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Polar Solvent Dynamics and Electron-Transfer Reactions

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Polar solvents often exert a dramatic influence on reactions in solution. Equilibrium aspects of this influence involve differential solvation of reactants compared to the transition state that lead to alteration of the free-energy barrier to reaction. Such effects are well known, and often give rise changes in reaction rates of many orders of magnitude. Less well understood are effects arising from non-equilibrium, dynamical aspects of solvation. During the course of reaction, charge is rapidly redistributed among reactants. How the reaction couples to its solvent environment depends critically on how fast the solvent can respond to these changes in reactant charge distribution. In this article the dynamics of solvation in polar liquids and the influence of this dynamics on electron-transfer reactions are discussed. A molecular picture suggests that polar solvation occurs on multiple time scales as a result of the involvement of different types of solvent motion. A hierarchy of models from a homogeneous continuum model to one incorporating molecular aspects of solvation, combined with computer simulations, gives insight into the underlying dynamics. Experimental measures of solvation dynamics from picosecond and subpicosecond time-dependent Stokes shift studies are compared with the predictions of theoretical models. The implication of these results for electron-transfer reactions in solution are then briefly considered.

A SOLVENT CAN INFLUENCE A CHEMICAL REACTION IN A number of ways. It can act in a static sense to change the energies of the reactants and products (that is, the potential surface on which the reaction occurs) compared with their energies in the gas phase. The solvent can also enter into the proceedings in a more dynamic way by exchanging energy and momentum with reacting species and by responding to their changing distributions of charge. Expressing the rate constant k of a chemical reaction as

$$k = A \exp(-\Delta G^{\ddagger}/k_{\mathrm{B}}T) \tag{1}$$

where k_{B} is the Boltzman constant and T the temperature, static solvent effects exert their major influence on the free energy of activation $\Delta G^{\ddagger}$. Dynamical solvent effects, on the other hand, appear in the frequency factor A. We focus our attention on this latter, dynamical aspect of the problem.

Dynamical solvent effects are usually discussed in terms of friction, which can be either of a collisional or dielectric origin. Collisional friction is important for reactions involving large-amplitude motion, such as isomerization and dissociation reactions. In these cases the solvent most often impedes reaction by being in the way of the desired reactive motion. The cage effect is a classic example of this type of interaction. Alternatively, under low-density conditions, collisions can also aid the progress of reaction by providing a source of energy needed to surmount the reactive barrier. Study of such collisional effects has a long history and many aspects of their dynamical solvent influence are well understood. Rather than discuss this first type of solvent friction further, we refer the interested reader to several excellent reviews (*1*).

The latter type of dynamical solvent effect involves the "dielectric" friction that arises in polar solvents. The coupling between solvent and reacting system in this case is electrostatic in origin. For electron and other charge-transfer reactions, such polar interactions can be quite strong, and it has long been recognized that the static aspects of this interaction can significantly affect reaction rates. For example, rate constants can change by many orders of magnitude when these reactions are studied in different solvents. Such dramatic changes mainly involve modification of the reactive barrier $\Delta G^{\ddagger}$ by polar solvation. However, dynamical aspects of polar interactions also play an important role in determining reaction rates. This fact has only been appreciated relatively recently. Current theories show that

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the extent to which a reaction couples to its solvent environment depends markedly on the "intrinsic" (that is, unsolvated) reaction rate compared with the rate at which the polar solvent can respond to charge redistribution that occurs during the reaction.

Although a good deal of experimental attention is currently being focused on establishing such a dynamical connection, the field is still a young one. In fact, an understanding of even what sorts of time scales are involved in polar solvation is very much under development. The purpose of the present article is to provide a simple introduction to some of the key ideas emerging from this rapidly developing field in a form useful to nonspecialists. We also direct the reader to reviews on related topics by Barbara and Jarbeza (*2*) and Simon (*3*).

The remainder of the article is divided into two parts. The first describes recent experiments, computer simulations, and theory aimed at learning about solvation dynamics in simple, nonreactive situations. An understanding of these cases is an obvious prerequisite to describing the more complex problem of dynamical solvent effects on reaction. The second part consists of a brief discussion of electron-transfer reactions, in which we attempt to survey the recent theoretical predictions linking solvent dynamics to reaction rates and review the experimental evidence thus far accumulated for this connection. Some opinions on the status of research in both areas are offered in the conclusion.

The Dynamics of Polar Solvation

If we are to consider how the dynamics of polar solvation influences chemical reactions, we must first address the question "How fast is solvation?" In particular, we need to know how the energy of solvation relaxes in response to an instantaneous change in the charge distribution of a dissolved solute. To quantify the time dependence we use the normalized response $S(t)$ to a step-function perturbation of the solute applied at $t = 0$:

$$S(t) = \frac{G_{\mathrm{solv}}(t) - G_{\mathrm{solv}}(\infty)}{G_{\mathrm{solv}}(0) - G_{\mathrm{solv}}(\infty)} \tag{2}$$

In this expression $G_{\mathrm{solv}}(0)$, $G_{\mathrm{solv}}(t)$, and $G_{\mathrm{solv}}(\infty)$ represent free energies of solvation at times 0, t, and at infinity, respectively.

The molecular mechanism of solvation of polar molecules has generally been considered to be rotational in character, that is, dipolar solvent molecules respond to a change in the charge distribution of a solute by reorienting. Although this process is the dominant relaxation mechanism in polar liquids, other types of motion also contribute to the solvation response. As we describe below, translational motion of nearest-neighbor solvent molecules may play a role. On short time scales, librational motions (*4*) become important, whereas at even shorter times vibrational and electronic motions contribute. Thus thinking of solvation as having a single time scale is an oversimplification. Nevertheless, describing solvation dynamics in terms of the reorientational part of the response alone does provide a reasonable starting point for discussion.

