalysis by enzymes). A primary purpose of this paper is therefore to obtain and briefly discuss this particular result.

Section 2 presents the required general treatments. Section 3 presents specific results to which the general results of Section 2 reduce for the particular example of a second order reaction. Section 4 gives the brief discussion of the possible role of the "number of states" in catalysis. A subsequent paper⁽¹²⁾ will focus attention on that part of Section 3 that pertains to dilute gas reactions and will display more specifically the relation between the stochastic-theory results of Section 3 for these cases and the results obtainable from collision theory⁽⁴⁾ in these gas-phase cases.

2. TREATMENT OF THE GENERAL MODEL

As stated above, the principal assumptions defining the model treated here are that (1) transitions among microstates of the system-cum-reservoir are governed by a stochastic master equation and (2) the transition probabilities for nonreactive events greatly exceed those for reactive events. The latter will allow use of an equilibrium expression for the *ratio* of the population of any microstate (e.g., quantum level) of a given molecular species (reactant or product) to the population of any other microstate *of the same*

molecular species. It will in some cases also permit a similar treatment of the ratio of the population of any microstate of an "activated complex" to that of any other microstate of the "activated complex." It certainly does not permit the use of an equilibrium expression for the changing (as the reaction proceeds) ratio of the population of any (combined) microstate of (a stoichiometric combination of) reactant molecule(s) to the population of any microstate of a (stoichiometric mixture of) product(s). More to the point, it does not permit the use of an equilibrium expression for the ratio of the population of any microstate of activated complex to that of any microstate of a stoichiometric combination of reactant molecules (or product molecules).

Consider a chemical reaction of the general form

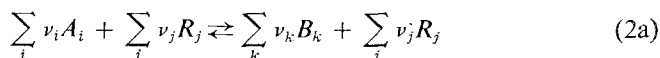


We will find it necessary to discuss two kinds of reactions. The first class includes reactions in which reactants go to products via an identifiable "activated complex" that persists long enough to equilibrate internally via nonreactive events ("collisions") before reacting to form products. The other class includes reactions that proceed via a very short-lived or virtual "activated complex" that decomposes to products before any nonreactive event has time to occur. In this case the "activated complex" is defined only via the requirement of a "threshold" energy for the single reactive collision event.⁽¹⁾ Clearly there is no sharp distinction between these two classes of "activated complexes." However, we would have suspected a priori that there would be a marked distinction between the two limiting cases. As we shall see, however, there proves to be no discernable differences between the important temperature dependencies in the limiting cases, and at least for low densities^(1,2) there proves to be very little difference between the "pre-exponential" factors that appear in the two limits.

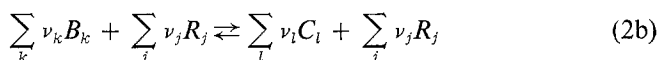
The net reaction (1) is unchanged by the inclusion (on both sides) of arbitrary numbers of "reservoir" molecules, which do not change their identity during the course of the reaction but do play a "reservoir" role in that certain of their degrees of freedom exchange energy (and momentum) with the reactants and products. We note that this role may be played either by molecules of a separate inert species or by molecules of the reacting species that, for a particular event, maintain their identity.

2.1. Long-Lived Complex

For the case involving the long-lived equilibrated "activated complex" we need to consider "activating" processes of the form



and “deactivating” processes of the form



in which R_j indicates a reservoir species (which, as explained above, may or may not be of the inert variety). In many cases the “transition state” $\sum_k \nu_k B_k$ can simply be conceived as a single ($k = 1$ only, $\nu_1 = 1$) “activated complex” B_1 . Mathematically, we only need investigate reactions of the form (2a), since these only differ by label changes from either those of the form (2b) or those of the direct $A \rightarrow C$ case (the case in which the “activated complex” is short-lived).

We use lower case notation, a_i , b_k , c_l , or r_j , to specify the particular (quantum or classical) microstate of a particular molecule of the chemical species denoted by the upper case symbol A_i , B_k , C_l , or R_j , respectively. With the general symbols x_s and X_s , where x_s represents a_i , b_k , c_l , or r_j , and where X_s represents A_i , B_k , C_l , or R_j , we bear in mind that for a particular choice of X_s the symbol x_s runs over its characteristic values (which may be discretely or continuously distributed), each value denoting a particular microstate of X_s .

We will need to consider each possible set \mathbf{a} of specifications of microstates a_i of a stoichiometric combination of interaction reactant molecules that collectively undergo a reactive transition. For every a_i of every A_i , the set \mathbf{a} contains ν_{a_i} molecules of type A_i in microstate a_i . The ν_{a_i} are constrained by the condition that their total must be just the stoichiometric coefficient ν_i in (1) and (2), i.e., that

$$\sum_{a_i} \nu_{a_i} = \nu_i \quad (3)$$

Inasmuch as the symbol \mathbf{a} designates for all reactant species A_i the number of molecules in each microstate a_i in the particular set \mathbf{a} , it clearly designates the composite microstate of the molecules in this interacting set of reactant molecules. We will of course need to consider all possible sets \mathbf{a} .

In exactly analogous fashion we introduce for “activated complex,” “product,” and “reservoir” molecules the concept of microstates of sets \mathbf{b} , \mathbf{c} , and \mathbf{r} , respectively. When we are dealing with statements that are true for all of these types of sets we shall naturally use the notation \mathbf{x} . Accordingly, we write, for each set \mathbf{x} ,

$$\sum_{x_s} \nu_{x_s} = \nu_s \quad (3')$$

the generalization of (3).

In the master equation that we shall use to describe the rate of (2a), for example, we shall assume that the rate of each transition contributing

to the forward component, for example, of process (2a) will be proportional to the relevant products of microstate concentrations $(n_{a_1})^{v_{a_1}} \cdots (n_{a_2})^{v_{a_2}} \cdots$ of reactant species A_1, A_2, \dots and of reservoir microstate concentrations $(n_{r_1})^{v_{r_1}} \cdots (n_{r_2})^{v_{r_2}} \cdots$. Thus it will be convenient to introduce the “concentration” $\bar{n}_{\mathbf{x}}$ of composite microstate \mathbf{x} by

$$\bar{n}_{\mathbf{x}} = \prod_s \prod_{x_s} (\bar{n}_{x_s})^{v_{x_s}} \quad (4)$$

where \bar{n}_{x_s} is a dimensionless³ measure of the concentration of chemical species X_s in microstate x_s .

With this notation we can write the “master equation” in an especially concise form. The obvious generalization of the master equation used in I for the flux $q_{\mathbf{AB}}(t)$ of conversion of reactants to activated complexes at time t is

$$\begin{aligned} q_{\mathbf{AB}}(t) &\equiv -(1/v_i) d\bar{n}_{A_i}(t)/dt \\ &= \sum_j \sum_{v_j=0}^{\infty} \sum_{\substack{\mathbf{a}, \mathbf{b}, \\ \mathbf{r}, \mathbf{r}'}} [W(\mathbf{ar}'|\mathbf{br})\bar{n}_{\mathbf{r}'}(t)\bar{n}_{\mathbf{a}}(t) \\ &\quad - W(\mathbf{br}|\mathbf{ar}')\bar{n}_{\mathbf{r}}(t)\bar{n}_{\mathbf{b}}(t)] \end{aligned} \quad (5)$$

where $\bar{n}_{A_i}(t) = \sum_{a_i} \bar{n}_{a_i}(t)$ and $W(\mathbf{ar}'|\mathbf{br})$ is the transition probability for (composite) microstates \mathbf{a} and \mathbf{r}' going to microstates \mathbf{b} and \mathbf{r} . $W(\mathbf{br}|\mathbf{ar}')$ is the corresponding transition probability for the inverse process.

