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Inhomogeneous Fluid Approach to Solvation Thermodynamics. 1. Theory

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The solvation energy and entropy at infinite dilution consist of a solute–solvent term and a solvent reorganization term representing the contributions of changes in solvent structure upon solute insertion. In the standard, homogeneous treatment of solutions, changes in solvent structure are expressed through derivatives of the homogeneous pair correlation function, which are very difficult to obtain by simulation. Tractable expressions for the solvation energy and entropy are here derived by viewing the solution as an inhomogeneous system with the solute fixed at a certain point. The solvent reorganization terms in the inhomogeneous view contain two contributions: the local, “correlation” contributions, which are due to correlations between the solute and the solvent and dominate at high densities, and the nonlocal, “liberation” contributions, which are due to the effective dilution of the solvent caused by the thermal motion of the solute and dominate at low densities. The liberation contributions are independent of the nature or size of the solute and depend only on the properties of the solvent. For common liquid solvents the nonlocal terms are negligible and the solvation properties arise almost entirely from effects localized around the solute. The new expressions are tested by calculations of the solvent reorganization energy and entropy in ideal hard-sphere and Lennard-Jones mixtures (solute identical to solvent). The solvent reorganization energy and entropy make distinct and significant contributions to the solvation free energy. The theory can be applied to truly inhomogeneous systems as well as small solute solvation, thus providing a connection between interfacial phenomena and microscopic solvation.

I. Introduction

The thermodynamics of solvation, especially aqueous solvation, is rife with controversy. One source of confusion is that several theoretical approaches to solvation exist and the correspondence between the various terms appearing in different theories is not clear. Establishing a connection between theoretical terms and the many intuitive ideas about solvation has been difficult as well. This sometimes leads to different qualitative conclusions as to the physical origin of the solvation free energy. Another source of confusion is that because solvation in real fluids is complex, insights are commonly obtained by studies of simple hard-sphere (HS) or Lennard-Jones (LJ) fluids. The conclusions drawn from these studies are then extrapolated to real fluids. Since there is no unique way of doing this, the results may differ depending on the scheme of extrapolation adopted. Finally, much of the confusion stems from the fact that the nature of the entropic contributions to solvation is not well understood.

A possible solution to the latter problem has emerged recently. It is an expansion of the entropy of a fluid in terms of multiparticle correlation functions,^{1,2} with the major contribution coming from the two-particle term. The two-particle correlation function can be readily and accurately obtained from simulations. The method has been applied to a variety of simple fluids, such as the hard sphere fluid,^{3–7} Lennard-Jones fluids,^{2,6,8} liquid argon,⁹ mixtures of hard spheres,¹⁰ as well as molten salts,¹ liquid metals,¹¹ and model electrolytes.¹² The method has also

been used to calculate the contributions of solute–solvent translational and orientational correlations to the entropy of hydrophobic hydration^{13–15} and the contribution of pair correlations to the entropy of pure liquid water.¹⁶

The practical utility of the entropy expansion depends on its convergence properties; i.e., whether accurate results can be obtained with a small number of terms. In practice, only the two-particle term can be calculated easily. Truncation of the expansion at this level is equivalent to the Kirkwood superposition approximation (KSA);¹⁷ i.e., $\delta g^{(3)} = 1$ in the expression for the triplet correlation function in terms of pair correlation functions:

$$g^{(3)}(1,2,3) = g^{(2)}(1,2) g^{(2)}(1,3) g^{(2)}(2,3) \delta g^{(3)}(1,2,3) \quad (1)$$

The KSA has been tested by simulations of simple fluids and was found to be qualitative correct but quantitatively inadequate.^{18–20} Therefore, neglect of the third and higher correlations is expected to lead to nonnegligible errors. However, most of the calculations on simple fluids listed above showed that the two-particle term contribution to the entropy agrees with the exact entropy to within 10 or 15%. Slightly better or worse results are obtained depending on how the higher order excluded volume terms are treated. In particular, if they are determined in the incompressible fluid limit, truncation at the two-particle level gives excellent agreement with the exact entropy at high densities.^{1,4,6,10,11} Even in liquid water the truncated expansion gives results in close agreement with free-energy simulations and experiment.¹⁶ Explicit calculations of the three-particle term for the Lennard-Jones fluid⁸ and the hard-sphere fluid⁵ indicate that this agreement probably results from cancellations among the higher order terms. Nevertheless, these

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results are encouraging and warrant further development of the method, particularly for obtaining an understanding of the factors involved in determining the entropy of liquids and liquid mixtures. This is of primary interest since in most cases experimental measurements of thermodynamic properties of solvation of small molecules are either available or easy to obtain and theory does not add anything if it only duplicates the experimental numbers.

To apply this distribution function approach to the problem of solvation, we consider what happens when a solute is dissolved in a solvent. The solvation energy is the sum of the solute–solvent interaction and the change in solvent–solvent interactions. Similarly, the solvation entropy arises from the introduction of solute–solvent correlations and the changes in solvent–solvent correlations upon solute insertion.¹⁴ The solute–solvent terms are similar to those for pure fluids and can be easily evaluated. The solvent–solvent terms are more difficult to obtain directly because they correspond to small differences between large numbers. For example, the solvent–solvent energy before and after solute insertion will exhibit statistical fluctuations as large or larger than the solvent reorganization energy itself.

In this paper we develop tractable expressions for the solvent–solvent contributions to the solvation energy and entropy by viewing the solution as an inhomogeneous fluid. The solute is considered “fixed” at the origin, so that it generates an external field that creates solvent density fluctuations around it. This trick (the “source particle method”) was first used by Percus²¹ to derive integral equations through the technique of functional differentiation and was extended to polyatomic fluids by Chandler et al.²² More recently it was used to obtain accurate three-particle correlation functions in simple fluids.^{23,24} In the present work, the inhomogeneous fluid device is used to obtain the solvent reorganization thermodynamic properties. The inhomogeneous point of view has been taken in a study of the solvation energy²⁵ and excess volume and compressibility²⁶ of a hydrophobic solute in water and in the prediction of the solvent density distribution around biomolecules,^{27,28} but a systematic formulation of the approach for the calculation of thermodynamic properties has not been presented.

In the paper we employ the canonical ensemble (CE) because it is conceptually and formally simpler and gives partial molar properties in a straightforward way (we have no control over the number of particles in the grand canonical ensemble (GCE)). It is emphasized that although we are using the CE, we consider solvation at constant pressure. That is, when a solute is inserted into a volume V_0 of pure solvent, we allow the volume of the mixture to increase by the partial molar volume of the solute so as to keep the pressure constant. However, each of the two systems, the pure solvent and the mixture, are treated in the CE.

Section II presents the inhomogeneous fluid theory of solvation. For simplicity, the development will be performed for monatomic solvent particles. The equations can easily be generalized by adding integrations over orientational degrees of freedom and dividing by the appropriate factor ($8\pi^2$ for nonlinear molecules and 4π for linear molecules²⁹). The new expressions are tested in simple ideal mixtures in section III. Section IV contains a brief discussion of the results. Appendix A shows the equivalence of the homogeneous and inhomogeneous description of a mixture, and Appendix B explores the reasons for the discrepancies observed in the numerical results. The following paper contains applications to a variety of simple

fluid mixtures. Application to an infinitely dilute mixture of methane in water will be reported shortly.

