FEATURE ARTICLE

The Effect of Solvent Density Inhomogeneities on Solute Dynamics in Supercritical Fluids: A Theoretical Perspective

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The solvating properties of supercritical fluids (SCF) in the compressible region of the phase diagram may be varied dramatically with modest changes in temperature and pressure, making these solvents a promising reaction medium for chemical syntheses. However, it is in just this compressible regime that SCFs exhibit unusual behaviors, such as solvent and solute "clustering," which complicate the prediction of SCF solvent effects on solute dynamics and reaction. Herein we describe the current understanding of solvent "clustering," both in pure SCFs and in SCF solutions, and we discuss the effect that these *average* solvent density inhomogeneities may have on solvation and on activated solute reactions, as well as the methods by which these effects may be calculated. Additionally, dynamic solute processes may be sensitive to fluctuations of the solvent environment away from its inhomogeneous average, especially if the solvent fluctuations are slow. We thus present a method for examining the distribution of solvent environments experienced by solute molecules, and show that this distribution is indeed both slowly relaxing and broad, spanning a range of behaviors from vapor-like to solid-like. Finally, we point out promising new directions and outstanding questions in the area of solute dynamics in compressible SCFs.

I. Introduction

Supercritical fluids (SCFs) are a promising class of solvents for use in the development of environmentally benign chemical syntheses.[1−8] These solvents have already found many uses in the food and fragrance industries, where, in particular, super-critical (SC) CO_2 is used for numerous separation processes, including coffee decaffeination.[2,9−12] Over the past decade there has been a growing interest in using SCFs to promote reaction processes, stimulated in part by the observation of extremely high oxidation efficiencies for the destruction of hazardous organic compounds in SC water.[1,3] Subsequent investigations have demonstrated that chemistry in SCFs frequently yields unexpected reaction products, mechanisms, and rates.[1,6,7,13−16] And, while there exists a wealth of potential applications of SCF chemistry, realization of this potential is severely hindered by our inability to predict reactivity in SCFs. This failure reflects the fact that our current theories of solvation and its effect on chemical reaction dynamics do not extrapolate well to this solvent regime.[4,7,16−21] Herein we discuss some recent advances in our understanding of SCFs and how they may affect solute reaction.

Solvents may affect industrial reaction processes through their effect on solubilities, transport properties, and phase separations, in addition to their effect on the rates of competing elementary processes. While the focus of this work will be restricted to understanding the dynamics of elementary reactions in SCFs, it is important to keep in mind that the effect of SCF solvents on other factors may differ substantially from that expected for non-SCF solvents, and the reader should consult refs 1, 4, 5, and 9 for further information.

An SCF is defined as a fluid at a temperature (T) greater than its critical temperature (T_c),[22] such that increases in pressure can be used to change the fluid's density continuously, from gas-like to liquid-like values. The first source of unusual reactivity in SCFs is their elevated temperatures, which change the relative rates of competing reaction steps exponentially, according to the Arrhenius expression

$$\frac{k_1}{k_2} \propto \exp[(\Delta G_2^{\ddagger} - \Delta G_1^{\ddagger})/RT] \tag{1}$$

Here k_1/k_2 is the ratio of the rate constants for the competing steps, which have activation energy barriers $\Delta G_1^{\ddagger}$ and $\Delta G_2^{\ddagger}$, respectively, and R is the ideal gas constant. This effect is particularly dramatic in SC water, which has a critical temperature of 374 °C. Thus, if the respective energy barriers of two processes differ by 1 kcal/mol, their rates at room temperature will differ by an order of magnitude; yet, at supercritical temperatures, their rates will differ by only a factor of 3 (or less, as the temperature is raised further above T_c).

A second, more exciting source of the unexpected reactivity observed in SCFs is the tunability of SCF solvent densities with pressure, as well as the concomitant accessibility of unexplored intermediate-density states. Many of a fluid's solvating properties are strongly density dependent, and thus the properties of intermediate density SCFs will often differ substantially from those of the corresponding liquid and vapor states. Of particular importance to solute reaction are a solvent's dielectric properties and its viscosity, both of which are sensitive to density. The ability to use pressure to select particular intermediate densities
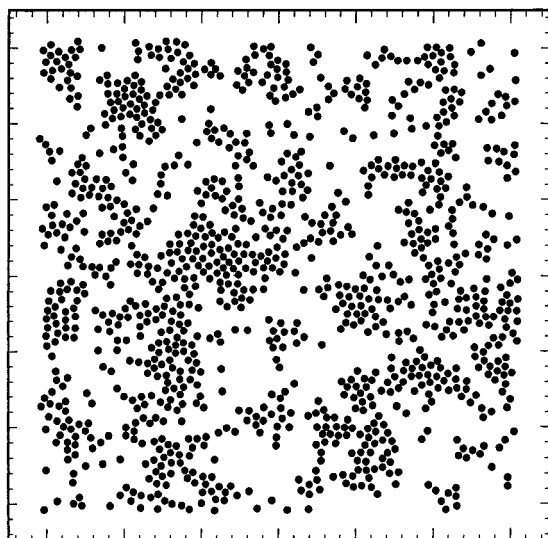
Figure 1. Configurational snapshot of a pure two-dimensional Lennard-Jones SCF at $T_r = 1.17$ and $\rho_r = 0.86$.

enables one to select the fluid's solvating properties. As an example, consider the dielectric properties of SC water at a temperature ($T = 380$ °C) slightly above its critical temperature, $T_c = 374$ °C. Here, a continuous variation in pressure from 21 to 27 MPa causes a smooth variation in density from 0.14 to 0.50 g cm^{-3} and, consequently, a continuous variation in the dielectric constant from a nonpolar value of $\epsilon = 2$ to a polar value of $\epsilon = 10$.[23] This thermodynamic tunability of solvent properties suggests that it may be possible to conduct a multistep synthesis in one solvent by using a series of different thermodynamic conditions, or to replace organic solvents in such syntheses with environmentally benign SCFs, such as SC water or carbon dioxide. In fact, a number of such SCF-replacement synthesis have already been developed.[1,13,24−26]

The theory of critical phenomena[27,28] tells us that, as the critical point of a fluid is approached ($T \rightarrow T_c$ from above, along the scaling axis[29]), the isothermal compressibility diverges (*i.e.*, it becomes infinite). Since this divergence occurs smoothly, there must exist a region of the phase diagram with $T > T_c$ for which the compressibility κ is large, by which we mean that $\kappa > \kappa^0$, the compressibility of an ideal gas. As it turns out, this region of large κ, which we shall call the "compressible regime," extends well beyond the near-critical region of the phase diagram in which all fluids behave universally and the theories of critical phenomena apply. It is just this compressible regime which is of experimental interest, because it is here that large changes in solvent density may be achieved and that intermediate density solvent states, within which novel reactivity is expected, may be found. However, SCF solvents exhibit anomalous behaviors under just these same conditions, because, as will be discussed below, these anomalous behaviors are fundamentally and inexorably connected with the large compressibilities of these solvents.

Macroscopically, a large compressibility means that there is very little cost associated with increases in solvent density. From a molecular point of view, this low cost is a result of a near balance between the entropic loss and energetic gain of "condensing" dispersed molecules into regions of higher-than-bulk density. This low cost implies that large fluctuations in local solvent densities may occur. As shown in Figure 1 for a two-dimensional SC Lennard-Jones fluid, such fluctuations in the pure solvent cause regions of high and low density, the range of which, ξ, becomes macroscopic as the critical point is

approached[27,30] and two phases are formed. In the compressible regime, where the range of the high- and low-density regions are of mesoscopic length, the microscopic environment around any given solvent molecule at a particular instant of time will depend upon whether that molecule is residing in a high- or low-density region.[31] Similarly, a solute, even one which does not perturb the solvent structure, will likely feel a solvent microenvironment which differs from the macroscopic average, or bulk, solvent environment. In such compressible solvents, however, the solute molecules may also substantially alter the solvent density in their vicinity.[7,32−57]

There are two types of experimental measurements on dilute SCF solutions which have suggested that solutes may greatly alter the average density distribution of the surrounding solvent. The first measurements of this ilk in SCFs were of solute partial molar volumes, $\bar{v}_2^\infty$, which were found to be extremely large and negative.[56,58−61] Initially, these results were thought to mean that there was some sort of solvent density collapse, involving hundreds of solvent molecules, around the solute. However, recent work has shown that this interpretation is incorrect and requiring of considerable refinement,[62] as discussed below. Subsequent to the partial molar volume measurements, spectroscopic shift measurements (*i.e.,* measurement of the spectrum of a probe molecule whose spectral lines shift in response to the properties of the surrounding solvent) were used to characterize the local SCF solvent environments.[32,43,45−48,52,63,64] The local solvent properties were found to be those that would have been expected for a solvent density greater than the actual bulk density, again implying the existence of a high-solvent-density region around the solute. Additional investigations have shown that some solutes yield instead large *positive* partial molar volumes,[57] suggesting depleted solvent density in the region around each solute, and computer simulations of such solutes have predicted lower-than-bulk-density surrounding local solvent environments.[36,37,53,65] In the following discussion we will focus on the more common phenomenon of enhanced solvent densities, rather than on this less common phenomenon of depleted solvent densities.

While it is tempting to substitute the word "cluster" for the awkward construction "enhanced solvent density," the terminology "clustering" has been the source of much confusion and controversy.[48,66,67] This is largely because the partial molar volume results do not imply the existence of *stable* physical clusters involving hundreds of solvent molecules (see below). In contrast, the spectral shift results, which probe only the "local" solvent environment, are much more readily interpreted in terms of a physical cluster picture (although this picture may be suspect even for this case). It is now understood that in the compressible regime the microscopic origins of the average density enhancements sampled in the two measurements are different, although related.[39,43,48,68]

The anomalously large partial molar volumes observed in the compressible regime arise only indirectly from the solute−solvent interactions. Instead they reflect correlations in the solvent density fluctuations (*i.e.*, in the density enhancements) out to lengths of order ξ from the solute.[39,40,54,59] Such correlations, however, mean only that there is an enhancement in the *ensemble average* of the surrounding solvent density and do not imply a static density enhancement. Note also that these density correlations are the same ones as give rise to regions of high and low density in the pure solvent. The anomalously large partial molar volumes reflect the divergence of the correlation length of these fluctuations, ξ, as the critical point is approached and is thus truly a critical phenomenon. We refer

to this effect as an "indirect" effect because of its indirect dependence on the solute−solvent interactions.

In contrast, the local solvent density enhancements around solutes observed spectroscopically, which we refer to as "direct" effects, arise primarily from direct solute−solvent correlations,[39,48] which to leading order, are determined by the solute−solvent potential interactions.[30] While these effects are affected by the proximity of the solvent's critical point, they are nondivergent as the critical point is approached and are thus not representative of critical phenomena in the same sense that the indirect effects are.[28,30] In addition, these direct effects are the primary determinant of the local microenvironment experienced by solutes in a dilute SCF. And, since it is the solute's local microenvironment, rather than its extended surroundings, which determines solvation,[39,48,69−71] the direct density enhancement effects can strongly influence this behavior. This is again in contrast with the indirect effects, which, because they primarily control the *range* of solvent density enhancements around a solute as the critical point is approached,[72] will not have much of an effect on solvation.

While the distinction between direct and indirect solvent density enhancements has resolved much of the controversy surrounding solvent−solute density inhomogeneities, there are still gaps in our microscopic understanding of this phenomena. For example, we really do not know how valid the physical cluster picture is for direct density enhancements. Are these enhancements best thought of as static clusters or as dynamically fluctuating entities? And, given that the solvent density around a solute is, *on average*, enhanced, what would be the distribution of observed solvent densities around this average value? Also, we don't know how these behaviors depend upon thermodynamic condition or the details of the solute and solvent molecular interaction potentials.