In conventional uses of master equations the dependence on reservoir microstate concentrations is usually lumped together with that on transition probabilities. Thus, transition probabilities $W(\mathbf{a}|\mathbf{b})$ are used; these bring averages over all reservoir processes that can supply the energy requisite to the $\mathbf{a} \rightarrow \mathbf{b}$ activation. The advantage, to be realized below, of explicit retention of this summation over \mathbf{r}, \mathbf{r}' , as well that over \mathbf{a}, \mathbf{b} , is that each term of the sum over $\mathbf{r}', \mathbf{r}, \mathbf{a}, \mathbf{b}$ corresponds to complete specification of a total transition that must both conserve energy,

$$E_{\mathbf{a}} + E_{\mathbf{r}'} = E_{\mathbf{b}} + E_{\mathbf{r}} \quad (6)$$

and obey microreversibility,

$$W(\mathbf{ar}'|\mathbf{br}') = W(\mathbf{br}'|\mathbf{ar}) \quad (7)$$

³ \bar{n}_{x_s} is related to the number density n_{x_s} of species X_s in microstate x_s by

$$\bar{n}_{x_s} = \gamma_{x_s} n_{x_s}$$

where γ_{x_s} , having dimensions of a volume, is a measure of the volume unit appropriate for the species X_s . In a subsequent paper⁽¹²⁾ we shall see that at low densities γ_{x_s} is just the cube of the thermal wavelength of the X_s th species. The total density of chemical species X_s is related to all the \bar{n}_{x_s} by

$$n_{X_s} = \sum_{x_s} n_{x_s} = (1/\gamma_{x_s}) \sum_{x_s} \bar{n}_{x_s}$$

Before utilizing these, however, we introduce the assumption discussed above concerning the ratio of populations of states internal to a particular species. Thus we write

$$\bar{n}_{x_s}(t) = \bar{n}_{X_s}(t) \exp[-\beta(E_{x_s} - F_{X_s})] \equiv \bar{n}_{X_s}(t) P_{x_s} \quad (8)$$

where

$$\exp(-\beta F_{X_s}) = \sum_{x_s} \exp(-\beta E_{x_s}), \quad \beta = 1/kT$$

and where we recognize that each total (dimensionless) concentration \bar{n}_{X_s} (e.g., each \bar{n}_{A_i} and each \bar{n}_{C_i}) may change as the reaction proceeds and is not necessarily equilibrated with any other \bar{n}_{X_s} (\bar{n}_{A_i} , \bar{n}_{C_i} , or \bar{n}_{B_r}). From this and Eqs. (3) and (4) it follows that

$$\bar{n}_{\mathbf{x}}(t) = \bar{n}_{\mathbf{X}}(t) \exp[-\beta(E_{\mathbf{x}} - F_{\mathbf{X}})] \equiv \bar{n}_{\mathbf{X}}(t) P_{\mathbf{x}} \quad (9)$$

where

$$\bar{n}_{\mathbf{X}}(t) = \prod_s [\bar{n}_{X_s}(t)]^{\nu_s}$$

and

$$E_{\mathbf{x}} = \sum_s \sum_{x_s} \nu_{x_s} E_{x_s}, \quad F_{\mathbf{X}} = \sum_s \nu_s F_{X_s}$$

When (9) and (7) are substituted into the master equation (5) the latter becomes

$$q_{\mathbf{AB}}(t) = \sum_{j, \nu_j} \sum_{\substack{\mathbf{ab} \\ \mathbf{rr}'}} W(\mathbf{ar}'|\mathbf{br}) [\bar{n}_{\mathbf{A}}(t) P_{\mathbf{a}} P_{\mathbf{r}'} - \bar{n}_{\mathbf{B}}(t) P_{\mathbf{b}} P_{\mathbf{r}}] \bar{n}_{\mathbf{R}}(t) \quad (10)$$

Now utilizing energy conservation, (6), we have

$$P_{\mathbf{a}} P_{\mathbf{r}'} = P_{\mathbf{b}} P_{\mathbf{r}} \exp[-\beta(F_{\mathbf{B}} - F_{\mathbf{A}})] \quad (11)$$

an expression the validity of which does *not* imply an equilibrium between *a* and *b*.

When (11) is substituted into (10) the latter reduces to

$$q_{\mathbf{AB}}(t) = \{\bar{n}_{\mathbf{A}}(t) \exp[-\beta(F_{\mathbf{B}} - F_{\mathbf{A}})] - \bar{n}_{\mathbf{B}}(t)\} \\ \times \sum_{j, \nu_j} \sum_{\substack{\mathbf{ab} \\ \mathbf{rr}'}} W(\mathbf{ar}'|\mathbf{br}) P_{\mathbf{b}} \bar{n}_{\mathbf{r}}(t) \quad (12)$$

The physical basis of this appearance of a "free energy of activation" is the subject of a brief commentary in the discussion in Section 5.

To simplify notation, we define a quantity $W_{\mathbf{AB}}^{\nu}$ by

$$W_{\mathbf{AB}}^{\nu} = \sum_{\substack{\mathbf{ab} \\ \mathbf{rr}'}} W(\mathbf{ar}'|\mathbf{br}) P_{\mathbf{b}} P_{\mathbf{r}} \quad (13)$$

where the superscript denotes an average for a fixed set ν of ν_j 's, and the general rate equation becomes

$$q_{\mathbf{AB}}(t) = \{\bar{n}_{\mathbf{A}}(t) \exp[-\beta(F_{\mathbf{B}} - F_{\mathbf{A}})] - \bar{n}_{\mathbf{B}}(t)\} \sum_{\nu} W_{\mathbf{AB}}^{\nu} \bar{n}_{\mathbf{R}}(t) \quad (14)$$

where we have written the sum over all j, ν_j , as a sum over all sets ν .

In the case in which all the reservoir species are distinct from reactants (large excess of inert species) $n_{\mathbf{R}}(t)$ is independent of time. For this case (14) is formally similar to the equation obtained in I,

$$q_{\mathbf{AB}}(t) = W_{\mathbf{AB}} \{\bar{n}_{\mathbf{A}}(t) \exp[-\beta(F_{\mathbf{B}} - F_{\mathbf{A}})] - \bar{n}_{\mathbf{B}}(t)\} \quad (15)$$

where

$$W_{\mathbf{AB}} = \sum_{\nu} W_{\mathbf{AB}}^{\nu} \bar{n}_{\mathbf{R}}$$

From similar consideration of (2b) we obtain an equation for $q_{\mathbf{CB}}(t)$ that is exactly analogous to (15).