II. Theory

A. Overview of the Homogeneous Approach to Solvation Energy and Entropy. If the potential energy of a pure monatomic fluid is given by a sum of pairwise interactions, the molar energy is given by³⁰

$$e = \frac{3}{2}kT + \frac{1}{2}\rho \int g^{(2)}(\mathbf{r}) u(\mathbf{r}) d\mathbf{r} \quad (2)$$

where k is Boltzmann’s constant, ρ the number density, $g^{(2)}$ the pair correlation function (PCF), u the interaction potential, and \mathbf{r} represents the relative position of two particles.

For the entropy, we can write

$$s = s^{\text{id}} + s^{(2)} + s^{(3)} + \dots \quad (3)$$

where s^{id} is the entropy of an ideal gas at the same temperature and density ($\frac{5}{2}k - k \ln(\rho\Lambda^3)$) and $s^{(2)} + s^{(3)} + \dots$ corresponds to the excess part of the molar entropy. The terms $s^{(2)}$ and $s^{(3)}$ can be expressed in terms of multiparticle correlation functions as follows:^{1,2}

$$s^{(2)} = -\frac{1}{2}k\rho \int [g^{(2)} \ln g^{(2)} - g^{(2)} + 1] d\mathbf{r} \quad (4)$$

$$s^{(3)} = -(1/3!)k\rho^2 \int [g^{(3)} \ln \delta g^{(3)} - g^{(3)} + 3g^{(2)}g^{(2)} - 3g^{(2)} + 1] d\mathbf{r} d\mathbf{r}' \quad (5)$$

where \mathbf{r} and \mathbf{r}' represent the positions of two particles with respect to a central particle, $g^{(3)}$ is the triplet correlation function, and $\delta g^{(3)}$ is the deviation of the triplet correlation function from the KSA (eq 1). Baranyai and Evans² showed that eqs 3–5 are valid for both the CE and GCE.

For a binary solution of a solute s and a solvent w and for pairwise additive interactions, the total energy is given by the standard formula:

$$E = \frac{3}{2}(N_s + N_w)kT + N_s\rho_w \int g_{sw}u_{sw} d\mathbf{r} + \frac{1}{2}N_s\rho_s \int g_{ss}u_{ss} d\mathbf{r} + \frac{1}{2}N_w\rho_w \int g_{ww}u_{ww} d\mathbf{r} \quad (6)$$

where N_s and N_w are the number of molecules of solute and solvent, respectively, ρ_s and ρ_w the solute and solvent number densities, respectively, g_{ij} the PCFs, and u_{ij} the pair interaction potentials.

The analogous expression for the total entropy of the system is^{31,13}

$$S = N_s(\frac{5}{2}k - k \ln(\rho_s\Lambda_s^3)) + N_w(\frac{5}{2}k - k \ln(\rho_w\Lambda_w^3)) - kN_s\rho_w \int (g_{sw} \ln g_{sw} - g_{sw} + 1) d\mathbf{r} - \frac{1}{2}kN_s\rho_s \int (g_{ss} \ln g_{ss} - g_{ss} + 1) d\mathbf{r} - \frac{1}{2}kN_w\rho_w \int (g_{ww} \ln g_{ww} - g_{ww} + 1) d\mathbf{r} + \dots \quad (7)$$

As can be seen in eq 7, perfect separation of the entropy into solute–solvent, solvent–solvent, and solute–solute terms is possible if the higher order terms in eq 7 are neglected.

The partial molar energy and entropy of the solute are obtained from eqs 6 and 7 by taking the derivative with respect to the number of solute particles at constant temperature and

pressure.^{14,32} At infinite dilution ($\rho_s \rightarrow 0$) these are

$$\bar{e}_s^\infty = \frac{3}{2}kT + \rho_w \int g_{sw} u_{sw} \mathbf{dr} + \frac{1}{2} N_w (\partial/\partial N_s)_{T,P} \{ \rho_w \int g_{ww} u_{ww} \mathbf{dr} \} \quad (8)$$

$$\bar{s}_s^\infty = (\frac{5}{2}k - k \ln(\rho_s \Lambda_s^3)) - k(1 - \rho_w \bar{v}_s^\infty) - k \rho_w \int (g_{sw} \ln g_{sw} - g_{sw} + 1) \mathbf{dr} - \frac{1}{2} k N_w (\partial/\partial N_s)_{T,P} \{ \rho_w \int (g_{ww} \ln g_{ww} - g_{ww} + 1) \mathbf{dr} \} + \dots \quad (9)$$

where \bar{v}_s^∞ is the partial molar volume of the solute, $(\partial V/\partial N_s)_{T,P}$. The first integral in eq 8 is the solute–solvent interaction energy, E_{sw} , and the last term represents the change in solvent–solvent energy upon solute insertion, ΔE_{ww} . This term has been referred to as cavity energy³³ or solvent reorganization energy.^{14,32,34} The value of the solvent reorganization energy will be significantly different for solute insertion at constant volume or constant pressure.^{25,32,35}

The partial molar entropy expression, eq 9, is analogous to the energy expression. The first integral in eq 9 is the entropy due to solute–solvent correlations, i.e., the solute–solvent entropy, S_{sw} . The following term, ΔS_{ww} , describes the change in solvent–solvent correlations upon addition of the solute, and in analogy to the energy expression, we will refer to it as the solvent reorganization entropy. In eq 9 there is an additional term, $k(1 - \rho_w \bar{v}_s^\infty)$, which arises from the derivatives of the ideal part of the entropy. The term $k \rho_w \bar{v}_s^\infty$ is closely related to the solute–solvent entropy due to the Kirkwood–Buff³⁶ expression for the partial molar volume, which at infinite dilution becomes

$$\bar{v}_s = \kappa kT = \int (1 - G_{sw}) \mathbf{dr} \quad (10)$$

where κ is the solvent compressibility and G_{sw} is the grand-canonical solute–solvent PCF. It differs from the canonical PCF, g_{sw} , in that it tends to unity at long separations whereas g_{sw} does not.^{29,30} For a pure fluid, $\bar{v}_s = 1/\rho$, and eq 10 becomes the well-known compressibility equation.³⁰

The integral in eq 10 represents the change in volume due to solute–solvent correlations. It includes the excluded volume effect of the solute upon the solvent and the effect of solvent packing around the solute. For simplicity, we will refer to it as the “excluded volume” and denote it by V_{ex} , although this term is often reserved for the value of the integral over the region where G is zero.^{26,37,38} The physical meaning of the first term, κkT , can be understood by considering an ideal gas mixture. In this case, the integral in eq 10 vanishes, i.e., there is no excluded volume. The partial molar volume, $\kappa kT = kT/P = 1/\rho$, is entirely due to the thermal motion of the solute. Generalizing to any fluid, κkT is the change in volume due to the thermal motion of the solute. If the solute were inserted at a fixed point without thermal motion, the only change in volume would be due to solute–solvent correlations. The same is true for an incompressible solvent; the thermal motion of the solute has no effect against the incompressible solvent.

