

## 5.2

# A MODERN PERSPECTIVE ON TRANSITION STATE THEORY

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Chemical rates, the temporal evolution of the populations of species of interest, are of fundamental importance in science. Understanding how such rates are determined by the microscopic forces involved is, in turn, a basic focus of the present discussion.

Before delving into the details, it is valuable to consider the general nature of the problem we face when considering the calculation of chemical rates. In what follows we shall assume that we know:

- the relevant physical laws (classical or quantum) governing the system,
- the molecular forces at work,
- the identity of the chemical species of interest, and
- the formal statistical-mechanical expressions for the desired rates.

Given all that, what is the “problem?” In principle, of course, there is none. “All” that we need do is to work out the “details” of our formal expressions and we have our desired rates. The kinetics of any conceivable physical, chemical, or biologic process are thus within our reach. We can predict fracture kinetics in complex materials, investigate the effects of arbitrary mutations on protein folding rates, and optimize the choice of catalyst for the decomposition/storage of hydrogen in metals, right?

Sadly, “no.” Even assuming that all of the above information is at our disposal, at present it is not possible in practice to carry out the “details” at the level necessary to produce the desired rates for arbitrary systems of interest.

Why not?

The essential problem we face when discussing chemical rates is one of greatly differing time scales. If, for example, a species is of sufficient interest that it makes sense to monitor its population, it is, by default, generally relatively “stable.” That is, it is a species that tends to live a “long” time on the scale

of something like a molecular vibration. On the other hand, if we are to understand the details of chemical events of interest, then we must be able to describe the dynamics of those events on a time scale that is “short” on the molecular level. If we do otherwise, we risk losing the ability to understand how those detailed molecular motions influence and/or determine the rates at issue. What happens then when we confront the problem of describing a rate process whose natural time scale is on the order of seconds? If we are not careful we end up drowning in the detail imposed by being forced to describe events on macroscopic time scales using microscopic dynamical methods. In short, we spend a great deal of time (and effort) watching things “not happen.”

Is there a better way to proceed?

Fortunately, “yes.” Using methods developed by a number of investigators [1–9], it is possible to formulate practical and reliable methods for estimating chemical rates for systems of realistic complexity. While there are often assumptions involved in the practical implementation of these approaches, it is increasingly feasible to quantify and often remove the effects of these assumptions albeit at the expense of additional work.

It is our purpose to review and illustrate these methods. Our discussion will focus principally on classical level implementations. Quantum formulations of these methods are possible and are considered elsewhere in this monograph. While much effort has been devoted to the quantum problem, it remains a particularly active area of current research. In the present discussion, we purposely utilize a sometimes nonstandard language in order to unify the discussion of a number of historically separate topics and approaches.

The starting point for any discussion of chemical rates is the identification of various species of interest whose population will be monitored as a function of time. While there are many possible ways in which to do this, it is convenient to consider an approach based on the Stillinger/Weber inherent structure ideas [10, 11]. In this formulation, configuration space is partitioned by assigned each position to a unique potential energy basin (“inherent structure”) based on a steepest descent quench procedure. The relevant mental image is that of watching a “ball” roll slowly “downhill” on the potential energy surface under the action of an over-damped dynamics.

In many applications the Stillinger/Weber inherent structures are themselves of primary interest. Although the number of such structures grows rapidly (exponentially) with system size [12], this type of analysis and the associated graphical tools it has spawned [13], provide a valuable language for characterizing potential energy surfaces. Wales, in particular, has utilized variations of the technique to great advantage in their study of the minimization problem [14].

In our discussion, it is the evolution of the populations of the inherent structures rather than the structures themselves that are of primary concern. Inherent structures, by construction, are associated with local minima in the

potential energy surface. They thus have an intrinsic equilibrium population that can, if desired, be estimated using established statistical–mechanical techniques. Since the dynamics in the vicinity of the inherent structures is locally stable, the inherent structure populations tend to be (relatively) slowly varying and thus provide us with a natural set of populations for kinetic study.

