MOLECULAR-SCALE MODELING
OF REACTIONS AND SOLVATION

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Abstract

This paper presents an overview of recent developments in molecular modeling of reactions and solvation. It includes both electronic structure and dynamics, and it considers both electronically adiabatic processes and electronically nonadiabatic ones.

Keywords

Continuous surface switching, Density functional theory, Diabatic representations, Direct dynamics, Ehrenfest method, Electron correlation, Hybrid Hartree-Fock-density-functional theory, Hybrid quantum mechanical molecular mechanical methods, Integrated molecular orbital methods, Multi-coefficient correlation methods, Multi-configuration molecular mechanics, Nonequilibrium effects, Specific reaction parameters, Tight binding theory, Trajectory surface hopping, Variational transition state theory.

Introduction

Molecular modeling of gas-phase molecular structure has achieved tremendous success in recent years. In many cases, theoretical structures and energies are more accurate than experimental results. Perhaps even more important though is the availability of reasonably reliable theoretical results where no experiments are practical or available. Theoretical chemistry can also be used to predict dynamics and spectroscopy, and it can model systems in the condensed phase as well as the gas-phase. This paper summarizes some recent advances in these areas, especially for molecular modeling of reaction energies, activation barriers, and solvation.

Chemical reactions may be divided into two types, electronically adiabatic and electronically nonadiabatic. Even when one calculates the electronic structure step-by-step along with the nuclear motion, the questions of interaction potentials and dynamics are conceptually separable. Interaction potentials will be discussed first, then dynamics. The discussion of dynamics focuses on rate constants and overall rate processes when state-to-state information is not required.

Interactions and Forces

For electronically adiabatic reactions, i.e., those in which the adiabatically defined electronic state does not change during the collision, the forces on the nuclei may be obtained as the gradient of a single-valued adiabatic potential energy function (PEF), also called the potential surface (Truhlar et al. 1987, Schatz 1989, Truhlar 1992). A potential surface is the expectation value of the electronic Hamiltonian (including nuclear repulsion) for a given electronic wave function with fixed nuclei; the surface is a function of the positions of the nuclei. Thus the calculations of forces between nuclei (i.e., between atoms and atomic ions) eventually reduce to calculating electronic wave functions as functions of coordinates. Technically, however, some electronic structure methods work directly with electronic densities rather than electronic wave functions, or—in a hybrid way—they work with wave functions and densities.

For electronically nonadiabatic reactions involving a small number N of electronic states, which is the usual situation for gas-phase photochemistry or condensed-

phase photochemistry in non-electronically–conducting media, the forces on the nuclei may be derived from N adiabatic potential surfaces, V_1, V_2, ... V_N, and $(N^2 - N)/2$ matrix elements of the nuclear momentum operator, which is a $3N_{atoms}$-dimensional vector (thus one requires $3N_{atoms}(N^2 - N)/2$ elements). (Note: N_{atoms} is the number of atoms.) When, as is usually the case for interesting applications, the electronically nonadiabatic coupling may be assumed to arise from changes in orbital occupation rather than from the inability of electrons in a given orbital to completely follow the nuclei due to their finite speed, one may change the electronic representation from an adiabatic one to a diabatic one (Garrett and Truhlar 1981, Sidis 1992). In the diabatic representation, the forces may be derived to a good approximation—but not exactly (Mead and Truhlar 1982)—from N diabatic potential surfaces, U_{11}, U_{22}, ..., U_{NN}, which are again expectation values, but now calculated with diabatic electronic wave functions, plus $(N^2 - N)/2$ off-diagonal matrix elements of the electronic Hamiltonian, which is a scalar operator. This is a great simplification. The final situation is the case of chemical reactions in or on an electronically conducting medium, such as reactions at a metal surface. This case is hardest to treat although there is some justification for continuing to use potential surfaces, possibly with the addition of electron-hole pairs to the model (Chester 1961, Marcus, 1964, Wonchoba et al. 1994, Head-Gordon and Tully 1995, Billing 1998).