Using eq 10, eq 9 becomes

$$\bar{s}_s^\infty = (\frac{3}{2}k - k \ln(\rho_s \Lambda_s^3)) + k \rho_w \kappa kT - k \rho_w \int G_{sw} \ln G_{sw} \mathbf{dr} - \frac{1}{2} k N_w (\partial/\partial N_s)_{T,P} \{ \rho_w \int (g_{ww} \ln g_{ww} - g_{ww} + 1) \mathbf{dr} \} + \dots \quad (11)$$

B. Inhomogeneous Theory. The solute–solvent terms in eqs 8 and 9 are relatively easy to evaluate using correlation

functions generated by computer simulations or integral equation theories. The solvent reorganization terms are more difficult to obtain, particularly in the form in which they appear in eqs 8 and 9. The solvent–solvent correlation functions in that expression are averages over the whole volume of the solution and therefore contain contributions from large amounts of essentially pure, unperturbed solvent. In practice, if one calculates by simulation the solvent–solvent correlation function for even a small box of solvent with one solute molecule, the calculated correlation function will be practically indistinguishable from that of pure solvent. What is needed is a formalism that will isolate the effect of the solute on the structure of the solvent next to it without having to deal with the large amounts of unperturbed solvent. One such formalism is obtained by viewing the solution as an inhomogeneous system. The solute is considered “fixed” at the origin, generating an external field that creates solvent density fluctuations around it.²¹

Morita and Hiroike in their classic work of 1961³⁹ presented formulas similar to eqs 2 and 3 for a general, inhomogeneous system. For a pure fluid of N molecules interacting with a pairwise potential under the influence of an external field u_{ext} , these formulas are

$$E = \frac{3}{2} N kT + \int \rho(\mathbf{r}) u_{ext}(\mathbf{r}) \mathbf{dr} + \frac{1}{2} \int \rho(\mathbf{r}) \rho(\mathbf{r}') g(\mathbf{r}, \mathbf{r}') u(\mathbf{r}, \mathbf{r}') \mathbf{dr} \mathbf{dr}' \quad (12)$$

$$S/k = \frac{5}{2} N - \int \rho(\mathbf{r}) \ln \Lambda^3 \rho(\mathbf{r}) \mathbf{dr} - \frac{1}{2} \int \rho(\mathbf{r}) \rho(\mathbf{r}') \{ g(\mathbf{r}, \mathbf{r}') \ln g(\mathbf{r}, \mathbf{r}') - g(\mathbf{r}, \mathbf{r}') + 1 \} \mathbf{dr} \mathbf{dr}' +$$

$$+ \left[\begin{array}{c} \rho \\ \text{triangle} \end{array} \right]^{g-1} - \left[\begin{array}{c} \text{square} \end{array} \right] + \dots \quad (13)$$

+ {sum of all the more than doubly connected diagrams of black ρ circles and $(g - 1)$ bonds}

In the above expressions $\rho(\mathbf{r})$ is the fluid density at point \mathbf{r} and $g(\mathbf{r}, \mathbf{r}')$ is the inhomogeneous PCF at \mathbf{r} and \mathbf{r}' defined by the relation

$$\rho^{(2)}(\mathbf{r}, \mathbf{r}') = \rho(\mathbf{r}) \rho(\mathbf{r}') g(\mathbf{r}, \mathbf{r}') \quad (14)$$

where $\rho^{(2)}(\mathbf{r}, \mathbf{r}')$ is the two-particle density at \mathbf{r} and \mathbf{r}' . The graphs are defined in the standard fashion (see, for example, ref 40).

In the absence of an external field ($u_{ext} = 0$) the density becomes uniform ($\rho(\mathbf{r}) = \rho(\mathbf{r}') = \rho$) and we obtain expressions for a homogeneous fluid. The expression for the energy is identical to eq 2 and the expansion for the entropy is identical to eq 3 up to and including the two-particle term. The Morita–Hiroike expansion does not have the $\ln g^{(n)}$ terms. It should be possible to rearrange the higher order terms in the two expressions and prove that they are equivalent, but it is not necessary for the present work since we focus on the two-particle terms. Equation 13 was derived in the GCE. We assume it is valid in the CE as well, based on the ensemble invariance of the corresponding homogeneous expression.²

Equations 12 and 13 hold for any external field, u_{ext} . In a mixture of 1 solute and N_w solvent particles, the solute can be considered “fixed” at the origin, giving rise to an external field $u_{ext} = u_{sw}^{21}$

$$u_{ext}(\mathbf{r}) \rightarrow u_{sw}(\mathbf{r}) \quad (15)$$

In this case the one-particle density in the inhomogeneous

system corresponds to the pair density in the homogeneous system:

$$\rho(\mathbf{r}) \rightarrow \rho_w g_{sw}(\mathbf{r})$$

In the CE, pair correlation functions do not approach unity at long distances because the number of particles in the CE is fixed.^{29,30} Therefore, the conditional density at any point given that one particle is at another point is less than the (unconditional) average density. In a pure fluid, this conditional density can be estimated in the following way: with the central particle being at the origin, the volume available to the other $(N - 1)$ particles is $(N - 1)/\rho$ plus the “thermal volume” of the central particle, κkT . Thus the overall density in this available volume will be

$$\rho^\infty = \frac{N - 1}{(N - 1)/\rho + \kappa kT} = \frac{\rho}{1 + \kappa kT\rho/(N - 1)} \approx \rho \left(1 - \frac{\kappa kT}{V}\right) \quad (16)$$

This will also be the value of the conditional density far from the “fixed” particle, where density oscillations due to its presence have vanished. This result was obtained much more rigorously and generally by Lebowitz and Percus.⁴¹ For an incompressible fluid or for a central particle that is truly fixed and lacks thermal motion, this density becomes equal to the bulk fluid density.

For an infinitely dilute mixture in the CE the solute–solvent correlation function will also not tend to unity even in the limit of zero compressibility. The reason is that g_{sw} is defined with respect to the density of the solvent in the mixture, $\rho_w = N_w/V$, which is slightly smaller than the pure solvent density, $\rho_w^\circ = N_w/V_0$, where V_0 is the volume of the pure solvent (before solute insertion at constant P). In this case the asymptotic value of the conditional density of the solvent given the position of the solute is $\rho_w^\infty \approx \rho_w^\circ(1 - \kappa kT/V)$.

Knowing the asymptotic conditional density in the CE, ρ_w^∞ , one can define a new PCF in the CE with respect to ρ_w^∞ , rather than ρ_w :

$$\rho(\mathbf{r}) \rightarrow \rho_w^\infty G_{sw}(\mathbf{r}) \quad (17)$$

The function G_{sw} is for all practical purposes identical to the GCE PCF and goes to unity at long separations whereas g_{sw} does not. We will use the notation g for the canonical PCF and G for the grand canonical or normalized canonical PCF.