Whether the reservoir species are reacting or not, the activation free energy differences will dominate the temperature dependence of these rates. With regard to the magnitude of the residual temperature dependence in $W_{\mathbf{AB}}$, it should be recalled that in the analysis leading from Eq. (5) to Eq. (12), we eliminated the "concentration" $\bar{n}_{\mathbf{r}}$, of the higher energy member of the pair of reservoir microstates involved in a transition by expressing it in terms of the concentration $\bar{n}_{\mathbf{r}}$, of the corresponding lower energy member⁴ with use of the Boltzmann distribution in the reservoir. Thus it is the weighting $P_{\mathbf{r}}$ of the lower energy member \mathbf{r} that survives in the expression (13) for $W_{\mathbf{AB}}^{\nu}$. Since nonzero values of $W(\mathbf{ar}'|\mathbf{br})$ are permissible for "lower" reservoir microstates \mathbf{r} of any energy, and since $P_{\mathbf{r}}$ is normalized, there is no reason to expect a large temperature dependence in $W_{\mathbf{AB}}$. If, on the other hand, we had alternatively used the Boltzmann expression to eliminate the concentration $\bar{n}_{\mathbf{r}}$ of the lower energy member of the reservoir microstate pair in favor of that, $\bar{n}_{\mathbf{r}'}$, of the higher energy member, we would have obtained an expression for $W_{\mathbf{AB}}$ involving the weighting factor $P_{\mathbf{r}'}$. With respect to \mathbf{r}' , nonzero values of $W(\mathbf{ar}'|\mathbf{br})$ do not begin with the lowest energy that a reservoir microstate \mathbf{r}' can possess but rather with an energy lying above the lowest by the quantity $E_{\mathbf{b}} - E_{\mathbf{a}}$ (see footnote 4). As a consequence of this "gap," the presence of the normalized factor $P_{\mathbf{r}'}$ in an expression for the preexponential quantity $W_{\mathbf{AB}}^{\nu}$ would introduce into it an enormous temperature dependence, which would be correspondingly compensated by the

⁴ Of course we recognize that we may include, in the sum over transition probabilities, transitions in which $E_{\mathbf{a}} > E_{\mathbf{b}}$ for some \mathbf{a} and \mathbf{b} . In this case the "concentration" $\bar{n}_{\mathbf{r}}$ of "lower" energy member of the pair of reservoir microstates is really that of the higher energy member. This contradiction in terminology is of no consequence so long as the terms in which $E_{\mathbf{b}} > E_{\mathbf{a}}$ dominate the sum. This is assured if $F_{\mathbf{B}} > F_{\mathbf{A}}$.

altered sign [as compared with (15)] in the exponential factor that such an ill-considered formulation would entail. In the formulation used here and in I, however, the principal recognizable temperature dependence has been compressed into a single factor, which is then found to be of the form of the familiar simple exponential dependence on a free energy of activation. Further, but hardly exhaustive, discussion of the possible temperature dependence of an averaged transition probability proportional to $W_{\mathbf{AB}}$ can be found in Section IV of I.

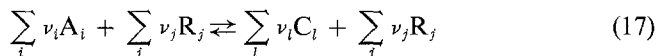
As in I, we can eliminate the "activated complex" concentration $\bar{n}_{\mathbf{B}}(t)$ from (15) and its analog for $q_{\mathbf{CB}}$ via a steady state approximation. This procedure yields

$$\begin{aligned} q(t) &= q_{\mathbf{AB}}(t) = q_{\mathbf{BC}}(t) = -q_{\mathbf{CB}}(t) \\ &= \frac{W_{\mathbf{AB}}W_{\mathbf{CB}}}{W_{\mathbf{AB}} + W_{\mathbf{CB}}} \\ &\quad \times \{\bar{n}_{\mathbf{A}}(t) \exp[-\beta(F_{\mathbf{B}} - F_{\mathbf{A}})] - n_{\mathbf{C}}(t) \exp[-\beta(F_{\mathbf{B}} - F_{\mathbf{C}})]\} \quad (16) \end{aligned}$$

When the reacting species also play the role of reservoir, the W 's in (16) will be time dependent as a consequence of their dependence on $\bar{n}_{\mathbf{R}}(t)$.

2.2. Short-Lived Complex

When the reaction (1) proceeds via a short-lived or "virtual" "activated complex" it is meaningless to employ (8) and (9) for \mathbf{B} along with a steady state approximation. In this case the intermediate complex reacts to form products before it has a chance to undergo equilibrating "collisions." It is then necessary to consider the rate equation for the direct process



By the same argument as presented above, we obtain a rate equation for (17),

$$q(t) = q_{\mathbf{AC}}(t) = \sum_{\mathbf{v}} W_{\mathbf{AC}}^{\mathbf{v}} \bar{n}_{\mathbf{R}}(t) \{\bar{n}_{\mathbf{A}}(t) \exp[-\beta(F_{\mathbf{C}} - F_{\mathbf{A}})] - \bar{n}_{\mathbf{C}}(t)\} \quad (18)$$

where

$$W_{\mathbf{AC}}^{\mathbf{v}} = \sum_{\substack{\mathbf{ac} \\ \mathbf{r}\mathbf{r}'}} W(\mathbf{ar}' | \mathbf{cr}) P_{\mathbf{c}} P_{\mathbf{r}}$$

and where

$$E_{\mathbf{a}} + E_{\mathbf{r}'} = E_{\mathbf{c}} + E_{\mathbf{r}} \quad (19)$$

Written in this form, Eq. (18) in this case still carries in its preexponential factor $W_{\mathbf{AC}}^{\mathbf{v}}$ the principal temperature dependence caused by a potential

barrier. The main effect of a potential barrier in this case of a direct $A \rightarrow C$ process is to impose a threshold energy condition on microstate combinations \mathbf{a} , \mathbf{r}' and \mathbf{c} , \mathbf{r} that are to yield nonzero transition probabilities $W(\mathbf{ar}'|\mathbf{cr})$. We therefore look for a version of (19) in which this energy "gap" and consequent temperature dependence have been removed from the pre-exponential factor.

Since we are assuming in this case that the reaction proceeds via the formation of a set of complexes \mathbf{B} (often a single complex) that decay into products before any nonreactive event can occur, the intermediate complexes in each reactive event must have the same energy as both the reactant combination and the product combination. Thus for each set of complexes \mathbf{b} formed in a given event there are sets \mathbf{a} and \mathbf{r}' such that

$$E_b = E_a + E_{r'} = E_c + E_r \quad (20)$$

We assume that the nonzero $W(\mathbf{ar}'|\mathbf{cr})$ all satisfy

$$E_b = E_a + E_{r'} \geq E_b^0 \quad (21)$$

i.e., that E_b^0 is the "threshold" energy for the reaction.