Table 1. Solvent properties at 298 K. Dielectric properties for the main Debye dispersions of acetonitrile, DMSO, and water are from (*56–58*), respectively. Dielectric data for the remaining solvents were obtained from fits of collected data as described in (*14*) and (*15*). The self-diffusion constants D_T were estimated from molar volume and viscosity data using the method described by Dullien (*59*), except for water and methanol, for which we report experimental values (*59*).

Solvent	ϵ_0	ϵ_∞	τ_D (ps)	τ_L (ps)	D_T (10^5 cm^2 s^{-1})	P
Acetonitrile	37.3	~1.8	4.0	0.2	5.3	0.42
Dimethylsulfoxide	46.5	4.8	20.6	2.1	0.83	0.25
Propylene carbonate	63.9	~11	43.5	8	0.55	0.33
N-methylpropionamide	163	~6	125	5	0.26	0.41
Water	78.36	5.16	8.27	0.54	2.51	1.0
Methanol	33.7	5.6	55.6	9.2	2.32	3.0
n-Propanol	20.6	3.65	435	77	0.70	4.6

Let us consider what sort of times are expected for the reorientational solvation response. As a first guess, one might anticipate that $S(t)$ would decay with a time constant characteristic of single-particle rotational diffusion of solvent molecules. A simple thought experiment suffices to show that this estimate is not correct. Consider instantaneously "switching off" the charge on an ion in two different solvent environments. In the first case, suppose that the solvent is predominately nonpolar such that only a single polar solvent molecule is near to the solute and the solvation energy is determined by this molecule alone. Originally the dipole of the polar solvent would be aligned so as to lower the electrostatic solvation energy. Once the charge is switched off, there is no longer an energetic preference for any particular orientation and the dipole randomly diffuses away from its original direction. In this case, the time for the relaxation of solvation free energy is the single-molecule rotational diffusion time. Now consider what happens in a solvent in which all of the molecules are polar. Initially, neighbors of the ion are all oriented so as to achieve favorable electrostatic interactions with the solute. By being so aligned, they accept some unfavorable interactions with their solvent neighbors. In this case, once the charge is switched off, solvent molecules are affected by only these residual unfavorable interactions. For any particular solvent molecule, the remaining solvent creates an electric field in opposition to its dipole direction. Thus the dipole in question undergoes a forced reorientation that is considerably faster than its random diffusive dynamics. All of the solvent molecules experience such driving forces and thus the solvation energy relaxes much more rapidly than in the first case.

From these examples, we conclude that in a polar solvent the solvation response $S(t)$ involves coupled reorientational dynamics that occur on shorter time scales than single-particle diffusion. It is this cooperative, many molecule aspect that makes solvation challenging to describe both in words and in quantitative theory. In general, we should expect that the more polar the solvent, the stronger the coupling between molecules and the faster the solvation response. Furthermore, there is no reason to anticipate that even the reorientational part of the response should involve just a single time scale.

To gain a more quantitative appreciation for the above ideas, we now consider the lowest level theoretical treatment of solvation dynamics. A number of workers (*5–9*) have used what we call "simple continuum" models to study this problem. These models represent the solute as a point charge or point dipole in a spherical cavity. The solute is pictured as being immersed, like a macroscopic object, in a continuum solvent. The key feature of such models is their representation of the solvent as a structureless fluid whose only relevant property is its bulk, frequency-dependent dielectric function $\epsilon(\omega)$. The major contribution to $\epsilon(\omega)$ at the frequencies studied experimentally is reorientational motion, and thus the predicted relaxation is also confined to such motions. The dielectric function of many solvents is adequately represented by the phenomenological Debye form:

$$\epsilon(\omega) = \epsilon_\infty + \frac{\epsilon_0 - \epsilon_\infty}{1 + i\omega\tau_D} \tag{3}$$

where ϵ_0 is the static dielectric constant, ϵ_∞ is the limiting, high-

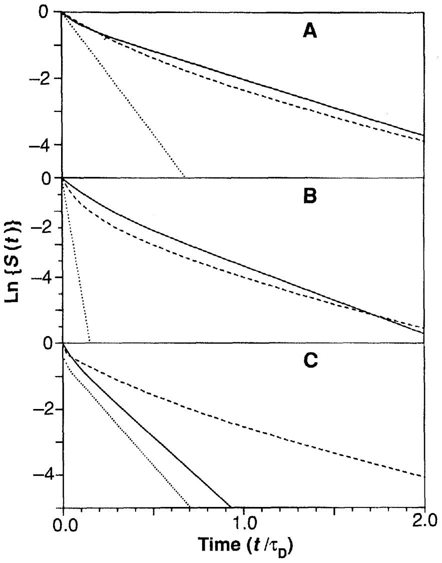

Fig. 1. Solvation response functions of the probe solute coumarin 153 in three solvents: (**A**) propylene carbonate (237 K); (**B**) *N*-methyl propionamide (273 K); and (**C**) *n*-propanol (251 K) [data from (*14*)]. The solid curve in each panel is the experimental response obtained from the time-dependent fluorescence shift with Eq. 6. The dotted curve is the prediction of the simple continuum model, the dashed curve that of the dynamical MSA model (*27*) (see text). The latter curves were calculated based on a single Debye $\epsilon(\omega)$ representation of the solvent and a dipolar solute of the same size as the solvent.