The PCF in the inhomogeneous system will be labeled as such to distinguish it from the homogeneous PCF, g_{ww} , which is an average over the whole volume of the fluid:

$$g(\mathbf{r}, \mathbf{r}') \rightarrow g_{ww}^{\text{inh}}(\mathbf{r}, \mathbf{r}') \quad (18)$$

With these substitutions, eqs 12 and 13 become

$$E = \frac{3}{2}N_w kT + \rho_w^\infty \int G_{sw}(\mathbf{r}) u_{sw}(\mathbf{r}) d\mathbf{r} + \frac{1}{2}\rho_w^{\infty 2} \int G_{sw}(\mathbf{r}) G_{sw}(\mathbf{r}') g_{ww}^{\text{inh}}(\mathbf{r}, \mathbf{r}') u_{ww}(\mathbf{r}, \mathbf{r}') d\mathbf{r} d\mathbf{r}' \quad (19)$$

$$S = N_w \left(\frac{5}{2}k - k \ln(\rho_w^\infty \Lambda_s^3) \right) - k\rho_w^\infty \int G_{sw}(\mathbf{r}) \ln G_{sw}(\mathbf{r}) d\mathbf{r} - \frac{1}{2}k\rho_w^{\infty 2} \int G_{sw}(\mathbf{r}) G_{sw}(\mathbf{r}') \{ g_{ww}^{\text{inh}}(\mathbf{r}, \mathbf{r}') \ln g_{ww}^{\text{inh}}(\mathbf{r}, \mathbf{r}') - g_{ww}^{\text{inh}}(\mathbf{r}, \mathbf{r}') + 1 \} d\mathbf{r} d\mathbf{r}' \quad (20)$$

where in eq 20 and all subsequent derivations from this point on the higher order terms are omitted. Appendix A shows that the inhomogeneous description (eqs 19 and 20) and the

homogeneous description (eqs 6 and 7) of an infinitely dilute mixture are equivalent.

The partial molar energy and entropy in the inhomogeneous view are obtained by subtracting the energy and entropy of the pure, homogeneous solvent from the energy and entropy of the solution (eqs 19 and 20):

$$\bar{e}_s^\infty = \frac{3}{2}kT + \rho_w^\infty \int G_{sw} u_{sw} d\mathbf{r} + \frac{1}{2}\rho_w^{\infty 2} \int G_{sw}(\mathbf{r}) G_{sw}(\mathbf{r}') g_{ww}^{\text{inh}} u_{ww} d\mathbf{r} d\mathbf{r}' - \frac{1}{2}N_w \rho_w^\circ \int g_{ww}^\circ u_{ww} d\mathbf{r} \quad (21)$$

$$\bar{s}_s^\infty = \left(\frac{3}{2}k - \ln(\rho_s \Lambda_s^3) \right) + k\rho_w \kappa kT - k\rho_w^\infty \int G_{sw} \ln G_{sw} d\mathbf{r} - \frac{1}{2}k\rho_w^{\infty 2} \int G_{sw}(\mathbf{r}) G_{sw}(\mathbf{r}') \{ g_{ww}^{\text{inh}} \ln g_{ww}^{\text{inh}} - g_{ww}^{\text{inh}} + 1 \} d\mathbf{r} d\mathbf{r}' + \frac{1}{2}kN_w \rho_w^\circ \int \{ g_{ww}^\circ \ln g_{ww}^\circ - g_{ww}^\circ + 1 \} d\mathbf{r} \quad (22)$$

where the solute kinetic energy and one-particle entropy^{1,13} (equal to the derivative of the solute ideal entropy with respect to N_s) have been added. In eqs 21 and 22 g_{ww}° is the PCF and ρ_w° the density of pure solvent. The $k\rho_w \kappa kT$ term in eq 22 arises from the difference in the solvent ideal entropy ($kN_w \ln(\rho_w^\circ/\rho_w^\infty)$). These equations are the inhomogeneous fluid analogues of eqs 8 and 9. If we add and subtract

$$\frac{1}{2}\rho_w^{\infty 2} \int G_{sw}(\mathbf{r}) g_{ww}^\circ u_{ww} d\mathbf{r} d\mathbf{r}'$$

from the energy equation and

$$\frac{1}{2}k\rho_w^{\infty 2} \int G_{sw}(\mathbf{r}) \{ g_{ww}^\circ \ln g_{ww}^\circ - g_{ww}^\circ + 1 \} d\mathbf{r} d\mathbf{r}'$$

from the entropy equation and use the identities

$$\int G_{sw} d\mathbf{r} = V\rho_w/\rho_w^\infty \quad (23)$$

$$\lim_{V \rightarrow \infty} [N_w(\rho_w^\infty - \rho_w^\circ)] = -\rho_w^{\circ 2} \kappa kT \quad (24)$$

Equations 21 and 22 can be rewritten as

$$\bar{e}_s^\infty = \frac{3}{2}kT + \rho_w^\infty \int G_{sw} u_{sw} d\mathbf{r} + \frac{1}{2}\rho_w^{\infty 2} \int G_{sw}(\mathbf{r}) [G_{sw}(\mathbf{r}') g_{ww}^{\text{inh}} - g_{ww}^\circ] u_{ww} d\mathbf{r} d\mathbf{r}' - \frac{1}{2}\rho_w^\circ \kappa kT \rho_w^\infty \int g_{ww}^\circ u_{ww} d\mathbf{r} \quad (25)$$

$$\bar{s}_s^\infty = \left(\frac{3}{2}k - \ln(\rho_s \Lambda_s^3) \right) + k\rho_w \kappa kT - k\rho_w^\infty \int G_{sw} \ln G_{sw} d\mathbf{r} - \frac{1}{2}k\rho_w^{\infty 2} \int G_{sw}(\mathbf{r}) [G_{sw}(\mathbf{r}') \{ g_{ww}^{\text{inh}} \ln g_{ww}^{\text{inh}} - g_{ww}^{\text{inh}} + 1 \} - \{ g_{ww}^\circ \ln g_{ww}^\circ - g_{ww}^\circ + 1 \}] d\mathbf{r} d\mathbf{r}' + \frac{1}{2}k\rho_w^\circ \kappa kT \rho_w^\infty \int \{ g_{ww}^\circ \ln g_{ww}^\circ - g_{ww}^\circ + 1 \} d\mathbf{r} \quad (26)$$