With this condition the summation in (18) can be written as

$$\begin{aligned} W_{\mathbf{AC}}^y &= \sum_{\substack{\mathbf{a}, \mathbf{b}, \mathbf{c} \\ \mathbf{r}, \mathbf{r}'}} \Delta(E_a + E_{r'}|E_b) W(\mathbf{ar}'|\mathbf{cr}) \exp[-\beta(E_b - F_{\mathbf{C}} - F_{\mathbf{R}})] \\ &= \{\exp[-\beta(F_{\mathbf{B}} - F_{\mathbf{C}} - F_{\mathbf{R}})]\} \\ &\quad \times \sum_{\mathbf{b}} P_{\mathbf{b}} \left[\sum_{\substack{\mathbf{a}, \mathbf{c} \\ \mathbf{r}, \mathbf{r}'}} \Delta(E_a + E_{r'}|E_b) W(\mathbf{ar}'|\mathbf{cr}) \right] \end{aligned}$$

where

$$\Delta(E_a + E_{r'}|E_b) = \begin{cases} 1 & \text{if } E_b = E_a + E_{r'} \\ 0 & \text{otherwise} \end{cases} \quad (22)$$

We see that $W_{\mathbf{AC}}^y$ is of the form

$$W_{\mathbf{AC}}^y = \bar{W}_{\mathbf{AC}}^y \exp[-\beta(F_{\mathbf{B}} - F_{\mathbf{C}} - F_{\mathbf{R}})] \quad (23)$$

where

$$\bar{W}_{\mathbf{AC}}^y = \sum_{\mathbf{b}} P_{\mathbf{b}} \left[\sum_{\substack{\mathbf{a}, \mathbf{c} \\ \mathbf{r}, \mathbf{r}'}} \Delta(E_a + E_{r'}|E_b) W(\mathbf{ar}'|\mathbf{cr}) \right]$$

With this substitution, (18) becomes

$$\begin{aligned} q(t) &= \sum_{\mathbf{y}} \bar{W}_{\mathbf{AC}}^y \bar{n}_{\mathbf{R}}(t) \\ &\quad \times \{\bar{n}_{\mathbf{A}}(t) \exp[-\beta(F_{\mathbf{BR}} - F_{\mathbf{A}})] - \bar{n}_{\mathbf{C}}(t) \exp[-\beta(F_{\mathbf{BR}} - F_{\mathbf{C}})]\} \quad (24) \end{aligned}$$

where

$$F_{\mathbf{BR}} = F_{\mathbf{B}} - F_{\mathbf{R}}$$

A difficulty is that each $F_{\mathbf{BR}}$ depends on its set \mathbf{v} . However, we can rewrite (24) in terms of an average "free energy of activation" when the time dependence of $n_{\mathbf{R}}$ may be neglected. Thus we may write

$$q_{\mathbf{AC}}(t) = \overline{W}_{\mathbf{AC}}\{\bar{n}_{\mathbf{A}}(t) \exp[-\beta(\bar{F}_{\mathbf{B}} - F_{\mathbf{A}})] - \bar{n}_{\mathbf{C}}(t) \exp[-\beta(\bar{F}_{\mathbf{B}} - F_{\mathbf{C}})]\} \quad (25)$$

where

$$\exp(-\beta\bar{F}_{\mathbf{B}}) = \sum_{\mathbf{v}} \exp(-\beta F_{\mathbf{BR}})$$

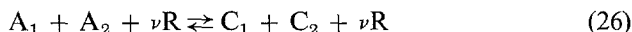
and

$$\overline{W}_{\mathbf{AC}} = \sum_{\mathbf{v}} W_{\mathbf{AC}}^{\mathbf{v}} \bar{n}_{\mathbf{R}} \exp[-\beta(F_{\mathbf{BR}} - \bar{F}_{\mathbf{B}})]$$

Thus we see that, regardless of the lifetime of the intermediate, an "activation free energy" appears in the rate expression wherever the formation of the "activated complex" involves a true activation. In a subsequent paper we will see that, for a particular case at low densities with no inert reservoir present, the rate expressions (16) and (25) are simply related. Equation (25) is a generalization of the results of the classic paper of Ross and Mazur,⁽¹⁾ in which it was shown that a free energy of activation appears whenever the reactive cross section for a bimolecular reaction has a threshold. We will make more detailed contact with their results as well as with those of Eu and Ross⁽²⁾ in a subsequent paper.⁽¹²⁾

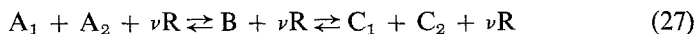
3. ILLUSTRATIVE EXAMPLE

Here we illustrate the results of Section 2 by considering the particular example of a second order reaction. Thus we consider



where R is a single reservoir species (e.g., solvent) and ν can take on arbitrary nonnegative integral values. To keep the example simple, however, we retain only $\nu = 0$ and $\nu = 1$; the essential structure of the equations including arbitrary ν will be obvious.

First we treat the case in which (26) proceeds via a relatively long-lived "activated complex." We depict this mechanism as



For this reaction (16) is

$$\begin{aligned} q(t) = q_{\mathbf{AB}}(t) = -q_{\mathbf{CB}}(t) &= \frac{W_{A_1 A_2 B} W_{C_1 C_2 B}}{W_{A_1 A_2 B} + W_{C_1 C_2 B}} \\ &\times \{\bar{n}_{A_1}(t) \bar{n}_{A_2}(t) \exp[-\beta(F_B - F_{A_1} - F_{A_2})] \\ &- \bar{n}_{C_1}(t) \bar{n}_{C_2}(t) \exp[-\beta(F_B - F_{C_1} - F_{C_2})]\} \quad (28) \end{aligned}$$

where

$$W_{A_1A_2B} = W_{A_1A_2B}^0 + W_{A_1A_2B}^1 \bar{n}_R$$

with

$$W_{A_1A_2B}^0 = \sum_{a_1 a_2 b} W(a_1 a_2 | b) P_b$$

and

$$W_{A_1A_2B}^1 = \sum_{\substack{a_1 a_2 b \\ r r'}} W(a_1 a_2 r' | b r) P_b P_r$$

$W_{C_1C_2B}$ is given by a totally analogous expression.

We wish to compare this with the "direct" bimolecular reaction, also of the form (26), in which the "activated complex" decays so rapidly that it never encounters a nonreactive event. Then (25) reduces to

$$\begin{aligned} q(t) = & \bar{W}_{A_1A_2C_1C_2} \{ \bar{n}_{A_1}(t) \bar{n}_{A_2}(t) \exp[-\beta(\bar{F}_B - F_{A_1} - F_{A_2})] \\ & - \bar{n}_{C_1}(t) \bar{n}_{C_2}(t) \exp[-\beta(\bar{F}_B - F_{C_1} - F_{C_2})] \} \end{aligned} \quad (29)$$

where

$$\exp(-\beta\bar{F}_B) = \exp(-\beta F_B) + \exp[-\beta(F_{B_1} - F_R)]$$

and

$$\begin{aligned} \bar{W}_{A_1A_2C_1C_2} = & \bar{W}_{A_1A_1C_1C_2} \exp[-\beta(F_B - \bar{F}_B)] \\ & + \bar{W}_{A_1A_2C_1C_2}^1 \{ \exp[-\beta(F_{B_1} - F_R - \bar{F}_B)] \} \bar{n}_R \end{aligned}$$

with

$$\bar{W}_{A_1A_2C_1C_2} = \sum_b P_b \sum_{\substack{a_1 a_2 \\ b_1 b_2}} \Delta(E_{a_1} + E_{a_2} | E_b) W(a_1 a_2 | c_1 c_2)$$

$$\exp(-\beta F_B) = \sum_b \exp(-\beta E_b)$$

$$\bar{W}_{A_1A_2C_1C_2}^1 = \sum_{b_1} P_{b_1} \sum_{\substack{a_1 a_2 r' \\ b_1 b_2 r}} \Delta(E_{a_1} + E_{a_2} + E_{r'} | E_{b_1}) W(a_1 a_2 r' | c_1 c_2 r')$$

and

$$\exp(-\beta F_{B_1}) = \sum_{b_1} \exp(-\beta F_{b_1})$$

Noting that, when $F_{B_1} = F_B + F_R$, $\bar{F}_B = F_B$, we see that (29) and (28) are similar in form not only to each other but also to the corresponding equation of the classical transition state theory, with the exception that the frequency factors in (29) and (28) involve the fundamental couplings in the

system (through the microscopic transition probabilities) and are not simply kT/h .