In addition to the density inhomogeneities in the pure solvent, and the solute-induced solvent density inhomogeneities just discussed, recent work has demonstrated that inhomogeneities in the distribution of solute molecules also occur, even in relatively dilute SCF solutions. Presently, not much is known about these inhomogeneities beyond the fact that theoretical calculations predict them[38,73−80] and experiments detect them.[68,75,76,81−86] Discussions about how solute and solvent density inhomogeneities are interrelated are largely speculative, and pressure and temperature studies of these effects are limited. The issue of solute density inhomogeneities, however, is outside the scope of this article, and the interested reader is referred to the above references for more information.

The ways in which solvent density inhomogeneities affect solute reaction and other dynamic solute processes are only partially understood. Both experimental and theoretical studies of solute activated barrier reactions suggest that direct solvent density enhancement effects can alter the relative solvation energies of the reactant and activated complexes, thus altering the barrier height and the reaction rate.[7,17,18,33,34,42,63,87,88] Very little is known, however, about how solvent density inhomogeneities affect other dynamic processes which may be important for reaction, such as solute rotational reorientation[49,50] and diffusion,[16,89−93] solute−solvent energy transfer[20,94−96] and solvent reorganizational response to solute changes.[71] For such processes, the fluctuations in the solvent density away from the average inhomogeneous distribution[31,97] and the time scale of such fluctuations,[31,53,89] both of which we know little about, could be determining factors. Here again it may be helpful to separate out the behavior and effects of directly and indirectly correlated density fluctuations. For example, it has been suggested that indirect solvent−solvent density fluctuations may play a role in solute vibrational relaxation.[20]

Another interesting problem that will not be addressed in this article is whether indirect solvent density inhomogeneities affect diffusion controlled reactions. We speculate that, since these inhomogeneities appear in the pure solvent as domains of high and low density,[31] they will lead to unusual solute diffusion[89,98] and alter diffusion controlled reaction rates. Yet, only one[16] of the handful of studies of such reactions in SCFs uncovered any anomalous behavior.[90−93] It is unknown whether this is because of (1) the state points considered in these studies and their proximity to the critical point (*e.g.*, generally only densities higher than the critical value were considered); (2) the types of solutes considered; or (3) whether details of the density inhomogeneities, such as the time scale of their fluctuations, mitigate the effect of these inhomogeneities on solute diffusion.

The present article will focus on the nature of solvent density inhomogeneities in SCFs, how they may be characterized and understood, and how they may affect dynamic solute processes, particularly solute reaction. In section 2 we consider the average solvent density inhomogeneities and their effects, while in section 3 we turn to the distribution of solvent densities around the average inhomogeneity. Since more is known about the average solvent density inhomogeneities than about their fluctuations, section 2 contains a background on the nature of these average inhomogeneities and the effects they have on static solute properties, in addition to describing what is known about the effect of these inhomogeneities on activated barrier reactions. In contrast, in section 3 we present a new method for characterizing the distribution of solvent inhomogeneities in pure and dilute SCF solutions. This method, which goes beyond that which we presented in ref 31, enables us to examine both the structure and dynamics of these distributed solvent environments. A summary section follows.

II. Average Solvent Density Inhomogeneities

The average solvent density enhancement around solutes in dilute SCF solutions can be described by fluctuation theory. Further refinement of the theory then enables the formal separation of the direct and indirect density enhancements, such that the contribution of each of these two phenomena toward various thermodynamic properties may be determined. In section II.A.1 we describe the application of fluctuation theory[54,59,63,99] to dilute SCF solutions, summarizing Debenedetti's 1987 treatment,[54] and show how this formalism leads naturally to a classification of solutes according to the "overall" density-fluctuation-response they induce in the solvent.[40,100] Chialvo and Cummings' refinement of this theory to separate out the direct and indirect components of these fluctuations is then presented in section II.A.2.[39] In section II.B, we discuss the effect of such average density inhomogeneities on static solute properties, emphasizing the separate contributions of the direct and indirect density enhancements (section II.B.1). We also discuss the external pressure (bulk density) dependence of these density enhancements effects (section II.B.2) and describe the computational methods available for determining them (section II.B.3). Then, in section II.C, we describe what is known about how SCF solvents may affect activated barrier reactions, highlighting the unusual behaviors which arise as a result of direct density inhomogeneity effects.

A. Nature of the Average Density Inhomogeneities. *1. Fluctuation Theory.* The formal theory of density fluctuations in fluids is couched in terms of pair correlation functions. The radially averaged pair correlation function for atom-type *i* around

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atom-type j, $g_{ij}(r)$, is called the radial distribution function.[30,101] This function gives the conditional probability that, given an atom of type j located at a particular position, there will be an atom of type i located a distance r away from this position. The normalization used for this probability distribution is that distribution which would result for completely random, uncorrelated particles, which is just the bulk density of component i, ρ_i. Hence, as r becomes large and the positions of particles i and j become uncorrelated, $g_{ij}(r) \rightarrow 1$. Indeed, as r gets large, the envelope of the function $[g_{ij}(r) - 1]$ falls off exponentially,[102,103] (*i.e.*,

$$g_{ij}(r) - 1 \sim \frac{1}{r} \exp(-r/\xi) \tag{2}$$

where the decay constant ξ gives the range of the ij correlations; ξ is called the correlation length[28,30]).

The average excess number of atoms of type i found around an atom of type j, as compared to the number that would be found in an uncorrelated (random) system, can be determined from the radial distribution function $g_{ij}(r)$ (in the grand canonical ensemble) as[30]

$$N_{ij}^{ex} = \rho_i G_{ij} = \rho_i \int_0^\infty [g_{ij}(r) - 1] \, d\mathbf{r} \tag{3}$$

Note that the correlation function integral G_{ij} is the zero frequency Laplace transform of $[g_{ij}(r) - 1]$. The average excess number $\rho_i G_{ij}$ can also be expressed in terms of correlated density, or number, fluctuations. For a two-component system, one finds[30,54]

$$\rho_1 G_{11} = \frac{\langle (\delta N_1)^2 \rangle}{\langle N_1 \rangle} - 1 \tag{4}$$

(where the -1 arises because δN_1 includes the central particle, whereas the excess number $\rho_1 G_{11}$ does not, eq 3), and

$$\rho_1 G_{12} = \frac{\langle \delta N_1 \delta N_2 \rangle}{\langle N_2 \rangle} \tag{5}$$

where $\delta N_i = N_i(t) - \langle N_i \rangle$ is the fluctuation, at time t, in the number of particles of type i ($N_i(t)$) away from the average number ($\langle N_i \rangle$) in a fixed volume, open system. The excess number $\rho_i G_{ij}$ (or lack, if $\rho_i G_{ij} < 0$) may be loosely interpreted as a density enhancement (depletion) phenomenon; however, this excess (lack) represents only a density correlation *on average*, and does not tell us whether or not this excess (lack) undergoes large fluctuations about its average value over time. Note also that, when these density fluctuations away from the bulk density are correlated over a long range (*i.e.*, $\xi \sim$ large), the excess number $\rho_i G_{ij}$ will be large, as can be seen from eqs 2 and 3.

The partial molar volume of an infinitely dilute solution $\bar{v}_2^\infty$, where component 2 refers to the solute and 1 will refer to the solvent, can be written in terms of these excess numbers as follows. At infinite dilution, $\rho \bar{v}_2^\infty$, where we have dropped the subscript 1 on the bulk solvent density, gives the change in the average excess number of solvent molecules $\langle \delta N_1 \rangle$ upon addition of a solute molecule (per mole of added solute molecules). And, $\rho \bar{v}_2^\infty$ can be decomposed as the change in N_1 upon addition of a *solvent* particle (*i.e.* + 1), plus a correction for the difference between the average excess number of solvent molecules found around a central solvent molecule, ρG_{11}, and this excess when the central molecule has been converted to a solute molecule,

ρG_{12}. Hence,[39,54,59,63,104]

$$\rho \bar{v}_2^\infty = 1 + \rho G_{11} - \rho G_{12} \tag{6}$$

Note that if one defines a volume V_G beyond which the contribution to G_{ij} is zero for all ij, then the excess density within this volume, upon insertion of a solute molecule, is $\rho \bar{v}_2^\infty V_G^{-1}$, and the excess density relative to the bulk value is $\bar{v}_2^\infty V_G^{-1}$. Since V_G is a constant, $\bar{v}_2^\infty$ carries the bulk-density dependence of this excess solvent density found around a solute. Returning to the main argument, we substitute eqs 4 and 5 into eq 6 to yield an expression for the partial molar volume $\rho \bar{v}_2^\infty$ in terms of density fluctuation correlations:[54]

$$\rho \bar{v}_2^\infty = \frac{\langle (\delta N_1)^2 \rangle}{\langle N_1 \rangle} - \frac{\langle \delta N_1 \delta N_2 \rangle}{\langle N_2 \rangle} \tag{7}$$

This density fluctuation expression for the partial molar volume leads naturally to a classification of solute behaviors in terms of the solute−solvent and solvent−solvent density-fluctuation correlations. Debenedetti and coworkers identified 3 solute behaviors: repulsive, weakly attractive, and attractive, as follows.[40,100]

(1) Repulsive solutes are those for which the repulsive part of the solute−solvent potential dominates the solute−solvent interactions. (Note that the dominant behavior will be thermodynamic condition dependent, ref 40.) In this case, the solute and solvent molecules repel each other and, consequently, their fluctuations will be anticorrelated (*i.e.*, a decrease in the number of solvent molecules will tend to occur when there is an increase in the number of solute molecules). Thus $\langle \delta N_1 \delta N_2 \rangle < 0$, and by eq 5 the correlation integral $G_{12} < 0$, indicating that the *average* solvent density around a solute is less than the bulk density. Thus, addition of solute increases the volume of the solution, which is confirmed by substitution of $G_{12} < 0$ into eq 6, to give $\rho \bar{v}_2^\infty > 0$.

(2) Weakly attractive solutes are those for which the solute−solvent potential interaction is dominantly attractive but are less so than the solvent−solvent potential interaction. The attractive interaction assures that solute and solvent density fluctuations will have a positive correlation (*i.e.*, that $\langle \delta N_1 \delta N_2 \rangle > 0$ and therefore that $G_{12} > 0$), and the *average* solvent density around such a solute will be greater than the bulk solvent density. But, because the solute−solvent interaction is less strong than the solvent−solvent interaction, the solvent−solute number density correlation $\langle \delta N_1 \delta N_2 \rangle / \langle N_2 \rangle$ is less strong than the solvent−solvent correlation $\langle (\delta N_1)^2 \rangle / \langle N_1 \rangle$ and, by eqs 4 and 5, we find $\rho G_{12} < (\rho G_{11} + 1)$. From eq 6, then, we find $\rho \bar{v}_2^\infty > 0$ and the addition of solute still increases the volume of the solution. One might wonder how it is possible for the volume of the solution to *increase* upon addition of a solute which is surrounded, on average, by a solvent number density which is *greater* than the bulk solvent density. To understand this behavior, remember that what is relevant to $\rho \bar{v}_2^\infty$ is not the average excess number of solvent molecules around a solute molecule, but rather it is the difference between the average excess number of solvent molecules around a solute molecule and the average excess number around a solvent molecule. From Figure 1 (and also eq 2) it can be seen that, on average, the solvent density around a solvent molecule will be greater than the bulk solvent density, a result arising because solvent molecules are more likely to reside in the high-solvent-density regions. Thus, the average excess number of solvent molecules around any given solvent molecule will be $(\rho G_{11} + 1) > 0$. While this behavior is simply

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a consequence of positive self-correlation, $\langle(\delta N_1)^2\rangle > 0$, it can produce a very large effect in an SCF in its compressible regime where ξ is large. So, for a weakly attractive solute, the average excess number of solvent molecules around the solute is not as large as the average excess number around a solvent molecule, and thus, upon addition of solute, the average density enhancement decreases and the fluid expands.

(3) Lastly, attractive behavior results when the dominant solvent−solute interaction is more attractive than the solvent−solvent interaction, so that the solute−solvent correlations exceed the solvent−solvent correlations. Now $G_{12} > 0$ *and* $\rho G_{12} > (\rho G_{11} + 1)$ (*i.e.*, the solute−induced density enhancement exceeds that induced by a solvent molecule, and, as seen from eq 6, $\rho \bar{v}_2^\infty > 0$). In this case addition of solute decreases the volume of the solution.

For a single component, open system, there is a direct relationship between the average excess number ρG_{11} and the fluid's compressibility, *i.e.*[30]

$$\tilde{\kappa} = 1 + \rho G_{11} \tag{8}$$

where $\tilde{\kappa} = \kappa/\kappa^0$ is the ratio of the fluid's compressibility κ to that for an ideal gas, $(\kappa^0 = \rho k_b T)^{-1}$. As the fluid approaches its critical point from above, $T \to T_c^+$, the correlation length becomes large, and the asymptotic form of the radial distribution function (eq 2) may be used in the correlation function integral G_{11} (eq 3), such that[102]

$$\tilde{\kappa} \sim 1 + \rho \int_0^\infty \frac{e^{-r/\xi}}{r} \, dr \tag{9}$$

which illustrates the direct relationship between the solvent's reduced compressibility $\tilde{\kappa}$ and the correlation length of the density fluctuations ξ. From this relation one sees that large reduced compressibilities reflect the correlation of density fluctuations over long range, and the experimentally observed divergence of $\tilde{\kappa}$ as $T \to T_c^+$ reflects a concomitant divergence of ξ. Note, however, that the relationship between $\tilde{\kappa}$ and ξ is nonlinear and that, in fact, a small wave vector expansion of the Fourier transform of $g_{11}(r)$, valid as $T \to T_c^+$, yields $\tilde{\kappa} \propto \xi^2$.[105] Thus, there is a region of the phase diagram above T_c within which modestly large correlation lengths yield very large compressibilities, and this region is of great interest in SCF chemistry.

In an infinitely dilute SCF solution, eq 9 implies that as the critical point of the solvent is approached from above and $\tilde{\kappa}$ diverges, the correlation length of the solvent must become very large, such that G_{11} will diverge as does $\tilde{\kappa}$ (eq 8).[28,30] Similarly, the solute−solvent correlations, and thus the integral G_{12}, will diverge with the same correlation length.[54,59,106,107] Why this is so will be addressed below. What is important here is that, as a result of the divergence of both G_{11} and G_{12}, the change in the excess number of solvent molecules $\rho \bar{v}_2^\infty$ (eq 6), and thus of the partial molar volume of the solute $\bar{v}_2^\infty$, will also diverge as does the solvent's compressibility $\tilde{\kappa}$ (except in the limit that the solute becomes identical to the solvent and $\rho G_{12} = \rho G_{11}$ such that $\rho \bar{v}_2^\infty = 1$).[54,59,106]

2. Direct vs Indirect Density Components. The theory of density fluctuations just presented can be refined to formally separate the direct and indirect components of the average solvent density inhomogeneities (enhancements or depletions) in dilute SCF solutions.[39] This separation is accomplished by making use of the infinite dilution Ornstein−Zernike relation,[30] which describes the total correlation between solvent (1) molecule i and solute (2) molecule u, $g_{12}(r)$, as a sum of the

direct correlation between these two molecules $c_{12}(r_{iu})$ and all possible indirect correlations proceeding via an intermediate solvent molecule k (*i.e.*, $u \to k \to i$). Thus,

$$[g_{12}(r_{iu}) - 1] = c_{12}(r_{iu}) + \rho \int c_{12}(r_{uk})[g_{11}(r_{ki}) - 1] \, d\mathbf{r}_k \tag{10}$$

where r_{iu}, r_{uk}, and r_{ki} are interparticle distances, and the integral runs over all possible positions of the kth intermediate solvent molecule. This equation defines the direct solvent−solute correlation function $c_{12}(r)$, which accounts for both the effect of the solute−solvent intermolecular potential V_{12} (*i.e.*, $\exp(-\beta V_{12}(r))$) and of the local solvent environment on the distribution of solvent molecules around a solute molecule $g_{12}(r)$. Since, to leading order in r as r becomes large, the direct correlation function can be written as $c_{12} \sim -\beta V_{12}[1 + ...]$, the range of the direct correlation function is of the order of the range of the intermolecular potential, which ensures that its integral, $C_{12} = \int c_{12}(r) \, d\mathbf{r}$, will remain finite even as the critical point of the solvent is approached (*i.e.*, $T \to T_c^+$).[28,30,108] The known divergence of the range of the total solvent−solute correlation function $g_{12}(r)$ as the critical point of the solvent is approached[54,59] must then arise from the diverging range of the solvent−solvent density-fluctuation correlations $g_{11}(r)$, which appear in the indirect term on the right-hand side (rhs) of eq 10.

To further understand this second, indirect term in eq 10, we use the fact that the total solvent−solvent correlation function may also be separated into direct and indirect components as[30]

$$[g_{11}(r_{ij}) - 1] = c_{11}(r_{ij}) + \rho \int c_{11}(r_{jk})[g_{11}(r_{ki}) - 1] \, d\mathbf{r}_k \tag{11}$$

Repeated substitution of this equation for g_{11} into itself (on the rhs) yields $[g_{11} - 1]$ as a series of integrals over direct solvent−solvent correlation functions only. Substitution of this expression into eq 10 gives the total solvent−solute correlation function (at infinite dilution) in terms of a 'chain' of direct correlation functions, *i.e.*[30]

$$\tag{12}$$

Here $\square$ and $\bigcirc$ represent solute and solvent molecules u and i, respectively, and filled circles, $\bullet$, represent solvent particles whose positions are integrated over. From such an expansion it becomes clear that all solvent−solute correlations which act over ranges longer than the range of c_{12} (*i.e.*, longer than the range of the solute−solvent interaction potential) arise from chains of solvent−solvent direct correlations c_{11}. This form reflects the fact that any solvent molecule which lies within the range of the solute−solvent interaction potential, and thus has a direct interaction with the solute, may itself be correlated with other solvent molecules far outside of this local range (via chains of other intermediate solvent molecules), thus providing an indirect correlation between the solute and these more distant solvent molecules. It is these chains of solvent−solvent interactions which cause the range of the solvent−solvent density correlations to diverge as $T \to T_c^+$, and it is clear that their presence in eq 12 ensures that the solute−solvent density correlations $g_{12}(r)$ will also diverge.

The Ornstein−Zernike formulation provides a natural division of the average solvent density inhomogeneity around a solute into direct and indirect components. The nondivergent direct, or "local", component is defined by the integral C_{12} and thus

arises from the direct correlation between the solute and solvent molecules residing (roughly) within the range of the solute−solvent interaction potential. Note that this identification defines "local" as the range of this potential, even if this potential is of long range. The indirect component I_{12} is then defined as all those correlations which are not included in C_{12} (*i.e.*, $I_{12} \equiv G_{12} - C_{12}$). Because G_{12} is the integral of $g_{12}(r)$ (eq 3), I_{12} will diverge as does the range of $g_{12}(r)$ when $T \rightarrow T_c^+$.[39]

An explicit expression for this indirect component of the solvent−solute correlations is found from a zero-frequency Laplace transform of the Ornstein−Zernike equation (eq 10) to be

$$I_{12} = \rho C_{12} G_{11} \tag{13}$$

showing that the divergence of the indirect component arises from the divergence of G_{11}, as expected on the basis of eqs 10 and 12. Combining eq 8 with the Laplace transform of eq 11 yields $G_{11} = C_{11}\tilde{\kappa}$, which, when substituted into eq 13, gives

$$I_{12} = \rho C_{12} C_{11} \tilde{\kappa} \tag{14}$$

showing explicitly the divergence of this indirect component with the solvent's reduced compressibility $\tilde{\kappa}$ as $T \rightarrow T_c^+$. Note that the Laplace transform of eq 11 also yields the division of the solvent density inhomogeneity around a solvent molecule into a direct component C_{11} and an indirect component,

$$I_{11} = \rho C_{11}^2 \tilde{\kappa} \tag{15}$$

Finally, note that as one moves away from the solvent's critical point, the correlation length ξ will decrease while the potential interaction range remains the same, such that length scale will cease to be a good identifier of the direct and indirect effects. It is for this reason that we have chosen to use the nomenclature "direct" and "indirect" instead of the more common terminology of "local" and "long range".

B. Effect on Static Properties. *1. Direct vs Indirect Components.* The Ornstein−Zernike separation of the correlation function integrals into direct and indirect components, $G_{\alpha,\alpha'} = C_{\alpha,\alpha'} + I_{\alpha,\alpha'}$, can be used to determine how these two components of the solvent density inhomogeneity affect the thermodynamic properties of the solution. In particular, the solute partial molar volume, eq 6, can be partitioned into direct and indirect components. As shown by Chialvo and Cummings,[39]

$$\bar{v}_2^\infty = \rho^{-1} + C_{11} - C_{12} + I_{11} - I_{12}$$

$$= \{\rho^{-1} + C_{11} - C_{12}\} + \rho\{\tilde{\kappa} C_{11}(C_{11} - C_{12})\}$$

$$\equiv \bar{v}_{2,D}^\infty + \bar{v}_{2,I}^\infty \tag{16}$$

where the second relation follows from eqs 14 and 15. The direct component $\bar{v}_{2,D}^\infty$ is given by the difference between the solvent−solvent and solvent−solute *direct* correlation function integrals. Hence, it accounts for density enhancements (or depletions) around the solute arising from direct correlations of the solute with solvent molecules that fall roughly within the range of the solute−solvent interaction potential (relative to the direct enhancement that would be found around a solvent molecule). And, because $\bar{v}_{2,D}^\infty$ contains only direct correlation function integrals, it will remain finite as the critical point of the solvent is approached ($T \rightarrow T_c^+$).

In contrast to the direct component of the partial molar volume, the indirect component $\bar{v}_{2,I}^\infty$ accounts for density enhancements due to the indirect correlations and thus diverges as does the reduced compressibility $\tilde{\kappa}$, as can be seen from eq 16. Clearly, as $\bar{v}_{2,I}^\infty$ diverges, $\bar{v}_2^\infty \approx \bar{v}_{2,I}^\infty$, and it is the indirect component which is responsible for the extremely large partial molar volumes observed experimentally as the critical point of the solvent is approached. Note, however, that the indirect density enhancement $\bar{v}_{2,I}^\infty$ is proportional to the difference between the direct correlation function integrals around solute and solvent. The dependence of the indirect component of the density enhancement on the direct component arises as follows: The central solute molecule causes a "local" solvent density fluctuation by virtue of its direct correlation with the solvent C_{12}. It is then this local density fluctuation which induces additional, correlated density fluctuations over the range ξ by virtue of the total solvent−solvent correlations. Similarly, a central solvent molecule's directly correlated fluctuations give rise to long range fluctuations. Since the long-range correlations are purely a solvent property, the relative magnitude of the average long-range fluctuations in the two cases is given by the difference in the local, direct fluctuations (*i.e.*, by $(C_{11} - C_{12})$). As a result, the sign of the divergence of $\bar{v}_{2,I}^\infty$ is governed by the direct correlation function integrals, while the divergence itself is controlled by the compressibility $\tilde{\kappa}$.

Chialvo and Cummings considered the contribution of the direct and indirect density fluctuations to a number of other thermodynamic properties of dilute SCF solutions.[39] Of import to the present discussion is their finding that free energies of solvation may be expressed entirely in terms of direct correlation functions[109]—a sensible result, given that only solvent density increases that occur within the range of the solute−solvent interaction potential, which are described primarily by C_{12}, will affect the solute energetics. Note that the accompanying indirect (long-range) density fluctuations (I_{12}) result precisely because there is little to no free energy change associated with the formation of such spatially extensive density fluctuations. Similarly, spectroscopic shift measurements, which rely on a solvation differential between ground and excited states, will be sensitive only to the direct ("local") solvent density enhancements. Finally, note that the quantity, which determines solvation energetics, is the actual average "local" density, given by the bulk density plus the local density enhancements, $\rho + \rho C_{12}$.

2. Pressure Dependence. Because a major goal in SCF chemistry is to understand the pressure, or bulk density, dependence of solvation and reaction, we here examine the bulk-density dependence of the solvent density inhomogeneities around solutes. As was observed by Knutson *et al.*[43] and pointed out by Carlier and Randolph,[48] spectroscopic shift measurements indicate that the largest relative solute-induced density enhancements (ρ_{loc}/ρ) occur at values of the bulk density ρ_{max}, which are substantially below the critical density $\rho_{max} \approx (1/2 \text{ to } 1/3)\rho_c$,[39,43,45,48,70,89] in contrast to partial molar volume results which indicate a maximum average density enhancement at the critical density, $\rho_{max} \approx \rho_c$.[39,54−56,59,60] This discrepancy results because the two measurements sample different components of the density enhancements C_{12} and I_{12}, which have differing bulk-density dependences.[39]

As stated previously, the solute's partial molar volume $\bar{v}_2^\infty$ depends upon both the direct and indirect correlation function integrals (eq 16) and is thus dominated by the indirect

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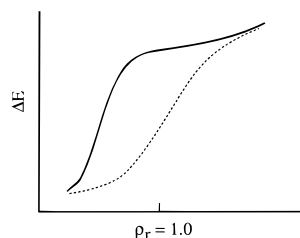*J. Phys. Chem. B, Vol. 102, No. 14, 1998* **2443**

Figure 2. Schematic diagram of the typical bulk-density-dependence observed for solvation energy differences in highly compressible SCFs (solid line) and the behavior expected on the basis of the bulk density (dashed line) for polar solvents.

component, which diverges as does $\tilde{\kappa}$, for temperatures near T_c. As a result, $\bar{v}_2^{\infty}$ will be maximized at $\rho = \rho_c$ where $\tilde{\kappa}$ grows large.[39,54,59]

In contrast, as shown by Chialvo and Cummings,[39] the solute free energy, like $\bar{v}_{2,D}^{\infty}$, reflect only the direct density enhancements. It follows that the spectral shifts, which reflect the relative solvation of different solute states, will also depend only upon the direct density enhancements.[45,48,63] For attractive solutes, the maximum relative "local" density enhancement is achieved at bulk densities below the critical value, where $\tilde{\kappa}$ is less than its maximal value.[39,48] To understand this result, realize first that the final, equilibrium density distribution around the solute will be that which balances the "energetic gain of bringing more solvent molecules into the range of the solute's interaction potential" with the "free energy cost of increasing the local solvent density". Then consider the approach of the local density to this final equilibrium distribution upon introduction of an attractive solute molecule into the solution. If the bulk solvent density is below the critical density, then the initial compression in response to the solute field, which increases the local solvent density, will increase the local compressibility, thus lowering the cost of further compression. Once the local density exceeds the critical density, any further compression will lower the local compressibility, such that additional compression will become less and less favorable. In contrast, if the initial bulk density is already above the critical density, even the initial compression would cause the cost of additional compression to increase. As a result, the degree of compression supported by the solute's interaction potential will be greater when the initial density is below the critical density than when it is at or above the critical density ρ_c. Thus, the maximum relative density enhancement should occur below ρ_c, as is seen experimentally. We note that the situation is different for repulsive solutes; here calculated values of $\bar{v}_{2,D}^{\infty}$ as a function of bulk density show no extremum (except as $\rho \rightarrow 0$), at least for the cases considered to date.[39,110] The limited number of spectroscopic studies conducted on these less usual solutes suggest little unusual bulk density behavior, in accordance with this theoretical prediction.[111]

The density dependence of the direct density enhancement around attractive solutes gives rise to a characteristic density dependence of solvation free energies and spectral shifts.[7,32,45,46,48,52,112] As shown in Figure 2, the ground-to-excited-state energy difference moves from the value expected in a gas-like solvent to that expected in a liquid-like solvent as the bulk density of the solvent is increased. The dashed line interpolating between these two values represents the energetics that would be expected in a polar homogeneous solvent of the same bulk density; the nonlinearity in this case arises from the nonlinear effect of a linearly increasing dielectric constant.[17,71] Thus, for nonpolar solvents a straight line would be expected.[48,52] In contrast, the solid line represents the

characteristic behavior observed at temperatures near the critical temperature, for which direct density enhancement effects are present. This behavior includes a very rapid change in the energy difference at densities below ρ_c, followed by a near-invariance in the region of the critical density ρ_c. The rapid change at $\rho < \rho_c$ results from a rapid build-up of the local solvent density enhancement, which is maximized in this region and causes the solute to feel a more liquid-like solvent environment than the bulk density presents. Once the first few solvation shells have attained liquid-like densities, further bulk density increases have little effect on the local environment, and the solvation energy difference remains fairly invariant in this region near ρ_c. Eventually, beyond ρ_c, the bulk density "catches up" with the local values. At this point, further increases in pressure yield only slow changes in the solvation energy difference as the increasing bulk density compresses the local structure. Note that when the relative energies of two states are involved, it is conceivable that the solvent density enhancements around the two states, which will depend on their respective solute−solvent interaction potentials, could be sufficiently different that their relative energy would take on a value outside the range between the gaseous and liquid values. Such a scenario has not yet been proven, although the experimental results of Jessop *et al.* could be explained in this fashion.[113] Note also that nonlinearities in the dependence of the solute energetics on solvent density enhancements could also affect the shape of the bulk density dependence;[71] however, the characteristic behavior described above appears to be fairly universal.

3. Methods of Computation. Average density inhomogeneities in SCF solutions and their effects on physical properties are generally computed in one of three ways:[19] computer simulation,[114,115] integral equation formulations,[30,38,59,116,117] or compressible electrostatic continuum methods.[33,118−120] Computer simulation, which is perhaps the most widely applied method, can be used to evaluate the total correlation function, $g_{12}(r) - 1$ (or $g_{11}(r) - 1$), which describes the combined effect of both the direct and indirect solvent density enhancements. Theoretically the direct component could then be isolated by using the Ornstein−Zernike equation (eqs 10 and 11) and solving for $c_{ij}(r)$, but this has not been done for SCF solutions. Additionally, simulation can be used to compute solvation energies. The advantage of simulation is that it may be straightforwardly applied to attractive, weakly attractive, and repulsive solutes, as well as to complicated systems. The disadvantages of this method are as follows: First, the correlation length of the solvent is limited by the simulation cell size. In the vicinity of the critical point, this limits the range of validity of the computed correlation functions unless costly simulations on very large systems are performed. Additionally, the presence of long correlation lengths means slow, collective-solvent fluctuations, which may make convergence of equilibrium averages difficult. Thus, simulation is most useful when one is interested in state points that are not too close to the critical point[121] and/or in short-range properties which are not sensitive to the long-range fluctuations. Next, computer simulations make use of simple models of the solvent−solvent interaction potential which generally have their critical points at significantly different state points than does the real fluid they are meant to represent.[122−124] In order to reliably simulate an SCF anywhere near its critical point, one needs to know the critical point of the model potential used, the determination of which is nontrivial. This hurdle has been a primary factor in the absence of realistic simulations (*i.e.*, including the quadru-

pole moment) of the favored experimental solvent, SC CO_2, in its compressible regime, as such critical parameters have only recently been established.[125]

Integral equation techniques yield similar information to computer simulation, but under a different set of approximations, generally referred to as closures.[30] These closures, the description of which is beyond the scope of this article, are effectively approximations to the correlation functions. However, in these methods the correlation length is not restricted, and thus integral equation calculations and computer simulations can be used to provide checks on their mutual validities in the SC regime.[59] Note also that the validity of different closures in near critical SCFs has been examined.[38,59,116,117]

A very different approach is the use of compressible electrostatic continuum solvation models.[33,118−120] These models take the solvent to be a continuous dielectric media characterized by density-dependent compressibility and dielectric-constant functions. The solute is represented by a charge distribution in a cavity, and the position-dependent solvent density distribution $\rho(\mathbf{r})$ is allowed to respond to the solute-induced electric field. Then, the governing electrostatic equation (Poisson's equation) must be solved self-consistently for the electric field and the solvent density distribution. This is because the electric field at each point is affected by the solvent's dielectric-constant distribution, which in turn depends upon the solvent density distribution, which itself depends upon the electric field. The final, normalized density distribution, $\rho(\mathbf{r})/\rho$, is a continuum approximation to the solvent−solute correlation function (*i.e.*, it contains no molecular structure information). The density enhancements predicted by this model result entirely from *direct* interactions between the continuum solvent and the solute's potential field. That is, the fluid density at each point $\mathbf{r}$ responds to the electrostatic interaction with the solute but does *not* respond to the density fluctuation of the solvent at any other point $\mathbf{r}'$ (except in so far as these fluctuations alter the solute induced electric field at $\mathbf{r}$). Thus, this method isolates the direct effect (within the continuum approximation of the model), but provides no information on the indirect effects; consequently, the density profile computed in this model, $\rho(\mathbf{r})$, is most closely equated with the direct correlation function $\rho c_{12}(\mathbf{r})$. Finally, note that in this method the response function for each volume element of the fluid at $\mathbf{r}$ is approximated by the compressibility of a macroscopic volume of fluid at the same density $\rho(\mathbf{r})$. This macroscopic response function (*i.e.*, the compressibility), of course depends on the indirect density fluctuations (see eq 8). Thus, use of this response function means that some aspects of the indirect fluctuation effects are implicitly included in the model.

Within such compressible continuum models, solvation energies in the presence of the average direct density enhancements, ΔG_{CC}, may be evaluated from the final (approximate) equilibrium density distribution. Comparison of ΔG_{CC} with solvation energies computed using a constant bulk density instead (*i.e.*, an incompressible continuum calculation),[126−130] ΔG_{IC}, isolates the density-enhancement-induced component of the free energy, $\Delta G_C = \Delta G_{CC} - \Delta G_{IC}$.