In the limit of long separation from the solute, the CE inhomogeneous PCF g_{ww}^{inh} does not become exactly equal to the pure solvent PCF because of the slight difference in conditional density ($\Delta\rho = \rho_w^\infty - \rho_w^\circ = -\rho_w^\circ \kappa kT/V$).⁴¹ Therefore, we can separate the integrals involving g_{ww}^{inh} into two regions: one local around the solute, and the other in the region distant from the solute. The exact boundary between the two regions has no significance, and in the thermodynamic limit the volume of the distant region is essentially equal to the volume of the

mixture. Noting that in the distant region $G_{sw} = 1$ we obtain for the energy

$$\begin{aligned} & \frac{1}{2}\rho_w^{\infty} \int G_{sw}(\mathbf{r})[G_{sw}(\mathbf{r}')g_{ww}^{\text{inh}} - g_{ww}^{\circ}]u_{ww} \, d\mathbf{r} \, d\mathbf{r}' = \\ & \frac{1}{2}\rho_w^{\infty} \int_{\text{local}} G_{sw}(\mathbf{r})[G_{sw}(\mathbf{r}')g_{ww}^{\text{inh}} - g_{ww}^{\circ}]u_{ww} \, d\mathbf{r} \, d\mathbf{r}' + \\ & \frac{1}{2}V\rho_w^{\infty} \int_V [g_{ww}^{\text{inh}} - g_{ww}^{\circ}]u_{ww} \, d\mathbf{r} \quad (27) \end{aligned}$$

The difference between g_{ww}^{inh} and g_{ww}° at long distances from the solute is essentially due to the difference in density, therefore the last integral in eq 27 is

$$\begin{aligned} & \frac{1}{2}V\rho_w^{\infty} \frac{\partial}{\partial \rho} [\int g_{ww}^{\circ} u_{ww}] \Delta \rho = \\ & -\frac{1}{2}V\rho_w^{\infty} \frac{\partial}{\partial \rho} [\int g_{ww}^{\circ} u_{ww}] \rho_w^{\circ} \frac{\kappa kT}{V} \rightarrow -\frac{1}{2}\rho_w^{\circ 3} \kappa kT \frac{\partial}{\partial \rho} \\ & [\int g_{ww}^{\circ} u_{ww}] \quad (28) \end{aligned}$$

where the replacement of ρ_w^{∞} by ρ_w° makes a negligible difference when they multiply a quantity of $\mathcal{O}(1)$. Similarly for the entropy

$$\begin{aligned} & -\frac{1}{2}V\rho_w^{\infty} \int_V [\{g_{ww}^{\text{inh}} \ln g_{ww}^{\text{inh}} - g_{ww}^{\text{inh}} + 1\} - \\ & \{g_{ww}^{\circ} \ln g_{ww}^{\circ} - g_{ww}^{\circ} + 1\}] \, d\mathbf{r} \rightarrow \\ & \frac{1}{2}\rho_w^{\circ 3} \kappa kT \frac{\partial}{\partial \rho} [\int \{g_{ww}^{\circ} \ln g_{ww}^{\circ} - g_{ww}^{\circ} + 1\}] \quad (29) \end{aligned}$$

Using eqs 28 and 29 in eqs 25 and 26, combining the κkT -dependent terms, and replacing ρ_w^{∞} by ρ_w° for simplicity, the equations for the partial molar energy and entropy become

$$\begin{aligned} \bar{e}_s^{\infty} &= \frac{3}{2}kT + \rho_w^{\circ} \int G_{sw} u_{sw} \, d\mathbf{r} + \\ & \frac{1}{2}\rho_w^{\circ 2} \int_{\text{local}} G_{sw}(\mathbf{r})[G_{sw}(\mathbf{r}')g_{ww}^{\text{inh}} - g_{ww}^{\circ}]u_{ww} \, d\mathbf{r} \, d\mathbf{r}' - \\ & \rho_w^{\circ 2} \kappa kT \frac{\partial}{\partial \rho} [\frac{1}{2}\rho_w^{\circ} \int g_{ww}^{\circ} u_{ww}] \quad (30) \end{aligned}$$

$$\begin{aligned} \bar{s}_s^{\infty} &= (\frac{3}{2}k - \ln(\rho_s \Lambda_s^3)) + k\rho_w^{\circ} \kappa kT - k\rho_w^{\circ} \int G_{sw} \ln G_{sw} \, d\mathbf{r} - \\ & \frac{1}{2}k\rho_w^{\circ 2} \int_{\text{local}} G_{sw}(\mathbf{r})[G_{sw}(\mathbf{r}')\{g_{ww}^{\text{inh}} \ln g_{ww}^{\text{inh}} - g_{ww}^{\text{inh}} + 1\} - \\ & \{g_{ww}^{\circ} \ln g_{ww}^{\circ} - g_{ww}^{\circ} + 1\}] \, d\mathbf{r} \, d\mathbf{r}' - \\ & \rho_w^{\circ 2} \kappa kT \frac{\partial}{\partial \rho} [-\frac{1}{2}k\rho_w^{\circ} \int \{g_{ww}^{\circ} \ln g_{ww}^{\circ} - g_{ww}^{\circ} + 1\}] \quad (31) \end{aligned}$$

Following Ben-Naim,^{42,43} we consider the process of solvation as consisting of two steps, one inserting the solute at a fixed point in a solvent without thermal motion, and a second where the solute is allowed to move (“liberated”). In the first step the volume of the system changes by the excluded volume of the solute, V_{ex} . The solvent far from the solute is identical to pure solvent, with density ρ_w° and PCF g_{ww}° . In the second step the volume changes by κkT . This volume change produces a global dilution of the solvent. This effect is not localized around the solute but affects the whole body of the fluid. The conditional density far from the solute now becomes ρ_w^{∞} . In eqs 30 and 31, the solvent reorganization energy and entropy have been split into two types of terms: (a) terms that describe the effect of the solute locally on the solvent structure around it and (b) terms that describe the effect of the thermal motion of the solute on the whole body of the solvent and depend on the compressibility of the solvent. Evidently, the local terms describe the change in thermodynamic properties for the first

step in the solvation process, insertion at a fixed point, and will be referred to as “correlation” terms. The compressibility-dependent terms correspond to the change in thermodynamic properties upon “liberation” of the solute and will be referred to as “liberation” terms. Thus, the partial molar energy can be written

$$\bar{e}_s^{\infty} = E_{\text{kin}} + E_{\text{sw}} + \Delta E_{\text{ww}}^{\text{cor}} + \Delta E_{\text{ww}}^{\text{lib}} \quad (32)$$

where the terms correspond to those in eq 30 in the same order. Similarly, the partial molar entropy can be written

$$\bar{s}_s^{\infty} = S_{1p} + S_{\text{id}}^{\text{lib}} + S_{\text{sw}}^{\text{ord}} + \Delta S_{\text{ww}}^{\text{cor}} + \Delta S_{\text{ww}}^{\text{lib}} \quad (33)$$

where the terms correspond to those in eq 31 in the same order. $S_{\text{id}}^{\text{lib}}$ is the liberation contribution to the change in ideal solvent entropy and $S_{\text{sw}}^{\text{ord}}$ is the “ordering” contribution to the solute–solvent entropy. Ben-Naim’s standard energy and entropy of solvation (quite aptly called “local” standard properties)^{42,43} then correspond to