Electronically Adiabatic Reactions

Electronic structure calculations have so far had the most success in the electronically adiabatic case, in part because the adiabatic states are uniquely defined, and the variational principle provides a convenient way to approximate the lowest adiabatic state. Two developments in this area have been the backbone of most other advances:

- Coupled cluster-type methods including the "parentheses T" terms, which is an explicit-correlation approach, and which includes coupled clusters with single and double excitations and quasiperturbative triple excitations, CCSD(T), and also quadratic configuration interaction with single and double excitations and quasiperturbative triple excitations, (QCISD(T)) (Raghavachari and Anderson 1996), and

- A density-based approach using hybrid Hartree-Fock-density functional theory (HF-DFT), which is justified on the basis of the adiabatic connection method (ACM) (Harris and Jones 1974, Harris 1984, Becke 1993).

Whereas CCSD(T) and QCISD(T) methods and Møller-Plesset perturbation theory, which may be thought of as an approximation to these methods, employ explicit forms for the many-electron wave function, DFT is based—in principle—directly on the one-electron density. But even so-called pure DFT methods are usually based on the Kohn-Sham formulation, and therefore they use a wave function to calculate the kinetic energy; whereas so-called hybrid HF-DFT methods use a hybrid formulation for the exchange part of the potential energy, calculating a fraction of it by Hartree-Fock exchange integrals and the rest by a functional of the density or a functional of the density and its gradient.

Explicitly Correlated Wave Functions

The quasiperturbative triple excitations in the CCSD(T) and QCISD(T) methods include both a fourth-order term and a fifth-order term in a well balanced way (Scuseria and Lee 1990, Stanton 1997), and they are generally believed to give a result that is often close to full configuration interaction for a given one-electron basis (Lee and Scuseria 1995). However, (i) the methods are expensive even for moderate (unconverged) basis sets, and (ii) convergence with respect to the one-electron basis is slow. There are four strategies for coping with these problems.

The first is the Gaussian-x strategy (Curtiss and Raghavachari 1998, Curtiss et al. 1999). To overcome difficulty (i) by this strategy, one performs less complete correlated calculations with a large basis and QCISD(T) or CCSD(T) calculations with a small basis and assumes that higher-order correlation effects and extended-basis-set effects are additive. To make up for systematic errors and help overcome difficulty (ii), one also adds in a so-called higher-level correction, which contains 2 to 4 parameters and changes discontinuously when the number of paired electrons change, e.g., during the process R· + H· → RH.

The second strategy is basis set extrapolation. Originally, this strategy was aimed primarily at very small molecules by testing how well one could extrapolate from very large basis sets (e.g., correlation-consistent polarized valence quadruple zeta or higher) to the infinite basis set limit (Montgomery et al. 1994, Martin 1998). More recently, it has been developed for the more affordable choice of extrapolating from polarized double and triple zeta to the infinite basis set limit (Ochterski et al. 1996, Fast et al. 1999).

The third strategy is to extrapolate the many-electron level of the treatment correlation energy, either *ab initio* or semiempirically. Examples of the latter are the scaling external correlation (SEC) and scaling all correlation (SAC) methods (reviewed elsewhere: Corchado and Truhlar 1998).

The fourth strategy is the multi-coefficient (MC) approach that attempts to combine the advantages of all three of these approaches (Tratz et al. 1999, Fast and Truhlar 2000). The most general class of MC methods is called multi-coefficient correlation methods (MCCMs),

Table 1. Mean Unsigned Errors Per Bond for
82 Atomization Reactions[a].

Scaling	Method	MUE/bond (kcal)	Cost[b] (relative)
N^5 methods	single-level		
	MP2/cc-pVDZ	7.8	8
	MP2/MG3	2.4	100
	MP2/cc-pVTZ	2.0	160
	multi-level		
	SAC-MP2/cc-pVTZ	3.1	8
	SAC-MP2/cc-pVTZ	1.9	160
	MCCM-CO-MP2	1.5	170
	MCCO-CO-MP2; MG3; 6-31+G*	1.3	150
N^6 methods	single-level		
	MP4SDQ/cc-pVDZ	11.5	17
	CCSD/cc-pVDZ	11.9	120
	MP4SDQ/cc-pVTZ	5.6	250
	CCSD/cc-pVTZ	6.1	2300
	multi-level		
	SAC-MP4SDQ/cc-pVDZ	2.1	17
	MCSAC-QCISD/6-31G*	2.6	25
	MCCM-UT-QCISD/6-31G(2df,p); 6-31G*	1.0	74
	MCCM-UT-MP4SDQ	0.8	180
	MC-QCISD	0.7	120
N^7 methods	single-level		
	QCISD(T)/6-31G*	10.2	42
	MP4/cc-pVDZ	9.6	92
	QCISD(T)/6-311G(d,p)	8.0	130
	CCSD(T)/cc-pVDZ	10.3	260
	MP4/6-311G(2df,p)	3.5	540
	MP4/cc-pVTZ	2.6	2250
	CCSD(T)/cc-pVTZ	3.7	3600
	multi-level		
	Gaussian-3	0.36	720
	MCG3	0.31	210

[a] based on Tratz et al. (1999) and Fast and Truhlar (2000).

[b] Cost: an average based on single-point energies for molecules with 5–11 atoms. MP2/MG3 ≡ 100.

and it includes the MCSAC, EIB, MCCM-CO, MCCM-UT, MCCM-NM, MCG2, MCG3, G3S, and MC-QCISD approaches. In the two papers just referenced, we recommended eleven of these methods as providing the best compromise of accuracy and economy for calculating bond energies (or, more generally, for calculating any gas-phase thermochemical quantities for stable species). Table 1 compares the performance (mean unsigned errors) of some of these methods (which, like the Gaussian-x methods, may all be called multi-level or dual-level methods) to the more traditional single-level electronic structure methods. The computational efficiency (defined as the cost for achieving a given average accuracy) is striking, even though the cost function is based on molecules with inly 5–11 atoms. As system size is increased, the costs of the methods eventually scale as $(N_{\_\_\_})^n$, where n is 5, 6, or 7. Because of these scaling properties, Table 1 has subsections for each of these values of n. For very large systems, only the smallest n calculations will be affordable. However, for any n, the multi-level methods are much more accurate for a given cost than the single-level methods. An important area of current research is linear scaling methods in which the algorithms are reformulated such that $n = 1$. Only recently has there been progress on developing linear scaling algorithms for methods with $n = 5$ and 6 (Ayala and Scuseria 1999, Schultz et al. 1999, Scuseria and Ayala 1999).

All electronic structure methods become less accurate when attention changes from stable species to transition states. A special problem occurs for doublet and triplet transition states; for these cases the most popular explicitly correlated treatments, which are based on unrestricted Møller-Plesset perturbation theory, often lead to wave functions that have significant contributions from states with an incorrect expectation value of S^2, where S is electronic spin. This so-called spin contamination problem is corrected by restricted open-shell Møller-Plesset theory, but it appears that the fix-up is not physical enough to guarantee more accurate results (Chuang et al. 2000). The CCSD and QCISD approaches, and especially CCSD(T) and QCISD(T), appear to be more accurate in this respect, but a truly satisfactory procedure seems to require a multi-configuration wave function as a zero-order state for perturbation theory or as a reference state for configuration interaction. Conventional configuration interaction methods, whether based on single-configuration references or multi-configuration references, are not size-cßonsistent, and this is a serious problem in predicting potential energy surfaces. One promising method that includes both size-consistency and multi-configuration reference states is the MRPT2 method of Hirao and Nakano (Nakano et al. 1997, Roberto-Neto et al. 1999, Kobayashi et al. 2000). It will be interesting to test this method further when computer code for analytic gradients (Nakano et al. 1998) becomes available. Other multireference perturbation theory methods may also be recommended (e.g., Finley and Freed 1995, Kozlowski et al. 1995, Staroverov and

Table 2.   Mean Unsigned Errors in Barrier Heights and Reaction Energies for 20 Reactions[a].

Basis	Method	Mean |error| (kcal)		Cost[b] (relative)
		$V^{\ddagger}$	ΔE	
MG3	MP2	4.3	2.9	100
	B3LYP	3.9	2.1	50
	BH&HLYP	2.3	3.0	50
	MPW1PW91	3.6	1.5	50
	MPW1K	1.6	1.7	50
	QCISD(T)// MPW1K	1.3	1.4	100
6-31+G(d,p)	MPW1K	1.6	2.0	7
	QCISD(T)// MPW1K	3.1	3.1	12
multi-basis	MC-QCISD// MPW1K	1.5	1.2	10

[a] based on Lynch et al. (2000).

[b] Cost: an estimate for 10 energies, 10 gradients, and 1 Hessian based primarily on the reaction of amino radical with ethane. MP2/MG3 ≡ 100.

Davidson 1998, Celani and Werner 2000; see also additional references in Sect. 1.2).

With these caveats about single-configuration reference methods in mind, the MCCM methods may still be recommended for transition states if used with appropriate caution. We shall return to this subject in the section below.

Density Functional Methods

Local density functional methods, with or without gradient corrections, systematically overestimate binding energies (Van Leuwen and Baerends 1994, Yxkinten et al. 1997, Perdew 1999) and systematically underestimate barrier heights (Porezag and Pederson 1995, Baker et al. 1996). (Sometimes gradient-corrected functionals are called nonlocal, but here we reserve the word "nonlocal" for integral operators like the Hartree-Fock exchange operator.) Although the situation may improve in the future with better density functionals or by including multireference character in the computational scheme (see next section), at the present time pure DFT cannot be recommended for quantitative work on molecules (it is better for solids).

Hybrid HF-DFT

The poor performance of local density functional methods for molecular energies has been explained theoretically (Becke 2000) in terms of the implied locality of the exchange hole, and this explanation, combined with the adiabatic connection method (Harris and Jones 1974, Harris 1984), points to the need for incorporating nonlocal operators, such as Hartree-Fock exchange. Apparently, at least 12% Hartree-Fock exchange is required to incorporate the necessary nonlocality (Becke 2000). Methods that mix local density functionals (usually gradient-corrected) with nonlocal Hartree-Fock exchange (Becke 1993) are called hybrid HF-DFT methods. When compared to using explicitly correlated wave functions, hybrid HF-DFT methods provide remarkably high accuracy on a price-performance basis, and for moderate-sized and large systems, they will often give the best results of all affordable methods. The most widely used hybrid method is B3LYP (Stephens et al. 1994), with 20% Hartree-Fock exchange, although a method employing the same functionals but with 50% Hartree-Fock exchange has often been reported to be more accurate for chemical reaction barrier heights and for applications in surface science. The newer MPW1K hybrid method, with a modified exchange functional and 42.8% Hartree-Fock exchange, is even more accurate; see Table 2 (Lynch et al. 2000). Nevertheless, one must still be very cautious about the reliability of DFT and hybrid HF-DF theory for molecular modeling, as indicated by the poor performance of DFT for hydration effects (Hall et al. 2000). The methods can be very useful when used in situations where they have been validated, but they cannot be used universally or uncritically.

Even with improved functionals of the one-electron density, DFT or hybrid HF-DFT based on the Kohn-Sham equations and a non-interacting single-determinant reference state cannot handle all situations equally well. That is because such a DFT formulation includes dynamical (external) correlation effects but not static (internal) ones; inclusion of static correlation requires a multi-reference treatment, i.e., the use of a multiconfiguration reference state, or taking account of the two-electron density. In recent work good progress has been made in sorting out the relevant issues and taking initial steps toward practical multi-reference DFT (Sancho-Garciá et al. 2000, Gräfenstein and Cremer 2000).

A separation of the kinetic or potential energy into non-exchange and exchange parts is not unique, and one must be careful not to overinterpret individual components of the energy. Nevertheless such analyses may be useful for designing better DFT methods. The exchange kinetic energy, for example, is known to play a critical role in realistic descriptions of bonding (Goddard and Wilson 1972).

Another idea illustrated in Table 2 is the use of DFT to optimize geometries. The notation "X//Y" refers to optimizing a stationary point or calculating a reaction path at level Y and then carrying out energy calculations at these geometries (so-called single-point energies) by method X. Table 2 shows that single-point energies with the MC-QCISD method at MPW1K stationary-point geometries provides an economical way to calculate

reasonably accurate barriers for chemical reactions. The // scheme can also be applied along reaction paths, where it is called ISPE or IRCmax, but it is less successful than a method called /// that involves limited geometry optimizations at the higher level (Chuang et al. 1999a).

Large Systems

Very large systems typically require the use of lower-level methods. Even DFT calculations may be too expensive for some applications, or they may be insufficiently accurate. One therefore turns to simpler, less expensive methods, especially those with parameters that may be adjusted semiempirically. Molecular mechanics (i.e., the use of valence force fields) is very popular for conformational analysis of stable species, but is inapplicable in its original form to reactions. Empirical valence bond (Åqvist and Warshel 1993) and multi-configuration molecular mechanics (Kim et al. 2000) provide two ways to extend molecular mechanics to reactive systems. Another approach is constituted by the so-called quantum-mechanical-molecular-mechanical (QM/MM) methods (Gao and Thompson 1998) in which quantum mechanical methods, often semiempirical ones, are used for a subsystem, and molecular mechanics is used for the rest of the system. When the subsystem is an entire solute not connected by bonds to the rest of the system, a method based on link atoms (Field et al. 1990) appears to be very useful. This approach has also been used successfully (Ridder et al. 1998) when the subsystem boundary is in the middle of a bond (which is essential for modeling the critical residues of enzymes), although in this case the generalized hybrid orbital method (Gao et al. 1998, Alhambra et al. 1999), which involves boundary atoms, and the use of adjusted connection atoms (Antes and Thiel 1999) appear more robust. Another QM/MM method that allows the boundary of the subsystem to be in the center of a bond is the integrated-molecular-orbital-molecular-orbital (IMOMO) method (Humbel et al. 1996, Svensson et al. 1996, Corchado and Truhlar 1998b) or the IMOHC extension for optimizing geometries (Corchado and Truhlar 1998a). The IMOMO method is very flexible and allows one to use explicitly correlated wave functions for the subsystems, which is called the correlated capped subsystem (CSS) method (Coitiño et al. 1996, Noland et al. 1997, Coitiño et al. 1997); it is particularly powerful for calculating substituent effects. Another approach, which is similar in some respects to IMOMO but both less flexible (a disadvantage) and simpler (a definite advantage) is the use of locally dense basis sets (LDBSs), as demonstrated by DiLabio and Wright (1998).

Atoms and molecules at nanosurfaces show different behavior and reactivity from that of ordinary materials. Furthermore, the properties of nanoparticles may be tuned by size as well as constitution. Modeling the reactivity of nanoparticles and large clusters efficiently may require specialized models. When one is modeling a specific system, one can often obtain more accurate results by using specific reaction parameters (SRPs) (Gonzalez-Lafont et al. 1991, Rossi and Truhlar 1995, Bash et al. 1996). For example, in work mentioned above, general parameters have been optimized to give improved thermochemistry via hybrid Hartree-Fock/density-functional theories (HF-DFT) (Becke 1993, Lynch et al. 2000). Although these parameters have been optimized to make the methods robust for a diverse set of applications, for any one application, other values of the parameters may prove more effective (Chuang et al. 1999b). This approach can be implemented by means of various bootstrap strategies. For example, if one can afford to calculate the barrier height and/or transition state geometry for a given reaction system by a more accurate method, one can adjust an SRP (or SRPs) to reproduce this critical region of the potential energy surface. Then the specifically recalibrated HF-DFT-SRP method provides an affordable engine for direct dynamics calculations that should yield useful results for that reaction system. Other strategies are also possible, e.g., one can optimize parameters on a smaller but similar system or on a subsystem of a larger system.

As we move up in size in the intermediate-size cluster systems, at some point we may find that even hybrid HF-DFT-SRP methods present a prohibitive cost. In that case there are two general strategies: (i) use an intrinsically less accurate level of theory, but use SRPs to calibrate it for the system of interest; (ii) use multilevel techniques based on treating a subset of the atoms in the cluster at a higher level than the full cluster.

Ab initio and hybrid HF-DF electronic structure techniques can be used to understand which lower-level methods are most reliable for various kinds of systems (e.g., systems without ions or polar bonds) and, when appropriate, to validate lower-level methods for such properties. Even more powerful is the use of high-level methods to parameterize semiempirical models that can be applied to larger systems. There is a hierarchy of such semiempirical methods that may be used. With respect to using lower level theory with SRPs we note that we have had considerable success using neglect-of-diatomic-differential-overlap (Pople and Beveridge 1970) theories as the lower level (Gonzalez-Lafont et al. 1991, Liu et al. 1993, Corchado et al. 1995, Chuang et al. 1999b). One can use genetic algorithms to optimize the parameters, a procedure that we have demonstrated successfully for other systems (Rossi and Truhlar 1995, Bash et al. 1996, Liu and Truhlar 2000). For even larger clusters, one can use tight binding theory (Sutton et al. 1988, Ducastelle 1991, Galli and Mauri 1994, Wang and Mak 1995, Wasserman et al. 1996, Elstner et al. 1998, Horsfield 1997, Galli et al. 1998, Liu and Truhlar 2000) to generate the potentials. Tight-binding methods are especially alluring when reformulated so the computational cost scales linearly with N_{atoms} (Goedecker and Teter 1995, Jayanthi et al. 1996, Horsfeld et al. 1998, Sternberg et al.

1999, Bowler and Gillan 1999). As an example of the size limitations, nonorthogonal, non-self-consistent tight binding could be used for long simulations of up to 5000 atoms, but nonorthogonal, self-consistent tight binding is probably most useful for long simulations in which the system size is restricted to 2000 or less atoms. As a starting point, it is important to understand the accuracies of various general levels as well as to have universal parameterizations available as starting points for specific reaction parameterization. Tight-binding methods have been most successful for homonuclear systems (e.g., silicon) and systems where all atoms have similar electronegativity (e.g., hydrocarbons).

Potential surfaces for liquid-phase condensed-phase systems may be modeled in the full space of solute and solvent (this is called the explicit-solvent approach) (for collections of articles, see Jensen and Truhlar 1987, Gao and Thompson 1998), or the effect of solvent may be taken into account implicitly by replacing the solute potential energy by a potential of mean force (for a recent review, see Cramer and Truhlar 1999). The explicit approach includes both nonequilibrum solvation effects and equilibrium ones, whereas the implicit approach usually includes only equilibrium solvation. In the implicit approach, nonequilibrium effects, if significant, can be added by using collective solvent coordinates representing the deviation from equilibrium (Chuang and Truhlar 1999). Explicit methods also have the advantage of providing a seemingly more natural way to include specific interactions in the first solvation shell, although these can be included in an average way in implicit models via atomic surface tensions. However, explicit-solvent methods have several severe drawbacks, most especially that they are expensive. As a result of this chief drawback, such treatments usually neglect solute and/or solvent polarizability effects or treat these in a parameterized way.

Whereas explicit-solvent models require new parameters for every new solvent to be considered, implicit-solvent models have been parameterized in a "universal" way for general organic solvents by representing the solvents in terms of a small number (about a half dozen) of solvent descriptors such as dielectric constant, hydrogen bond acidity, and so fourth (Zhu et al. 1998, Hawkins et al. 1999). The dielectric constant accounts for bulk electric polarization of the solvent, and the other descriptors account for deviations from this due to cavitation, short-range forces, such as dispersion forces and hydrogen bonding, and solvophobic effects, if any. A critical element in calculating the electric polarization effects is a realistic model of liquid-phase electrostatics. Class IV charges calculated by the self-consistent reaction field method in the liquid phase provide a semiempirical, low-cost means of including solute polarizability in such calculations (Zhu et al. 1998).

Electronically Nonadiabatic Reactions and Spectroscopy

The best current methods for calculating excited-state potential curves or sets of coupled ground and excited surfaces are multiconfiguration SCF (MCSCF) calculations combined with perturbation theory for dynamical electron correlation (both diagonalize-then-perturb, e.g., CASPT2 (Roos et al. 1994, Roos et al. 1996, Merchan et al. 1999), and perturb-then-diagonalize, e.g., QCMRPT2 (Nakano 1993, Hoffmann and Khait 1999), procedures are available) and MCSCF followed by multi-reference configuration interaction (MRCI) (Harrison and Shepard 1994, Werner 1995, Dachsel et al. 1977). Diabatic states are usually defined by using valence bond configurations, or state-averaged natural orbitals (García et al. 1997, Klüner et al. 1999) but more systematic (and systematically improvable) methods are available (Atchity and Ruedenberg 1997), although they are not still completely general.

Recent work has shown progress in practical extensions of DFT methods to excited states, and there is now considerable activity in this area.

A problem on the borderline between structure and dynamics is the calculation of vertical excitation spectra in the condensed phase. By the Franck-Condon principle, the excitation is sudden on the time scale of nuclear motion, but electronic polarization occurs on a faster time scale. Recent progress has been made by combining a two-time-scale treatment of electric polarization of the solvent (treated as a continuous dielectric medium) with additional terms for dispersion effects and hydrogen bonding (Aguilar et al. 1993, Li et al. 2000).

Dynamics

Electronically Adiabatic Processes

A variety of molecular dynamics methods can be used for the dynamics of the interacting atoms once accurate forces are known. The most straightforward methods are based on classical trajectories. For statistically averaged (i.e., microcanonical or canonical) chemical reaction rate constants, generalized transition state theory has some advantages. One advantage of transition state theory is that although the original fundamental justification of the theory was classical, it has been shown that quantal effects may be incorporated by a two-step process (Garrett et al. 1980, Truhlar et al. 1982, Isaacson and Truhlar 1982). First, one replaces the classical phase space integrals that define the partition functions of transition state theory by quantum mechanical sums over states. This quantizes all degrees of freedom of the reactant and all degrees of freedom of the transition state except the reaction coordinate (which is missing in the transition state partition coefficient). This is done prior to optimizing the location of the variational transition state so as to include quantum effects on the location of the variational transition state as

well as on the reactive flux that passes through it. In the second step, one multiplies by a transmission coefficient that accounts for the competition between tunneling and overbarrier processes; this includes the quantum effects on the reaction-coordinate motion. Variational transition state theory with semiclassical multidimensional transmission coefficients (VTST/SMT) has been well validated against accurate quantum dynamics for a diverse set of few-body systems (Allison and Truhlar 1998), but accurate quantum dynamics rapidly becomes prohibitively expensive as system size grows.

At a deeper level, we now recognize that the transition state partition function, usually interpreted as a Boltzmann average of sharp energy levels of the transition state, can be also interpreted as a Boltzmann average of transition state resonances with finite energy widths (due to their finite lifetimes) (Truhlar and Garrett 1992) or as a Boltzmann average of the transmission probability for flux passing the quantized dynamical bottlenecks (Chatfield et al. 1992, Chatfield et al. 1996)— either of these methods automatically includes tunneling and other quantum effects on the reaction coordinate, and they provide an alternative to the two-step procedure.

Other (closely related) approaches to including quantum effects in transition state theory are called path integral quantum transition state theory, PI-QTST (Gillan 1988, Voth et al. 1989; for a comparison to VTST/MT, see Truhlar et al. 1996) and the instanton approach (Miller 1975, Bendarskii et al. 1993, Smedarchina et al. 1995). The PI-QTST method has similar accuracy to VTST/MT for symmetric bimolecular reactions in regions of its validity (McRae et al. 1992), and work is in progress on extending it to asymmetric systems and metastable potentials (Jang et al. 1999). The instanton approach has had considerable success for proton tunneling rearrangements (Fernández-Ramos et al. 1999), but in its current form it is not applicable to bimolecular reactions or to unimolecular reactions with reaction paths involving large-amplitude motions.

An alternative approach that is being developed for proton and hydride transfer reactions is to treat the transferred atom quantum mechanically with the rest of the system treated by classical mechanics (Hammes-Schiffer 1998).

It is useful to compare transition state theory to classical trajectories even in a classical mechanical world. If a rate process is dominated by a single dynamical bottleneck region, a very efficient way to calculate the reactive flux by trajectories would be to sample at the dynamical bottleneck region and integrate the trajectories just far enough forward and backward to count how many times they recross the bottleneck region. If one has identified a true dynamical bottleneck, the trajectories with positive momentum at the saddle point will proceed directly to products and those with negative momentum along the reaction coordinate will proceed directly to

reactants, where "directly" means without recrossing the dynamical bottleneck. This no-recrossing limit is transition state theory, and it is often an excellent approximation (Truhlar and Garrett 1980, Truhlar et al. 1996). Thus, in a classical world, transition state theory may be thought of as an efficient way to carry out trajectory simulations, i.e., as a form of rare event sampling.

When one considers condensed-phase systems, the number of possible dynamical bottlenecks can become large. Nevertheless in some cases one can still calculate all the rate constants for elementary steps and predict the complex-systems kinetics by a master equation or by kinetic Monte Carlo algorithms However, when the number of possible elementary processes becomes too large to catalog, a classical mechanical simulation of the entire complex system may still be used. At first it might seem that transition state theory becomes less useful here, but that is not true. Voter has shown that combining transition state theory ideas with full-system classical dynamics provides an efficient means of rare event sampling even when the dynamical bottlenecks are not pre-identified; the resulting method is called hyperdynamics (Voter 1997, Voter and Sorensen 1999, Rudd and Voter 1999). In a rough description, hyperdynamics consists in flooding (filling in) the minima to make it easier to surmount the barriers. This may be compared to an alternative strategy (Ota and Brünger 1997) of scaling down the barriers when the goal is the computation of free energies of flexible molecules rather than dynamics.

If energy transfer processes that replenish the reactant Boltzmann distribution for reactive states are slow compared to reaction, or if energy transfer events that stabilize highly reactive states of reactants formed by reverse reaction are slow, then one must add corrections for nonequilibrium effects to either trajectory calculations or to transition state theory, because the assumption that reaction is sampling an equilibrium ensemble breaks down (Lim and Truhlar 1986). A second circumstance in which one must consider nonequilibrium effects is when one or more of the reactants is a solute, and it is assumed that the solvent is at equilibrium with it. This is often a good first-order assumption, but we must consider quantitative nonequilibrium corrections (Chuang and Truhlar 1999).

Direct dynamics is the use of electronic structure theory to calculate energies, gradients, and Hessians on an "as needed" basis, or perhaps by local interpolation, but without fitting this data to a global or semiglobal potential energy function (Wang and Karplus 1973, Leforestier 1978, Truhlar et al. 1982). In other words, the dynamics are generated directly from the electronic structure calculations. Car and Parrinello (1985) pioneered an extended Lagrangian formulation for the interface between the two elements in direct dynamics calculations combining density functional theory (DFT)

for the electronic structure element with purely classical trajectories for the dynamics. In their method, the electronic degrees of freedom are treated by fictitious dynamics while the nuclei are treated with classical dynamics. Direct dynamics has also been widely used with other computational strategies and with other dynamics methods. For example, there has been a considerable amount of work on direct dynamics methods for generalized transition state theory in the gas phase (Truhlar and Gordon 1990, Truhlar 1995, Corchado et al. 1998c, Chuang et al. 1999a) and in the liquid state (Chuang et al. 1999b).

An especially difficult challenge for condensed-phase dynamical studies is the incorporation of quantal dynamical effects into enzyme catalysis, but recently progress has been reported in this area by two especially promising approaches (Hwang and Warshel 1996, Alhambra et al. 1999, Alhambra et al. 2000).

Electronically Nonadiabatic Dynamics

The treatment of electronically nonadiabatic collisions is much less developed than the treatment of reactions that proceed on a single potential energy surface. In some cases when there is a dense manifold of closely coupled electronic states, one may use statistical theories even for electronic degrees of freedom (Truhlar and Dixon 1979). For the coupling of the ground state to this manifold or for couplings among a few low-lying, widely separated electronic states, there are three main approaches under current study: trajectory surface hopping (Tully 1998), self-consistent potential methods (Meyer and Miller 1979, Topaler et al. 1998), and density matrix evolution (Martens and Fang 1997). Recently we have developed a method, called continuous surface switching (CSS), that combines some of the more desirable features of the TSH and Ehrenfest methods, without having their worst drawbacks (Volobuev et al. 2000, Hack and Truhlar 2000). An alternative method that accomplishes some of the same objectives by using a stochastic Schrödinger equation has also been proposed (Prezhdo 1999).

Methods are also available for the treatment of electronically nonadiabatic processes in condensed-phase systems (Prezhdo and Rossky 1997, Rabani et al. 1999), and a review is available (Egorov et al. 1999).

Concluding Remarks

It is now well established that molecular-scale modeling competes with experiment for accuracy and convenience on small systems, and the size of the system that can be treated with useful accuracy is rapidly increasing. For complex systems, molecular-scale modeling is not only a technique for predicting accurate numerical values of system parameters, but also it serves as a techniques of gaining insight and understanding.

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