frequency dielectric constant, and τ_D the dielectric (or Debye) relaxation time. (Note that this form is an idealization and that the other, nonreorientational polarization mechanisms mentioned earlier cause deviations from Debye behavior at high frequencies.) The time-domain response corresponding to such an $\epsilon(\omega)$ is one in which a step-function change in applied electric field produces exponential relaxation of the polarization of the dielectric with time constant τ_D. Simple continuum models predict that solvents with this type of dielectric function have an exponential solvation response

$$S(t) = \exp(-t/\tau_L) \tag{4}$$

whose time constant is the so-called "longitudinal" relaxation time of the solvent (*10*)

$$\tau_L = (\epsilon_\infty/\epsilon_0)\tau_D \tag{5}$$

The central result of simple continuum models is that the solvation time is equal to τ_L. Since the ratio $\epsilon_\infty/\epsilon_0$ normally lies between 1/10 and 1/50 for polar solvents, this longitudinal relaxation time is much shorter than the Debye time (τ_D) and is in the range of 10^{-13} to 10^{-10} s (Table 1). For nonassociated liquids, τ_D is comparable to the single-particle rotational diffusion time, so that solvation is indeed much faster than diffusion. In simple continuum theories, the ratio $\epsilon_\infty/\epsilon_0$, by which τ_L differs from τ_D, in some sense gauges the degree of cooperativity of the solvation response. Although in many respects simple continuum models are a poor representation of the solvation of molecular solutes, the above treatment yields simple predictions that serve as benchmarks for comparison of experimental results and more refined theories.

In order to see how realistic predictions of this simple model are, we now consider direct experimental measurements of solvation. The dynamics of polar solvation can be studied experimentally through observation of the time-dependent frequency shift of the fluorescence spectrum of a probe solute after ultrafast excitation. Such "dynamic Stokes shift" measurements are analogous to well-known steady-state "solvatochromic" shifts that have long been used for studying equilibrium aspects of solvation (*11*). In both cases, relative frequency shifts are used to provide an instantaneous measure of energy differences between the ground (S_0) and excited (S_1) electronic states of a solute. The idea behind the dynamical measurement is as follows. Prior to excitation, the solvent environment surrounding a solute is in equilibrium with its ground-state electronic charge distribution. Excitation is instantaneous on the time scale of solvent reorientation, so that the solute excited state is initially prepared in this ground-state solvent configuration. If the charge distribution (dipole moment) of the solute is appreciably different in S_1 and S_0, the state prepared is thus a nonequilibrium one with respect to solvation. As the solvent reorganizes so as to achieve equilibrium with the new (S_1) charge distribution, the fluorescence spectrum shifts, and this shift monitors the progress of the solvation energy relaxation. Explicitly, the time-evolving spectra are used to determine an experimental response function

$$S_{\mathrm{obs}}(t) = \frac{\nu(t) - \nu(\infty)}{\nu(0) - \nu(\infty)} \tag{6}$$

where the ν's refer to the frequency of some characteristic point on the spectrum, for example, its maximum. Under the assumption that the solvation response is linear, the spectral response $S_{\mathrm{obs}}(t)$ is a direct measure of the desired solvation response function $S(t)$.

Although dynamical Stokes shift measurements have been reported for a number of years (*12*), only recently have both sufficient time resolution and theoretical understanding become available to make such measurements fruitful. Recent work by several groups, including our own (*13–15*) and those of Simon (*16*) and Barbara (*17–19*), have provided measures of solvation times of a variety of solute-solvent combinations (*13–21*) whose time scales span over five orders of magnitude. For experimental reasons, the probe solutes used have been large aromatic molecules (typically laser dyes) that have $S_0 \rightarrow S_1$ absorptions with substantial charge-transfer character. The solvents studied have included both associated, hydrogen-bonding solvents as well as nonassociated, polar aprotic solvents. Some of the main features observed in these studies can be summarized as follows:

1) The solvation time scale is determined primarily by the solvent. There is general agreement (to within a factor of 2) between solvation times measured in the same solvent with different probe solutes (*15, 18*). Much greater variations are observed as a function of solvent with a given probe.

2) In experiments with dynamic range sufficient to provide $S_{\mathrm{obs}}(t)$ over several orders of magnitude, the solvation response has been found to decay nonexponentially in time (*14, 18*). Contrary to predictions of simple continuum models, such nonexponential decays are observed even for solvents that are adequately represented by a Debye $\epsilon(\omega)$. Typical response functions observed (solid curves) with coumarin 153 in three solvents (*14*) are shown in Fig. 1. The predictions of the continuum model are shown as the dotted lines. The dashed lines are predictions of another theory discussed below.

3) In most cases the observed solvation response is slower than predicted by continuum theory (Fig. 1, A and B). In Fig. 2 we summarize virtually all of the solvation times that have been reported thus far. The ordinate of this plot is the ratio of the average observed solvation time [$\langle\tau_{\mathrm{obs}}\rangle$, defined as the area under $S_{\mathrm{obs}}(t)$] to τ_L. With the exception of the alcohols, nearly all points fall above the horizontal line that marks agreement with continuum predictions.

4) There is an apparent correlation between the deviation of $\langle\tau_{\mathrm{obs}}\rangle$ from τ_L and the ratio $\epsilon_0/\epsilon_\infty$ (Fig. 2). For the highest values of this ratio (where $\epsilon_0 > 200$), $\langle\tau_{\mathrm{obs}}\rangle$ is more than an order of magnitude greater than τ_L.

5) Results in alcohols differ from those in other solvents, in that $\langle\tau_{\mathrm{obs}}\rangle$ is here close to and often less than τ_L. At temperatures below ~200 K, solvation times much less than τ_L are observed (*10, 16*) in alcohols.