$$\begin{aligned} \Delta E^* &= E_{\text{sw}} + \Delta E_{\text{ww}}^{\text{cor}} = \rho_w^{\circ} \int G_{sw} u_{sw} \, d\mathbf{r} + \\ & \frac{1}{2}\rho_w^{\circ 2} \int_{\text{local}} G_{sw}(\mathbf{r})[G_{sw}(\mathbf{r}')g_{ww}^{\text{inh}} - g_{ww}^{\circ}]u_{ww} \, d\mathbf{r} \, d\mathbf{r}' \quad (34) \end{aligned}$$

$$\begin{aligned} \Delta S^* &= S_{\text{sw}}^{\text{ord}} + \Delta S_{\text{ww}}^{\text{cor}} = -k\rho_w^{\circ} \int G_{sw} \ln G_{sw} \, d\mathbf{r} - \\ & \frac{1}{2}k\rho_w^{\circ 2} \int_{\text{local}} G_{sw}(\mathbf{r})[G_{sw}(\mathbf{r}')\{g_{ww}^{\text{inh}} \ln g_{ww}^{\text{inh}} - g_{ww}^{\text{inh}} + 1\} - \\ & \{g_{ww}^{\circ} \ln g_{ww}^{\circ} - g_{ww}^{\circ} + 1\}] \, d\mathbf{r} \, d\mathbf{r}' \quad (35) \end{aligned}$$

and the liberation terms correspond to

$$e^{\text{lib}} = E_{\text{kin}} + \Delta E_{\text{ww}}^{\text{lib}} = \frac{3}{2}kT - \rho_w^{\circ 2} \kappa kT \frac{\partial}{\partial \rho} [\frac{1}{2}\rho_w^{\circ} \int g_{ww}^{\circ} u_{ww}] \quad (36)$$

$$\begin{aligned} s^{\text{lib}} &= S_{1p} + S_{\text{id}}^{\text{lib}} + \Delta S_{\text{ww}}^{\text{lib}} = (\frac{3}{2}k - \ln(\rho_s \Lambda_s^3)) + k\rho_w^{\circ} \kappa kT - \\ & \rho_w^{\circ 2} \kappa kT \frac{\partial}{\partial \rho} [-\frac{1}{2}k\rho_w^{\circ} \int \{g_{ww}^{\circ} \ln g_{ww}^{\circ} - g_{ww}^{\circ} + 1\}] \quad (37) \end{aligned}$$

Note that the liberation terms depend only on the properties of the pure solvent and not on the nature of the solute–solvent interactions. The significance of eqs 34 and 35 is that they provide an explicit connection between the solvation energy and entropy and the structure of the solvent around the solute (the pair correlation functions).

The second integral in eq 34 is equivalent to the equation for the solvent reorganization energy given by Matubayasi et al.²⁵ in terms of the binding energy of solvent molecules in the solvation shell and in the bulk. They also give, without derivation, an equation for the entropy similar to the second integral of eq 35, except for the absence of the $(-G + 1)$ terms. No liberation terms were derived by these authors. As will be shown in the next section, these terms are negligible for common liquids at room temperature but are significant under conditions of high compressibility, as in gases or near the critical point.

III. Numerical Tests in Simple Ideal Solutions

One instructive case where the solvent reorganization energy and entropy contributions are known exactly is a solution where solute and solvent have identical molecular properties, i.e., an ideal solution. In fact, one can consider solvation of a particle in its own pure fluid. The newly inserted particle is considered to be the “solute”, and the rest of the particles comprise the

“solvent”. This “mixture” is equivalent to a pure fluid with $N + 1$ particles. The “solvent–solvent” potential energy in the “mixture” is $(N + 1)e^{\text{ex}}$ minus the binding energy of the “solute” (the interaction energy of the “solute” with the rest of the system), which is equal to $2e^{\text{ex}} = \rho f g u \, \text{dr}$. The “solvent–solvent” energy before “solute” insertion is Ne^{ex} . Therefore, the change in “solvent–solvent” energy is

$$\Delta E_{\text{ww}} = \{(N + 1)e^{\text{ex}} - 2e^{\text{ex}}\} - Ne^{\text{ex}} = -e^{\text{ex}} = -\frac{1}{2}\rho f g u \, \text{dr} = -\frac{1}{2}E_{\text{sw}} \quad (38)$$

Similarly, the solvent reorganization entropy is equal to one-half of the solute–solvent entropy and opposite in sign:

$$\Delta S_{\text{ww}} = -s^{(2)} = \frac{1}{2}k\rho f(g \ln g - g + 1) \, \text{dr} = -\frac{1}{2}S_{\text{sw}} \quad (39)$$

In this section the inhomogeneous expressions for the solvent reorganization energy and entropy (eqs 30 and 31) are applied to ideal infinitely dilute hard sphere and Lennard-Jones mixtures (solute identical to the solvent), and the results are compared to the excess molar energy and two-particle entropy in eqs 2 and 3–5. For the calculations we need the inhomogeneous PCF at short range, $g_{\text{ww}}^{\text{inh}}$. For now, we assume that $g_{\text{ww}}^{\text{inh}} = g_{\text{ww}}^{\circ}$, which is equivalent to the KSA (eq A5). Thus, for a pure fluid all pair correlations in eqs 30 and 31 are identical:

$$\begin{aligned} \Delta E_{\text{ww}} &= \frac{1}{2}\rho^2 \int G(\mathbf{r})[G(\mathbf{r}') - 1]G(\mathbf{r}, \mathbf{r}') u(\mathbf{r}, \mathbf{r}') \, \text{dr} \, \text{dr}' - \\ &\quad \rho^2 \kappa kT \frac{\partial}{\partial \rho} \left[\frac{1}{2}\rho \int G u \right] \quad (40) \\ \Delta S_{\text{ww}} &= -\frac{1}{2}k\rho^2 \int G(\mathbf{r})[G(\mathbf{r}') - 1]\{G(\mathbf{r}, \mathbf{r}') \ln G(\mathbf{r}, \mathbf{r}') - \\ &\quad G(\mathbf{r}, \mathbf{r}') + 1\} \, \text{dr} \, \text{dr}' - \rho^2 \kappa kT \frac{\partial}{\partial \rho} \left[-\frac{1}{2}k\rho \int \{G \ln G - \right. \\ &\quad \left. G + 1\} \right] \quad (41) \end{aligned}$$

As input to the above equations we used the radial distribution functions (RDF) obtained from the Percus–Yevick (PY) integral equation for HS^{44,45} and LJ⁴⁶ fluids at a number of thermodynamic states. Of course, we could have used RDFs from any other source, such as simulations. For the compressibility we used the Carnahan–Starling equation of state (EOS) for HS⁴⁷ and a recent empirical EOS for the LJ fluid.⁴⁸ We then performed numerical evaluation of the integrals in eqs 40 and 41. The RDFs are truncated at the point (R_c) that most closely satisfies the compressibility equation. The cutoffs used for the systems studied are for HS 3.4, 3.5, 5.3, 5.75, 5.7 for $\rho^* = 0.1, 0.3, 0.5, 0.7, 0.9$, respectively, and for LJ 6.0, 6.0, and 5.25 for $\rho^* = 0.1, 0.5$, and 0.85 , respectively. One-particle integrals for the spherically symmetric solutes considered here are trivially transformed into one-dimensional integrals ($\int \text{dr} \rightarrow \int_0^{R_c} 4\pi r^2 \, \text{dr}$). Two particle integrals are evaluated using bipolar coordinates ($\int \text{dr} \, \text{dr}' \rightarrow 4\pi \int_{r_2}^{2R_c} \text{dr} (2\pi/r) \int_0^{R_c} \text{ds} \int_{|r-s|}^{r+s} t \, \text{dt}$). Integration over r is carried out up to $2R_c$ because only at that distance the second particle (\mathbf{r}') becomes uncorrelated from the “fixed” solute. All integrations were carried out with the extended trapezoidal rule and an increment of 0.05 dimensionless units.

