

Reaction rate theory: What it was, where is it today, and where is it going?

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A brief history is presented, outlining the development of rate theory during the past century. Starting from Arrhenius [Z. Phys. Chem. **4**, 226 (1889)], we follow especially the formulation of transition state theory by Wigner [Z. Phys. Chem. Abt. B **19**, 203 (1932)] and Eyring [J. Chem. Phys. **3**, 107 (1935)]. Transition state theory (TST) made it possible to obtain quick estimates for reaction rates for a broad variety of processes even during the days when sophisticated computers were not available. Arrhenius' suggestion that a transition state exists which is intermediate between reactants and products was central to the development of rate theory. Although Wigner gave an abstract definition of the transition state as a surface of minimal unidirectional flux, it took almost half of a century until the transition state was precisely defined by Pechukas [*Dynamics of Molecular Collisions B*, edited by W. H. Miller (Plenum, New York, 1976)], but even this only in the realm of classical mechanics. Eyring, considered by many to be the father of TST, never resolved the question as to the definition of the activation energy for which Arrhenius became famous. In 1978, Chandler [J. Chem. Phys. **68**, 2959 (1978)] finally showed that especially when considering condensed phases, the activation energy is a free energy, it is the barrier height in the potential of mean force felt by the reacting system. Parallel to the development of rate theory in the chemistry community, Kramers published in 1940 [Physica (Amsterdam) **7**, 284 (1940)] a seminal paper on the relation between Einstein's theory of Brownian motion [Einstein, Ann. Phys. **17**, 549 (1905)] and rate theory. Kramers' paper provided a solution for the effect of friction on reaction rates but left us also with some challenges. He could not derive a uniform expression for the rate, valid for all values of the friction coefficient, known as the Kramers turnover problem. He also did not establish the connection between his approach and the TST developed by the chemistry community. For many years, Kramers' theory was considered as providing a dynamic correction to the thermodynamic TST. Both of these questions were resolved in the 1980s when Pollak [J. Chem. Phys. **85**, 865 (1986)] showed that Kramers' expression in the moderate to strong friction regime could be derived from TST, provided that the bath, which is the source of the friction, is handled at the same level as the system which is observed. This then led to the Mel'nikov-Pollak-Grabert-Hänggi [Mel'nikov and Meshkov, J. Chem. Phys. **85**, 1018 (1986); Pollak, Grabert, and Hänggi, *ibid.* **91**, 4073 (1989)] solution of the turnover problem posed by Kramers. Although classical rate theory reached a high level of maturity, its quantum analog leaves the theorist with serious challenges to this very day. As noted by Wigner [Trans. Faraday Soc. **34**, 29 (1938)], TST is an inherently classical theory. A definite quantum TST has not been formulated to date although some very useful approximate quantum rate theories have been invented. The successes and challenges facing quantum rate theory are outlined. An open problem which is being investigated intensively is rate theory away from equilibrium. TST is no longer valid and cannot even serve as a conceptual guide for understanding the critical factors which determine rates away from equilibrium. The nonequilibrium quantum theory is even less well developed than the classical, and suffers from the fact that even today, we do not know how to solve the real time quantum dynamics for systems with "many" degrees of freedom. © 2005 American Institute of Physics. [DOI: 10.1063/1.1858782]

Rate theory provides the relevant information on the long-time behavior of systems with different metastable states and therefore is important for the understanding of many different physical, chemical, biological, and technical processes. Einstein indirectly contributed to this theory by clarifying the nature of Brownian motion as being caused by the thermal agitation of surrounding molecules on an immersed small particle. Kramers later

pointed out that the thermally activated escape from a metastable state is nothing else but the Brownian motion of a fictitious particle along a reaction coordinate leading from an initial to a final locally stable state. In order to overcome the energetic barrier separating the two states, the particle has to "borrow" energy from its surroundings, an extremely rare event if as is usually the case the activation energy is much larger than the thermal energy.

So, many attempts will take place until the particle has overcome the barrier separating the two states. During these many unsuccessful events, the particle completely loses any memory on how it had come to its initial state. Due to this loss of memory, the waiting time in the initial well will be random with an exponential distribution whose average coincides with the inverse of the decay rate. In this article the historical development of rate theory is outlined, the concepts are discussed, and present day generalizations to quantum nonequilibrium systems are presented. Our review ends with a brief summary of some challenges facing rate theory which remain open even a century after Einstein's seminal paper.

I. RATE THEORY IN THE FIRST HALF OF THE 20TH CENTURY: ARRHENIUS, WIGNER, EYRING AND KRAMERS

A. Arrhenius and activated molecules

The father of reaction rate theory is Arrhenius who in his famous 1889 paper¹ investigated the temperature dependence of the rates of inversion of sugar in the presence of acids. As noted by Hänggi *et al.*,² Arrhenius himself cites van't Hoff³ as the person who suggested an $e^{-A/T}$ temperature dependence of reaction rates. However, Arrhenius is the father of rate theory since he postulated that this relationship indicates the existence of an "activated sugar" whose concentration is proportional to the total concentration of sugar, but is exponentially temperature dependent.

But perhaps there is another reason why Arrhenius is so highly respected by the physical chemistry community. In 1911 he traveled to the United States and gave there a series of lectures, summarized in his book *Theories of Solutions*.⁴ In the Introduction he made the following observations: "Chemistry works with an enormous number of substances, but cares only for some few of their properties; it is an extensive science. Physics on the other hand works with rather few substances, such as mercury, water, alcohol, glass, air but analyzes the experimental results very thoroughly; it is an intensive science. Physical chemistry is the child of these two sciences; it has inherited the extensive character from chemistry...it has its profound quantitative character from the science of physics." He ends his Introduction by noting that, "The theoretical side of physical chemistry is and will probably remain the dominant one."

It is this theoretical side which lies at the heart of this review. We will try briefly to follow the history of the development of rate theory in chemistry and physics, its impact on present day science, and its prospect for the 21st century—is there still anything that can be added to it?

B. Wigner and Eyring: The transition state method

Arrhenius' idea of an activated intermediate was amplified by a number of authors during the next 35 years. Christiansen and Kramers⁵ were able to provide a rationale for the Arrhenius form based on the kinetic theory of gases. They realized already in 1923 that the activation energy could be understood by assuming that a minimum amount of energy is needed before reaction could occur. The probability

for attaining this energy is given by the canonical distribution and thus one obtains the Arrhenius factor. They then provided a heuristic estimate for the magnitude of the prefactor.

In 1935, Eyring published a paper titled "The Activated Complex in Chemical Reactions."⁶ By this time, it was well established that reaction rates (k) should be written in the form

$$k = \nu e^{-E/k_B T}, \quad (1.1)$$

where ν is a prefactor with the dimensions of 1/s for unimolecular reactions and 1/(s · cm³) for bimolecular reactions. Eyring proposed a method by which one could calculate the "absolute reaction rate." Eyring, though a devout Mormon, probably did not really mean "absolute" in the divine sense, rather his claim to fame at this point was that he wrote down a formula for the rate which allowed one to estimate the prefactor in the rate expression. While most previous works dealt with the relative rates of reactions, in which the prefactor would be eliminated, Eyring gave a heuristic derivation of an expression for the prefactor based on the assumption of an equilibrium between the activated complex and reactants. To obtain the time constant, he postulated, that at the saddle point, any quantum state perpendicular to the reaction coordinate reacts with the same universal time constant $k_B T / 2\pi\hbar$. The rate is then given by the product of this universal time constant with the ratio of the partition function of the activated complex (which has one degree of freedom less than the reactants) to the partition function of the reactants. Eyring's formulation, in terms of partition functions allowed a heuristic quantum mechanical formulation for the rate constant and indeed in his 1935 paper he used quantum mechanical partition functions.⁶

Noteworthy also is the work of Farkas⁷ and Szilard (who was credited by Farkas, but a specific citation was not given) who realized and implemented the flux over population definition of the rate constant. This was then picked up by Pelzer and Wigner in their 1932 paper⁸ in which they estimated the rate of conversion of parahydrogen into normal hydrogen. In this very early paper one may find all the elements of much more sophisticated work which abounded in the second half of the 20th century. They adapt the Eyring–Polanyi representation⁹ of the ground Born–Oppenheimer potential energy surface for the motion of the nuclei, even showing a fictitious trajectory leading from reactants to products. They estimate the effect of electronically nonadiabatic interactions and show that they are negligible.

To compute the reaction rate, they use a thermal equilibrium distribution in the vicinity of the saddle point of the potential energy surface and estimate the unidirectional classical flux in the direction from reactants to products. Already here, they note that they ignore the possibility of recrossings of the saddle point, pointing out that their probability at room temperature would be rather small. To get the rate they use the flux over population method after harmonically expanding the potential energy surface about the saddle point. The Pelzer and Wigner paper⁸ is the very first use of transition state theory to estimate reaction rates. It is however written in a rather specific form, as applied to the hydrogen ex-

change reaction. Eyring's later paper of 1935⁶ provides general formulas which were then applied to many different activated reactions.

In 1932 Wigner¹⁰ made an additional seminal contribution to rate theory by providing an estimate for the tunneling contribution to the thermal flux of particles crossing a barrier. Using the same parabolic barrier expansion as in the work with Pelzer and his recently formulated quantum distribution function in phase space, he derives a series in \hbar^2 for the thermal tunneling corrections. His derivation is heuristic, he uses quantum mechanics for the thermal density of particles but treats the motion across the barrier as classical.

The competition between Wigner and Eyring seems to have reached a head at a Faraday discussion, the papers of which were published in 1938. Wigner¹¹ and Eyring¹² had back-to-back papers; Wigner's was titled "The Transition State Method," Eyring used "The Theory of Absolute Reaction Rates." Wigner notes here that the transition state method is inherently a classical theory, since the uncertainty principle forbids the simultaneous determination of a dividing surface and the sign of the momentum across the surface. Eyring ignores this, and uses his heuristic thermodynamic formulation within a quantum mechanical context, applying the theory to the reaction of NO with O₂.

One of the most interesting aspects of this Faraday meeting was the emerging ambiguity with respect to the definition of the "activated complex." In Wigner's approach it is defined through the dividing surface. However, when using equilibrium thermodynamics as a basis for the theory, ambiguities arise. Evans¹³ in his paper titled "Thermodynamical Treatment of the Transition State" defines it as "The least probable configuration along the reaction path" but does not really define this probability. Guggenheim and Weiss in their paper "The Application of Equilibrium Theory to Reaction Kinetics"¹⁴ are very forthcoming: "We are not always quite sure whether the expression the activated complex refers to A' (an energetic molecule) or A* (a reacting molecule) or to something intermediate between the two."

This ambiguity continues for three more decades. In a symposium held in Sheffield, in April 1962 a lively discussion takes place between G. Porter and Eyring.¹⁵ Porter asks: "May we begin by making sure that we know what we are talking about? In the papers presented at this meeting...potential-energy and free energy maxima are used rather indiscriminately to define the transition state.... Would Professor Eyring give us a rigorous definition to the transition state?" Eyring's answer is "the concept of an activated complex...provides us with the same theoretical tools for discussing reaction kinetics that have been so successfully used in discussing the equilibrium constants. The current literature is an eloquent testimonial to the fecundity of the concept."

It is noteworthy, that this kind of discussion did not arise through Wigner's work. Wigner's approach was based on classical mechanics. Early on, Wigner realized that classical transition state theory provides an upper bound for the classical canonical net flux going from reactants to products. In his 1937 paper¹⁶ he used this property to derive an upper bound to the rate of association reactions, using a dividing

surface in energy rather than in configuration space. The upper bound leads to the variational property, which says that the best dividing surface is that which minimizes the unidirectional flux from reactants to products. With this definition, there is no ambiguity. The classical formulas for estimating this unidirectional flux are identical to the classical limit of the formulas used by Eyring and the chemistry community, this is not an accident, we remember that Pelzer and Wigner⁸ had already given the foundations for the transition state theory (TST) method in their 1932 paper and that Eyring made sure that his formulation would correctly reduce to theirs. Wigner's interest in the TST method waned after 1938. In a personal meeting with him in the early 1980s, he showed no further interest in the issue.

C. Kramers–Brownian motion in a field of force

Kramers, whose earlier paper on rate theory was with Christiansen⁵ as mentioned above, published a seminal paper of his own in 1940 titled "Brownian Motion in a Field of Force and the Diffusion Model of Chemical Reactions,"¹⁷ which may be thought of as the direct descendent of Einstein's famous paper of 1905. Although he does not provide a citation to Einstein's work¹⁸ he does note, "A theory of Brownian motion on the Einstein pattern can be set up..." under appropriate conditions. Using the Langevin equation as a model in which a particle is moving under the influence of a field of force and a frictional force characterized by a damping coefficient γ he derives a Fokker–Planck equation in phase space (known also as the Kramers equation) for the motion.

Kramers then proceeds to use the flux over population method to derive the rate of passage over a barrier in three limits—weak damping, intermediate, and strong damping. He derives the famous prefactor for the rate which is valid for the intermediate to strong damping regimes and independently a different prefactor, obtained by deriving a diffusion equation in energy in the underdamped limit, where the reaction rate is limited by the rate of flow of energy from the surrounding to the particle. Kramers notes that the intermediate friction range is the one in which one obtains the transition state limit for the rate. His paper also presented a challenge—deriving a uniform expression for the rate valid for all values of the friction, known as the turnover problem.

Kramers realized that in the intermediate friction range his expression for the rate is identical to the ones derived by Pelzer and Wigner⁸ and Eyring⁶ and cites them accordingly. He considers his derivation as support for the transition state method, noting that "the transition state method gives results which are correct, say within ten percent in a rather wide range of η (friction coefficient) values." However, Kramers does not state nor does he derive any formal equivalence between his results and transition state theory. Moreover, he refers to the ambiguity of choice of transition state, noting that for small friction it should be a state of definite energy while for larger friction it is characterized by the spatial coordinate.

His work which was used by the physics community for the next four decades or so, evolved independently of the TST approach to rate theory used by the chemistry commu-

nity. Kramers' equation was put to use for solving a variety of problems, and was even generalized to include quantum effects such as tunneling by Caldeira and Leggett in 1983.¹⁹ Kramers himself considered his model as having no room for quantum mechanical effects such as tunneling.

Kramers' rate theory was generalized by a number of groups mainly in the 1970s and 1980s to systems with more than one degree of freedom^{20,21} and to systems with memory friction in the moderate to strong friction regime^{22–24} and in the weak friction regime.²⁵ These authors determined the rate by a flux over population expression where the flux is considered as the number of particles per unit time crossing a conveniently chosen hypersurface in the phase space of the system that divides between reactants and products. The population is by definition the density of reactants. The flux and the population are calculated for a stationary distribution in which those particles that have escaped from the state of reactants through the separating hypersurface are replenished. The validity of this method is based on the assumption that the reinjected particles thermalize before they escape the next time. This requires that the reactants are separated from the products by a barrier that is substantially higher than the thermal energy. The necessary minimal barrier height for the flux over population method to hold strongly depends on the considered system. In the presence of a slow degree of freedom which is different from the reaction coordinate the true rates may be strongly suppressed compared to the classical Kramers–Langer–Grote–Hynes expression.^{26–29}

Another approach that basically gives the same rate expressions as the flux over population method relies on the determination of the mean time that the reactants need to transform into the activated complex, or more precisely, on the mean first passage time of trajectories leading from the reactant state to the separating hypersurface. Elaborate asymptotic methods have been developed^{30–32} for the calculation of the mean first passage time.

In passing we note that any inverse mean first passage time which results from a Fokker–Planck equation can formally be represented as a flux over population expression.^{2,33} Recently the same result was obtained for mean first passage times of any time-homogeneous process.³⁴ Yet there are conceptual differences between the two methods. For the mean first passage time, trajectories arriving at the considered separating surface are immediately stopped. Consequently any recrossings of this surface are strictly excluded from the corresponding formal rate. This is quite in contrast to the Kramers flux over population expression which allows for recrossings of the barrier. Absorption only takes place beyond the barrier from where it is most likely that reaction will be completed before any eventual back reaction takes place. In simple cases, the effect of recrossings can be incorporated in the rate resulting from a mean first passage time by a numerical factor which is 1/2 if the separating surface coincides with the so-called stochastic separatrix.^{35–37} In these works it was also shown that the stochastic separatrix coincides with the usual, deterministic separatrix in the limit of infinitely high barriers. On the other hand, the recrossings become immaterial for mean first passage times of a separat-

ing surface that is sufficiently close to the final product state. In general, however, there is no easy way to infer the true rate from a mean first passage time.^{38–41}

II. RATE THEORY IN THE SECOND HALF OF THE 20TH CENTURY

A. Variational transition state theory

The next milestone in the development of rate theory is what is termed variational transition state theory (VTST). Keck⁴² used the ideas of Marcelin,⁴³ Wigner,^{10,11,16} and Horiuti⁴⁴ and in his definitive review of 1967⁴⁵ presented the systematic application of the variational property to activated chemical reactions.

In VTST one varies a surface that divides between reactants and products so as to minimize the unidirectional flux through the surface. Considering that the rate is given by the ratio of the reactive flux and the population of reactants one has that “such a calculation gives an upper limit to the true reaction rate since passage at least once through the trial surface is a necessary condition for reaction.” Keck specifically shows that VTST reduces to Eyring's TST under appropriate conditions. For Keck, as for Wigner and Horiuti, there is no ambiguity in the definition of the activated complex, it is the solution of the variational minimization problem. If the activation energy is large as compared with $k_B T$ then naturally this surface will be in the vicinity of the barrier and will be very close to the surface perpendicular to the unstable mode at the saddle point.

Keck had an additional contribution. The chemistry community became interested not only in thermal reaction rates but also in energy dependent microcanonical rates. For this purpose, he formulated a statistical theory of reaction rates⁴⁶ which could be considered as an adaptation to molecular dynamics of the statistical theories of nuclear reaction rates⁴⁷ developed earlier in the physics community.

Rate theory and especially TST became an object of quantitative studies with the introduction of computers. In the early 1960's people started using them to solve numerically the classical motion of atoms and molecules evolving on a single Born–Oppenheimer potential energy surface. They were able to compute numerically exact reaction rates and compare them with theory. One of the interesting results was that microcanonical TST gave energy dependent reaction probabilities that were greater than unity.⁴⁸ This problem was actually realized already back in the Faraday discussion by Hinshelwood.⁴⁹ It usually does not arise in practice in activated reactions for which the barrier height is much larger than $k_B T$, but it is striking when considering microcanonical reaction rates.

This difficulty was also resolved through use of VTST. The variational dividing surface which truly minimizes the reactive flux will never lead to reaction probabilities that are greater than unity. Only when one uses a “bad” dividing surface for which there are many recrossings does one encounter the problem. When accounting for recrossings, it was shown⁵⁰ that the unidirectional flux across any dividing surface is identical to the average number of recrossings of the

dividing surface. This average number can of course be greater than unity. When it is less than unity, it gives a non-trivial upper bound on the reaction rate.

B. What is the activated complex?

In pioneering work, De Vogelaere and Boudart realized that periodic orbits play a special role in collinear atom diatom reactions.⁵¹ In 1976, Pechukas⁵² resolved the mystery by noting that classically, the solution to microcanonical variational TST is a classical bound state embedded in the continuum. For a system with N degrees of freedom, it is a phase space manifold with dimensionality $2 \times (N-1)$ and so it is truly an intermediate entity between reactant and products. For a system with two degrees of freedom the energy dependent activated complex is a periodic orbit dividing surface, named a pods,^{53,54} moving between the two equipotential energy surfaces. One can also show that the optimal canonical dividing surface in two degrees of freedom is a trajectory embedded in the continuum, however it moves on an effective temperature dependent surface.⁵⁵

For reactive systems with two degrees of freedom, one typically finds that for a small energy range above the saddle point energy, there exists only one pods between reactants and products. In this energy region, there are no recrossings and TST is exact.⁵⁶ When more than one pods exists, the flux through the pods leads to both upper and lower bounds to the microcanonical reaction probability.⁵⁷ The activated complex is by definition the pods with the minimal unidirectional flux through it.

The identity of the activation energy in the Arrhenius expression was resolved in 1978 by Chandler.⁵⁸ He presented a formal derivation of the classical transition state theory expression for the rate of reaction in liquids. Using the regression hypothesis, he identified the rate as the time rate of change of the reactants density autocorrelation function which can be expressed as the ratio of the “reactive flux” to the density of reactants. Then he noted that classical TST gives an upper bound to the reactive flux and used the unidirectional flux of TST to obtain the TST expression for the rate. His innocuous looking one-dimensional TST result is obtained by hiding the condensed phase in a one-dimensional potential of mean force. The activation energy in his expression is now a free energy, answering the 50-year-old question as to whether it is the energy or the free energy.

C. Unification of the TS method with Kramers' Brownian motion theory and solution of the Kramers turnover problem

Originally, Kramers' prefactor for the rate was considered as a dynamic friction induced correction to TST. Only in 1986 was it demonstrated that Kramers' result for the moderate-to-strong damping regime may be derived from classical variational transition state theory.⁵⁹ Until then, everyone used the “simple” dividing surface perpendicular to the system coordinate q . The identity between variational TST and Kramers' result was derived by (a) using the well-known identity of the Langevin equation with a Hamiltonian

in which the system is bilinearly coupled to a harmonic bath,⁶⁰ and then (b) allowing the dividing surface to be perpendicular to a collective mode reaction coordinate ρ which is a linear combination of the system and harmonic bath modes. The coefficients of the linear combination are determined by minimizing the unidirectional flux. For a parabolic barrier potential this exactly gives the Kramers result. In fact, the ratio of the “standard” TST result based on use of the dividing surface perpendicular to the system q coordinate and Kramers' expression is just a reflection of the large number of times that trajectories recross the “standard” dividing surface. For the parabolic barrier, the optimized collective mode ρ is separable from all other modes, trajectories cross the surface perpendicular to it only once and VTST is exact.

In the underdamped energy diffusion limited regime, a variational TST approach shows that the dividing surface is now in energy space,⁶⁵ similar to the dividing surface used by Wigner in his treatment of three-body dissociation.¹⁶ However, it is not possible to construct a simple surface which would totally eliminate the recrossings of this energy dividing surface.

The observation that in dissipative systems one should use collective mode reaction coordinates then led to a flurry of activity, culminating by a two step solution to the old Kramers' turnover problem. Mel'nikov and Meshkov showed how one could derive a uniform expression for the rate which covered the underdamped-to-moderate damping limit.⁶⁶ Pollak, Grabert, and Hänggi then used Mel'nikov and Meshkov's formalism but adapted it to the collective mode to derive an expression which is valid for all values of the damping as well as memory friction.⁶⁷

D. Quantum TST?

Another question which remains open even today is that of a quantum mechanical analog to TST. One can follow Eyring's approach⁶ and replace classical partition functions with quantum partition functions, make a separable approximation about the saddle point, and use it to treat the unstable mode quantum mechanically thus introducing tunneling corrections. This “engineering” approach was used rather successfully by Truhlar *et al.*,^{68,69} who devised strategies for calculating quantum reaction rates in rather complex systems. Although useful in practice, and typically accurate to within an order of magnitude and often much less, this approach remains unsatisfying due to its *ad hoc* nature.

A serious attempt to formulate a quantum mechanical TST comes in 1974 with the paper of McLafferty and Pechukas.⁷⁰ They demonstrated that although one could derive upper bounds of a TST form to the reaction rate the bounds were not very good even for a free particle or a parabolic barrier potential. The quantum upper bound property remained a topic of active research for the next two decades⁷¹⁻⁷⁴ however the quantum upper bounds to the rate are not as useful as in the classical theory. For deep tunneling they go as the amplitude of the tunneling, instead of the amplitude squared and for above barrier activation, they are not accurate enough to justify the numerical effort needed in computing them.

Classical canonical transition state theory relies on thermodynamic averages, so that the search for a quantum transition state theory is really a search for a rate theory which relies only on imaginary time data. An important milestone in this direction was the centroid based approximation for the rate developed during the past 15 years.⁷⁵⁻⁷⁷

In this approach, the rate expression is approximated as a product of a centroid density containing all closed paths with centroid at the transition state, multiplied by a thermal velocity factor. The centroid expression for the rate is exact for a parabolic barrier. However, due to the intuitive derivation, centroids do not give upper bounds to the rate and so the location of the transition state in asymmetric systems can become quite a problem. The centroid TST has been improved upon by employing centroid dynamics.^{78,79}

The great advantage of the centroid approach is that it can be computed for many dimensional systems, however, the lack of a derivation from first principles leaves one with an uneasy feeling. At this point, the search for a rigorous expansion, in which the centroid based formulas would be the first term in a series is open. Just as the Wigner ansatz for the tunneling correction was a wonderful guess, so is the centroid approach. But one should keep in mind that even to date, it is more of an ansatz than a theory.

The centroid approach served though as an impetus for other approximate thermodynamic rate expressions. Pollak and Liao⁸⁰ followed an earlier idea of Voth *et al.*⁸¹ and replaced the exact projection operator appearing in the rate expression with two choices, one being the parabolic barrier projection operator in phase space, this approximation was termed by them as quantum TST, the other using classical mechanics to compute the projection operator.^{80,82} This mixed quantum classical theory was rederived by Wang and coworkers⁸³ and termed the linearized approximation, since it also comes about from linearization of the action appearing in the path integral about the classical dynamics. The formal advantage of these two methods over the centroid method is that one can at least in principle write down quantum correction terms. In practice, although demonstrated to be useful for a one-dimensional symmetric Eckart potential,⁸² no one has attempted to compute these correction terms for reactions with two or more degrees of freedom.

A different thermodynamic approach was suggested by Hansen and Andersen⁸⁴ who noted that the first few initial time derivatives of the flux flux correlation function involve only thermodynamic averages. They used various extrapolation formulas to bridge the gap between the initial time and final time and thus derive a thermodynamic rate theory. Here too though, the extrapolation is fraught with danger, and it is difficult to obtain systematic corrections and convergence toward an exact result.⁸⁵

In the early 1970s Miller⁸⁶ showed that semiclassically the tunneling rate is determined by a periodic trajectory moving on the upside down potential energy surface, with period $\hbar/k_B T$. The physics community, rediscovered this same object^{87,88} and named it the instanton. In a seminal paper, Caldeira and Leggett derived the formulas for the instanton in the case of a particle moving under the influence of dissipation, introduced by coupling the system bilinearly to a har-

monic bath. In fact, for many years, starting with Kramers' paper of 1940, the physics community was interested in reaction rates in condensed matter and modeled the "bath" in terms of the Langevin equation, which had its roots in Einstein's paper of 1905. It was though only in 1983 that Caldeira and Leggett applied the Feynman-Vernon influence functional approach⁸⁹ to a quantum system bilinearly coupled to a harmonic bath to derive an instanton based rate expression for tunneling in the presence of dissipation. Their theory became the standard model of quantum friction, which continues to be a subject of intense study to this very day due to its applicability as a model for a broad variety of physical phenomena. In particular, the influence of temperature and friction on quantum rates has been studied extensively by means of this theory. For a review we refer to Hänggi *et al.*²

Originally, the concept of the instanton came from semiclassical. Only lately Miller and coworkers have managed to formulate a quantum mechanical object which in the semiclassical limit reduces to the instanton.⁹⁰ This quantum mechanical instanton turns out to be an extremum of the off diagonal matrix elements of the Boltzmann operator $\langle q | e^{-\beta H} | q' \rangle$ with respect to the positions q and q' . They then use the quantum instanton coupled with the short time Laplace inversion method of Plimak and Pollak⁹¹ to obtain a new rate expression. Although the tests on this quantum instanton theory were rather successful,⁹² this approach too suffers from the fact that it is not a theory in the sense of a set of approximations that converge towards the correct answer.

E. Reactive flux method

One of the central difficulties in computing reaction rates for large systems is the rare sampling of events that lead to reaction. Especially if the barrier height is large compared to $k_B T$ the probability of finding an initial condition which will lead to barrier crossing becomes small and the computational cost high. To overcome this problem, Chandler⁵⁸ used Onsager's regression hypothesis⁹³ to derive a reactive flux formula whose great advantage was that it provided a technique in which one could sample the phase space in the vicinity of the barrier to reaction instead of reactants, thus leading to an enormous saving in computational effort.⁹⁴ This approach later led to more sophisticated methods for identifying the barriers to reaction in multidimensional systems.^{95,96} The reactive flux method which originally was restricted to processes with a well-defined velocity, was later also generalized to jump and diffusion processes.⁹⁷

The reactive flux method also served as the basis for the application of variational TST to condensed phases,^{29,55,98,99} as the reactive flux is bounded from above by the unidirectional flux. By varying the dividing surface one could improve upon the Kramers-Grote-Hynes estimate of the rate in the spatial diffusion limit and obtain temperature dependent corrections.¹⁰⁰ The same corrections were also found in the framework of the Fokker-Planck description of thermally activated escape.¹⁰¹

One has to keep in mind though that any meaningful rate description is based on the assumption that the time scale on which the reaction takes place must be well separated from other time scales that describe the relaxation to, say, products once the separating barrier was crossed, and vice versa to reactants from the other side of the barrier. The time-scale separation is determined by the height of the separating barrier as seen from the reactants side. Recently Drozdov and Tucker¹⁰² determined the lowest nonvanishing eigenvalue of the Fokker–Planck equation and the reactive flux rate in a numerical study of an overdamped bistable Brownian oscillator. The lowest eigenvalue describes the asymptotic exponential approach to equilibrium and therefore can be identified with the equilibrium rate constant. If the rate picture holds, the equilibrium rate should agree with twice the reactive flux rate. For reduced barrier heights $\Delta V/k_B T$ smaller than 5 the deviation exceeds 1% and grows rapidly for lower barriers. For too low barriers the time scales start to merge and consequently the reactive flux rate no longer displays a pronounced plateau as a function of time because the population of reactants no longer can be considered as constant. If the correct time dependence of the reactant population is included the reactive flux rate converges to a plateau value.¹⁰³

F. Numerically exact quantum methods

The short paper by McLafferty and Pechukas⁷⁰ also provided the formulation of a precise quantum mechanical expression for the reactive flux as

$$\text{Flux} = \text{Tr}[j(x)P_+e^{-\beta H}] \quad (2.1)$$

with $j(x)$ being the standard quantum mechanical current operator. An important construct here is the projection operator P_+ which projects onto the scattering wave functions with the appropriate boundary conditions. At the same time Miller was interested in a semiclassical version of reaction rate theory and transition state theory. He too wrote down a quantum expression for the reactive flux which was identical to that of Pechukas and McLafferty, and then proceeded to estimate it semiclassically.¹⁰⁴ It took almost another decade until in 1983 Miller, Schwartz, and Tromp¹⁰⁵ formulated the exact quantum reaction rate in terms of flux correlation functions, which turned out to be generalizations of Yamamoto's expressions for reaction rates¹⁰⁶ which were based on linear response theory. McLafferty and Pechukas⁷⁰ and Miller and coworkers¹⁰⁵ used the known scattering theory expressions for the rate and rewrote them as a reactive flux divided by the density of reactants. It cannot be overstressed that the scattering theory based expression is correct. As discussed below, it has also been adapted to reactions in condensed phases where the boundary conditions differ from scattering boundary conditions. The formal proof of the validity of the flux–flux correlation function formalism for the quantum (and even classical mechanics) rate of reaction in condensed phases remains open to date, see also below.

Topaler and Makri,¹⁰⁷ in their ground breaking quantum numerical computations, used the reactive flux methodology to compute the numerically exact quantum rate in a symmetric double well potential coupled bilinearly to a harmonic

bath using what they called the quasiadiabatic path integral method. Their computations then served as benchmarks for many other approximate quantum theories. At the end of the day, we do not know whether the formal rate expression used by Topaler and Makri is exact. The reduced barrier height used in their computations was $\Delta V/k_B T=5$, where we already know classically that the reactive flux over population method starts to deviate from the lowest nonzero eigenvalue of the Kramers equation. Quantum rate theory in condensed phases remains an open problem.

Enormous progress has been made toward solution of the scattering dynamics of molecule–molecule collisions. Reviewing the molecular scattering theory literature is beyond the scope of the present review, suffice it to note that the present day state of the art is a full quantum mechanical solution for systems with up to seven degrees of freedom.¹⁰⁸ The limitation is that even the most sophisticated method relies on using grids in configuration space and their dimensionality grows exponentially with the number of degrees of freedom. It is therefore virtually impossible even with present day computers to go with these methods beyond at most ten dimensions.

The evident strategy to overcome the dimensionality problem is to resort to path integral methods. These are prohibitive for real time because of the sign problem, the integrand in the real time path integral is too oscillatory. However when considering imaginary time path integrals, the exponent is real and negative and so there is no serious convergence problem. Imaginary time path integrals have been computed for systems with more than 100 dimensions.¹⁰⁹ The natural extension of rate theory was then to attempt to devise a quantum mechanical framework which would rely only on imaginary time data. One natural choice is to use the inverse Laplace transform to get the real time results.^{110–112} The inverse Laplace transform is though ill behaved, the noise in the Monte Carlo estimates is typically too large to allow more than short time inversion and this is just not sufficient, even when using sophisticated numerical methods such as maximum entropy inversion.¹¹²

G. Rates in nonequilibrium systems

Thermal equilibrium is of eminent importance for the understanding of many processes in physics and chemistry but, in many other cases, as for example in living matter, fluxes of energy and matter prevent a system from approaching a thermal equilibrium state. Time and space dependent structures may then persist in the asymptotic long-time behavior of such a nonequilibrium system. In general, the presence of fluxes in nonequilibrium systems breaks the microscopic reversibility and consequently these systems do not obey the principle of detailed balance.^{93,113} Yet different locally stable states may coexist. Ubiquitous thermal or possibly also external noise will generally induce transitions between these states. The determination of the respective transition rates though is hampered by the fact that the asymptotic distribution of the system is not known in most cases due to the lack of detailed balance. Often, numerical simulations of the stochastic dynamics^{114,115} of the considered system are the only possible approach.

Before discussing some of the available approximate methods we note that a general distinction can be made between systems that are driven out of equilibrium by stationary fluxes of matter and energy and others on which time-dependent external forces act preventing the system from reaching equilibrium. In the first case the system's dynamics is still autonomous and, in presence of noise, a stationary probability distribution will be approached asymptotically at large times. In the second case, asymptotically, the probability distribution will still depend on time. Accordingly, different methods are needed to determine transition rates in these cases.

For autonomous nonequilibrium systems, in principle, both the flux over population method and the mean first passage time approach can be used to determine the rate. For each method, the asymptotic probability distribution is required, but most often is not known. In particular cases, perturbational treatments about known stationary distributions are feasible.^{116–119} For weak noise, a singular perturbation theory^{30,120,121} which is analogous to WKB theory in quantum mechanics, can be employed to first find the stationary distribution and then the transition rates. Within this approach, the stationary probability distribution contains an exponentially leading part $\exp\{-\Phi(x)/\epsilon\}$ where ϵ denotes the noise strength, $\Phi(x)$ is a generalized potential, and x a point in the respective state space. The generalized potential is a continuous function of x but may show discontinuities of its derivatives. These singularities must be compensated by a preexponential factor to assure that a smooth probability distribution results. Decay rates of metastable states were determined for special two-dimensional Fokker–Planck cases for which the generalized potential is sufficiently smooth¹²² and also for simple one-dimensional noisy maps.^{123,124} In the latter case, as a consequence of the singularities of the generalized potential, the prefactor of the rate depends on the noise strength in a nonanalytical way.

In the presence of time dependent driving, noise induced transitions give rise to important effects which are strictly absent in equilibrium systems. These effects comprise stochastic resonance,^{125,126} and resonance activation^{127,128} as well as the rectification of noise in ratchets or Brownian motors.^{129,130} In general, the time-dependent forcing leads to time-dependent rates, considerably complicating any analytical description. For a periodically driven bistable system time-dependent rates as well as the time averaged rates were determined in the limit of weak noise by means of the path integral representation of the transition probability from one locally stable state to the moving separatrix.¹³¹ For the same type of systems a different limit results if the noise strength is small but fixed and the external driving is much slower than the intrawell relaxation. The time dependent rate is then given by the adiabatic expression for the frozen force. For this approximation to hold, no further restriction is to be imposed on the period of the driving force which may still be larger or smaller than the resulting transition time. This kind of kinetic description has been applied to describe a large variety of phenomena^{132–134} but only recently a strict derivation from a Fokker–Planck model was provided.¹³⁵

III. FUTURE: OPEN PROBLEMS

A. Classical rate theory at equilibrium

Pechukas⁵² gave a clear identification for the activated complex in terms of a hypersurface of classical bound states embedded in the continuum. For closed systems with two degrees of freedom, the fixed energy surface is well characterized as a periodic orbit dividing surface. However for systems with more than two degrees of freedom, the nature of this surface remains elusive. It can no longer be considered as a dividing surface in configuration space, one must consider it as a dividing surface in phase space.¹³⁶ The study of variational dividing surfaces in systems with more than two degrees of freedom remains a topic of active research even to date¹³⁷ as the classical dynamics of such nonlinearly coupled systems is rather complicated.

We also noted that for canonical systems, the activated complex is identifiable as a pods with infinite period moving on an effective temperature dependent potential energy surface.⁵⁵ Although Miller gave a general formal solution to the problem¹⁰⁴ the actual solution for systems with more than two degrees of freedom remains an open problem.

B. Classical rate theory away from equilibrium

As detailed in this paper, equilibrium rate theory is by and large well understood. However, as also outlined above, classical rate theory for systems outside of equilibrium is poorly understood. There is not any clear characterization of the structures that determine the flow such as the pods in the equilibrium case. The variational minimum principle of Wigner no longer exists and except for numerical simulations, we do not have any good theory of reaction rates away from equilibrium except in a few particular limiting cases. The key information that in most cases is missing is the asymptotic probability distribution in the state space of the considered system. Once this distribution is known one further has to identify the relevant transition regions corresponding to the saddle points in the free energy landscape in equilibrium problems, and has to determine the local dynamics in these regions. In principle, this then would allow one to estimate the rate by means of the flux over population expression, or by a conveniently defined mean first passage time. A further complication may arise from the fact that the topology of the energy landscape may be very complicated as, for example, for glass-forming liquids,¹³⁸ or for the motion and folding of proteins.¹³⁹ In such cases the resulting relaxational dynamics is no longer governed by an exponential decay law, but by some slower, possibly stretched exponential or even algebraic law.

Another question that only recently has been posed is related to the influence of a possibly non-Gaussian, algebraically correlated, random force on the escape dynamics from a metastable state. Apart from numerical simulations, fractional Fokker–Planck equations might prove to be a convenient starting point for such investigations.¹⁴⁰

C. Quantum equilibrium rate theory

At this point, there are a few benchmark computations of numerically exact quantum rates for dissipative systems. One of the promising routes is the use of stochastic Schrödinger equations.^{141–143} However, even the best of available results runs into problems when the barrier crossing dynamics is not rapid on the molecular time scales. It is very difficult to obtain long real time quantum mechanical data. Various authors have been suggesting methods for overcoming this problem. We note especially the recent multiconfiguration time-dependent Hartree method¹⁴⁴ which claims to give numerically exact results for dissipative systems with up to 1000 bath modes.

A different approach is based on the semiclassical initial value series representation of the exact propagator.¹⁴⁵ Instead of using the path integral, one uses a semiclassical propagator, which is a leading order term in a series expansion. Since one knows all the terms in the expansion, one can now compute them one by one to obtain the exact propagator. Experience with some model systems shows that the series converges rapidly¹⁴⁶ so that it can be used to generate numerically exact real time quantum data using a classical trajectory based Monte Carlo algorithm.

When considering dissipative systems, it is very appealing to attempt and derive reduced equations of motion for the system. A recent review of these may be found in Ref. 147. In the weak damping regime, these lead to Redfield theory^{148–150} and there have been attempts at solution for quantum reaction rates using these equations. In the strong friction limit, Ankerhold¹⁵¹ has derived low temperature extensions of the Caldeira–Leggett reduced equation of motion.¹⁹ An application of these reduced equations of motion to quantum barrier crossing problems has recently been carried out.¹⁵² The resulting rate coincides with the large friction limit of Wolynes' rate expression.¹⁵³

D. Quantum rate theory away from equilibrium

This is perhaps the most open problem remaining today. Again, as for classical systems, one may distinguish between systems that are driven out of equilibrium by external time dependent fields and systems with different reservoirs maintaining currents of energy and matter in the system. Very little is known about this latter case in general, see also the article by Hänggi and Ingold⁶¹ in this Focus Issue. The brute force numerical approach, which allows one to get insight into the classical problem is not available. In the presence of time-dependent forcing, the Zwanzig–Caldeira–Leggett harmonic oscillator bath model¹⁹ and the related spin-boson model¹⁵⁴ can be extended to include the forcing.¹⁵⁵ Within this framework particular aspects of quantum stochastic resonance^{126,156} and quantum ratchets^{129,157} have been investigated. But a comprehensive theoretical understanding is still lacking. A serious general problem in the field of open quantum systems is that seemingly harmless and even plausible approximations may entail inconsistencies with general statistical mechanical laws¹⁵⁸ and may introduce Maxwell demons that survive even in thermal equilibrium.¹⁵⁹

E. Concluding remarks

This paper attempted to provide some insight into the development of rate theory. It is though limited, due to the strict length limitations set by the editors of this Focus Issue and the probably subjective point of view of the authors. We have brought almost no formulas, instead pointed out to the interested reader what we believe are the “important” references. The paper is not comprehensive; for example, we have not discussed the rates of electron transfer reactions, where much remains for future work, especially when considering molecular electronics or electron transfer in biological systems. We have not provided a detailed history of the development of quantum scattering theory. Here too, progress has been made in inventing algorithms which allow extension of the computational horizon to increasingly larger systems, though as already noted, the largest to date is with seven degrees of freedom. The theory of surface diffusion, surface reactions, and catalysis which is closely related to rate theory has also been left out. We also have not considered the coherent control of rate processes,¹⁶⁰ a topic of intensive activity and interest, whose details are becoming clearer as people devise better quantum methods for dealing with multidimensional systems.

Another “hot topic” having to do with classical-quantum correspondence and the influence of classical chaos on quantum dynamics has also been set aside.¹⁶¹ Interesting phenomena such as quantum tunneling in multidimensional systems and its relationship to the underlying real time classical dynamics, or the effects of external fields on quantum tunneling rates have also not been included in this review.

Our central purpose was to point out some of the important milestones in the development of rate theory and to encourage a new generation to continue the study of rate theory. Due justice to the many people who have contributed significantly to the theory and from whose knowledge we have all gained would probably be only possible if one would write up a comprehensive book on rate theory.

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