The above results indicate that the dynamics of solvation of molecular solutes deviate in several respects from the predictions of simple continuum theories. Such deviations are hardly surprising, and merely point out that molecular aspects of the solvent-solute interaction are important in determining the dynamics. In order to obtain a deeper understanding of the experimental results, dynamical theories have recently been advanced that attempt to improve on the simple continuum picture by incorporating some aspects of solvent molecularity. Approaches based on inhomogeneous continuum ideas (*22*) as well as approximate treatments of truly molecular solvents (*23–28*) have been used. To date, the most useful of these models is the dynamical mean spherical approximation (MSA) treatment proposed by Wolynes (*26*) and extended by other workers (*27, 28*). In this theory it is assumed that the molecular nature of the surroundings of a solute in a real solvent is roughly the same as that surrounding a hard-sphere ion or dipole in a hard-sphere dipolar liquid. The static structure in the idealized hard-sphere model can be solved for in closed form within the MSA model (*29*). The influence of this structure on the dynamics is analyzed in an approximate, semiempirical way with the experimental $\epsilon(\omega)$ of the solvent under consideration used as input. Such a model accounts semiquantitatively for many of the features of the experimental data (*27, 30*). As illustrated by the dashed lines in Fig. 1, the MSA model predicts highly nonexponential $S(t)$ decays, even for Debye solvents. The solvation times predicted by this theory are uniformly greater than the continuum τ_L prediction. The dashed curve in Fig. 2 is the dynamical MSA result for how $\langle\tau_{obs}\rangle/\tau_L$ should vary with $\epsilon_0/\epsilon_\infty$. The theoretical curve provides a reasonable representation of the experimental trend (Fig. 2) if the alcohol data is ignored.

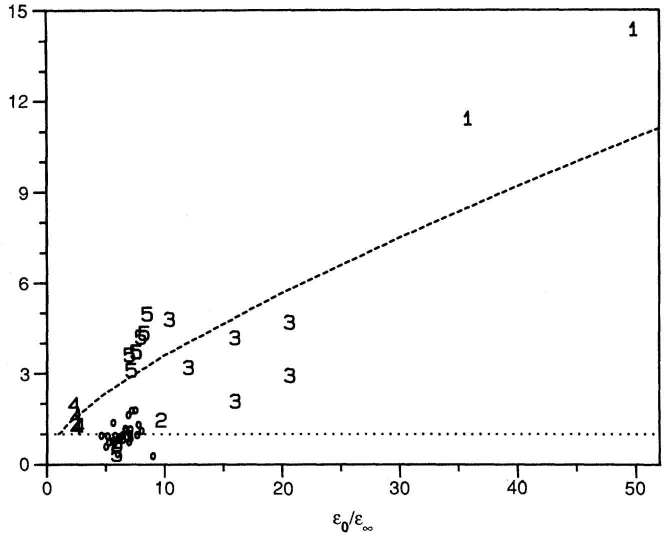

Fig. 2. Summary of observed solvation times. The ordinate of this plot is the ratio of observed time $\langle\tau_{obs}\rangle$ to the prediction of simple continuum models, τ_L. The ratio $\langle\tau_{obs}\rangle/\tau_L$ thus quantifies the departure from simple continuum predictions (dotted horizontal line). Note the apparent correlation between this ratio and the dielectric parameter ratio $\epsilon_0/\epsilon_\infty$ (see Eq. 3). The dashed curve is the prediction of the dynamical MSA model (*27*) [assuming a dipolar solute, a Debye $\epsilon(\omega)$ with $\epsilon_\infty = 2$, and equal solvent and solute sizes]. Numbers refer to different solvent types as: 0, alcohols (*13–18, 20*); 1, *N*-methylpropionamide (*14*); 2, dimethylsulfoxide (DMSO) (*13*); 3, nitriles (*13, 17, 18*); 4, acetates (*18*); and 5, propylene carbonate (*14, 18, 21*).

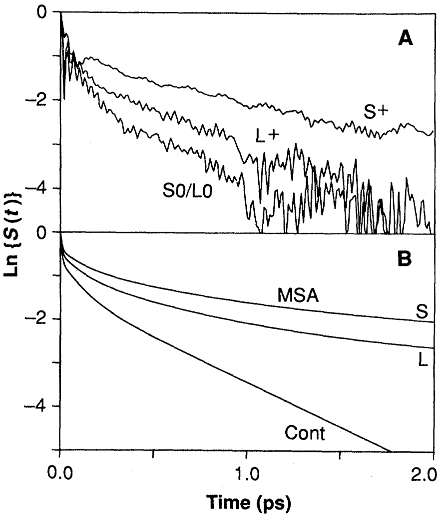

Fig. 3. (**A**) Solvation response functions observed in computer simulations of spherical solutes in ST2 water (*32*). All three curves show the response to a small step-function change in the solute charge. Different curves correspond to different solutes as: S+, "small" univalent cation, L+, "large" univalent cation, and S0/L0, uncharged solutes (small and large solutes are indistinguishable in this case). (**B**) Response functions predicted by the simple continuum (Cont) and MSA (*27*) theories. The dynamics predicted by the simple continuum treatment are independent of solute, whereas the MSA predictions depend on solute size but not solute charge.

The physical explanation provided by the MSA and other current models for why the dynamics observed experimentally deviate as they do from simple continuum predictions can be paraphrased as follows. Far from the solute, where its electrical field varies slowly compared with solvent dimensions, the response occurs with the continuum τ_L time. Near the solute, however, the field changes appreciably over distances comparable to the solvent size. As a result, the full cooperativity of the τ_L response, which is a limiting long wavelength property, is not achieved. Rather, the response here is slower and more like a single-particle time than the continuum prediction. As a function of distance from the solute, there is actually a continuous distribution of solvent reaction times that range from slow, single-particle times down to τ_L values. Counter to intuition, the solvation response is pictured to proceed from the outside in toward the solute. Such response was anticipated by Onsager in his "snowball" comment on electron solvation (*31*). The net relaxation is a superposition of all of these responses and so is both nonexponential and slower than τ_L, as is observed experimentally.

We now ask whether this physical picture is an accurate representation of the solvation process. Although the MSA model provides satisfying explanations for a number of experimental trends, it does not predict the behavior of alcohol solvents (Figs. 1C and 2). At least for these solvents, some important feature of the solvation has been neglected.

The soundness of the MSA description can be evaluated on a molecular level with computer simulation. We have recently completed a series of simulations of the dynamics of solvation of ionic solutes in water (*32*). Similar studies have also been carried out by Karim *et al.* (*33*) for the case of dipolar solutes. The dynamics observed in these studies were much more varied than could be accounted for on the basis of simple continuum ideas, the MSA treatment, or indeed any current theories. The simulated response functions corresponding to solvation energy relaxation after a small change in the charge of several solutes is shown in Fig. 3A. The MSA prediction in Fig. 3B depends on the solute size (L = large and S = small) but not on its charge. Contrary to this prediction, the observed dynamics are, in fact, size-independent for uncharged solutes S0 and L0, but depend strongly on the charge-to-size ratio (compare S+ and L+). Furthermore, for the uncharged solutes, the response is much faster than the MSA prediction, and is near that predicted by the simple continuum model (Fig. 3B). These latter solutes are most similar to the probes used in experimental studies and their fast response is consistent with the relaxation times near τ_L observed in alcohol experiments. Recently, Barbara and co-workers (*19*) have succeeded in achieving the experimental time resolution needed to measure the water response directly. The response these workers observe is in rough agreement with the simulation results, tending to confirm the apparent correspondence between the dynamics in water and the alcohols.

The computer simulations provide insight into why the solvation dynamics in water are faster than the MSA prediction. In Fig. 4 the total solvation energy response (Tot) has been decomposed into contributions from different regions as a function of distance from the solute. Also shown for reference is the time correlation function corresponding to single-molecule reorientational diffusion of the solvent. The vast difference in time scale between this single-particle behavior and the solvation response functions is a striking demonstration of the collective nature of solvation. A second important feature illustrated by Fig. 4 is how the first solvation shell contribution dominates the total response. The 16 water molecules in the first shell account for 85% of $S(t=0)$. The very rapid initial decay and the 20-fs oscillations in $S(t)$ are due almost entirely to a concerted librational motion of the first shell molecules. It is mainly this first shell response that leads to failure of the MSA predictions for water. Rather than contributing the slowest response as predicted, the first shell contribution to $S(t)$ is actually much faster than that of the second and third shells (Fig. 4). These latter shells behave roughly as expected. The molecular basis for the fast nearest-neighbor response is twofold. First, interaction of the solute with nearby solvent molecules involves the full molecular charge distribution of the solvent rather than simply its dipole moment, as is the case with more distant solvent. For this reason, small reorientational-librational motions are more effective (faster) for relaxing the solvation energy. The MSA theory, which is based on a point dipolar solvent model, misses this effect. Second, small translational motions of solvent molecules also take part in the energy relaxation process. This aspect, also not included in present formulations of the MSA theory, can serve to either speed up or slow down the relaxation time of the first shell compared with other solvent regions.

We can dissect these differing contributions by looking at the trajectories of a single first shell solvent molecule in different cases. Three observables that can be obtained from a calculation for a small uncharged probe S0 and a small unit-charged probe S+ are the solute-oxygen distance (Fig. 5A), the cosine of the angle between the solvent dipole and the radius vector (Fig. 5B), and the single-molecule contribution to the electrical potential at the center of the solute (Fig. 5C). This last observable determines the solvation energy. Comparison of Fig. 5, A and B, shows that, in each case, small-scale rotational motions occur with roughly four times the frequency of translational motions. These two motions contribute with different weights to the potential fluctuations in different solutes and are responsible for the differences in the solvation dynamics shown in Fig. 3. For the S0 solute, fluctuations in the potential arise mainly from rotational motions, but for the S+ solute, translational motions also play an important role. Water molecules in the first solvation shell of S+ point one of their negative charges directly at the solute and are rather tightly held. This binding is apparent in the S+ trajectory of Fig. 5, and the potential fluctuations match the excursions of the solvent center-of-mass distance. Thus the slower solvation observed for S+ is the result of slower translational mechanisms of relaxation in the former solute and not the latter.

These water simulations point out several shortcomings of the dynamical MSA theory as a complete description of the dynamics of aqueous solvation. Proper modeling of the first solvation shell is critical and must take into account the extended charge distribution of solvent molecules and the participation of translational modes of relaxation. Neither of these two aspects of the response of the solvent near to the solute is captured in its dielectric response [$\epsilon(\omega)$] or accounted for in the MSA theory. The operation of these two effects renders the qualitative idea of a slow first shell response incorrect for water. Whether such a picture is valid for polar aprotic solvents, for which the MSA model provides good agreement with experimental data, is open to question. Although the highly structured nature of aqueous solutions probably exaggerates their effect, the aspects of the nearest-neighbor response discussed above must operate in simpler solvents as well.

In light of our water results, it is interesting to ask whether the "anomalous" behavior exhibited by alcohols reflects the greater importance of translational modes of relaxation compared with other solvents. The influence of "polarization diffusion" on solvation dynamics has been explored with the use of a continuum solvent model by Van der Zwan and Hynes (*7*) and in a more microscopic approach through the use of Smoluchowski-Vlasov equation by Chandra and Bagchi (*34*). These latter authors used the MSA formulation of the direct correlation function and concluded that for values of a quantity $P = D_T\tau_D/R^2$ greater than unity,

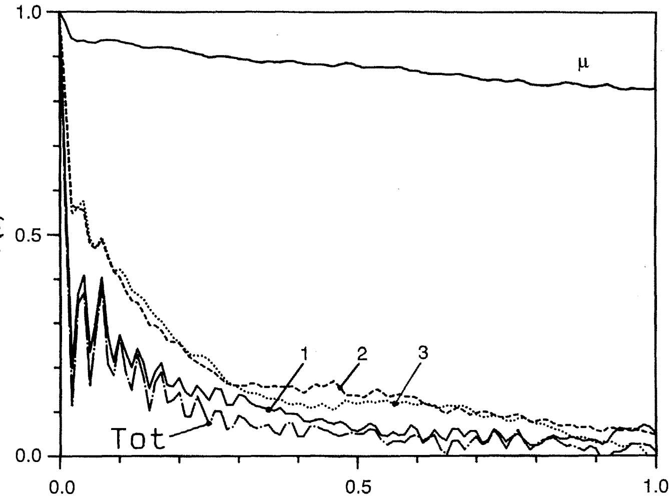

Fig. 4. Decomposition of the simulated solvation response into contributions from different solvent regions. The data are from simulations described in Fig. 3A for the uncharged S0 solute [see also (*32*)]. The solid curve (Tot) is the overall response, and the curves labeled 1, 2, and 3 are the contributions to this response made by solvent shell regions at increasing distance from the solute (the numbers of molecules included in these shells are 16, 43, and 83 for the first, second, and third shells, respectively). The top curve labeled μ is the diffusive reorientational response (dipole direction) of a single first shell solvent molecule and is included for comparison.

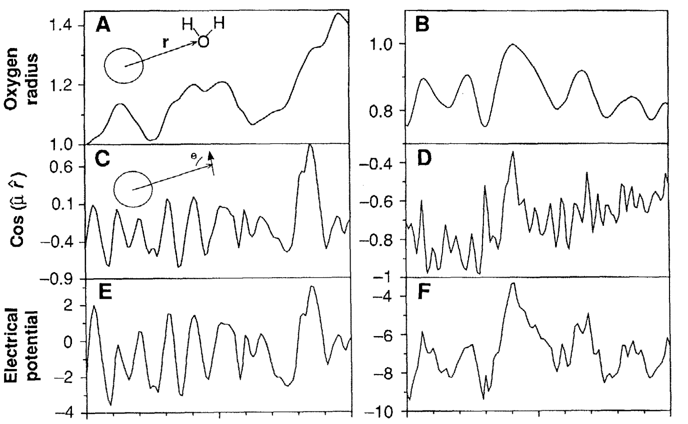

Fig. 5. Properties calculated from trajectories of single solvent molecules in the first solvation shells of S0 and S+ solutes [see caption to Fig. 3A and (*32*)]. The properties observed are: (**A** and **B**) solute-solvent (oxygen) distance; (**C** and **D**) cosine of the solvent dipole angle; and (**E** and **F**) the single-solvent contribution to the electrical potential at the solute charge site, for S0 and S+, respectively. The latter property determines the contribution to the solvation energy.

translational effects lead to relaxation occurring much more rapidly than predicted from the rotational MSA model (in this expression D_T is the solvent translational diffusion coefficient, τ_D the dielectric relaxation time, and R the solvent radius). Water and the *n*-alcohols have significantly larger P values than other solvents (Table 1). In addition, P increases with decreasing temperature. For example, P increases by a factor of 2 for *n*-propanol between room temperature and 200 K. As yet no quantitative comparison between theory and the experimental data has been attempted. Since the MSA representation is a crude model of a hydrogen-bonded liquid, the relative importance of translational effects in solvation by alcohols is not currently clear.

Electron-Transfer Reactions

Having considered the dynamics of polar solvation in some detail, we now briefly discuss how such dynamics influence solution-phase reactions. We limit the discussion to electron-transfer (ET) reactions, which have been extensively studied.

Theoretical understanding of solution phase ET reactions with regard to the role played by solvent dynamics has progressed rapidly in the last 5 years (*35–41*). A number of points are now relatively clear. First, dynamical solvent effects are expected to be observed only in reactions for which the dominant contribution to the activation energy comes from the solvent. That is, the "inner shell" or intramolecular component to ΔG^* (Eq. 1) should be small compared with that part contributed by solvation. In such cases, the energy of the reacting system is mainly a function of the solvent configuration, and thus the nuclear motions driving the ET process are mainly solvent motions. With this initial caveat in mind, the dynamical solvent effect depends on the adiabatic or nonadiabatic character of the reaction (*42*).

A nonadiabatic description is appropriate when the coupling between reactant and product states in the ET process is very weak, so that solvent fluctuations bring about occasional equalization of the energies of the reactant and product states. The electron, which is localized in a manner appropriate to the reactant state, can at such times transfer to the product state. In this weak coupling case, the probability for transfer is very low and is rate limiting; solvent dynamics do not dictate the overall rate. This nonadiabatic regime was the one considered by most of the early (intermolecular) ET theories (*43*).

The opposite extreme is the adiabatic limit. Here the product and reactant states interact strongly and the ET reaction is treated in terms of nuclear (solvent) motion on a single potential energy surface. The electronic distribution is assumed to adiabatically follow the nuclear dynamics, just as in "normal" chemical reactions. For outer-sphere ET, the nuclear motion involved is precisely that of the solvent, and thus ET rates (k_{ET}) in the adiabatic regime are predicted to be directly proportional to solvation rates. Most theories of ET have thus far used Debye-type (Eq. 3) continuum models for the solvent, and they therefore predict $k_{ET} \propto \tau_L^{-1}$ (*35–40*). Since, as we have discussed, τ_L is not a very accurate predictor of solvation times, a more general prediction might be that $k_{ET} \propto \langle\tau_{obs}\rangle^{-1}$, where $\langle\tau_{obs}\rangle$ is the experimental solvation time.

The nonadiabatic and adiabatic regimes described above are of course two limiting cases, and many ET reactions do not fit cleanly into either category. Rips and Jortner (*39*) and Sparpaglione and Mukamel (*40*) have recently formulated theories that attempt to incorporate both limits in a unified way. As expected, these theories predict behavior intermediate between the limiting $\tau_L{}^0$ and $\tau_L{}^{-1}$ dependences, as well as some more unusual behavior in special cases (*40*).

In all of the above theories, $\tau_L{}^{-1}$ (or $\langle\tau_{obs}\rangle^{-1}$) is predicted to be the maximal rate at which ET reactions can occur. Two effects can alter this prediction. The first is related to the shape of the activation barrier. Even when an adiabatic description of the ET process is appropriate, relatively weak coupling between reactant and product states is normal for ET reactions. The adiabatic potential surface in such weak coupling cases has a sharp, cusplike barrier. Hynes (*37*) has pointed out that crossing a barrier of this type depends in a biased way on the fastest components of the solvent response. For sharp barriers, the predicted k_{ET} is not proportional to average solvation times, but rather is more sensitive to the fastest components of the solvent motion. Zusman has recently drawn similar conclusions using a different theoretical approach (*41*). In a Debye continuum solvent model (Eq. 3), such effects are irrelevant because there is only a single time scale or frequency for dielectric (τ_D) and thus solvation relaxation (τ_L). All real molecular liquids, however, possess vibrational and librational motions that cause departure from the simple Debye $\epsilon(\omega)$ at high frequencies and that thus lead to other frequency components in the response. Taking such "frequency-dependent friction" effects into account leaves open the possibility that $k_{ET} > \langle\tau_{obs}\rangle^{-1}$. A similar result is also obtained when one considers the influence of intramolecular contributions to the reaction coordinate. The theories mentioned so far all consider a one-dimensional reaction coordinate that involves exclusively solvent motions. Sumi and Marcus (*35*) have examined the influence of intramolecular vibrational motions in the reaction coordinate. That is, they considered what happens when some inner shell barrier is present in addition to that brought about by solvation. They showed that adding this second degree of freedom can lead to nonexponential ET kinetics and ET rates that again are faster than solvation rates.

In summary, when ET rates depend on the dynamics of solvation, the general theoretical prediction is for $k_{ET} \propto \langle\tau_{obs}\rangle^{-1}$. A number of factors, such as the partial adiabaticity of the reaction, the barrier shape, and involvement of inner shell contributions, could, however, cause departure from this simple prediction.

Experimental evidence for dynamical solvent effects on ET has come from several sources. In early electrochemical studies of the heterogeneous oxidation of phenothiazine and 1,4-phenylenediamine, Opallo *et al.* (*44*) noted a correlation between the k_{ET} and the longitudinal relaxation time of the solvents studied. For both compounds there was a distinct difference between the k_{ET}-τ_L correlations observed in hydrogen bonding versus non–hydrogen bonding solvents. In another early study, McGuire and McLendon (*45*) measured the ET quenching of ruthenium compounds by methyl viologen in glassy glycerol matrices. Temperature-dependent quenching data were interpreted in terms of ET rates that varied with the solvent longitudinal relaxation time as $k_{ET} \propto \tau_L{}^{-\beta}$ with $\beta \sim 0.6$. Rips and Jortner (*46*) later quantitatively explained this fractional dependence on τ_L within the context of their theory of adiabatic ET and the non-Debye dielectric response of glycerol. In both of these cases there does seem to be a close relation between k_{et} and τ_L.

A number of workers have also observed a simple correlation between the rates of photoinduced intramolecular ET and solvation times. Kosower and co-workers (*47*) and Su and Simon (*48*) have observed that $k_{ET} \sim \tau_L{}^{-1} \sim \langle\tau_{obs}\rangle^{-1}$ for a variety of so-called "twisted intramolecular charge transfer" (TICT) reactions in alcohol solvents. Barbara and co-workers (*49*) have observed analogous behavior for bianthryl in polar aprotic solvents, except that in this case $k_{ET} \sim \langle\tau_{obs}\rangle^{-1}$ but $\langle\tau_{obs}\rangle^{-1} < \tau_L{}^{-1}$. Michele-Beyerle and co-workers (*50*) compared the temperature dependence of TICT formation of two model compounds in the solvents propionitrile and propylene glycol. They observed that the relative ET rates in these two solvents behaved as would be expected based on the adiabatic-nonadiabatic theory of Rips and Jortner *(39)*. They were able to quantitatively model the observed temperature dependence by assuming that propionitrile and propylene glycol corresponded, respectively, to the theoretical nonadiabatic and solvent-controlled adiabatic regimes. Not all of the data on TICT processes point to a simple relation between k_{ET} and solvent dynamics. The careful study of the TICT dynamics of dimethylaminobenzonitrile (DMABN) in alcohol solvents performed by Su and Simon *(51)* provides a good counterexample. These authors observed ET rates in DMABN that appeared to be correlated with, but much faster than, $\langle\tau_{\mathrm{obs}}\rangle^{-1}$. Su and Simon interpreted this behavior as indicating involvement of intramolecular vibrational dynamics within the framework of the Sumi-Marcus *(38)* theory. It is worth pointing out with respect to the above studies that in some cases attainment of the TICT state requires large-amplitude motion of the solute. This motion may involve (viscous) aspects of solvent-reaction coupling of a sort not considered in present theories.