The results for the HS fluid at different densities are given in Table 1. The “exact” entropy, calculated based on the Carnahan–Starling EOS⁴⁹

$$s^{\text{ex}} = -k\eta(4 - 3\eta)/(1 - \eta)^2 \quad (42)$$

TABLE 1: Solvent Reorganization Entropies for the Hard-Sphere Fluid^a

1 ρ^*	2 s^{ex}	3 $s^{(2)}$	4 $\Delta S_{\text{ww}}^{\text{cor}}$	5 $\Delta S_{\text{ww}}^{\text{lib}}$	6 tot ΔS_{ww}
0.1	−0.224	−0.21	0.04	0.14	0.18
0.3	−0.780	−0.67	0.24	0.23	0.47
0.5	−1.544	−1.28	0.65	0.24	0.89
0.7	−2.649	−2.25	1.60	0.26	1.86
0.9	−4.359	−4.27	3.42	0.30	3.72

^a 2. The “exact” excess entropy calculated by the Carnahan–Starling EOS (eq 42). 3. The two-particle contribution to the excess entropy. 4. The correlation contribution to the solvent reorganization entropy. 5. The liberation contribution to the solvent reorganization entropy. 6. Total solvent reorganization entropy. Should be compared to $-s^{(2)}$. All values in k units.

where η is the packing fraction ($\pi\rho^*/6$, $\rho^* = \rho\sigma^3$, where σ is the hard-sphere diameter), is also given to see the level of agreement with the calculated two-particle contribution. The deviation between these two quantities is largest at intermediate density (17% error) and decreases for both low and high density (6% and 3%, respectively).

The liberation contributions can be calculated based on eq 31 and using the compressibility from the Carnahan–Starling EOS. To determine the density derivative of the entropy integral required for the liberation contribution, the values of this integral using the PY RDFs as a function of density were fitted to a polynomial and the derivative was taken analytically.

An alternative way to calculate the liberation contributions is through the thermodynamic relation

$$\begin{aligned} \frac{\partial S}{\partial V} \kappa kT &= \left[\frac{\partial S^{\text{id}}}{\partial V} + \frac{\partial S^{\text{ex}}}{\partial V} \right] \kappa kT = kT\alpha \Rightarrow \\ \frac{\partial S^{\text{ex}}}{\partial V} \kappa kT &= k(T\alpha - \rho \kappa kT) \quad (43) \end{aligned}$$

and the EOS values for the thermal expansion coefficient α and the compressibility κ . However, the latter method gives the liberation contribution to the exact excess entropy rather than to the two-particle contribution alone. The values of eq 43 are similar to those obtained from the density derivative of the entropy integral (not shown).

As shown in Table 1, the values of the liberation contribution calculated using the EOS compressibility and the density derivative of the PY correlation functions vary modestly with density. The correlation contribution, on the other hand, is small at low densities and increases rapidly with density. As a result, the liberation term is dominant at low densities and the correlation term is dominant at high densities. The sum of the correlation term and the liberation term is close to minus the two-particle entropy, as it should, but systematically smaller in magnitude. The deviation is largest at intermediate density (about 30%) and decreases at both low and high density (14 and 12%, respectively), just like the deviation of the two-particle entropy from the total excess entropy. Appendix B clarifies the source of this discrepancy between ΔS_{ww} and $-s^{(2)}$.

The same HS systems were studied with a perturbation potential of the LJ type:

$$u/kT = 4(r^{*-12} - r^{*-6}) \quad (44)$$

where $r^* = r/\sigma$. The excess molar energy at the first-order perturbation theory level is

$$e^{\text{ex}} = \frac{1}{2}\rho f g^{\text{HS}} u \, \text{dr} \quad (45)$$

TABLE 2: Solvent Reorganization Energies for the Perturbed Hard-Sphere Fluid^a

1 ρ^*	2 e_{ex}	3 $\Delta E_{\text{ww}}^{\text{cor}}$	4 $\Delta E_{\text{ww}}^{\text{lib}}$	5 total ΔE_{ww}
0.1	-0.56	0.17	0.39	0.56
0.3	-1.83	1.22	0.61	1.83
0.5	-3.32	2.82	0.51	3.33
0.7	-4.83	4.42	0.26	4.68
0.9	-6.19	4.80	0.004	4.80

^a 2. The excess molar energy (eq 45). 3. The correlation contribution to the solvent reorganization energy. 4. The liberation contribution to the solvent reorganization energy. 5. Total solvent reorganization energy. Should be compared to $-e^{\text{ex}}$. All values in kT units. No long-range corrections included.

TABLE 3: Solvent Reorganization Entropies for the Lennard-Jones Fluid^a

1 ρ^*	2 T^*	3 s^{ex}	4 $s^{(2)}$	5 $\Delta S_{\text{ww}}^{\text{cor}}$	6 $\Delta S_{\text{ww}}^{\text{lib}}$	7 tot ΔS_{ww}
0.1	1.2	-0.32	-0.33	-0.69	0.99	0.30
0.5	1.4	-1.36	-1.17	-0.13	1.58	1.45
0.85	0.88	-3.44	-3.28	2.57	0.28	2.85

^a 3. The "exact" excess entropy calculated by the LJ EOS.⁴⁸ 4. The two-particle contribution to the excess entropy. 5. The correlation contribution to the solvent reorganization entropy. 6. The liberation contribution to the solvent reorganization entropy. 7. Total solvent reorganization entropy. Should be compared with $-s^{(2)}$. All values in k units.

TABLE 4: Solvent Reorganization Energies for the Lennard-Jones Fluid^a

1 ρ^*	2 T^*	3 e^{ex} (EOS)	4 e^{ex} (PY)	5 $\Delta E_{\text{ww}}^{\text{cor}}$	6 $\Delta E_{\text{ww}}^{\text{lib}}$	7 tot ΔE_{ww}
0.1	1.2	-0.69	-0.70	-1.38	2.05	0.67
0.5	1.4	-2.40	-2.39	0.41	2.15	2.56
0.85	0.88	-7.26	-6.55	5.33	0.25	5.58

^a 3. The excess molar energy from the EOS.⁴⁸ 4. The excess molar energy from the PY radial distribution functions. 5. The correlation contribution to the solvent reorganization energy. 6. The liberation contribution to the solvent reorganization energy. 7. Total solvent reorganization energy. Should be compared to $-e^{\text{ex}}$ (PY). All values in kT units.