The main advantage of such compressible continuum models is their ease of application and low computational cost. Additionally, the solvent can be characterized by the experimentally determined equation of state and dielectric properties, eliminating the need for model potential functions. And, despite the approximations inherent in continuum models,[17,127,131−133] very good relative solvation energies and solvent density distributions have been obtained with this type of model, when compared to simulation results.[34] Such models suffer from a number of limitations, however. First, they are only applicable to attractive and weakly attractive solutes in dipolar (or polarizable) fluids.[134] Second, these models treat the local density enhancement effects, which are inherently molecular in nature for at least the first few solvation shells, with a continuous density function. Although rapid decreases in the compressibility at high solvent density keep the continuum solvent model from predicting densities which violate molecular excluded volume requirements near the solute, purely molecular effects, such as hydrogen bonding, cannot be accounted for in these models. This is one reason these models more accurately predict relative rather than absolute solvation energetics.[17,34] The other primary reason is that the absolute computed solvation energies are sensitive to the rather arbitrary choice of solute cavity size, as well as to quality of the solute charge distribution.[127,130,132,135−137]

A simplified alternative to the compressible continuum models are incompressible continuum models in which the solute is surrounded by a region of enhanced solvent density, represented by a constant higher-than-bulk-value dielectric constant, outside of which the bulk-density solvent region is represented by the constant bulk-value dielectric constant.[138,139] While these methods are very simple to evaluate, they suffer from the disadvantage that both the size and dielectric constant of the enhanced density solvent region must be known in advance. These methods may become very useful for back-of-the-envelope estimates of solvation in compressible SCFs if a method of estimating these quantities from known empirical parameters is found; initial efforts in this direction appear promising.[140]

C. Effect on Activated Reaction Dynamics. Dynamic processes depend fundamentally upon the fluctuation of some property away from its equilibrium value, and the rates of these processes are controlled by the rate at which the relevant fluctuations decay back to equilibrium. At present, little is known about solvent density fluctuations away from the equilibrium average density distribution in highly compressible SCFs or about how such density fluctuations affect the dynamics of solutes in these fluids. We delay discussion of what we do know about such fluctuations until section III, where we present some new results in this area. For the moment, suffice it to say that our present understanding of the dynamics in these fluids is far from complete, and that, as a result, we do not have the requisite foundation for examining reaction rates in SCFs from such a first principles point of view. (Detailed reaction dynamics could be examined by using computer simulation to follow the relevant solute populations fluctuations directly,[141−145] but this has not yet been done in SCFs).

Given such a bleak state of affairs, how can we say anything about how solvent inhomogeneities affect solute reaction rates? To do so, we must rely on the fact that for chemical reactions in which the reactant must surmount an energy barrier, the rate may be described entirely in terms of equilibrium and quasi-equilibrium quantities,[146−152] such that a detailed description of the dynamic fluctuations is not required. As a result, the possibly inhomogeneous, average solvent density distributions (as opposed to the fluctuations around these averages) can be used to determine the effect of the solvent density inhomogeneities on reaction rates.

The formalism which enables such a quasi-equilibrium description of activated chemical reactions is transition state theory.[146−152] Within this formalism, the rate constant for reaction is given in terms of the difference between the free

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energy of the reactants G_R and the quasi-free energy $G^{\ddagger}$ of the transient intermediate complex known as the transition state. Note that because the transition state is transient rather than stable its free energy is not a true free energy, rather it is the free energy of the complex when the reactive degree of freedom is fixed at its transition state value, hence its designation as a quasi-free energy.[147]

The transition state theory rate constant is given in terms of this standard state, molar free energy difference, $\Delta G^{\ddagger} = G^{\ddagger} - G_R$, as[147,149]

$$k = \kappa_{TST} \frac{k_b T}{h} K_0 e^{-\Delta G^{\ddagger}/RT} \qquad (17)$$

where k_b is Boltzmann's constant, h is Planck's constant, and the factor K_0 is the reactant-to-transition-state reaction quotient evaluated at the standard states for these species and carries the rate constant's units of inverse concentration.[147,149] The transmission coefficient κ_{TST}[149−152] is a correction factor for cases in which transition state theory breaks down. The primary causes of transition state theory breakdown are (i) an incorrect choice of transition state complex, either in location along the reaction path or in the identification of the reactive degree of freedom, which, remember, must be removed from the calculated quasi-free energy, and (ii) cases in which energy transfer into the reactive mode is rate limiting, as may occur, for example, in dense gasses. A great deal of recent work has been devoted to the study of situations in which transition state theory fails and to the methods by which the corrections to transition state theory, κ_{TST}, may be determined. Except for speculations as to the likelihood of transition state theory breakdown in SCFs (see section III.C.2), further discussions of these issues is outside the scope of this article, and the reader is referred to refs 149−152.

For reactions in solution, it is usually assumed that the solute follows the same reaction path as it would if the same reaction were to occur in the gas phase, and that the transition state complex is taken to be located at some point along this path, most frequently at the free energy maximum. Additionally, the solute reaction path is nearly always identified as the reactive degree of freedom,[153] and then κ_{TST} is taken to be one. Note that this set of assumptions, known as the equilibrium solvation approximation, is equivalent to assuming that the solvent rapidly readjusts in response to changes in the solute, such that at all times during the course of the reaction the solvent remains in equilibrium with the reacting solute.[150,151] Within this approximation, the activation energy $\Delta G^{\ddagger}$ can be written as

$$\Delta G^{\ddagger} = (U^{\ddagger} + \Delta G_{solv}^{\ddagger}) - (U^R + \Delta G_{solv}^R) \qquad (18)$$

where the free energy at each location along the solute reaction path is given by the sum of the potential energy,[154] U, of the isolated solute at this location plus the equilibrium solvation free energy of the solute at this location ΔG_{solv}. Hence, the effect of the solvent on the chemical reaction rate constant can, in this approximation, be determined by evaluating the equilibrium solvation energy of each solute configuration along the solute reaction path, locating the transition state, and evaluating eqs 18 and 17 with $\kappa_{TST} = 1$.

In SCF solutions, one wishes to be able to predict the pressure (and bulk density) dependence of chemical reaction rates. As formulated in eq 17 (under the equilibrium solvation approximation, $\kappa_{TST} = 1$), the pressure dependence appears in the free energy term, $K_0 \exp(-\Delta G^{\ddagger}/RT)$, such that[155,156]

$$\frac{\partial \ln k}{\partial P} = -\frac{1}{RT} \frac{\partial \Delta G^{\ddagger}}{\partial P} + \frac{1}{K_0} \frac{\partial K_0}{\partial P}$$

$$= -\frac{\Delta V^{\ddagger}}{RT} + \frac{1}{K_0} \frac{\partial K_0}{\partial P} \qquad (19)$$

When pressure independent units (*e.g.*, mole fractions) are used, $(1/K_0) \partial K_0 / \partial P = 0$, whereas when pressure dependent units such as molarities are used this term gives $-\Delta n \kappa$, where Δn is the $\ddagger$ to R stoichiometric change.[1] The second equality in eq 19, which follows because the thermodynamic derivative of a free energy with respect to pressure gives a volume, defines the activation volume $\Delta V^{\ddagger}$. The conventional interpretation of the activation volume $\Delta V^{\ddagger}$ is that it is an intrinsic solute property (or solute-plus-local solvent property for solution phase reactions), which represents the difference in the effective volumes of the transition state and reactant complexes.[155] To see the relationship between $\Delta V^{\ddagger}$ and pressure, consider the case where the transition state volume is smaller than that of the reactants $(\Delta V^{\ddagger})$. In this case an increase in pressure would shift the assumed equilibrium between the transition state and reactants toward the transition state, increasing the rate as given by eq 19 when $\Delta V^{\ddagger} < 0$. Although there is in principle nothing wrong with the activation volume approach, application of its traditional interpretation to the pressure dependence of reaction rates to SCFs can be misleading (as discussed below),[5,32,33,157,158] and our discussion of these effects will therefore be given in terms of the pressure dependence of the activation barriers, $\Delta G^{\ddagger}(P)$.

The first problem with the traditional interpretation of the activation volume is that it neglects the fact that other solvent properties, such as the dielectric constant, can be extremely pressure sensitive in compressible SCFs. When these properties affect the solvation of the transition state and reactants differently, the activation energy (*i.e.*, the reaction *energetics*) will vary rapidly with pressure, causing large changes in the reaction rate which are *not* representative of an actual volume effect.[17,33,34,42,87,158] In fact, pressure-induced changes in the bulk density, as well as in the local density enhancements (which are generally given *relative* to the bulk density), will contribute to this effect. This type of energetic effect has even been shown to generate a pressure dependence which is of opposite sign to that predicted by equation of state estimates of $\Delta V^{\ddagger}$.[87] A second problem arises because the idea of an activation volume has led numerous investigators to suggest that the large, equilibrium solute partial molar volumes $\bar{v}_2^{\infty}$ observed in SCFs mean that comparably large activation volumes, reflecting a difference in the long range, indirect density enhancement around the transition state and reactants, will be found in these solvents. This idea is conceptually perplexing on two fronts. First, the physical relationship between this expected large activation volume, which would be dominated by long-range, indirect solvent density enhancements, and the activation free energy, which, because it is determined by solvation energies, is controlled by direct solvent density enhancements, is not intuitively obvious. Recently, Chialvo *et al.* have made an important step toward clarifying this relationship by deriving an expression for the activation volume in terms of both the direct components of the transition state and reactants partial molar volumes (*i.e.*, $\bar{v}_{2,D}^{\infty}$) and the compressibility.[159] The second difficulty associated with the idea of such large activation volumes is that the transition state is a transient species, and it seems unlikely that such long-range solvent density fluctuations involving hundreds of solvent molecules are actually formed

during its lifetime (which is typically on the order of femtoseconds).[145] Note that if these large density fluctuations were required for the reaction to occur, then the reaction rate would be controlled by the time scale of these fluctuations rather than by that for solute coordinate motion, leading to a breakdown of the equilibrium solvation approximation and a very small transmission factor, $\kappa_{TST} \ll 1$, reflecting this large reduction of the rate. However, if these fluctuations are not required for the reaction to occur (*e.g.*, because they have little effect on the solvation free energy of the transition state), then their time scale of motion will be irrelevant to the reaction, allowing them to be neglected.

1. Bulk Density Effects. Because the bulk density of an SCF may vary dramatically with pressure, the effects of this density variation on the pressure dependence of the solute activation energy can be quite large and must be taken into account (even if there are no local inhomogeneities). The potential magnitude of these effects was clearly demonstrated by incompressible electrostatic continuum model calculations[126,127] of the anisole hydrolysis reaction in SC water,[17,33] which yielded an expected free energy barrier decrease of $\Delta(\Delta G_{IC}^{\ddagger}) = 16.1$ kcal/mol for a pressure change of 4.1 MPa at 380 °C ($T_r = 1.02$), corresponding to a bulk density change of 0.25 g/cm³, from $\rho_r = 0.8$ to $\rho_r = 1.6$. This change in $\Delta G^{\ddagger}$ would yield a change in the rate constant of 5 orders of magnitude. Incompressible continuum model calculations on the $Cl^- + CH_3Cl$ exchange reaction in SC water at $T = 374$ °C ($T_r = 1.00$) show a similarly large change in barrier height, $\Delta G_{IC}^{\ddagger} = 5$ kcal/mol, from $\Delta G_{IC}^{\ddagger} = 12$ kcal/mol at $\rho_r = 0.5$ to $\Delta G_{IC}^{\ddagger} = 17$ kcal/mol at $\rho_r = 1.5$.[18] Note that, because this reaction goes through a charge delocalized transition state, $[Cl \cdots CH_3 \cdots Cl]^{-1}$,[160] the effect of increasing solvent density is to increase the activation barrier and slow reaction, in contrast to the anisole case. While numerous experiments have demonstrated large changes in activated rate constants with pressure, the pressure dependence of the activation barriers have not been analyzed nor have the local and bulk contributions been isolated.[1]