Some of the most thorough studies of dynamical solvent effects on ET are the intermolecular electron-exchange measurements of Weaver and co-workers *(52)*. These researchers have measured self-exchange rates for couples such as $\mathrm{Co[cp]_2}^0/\mathrm{Co[cp]_2}^+$ (cp is cyclopentiadienyl) using both electrode half-reaction measurements as well as nuclear magnetic resonance (NMR) linewidth measurements of the homogeneous reactions. In polar aprotic solvents, the prefactors A_{ET} (see Eq. 1) of the electron-exchange rates were observed to correlate reasonably well with $\tau_{\mathrm{L}}{}^{-1}$ as a function of solvent. These authors are careful to point out that, in studies performed in different solvents, it is important to account for any solvent-dependent changes in the free-energy barrier $\Delta G^{\ddagger}$ before looking for dynamical solvent effects. As discussed in the introduction, dynamical effects manifest themselves in the prefactor A and can be confused or obscured by equilibrium solvation effects if changes in $\Delta G^{\ddagger}$ are ignored (as has indeed been the case with many other studies). Weaver and co-workers *(52)* also noted that there was some deviation between the effective solvation time scale inferred from the ET rates (assuming $A_{\mathrm{ET}} \propto \tau_{\mathrm{eff}}{}^{-1}$) and the solvent longitudinal relaxation times. Curiously, the deviation seems to correlate with solvent dielectric constant but with the opposite dependence exhibited by Fig. 2 *(53)*. They also observed that k_{ET} was much greater in alcohols than would be expected based on τ_{L} (or $\langle\tau_{\mathrm{obs}}\rangle$). Using the frequency-dependent friction approach of Hynes *(37)*, McManis and Weaver *(54)* found that inclusion of a relatively small amplitude rapid component in the dielectric response leads to a large enhancement in the frequency factor in excess of that expected for a single Debye response. The effect is particularly marked in alcohol solvents and accounts for a substantial fraction of the enhanced rates observed in these solvents. It is clear that great care must be exercised in relating the dielectric response of a solvent to the frequency factor for an electron-transfer reaction.

Conclusions

Research into the relation between dynamical aspects of polar solvation and the influence that a solvent exerts on a reaction has been vigorous over the last few years. Understanding this connection first requires a knowledge of the dynamics of the solvation process itself. Considerable progress on this part of the problem has been made. Solvation times have been measured with several probe solutes in a wide variety of solvents. One clear result of these measurements is that naïve theoretical treatments, which neglect molecular aspects of solvation, provide a poor description of the dynamics. Simple semimolecular models, such as the dynamical MSA model, have been developed that are able to account for many of the shortcomings of purely continuum solvent descriptions. However, computer simulations have shown that such improved models are still far from providing a true picture of dynamical solvation. Water simulations point out that details of the solute-solvent interaction in the first solvation shell largely control the dynamics. A similar situation is expected for less structured solvents as well. It is not obvious how to begin to model such first solvation shell dynamics, and additional computer simulations of different model solvents should help guide further theoretical development in this area.

The theoretical connection between solvent dynamics and ET reaction rates has been firmly established. Theories developed thus far have relied on continuum descriptions of the solvent. Because such descriptions provide poor representations of the true solvent dynamics, further theoretical development of ET models, including a molecular solvent description, are desirable. However, further experimental work aimed at verifying the theoretical predictions already available is probably a more pressing concern. Although unambiguous evidence for dynamical solvent involvement in ET reactions is still rather limited, a number of groups are actively pursuing this goal, and we expect that the picture will change rapidly over the next few years. Especially valuable will be experiments on rigid intramolecular ET systems, since such experiments will provide the most direct comparison to theory. Finally, we note that computer simulations of ET and related processes should also be of great value in understanding dynamical solvent involvement. Although no full dynamical simulations of ET reactions are yet available, the simulations of Hynes, Wilson, and co-workers *(55)* on $\mathrm{S_N2}$ reactions in water highlight the potential of such approaches.

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Research Articles

The DNA Binding Domain of the Rat Liver Nuclear Protein C/EBP Is Bipartite

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C/EBP is a rat liver nuclear protein capable of sequence-specific interaction with DNA. The DNA sequences to which C/EBP binds in vitro have been implicated in the control of messenger RNA synthesis. It has therefore been predicted that C/EBP will play a role in regulating gene expression in mammalian cells. The region of the C/EBP polypeptide required for direct interaction with DNA has been identified and shown to bear amino acid sequence relatedness with the product of the *myc*, *fos*, and *jun* proto-oncogenes. The arrangement of these related amino acid sequences led to the prediction of a new structural motif, termed the "leucine zipper," that plays a role in facilitating sequence-specific interaction between protein and DNA. Experimental tests now provide support for the leucine zipper hypothesis.

A FUNDAMENTAL QUESTION IN THE STUDY OF GENE REGULATION has been how regulatory proteins bind DNA selectively. Given the relatively uniform structure of double helical DNA, how do regulatory proteins achieve the binding specificity necessary to execute precise decisions? The simple answer is that regulatory proteins detect differences in the nucleotide sequence of DNA. Whether by establishing a series of direct atomic contacts with a sequence of base pairs, or by detecting subtle, nucleotide sequence–induced deformity in DNA, a regulatory protein is somehow able to lock onto its cognate sites on DNA with unusual avidity.

Recent x-ray crystallographic studies on a related class of repressor proteins from bacteria have begun to provide an account of the molecular forces that mediate sequence-specific interaction between protein and DNA (*1*). These related bacterial proteins adopt, within their respective DNA binding domains, similar three-dimensional structures. The common structural motif consists of two α helices bridged by a sharp β turn (helix-turn-helix). One of the two α helices is oriented in a manner that allows its close apposition to the major groove of DNA. The distinctive binding specificity inherent to different repressors is established by small differences in the shape or projection of the helix-turn-helix motif, by variations in the amino acid side chains that project from it, and by a limited number of additional interactions donated by amino acid residues outside of the helix-turn-helix motif.

The basic principles emerging from studies on bacterial proteins have illuminated the problem of DNA binding selectivity in eukaryotic cells. A structure similar to the helix-turn-helix motif has been hypothesized to form in a class of eukaryotic regulatory proteins that share a highly conserved amino acid sequence termed the homeobox (*2*). Homeobox proteins have now been shown to be capable of sequence-specific interaction with DNA (*3*), and to be dependent on the integrity of the homeobox for this interaction (*4*).

Owing to the widespread occurrence of the helix-turn-helix motif, one might have anticipated that it would constitute the sole three-dimensional structure used to interface protein with DNA—perhaps comparable to the ubiquitous use of immunoglobulins for antigen

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