4. PRE-EXPONENTIAL FACTORS AND THE IMPLICATIONS FOR CATALYSIS BY LARGE MOLECULES OR CRYSTALS

The pre-exponential factors W_{AB} and W_{CB} in (16) can be observed to contain strong dependences on effective numbers of initial states and final states, respectively. This point was originally recognized in I for the special case treated there and will be examined both more generally and more precisely here. Consider, for example, W_{AB}^{ν} in Eq. (13),

$$W_{\text{AB}}^{\nu} = \sum_{\substack{\mathbf{ab} \\ \mathbf{r}\mathbf{r}'}} W(\mathbf{ar}'|\mathbf{br})P_{\mathbf{b}}(T)P_{\mathbf{r}}(T) \quad (30)$$

where we explicitly indicate that the thermal weighting factors are evaluated at temperature T .

We observe that only the sums over \mathbf{r} and \mathbf{b} in (30) are weighted thermal averages. The sums over \mathbf{a} and \mathbf{r}' are unweighted as they stand. If the transition probabilities $W(\mathbf{ar}'|\mathbf{br})$ were all to have the same value W_0 for total energy ($E_{\mathbf{a}} + E_{\mathbf{r}'} = E_{\mathbf{b}} + E_{\mathbf{r}}$) less than some cutoff energy (a cutoff being necessary to make the sum converge in this unrealistic example), then W_{AB}^{ν} would be equal to W_0 times the number of states $\{\mathbf{a}, \mathbf{r}'\}$ having total energy less than this cutoff energy. Indeed we may in general expect the sum to be given by

$$W_{\text{AB}}^{\nu} = \Omega_{\text{AR}}^{\nu} \overline{W}_{\text{AB}}^{\nu} \quad (31)$$

where Ω_{AR}^{ν} is an effective number of initial states that contribute to the reaction and $\overline{W}_{\text{AB}}^{\nu}$ is an average transition probability. In the appendix we show that the identification

$$\Omega_{\text{AR}}^{\nu} = [\delta E_{\text{AR}}^w / \delta E_{\text{AR}}(T_w^{\nu})] \exp\{[S_{\text{A}}(T_w^{\nu}) + S_{\text{R}}(T_w^{\nu})]/k\} \quad (32)$$

is an especially convenient one. $S_{\text{A}}(T_w^{\nu})$ and $S_{\text{R}}(T_w^{\nu})$ are the reactant and reservoir entropies evaluated at the "effectiveness temperature" T_w^{ν} . This temperature is defined by Eq. (A.15) of the appendix. The variances $\delta E_{\text{AR}}(T)$ and δE_{AR}^w are just rms energy fluctuations defined in Eqs. (A.8) and (A.16) of the appendix. The ratio of these variances should be of order unity. Thus the principal contribution of Ω_{AR}^{ν} comes from the entropy factors. The energy kT_w^{ν} determines the effective cutoff energy for the purpose of counting the number of effective initial states.

Although the factors Ω_{AR}^{ν} and $\overline{W}_{\text{AB}}^{\nu}$ of the expression (31) for W_{AB}^{ν} and the analogous factors Ω_{CR}^{ν} and $\overline{W}_{\text{CB}}^{\nu}$ are no easier to evaluate precisely than W_{AB}^{ν} and W_{CB}^{ν} , this decomposition into factors representing effective

numbers of states and average transition probabilities does assist in the identification of situations in which the overall "frequency factor" may be exceptionally large. Specifically it suggests that "large" catalysts, that is catalysts containing large numbers of degrees of freedom and therefore large numbers of microstates, may accelerate reactions in part by raising the effective number of states participating in the reaction. Consider, for example, situations in which the rates of binding of reactants to enzymes or to solid catalysts are fast relative to the subsequent reactions taking place in the enzyme-substrate or solid-substrate complexes and in which rates of release of products from enzymes or solids are also fast in this sense. In such cases the transformations occurring within the complexes are the rate-controlling steps and the enhancements of the factors Ω_{AR}^{ν} and Ω_{CR}^{ν} that the bound enzymes or solid catalysts may contribute to these steps can be significant for the rates of the overall reactions.

In cases in which a reactant molecule is actually chemically bound to an enzyme it would seem most natural to treat the enzyme as part of the initial species **A** for the rate-controlling reaction step. In cases in which the binding is less strong, it might seem more natural to treat the enzyme as part of the reservoir **R**. If the enzyme remains chemically unaltered in this step (as well as for the overall reaction), the choice is an arbitrary one, a circumstance which must be reflected in the theory. We note that the factor Ω_{AR} is indeed symmetric with respect to reactant **A** and reservoir **R**.

This discussion has been given in terms of the case involving a "long-lived activated complex" and involving only a single important value of ν . In the appendix it is shown that similar conclusions are obtained when all values of ν are considered as well as when the "activated complex" is "short-lived."

A typical enzyme has on the order of 10^5 vibrational degrees of freedom. (It will be shown in a subsequent paper that, at least at low densities, only internal, as opposed to translational, degrees of freedom contribute significantly to Ω). If, for example, four of these can effectively couple to the reaction and each possesses roughly ten discrete quantum levels, then the density of initial states Ω_{AR} will be greater by a factor 10^4 in the enzymatically catalyzed case than in the case in which no such large catalyst is present.

5. DISCUSSION

The principal results are most concisely stated in the general equations (13), (16), (25), and (31).

It was emphasized in Section 1 that the familiar assumption of equilibrium between initial state and transition state (or activated complex) is not required in the formulation of this stochastic model of chemical kinetics.

It should now also be clear that the physical basis of the appearance of an exponential dependence on a "free energy of activation" in the analysis leading to Eqs. (16) and (25) is different from that which underlies the conventional treatment. In the latter no such exponential dependence on a free energy of activation appears in any expression for the net flux of activation, which we have here called q_{AB} in the case of the "long-lived" activated complex (the only case considered in the conventional treatment). Rather, it originates, in the conventional treatment, in the expression for what we have here called q_{BC} for this case; its origin in q_{BC} is a consequence of the dependence of q_{BC} on n_B , which is assumed, in the conventional treatment, to be in Boltzmann equilibrium with n_A . In the present formulation, however, equilibrium between **A** and **B**, i.e., $q_{AB} = 0$, is a condition for no net reaction at all. Rather, the exponential dependence of a nonzero reaction flux on a "free energy of activation" originates in q_{AB} (as well as q_{BC}). Its appearance in q_{AB} is a consequence of the fact that q_{AB} depends not only on all the n_a but also on all the n_r (Eqs. (3) and (5)). In accordance with energy conservation, each reservoir microstate r' that is to supply effectively the requisite activation energy $E_b - E_a$ must lie above the microstate r to which it decays by precisely the amount $E_b - E_a$. Since $n_{r'}$ and n_r are, in the model, governed by rapid, frequent nonreactive events, they are in relative equilibrium, so that $n_{r'}$ can be expressed in terms of n_r by a Boltzmann formula involving $E_{r'} - E_r = E_b - E_a$ [Eq. (11)]. With summation over r the latter accounts for the Arrhenius factor in terms of $E_b - E_a$. When the summation over all **a**, **b** is performed, the Arrhenius energy dependence emerges as a free energy dependence.

Equations (16) and (25) show that the zero-flux, i.e., equilibrium, condition is precisely the thermodynamic condition, according to which the (standard) free energy change $F_C - F_A$ for the overall (**A** \rightarrow **C**) reaction is related to the "equilibrium constant" \bar{n}_C/\bar{n}_A by

$$F_C - F_A = -kT \ln(\bar{n}_C/\bar{n}_A) \quad (33)$$

That this result has been obtained in this stochastic treatment may, at first sight, appear to be simply a consequence of the assumption of Boltzmann equilibrium in the reservoir. However, the fact that the reacting system reaches its state of zero flux at precisely the point where it has been locked into a distribution function of the same form as that in the reservoir is a consequence of energy conservation [Eq. (8)] and microscopic reversibility [Eq. (9)]. Indeed the Boltzmann distribution itself can be very simply derived by use of these principles in conjunction with a stochastic master equation of the form of (7), with only the added assumption that the zero-flux condition is obtained by "detailed balancing."⁽¹⁴⁾

We have thus seen that this stochastic model does yield the well-known

factors involving free energies of activation, and therefore energies and entropies of activation, for forward and backward rates, which combine in the long-time (zero-flux) limit in the familiar fashion to reduce to the correct description of equilibrium concentrations in terms of energy and entropy changes for the overall reaction. It is nonetheless true, however, that the total dependence of the absolute values of the forward and backward rates on entropy factors associated with the reacting molecules, including the entropy dependence now identifiable in the "frequency factor," is not primarily a dependence on entropies of activation (ΔS^\ddagger in the usual notation) but is often more nearly a dependence on the absolute value of the entropy S^\ddagger of the activated state alone. To see this, consider the special case in which the shape and depth of the initial state potential well are similar to those of the final state. In such a situation

$$\overline{W}_{\mathbf{AB}}^{\mathbf{v}} = \overline{W}_{\mathbf{CB}}^{\mathbf{v}} = W \quad (34)$$

$$\Omega_{\mathbf{AR}}^{\mathbf{v}} = \Omega_{\mathbf{CR}}^{\mathbf{v}} = \Omega \quad (35)$$

and

$$\Omega \approx \exp\{[S(T_w) + S_{\mathbf{R}}(T_w)]/k\} \quad (36)$$

[where $S(T) = S_{\mathbf{A}}(T) = S_{\mathbf{C}}(T)$] in accordance with Eq. (A.19) [the ratio of variances has been omitted from (36) because it is generally of order unity]. If $T_w \approx T$, then the factor $e^{S(T_w)/k}$ from the frequency factor may be readily combined with the common factors $e^{-S(T)/k}$ from the (exponentials of) free energies of activation for forward and reverse reactions to yield for the forward and reverse rate constants

$$\begin{aligned} k_f &= \frac{1}{2}W \exp[-\beta(E_{\mathbf{B}} - E_{\mathbf{A}})] \exp[(S_{\mathbf{B}} + S_{\mathbf{R}})/k] \\ &\equiv \frac{1}{2}W \exp(-\beta \Delta E_f^\ddagger) \exp(S^\ddagger/k) \end{aligned} \quad (37)$$

and

$$\begin{aligned} k_r &= \frac{1}{2}W \exp[-\beta(E_{\mathbf{B}} - E_{\mathbf{C}})] \exp[(S_{\mathbf{B}} + S_{\mathbf{R}})/k] \\ &\equiv \frac{1}{2}W \exp(-\beta \Delta E_r^\ddagger) \exp(S^\ddagger/k) \end{aligned} \quad (38)$$

The reasonableness of this result is most clearly seen by application of the same considerations to the expression (14) for $q_{\mathbf{AB}}$ rather than, as above, to the expression (16) for the overall reaction flux. As applied to the forward component, for example, of $q_{\mathbf{AB}}$, these considerations indicate that the rate of transition from initial state to transition state depends on the "number of states" of activated complex [i.e., on $\exp(S^\ddagger/k)$] but not on the number of initial states. Inasmuch as the activated complex is the "final state" of this forward component of $q_{\mathbf{AB}}$, we see that this result conforms to the "golden

rule" of Fermi, according to which the flux associated with a simple transition is proportional to the density of final states for the simple transition but is not dependent on the density of initial states.⁵

It is, of course, this primary entropic dependence of a reaction rate on $\exp(S^\ddagger/k)$ rather than on $\exp(\Delta S^\ddagger/k)$ that underlies the considerations of section 4 concerning a possible feature of catalysis by enzymes or solid catalysts. If, in addition to the oft-considered catalytic lowering of ΔE^\ddagger there existed only the possibility of catalytic alteration of ΔS^\ddagger (i.e., if the constant factor kT/h were the correct frequency factor), then binding of reactants to particles with large densities of states, such as enzymes and solids, would not of itself have any obvious effect, since the entropies of the initial and activated states would be raised by roughly the same amounts and these changes would be cancelled out in ΔS^\ddagger . The present analysis indicates, however, that the larger values of S^\ddagger attributable to enzyme-reactant or solid-reactant activated complexes, as compared with those of unbound reactant activated complexes, are not totally offset in their influence on reaction rate by the correspondingly larger values of entropies of initial states.

It should be borne in mind, however, that, as shown in the analysis in Section 4 and in the appendix, to count as part of $\exp(S^\ddagger/k)$, the microstates (levels) of a catalyst degree of freedom must be effectively coupled⁶ (through significant values of associated transition probabilities) to the appropriate reactive degrees of freedom of the reacting molecules. For this reason it cannot be stated that this observation concerning a possibly important entropic effect of catalysis by large particles is a necessary consequence of the stochastic model for kinetics presented here. The stochastic model raises this as a possibility but by itself cannot ensure that the transition probabilities W have the requisite properties for realization of the effect.

The foregoing extension of an adaptation⁽¹⁰⁾ of the stochastic approach to chemical kinetics suggests that the stochastic model may provide the structure for an at least didactically useful bridge between, on one hand, some of the concepts of the transition state theory⁽⁴⁾ and, on the other hand, the various aspects of collision theory. The approach leading to the rather firm ground of the collision treatment^(1,2) of bimolecular dilute gas reactions will be discussed in a subsequent paper. Tests of the structural integrity of the bridge, in particular the validity of the stochastic master equation and of the assumption that nonreactive events have significantly larger transition probabilities than reactive ones, must be subjects of further investigation.

⁵ Our results have not, however, been derived from the Fermi rule. The conformity with it seen here is instead a consequence of the fact that the physical basis of this particular feature of the Fermi rule is also contained in the master equation (9).

⁶ This is most easily seen when the catalyst is treated as part of the reservoir.

As mentioned in Section 1, the latter assumption would seem to be variable in its accuracy as it is applied to different cases, the best cases for its applicability clearly being those of reactions (other than unimolecular reactions) in sufficiently dilute solution with inert solvent.

APPENDIX. IDENTIFICATION OF Ω FACTORS

In this appendix we provide definitions of the Ω factors introduced in Section 4, which are directly related to the "effective number of initial states" that can affect reaction. Consider Eq. (15), which can be written in the form

$$W_{\mathbf{AB}}^{\nu} = \sum_{\mathbf{ar}} W(\mathbf{ar}) \quad (\text{A.1})$$

where

$$W(\mathbf{ar}') = \sum_{\mathbf{br}} W(\mathbf{ar}'|\mathbf{br})P_{\mathbf{b}}P_{\mathbf{r}}$$

We can replace the sum over \mathbf{a} and \mathbf{r} by an integration over a density of states

$$\sum_{\mathbf{ar}} W(\mathbf{ar}) = \int dE \rho_{\mathbf{AR}}(E) W_{\mathbf{AB}}^{\nu}(E) \quad (\text{A.2})$$

where

$$\rho_{\mathbf{AR}}(E) = \sum_{\mathbf{av}} \delta(E - E_{\mathbf{a}} - E_{\mathbf{r}})$$

This expression should be compared with the corresponding integral expression involving $F_{\mathbf{A}}$ and $F_{\mathbf{R}}$,

$$\exp[-\beta(F_{\mathbf{A}} + F_{\mathbf{R}})] = \sum_{\mathbf{ar}} \exp[-\beta(E_{\mathbf{a}} + E_{\mathbf{r}})] = \int dE \rho_{\mathbf{AR}}(E) \exp(-\beta E) \quad (\text{A.3})$$

If we assume that the states $\{ar\}$ in the sums are sufficiently closely spaced that $\rho_{\mathbf{AR}}(E)$ can be effectively replaced by a continuous function of the energy, we then can estimate the integrals (A.2) and (A.3) by the method of steepest descent.

For (A.3) this procedure yields

$$\exp[-\beta(F_{\mathbf{A}} + F_{\mathbf{R}})] = \{\exp[-\beta E_{\mathbf{AR}}(T)]\} \rho_{\mathbf{AR}}(E_{\mathbf{AR}}(T)) (2\pi)^{1/2} \delta E_{\mathbf{AR}}(T) \quad (\text{A.4})$$

where $E_{\mathbf{AR}}$ is defined as the solution of

$$\beta = \partial[\ln \rho_{\mathbf{AR}}(E_{\mathbf{AR}})]/\partial E_{\mathbf{AR}} \quad (\text{A.5})$$

and

$$[\delta E_{\mathbf{AR}}(T)]^2 = - \left[\frac{\partial^2 \ln \rho_{\mathbf{AR}}(E_{\mathbf{AR}})}{\partial E_{\mathbf{AR}}^2} \right]^{-1} = \frac{C}{k\beta^2} = \frac{C_{\mathbf{A}} + C_{\mathbf{R}}}{k\beta^2} \quad (\text{A.6})$$

C_A (C_R) is identified as the total specific heat of reactant species A (reservoir species R).

When we neglect higher derivatives of $\partial^2 \ln \rho / \partial E^2$ (that these are small is implicit in the steepest descent assumption), it is easy to show that

$$E_{AR}(T) = E_A + E_R = \partial(\beta F) / \partial \beta = \sum_{ar} (E_a + E_r) P_a(T) P_r(T) \quad (\text{A.7})$$

and

$$[\delta E_{AR}(T)]^2 = \sum_{ar} [E_a + E_r - E_{AR}(T)]^2 P_a(T) P_r(T) \quad (\text{A.8})$$

The entropy is then obtained simply as

$$\begin{aligned} \frac{S_{AR}(T)}{k} &= \frac{S_A(T) + S_R(T)}{k} = \beta(E_{AR} - F_A - F_R) \\ &= \ln[(2\pi)^{1/2} \delta E_{AR}(T) \rho_{AR}(E_{AR})] \end{aligned} \quad (\text{A.9})$$

From (A.9) it is seen that (A.5) is just the thermodynamic relation

$$\beta = 1/kT = (1/k) \partial S_{AR}(E_{AR}) / \partial E_{AR} \quad (\text{A.10})$$

By a similar procedure we can approximately evaluate (A.2)

$$\int dE \rho_{AR}(E) W_{AB}(E) = \rho_{AR}(E_{AR}^w) W_{AB}^v(E_{AR}^w) (2\pi)^{1/2} \delta E_{AR}^w \quad (\text{A.11})$$

where E_{AR}^w is given as the solution to the equation

$$\frac{\partial \ln \rho_{AR}(E_{AR}^w)}{\partial E_{AR}^w} = \frac{-\partial \ln W_{AB}(E_{AR}^w)}{\partial E_{AR}^w} \quad (\text{A.12})$$

and where

$$[\delta E_{AR}^w]^2 = - \left[\frac{\partial \ln [\rho_{AR}(E_{AR}^w) W_{AB}^v(E_{AR}^w)]}{(\partial E_{AR}^w)^2} \right]^{-1} \quad (\text{A.13})$$

We see that (A.5) and (A.12) define an effective temperature

$$\beta_w^v = 1/kT_w^v = \partial[\ln \rho_{AR}(E_{AR}^w)] / \partial E_{AR}^w \quad (\text{A.14})$$

Then clearly we have (neglecting higher derivatives of δE as before) from (A.7)

$$E_{AR}^w = \sum_{ar} (E_a + E_r) w_{ar} = E_{AR}(T_w^v) \quad (\text{A.15})$$

where

$$w_{ar} = W(ar) / W_{AB}^v$$

The variance δE_{AR}^w of course will in general be different from that obtained from (A.8) evaluated at T_w^v . This is clearly seen when (A.6) is

compared with (A.13). Instead $\delta E_{\mathbf{AR}}^w$ is the variance of the weighting factor $w_{\mathbf{ar}}$

$$[\delta E_{\mathbf{AR}}^w]^2 = \sum_{\mathbf{ar}} [E_{\mathbf{a}} + E_{\mathbf{r}} - E_{\mathbf{AR}}(T_w^\nu)]^2 w_{\mathbf{ar}} \quad (\text{A.16})$$

We now make an identification of $\Omega_{\mathbf{AR}}^\nu$. In particular a comparison of (A.11) with (31) suggests

$$\Omega_{\mathbf{AR}}^\nu = (2\pi)^{1/2} \delta E_{\mathbf{AR}}^w \rho_{\mathbf{AR}}(E_{\mathbf{AR}}^w) \quad (\text{A.17})$$

and

$$\overline{W}_{\mathbf{AB}}^\nu = W_{\mathbf{AB}}^\nu(E_{\mathbf{AB}}^w) \quad (\text{A.18})$$

The expression (A.17) for $\Omega_{\mathbf{AR}}^\nu$ has precisely the properties we expect. It says that the effective number of initial states that contribute to the reaction is equal to an effective density of states times a width in energy within which the corresponding transition probabilities are effective in inducing reactive transitions. In addition (A.17) allows us to identify $\Omega_{\mathbf{AR}}^\nu$ with the corresponding entropy evaluated at the effectiveness temperature T_w^ν . Comparison of (A.9) with (A.17) yields

$$\Omega_{\mathbf{AR}}^\nu = [\delta E_{\mathbf{AR}}^w / \delta E_{\mathbf{AR}}(T_w^\nu)] \exp\{[S_{\mathbf{A}}(T_w^\nu) + S_{\mathbf{R}}(T_w^\nu)]/k\} \quad (\text{A.19})$$

We notice that this expression makes reference to neither the ‘‘smoothness’’ assumption about the density of states, nor to the assumption that the sum can be approximately evaluated by integration via the method of steepest descent. Therefore we can define all relevant quantities $[T_w^\nu \delta E_{\mathbf{AR}}(T_w^\nu)$, and $\delta E_{\mathbf{AR}}^w]$ by Eqs. (A.15), (A.8), and (A.16).

In a similar manner we can write (15) as

$$W_{\mathbf{AB}} = \Omega_{\mathbf{A}} \overline{W}_{\mathbf{AB}} \quad (\text{A.20})$$

where

$$\Omega_{\mathbf{A}} = [\delta E_{\mathbf{A}}^w / \delta E_{\mathbf{A}}(T_w)] \exp[S_{\mathbf{A}}(T_w)/k] \quad (\text{A.21})$$

T_w is defined by

$$E_{\mathbf{A}}(T_w) = \sum_{\mathbf{a}} E_{\mathbf{a}} P_{\mathbf{a}}(T_w) = \sum_{\mathbf{a}} E_{\mathbf{a}} W_{\mathbf{a}} \quad (\text{A.22})$$

$$[\delta E_{\mathbf{A}}(T_w)]^2 = \sum_{\mathbf{a}} [E_{\mathbf{a}}(T_w)]^2 P_{\mathbf{a}}(T_w) \quad (\text{A.23})$$

and

$$[\delta E_{\mathbf{A}}^w]^2 = \sum_{\mathbf{a}} [E_{\mathbf{a}} - E_{\mathbf{A}}(T_w)]^2 w_{\mathbf{a}} \quad (\text{A.24})$$

where

$$w_{\mathbf{a}} = \left[\sum_{\nu} \sum_{\mathbf{r}\mathbf{r}'} W(\mathbf{ar}'|\mathbf{br}) P_{\mathbf{b}}(T) \bar{n}_{\mathbf{r}} \right] / W_{\mathbf{AB}}$$

The T_w defined by (A.22) need not be equal to any T_w^ν defined for a particular ν by (A.15). However, T_w is a sort of average of the T_w^ν 's.

We see from (A.20) that

$$\bar{W}_{\mathbf{AB}} = \sum_{\nu} \bar{W}_{\mathbf{AB}}^{\nu} \bar{\Gamma}_{\mathbf{R}} \Omega_{\mathbf{AR}}^{\nu} / \Omega_{\mathbf{A}} \quad (\text{A.25})$$

implicitly contains enhancement factors $\Omega_{\mathbf{AR}}^{\nu} / \Omega_{\mathbf{A}} \approx \Omega_{\mathbf{R}}$ (exact equality if all the T_w^ν 's are the same), which count, for fixed ν , the effective number of initial reservoir states that can effectively transfer energy.

Next we consider the Ω factor appropriate for the direct reaction (17.) We can easily show that in (23)

$$\bar{W}_{\mathbf{AC}}^{\nu} = \Omega^{\nu} \bar{\bar{W}}_{\mathbf{AC}}^{\nu} \quad (\text{A.26})$$

where

$$\Omega^{\nu} = [\delta E_w^{\nu} / \delta E^{\nu}(T_w^{\nu})] \exp\{[S_{\mathbf{A}}(T_w^{\nu}) + S_{\mathbf{c}}(T_w^{\nu}) + 2S_{\mathbf{R}}(T_w^{\nu})] / k\} \quad (\text{A.27})$$

T_w is defined by

$$E(T_w^{\nu}) \equiv E_{\mathbf{A}}(T_w^{\nu}) + E_{\mathbf{c}}(T_w^{\nu}) + 2E_{\mathbf{R}}(T_w^{\nu}) = \sum_{\mathbf{ac}} (E_{\mathbf{a}} + E_{\mathbf{c}} + E_{\mathbf{r}} + E_{\mathbf{r}'}) w(\mathbf{ar}' | \mathbf{cr}) \quad (\text{A.28})$$

where

$$w(\mathbf{ar}' | \mathbf{cr}) = \left\{ \sum_{\mathbf{b}} P_{\mathbf{b}} \Delta(E_{\mathbf{a}} + E_{\mathbf{r}' | \mathbf{E}_{\mathbf{b}}}) W(\mathbf{ar}' | \mathbf{cr}) \right\} / \bar{W}_{\mathbf{AC}}^{\nu}$$

The variances δE_w^{ν} and $\delta E^{\nu}(T_w^{\nu})$ are defined in the obvious manner in terms of $w(\mathbf{ar}' | \mathbf{cr})$ and $P_{\mathbf{a}} P_{\mathbf{c}} P_{\mathbf{r}} P_{\mathbf{r}'}$.

Finally, we note that (25) can be written as

$$\bar{W}_{\mathbf{AC}} = \Omega \bar{\bar{W}}_{\mathbf{AC}} \quad (\text{A.29})$$

where

$$\Omega = [\delta E_{\mathbf{AC}}^{\bar{w}} / \delta E_{\mathbf{AC}}(T_{\bar{w}})] \exp\{[S_{\mathbf{A}}(T_{\bar{w}}) + S_{\mathbf{c}}(T_{\bar{w}})] / k\} \quad (\text{A.30})$$

$T_{\bar{w}}$ is defined by

$$E_{\mathbf{AC}}(T_{\bar{w}}) = E_{\mathbf{A}}(T_{\bar{w}}) + E_{\mathbf{c}}(T_{\bar{w}}) = \sum_{\mathbf{ac}} (E_{\mathbf{a}} + E_{\mathbf{c}}) \bar{w}_{\mathbf{ac}} \quad (\text{A.31})$$

where

$$\begin{aligned} \bar{w}_{\mathbf{ac}} &= (\bar{W}_{\mathbf{AC}})^{-1} \sum_{\nu} \{ \exp[-\beta(F_{\mathbf{BR}} - \bar{F}_{\mathbf{B}})] \} \\ &\quad \times \sum_{\mathbf{brf}'} P_{\mathbf{b}} \Delta(E_{\mathbf{a}} + E_{\mathbf{r}' | \mathbf{E}_{\mathbf{b}}}) W(\mathbf{ar}' | \mathbf{cr}) \end{aligned}$$

The variances $\delta E_{\mathbf{AC}}^{\bar{w}}$ and $\delta E_{\mathbf{AC}}(T_{\bar{w}})$ are defined in the obvious manner.

As before, $T_{\bar{w}}$ is a sort of average of the $T_{\bar{w}}^{\nu}$'s. We see that

$$\begin{aligned}\bar{\bar{W}}_{AC} &= \sum_{\nu} \{\exp[-\beta(F_{BR} - \bar{F}_B)]\} (\Omega^{\nu}/\Omega) \bar{n}_R \bar{\bar{W}}_{AC}^{\nu} \\ &\approx \sum_{\nu} \{\exp[-\beta(F_{BR} - \bar{F}_B)]\} \Omega_R^{-2} \bar{n}_R \bar{\bar{W}}_{AC}\end{aligned}\quad (\text{A.32})$$

also contains enhancement factors for each value of ν in the sum.

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