2. Density Inhomogeneity Effects. a. Evaluated within the Equilibrium Solvation Approximation. As first pointed out by Johnston and co-workers, local solvent density inhomogeneities can significantly alter reaction rate constants, thus changing the way in which experimental data should be interpreted.[7,63,161] These authors used solvatochromic shift data on phenol blue to predict the pressure-dependent local density enhancements, and thus local dielectric constants, around α-chloromethyl benzyl ether in 1,1-difluoroethane. These local dielectric constants were then used in the continuum solvation model of Kirkwood,[155] in order to fit the rate data. While the data could be fit reasonably well using either the bulk or local dielectric constants, the bulk-dielectric-based fit predicts a much less polar transition state structure than does the more realistic local-dielectric-based fit.[7]

Even more convincing are the two reactions discussed above—$Cl^- + CH_3Cl$ and $PhOCH_3 + OH_2$—for which the pressure dependence of the activation barriers computed on the basis of the solvents' bulk density changes, $\Delta G_{IC}^{\ddagger}(P)$, are unable to explain those predicted by molecular dynamics simulation (methyl chloride reaction)[18,42] or derived from experimentally observed rate constants (anisole reaction).[14,33] In both cases the observed deviations of $\Delta G^{\ddagger}(P)$ from that predicted by an incompressible solvent model were attributed to the neglected density inhomogeneity effect, and this attribution has been confirmed by compressible continuum model calculations which
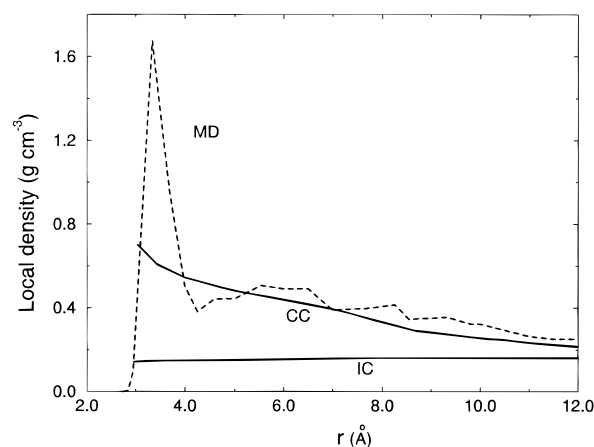

Figure 3. Radial density distribution around the $Cl^- \cdot CH_3Cl$ ion–dipole complex in SC water at $T_r = 1.03$ and $\rho_r = 0.51$ ($\rho = 0.165$ g cm⁻³), from molecular dynamics (MD; ref 42), a compressible continuum model (CC), and an incompressible continuum model (IC). From ref 34.

include direct density enhancement effects explicitly (see section II.B.3), as discussed below.

The molecular dynamics simulation results[42] for the $Cl^- + CH_3Cl$ reaction in SC water have provided a good check on the usefulness of continuum model formulations for evaluating the effect of solvent density enhancements on solvation free energies.[34] Of primary importance is the ability of such models to provide a good approximation to the density profile around the solute, $\rho c_{12}(r)$. In Figure 3, the compressible continuum prediction[34] of the radially averaged solvent density distribution $\rho_{cc}(r)$ around the $Cl^- \cdot CH_3Cl$ ion–dipole complex in SC water at $T_r = 1.0$ and $\rho_r = 0.5$ is compared to $\rho g_{12}(r)$ computed from simulation of the same system.[42] Although the continuum prediction contains no molecular structure peaks, including the strong first hydrogen bonding peak present in the simulation results, the gross decay of the density enhancement with distance is well represented by the continuum result. Note that comparison of the compressible continuum density profile with $\rho g_{12}(r)$ is not rigorously correct, as $\rho g_{12}(r)$ may contain indirect density enhancement effects not accounted for in the continuum model results. Although the larger value of $\rho g_{12}(r)$ compared to that of $\rho_{cc}(r)$ at large r could be a result of such indirect effects, the deviations are small enough as to be unreliable.

The effect of solvent density enhancements on the reaction-path-dependent, relative solvation free energies for the $Cl^- + CH_3Cl$ reaction at this state point is shown in Figure 4.[34,42] Notice first that the compressible continuum results (circles) agree exceptionally well with the simulation results (line). This accuracy is probably somewhat fortuitous, being due in part to the cancellation of neglected molecular effects, such as hydrogen bonding, along the reaction path. Comparison with incompressible continuum model estimates of the relative free energies (squares), which lie substantially below the compressible continuum and simulation results in the barrier region, demonstrates that the compressible continuum model captures the essential physics missing from the incompressible calculations and can predict the density enhancement effects on the relative solvation free energies with reasonable accuracy. Notice that the density-enhancement induced change to the reaction free energy barrier, $\Delta G_C^{\ddagger} = \Delta G_{CC}^{\ddagger} - \Delta G_{IC}^{\ddagger}$, is 7 kcal/mol at this state point, which translates to a density-enhancement-induced rate decrease of more than 2 orders of magnitude.

Compressible continuum model calculations on the effects of solvent density enhancements of the anisole hydrolysis
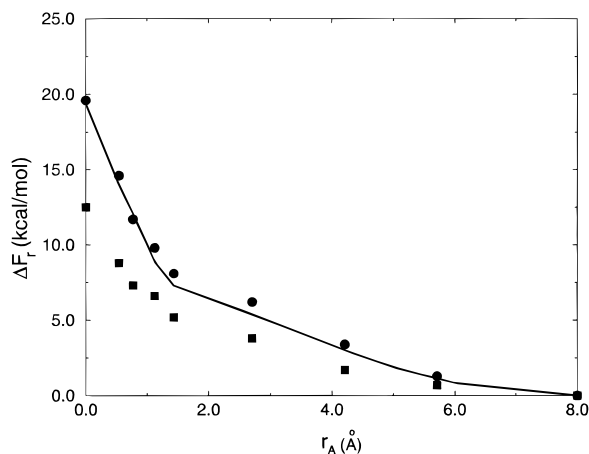
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Figure 4. Reaction-path-dependent relative solvation free energies for the $Cl^- + CH_3Cl$ reaction in SC water at the same state as in Figure 3. From molecular dynamics (line; ref 42), a compressible continuum model (circles), and incompressible continuum model (squares). From ref 34.

reaction show that solvent density enhancements may also alter the location of the transition state.[33] Because this reaction involves the creation of separated charges ($PhO^- + CH_3O$ H_2^+) from neutrals ($PhOCH_3 + OH_2$), the dielectric solvation of the products exceeds that of the reactants. Such asymmetric solvation, already present in an incompressible solvent, is enhanced by solvent compression effects. That is, because the magnitude of the direct density enhancements grow with increasing solute electric field, the product ions induce a much greater density enhancement than do the neutral reactants. Hence, the compression-induced stabilization of the solvation free energies increases along the reaction path, increasing the solvation asymmetry. Because such asymmetric solvation shifts the transition state to an earlier location along the reaction path, the compression-induced asymmetry causes the transition state to move to an earlier location than it would have had in the absence of density enhancement effects. This density-enhancement-induced asymmetry will initially, at low bulk densities, increase with increasing pressure (and increasing bulk density and solvent compressibility) as the density enhancements grow in magnitude. Then, as the pressure is increased further, and the density enhancements decrease in importance, the density-enhancement-induced asymmetry will decrease. This latter trend counteracts the trend of the bulk density to increase the incompressible solvation asymmetry at all pressures. A little thought, however, suggests that the decrease in the density enhancement asymmetry with pressure will never exceed the increase in the bulk density asymmetry, because, while the density enhancements decrease with increasing pressure at high pressures, the actual density around the solute does not decrease. As a result, the overall trend with pressure will always be to increase the solvation asymmetry. Thus, when there are compression effects, the initial transition towards an earlier transition state location will occur more rapidly at low bulk densities and then more slowly at higher bulk densities, as compared to the case of no compression effects. This behavior is consistent with the universal trend associated with density enhancement effects discussed in section II.B.2.

Finally, we note that Chialvo and co-workers have extensively examined the reaction-path-dependent activation free energy (potential of mean force)[150] for ion pair separation in super-critical water under varying thermodynamic conditions with a variety of potential models.[115,162,163] They have also evaluated

transition state theory rate constants for the interconversion between contact and solvent-separated ion pairs.[164]

b. Breakdown of the Equilibrium Solvation Approximation. The fact that the direct-density enhancements, or clustering, must vary along the reaction path for the equilibrium solvation energetics to be attained suggests that if these variations cannot be achieved rapidly enough, the reaction will be hindered.[150,151] This situation would cause a breakdown of transition state theory in the equilibrium solvation approximation, because the true reactive degree of freedom would not be the solute reaction path, but would instead involve the solvent degrees of freedom associated with this clustering phenomenon. And, because the number of molecules involved in the direct component of the equilibrium solvent "clusters" can be extremely large when the solute−solvent interaction is long range (*e.g.*, charge−dipole),[34,35] one might expect the formation of such clusters to be very slow and thus that the associated nonequilibrium solvation, or caging, effect would be unusually important in highly compressible SCFs. However, a preliminary study[71] suggests that when such electrostatic forces are involved, only a small fraction of the equilibrium cluster is required to attain the bulk of the equilibrium cluster-induced solvation energy. It was therefore hypothesized that the magnitude of nonequilibrium solvation effects in SCFs will be of the same order as found in liquids (*i.e.*, a factor of 10 or less),[151] in spite of reaction-path-dependent solvent clustering.[34] This conclusion is indirectly supported by a few experimental studies, which have found only small or nonexistent caging effects in SCFs.[165−167]

As mentioned previously, transition state theory will also break down when energy transfer into the solute is rate limiting. Some initial studies by Randolph, O'Brien, and co-workers have shown that the solvent−solute collision rate, which is proportional to the energy transfer rate in simple collision theory, is increased over the expected value when direct density enhancements are present.[95]

III. Fluctuations

A. General Considerations. So far, we have focused primarily on the average solvent density distribution around solutes and on the effects which arise as a result of inhomogeneities in these average distributions. Yet, SCFs also exhibit unusually broad distributions of solvent environments around these inhomogeneous averages.[31,97] Such a broad distribution of solvent environments is clearly evident in the configurational snapshot of a pure SC two-dimensional Lennard-Jones fluid, Figure 1. There it is seen that, while a large percentage of the atoms lie in regions of relatively high local density, a number of atoms reside in regions nearly void of other atoms. The radial solvent-density distribution around an atom in a high-local-density environment, which would be characterized by a nearly full, liquid-like solvation shell, is evidently quite different from that around an atom in a low density environment, which would be characterized by a nearly empty, vapor-like solvation shell.[31]

If solutes experience a similarly broad array of solvent environments, again distributed around an inhomogeneous average, this distribution could be an important factor in solute dynamics. In particular, if the time scale of the solvent environment reorganization (*i.e.*, the time required for the solute to sample this distribution of equilibrium environments) is long compared to the time scale of a given dynamic process, then an inhomogeneous description of the solvent environment effect on this process would be required. Thus, the average lifetime of, for example, vibrational excitation in a solute, would not be given by the excitation lifetime in the average solvent environ-

ment (described by $g_{12}(\mathbf{r})$), but rather by the average of the excitation lifetimes in each of the possible solvent environments. The need for such an inhomogeneous description will be magnified if the process of interest is sensitive to the nature of the local environment. In contrast, if the time scale of the dynamic process is long (*i.e.*, the process is slow compared to the rate of solvent environment reorganization), the solute will, to good approximation, feel the mean solvent environment (which could itself have an *average* inhomogeneity described by $g_{12}(r)$).

These considerations give rise to a number of unanswered questions about SCF solvents in their compressible regimes. In particular, what is the distribution of solvent environments in such fluids, and how does this distribution vary with thermodynamic conditions? Additionally, how do these distributions depend on thermodynamic condition and upon the details of the intermolecular interaction potential? We also do not know the microscopic details of the solvent structure in these differing environments. And, of critical importance to dynamic processes, what are the lifetimes of these microenvironments? That is, how fast do these environments interconvert? Then, we need to ask these same questions about the solvent environment around solutes. Answers to these basic questions will provide a much-needed foundation from which to interpret the effect of SCF solvents on dynamic processes.

B. Previous Work. In order to examine the distribution of environments found in SCFs, it is necessary to go beyond the description provided by the radial distribution functions, as these structural indicators describe only the average of all environments found within the fluid. Initial efforts to go beyond this standard, average description in computer simulations of pure and dilute SCFs have yielded some interesting results. In an early study of three-dimensional Lennard Jones (LJ) SCFs, Petsche and Debenedetti[53] examined the size distribution of clusters — energetically "bonded" networks — found in the pure SCF, as well as in dilute solution. For the state point considered, $T_r = 1.04$, $\rho_r = 1.0$, the distribution of cluster sizes in the pure SCF was found to be very broad. For example, even though isolated molecules and dimers account for 50% of the observed clusters, the mean cluster size is 16, and clusters of more than 50 atoms accounted for 10% of the distribution. These observations are consistent with the inhomogeneous solvent distribution pictured in Figure 1 for a two-dimensional LJ SCF. For an attractive solute, the distribution of clusters containing the solute was found to be shifted to a higher mean size, 75, than that for the pure solvent. The situation is reversed for the repulsive solute considered, which was found to be completely isolated 90% of the time. These authors also examined the length of time over which the *identity* of the solvent molecules in a specified cluster are maintained. For pure SC Ne they found an identity persistence lifetime of 0.5 ps, while for the strongly attractive solute, Xe in SC Ne, they found the lifetime to be greater than 2 ps, this time being limited by the length of the simulated trajectory. This general time scale of a few picoseconds has been used to assist in the interpretation of a number of experimental results, despite the fact that these time scales should be expected to be very sensitive to both the SCF state point being considered and the nature of the intermolecular potential interactions. Reliance on this one set of time scale estimates arises simply because no other estimates are presently available.

More recently, Flanagin *et al.* computed such identity persistence times for water molecules initially in the first solvation shell around the $Cl^- + CH_3Cl$ reaction complex, and
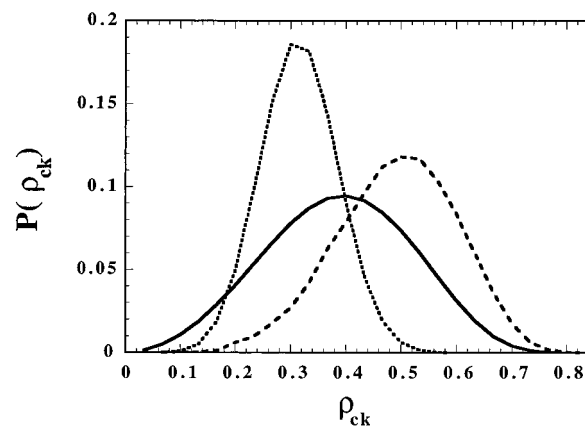
Figure 5. The distribution of local solvent environments, $P(\rho_{ck})$, found around a solvent atom at $T_r = 1.17$ (solid line) and $T_r = 10.6$ (dotted line) and an attractive solute (see text) at $T_r = 1.17$ (dashed line) in a two-dimensional Lennard-Jones SCF at $\rho_r = 0.86$.

found them to be on the order of 3 ps for a number of state points in the compressible regime. This is in contrast to the first shell, identity-persistence lifetime under ambient conditions, which was found to be on the order of $10-14$ ps.[42]

Additional evidence of broad distributions in SCF solvent environments can be found in simulation studies of Randolph, O'Brien, and their co-workers.[89] These authors found the standard deviation of computed average cluster sizes in a dilute three-dimensional LJ SCF solution ($T_r = 1.08$, $0.25 < \rho_r < 1.5$) to be very large, even over simulation runs of 67 ps. Similarly, these authors found extremely large fluctuations in the computed solute diffusion coefficient, here over simulations of 1.35 ns.

C. Distribution of Local Environments. Because our final goal is to understand the effect that such broad distributions of solvent environments will have on solute dynamics, we take an atom-centered approach to characterizing the distribution of solvent environments in SCFs. This approach is an extension of that proposed by Martinez, Ravi, and Tucker.[31] In this type of approach, we need a handle for indexing the local solvent environments found around a central atom (which could be either solute or solvent). A conceptually appealing method for classifying the local solvent environment around an atom would be to use the integral of an instantaneous direct correlation function. However, given the impracticality of this suggestion, we choose instead to simply count the number of surrounding solvent atoms, n_{ck}, which lie within a distance r_{ck} of the central atom at time t. Note that this definition of local environment is the same as used by O'Brien *et al.* to define cluster sizes.[89] We also define the local density within the check radius, ρ_{ck}, based upon the total number of atoms in this region, $n_{ck} + 1$, and the size of this region.

The equilibrium distribution of solvent environments is then characterized by the probability distribution, $P(\rho_{ck})$, of observing a particular density ρ_{ck} within the radius r_{ck} given that there is an atom at the origin. This probability distribution is shown in Figure 5 for a pure two-dimensional LJ SCF. Here we consider the same two-dimensional LJ system as in ref 31. The exact details of the potential used and the estimated critical parameters ($T_c \approx 0.47$, $\rho_c \approx 0.35$)[31,168,169] can be found therein. Note that the reduced variables we use in the present work are reduced relative to the specified critical parameters, such that, *e.g.*, $T_r = T/T_c = T/0.47$ and nonreduced variables are given in the standard LJ reduced units, see ref 114. At at $\rho = 0.30$ ($\rho_r = 0.86$) and a high temperature of $T_r = 10.6$, this atom-centered distribution of local densities approaches the limiting case of

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hard sphere behavior. As the temperature of the fluid is lowered toward T_c (with ρ held constant), the distribution of local densities broadens substantially, as seen in Figure 5 for $T_r = 1.17$. This behavior, which is exactly opposite of the decrease in thermal fluctuations with decreasing temperatures that one would expect for homogeneous fluids, reflects the inhomogeneities apparent in the instantaneous configurational snapshot of this same fluid shown in Figure 1.[170] These results are in concert with the large deviation of cluster sizes observed by O'Brien and co-workers mentioned above.[89]

Additionally, the maximum in $P(\rho_{ck})$, which gives the most probable local density, ρ_{mp}, shifts to higher densities as $T \rightarrow T_c$ (*i.e.*, $\rho_{mp} > \rho$), reflecting the propensity of atoms to be found in the higher density regions. That is, since $P(\rho_{ck})$ is an atom-centered function, it samples only those regions of space containing atoms, thus giving less and less weight to the void-like regions as $T \rightarrow T_c$.

The local environment probability distribution, $P(\rho_{ck})$, around an attractive solute, also at $T_r = 1.17$, $\rho_r = 0.86$, is shown in Figure 5. The LJ solute considered has the same diameter as the solvent (σ), but the solute−solvent interaction energy is 6 times that of the solvent−solvent interactions (ϵ). The distribution of environments around this solute is shifted to higher density compared to that around a solvent atom under the same conditions, consistent with the solvent−solute clustering that is expected on average for such systems. Note that, because we sample only the local environment ($r_{ck} = 3.09\sigma$ compared to an interaction potential cutoff of 2.5σ), this distribution reflects primarily the direct density enhancement effects. Also, notice that the distribution of environments around the solute is still quite broad, suggesting that the local environment fluctuations may be important, even for very attractive solutes.

D. Time Scales. Prediction of the relevance of this distribution of local solvent environments to dynamic processes will require information about the time scale of the solvent−environment interconversion process. Toward this end, we define a time-dependent, per atom, local-density fluctuation variable $\delta\rho_{ck}(t) = \rho_{ck}(t) - \bar{\rho}_{ck}$, where $\bar{\rho}_{ck}$ is the average local density given by $\bar{\rho}_{ck} = \sum_{\rho_{ck}} \rho_{ck} P(\rho_{ck})$. The local density autocorrelation function[101,171]

$$C_\rho(t) = \frac{\langle \delta\rho_{ck}(t)\delta\rho_{ck}(0) \rangle}{\langle [\delta\rho_{ck}(0)]^2 \rangle} \qquad (20)$$

then describes the time it takes for the local environment around a solvent atom to become uncorrelated with the initial value of this environment at $t = 0$. Initially, at very short times, every atom remains in the same local environment as it had at $t = 0$, and $C_\rho(t) = 1$. As time progresses, solvent atoms will move in and out of a specified atom's check radius sphere, causing $\delta\rho_{ck}$ to vary away from its initial value. The initial variations will be small, such that $\delta\rho_{ck}(t)$ retains a knowledge of its initial value. As variations become large, $\delta\rho_{ck}(t)$ will sample the equilibrium distribution of environments, $P(\rho_{ck})$, and the value of $\delta\rho_{ck}(t)$ will become independent of its initial value. At this point $\langle \delta\rho_{ck}(t)\delta\rho_{ck}(0) \rangle = \langle \delta\rho_{ck}(t) \rangle \langle \delta\rho_{ck}(0) \rangle = 0$, such that $C_\rho(t_{large}) = 0$. Thus, the rate of decay of $C_\rho(t)$ from 1 to 0 describes the rate of interconversion of the local solvent environments. Note that the lifetime we compute is qualitatively different from the identity lifetime studied by Petsche and Debenedetti,[53] in that we examine the persistence of the local number density away from its average value, independent of the identity of the atoms.

Figure 6 shows the local environment correlation function for the pure two-dimensional LJ SCF at $T_r = 10.6$ and $T_r =$
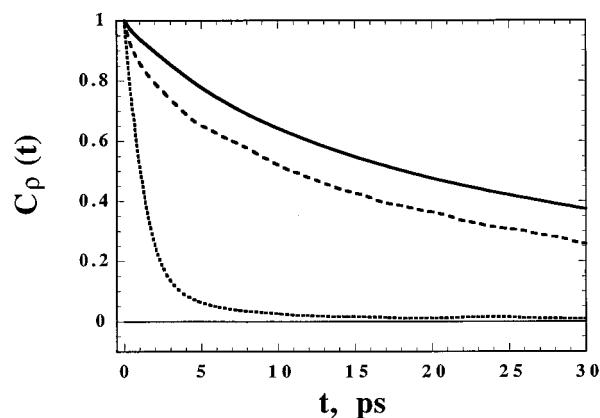

Figure 6. Local environment autocorrelation function, $C_\rho(t)$, for the solvent and solute environments shown in Figure 5; time units were computed assuming an atom mass equal to that of Ar.

1.17 for $\rho_r = 0.86$. The times were converted from LJ reduced times to picoseconds by assuming the parameters for Ar. The rate of decay, or rather, the rate of local-solvent-environment interconversion is much slower at the lower, more near critical temperature, where $\sim$20 ps are required for 50% decay of $C_\rho(t)$, compared to $\sim$1 ps required at $T_r = 10.6$. These results illustrate that the time scale of local solvent interconversion is very sensitive to thermodynamic condition and thus that applying a single estimated value to data taken under varying conditions is extremely risky. Also, for the decay time scale observed at the more near critical temperature, there are dynamic processes, such as rotational reorientation, vibrational relaxation, or geminate recombination, which could be fast relative to the rate of solvent environment interconversion; for such processes an inhomogeneous description of the solvent would be appropriate. Obviously, this will be true for more and more processes as the critical point is approached. Finally, note that these decay curves cannot be fit with a single exponential, indicating multiple time scale decay.

The solvent environment autocorrelation function around the attractive solute described above is also shown in Figure 6 for $T_r = 1.17$. Perhaps surprisingly, the fluctuations of the solute's local solvent environment away from its average value occur on a similar time scale as do those around a solvent atom (except for times less than 5 ps). Although the stronger solute-solvent interaction assures a higher average local density around the solute (Figure 5), the *fluctuations* around this average need not be slower than those in the pure solvent, and in fact, in this case it appears that the solute has little effect on the fluctuation behavior of the surrounding solvent.

E. Structure. While the local density distribution $P(\rho_{ck})$ provides information about the distribution of local environments in SCF solvents, it provides no structural information, neither about the local solvent structure nor about correlations between the local and long-range densities. Such information can be determined from a *distribution* of pair correlation functions. The time scale separation between the time scale for atomic motions and the time scale for local environment changes at $T_r = 1.17$ (Figure 6) allows one to treat atoms in differing local solvent environments as separate species. One is then justified in defining a radial correlation function $g(r; \rho_{ck})$ which gives the conditional probability of finding a particle at a radial distance r, given that there is a particle located at the origin having a surrounding local solvent environment of density ρ_{ck}. Thus, for each local environment appearing in the distribution $P(\rho_{ck})$, a separate radial correlation function is computed.[172]
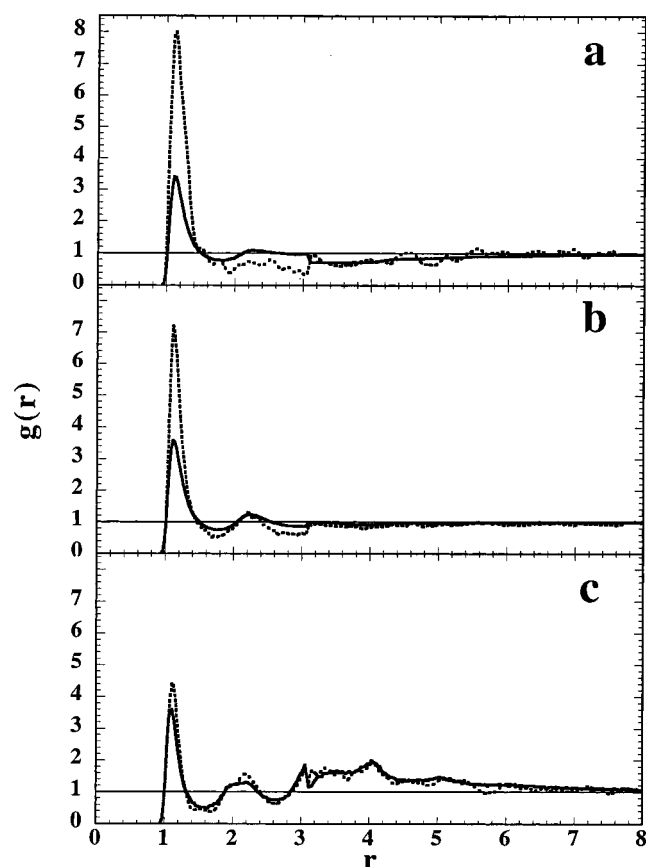
Figure 7. Local environment-specific radial distribution functions $g(r; \rho_{ck})$ around a solvent atom (solid line) and a solute atom (dashed line, see text) in the same two-dimensional Lennard-Jones SCF ($\rho = 0.30$; $\rho_r = 0.86$) at $T_r = 1.17$. For local densities (a) $\rho_{ck} = 0.17$, (b) $\rho_{ck} = 0.30$, and (c) $\rho_{ck} = 0.77$.

A sampling from the distribution of local-environment-specific radial correlation functions for the $T_r = 1.17$, $\rho_r = 0.86$ ($\rho = 0.30$) two-dimensional LJ SCF system are shown in Figure 7. The solid lines correspond to the solvent-centered correlation functions from the pure SCF, while the dashed lines correspond to the solute-centered functions from the infinitely dilute SCF solution defined above. First notice that as the local density moves from below to above the bulk density, the short-range structure around both solvent and solute changes from a characteristic vapor-like structure to a characteristic liquid-like, and then even solid-like, structure. (Note, however, that since the solid-like structure is observed only over very short range, it is more accurately referred to as "glass-like"). Hence, the broad distribution of local densities exhibited by $P(\rho_{ck})$ in Figure 5 indeed corresponds to a distribution of structurally distinct local solvent environments spanning the range of behaviors from vapor-like to solid-like.

Another interesting feature of the ρ_{ck}-specific correlation functions is the long-range decay of these functions, which is indicative of the correlated densities over long range. In particular, notice that for atoms in low-ρ_{ck} environments (Figure 7a), the long-range correlation approaches its asymptotic value from below, because atoms with low density local environments are generally found in the large empty regions evident in the configurational snapshot, Figure 1. In contrast, for atoms with high local densities (Figure 7c), large ρ_{ck}, the long range correlation approaches its asymptotic value from above, because atoms with high local densities are generally found in the extensive regions of higher density apparent in Figure 1. And, since atoms having intermediate local densities (Figure 7b) tend

to be found in boundary regions, and thus be surrounded on one side by higher density and on the other by lower density, there is a cancelation in the radial density correlations over long range, yielding a much smaller amplitude asymptotic tail for these atoms.

The correlation between the local solvent environment and the sign of the long-range decay can be understood from consideration of the expressions for the indirect (long-range) correlations in the total radial correlation function, eq 15. These expressions show that the sign of long range correlations depend upon the nature of the local fluctuation (represented by the direct correlation function integral) around the central atom. Hence, a local density variation (*i.e.*, depletion or enhancement) should induce the same kind of long range density variation (*i.e.*, depletion or enhancement, respectively) with corresponding magnitude. This is exactly the correlation of local and long range behavior we observe upon separation of the correlation functions according to the local density environments.

The solute-centered local-density-specific correlation functions for the very attractive solute described above are shown for comparison. The main difference between the two functions is that the short-range structure around the solute contains sharper peaks, indicating a more pronounced solvent structure. This difference is magnified at the lower densities, indicating that the solute never relinquishes its nearest neighbors, unlike solvent atoms, which may become isolated. In contrast, the long range asymptotic decay of these correlation functions is nearly the same for both the solute- and solvent-centered cases. (The deviations are well within the noise of the solute simulations, which are much more CPU intensive because there is but one solute to average over.) This similarity arises because we are comparing the long range asymptotic decay around solute and solvent atoms having the same fixed local density ρ_{ck} (*i.e.*, $C_{12} \approx C_{11}$), and, as just mentioned, the asymptotic decay is strongly correlated with this variable (cf. eqs 14 and 15). Thus, the difference between the average structure found around solute and solvent atoms is carried primarily by the difference in the distribution of local environments $P(\rho_{ck})$, Figure 5, for these two cases.

IV. Summary

One of the most appealing features of supercritical fluids (SCF) is the large variation in their solvating properties which may be achieved through variation of the temperature and pressure. This tunability is maximized in a region of the phase diagram relatively close to the critical point, where SCF compressibilities are large, and therefore large density changes may be effected with modest changes in pressure. However, these large compressibilities go hand-in-hand with large fluctuations in the solvent density that are correlated over long ranges.

Recent studies of SCFs in this compressible regime have helped to characterize these density inhomogeneities, both in pure SCFs and in SCF solutions. In particular, the distinction between direct and indirect density enhancement (or depletion) effects has now been well established. That is, the *average* solvent density enhancement around a solute molecule is given by the total solute−solvent correlation function, which itself is comprised of direct and indirect parts. The direct component extends (roughly) over the range of the solute−solvent interaction potential and can be thought to reflect the effect of this potential on the compressible solvent, while the indirect component reflects the fact that, because there are density correlations between solvent molecules, the average enhancement in solvent density can be extended well beyond the range

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of the direct component. The distinction made between these two components of the average solute-induced solvent density enhancement (or depletion) is important, because these two effects are maximized under different thermodynamic conditions. Additionally, in the compressible regime the direct density enhancements strongly influence some physical properties, such as solvation energies, while the indirect density enhancements dominate others, such as the partial molar volume. Note that the importance of the direct effects to solvation energetics means that any treatment of solvation in SCFs must account for these effects, if they are to be valid in the compressible regime. These effects may be included as an *ad hoc*, after the fact addition, or, preferably, the treatment may be such that these effects are predicted in the computation, as in simulation and in compressible continuum methods.

Many different processes, such as relative solvation, energy transfer and diffusion, can be important for understanding chemical reactions in solution, and, in particular, in SCF solutions. Thus, to provide adequate descriptions of reactions in SCFs in their compressible regimes, it will be necessary to understand how solvent density inhomogeneities affect each of these processes. (Note that inhomogeneities in solute density have also been observed and found to affect reactivity, although we have not discussed this topic herein.) Solvent density-enhancement effects have already been explored to some extent for activated barrier reactions, for which one may assume as a first approximation that the solvent configuration remains equilibrated with the solute as the reaction proceeds. Under such an assumption, the solvent effect on the reaction rate is described by the relative solvation energies along the reaction path, and the effect of the reaction-path-dependent, average solute-induced direct density enhancements on these solvation energies. Initial studies suggest that such density enhancement effects can substantially alter the reaction energetics, changing solute rate constants by many orders of magnitude. At this point, application of techniques such as the compressible continuum model to study the implications of such density enhancement effects for activated reactions of technological interest are in order.

Much less is known about the ways in which SCF solvent behavior affects other dynamic processes which may be important to solute reaction. Understanding the influence of SCFs on many dynamic processes is, however, complicated by the fact that these processes may be affected by the *distribution* of solvent environments around the average inhomogeneous environment, as well as upon the nature of the average environment itself. Our simulations of two-dimensional Lennard-Jones SCF solutions show that under certain conditions a very broad distribution of local solvent environments is expected around solutes (and around tagged solvent molecules). And, at this point, we can only speculate as to the effects such broad distributions will have on different dynamic processes. Additionally, an important factor in determining the effect that such environmental distributions will have will be the time scale for the relaxation of these local environment fluctuations back to the average environment. Such lifetimes will be a factor determining whether or not solute dynamic processes should be thought of as occurring in an inhomogeneous solvent environment and whether such density fluctuations can couple to, and thus assist, such solute processes.

In conclusion, we have just begun to understand the nature of solvent density inhomogeneities in SCFs in their compressible regimes. This knowledge opens the door for studies to examine the ways in which such density inhomogeneities alter solute dynamics and reaction and the ways in which these effects contribute to the novel solute reactivity observed in these intriguing solvents.

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(172) The normalization of each ρ_{ck}-specific correlation function is taken to be the ρ_{ck}-specific correlation function for a completely random distribution of points. Because restricting ρ_{ck} fixes the density within a distance r_{ck} from the central point to a value which in general differs from the bulk density, this normalization function is a step function of density ρ_{ck} for $r < r_{ck}$ and $(\rho A - \rho_{ck}\mathcal{A})/(A - \mathcal{A})$ for $r > r_{ck}$, where A and $\mathcal{A}$ are the total area (or volume in 3D) of the simulation box and the local environment, respectively. This choice of normalization removes the effect of statistical clustering that occurs in a purely random system. The observed discontinuities in the ρ_{ck}-specific functions are not a result of this normalization, as will be discussed in future work.[110]