If followed as a function of time under the action of the dynamics generated by potential energy surface to which the inherent structures belong, the populations of the inherent structures will, aside from fluctuations, tend to remain constant at their various equilibrium values. Fluctuations in these populations, on the other hand, will result in a net flow of material between the various inherent structures. Such flows are the mechanism by which such fluctuations, either induced or spontaneous, “relax.” Consequently, they contain sufficient information to establish the desired kinetic parameters.

To make the discussion more explicit, we consider the simple situation of a particle moving on the bistable potential energy depicted in Fig. 1. Performing a Stillinger/Weber quench on this potential energy will obviously produce two inherent structures. Denoted A and B in the figure, these correspond to the regions to the left and right of the potential energy maximum, respectively.

We now imagine that we follow the dynamics of a statistical ensemble of  $N$  particles moving on this potential energy surface. For the purposes of discussion, we assume that the physical dynamics involved includes a solvent or “bath” (here unspecified) that provides fluctuating forces that act on the system

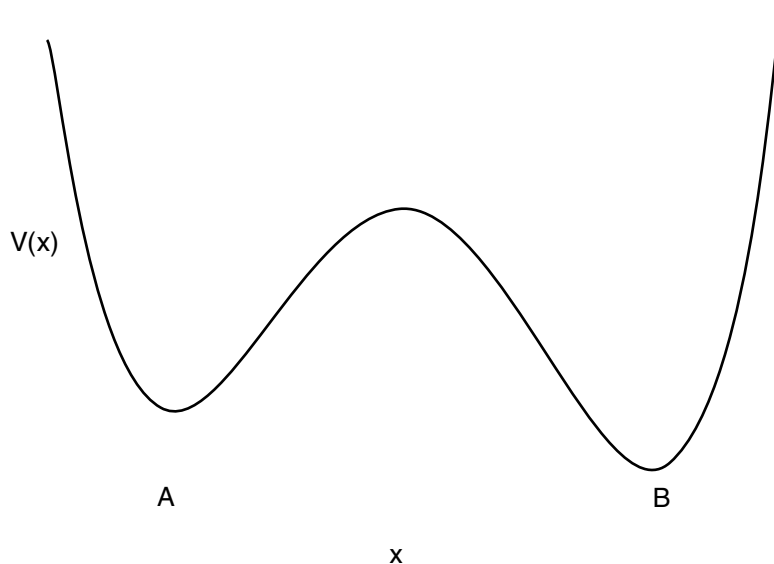


Figure 1. A prototypical, bistable potential energy. The two inherent structures, A and B, are separated by an energy barrier.

of interest. The bath dynamics acts both to energize the system (permitting it to acquire sufficient energy to sometimes cross the potential barrier) as well as to dissipate that energy once it has been acquired. It is important to note that these fluctuations and dissipations must, in some sense, be balanced if an equilibrium state is to be produced and sustained [7]. Were the dynamics in our example purely conservative and one-dimensional in nature, for example, the notion of rates would be ill-posed.

We now assume in what follows that we can monitor the populations of the inherent structures as a function of time. Denoting these populations  $N_A(t)$  and  $N_B(t)$ , we further assume, following Chandler [7], that the overall kinetics of the system can be described by the phenomenological rate equations

$$\begin{aligned}\frac{dN_A(t)}{dt} &= -k_{A \rightarrow B}N_A(t) + k_{B \rightarrow A}N_B(t) \\ \frac{dN_B(t)}{dt} &= +k_{A \rightarrow B}N_A(t) - k_{B \rightarrow A}N_B(t).\end{aligned}\tag{1}$$

If the total number of particles is conserved, then the two inherent structure populations are trivially related: the fluctuation in the population of one inherent structure is the negative of that for the other. Assuming a fixed number of particles, it is thus a relatively simple matter to show that

$$\frac{d\delta N_A(t)}{dt} = -(k_{A \rightarrow B} + k_{B \rightarrow A})\delta N_A(t),\tag{2}$$

where  $\delta N_A(t)$  indicates the deviation of  $N_A(t)$  from its equilibrium value. The decay of a fluctuation in the population of inherent structure A, relative to an initial value at time zero, is thus given by

$$\delta N_A(t) = \delta N_A(0) e^{-k_{\text{eff}}t},\tag{3}$$

where  $k_{\text{eff}}$  is given by the sum of the “forward” and “backward” rate constants

$$k_{\text{eff}} = (k_{A \rightarrow B} + k_{B \rightarrow A}).\tag{4}$$

As noted by Onsager [15], it is physically reasonable to assume that if they are small, fluctuations, whether induced or spontaneous, are damped in a similar manner. Accepting this hypothesis, we conclude from the above analysis that the decay of the equilibrium population autocorrelation function, denoted here by  $\rho(t)$ , is given in terms of  $k_{\text{eff}}$  by

$$\frac{\langle \delta N_A(0)\delta N_A(t) \rangle}{\langle \delta N_A(0)\delta N_A(0) \rangle} = e^{-k_{\text{eff}}t}.\tag{5}$$

Equivalently, taking the time derivative of both sides of this expression, we see that  $k_{\text{eff}}$  is given explicitly as

$$k_{\text{eff}} = -\frac{\langle \delta N_A(0)\delta \dot{N}_A(t) \rangle}{\langle \delta N_A(0)\delta N_A(t) \rangle}.\tag{6}$$

Equations (5) and (6) are formally exact expressions that relate the sum of the basic rate constants of interest to various dynamical objects that can be computed. Since we also know the ratio of these two rate constants (it is given by the corresponding ratio of the equilibrium populations), the desired rate parameters can be obtained from either expression provided that we can obtain the relevant time correlation functions involved.

Although formally equivalent, Eqs. (5) and (6) differ with respect to their implicit computational demands. Computing the rate parameters via Eq. (5), for example, entails monitoring the decay of the population autocorrelation function. To obtain reliable estimates of the rate parameters from Eq. (5), we have to follow the system dynamics over a time-scale that is an appreciable fraction of the reciprocal of  $k_{\text{eff}}$ . If the barriers separating the inherent structures involved are “large”, this time scale can become macroscopic. Simply stated, the disparate time-scale problem makes it difficult to study directly the dynamics of infrequent events using the approach suggested by Eq. (5).

Equation (6), on the other hand, offers a more convenient route to the desired kinetic parameters. In particular, it indicates that we might be able to obtain these parameters from short as opposed to long-time dynamical information. If the phenomenological rate expressions are formally correct for all times, then the ratio of the two time correlation functions in Eq. (6) is time-independent. However, since it is generally likely that the phenomenological rate expressions accurately describe only the longer-time motion between inherent structures, we expect in practice that the ratio on the right hand side of Eq. (6) will approach a constant “plateau” value only at times long on the scale of detailed molecular motions. The critical point, however, is that this transient period will be of molecular not macroscopic duration. With Eq. (6), we thus have a route to the desired kinetic parameters that requires only molecular or short time-scale dynamical input.

A valuable practical point concerning kinetic formulations based on Eq. (6) is that for many applications the final plateau value of the correlation function ratio involved is often relatively well approximated by its zero time value. Because the correlation functions required depend only on time differences, such zero-time quantities are purely equilibrium objects. Consequently, an existing and extensive set of equilibrium tools can be invoked to produce approximations to kinetic parameters.

The approach to the calculation of chemical rates based on Eq. (6) has several desirable characteristics. Most importantly, it has a refinable nature and can be implemented in stages. At the simplest level, we can estimate chemical rate parameters using purely zero-time, or equilibrium methods. Such approximate methods alone may be adequate for many applications. We are, however, not restricted to accepting such approximations blindly. With additional effort we can “correct” such preliminary estimates by performing additional dynamical studies. Because such calculations involve “corrections” to

equilibrium estimates of rate parameters, as opposed to the entire rate parameters themselves, the dynamical input required is only that necessary to remove the errors induced by the initial equilibrium assumptions. Because such errors tend to involve simplified assumptions concerning the nature of transition state dynamics, the input required to estimate the corrections is of a molecular, not macroscopic time scale.

We now focus our discussion on some of practical issues involved in generating equilibrium estimates of the rates. We shall illustrate these using the simple two-state example described above. We begin by imagining that we have at our disposal the time history of a reaction coordinate of interest,  $x(t)$ . As a function of time,  $x(t)$  moves back-and-forth between inherent structures A and B, which we assume to be separated by the position  $x = q$ . Using one of the basic properties of the delta function,

$$\delta(ax) = \frac{1}{|a|} \delta(x), \quad (7)$$

it is easy to show that  $N(\tau, [x(t)])$ , defined by

$$N(\tau, [x(t)]) = \int_0^\tau dt \left| \frac{dx(t)}{dt} \right| \delta(x(t) - q), \quad (8)$$

is a functional of the path whose value is equal to the (total) number of crossings of the  $x(t) = q$  surface in the interval  $(0, \tau)$ . Every time  $x(t)$  crosses  $q$ , the delta function argument takes on a zero value. Because the delta function in Eq. (8) is in coordinate space while the integral is with respect to time, the Jacobian factor into Eq. (8) creates a functional whose value jumps by unity each time  $x(t) - q$  sweeps through a value of zero.

If we form a statistical ensemble corresponding to various possible histories of the motion of our system and bath, we can compute the average number of crossings of the  $x(t) = q$  surface in the  $(0, \tau)$  interval,  $\langle N(\tau, [x(t)]) \rangle$ , using the expression

$$\langle N(\tau, [x(t)]) \rangle = \int_0^\tau dt \langle |\dot{x}(t)| \delta(x(t) - q) \rangle. \quad (9)$$

Here represents the time derivative of  $x(t)$ . Because we are dealing with a "stationary" or equilibrium process, the time correlation function that appears on the right hand side of Eq. (9) can be function only of time differences. Consequently, the integrand on the right hand side of Eq. (9) is time-independent and can be brought outside the integral. The result thus becomes

$$\langle N(\tau, [x(t)]) \rangle = \langle |\dot{x}| \delta(x - q) \rangle \int_0^\tau dt, \quad (10)$$

where the (now unnecessary) time labels have been dropped. We thus see that the number of crossings of the  $x(t) = q$  surface in this system per unit time is given by

$$\frac{\langle N(\tau, [x(t)]) \rangle}{\tau} = \langle |\dot{x}| \delta(x - q) \rangle. \quad (11)$$

Recalling that  $N$  measures the total number of crossings, the number of crossings per unit time in the direction from A to B (the number of “up zeroes” of  $x(t) - q$  in the language of Slater) is half the value in Eq. (11). Thus, the equilibrium estimate of the rate constant for the A to B transition, (i.e., the number of crossings per unit time from A to B per atom in inherent structure A) is given by

$$k_{A \rightarrow B}^{\text{TST}} = \frac{1}{2} \frac{\langle |\dot{x}| \delta(x - q) \rangle}{N_A}. \quad (12)$$

Equation (12) gives an approximate expression to the rate constant that involves an equilibrium flux between the relevant inherent structures. Because the relevant flux is associated with the “transition” of one inherent structure into another, the approach to chemical rates suggested by Eq. (12) is typically termed “transition state” theory (TST). Along with its multi-dimensional generalizations, it represents a convenient and useful approximation to the desired chemical rate constants. Being an equilibrium approximation to the dynamical objects of interest, it permits the powerful machinery of Monte Carlo methods [16, 17] to be brought to bear on the computational problem. The significance of this is that the required averages can be computed to any desired accuracy for arbitrary potential energy models. One can proceed analytically by making secondary, simplifying assumptions concerning the potential. Such approximations are, however, controllable in that their quality can be tested. Furthermore, Eq. (12) provides a unified treatment of the problem that is independent of the nature of the statistical ensemble that is involved. Applications involving canonical, microcanonical and other ensembles are treated within a common framework. It is historically interesting in this regard to note that if the reaction coordinate of interest is expressed as a superposition of normal modes, Eq. (12) leads naturally to the unimolecular reaction expressions of Ref. [4].

There is a technical aspect concerning the calculation of the averages appearing in Eq. (12) that merits discussion. In particular, it is apparent from the nature of the average involved that, if they are to be computed accurately, the numerical methods involved must be capable of accurately describing the reactant’s concentration profile in the vicinity of the transition state. If we are dealing with activated processes where the difference between transition state in inherent structure energies are “large”, then such concentrations can become quite small and difficult to treat by standard methods. This is

simply the equilibrium, “sparse-sampling” analog of the disparate time-scale dynamical problem. Fortunately, there are a number well-defined techniques for coping with this technical issue. These include, to name a few, umbrella methods [18], Bennett/Voter techniques [19, 20], J-walking [21, 22], and parallel tempering approaches [23]. These and related methods make it possible to compute the the required, transition-state-constrained averages.

The basic approach outlined above can be extended in a number of ways. One immediate extension involves problems in which there are multiple, rather than two states involved. Adams has considered such problems in the context of his studies on the effects of precursor states on thermal desorption [24]. A second extension involves using the fundamental kinetic parameters produced to study more complex events. Voter, in a series of developments, has formulated a computationally viable method for studying diffusion in solids based on such an approach [25]. In its most complete form (including dynamical corrections), this approach produces a computationally exact procedure for surface or bulk diffusion coefficients of a point defect at arbitrary temperatures in a periodic system [26]. In related developments, Voter [25] and Henkelmen and Jónsson [27] have discussed using “on-the-fly” determinations of TST kinetic parameters in kinetic Monte Carlo studies. Such methods make it possible to explore a variety of lattice dynamical problems without resorting to ad hoc assumptions concerning mechanisms of various elementary events. In a particularly promising development, they also appear to offer a valuable tool for the study of long-time dynamical events [28, 29].

An important practical issue in the calculation of TST approximations to rates is the identification of the transition state itself. In many problems, such as the simple two-state problem discussed previously, locating the transition state is trivial. In others, it is not. Techniques designed to locate explicit transition states in complex systems have been discussed in the literature. One popular technique, developed by Cerjan and Miller [30] and extended by others [31–33], is based on an “eigenvector following” method. In this approach, one basically moves “up-hill” from a selected inherent structure using local mode information to determine the transition state. Other approaches, including methods that do not require explicit second-order derivatives of the potential, have been discussed [34]. It is also important to mention a different class of methods suggested by Pratt [35]. Borrowing a page from path integral applications, this technique attempts to locate transition states by working with paths that build in proper initial and final inherent structure character from the outset. Expanding upon the spirit of the original Pratt suggestion, recent efforts have considered sampling barrier crossing paths directly [36].

We wish to close by pointing out what we feel may prove to be a potentially useful link between inherent structure decomposition methods and the problem of “probabilistic clustering” [37, 38]. An important problem in applied mathematics is the reconstruction of an unknown probability distribution given a



known statistical sampling of that distribution. So stated, the probabilistic clustering problem is effectively the inverse of the Monte Carlo sampling problem. Rather than producing a statistical sampling of a given distribution, we seek instead to reconstruct the unknown distribution from a known statistical sampling. This clustering problem is of broad significance in information technology and has received considerable attention. Our point in emphasizing the link between probabilistic clustering and inherent structure methods is that our increased ability to sample arbitrary, sparse distributions would appear to offer an alternative to the Stillinger/Weber quench approach to the inherent structure decomposition problem. In particular, one could use clustering methods both to “identify” and to “measure” the concentrations of inherent structures present in a system.

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