The liberation contribution was calculated using the density derivative of the PCF. The results are shown in Table 2. As for the entropy, the liberation term is dominant at low densities and the correlation term at higher densities. The total solvent reorganization energy agrees very well with $-e^{\text{ex}}$ at low densities but deviates from it at higher densities due to the KSA (see Appendix B).

Tables 3 and 4 show the results for the LJ fluid at three thermodynamic states. The EOS can be used to obtain the excess energy, entropy, and chemical potential. The two-particle entropy calculated using the PY RDF is in quite good agreement with the excess entropy from the EOS. The deviation is largest at the intermediate density. The excess energy from the PY RDFs is in good agreement with that from the EOS for the two lower densities but is smaller in magnitude at the highest density.

It is interesting that the correlation contributions in Tables 3 and 4 at low density are actually negative. This is due to the overall attraction of the "solvent" molecules to the "solute" (the "excluded volume" integral of eq 10 here is negative) which increases the interactions and correlations among the solvent molecules. The liberation contributions were calculated by using data from the EOS and eq 43, along with the correspond-

ing equation for the energy:

$$\frac{\partial E^{\text{ex}}}{\partial V} \kappa T = kT(T\alpha - \kappa P) \quad (46)$$

This term is found to be largest for the intermediate density—high temperature state. As for the HS systems, the total solvent reorganization energy and entropy agree well with $-e^{\text{ex}}$ and $-s^{(2)}$, respectively, at low density but deviate from them at higher densities.

The calculations presented here show the relative importance of the correlation and liberation terms under different conditions. The liberation terms correspond to the change in energy and entropy upon the slight expansion of the solvent caused by the thermal motion of the solute. Their sign is the same as the sign of the derivative of E and S with respect to the volume, usually positive. For common liquid solvents the liberation terms are negligible. For example, for water at room temperature, the liberation energy and entropy are calculated from eqs 43 and 46 to be 46 cal/mol and 0.03 cal/mol K, respectively. The correlation terms are also usually positive, reflecting the excluded volume effect of the solute; i.e., the solute breaks some of the solvent—solvent interactions and correlations. The correlation terms dominate at high densities. Numerically, eqs 40 and 41 give reasonable values, but the KSA introduces some error at high densities (see Appendix B).

IV. Discussion

Until now solvation thermodynamics has been analyzed in the standard, homogeneous view of solutions. Because of the lack of precision of free energy simulations, this analysis has been carried out mostly by integral equation methods.^{33,35,57,58} The correlation functions appearing in these theories are defined with respect to the overall densities and are averages over the whole body of the fluid. Therefore, it is difficult to isolate the effects of solvent structural perturbation in the vicinity of the solute, and one cannot take advantage of the fact that far from the solute we have essentially pure, unperturbed solvent. This can be accomplished by treating the solution as an inhomogeneous system.

In this paper expressions for the energy and entropy of solvation have been developed taking the inhomogeneous view and using the KSA for the truncation of the entropy expansion at the two-particle level. The expressions include a solute—solvent term, which depends on the one-particle distribution of the solvent around the solute and a solvent reorganization term, describing the change in solvent—solvent interactions and correlations when the solute is inserted and which depend on the two-particle distribution of the solvent around the solute. The solvent reorganization terms contain contributions from the structural effect of the solute on the solvent ("correlation" terms) and terms that depend on the compressibility and that arise from the dilution of solvent—solvent interactions and correlations due to the thermal motion of the solute ("liberation" terms). The correlation terms are local, i.e., they depend on the structure of the solvent in the vicinity of the solute and are dominant at high densities (liquidlike states). The liberation terms are nonlocal, i.e., they arise from changes in the whole body of the fluid. The liberation contributions to the solvation energy and entropy are independent of the solute—solvent interaction potential or the size of the solute. They are the same for every solute in a given solvent. They are, in a sense, "trivial" terms. However, they become dominant at low densities (gaslike states)

and need to be considered when comparison is made to experimental data.

For common solvents the nonlocal, liberation terms are negligible. The other nonlocal term in the excess chemical potential is the PV term, which is also negligible for common solvents. Therefore, for these solvents one can practically think of the solvation properties arising entirely from effects localized in the vicinity of the solute. Since both the solute–solvent and solvent–solvent terms are integrals over space, one can determine contributions from each region of space around the solute, for example, the first solvation shell, the second solvation shell, etc. This provides a theoretical justification for empirical “hydration shell” models of solvation.^{25,26,59,60} The expressions derived here provide a practical means of calculating solvent reorganization contributions and allow a detailed analysis of the contribution of solvent structure in each region of space to the solvation energy and entropy.

In a recent study Cann and Patey⁵⁸ indirectly separated the local from nonlocal contributions to the solvation energy and entropy by comparing the scaling of these properties with solute volume, surface, and diameter under constant volume and constant pressure solute insertion. Specifically, they estimated the nonlocal terms from the difference of the surface- and diameter-dependent terms at constant volume and at constant pressure. They concluded that nonlocal contributions in their liquidlike solvents are very important, even for constant pressure solvation. This is in sharp contrast to the conclusions of the present work. The discrepancy may be due to the fact that these authors use the molecular volume ($\pi\sigma^3/6$) instead of the excluded volume (V_{ex}) to isolate the nonlocal contribution at constant volume. Because the molecular volume is normally smaller than V_{ex} , some of the (global) solvent compression effects are inappropriately attributed to the (local) surface and diameter terms. This results in estimates of the local contributions at constant volume that are too negative.

The formulas have been numerically tested on simple hard-sphere and Lennard-Jones fluids at various thermodynamic states. The fact that the solvent reorganization energy and entropy for a pure fluid are equal to one-half of the solute–solvent term and opposite in sign was used as a consistency check for the method. This test is approximately satisfied at high densities when the KSA is employed. It appears that the KSA underestimates the solvent reorganization energy and entropy in the systems studied. Appendix B shows that if the liberation terms are calculated self-consistently within the KSA, this test is satisfied exactly.

The use of the inhomogeneous formalism allows us to take the limit of the solute to a macroscopic surface. In this case, the excess solvation energy and entropy, per surface area, become equal to the interfacial energy and entropy. The use of the same expressions for microscopic and macroscopic solvation should facilitate our understanding of the similarities and differences between the two phenomena. This is of interest since attempts have been made to use surface tension data to elucidate aspects of aqueous solvation of nonpolar solutes.⁵² The inhomogeneous approach is also more convenient in extrapolating results from small molecule solvation to larger molecules. Specifically, it can be used to define group contributions to the solvation properties (unpublished work).

On the basis of thermodynamic and statistical mechanical arguments, it has been argued that changes in “solvent structure” may influence the energy and entropy but not the free energy of solvation.^{53–56} In the present work the solvent reorganization energy and entropy partly compensate but certainly do not cancel

each other out. We can see this most clearly for the case of an ideal solution or a pure fluid, where the solvent reorganization energy and entropy are known to be exactly equal to minus the molar energy and entropy. