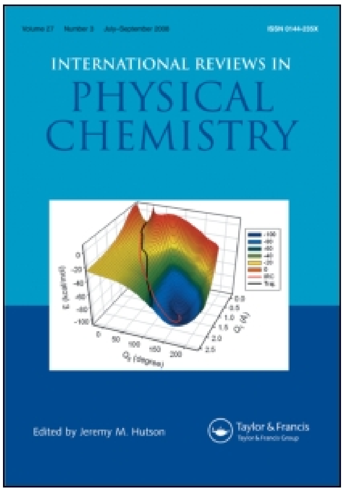

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Variational transition state theory for activated chemical reactions in solution

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An approach is outlined for including solvent effects in variational transition state theory calculations of rate constants for activated chemical reactions in solution. The focus is on methods capable of first-principles predictions of reaction rate constants from interatomic potential energy surfaces. The approach separates the system into a cluster model that is treated explicitly and the 'solvent' that is treated approximately, and includes both equilibrium solvation effects on interaction energies and non-equilibrium effects that enter through a solvent friction model. We discuss methods used to included quantum-mechanical effects on bound vibrational motions and quantum-mechanical effects on motion along a reaction coordinate (e.g. quantum tunnelling).

1. Introduction

Transition state theory (TST) (Glasstone *et al.* 1941, Bunker 1966, Johnston 1966, Pechukas 1976, Laidler 1987) has been the most widely used tool for analysis of rate constants for chemical reactions in both gas phase (for example Benson 1976) and solution (for example Moore and Pearson 1981). In addition, TST provides a convenient framework for first-principles predictions of reaction rate constants from a knowledge of the potential energy as a function of interatomic distance (the potential energy surface). The calculation of reaction rate constants from potential energy surfaces was first discussed by Eyring (1935) and progress towards this goal has been reviewed by Laidler and King (1983) and Truhlar *et al.* (1983). Over the past decade there has been great progress in developing methods for quantitative predictions of rate constants of gas-phase reactions (for a recent review see Steinfeld *et al.* 1989). One successful example of this is quantized variational transition state theory (VTST) with multidimensional semiclassical tunnelling corrections (Truhlar and Garrett 1980, 1984, Truhlar *et al.* 1985, Isaacson *et al.* 1987, Lu *et al.* 1992) that have been developed for reactions in the gas phase and at gas–surface interfaces. These methods are capable of accurate predictions of gas-phase rate constants; the accuracy of the potential energy surface is typically the major factor limiting the precision of the calculated rate constants. Applications of VTST have been reviewed by Truhlar and Garrett (1984) and Truhlar and Gordon (1990) and recent critical comparisons of VTST with accurate quantum mechanics include those by Garrett *et al.* (1986), Garrett and Truhlar (1991) and McRae *et al.* (1992). Here we examine a strategy for applying the quantized VTST with multidimensional semiclassical tunnelling methods to reactions in solution.

The thermodynamic formulation of TST (Glasstone *et al.* 1941) is the approach most used for analysing gas-phase reaction rate constants (Benson 1976) (see also Truhlar and Garrett 1989 for how this approach can be extended to include variational and tunnelling effects). In this approach a quasiequilibrium is postulated between reactants and the transition state. The rate constant is expressed as the product of the

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rate of decomposition of the transition state complex to products and the equilibrium constant for forming the transition state complex from reactants. The equilibrium constant is often interpreted in terms of a free energy of activation or, equivalently, in terms of separate contributions to the enthalpy and entropy of activation that are modelled empirically or theoretically (Benson 1976). The effect of the solvent on the reaction energetics is conveniently included in this formalism as the difference in free energies of solvation of the transition state and reactants (see Reichardt 1988, and references therein).

The dynamical formulation of TST (Wigner 1938) provides the best approach to examine the approximations in TST and also provides the basis for improvements to the conventional theory. In this approach, the classical equilibrium rate constant† is derived using a single approximation, the fundamental dynamical assumption of TST (Wigner 1938, Miller 1974, Pechukas 1976, Tucker and Truhlar 1989). The reactive flux through a dividing surface separating reactants from products is assumed to be the equilibrium flux of trajectories that crosses the dividing surface with momentum directed towards products; that is, it is assumed that all classical trajectories that reach the dividing surface from the reactant side are stabilized as products without recrossing the dividing surface. This obviates the need to know the detailed classical dynamics of the reaction; only the momentum at the dividing surface is required. Once this approximation is made, the rate constant calculation reduces to an equilibrium statistical mechanical evaluation of the volume of available phase space for trajectories to pass from reactants to products. Evaluation of this equilibrium average is constrained to a dividing surface and yields the classical partition function for the bound degrees of freedom that are defined by the dividing surface.

Classical trajectories that recross the dividing surface cause the breakdown of the fundamental dynamical assumption of TST. All reactive classical trajectories are required to cross the dividing surface at least once, but some non-reactive trajectories that recross the dividing surface are also counted as reactive in TST. Thus TST provides an upper bound to the exact reactive flux of classical trajectories through the dividing surface. This is the basis of classical variational VTSTs that optimize the location of the dividing surface to minimize the rate constant (Wigner 1937, Horiuti 1938, Keck 1960, 1967, Jaffe *et al.* 1973, Miller 1974, Pechukas 1976, Pollak and Pechukas 1978, Garrett and Truhlar 1979b). Although the dividing surface can, in principle be defined as a function of both coordinates and momenta, practical applications for complex systems generally require the use of simple functional forms such as planar functions of coordinates only.

The effect of the solvent on the reaction energetics can also be included in the dynamical formulation of classical transition state theory (Chandler 1978, Hynes 1985a, Berne *et al.* 1988). For reactions in solution, the equilibrium averages include ensemble averages over solvent degrees of freedom and they can be evaluated using

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†Throughout we shall use the term rate constant to denote equilibrium rate constant rather than the phenomenological non-equilibrium rate constant that may be observed experimentally. Approximating the observed rate constant by the equilibrium rate constant is often referred to as the local-equilibrium approximation, for example the assumption that transition state species which originated as reactants are in local equilibrium with reactants. We address only those approximations needed to obtain the equilibrium rate constant.

standard methods of statistical mechanics (McQuarrie 1976). The equilibrium averages yield partition functions for the transition state complex and reactants, and the ratio of these partition functions is just the equilibrium constant used in the thermodynamic formulation. If the dividing surface is defined to be a function of only the coordinates of the reacting solute molecules, then the thermodynamic averages over the solvent degrees of freedom give the solvent partition function that is related to the free energy of solvation.

The use of TST for solution-phase reactions dates back to the work of Evans and Polanyi (1935), but it is only within the past 15 years that the validity of the fundamental approximation of classical mechanical TST have been more closely examined for reactions in solution (for example Chandler 1978 and Hynes 1985a). As pointed out by these workers, collisions of solvent molecules with the reacting solute molecules can lead to recrossings of the dividing surface that do not occur in the gas phase and therefore lead to a breakdown of the fundamental dynamical assumption of TST. One advantage of the dynamical formulation of TST is that it provides a means to mitigate the effects of this breakdown by variationally optimizing the dividing surface in the space of both the solute and the solvent degrees of freedom. In this case the dividing surface is defined as a function of solvent coordinates as well as the coordinates of the reacting solute molecules. A procedure for using planar dividing surfaces that includes the explicit solvent coordinates in classical mechanical VTST has been discussed by Pollak (1991c). However, this does lead to a complication in the calculation of the ensemble averages since they are constrained to be evaluated on a dividing surface. It is much easier to evaluate the averages over the solvent degrees of freedom if they have no external constraint. For this reason, dividing surfaces are typically chosen to depend only on the solute coordinates, and solvent-induced recrossings are included using approximate models. This is discussed further below in the context of equilibrium and non-equilibrium solvent effects.

For many reactions, especially those including light atoms, such as hydrogen atom, proton or hydride transfer reactions, quantum-mechanical effects on the motion of the atoms must be included. Attempts at developing a rigorous formulation of a quantum-mechanical TST that provides an upper bound to the exact quantum-mechanical rate constant have not been successful to date (McLafferty and Pechukas 1974, Miller 1974, Pechukas 1976, Pollak and Proselkov 1993). Additional approximations are needed to include quantum-mechanical effects into TST. The standard approach is an *ad-hoc* procedure (Eyring 1935, Glasstone *et al.* 1941) that replaces classical partition functions by approximate quantum-mechanical functions and then correction factors for quantum-mechanical effects on the reaction coordinate motion (such as tunnelling) are included. That is the approach discussed here for including quantum-mechanical effects in VTST (Garrett and Truhlar 1979c, Truhlar *et al.* 1982, 1985, Isaacson *et al.* 1987, Lu *et al.* 1992).

Before proceeding we mention another approach that is gaining popularity, namely the Feynman path integral formulation (Feynman and Hibbs 1965, Feynman 1972) of quantum-mechanical TST (Voth *et al.* 1989) that was based on earlier work by Gillan (1987). This method has recently been reviewed by Voth (1993) including a review of applications and extensions of the method. It is interesting that both the VTST and the path integral approaches have been applied to a model reaction in solution (McRae *et al.* 1992, McRae and Garrett 1993) and, although they employ different approximations, they agree well with each other and with accurate benchmark results. To date, the VTST approach has been applied and tested for a more extensive set of systems and to more complex reactions, and in this work we examine how it can be extended to even more complex systems, namely solution-phase reactions. The approach taken here is to develop reduced-dimensional effective Hamiltonians that approximate the effects of the solvent. The path integral approach can be applied either to the Hamiltonians for the full system or to the reduced-dimensional Hamiltonians. In the future it will be interesting to see comparisons of these types of calculation as well as other comparisons of the VTST and path integral approaches for reduced-dimensional Hamiltonians.

The computational procedures used to perform VTST calculations that include quantum-mechanical effects are significantly different from those outlined above for the classical mechanical theory. The quantum-mechanical calculations require identification of a saddle point and a reaction path connecting the saddle point with reactants and products. For reactions in solution, there are many saddle points that are close in energy and that differ significantly only in the configuration of the solvent (for example Warshel 1979 and Harris and Stillinger 1990). The multiple saddle points are a reflection of the large anharmonicity in the solvent that makes the quantum-mechanical calculation of the partition functions impractical. In this case, it is much more difficult to see how to apply VTST methods to reactions in solution. The major focus of this work is the description of a procedure for making these calculations practical.

VTST including quantum-mechanical effects can be applied to solution-phase reactions by separating the system into a cluster model that contains the part of the system undergoing reaction and the solvent that is treated in an approximate manner (figure 1). This dichotomy is well founded in the literature (for example Adelman 1983, 1984, Warshel and Russell 1984, Robinson *et al.* 1990). The cluster model can include a finite collection of solvent molecules as well as the reactants or solute molecules. The effects of microsolvation on reaction dynamics has been studied using VTST by Tucker and Truhlar (1990), Gonzalez-Lafont *et al.* (1991) and Zhao *et al.* (1991, 1992) and using classical trajectories by Hu and Hase (1992). The VTST calculations have included only a small number of solvent molecules (one or two) but in principle this approach can be extended to larger clusters. As more solvent molecules are added, the VTST calculations become more difficult and applications to clusters of sufficient size to reproduce bulk liquid are not practical. In practice, the studies of cluster models will be limited to those that are sufficiently small to retain the ease of the gas-phase VTST calculations. Note that in this article we shall use the terminology solute to mean the cluster model even though it may contain some solvent degrees of freedom.

A convenient approach to approximating the influence of the extended solution on the solute reaction dynamics is by separating solvent equilibrium (static) and non-

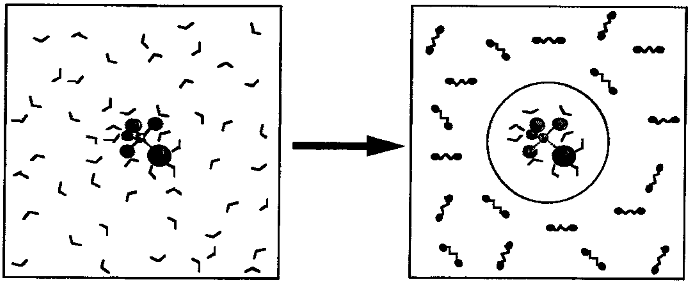

Figure 1. Approximation of solution-phase system by a cluster model (inside the circle) and an approximate model of the solvent (depicted by oscillators).

equilibrium (dynamic) effects.† Equilibrium solvation affects the reaction energetics of the solute. The constant proximity of solvent molecules around the solute changes the interaction potential of the solute. The resulting mean-field potential for the solute is obtained from an equilibrium ensemble average over solvent configurations. Since this mean-field potential is obtained from an equilibrium ensemble average at each solute configuration, the equilibrium solvation assumption implies that the solvent molecules instantaneously equilibrate to each new solute configuration. In the thermodynamic formulation of TST the effect of the solvent on the reaction energetics is included by the free energy of solvation that is obtained from equilibrium ensemble averages and is therefore an equilibrium solvent effect.

From a knowledge of the potential energy surface of the entire system, the free energy of solvation, or equivalently the potential of mean force, can be computed classically using statistical perturbation theory (Zwanzig 1954). This approach has been used to compute the free energy of activation for reactions in solution by Jorgensen and co-workers (for recent reviews see Jorgensen 1988, 1989). In some cases, such as when masses of either the solute or solvent are sufficiently light, a quantum-mechanical evaluation of the free energy may be necessary. In principle this can be accomplished using path integral methods (Feynman and Hibbs 1965, Feynman 1972).‡ The condition for validity of classical mechanics is that the de Broglie wavelengths of the particles are sufficiently small compared with the average length scale of their interactions with other particles in the solution. For most cases, except possibly for hydrogen atoms, classical mechanics should be adequate and in this article we consider only the classical mechanical evaluation of the free energies of solvation.

Equilibrium solvation includes the average effect of the solvent on the energetics of the interactions within the cluster for each cluster geometry. This neglects any dynamical influence that the solvent may have on the reaction dynamics as a result of solvent fluctuations. Non-equilibrium or dynamic solvent effects can be separated into local and collective effects. Local effects, such as solvent caging in which the solvent molecules must move out of the way of the reacting molecules, involve only a limited number of solvent molecules that can be included in the cluster model. Collective effects involve cooperative motions of the molecules in the bulk liquid and may be included with reduced-dimensional models. When the interaction potentials are dominated by electrostatic interactions (such as for a charge-transfer reaction in a polarizable medium), the collective effect may be best included by a non-equilibrium polarization model (Lee and Hynes 1988, Truhlar *et al.* 1993). Here we focus on situations where this collective non-equilibrium solvent effect on the solute dynamics is treated by a solvent friction model based on a generalized Langevin equation (GLE) (Zwanzig 1965, Mori 1965, Kubo 1966).

As mentioned above, one consequence of solvent dynamics is a breakdown of the no-recrossing approximation of TST. Methods for treating the solvent-induced recrossing based upon a solvent friction model include the early work of Kramers (1940) and more recent extensions by Grote and Hynes (1980). Recent reviews of the Kramers theory include those by Nitzan (1988) and Hänggi *et al.* (1990). These classical

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†The terminology of equilibrium and non-equilibrium solvent effects is very old (for example Kurz and Kurz 1972) but the concepts have been refined in more recent work (for example Chandler 1978, Truhlar *et al.* 1983, Hynes 1985a, b, Berne *et al.* 1988, Tucker and Truhlar 1990).

‡For a recent example of the calculation of a quantum-mechanical free energy of solvation see Gai and Garrett (1994).

mechanical methods estimate the recrossing of a dividing surface that is defined in terms of a single solute reaction coordinate using a GLE model. As has been shown by van der Zwan and Hynes (1983, 1984), a single reaction coordinate GLE model can be equivalent to a multidimensional solvent model. The formal relation between the Kramers and Grote–Hynes theories and multidimensional classical TST on an effective Hamiltonian that models the solvent friction by a collection of oscillators (Ford *et al.* 1965, Zwanzig 1973) has been demonstrated by Dakhnovskii and Ovchinnikov (1985) and Pollak (1986a). In this case, the dividing surface in the multidimensional TST is implicitly defined to be a function of effective solvent degrees of freedom as well as those of the solute. In the present paper we discuss how the friction model can be used in VTST calculations that include quantum-mechanical effects.

The notion that the friction model can be used in a quantum-mechanical calculation deserves further consideration. The GLE is a classical mechanical equation of motion for the solute degrees of freedom that includes the effect of solvent friction and random forces exerted by the solvent. In this model the influence of the solvent dynamics on the reaction is completely determined by the friction tensor. The friction tensor may be obtained from classical mechanical simulations of the autocorrelation function of the force exerted by the solvent on the solute. The use of classical mechanics to model the influence of the solvent dynamics on the reaction is most valid when the friction tensor is characterized by low-frequency intermolecular motions of the solvent. In the case where high-frequency intramolecular solvent motions contribute significantly to the friction tensor, it may be better to include explicitly some of these modes in the cluster model where they can be treated quantum-mechanically. The use of the classical mechanics to obtain the friction tensor is therefore on firm grounds; however, the use of this classically derived friction model in a quantum-mechanical calculation is less justified. Throughout this article we shall describe the approximate treatment of the solvent interaction with the solute in terms of reduced-dimensional effective Hamiltonians. The reduced system will then be solved in terms of a complete quantum-mechanical treatment. Classical mechanics is a convenient technique for parametrization of these Hamiltonians. If necessary, quantum mechanics may be employed. These issues will be discussed further in § 3.

One goal of this paper is to indicate how the equilibrium and non-equilibrium solvent effects can be incorporated in the computational procedures used in quantized VTST calculations. Although the focus is on a quantum-mechanical prescription, it is first necessary to consider classical mechanical rate theories since the solvent influence on the reaction dynamics of the solute is modelled using classical mechanics. Therefore, we explicitly show how the reduction of the multidimensional solvent to the approximate equilibrium and non-equilibrium models is carried out in classical mechanical rate theories. For the nonequilibrium model it is necessary to examine the exact classical dynamics in the reduced model; thus, the starting point for our discussions is the exact classical rate constant expression. Once the approximation to the dynamical influence of the solvent is made, the explicit dynamics are replaced by the transition state approximation. An effective Hamiltonian of reduced dimension results from the analysis. Quantum-mechanical corrections are then made to the classical mechanical generalized TST expression by an *ad-hoc* procedure.

Another objective here is to indicate the type of information that is needed to perform the VTST calculations. One advantage of VTST over other dynamical methods for gas-phase reaction is that a global potential energy surface is not needed (Garrett *et al.* 1981, Truhlar *et al.* 1986, Isaacson *et al.* 1987, Truhlar and Gordon 1990).

By knowing the potential in the region of a path connecting reaction and products (a 'reaction-valley potential' as termed by Truhlar and Gordon 1990), the VTST calculations can be performed. One approach is to use the potential and its first and second derivatives along the reaction path computed using *ab-initio* electronic structure theory (for recent applications of this approach see Garrett *et al.* 1990 and Garrett and Melius 1991). When necessary, selected higher-order derivatives can be included to account for some of the anharmonicity. In the present paper we present an approach to representing the solvent average potential along a reaction valley in terms of the value of the potential and its first and second derivatives along a path.

We start in §2 by reviewing the classical rate theories and the methods used to include quantum-mechanical effects in the VTST calculations. In §3 we consider a partitioning of the system into solute and solvent components and then discuss approximate methods for including solvent effects in the classical mechanical and quantum-mechanical theories. Both equilibrium and non-equilibrium solvation approximations are derived within the classical mechanical theories and prescription for treating the models quantum-mechanically are described. In §4, concluding remarks are presented.

2. Methods

We are interested in the application of VTST beginning from a knowledge of the potential energy surface and other important parameters of the system, such as the mass of the atoms and temperature. Throughout, it is assumed that the potential energy surface for the entire system is known. A discussion of methods for obtaining accurate potential energy surface information for the extended system of a reaction in solution is beyond the scope of this work. However, we shall try to indicate where the solvent effects can be approximated by reduced-dimensional models rather than a full potential energy surface.

We begin by discussing the general case where all degrees of freedom are explicit. In this case, all atoms are considered to be part of the cluster model or solute and the approach is identical with that used in a gas-phase reaction. The starting point is knowledge of the complete Hamiltonian for the system. We assume, with no loss of generality, that the Hamiltonian may be recast in the following mass-scaled form:

$$H(\mathbf{q}, \mathbf{p}) = \frac{\mathbf{p}^2}{2\mu} + V(\mathbf{q}), \tag{1}$$

where $\mathbf{q}$ and $\mathbf{p}$ are coordinates and conjugate momenta of the cluster model (or solute), μ is a reduced mass and $V(\mathbf{q})$ is the potential energy surface as a function of the coordinates. It is most convenient to take $\mathbf{q}$ to be the Cartesian coordinates of each atom in the system multiplied by a mass scaling factor that gives the same effective mass μ for each coordinate.

2.1. *Classical rate theories*

The reactive flux formalism (Miller 1974) provides a convenient formulation of the classical rate constant for chemical reactions in terms of the Hamiltonian.† It is assumed that the reactants may be distinguished from the products by a continuous

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†The reactive flux formalism of Miller is most convenient for gas-phase reactions and this is the approach taken here. The reactive flux correlation formalism of Yamamoto (1960) is convenient for both gas- and solution-phase reactions. In the latter the rate constant is derived from a time-dependent reactive flux correlation function. The phenomenological rate constant, if it exists, is defined as the plateau value of the time correlation function (Chandler 1978). In the reactive flux formalism used here, it is assumed that a plateau value exists.

function $Z(\mathbf{q}, \mathbf{p})$ that is negative for reactant regions and positive for product regions of phase space. (Often it is the case that a single coordinate, q_1 for example, is chosen to be a 'reaction coordinate', and Z is chosen to be a function of the reaction coordinate only, e.g. $Z = q_1$.) The classical equilibrium rate constant is expressed in terms of the flux of reactive trajectories across the dividing surface defined by the implicit equation, $Z = 0$. For a canonical ensemble at temperature T, the exact classical rate constant is given by

$$k_{\mathrm{cl}}(T) = \frac{\mathrm{Tr}_{\mathrm{cl},\mathbf{q}}[\exp(-\beta H)\,\delta(Z)\dot{Z}\chi]}{Q^{\mathrm{R}}_{\mathrm{cl}}(T)}, \tag{2}$$

where the classical trace is defined as a classical phase-space average:

$$\mathrm{Tr}_{\mathrm{cl},\mathbf{q}}[\ldots] = \int \frac{\mathrm{d}\mathbf{q}\,\mathrm{d}\mathbf{p}}{(2\pi\hbar)^N}\cdots, \tag{3}$$

N is the total dimension the system, $2\pi\hbar$ is Planck's constant, $\beta = 1/k_{\mathrm{B}}T$ and k_{B} is Boltzmann's constant. The phase-space average is over initial conditions for classical trajectories and the Dirac delta function restricts the average to the dividing surface (e.g. $Z = 0$). Each phase-space point is weighted by the classical phase-space density $\exp(-\beta H)$, and the flux through the dividing surface for the trajectory specified by the point in phase space is defined by

$$\dot{Z} = \frac{\partial Z}{\partial \mathbf{q}}\cdot\frac{\partial H}{\partial \mathbf{p}} - \frac{\partial H}{\partial \mathbf{q}}\cdot\frac{\partial Z}{\partial \mathbf{p}}. \tag{4}$$

The characteristic function $\chi(\mathbf{q}, \mathbf{p})$ (Pechukas and McLafferty 1973) projects out the reactive trajectories and may be written explicitly as (Chandler 1978)

$$\chi(\mathbf{q}, \mathbf{p}) = \theta(Z(t_{\mathrm{P}}))\theta(-Z(-t_{\mathrm{P}})), \tag{5}$$

where we have written $Z(t)$ for $Z[\mathbf{q}(t), \mathbf{p}(t)]$, $[\mathbf{q}(t), \mathbf{p}(t)]$ is the phase-space point resulting from propagating the point $(\mathbf{q}, \mathbf{p})$ for time t, θ is a unit step function, and t_{P} is the plateau time. Thus χ projects out those trajectories that begin in reactants (e.g. $Z(-t_{\mathrm{P}}) < 0$) and end in products (e.g. $Z(t_{\mathrm{P}}) > 0$). The product of the classical density, the flux through the dividing surface and the characteristic function form a microscopic reactive flux, and the product $Q^{\mathrm{R}}_{\mathrm{cl}}(T)k_{\mathrm{cl}}(T)$ is often referred to as the total 'reactive flux'. The normalization $Q^{\mathrm{R}}_{\mathrm{cl}}(T)$ is the reactant partition function, which may be written as

$$Q^{\mathrm{R}}_{\mathrm{cl}}(T) = \mathrm{Tr}_{\mathrm{cl},\mathbf{q}}[\exp(-\beta H)\,\chi^{R}], \tag{6}$$

where χ^{R} is a projector of the reactant region of phase space. For example, for a bimolecular reaction, χ^{R} can be chosen as a delta function in the relative Cartesian vector between the two reactants for a large internuclear separation giving a partition function per unit volume. For a unimolecular reaction, χ^{R} can be chosen as a unit step function in a reaction coordinate that limits the integration to the reactant region.

The transition state approximation is obtained by making a short-time approximation to the characteristic function in equation (5) (Chandler 1978). The TST approximation selects those trajectories that pass from the reaction to product side over a short period of time, e.g. $\chi^{\mathrm{TST}}(\mathbf{q}, \mathbf{p}) = \theta(\dot{Z})$. Using this approximation we obtain the generalized TST expression

$$k^{\mathrm{GT}}_{\mathrm{cl}}[Z, T] = \frac{\mathrm{Tr}_{\mathrm{cl},\mathbf{q}}[\exp(-\beta H)\,\delta(Z)\dot{Z}\theta(\dot{Z})]}{Q^{\mathrm{R}}_{\mathrm{cl}}(T)}. \tag{7}$$

The resulting value for the exact classical rate constant $k_{\mathrm{cl}}(T)$ obtained from equation (2) is independent of the choice of the dividing surface defined by $Z=0$. The TST expression is dependent on the dividing surface and in VTST the dividing surface is optimized to minimize the rate constant.

In our implementation of VTST, rather than allow arbitrary orientations of the dividing surface, a one-parameter sequence of dividing surfaces is considered by the following procedure. This is a compromise between a practical scheme that is applicable to complex problems and methods for obtaining the best variational solution. In applications the constrained variations of the dividing surface still provide practical improvements over the conventional choice of placing the dividing surface at the saddle point (for example Garrett and Truhlar 1979b). The reaction path is defined as the minimum-energy path (MEP), that is the path of steepest descent from the saddle point to reactants and products in the mass-scaled coordinates (Shavitt 1959, 1968, Weston 1959, Marcus 1966, 1968b, Truhlar and Kuppermann 1971, Fukui 1974, Schaefer 1975). Explicitly, this path is defined by $\mathbf{q}^{\mathrm{MEP}}(s)$ and is obtained from integrating the equation

$$\mathbf{q}'(s)=\frac{\mathrm{d}}{\mathrm{d}s}\mathbf{q}^{\mathrm{MEP}}(s)=-\left.\frac{\partial_{\mathbf{q}}V}{|\partial_{\mathbf{q}}V|}\right|_{\mathbf{q}=\mathbf{q}^{\mathrm{MEP}}(s)}, \tag{8}$$

starting from the saddle point at $s=0$ with an initial step along the eigenvector for the unbound mode. The reaction coordinate s along the MEP is the (signed) distance from the saddle point (negative on the reactant side and positive on the product side). The evaluation of the MEP requires calculation of the first derivatives of the potential along the MEP. Generalized transition state dividing surfaces are constrained to be hyperplanes that are orthogonal to the reaction path and are defined by their location s along the reaction coordinate. Given $\mathbf{q}'(s)$, a sequence of planar dividing surfaces may be defined as

$$Z_s(\mathbf{q},\mathbf{p})=\mathbf{q}'(s)[\mathbf{q}-\mathbf{q}^{\mathrm{MEP}}(s)]=0. \tag{9}$$

Given the MEP, one may define a local coordinate system (Garrett and Truhlar 1979b) based upon local normal modes at each s that are obtained from diagonalizing the matrix of mass-scaled second derivatives with the reaction coordinate motion projected out. This requires calculation of the Hessian matrix along the MEP. Explicitly, one diagonalizes the matrix (Miller *et al.* 1980)

$$\mathbf{F}^{\mathrm{P}}(s)=[1-\mathbf{q}'(s)\mathbf{q}'(s)^{\mathrm{T}}]\left.\left(\frac{\partial^2 V}{\partial\mathbf{q}^{\mathrm{T}}\partial\mathbf{q}}\right)\right|_{\mathbf{q}=\mathbf{q}^{\mathrm{MEP}}(s)}[1-\mathbf{q}'(s)\mathbf{q}'(s)^{\mathrm{T}}] \tag{10}$$

to give a set of normal mode eigenvectors $\mathbf{L}_m(s)$ and eigenvalues $\mu\omega_m^2(s)$. The normal mode coordinates are $(\mathbf{u},\xi)$, where the coordinate ξ is associated with the tangent eigenvector $\mathbf{q}'(s)$, and $\mathbf{u}$ is associated with the remaining $N-1$ bound modes orthogonal to the reaction coordinate. Transformation between the Cartesian and normal coordinates is given by

$$\mathbf{q}=\mathbf{q}^{\mathrm{MEP}}(s)+\sum_{m=1}^{N-1}\mathbf{L}_m u_m+\mathbf{q}'(s)\xi. \tag{11}$$

This series of dividing surfaces serve to define the s-dependent generalized TST expression for the gas-phase canonical rate constant (Truhlar *et al.* 1985):

$$k_{\mathrm{cl}}^{\mathrm{GT}}(s,T)=k_{\mathrm{cl}}^{\mathrm{GT}}[Z_s,T]=\frac{k_{\mathrm{B}}T}{h}\frac{Q_{\mathrm{cl}}^{\mathrm{GT}}(s,T)}{Q_{\mathrm{cl}}^{\mathrm{R}}(T)}\exp[-\beta V^{\mathrm{MEP}}(s)], \tag{12}$$

where $h=2\pi\hbar$, $V^{\mathrm{MEP}}(s)$ is the potential evaluated on the MEP at s, and the zero of energy of the potential is defined to be the reactant equilibrium geometry (e.g. $V^{\mathrm{MEP}}(s)$ at reactants is zero). The generalized transition state partition function for the bound modes orthogonal to the reaction path at s is given in terms of the local normal coordinates by

$$Q_{\mathrm{cl}}^{\mathrm{GT}}(s,T)=\mathrm{Tr}_{\mathrm{cl},\mathbf{u}}\left\{\exp\left[-\beta\left(\frac{|\mathbf{p}_u|^2}{2\mu}+V(\mathbf{u},\xi=0)-V^{\mathrm{MEP}}(s)\right)\right]\right\}, \tag{13}$$

where $\mathrm{Tr}_{\mathrm{cl},\mathbf{u}}$ is the classical trace over the $N-1$ bound modes and $V(\mathbf{u},\xi)$ is $V(\mathbf{q})$ with the Cartesian coordinates defined by equation (11). Note that the partition function is defined with its zero of energy at the local minimum of the potentials for the bound modes orthogonal to the reaction coordinate. The canonical variational theory (CVT) rate constant is obtained by minimizing equation (12) with respect to s (Garrett and Truhlar 1979b):

$$k_{\mathrm{cl}}^{\mathrm{CVT}}(T)=\min_{s}\left[k_{\mathrm{cl}}^{\mathrm{GT}}(s,T)\right]\sim k_{\mathrm{cl}}^{\mathrm{GT}}(s_{\mathrm{cl}}^{\mathrm{CVT}}(T),T), \tag{14}$$

where $s_{\mathrm{cl}}^{\mathrm{CVT}}(T)$ is the location of the dividing surface that minimizes equation (12) at temperature T.

2.2. *Quantum-mechanical variational transition state theory*

The classical expression for the rate constant given in equation (12) is the starting point for including quantum-mechanical effects in VTST. To obtain the appropriate quantum-mechanical expression for the rate constant, first the classical mechanical partition functions are replaced by their quantum-mechanical analogues (for example Garrett and Truhlar 1979c). The quantized generalized transition state rate constant is given by

$$k^{\mathrm{GT}}(s,T)=\frac{k_{\mathrm{B}}T}{h}\frac{Q^{\mathrm{GT}}(s,T)}{Q^{\mathrm{R}}(T)}\exp\left[-\beta V^{\mathrm{MEP}}(s)\right], \tag{15}$$

where $Q^{\mathrm{R}}(T)$ and $Q^{\mathrm{GT}}(s,T)$ are evaluated quantum-mechanically. In the quantum-mechanical generalization, the classical trace in equation (13) is replaced by a quantum-mechanical trace. Using an independent normal mode approximation, the potential becomes decoupled and one-dimensional energy levels for the bound modes may be computed. In this case, the quantized partition function is given by the product of partition functions for each mode:

$$Q^{\mathrm{GT}}(s,T)=\prod_{m} q_m^{\mathrm{GT}}(s,T), \tag{16}$$

where the partition function for mode m is given by the sum over Boltzmann factors for the energy levels in the mode, that is

$$q_m^{\mathrm{GT}}(s,T)=\sum_{n_m}\exp\left[-\beta\varepsilon_m^{\mathrm{GT}}(s,n_m)\right] \tag{17}$$

and $\varepsilon_m^{\mathrm{GT}}(s,n_m)$ is the generalized transition state energy level for level n_m in mode m. Within the harmonic approximation, the independent normal mode approximation becomes exact and equations (16) and (17) reduce to

$$Q_{\mathrm{h}}^{\mathrm{GT}}(s,T)=\prod_{m}\frac{1}{2\sinh\left[\frac{1}{2}\hbar\omega_m(s)\beta\right]}, \tag{18}$$

where $\omega_m(s)$ is the harmonic frequency for mode m at location s along the MEP. When low-frequency modes are present, the harmonic approximation is very often not valid and methods for including anharmonicity must be considered (Garrett and Truhlar 1979e, 1984, Truhlar *et al.* 1982). In these cases it is often possible to introduce quantum-mechanical corrections to the accurate classical partition functions (Pitzer and Gwinn 1942, Messina *et al.* 1993). This is discussed further below for reactions in solution when low-frequency modes of the solvent are present.

With the partition functions in equation (15) treated quantum-mechanically, the rate constant is a hybrid quantized expression in which the bound modes are treated quantum-mechanically but the reaction coordinate motion is treated classically. The adiabatic theory of reactions (Marcus 1966, 1967, 1968a, Truhlar 1970) provides a consistent route to include quantum-mechanical effects in reaction coordinate motion. In the adiabatic theory of reactions, coordinates orthogonal to the reaction coordinate are treated as 'fast' variables. Reaction probabilities $P(\mathbf{n}, E)$ for each adiabatic state are obtained by considering the dynamics on the one-mathematical-dimensional vibrationally adiabatic potential. In the independent normal-mode approximation the adiabatic potential is written

$$V_a(s, \mathbf{n}) = V^{\mathrm{MEP}}(s) + \sum_m \varepsilon_m^{\mathrm{GT}}(s, n_m), \tag{19}$$

where the sum is over the bound vibrational modes of the generalized transition state at s, and the energy levels $\varepsilon_m^{\mathrm{GT}}(s, n_m)$ are the same as those used in the partition functions. The reaction probabilities $P(\mathbf{n}, E)$ can then be thermally averaged to yield the rate constant. When reaction coordinate motion is treated classically, the adiabatic theory of reactions yields an expression for the thermal rate constant which is equivalent to that obtained from microcanonical variational theory (μVT) even though the approximations in the two theories are very different (Garrett and Truhlar 1979b, c). Since the one-dimensional scattering problem can be treated quantum-mechanically, a multiplicative tunnelling correction factor for the adiabatic theory of reactions can be obtained, and the equivalency of μVT and adiabatic theory makes it consistent to use the same correction factor to account for the quantization of reaction coordinate motion in the μVT.

Rather than compute the tunnelling through all adiabatic potentials that contribute significantly to the tunnelling correction factor, for gas-phase reactions the tunnelling correction factor is approximated by the tunnelling through the ground-state potential only (Garrett *et al.* 1980):

$$\kappa^{\mathrm{CVT/AG}}(T) = \beta \exp \beta V_a(s^{\mathrm{CVT}}(T), \mathbf{n} = \mathbf{0})] \int_0^{\infty} \mathrm{d}E \exp(-\beta E) P(\mathbf{n} = \mathbf{0}, E). \tag{20}$$

At low temperatures where tunnelling corrections are most important, quantized systems tend to be in the ground state, and this approach provides is a good approximation. As temperature increases, tunnelling through excited-state adiabatic potentials would contribute relatively more, but tunnelling becomes less important and the correction factor decreases until at sufficiently high temperatures it tends to unity. The ground-state method gives the correct high-temperature limit, and for intermediate temperatures, the tunnelling through excited-state adiabatic potentials is approximated (implicitly) by the tunnelling probabilities for the ground-state potential with the energy scale shifted by the difference in the excited-state and ground-state energies at the ground-state maximum. The resulting quantum-mechanical CVT rate constant with the tunnelling correction factor included is then given by

$$k^{\mathrm{CVT/AG}}(T) = \kappa^{\mathrm{CVT/AG}}(T)k^{\mathrm{CVT}}(T). \tag{21}$$

The adiabatic approximation is made in a curvilinear coordinate system and, although the potential term is simple, the kinetic energy term is complicated by factors dependent upon the curvature of the reaction path (Marcus 1964, 1966, Miller *et al.* 1980). As shown by Skodje *et al.* (1982), the most successful methods for including the multidimensional effect of the reaction path curvature in the adiabatic calculations of the reaction probabilities are those that specify a tunnelling path that 'cuts the corner' and shortens the tunnelling length. Marcus and Coltrin (1977) found the optimum tunnelling path for the collinear $H + H_2$ reaction by finding the path that gave the least exponential damping. The small-curvature semiclassical adiabatic ground-state (SCSAG) method (Skodje *et al.* 1981, 1982) extends the Marcus–Coltrin method to other reactions and to multidimensional reactions. It has been extensively tested and shown to be valid for systems in which only one bound mode is coupled to the reaction coordinate. The centrifugal-dominant (CD) SCSAG method (Lu *et al.* 1992) provides a more suitable approximation for systems with non-zero components of the reaction path curvature along several generalized normal modes. The CD SCSAG method reduces to the previous SCSAG method in the limit of one non-zero component of the reaction-path curvature. The adiabatic tunnelling methods are most valid for systems with small to intermediate reaction path curvatures.

The adiabatic approximation is expected to break down for reactions with large reaction path curvatures (e.g. for reactions involving the transfer of a light atom or fragment between two heavy moieties). For these systems it is most appropriate to use methods that do not rely on the adiabatic approximation in the interaction region. The large-curvature ground-state (LCG) tunnelling method approximates the tunnelling paths as straight-line tunnelling paths between adiabatic turning points in the reactant and product region (Garrett and Truhlar 1983, Garrett *et al.* 1983, Truhlar *et al.* 1985, Garrett *et al.* 1989). In the spirit of the approach used by Marcus and Coltrin (1977), the least-action ground-state (LAG) method chooses the optimum tunnelling path as the path with least exponential damping (least action) from a set of paths interpolated between the MEP and the straight-line LCG tunnelling path (Garrett and Truhlar 1983, Truhlar *et al.* 1985). The LAG method is the most computationally intensive method and, to date, only the LCG method has been implemented for general polyatomic reactions. A simpler but more approximate method is to choose the optimum tunnelling from the CD SCSAG and LCG methods (Truhlar *et al.* 1992, Liu *et al.* 1993).

For the adiabatic tunnelling methods, the information about the potential energy surface needed for the calculations of the tunnelling correction factor $\kappa^{\mathrm{CVT/AG}}(T)$ is the same as for evaluating the hybrid quantized rate constant in equation (15). For the CD SCSAG method, the necessary information about the curvature of the reaction path can be obtained from the gradient and Hessian matrix along the MEP (Miller *et al.* 1980). If a harmonic representation of the potential is sufficient, the calculation can be accomplished by knowing the potential, gradient vector and Hessian matrix along the MEP. Anharmonicity for bound modes is typically added as selective higher-order terms in the potential. In both the LCG and the LAG methods, the tunnelling path can sample regions of the potential energy surface far from the MEP and outside the region of validity of the expansion of the potential at the MEP. In this case a wider region of the potential is needed but is still limited compared with a global potential energy surface (Truhlar *et al.* 1986, Garrett *et al.* 1989). In the present work we focus on the use of methods for which only the expansion in the region of the MEP is sufficient. The approach discussed below can be extended to include the LCG and LAG methods, but these methods are not pursued here.

3. Solvent effects

We outlined above a general procedure for obtaining a rate constant for the general case where all degrees of freedom are explicit. The procedure required the identification of a path in the multidimensional configuration space, requiring the evaluation of gradients of a potential along the path. By defining coordinates normal to the path, a generalized transition expression for the rate constant is given by equation (12). With the Hessian along the path, within a harmonic approximation for the transverse motion, a quantum-mechanical rate constant is recovered. To extend this procedure to the condensed phase, we need to define appropriate procedures for obtaining the MEP and the effective potential, gradient and Hessian along that path.

To generalize the procedure to the condensed phase, we first start from the full microscopic description of the system. The Hamiltonian for the total system is partitioned into a gas-phase component for the cluster model in the absence of the solvent and the solvent component that includes coupling between the solvent and cluster model:

$$H(\mathbf{q}, \mathbf{p}, \mathbf{x}, \mathbf{p}_x) = H_{\text{gas}}(\mathbf{q}, \mathbf{p}) + H_{\text{solv}}(\mathbf{p}_x; \mathbf{q}), \tag{22}$$

where $\mathbf{q}$ and $\mathbf{p}$ are coordinates and conjugate momenta of the solute, and $\mathbf{x}$ and $\mathbf{p}_x$ are the solvent coordinates and conjugate momenta. The solute and solvent components take the same form as in equation (1):

$$H_{\text{gas}}(\mathbf{q}, \mathbf{p}) = \frac{|\mathbf{p}|^2}{2\mu} + V_{\text{gas}}(\mathbf{q}) \tag{23}$$

and

$$H_{\text{solv}}(\mathbf{x}, \mathbf{p}_x; \mathbf{q}) = \frac{|\mathbf{p}_x|^2}{2\mu} + V_{\text{solv}}(\mathbf{x}; \mathbf{q}), \tag{24}$$

where $V_{\text{gas}}(\mathbf{q})$ is the potential energy surface for the solute and $V_{\text{solv}}(\mathbf{x}; \mathbf{q})$ is the potential energy surface for the solvent including the solvent interactions with the solute. The total potential is defined as

$$V(\mathbf{q}, \mathbf{x}) = V_{\text{gas}}(\mathbf{q}) + V_{\text{solv}}(\mathbf{x}; \mathbf{q}). \tag{25}$$

Here we shall review two levels of approximation for obtaining the rate constant for a reactive process in solution. The levels of approximation are, firstly, modelling the solvent influence on the solute by assuming equilibrium solvation, and secondly, including dynamic solvent effects by using a linear response model.

3.1. *Equilibrium solvent effects*

3.1.1. *Classical mechanical rate theory*

First consider the case where there is weak dependence of H_{solv} on $\mathbf{q}$ and we define both the dividing surface Z and the reactant region of phase space by χ^{R} in terms of $(\mathbf{q}, \mathbf{p})$ only. Then we may factor out the solvent partition function

$$Q_{\text{cl,solv}}(\mathbf{q}, T) = \text{Tr}_{\text{cl},\mathbf{x}}[\exp(-\beta H_{\text{solv}})] \tag{26}$$

in both the expression for the rate constant and the reactant partition function. The reactant partition function is approximated by

$$\begin{aligned} Q^{\mathrm{R}}_{\mathrm{cl}}(T) &\approx Q_{\mathrm{cl,solv}}(\mathbf{q}, T)\,\mathrm{Tr}_{\mathrm{cl},\mathbf{q}}\,[\exp(-\beta H_{\mathrm{gas}})\,\chi^{R}] \\ &= Q_{\mathrm{cl,solv}}(\mathbf{q}, T)\,Q^{\mathrm{R}}_{\mathrm{cl,gas}}(T), \end{aligned} \tag{27}$$

and the rate constant reduces to that for the gas-phase reaction

$$k^{\mathrm{GT}}_{\mathrm{cl,gas}}[Z, T] = \frac{\mathrm{Tr}_{\mathrm{cl},\mathbf{q}}\,[\exp(-\beta H_{\mathrm{gas}})\,\delta(Z)\dot{Z}\theta(\dot{Z})]}{Q^{\mathrm{R}}_{\mathrm{cl,gas}}(T)}. \tag{28}$$

The above result shows that, within a TST approximation, the resulting gas-phase rate constant is not influenced if H_{solv} has a weak $\mathbf{q}$ dependence. In addition, the MEP required for adding quantum corrections is identical with the gas-phase MEP.

This result motivates the introduction of an equilibrium solvation description of the rate constant. In this case the dependence of H_{solv} on $\mathbf{q}$ is not ignored, but we still assume that the dividing surface Z and the reactant region of phase space are defined in terms of solute coordinates alone. An equilibrium solvation Hamiltonian is defined by

$$\begin{aligned} \exp[-\beta H_{\mathrm{ES}}(\mathbf{q}, \mathbf{p}, T)] &= \mathrm{Tr}_{\mathrm{cl},\mathbf{x}}\,[\exp(-\beta H)] \\ &= Q_{\mathrm{cl,solv}}(\mathbf{q}, T)\exp[-\beta H_{\mathrm{gas}}(\mathbf{q}, \mathbf{p})]. \end{aligned} \tag{29}$$

In the case of equilibrium solvation the rate constant expression for generalized transition state theory, analogous to equation (7), can be written

$$k^{\mathrm{GT}}_{\mathrm{cl,ES}}[Z, T] = \frac{\mathrm{Tr}_{\mathrm{cl},\mathbf{q}}\,[\exp(-\beta H_{\mathrm{ES}})\,\delta(Z)\dot{Z}\theta(\dot{Z})]}{Q^{\mathrm{R}}_{\mathrm{cl,ES}}(T)}, \tag{30}$$

where

$$Q^{\mathrm{R}}_{\mathrm{cl,ES}}(T) = \mathrm{Tr}_{\mathrm{cl},\mathbf{q}}\,[\exp(-\beta H_{\mathrm{ES}})\,\chi^{\mathrm{R}}]. \tag{31}$$

This expression is identical in form with the rate constant given in equation (7) except the full Hamiltonian is replaced by the equilibrium solvation Hamiltonian. The only assumption made in deriving equation (30) is that the dividing surface and reactant region of phase space are defined in terms of solute coordinates only.

For the form of the total Hamiltonian given in equations (23)–(25), the equilibrium solvation Hamiltonian can be rewritten

$$H_{\mathrm{ES}}(\mathbf{q}, \mathbf{p}, T) = \frac{|\mathbf{p}|^2}{2\mu} + V_{\mathrm{ES}}(\mathbf{q}, T), \tag{32}$$

where the equilibrium solvation potential is defined by

$$\partial_{\mathbf{q}} V_{\mathrm{ES}}(\mathbf{q}, T) = \langle \partial_{\mathbf{q}} V(\mathbf{q}, \mathbf{x}) \rangle_{\mathbf{q}} = \partial_{\mathbf{q}} V_{\mathrm{gas}}(\mathbf{q}) + \langle \partial_{\mathbf{q}} V_{\mathrm{solv}}(\mathbf{q}, \mathbf{x}) \rangle_{\mathbf{q}}, \tag{33}$$

and the $\mathbf{q}$ constrained average is given by

$$\langle \ldots \rangle_{\mathbf{q}} = \frac{\mathrm{Tr}_{\mathrm{cl},\mathbf{x}}\,[\exp(-\beta H)\ldots]}{\mathrm{Tr}_{\mathrm{cl},\mathbf{x}}\,[\exp(-\beta H)]}. \tag{34}$$

Thus, $V_{\mathrm{ES}}(\mathbf{q}, T)$ is just the potential of mean force (McQuarrie 1976) generalized to a multidimensional solute. It has long been realized that the effect of equilibrium solvation can be included in TST using the potential of mean force (Chandler 1978, Truhlar *et al.* 1983, Hynes 1985a, b, Berne *et al.* 1988); however, most previous calculations of equilibrium solvation contributions to the TST rate constant express the potential of mean force as a function of a single coordinate, namely the reaction coordinate. Equation (30) differs in the fact that the rate constant is written as a function of a multidimensional equilibrium solvation potential energy surface.

VTST calculations as outlined in §2 do not require a knowledge of the global potential energy surface, only the potential in a quadratic region around the MEP is needed. Note that the first-derivative information needed to define the MEP for the equilibrium solvation model is given directly by equation (33). The second-derivative information needed for the definition of the normal modes used in the evaluation of the partition functions are given by

$$\begin{aligned}\partial_{\mathbf{q}}\partial_{\mathbf{q}}V_{\mathrm{ES}}(\mathbf{q}) &= \langle\partial_{\mathbf{q}}\partial_{\mathbf{q}}V(\mathbf{q},\mathbf{x})\rangle_{\mathbf{q}} - \beta[\langle\partial_{\mathbf{q}}V(\mathbf{q},\mathbf{x})\partial_{\mathbf{q}}V(\mathbf{q},\mathbf{x})\rangle_{\mathbf{q}} - \langle\partial_{\mathbf{q}}V(\mathbf{q},\mathbf{x})\rangle_{\mathbf{q}}\langle\partial_{\mathbf{q}}V(\mathbf{q},\mathbf{x})\rangle_{\mathbf{q}}] \\ &= \partial_{\mathbf{q}}\partial_{\mathbf{q}}V_{\mathrm{gas}} + \langle\partial_{\mathbf{q}}\partial_{\mathbf{q}}V_{\mathrm{solv}}\rangle_{\mathbf{q}} - \beta(\langle\partial_{\mathbf{q}}V_{\mathrm{solv}}\partial_{\mathbf{q}}V_{\mathrm{solv}}\rangle_{\mathbf{q}} - \langle\partial_{\mathbf{q}}V_{\mathrm{solv}}\rangle_{\mathbf{q}}\langle\partial_{\mathbf{q}}V_{\mathrm{solv}}\rangle_{\mathbf{q}}). \qquad (35)\end{aligned}$$

The MEP and the harmonic expansion of V_{ES} along the MEP will be different from the gas-phase path. It is, however, restricted to span solute coordinate space alone. This will not be the case when dynamical solvent effects are introduced in the next section.

With the planar dividing surfaces defined in terms of the MEP, the classical generalized TST rate constant is given by

$$\begin{aligned}k^{\mathrm{GT}}_{\mathrm{cl,ES}}(s,T) &= \frac{k_{\mathrm{B}}TQ^{\mathrm{GT}}_{\mathrm{cl,ES}}(s,T)}{Q^{\mathrm{R}}_{\mathrm{cl,ES}}(T)}\exp[-\beta V^{\mathrm{MEP}}_{\mathrm{ES}}(s,T)] \\ &= \frac{k_{\mathrm{B}}T}{h}\frac{Q^{\mathrm{GT}}_{\mathrm{cl,ES}}(s,T)}{Q^{\mathrm{R,0}}_{\mathrm{cl,ES}}(T)}\exp\{-\beta[V^{\mathrm{MEP}}_{\mathrm{ES}}(s,T)-V^{\mathrm{R}}_{\mathrm{ES}}]\}, \qquad (36)\end{aligned}$$

where $V^{\mathrm{MEP}}_{\mathrm{ES}}(s,T)$ is the potential along the MEP on the equilibrium solvation potential, $V^{\mathrm{R}}_{\mathrm{ES}}$ is the value of the equilibrium solvation potential at the reactant equilibrium geometry in the equilibrium solvation potential, and the equilibrium solvation generalized transition state partition function is defined by an expression similar to equation (13) but with the potential replaced by V_{ES} and the normal mode coordinates determined from the Hessian matrix constructed from the second derivatives of the equilibrium solvation potential (e.g. equation 35). The generalized transition state partition functions are defined with their zeros of energy at the local minimum of the potentials for the bound modes. Since the equilibrium solvation potential does not necessarily go to zero at the reactant equilibrium geometry, the additional Boltzmann factor of the potential at reactants arises in the evaluation of the reaction partition function in equation (31). The reactant partition function with this zero of energy (at the local minimum at the reactant equilibrium geometry) $Q^{\mathrm{R,0}}_{\mathrm{cl,ES}}(T)$ is defined by equation (31) with the Boltzmann factor $\exp(-\beta V^{\mathrm{R}}_{\mathrm{ES}})$ removed. Because of the change in the equilibrium solvation potential from the gas-phase value, the potential $V^{\mathrm{MEP}}_{\mathrm{ES}}(s,T)$ along the MEP, the potentials for the bound vibrations and thereby the partition functions $Q^{\mathrm{GT}}_{\mathrm{cl,ES}}(s,T)$ and $Q^{\mathrm{R}}_{\mathrm{cl,ES}}(T)$ are also different from their gas-phase counterparts. The equilibrium solvation CVT rate constant is obtained by minimizing equation (36) with respect to the reaction coordinate.

It is instructive to examine the generalized transition state expression for the rate constant in terms of the thermodynamic formulation. We can rewrite equation (36) as (Garrett and Truhlar 1979a–d)

$$k^{\mathrm{GT}}_{\mathrm{cl,ES}}(s,T) = \frac{k_{\mathrm{B}}T}{h}K^0\exp[-\beta\,\Delta G^{\mathrm{GT,0}}_{\mathrm{cl,ES}}(s,T)], \qquad (37)$$

where K^0 is the reciprocal of the standard state concentration for bimolecular reactions and unity for unimolecular reactions, and $\Delta G^{\mathrm{GT},0}_{\mathrm{cl,ES}}(s,T)$ is the classical equilibrium solvation generalized transition state standard-state molar free energy of activation as a function of the reaction coordinate. Equating equations (36) and (37) and using the definition of $V_{\mathrm{ES}}(\mathbf{q})$ implied by equations (29) and (32) leads to

$$\Delta G^{\mathrm{GT},0}_{\mathrm{cl,ES}}(s,T) = V_{\mathrm{gas}}[\mathbf{q}^{\mathrm{MEP}}_{\mathrm{ES}}(s)] - V_{\mathrm{gas}}[\mathbf{q}^{\mathrm{R}}_{\mathrm{ES}}] - k_{\mathrm{B}}T\ln\left(\frac{Q^{\mathrm{GT}}_{\mathrm{cl,ES}}(s,T)Q_{\mathrm{cl,solv}}[\mathbf{q}^{\mathrm{MEP}}_{\mathrm{ES}}(s),T]}{K^0 Q^{\mathrm{R},0}_{\mathrm{cl,ES}}(T)Q_{\mathrm{cl,solv}}[\mathbf{q}^{\mathrm{R}}_{\mathrm{ES}},T]}\right), \tag{38}$$

where $\mathbf{q}^{\mathrm{MEP}}_{\mathrm{ES}}(s)$ is the MEP on the equilibrium solvation potential and $\mathbf{q}^{\mathrm{R}}_{\mathrm{ES}}$ is the equilibrium geometry on the equilibrium solvation potential. The free energy of activation in solution is often separated into a gas-phase free energy of activation plus a contribution from solvation:

$$\Delta G^{\mathrm{GT},0}_{\mathrm{cl,ES}}(s,T) = \Delta G^{\mathrm{GT},0}_{\mathrm{cl,gas}}(s,T) + \Delta G^{\mathrm{GT},0}_{\mathrm{cl,solv}}(s,T). \tag{39}$$

The gas-phase free energy of activation is given by

$$\Delta G^{\mathrm{GT},0}_{\mathrm{cl,gas}}(s,T) = V_{\mathrm{gas}}[\mathbf{q}^{\mathrm{MEP}}_{\mathrm{gas}}(s)] - k_{\mathrm{B}}T\ln\left(\frac{Q^{\mathrm{GT}}_{\mathrm{cl,gas}}(s,T)}{K^0 Q^{\mathrm{R}}_{\mathrm{cl,gas}}(T)}\right) \tag{40}$$

and the solvation part takes the form

$$\Delta G^{\mathrm{GT},0}_{\mathrm{cl,solv}}(s,T) = V_{\mathrm{gas}}[\mathbf{q}^{\mathrm{MEP}}_{\mathrm{ES}}(s)] - V_{\mathrm{gas}}[\mathbf{q}^{\mathrm{MEP}}_{\mathrm{gas}}(s)] - V_{\mathrm{gas}}[\mathbf{q}^{\mathrm{R}}_{\mathrm{ES}}] - k_{\mathrm{B}}T\ln\left(\frac{Q^{\mathrm{GT}}_{\mathrm{cl,ES}}(s,T)Q^{\mathrm{R}}_{\mathrm{cl,gas}}(T)}{Q^{\mathrm{GT}}_{\mathrm{cl,gas}}(s,T)Q^{\mathrm{R},0}_{\mathrm{cl,ES}}(T)}\right) - k_{\mathrm{B}}T\ln\left(\frac{Q_{\mathrm{cl,solv}}[\mathbf{q}^{\mathrm{MEP}}_{\mathrm{ES}}(s),T]}{Q_{\mathrm{cl,solv}}[\mathbf{q}^{\mathrm{R}}_{\mathrm{ES}},T]}\right). \tag{41}$$

Viewed this way, there are three types of contribution to the solvation part of the free energy of activation. In the first contribution, contained in the gas-phase potential terms in equation (41), solvation can change the reaction path and therefore change the contributions from the gas-phase potential along the MEP. The second to last term contains contributions arising from changes upon solvation in the potentials for the bound modes of the solute. The first two contributions are secondary effects that arise because solvation affects the interactions within the cluster model, thereby changing the MEP for the reaction and the internal vibrations in the cluster. The last term contains the actual mean contribution from the solvent on the reaction energetics.

Calculations of the equilibrium solvation free energy of activation have been performed by Jorgensen and coworkers (for reviews see Jorgensen 1988, 1989) using explicit microscopic evaluations. These calculations are carried out using a three-step procedure. First, the gas-phase MEP and potential profile along it are obtained from high-level *ab-initio* electronic structure calculations. Second, the solute–solvent and solvent–solvent interaction potentials are modelled using analytic functional forms. Third, the free energy of solvation of the rigid solute complex is computed from the model potentials using statistical perturbation theory.

It is important to note that equations (33) and (35) refer to explicit microscopic evaluations of the gradient and Hessian of V_{ES}. However, only a description of V_{ES} is required for the rate constant and its quantum-mechanical generalizations, and other approaches can be used to evaluate these quantities. For example, integral equation methods have been used to compute the solvation free energy of activation (Chiles and Rossky 1984, Huston *et al.* 1989). Ladanyi and Hynes (1986) carried out a careful study of equilibrium solvation effects within the context of VTST calculations. In this study the solvation contribution to the potential of mean force is computed from an extension of the equilibrium theory of solvent structure and thermodynamics developed by Chandler and Pratt (1976) (see also Pratt and Chandler 1977 and Chandler 1982). Also, it is entirely consistent to use an empirical model for V_{ES}, such as lattice dipole models (Warshel 1979, 1991) or one based on a continuum dielectric and an electric polarization field and a continuum model for the hydrophobicity of the solute (for example see the recent review by Cramer and Truhlar 1994).

The procedure reviewed above only obtains contributions to the solvation part of the free energy of activation contained in the last term in equation (41). The secondary solvation effects of changes to the MEP and the internal vibrations of the solute are neglected. There is evidence from the microsolvation studies of an S_N2 reaction by Tucker and Truhlar (1990) that the solvation effects on the location and energetics of the MEP may be small. The studies of Ladanyi and Hynes indicate that solvation effects on the internal vibrations of the solute are small for the case of an atom transfer reaction in a rare-gas liquid. Although these studies are encouraging that the inclusion of the more complicated contributions to the solvation free energy of activation may not be needed, more detailed studies are needed to test this for other types of reactions and solvents and for cases where quantum-mechanical effects (such as tunnelling) are important.

3.1.2. *Quantum-mechanical variational transition state theory*

For the equilibrium solvation model the quantum-mechanical VTST rate constant is obtained using the procedures outlined in § 2 but with the Hamiltonian H replaced by H_{ES} defined in equation (29). The quantized VTST rate constant is given by

$$k_{\mathrm{ES}}^{\mathrm{GT}}(s,T)=\frac{k_{\mathrm{B}}T}{h}\frac{Q_{\mathrm{ES}}^{\mathrm{GT}}(s,T)}{Q_{\mathrm{ES}}^{\mathrm{R}}(T)}\exp\left[-\beta V_{\mathrm{ES}}^{\mathrm{MEP}}(s,T)\right], \tag{42}$$

and the quantum-mechanical CVT rate constant with adiabatic ground-state transmission coefficient is given by

$$k_{\mathrm{ES}}^{\mathrm{CVT/AG}}(T)=\kappa_{\mathrm{ES}}^{\mathrm{CVT/AG}}(T)k_{\mathrm{ES}}^{\mathrm{CVT}}(T), \tag{43}$$

where $k_{\mathrm{ES}}^{\mathrm{CVT}}(T)$ is obtained by minimizing equation (42) with respect to s. As for the classical mechanical case, the change in the effective potential from the gas-phase value alters the bound energy levels $\varepsilon_{\mathrm{ES},m}^{\mathrm{GT}}(s,n_m)$, and thus the partition functions $Q_{\mathrm{ES}}^{\mathrm{GT}}(s,T)$ and $Q_{\mathrm{ES}}^{\mathrm{R}}(T)$ and also the adiabatice potential curve and tunnelling correction factor $\kappa_{\mathrm{ES}}^{\mathrm{CVT/AG}}(T)$, from their gas-phase counterparts.

Operationally, VTST calculations using the equilibrium solvation potential are the same as for the corresponding gas-phase system. The calculations involve only the solute degrees of freedom. The major complication arises in the evaluation of the effective potential that requires ensemble averages over the solvent coordinates. Although these types of calculations are computationally intensive, the fact that the VTST calculations outlined here only involve knowing the potential and its first and second derivatives along the MEP holds promise that these types of calculation may be possible in the near future.

On a more fundamental level, it may seem inconsistent to use an effective potential that is computed using classical mechanics in a quantum-mechanical calculation. However, the use of the classical mechanical free energy of solvation to correct the reaction energetics is well founded in the literature. This is equivalent to the approach outlined here, except that we also consider secondary solvation effects on the MEP and its energy profile and on bound energy levels. Of more concern is the fact that the tunnelling correction factor is computed in the same manner as for the gas phase. The solute vibrational modes are treated quantum-mechanically in the ground-state vibrationally adiabatic approximation but the solvent modes are treated classically. Therefore the solvent modes are not restricted to their ground state but are effectively thermally averaged. This is not such a bad situation since, for the low-frequency modes of the solvent, the ground-state vibrations are not representative of those states that contribute most significantly to the thermally averaged rate constant. This is true because the density of states rises very rapidly with energy in these low-frequency modes. Using the thermally averaged potential of mean force represents a physically motivated method that includes the important energy levels in an average sense. This issue has been discussed in greater detail by Truhlar *et al.* (1994) where they have tested the use of the ground-state tunnelling approximation on the potential of mean force for some model reactions in solution. Their conclusions are encouraging for this approach.

3.2. *Non-equilibrium solvent effects*

3.2.1. *Classical mechanical rate theory*

The equilibrium solvation model includes the average effect of the solvent on the solute energetics but neglects any dynamical influence of the solvent. At the next level of complexity, it is possible to introduce dynamical effects by considering the classical equations of motion for the solute coordinates $\mathbf{q}$ written as

$$\mu\ddot{\mathbf{q}} = -\partial_{\mathbf{q}} V(\mathbf{q}, \mathbf{x}) = -\partial_{\mathbf{q}} V_{\mathrm{ES}}(\mathbf{q}, T) + \delta\mathbf{F}(t), \tag{44}$$

where $\delta\mathbf{F}$ is the fluctuation in the force about the mean force:

$$\delta\mathbf{F}(t) = \langle \partial_{\mathbf{q}} V_{\mathrm{solv}}(\mathbf{q}, \mathbf{x}) \rangle_{\mathbf{q}} - \partial_{\mathbf{q}} V_{\mathrm{solv}}(\mathbf{q}, \mathbf{x}). \tag{45}$$

The time dependence of the fluctuating force arises from the time dependence of the solvent coordinates. Equation (44) is exact if the time dependence of the solvent coordinates is computed from the full dynamics of the system (solute plus solvent). In practice we use a reduced, approximate model for $\delta\mathbf{F}$ based upon linear response theory (for example Chandler 1987) that will not require the exact dynamics of the solvent.

To estimate $\delta\mathbf{F}$, a set of effective degrees of freedom $\mathbf{y}$ and $\mathbf{p}_y$ are introduced, and it is assumed that the dynamics are sufficiently described by the motion from the effective non-equilibrium solvation Hamiltonian

$$H_{\mathrm{NS}}(\mathbf{q}, \mathbf{p}, \mathbf{y}, \mathbf{p}_y, T) = \frac{|\mathbf{p}|^2}{2\mu} + V_{\mathrm{ES}}(\mathbf{q}, T) + \frac{|\mathbf{p}_y|^2}{2\mu} + \tfrac{1}{2}\mu(\mathbf{y} - \mathbf{C}\mathbf{q})^{\mathrm{T}}\boldsymbol{\Omega}^2(\mathbf{y} - \mathbf{C}\mathbf{q}), \tag{46}$$

where $\boldsymbol{\Omega}$ is the effective multidimensional frequency matrix of an oscillator bath and $\mathbf{C}$ is a matrix of constants coupling the oscillators to the solute coordinates. Note that $\boldsymbol{\Omega}$ need not be diagonal. (Other choices of a non-equilibrium solvation Hamiltonian are possible. This is discussed further in the appendix.) For this form of the effective Hamiltonian, the equations of motion of the solute coordinates can be written as a GLE in the limit of a continuum of oscillators (Ford *et al.* 1965, Zwanzig 1973). For the GLE the fluctuating force in equation (44) is written

$$\delta\mathbf{F}(t) = -\int_0^t \mathrm{d}t'\, \eta(t - t')\dot{\mathbf{q}}(t') + \mathbf{R}(t), \tag{47}$$

where the friction tensor $\boldsymbol{\eta}$ in equation (47) is related to the solute-constrained force–force correlation function by

$$\boldsymbol{\eta}(\mathrm{t})=\beta\langle\delta\mathbf{F}(t)\delta\mathbf{F}(0)^{\mathrm{T}}\rangle_{\mathbf{q}}. \tag{48}$$

With the solute fixed, $\delta\mathbf{F}(t)=\mathbf{R}(t)$, and the random force term $\mathbf{R}(t)$ is related to the friction tensor by the same relation, consistent with the second dissipation–fluctuation theorem (Kubo *et al.* 1985). For the Hamiltonian given in equation (46), the force–force correlation function is given by

$$\langle\delta\mathbf{F}(t)\delta\mathbf{F}(0)^{\mathrm{T}}\rangle_{\mathbf{q}}=\frac{1}{\beta}\mu\mathbf{C}^{\mathrm{T}}\boldsymbol{\Omega}^{2}\cos(\boldsymbol{\Omega}t)\ \mathbf{C}, \tag{49}$$

where averages are now defined in terms of H_{NS} as

$$\langle\ldots\rangle_{\mathbf{q}}=\frac{\mathrm{Tr}_{\mathrm{cl},\mathbf{y}}[\exp(-\beta H_{\mathrm{NS}})\ldots]}{\mathrm{Tr}_{\mathrm{cl},\mathbf{y}}[\exp(-\beta H_{\mathrm{NS}})]}, \tag{50}$$

so that $\partial_{\mathbf{q}}V_{\mathrm{ES}}(\mathbf{q})=\langle\partial_{\mathbf{q}}V(\mathbf{q},\mathbf{x})\rangle_{\mathbf{q}}$ and $\langle\delta\mathbf{F}\rangle_{\mathbf{q}}=0$.

The exact rate constant is given by equation (2) with the characteristic function χ determined from the dynamics of the entire system. For the partitioning of the Hamiltonian in equation (22) the *exact* expression (for the exact fluctuation about the mean force) for the classical rate constant can be rewritten

$$k_{\mathrm{cl}}(T)=\frac{\mathrm{Tr}_{\mathrm{cl},\mathbf{q}}[\exp(-\beta H_{\mathrm{ES}})\langle\delta(Z)\dot{Z}\chi\rangle_{\mathbf{q}}]}{\mathrm{Tr}_{\mathrm{cl},8}[\exp(-\beta H_{\mathrm{ES}})\langle\chi^{\mathrm{R}}\rangle_{\mathbf{q}}]}. \tag{51}$$

In an equilibrium solvation approximation it is assumed that the quantities inside the averages over the solvent coordinates are independent of the solvent coordinates. For the non-equilibrium solvation model, we wish to retain some dependence of the dividing surface, characteristic function and reactant projector on the solvent degrees of freedom. This is accomplished by approximating the total system Hamiltonian by the non-equilibrium solvation Hamiltonian in equation (46). Then the exact classical rate constant is approximated by

$$k_{\mathrm{cl,NS}}(T)=\frac{\mathrm{Tr}_{\mathrm{cl},\mathbf{q},\mathbf{y}}[\exp(-\beta H_{\mathrm{NS}})\,\delta(Z)\dot{Z}\chi]}{Q^{\mathrm{R}}_{\mathrm{cl,NS}}(T)}, \tag{52}$$

where the non-equilibrium reactant partition function is given by

$$Q^{\mathrm{R}}_{\mathrm{cl,NS}}(T)=\mathrm{Tr}_{\mathrm{cl},\mathbf{q},\mathbf{y}}[\exp(-\beta H_{\mathrm{NS}})\,\chi^{\mathrm{R}}]. \tag{53}$$

Equation (52) can be rewritten as equation (51), but with the averages over solvent coordinates given in terms of the effective solvent coordinates $\mathbf{y}$ (equation 50) instead of the original solvent coordinates $\mathbf{x}$ (equation 34).

The TST geneneralization of the above expression is simply

$$k^{\mathrm{GT}}_{\mathrm{cl,NS}}[Z,T]=\frac{\mathrm{Tr}_{\mathrm{cl},\mathbf{q},\mathbf{y}}[\exp(-\beta H_{\mathrm{NS}})\,\delta(Z)\dot{Z}\theta(\dot{Z})]}{Q^{\mathrm{R}}_{\mathrm{cl,NS}}(T)}. \tag{54}$$

Note that, if the dividing surface is chosen to be a function of solute coordinates only, the rate constant reduces to that obtained from the equilibrium solvation model, equation (30). However, here we wish to allow the dividing surface to depend on solvent coordinates also. For the calculation of the MEP and harmonic expansion along the path, one considers the total effective potential

$$V_{\mathrm{NS}}(\mathbf{q},\mathbf{y},T)=V_{\mathrm{ES}}(\mathbf{q},T)+\tfrac{1}{2}\mu(\mathbf{y}-\mathbf{C}\mathbf{q})^{\mathrm{T}}\boldsymbol{\Omega}^{2}(\mathbf{y}-\mathbf{C}\mathbf{q}), \tag{55}$$

so that in general the MEP spans the space of both the solute and the effective solvent coordinates. With the planar dividing surfaces defined in terms of the reaction coordinate s for the non-equilibrium potential, the classical generalized TST rate constant is given by

$$k^{\mathrm{GT}}_{\mathrm{cl,NS}}(s,T)=\frac{k_{\mathrm{B}}T}{h}\frac{Q^{\mathrm{GT}}_{\mathrm{cl,NS}}(s,T)}{Q^{\mathrm{R}}_{\mathrm{cl,NS}}(T)}\exp\left[-\beta V^{\mathrm{MEP}}_{\mathrm{NS}}(s,T)\right], \tag{56}$$

where $V^{\mathrm{MEP}}_{\mathrm{NS}}(s,T)$ is the potential along the MEP on the non-equilibrium solvation potential and the non-equilibrium solvation generalized transition state partition function is defined by an expression similar to equation (13) but with the potential replaced by V_{NS} and the normal mode coordinates determined from the Hessian matrix constructed from the second derivatives of the non-equilibrium solvation potential. Unlike the equilibrium solvation model, the non-equilibrium solvation model includes effective solvent modes in addition to the solute modes. The partition functions $Q^{\mathrm{GT}}_{\mathrm{cl,NS}}(s,T)$ and $Q^{\mathrm{R}}_{\mathrm{cl,NS}}(T)$ include contributions from all the modes in the extended model system.

The Hamiltonian in equation (46) includes frictional effects on reaction dynamics in the vicinity of the saddle point but also predicts a non-equilibrium effect on the reactants and products. Since we do not want to include non-equilibrium solvation effects in the (equilibrium) reactant partition function, the projector χ^{R} is chosen to be a function of the solute coordinates only, for example $\chi^{\mathrm{R}}=\chi^{\mathrm{R}}(\mathbf{q})$. With this form for the projector, the reactant partition function is written

$$Q^{\mathrm{R}}_{\mathrm{cl,NS}}(T)=Q^{\mathrm{R}}_{\mathrm{cl,ES}}(T)Q^{\mathrm{C=0}}_{\mathrm{cl,y}}(T) \tag{57}$$

where $Q^{\mathrm{R}}_{\mathrm{cl,ES}}$, as defined in equation (31), is the classical equilibrium solvation partition function for the solute modes at reactants and $Q^{\mathrm{C=0}}_{\mathrm{cl,y}}$ is the partition function for effective solvent modes in the zero-coupling limit. Alternatively, the non-equilibrium solvation can be modelled by a reaction-coordinate-dependent friction (see the appendix) so that the coupling goes to zero in the reactant region. This method also recovers the desired result, equation (57), for the reactant partition function.

As in the equilibrium solvation case, the expression for the rate constant depends only on an effective potential V_{NS} in the case of non-equilibrium solvation. To describe non-equilibrium solvation, both the equilibrium solvation potential $V_{\mathrm{ES}}(\mathbf{q},T)$ and the friction tensor $\boldsymbol{\eta}(t)$ are required. As $V_{\mathrm{ES}}(\mathbf{q},T)$ is determined from the constrained average of the total potential over the solvent coordinate (equation 33), the friction tensor is specified by the constrained average of the force–force correlation function. The parameters of the oscillator model, the effective frequency matrix $\boldsymbol{\Omega}$ and the coupling constants $\mathbf{C}$, are obtained by fitting the force–force correlation function to the cosine expansion in equation (49). Some freedom is allowed in choosing these parameters. For instance, in the work of Ford *et al.* (1965) and Zwanzig (1973), the frequency matrix is taken as diagonal and there are non-zero coupling constants between multiple oscillators and a solute coordinate. On the other hand, Adelman (1983) chooses the frequency matrix to be tridiagonal where $\mathbf{C}$ is chosen to couple only one oscillator to each solute coordinate. These two forms for the parameters, as well as other choices, can be related to each other by similarity transformations. Adelman has suggested fitting the parameters using moments of the spectral density of the force–force correlation function. In our work, the parameters are obtained by a consistent procedure of fitting the cosine expansion (Schenter *et al.* 1992).

The evaluation of the friction tensor using classical molecular dynamics simulations is computationally intensive. It has been carried out for several reactions in solution for comparisons of the GLE dynamics with exact classical dynamics. This work has been recently reviewed by Whitnell and Wilson (1993). The general conclusion from these studies is that the linear response theory gives an accurate description of the influence of the solvent friction on the reaction dynamics for the systems studied. As V_{ES} may be obtained from an empirical model, the present analysis is consistent if the friction tensor is obtained from an empirical model instead of classical microscopic simulations of equation (48). Examples of different approaches are an integral equation method (Huston *et al.* 1989) and a polarizable continuum model (Bianco *et al.* 1992).

The Hamiltonian in equation (46) has been widely used to model solvent friction on reaction dynamics. This has been reviewed recently by Hänggi *et al.* (1990). For a reaction model of a one-dimensional solute (a reaction coordinate) coupled to an oscillator bath, Dakhnovskii and Ovchinnikov (1985) and Pollak (1986a) have shown how the Grote–Hynes (1980) expression for the rate constant can be obtained from this Hamiltonian using conventional TST in which the dividing surface is allowed to be a function of the effective solvent coordinates as well as the solute coordinate. More recently, variational optimization of the dividing surface has been employed to obtain a better bound to the exact classical rate constant for this model system (Pollak 1990, 1991a, b, Pollak *et al.* 1990, Tucker *et al.* 1991, Berezhkovskii *et al.* 1992, Tucker and Pollak 1992, Frishman and Pollak 1992, 1993). Extension of this approach to include nonlinearities in the coupling and anharmonicities in the potentials using VTST have also appeared (Pollak 1991c).

Most previous investigations of solvent friction effects on the rate constants for activated reactions have studied the simple model of a single solute coordinate, the reaction coordinate, coupled to the reduced model of the solvent. Reducing the full solute-plus-solvent system to a single reaction coordinate plus a solvent bath requires including effects of internal motions of the reacting molecules in the friction kernel. The linear response theory will not adequately model large-reaction-path-curvature coupling that can occur between the reaction coordinate and internal vibrational motions of the solute. This type of coupling can cause classical recrossing of the transition state dividing surface that is intrinsic to the solute molecule and is not described by a GLE. This has been demonstrated in recent studies of multidimensional solute systems coupled to an oscillator bath (Schenter *et al.* 1992). For a model A + BC reaction it was found that classical VTST can mitigate these recrossings when the coupling to the solvent is sufficiently large, but that at low values of the solvent friction (and coupling) the variational theory offered no improvement over conventional TST.

3.2.2. *Quantum-mechanical variational transition state theory*

As for the equilibrium solvation model, the quantum-mechanical VTST rate constant for the non-equilibrium solvation model is obtained using the procedures outlined in § 2, but with the Hamiltonian H replaced by H_{NS}. The quantized version of equation (56) is written

$$k_{\mathrm{NS}}^{\mathrm{GT}}(s,T)=\frac{k_{\mathrm{B}}T}{h}\frac{Q_{\mathrm{NS}}^{\mathrm{GT}}(s,T)}{Q_{\mathrm{NS}}^{\mathrm{R}}(T)}\exp\left[-\beta V_{\mathrm{NS}}^{\mathrm{MEP}}(s,T)\right], \tag{58}$$

where the quantized generalized partition function is obtained by summing the Boltzmann factors for the bound energy levels $\varepsilon_{\mathrm{NS},m}^{\mathrm{GT}}(s,n_m)$. The bound energy levels

$\varepsilon^{\mathrm{GT}}_{\mathrm{NS},m}(s, n_m)$ are those for the coupled solute–solvent system, and therefore there are more modes than in the equilibrium solvation model. The reactant partition function $Q^{\mathrm{R}}_{\mathrm{NS}}(T)$ is the quantized version of equation (57) where both the equilibrium solvation reactant partition function and the solvent partition function are quantized. The quantum-mechanical CVT rate constant for the non-equilibrium solvation model is given by

$$k^{\mathrm{CVT/AG}}_{\mathrm{NS}}(T) = \kappa^{\mathrm{CVT/AG}}_{\mathrm{NS}}(T) k^{\mathrm{CVT}}_{\mathrm{NS}}(T), \tag{59}$$

where $k^{\mathrm{CVT}}_{\mathrm{NS}}(T)$ is obtained by minimizing equation (58) with respect to s and $\kappa^{\mathrm{CVT/AG}}_{\mathrm{NS}}(T)$ is the tunnelling correction factor. The adiabatic potential is computed using the potential $V^{\mathrm{MEP}}_{\mathrm{NS}}(s, T)$ along the MEP and the ground-state energy levels $\varepsilon^{\mathrm{GT}}_{\mathrm{NS},m}(s, n_m)$. The tunnelling correction factor $\kappa^{\mathrm{CVT/AG}}_{\mathrm{NS}}(T)$ is computed from an expression similar to equation (20) but using the ground-state adiabatic potential for non-equilibrium solvation.

As for the equilibrium solvation model, the procedures are operationally the same as used in the gas phase; the major complication that arises is obtaining the non-equilibrium solvation potential. In addition to the equilibrium solvation potential, the friction tensor needs to be evaluated. However, for the simple non-equilibrium solvation model described above, the friction tensor only needs to be evaluated at the saddle point. More general models to the friction include dependence of the parameters $\mathbf{\Omega}$ and $\mathbf{C}$ on the reaction coordinate s or, more generally, on the solute coordinates $\mathbf{q}$ (see appendix and Straus *et al.* 1993, Straus and Voth 1992, Haynes *et al.* 1993, and Haynes and Voth 1992). Even for these more complicated models of the friction, the information will still only be needed along a MEP. Classical mechanical studies have indicated that the saddle-point model of the friction provides a good approximation to the solvent dynamical effects. This makes sense because the solvent friction in the region of the barrier maximum influences the recrossing dynamics most greatly. However, quantum-mechanical tunnelling is controlled by greater regions of the MEP and may be more sensitive to the friction away from the saddle point.

The issue of using V_{ES} (or a classical potential of mean force) in the tunnelling calculation was discussed above and another complication in the tunnelling calculation arises for the non-equilibrium solvation model because of the explicit solvent modes. The solvent modes are used to model collective solvent motions that typically have low frequencies. This calls into question the validity of the vibrationally adiabatic approximation employed in these calculations. As a test of this approximation we have recently presented a critical comparison of accurate quantum mechanics with the VTST plus tunnelling for a model reaction in solution (McRae *et al.* 1992). This work showed that the worst agreement in the rate constants was a factor of about three, indicating that the approximate method was still capable of at least semiquantitative agreement. Those preliminary results used the harmonic approximation to describe the bound vibrational modes. Subsequent studies by McRae and Garrett (1993) showed that the largest portion of the error of a factor of three was attributed to the harmonic approximation. The VTST calculations with SCSAG tunnelling corrections for the model reaction in solution were found to be limited more by the treatment of anharmonicity rather than by errors inherent in the approximations to the reaction dynamics.

Another issue arises concerning the quantum-mechanical tunnelling calculations. It may seem inconsistent to take a classically derived model Hamiltonian H_{NS} and to use it in a quantum-mechanical calculation. Ford *et al.* (1965, 1988) have shown that the same form for the Hamiltonian can be derived from a 'quantum GLE'. Thus the problem reduces to whether the classical mechanical parametrization of the model Hamiltonian is a good approximation to the actual quantum mechanics. It seems that parameters derived from classical mechanics should be adequate for describing the low-frequency fluctuations of most liquids. In addition, the model non-equilibrium solvation Hamiltonian has been used to describe quantum-mechanical tunnelling in dissipative systems starting with the work of Caldeira and Leggett (1981) (see Hänggi *et al.* 1990 for a recent review). In particular, the quantization of conventional TST for the model of a single reaction coordinate coupled to the oscillator bath was presented by Pollak (1986b, c).

4. Concluding remarks

VTST with semiclassical tunnelling correction factors has been successfully implemented for practical calculations of rate constants for gas-phase reactions based upon potential energy surfaces. When quantum-mechanical effects, including tunnelling, are accurately included, these methods are capable of quantitative predictions of rate constants. In the present article we have outlined the steps needed to extend to solution-phase reactions the VTST with tunnelling calculations based upon potential energy surfaces. Consistent procedures for treating quantum-mechanical effects in solution have been discussed, including quantization of bound vibrational modes as well as quantum-mechanical tunnelling effects.

The procedures outlined here are computationally intensive but, given the recent advances in computational hardware and software, these calculations are possible. Solvent effects on the reaction are included through equilibrium and non-equilibrium solvation models. This approach requires explicit treatment of only a limited number of degrees of freedom (of the solute and possibly some explicit solvent molecules) and information about the effective potential energy surface for these explicit coordinates is needed only in the region of a reaction valley. Explicitly treating only a limited number of coordinates obviates some of the difficulties inherent in quantum-mechanical TST calculations on solution-phase reactions (the multiple-saddle-point problem) and also allows the quantum-mechanical effects to be included by the standard *ad-hoc* procedure.

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APPENDIX

Here we give an example of an extension to the non-equilibrium solvation model of § 3.2. The choice of our effective non-equilibrium solvation Hamiltonian given by equation (46) is modified to include nonlinear coupling of the solute to the solvent bath and coordinate-dependent frequencies. To retain the simplicity of the model, we still require the solvent bath to be harmonic for a fixed solute configuration. An appropriate form for the non-equilibrium solvation Hamiltonian is

$$H_{\mathrm{NS}}(\mathbf{q},\mathbf{p},\mathbf{y},\mathbf{p}_y,T)=\frac{|\mathbf{p}|^2}{2\mu}+\tilde{V}_{\mathrm{ES}}(\mathbf{q},T)+\tfrac{1}{2}k_{\mathrm{B}}T\ln\left[\det\left(\frac{\boldsymbol{\Omega}_0^2}{\boldsymbol{\Omega}^2(\mathbf{q})}\right)\right]$$
$$+\frac{|\mathbf{p}_y|^2}{2\mu}+\tfrac{1}{2}\mu[\mathbf{y}-\mathbf{C}(\mathbf{q})]^{\mathrm{T}}\boldsymbol{\Omega}^2(\mathbf{q})[\mathbf{y}-\mathbf{C}(\mathbf{q})], \qquad \text{(A 1)}$$

where we introduce the arbitrary coordinate-dependent coupling function $\mathbf{C}(\mathbf{q})$ and the coordinate-dependent bath frequency matrix $\boldsymbol{\Omega}(\mathbf{q})$. Here $\boldsymbol{\Omega}_0$ is an arbitrary constant matrix that only shifts the zero of energy of the Hamiltonian. A similar form of an effective Hamiltonian with only the coordinate-dependent coupling was considered in Zwanzig's (1973) general treatment of non-linear generalized Langevin equations (see also Haynes and Voth 1992). The purpose of this appendix is to show how the parameters $\tilde{V}_{\mathrm{ES}}(\mathbf{q},T)$, $\boldsymbol{\Omega}(\mathbf{q})$ and $\mathbf{C}(\mathbf{q})$ the Hamiltonian can be fitted using microscopic simulations.

As in § 3.2., we approximate the force of the solvent on the solute by

$$\mathbf{F}(t)=-\partial_{\mathbf{q}}H_{\mathrm{NS}} \qquad \text{(A 2)}$$

and define fluctuations to this force by

$$\delta\mathbf{F}(t)=\langle\partial_{\mathbf{q}}H_{\mathrm{NS}}\rangle_{\mathbf{q}}-\partial_{\mathbf{q}}H_{\mathrm{NS}}, \qquad \text{(A 3)}$$

where the averages $\langle\ldots\rangle_{\mathbf{q}}$ are given by equation (50). Since $\ln[\det(\mathbf{A})]=\mathrm{Tr}[\ln(\mathbf{A})]$, where Tr is a matrix trace of the dimensionality of the bath, the mean force may be written as

$$\langle\mathbf{F}\rangle_{\mathbf{q}}=-\partial_{\mathbf{q}}\tilde{V}_{\mathrm{ES}}-\tfrac{1}{2}k_{\mathrm{B}}T\,\mathrm{Tr}\left(\frac{\partial_{\mathbf{q}}\boldsymbol{\Omega}^2(\mathbf{q})}{\boldsymbol{\Omega}^2(\mathbf{q})}\right)$$
$$+\tfrac{1}{2}\mu\,\mathrm{Tr}\left\{\partial_{\mathbf{q}}\boldsymbol{\Omega}^2(\mathbf{q})\langle[\mathbf{y}-\mathbf{C}(\mathbf{q})][\mathbf{y}-\mathbf{C}(\mathbf{q})]^{\mathrm{T}}\rangle_{\mathbf{q}}\right\}. \qquad \text{(A 4)}$$

Here we have used the fact that $\langle[\mathbf{y}-\mathbf{C}(\mathbf{q})]\rangle_{\mathbf{q}}=0$. For fixed $\mathbf{q}$, H_{NS} is harmonic, so that all higher moments of $\mathbf{y}$ may be written in terms of

$$\langle[\mathbf{y}-\mathbf{C}(\mathbf{q})][\mathbf{y}-\mathbf{C}(\mathbf{q})]^{\mathrm{T}}\rangle_{\mathbf{q}}=\frac{k_{\mathrm{B}}T}{\mu\boldsymbol{\Omega}^2(\mathbf{q})}. \qquad \text{(A 5)}$$

Inserting this expression into equation (A 4) gives

$$\langle\mathbf{F}\rangle_{\mathbf{q}}=-\partial_{\mathbf{q}}\tilde{V}_{\mathrm{ES}}. \qquad \text{(A 6)}$$

Since this takes the same form as equation (33), $\tilde{V}_{\mathrm{ES}}(\mathbf{q},T)$ can be replaced by the potential of mean force $V_{\mathrm{ES}}(\mathbf{q},T)$. The additional term in H_{NS} that involves the determinant of frequencies was chosen to offset contributions from the nonlinear bath when the potential of mean force is calculated at a fixed coordinate configuration $\mathbf{q}$. See Straus and Voth (1992) for studies involving a Hamiltonian of this form.

The other parameters of H_{NS} can be fitted using the autocorrelation function of the fluctuating force that is obtained from dynamics of the bath with solute coordinates 'clamped' at a solute configuration (see equation 49) for the analogous expression for the linear coupling case). We now consider the coordinate-dependent friction tensor

$$\eta(\mathbf{q},t)=\beta\langle\delta\mathbf{F}(t)\delta\mathbf{F}(0)^{\mathrm{T}}\rangle_{\mathbf{q}}. \qquad \text{(A 7)}$$

Through the careful evaluation of harmonic averages, this expression may be written in closed form as

$$\boldsymbol{\eta}(\mathbf{q},t)=\mu(\partial_{\mathbf{q}}\mathbf{C})^{\mathrm{T}}\boldsymbol{\Omega}^2\cos(\boldsymbol{\Omega}t)\,\partial_{\mathbf{q}}\mathbf{C}+\Delta\boldsymbol{\eta}(\mathbf{q},t). \tag{A 8}$$

with

$$\Delta\eta_{ij}(\mathbf{q},t)=\frac{1}{2\beta}\mathrm{Tr}\left[\partial_{q_i}\boldsymbol{\Omega}^2\frac{\cos(\boldsymbol{\Omega}t)}{\boldsymbol{\Omega}^2}\partial_{q_j}\boldsymbol{\Omega}^2\frac{\cos(\boldsymbol{\Omega}t)}{\boldsymbol{\Omega}^2}\right]. \tag{A 9}$$

Throughout this analysis we require $\boldsymbol{\Omega}^2$ to be symmetric. For every clamped value of the solute coordinates, $\mathbf{q}$, $\mathbf{C}$ and $\boldsymbol{\Omega}^2$ must be chosen to reproduce $\boldsymbol{\eta}(\mathbf{q},t)$. In the case where $\mathbf{C}$ is linear in $\mathbf{q}$ and $\boldsymbol{\Omega}^2$ has no $\mathbf{q}$ dependence, we see that this expression reduces to equation (49).

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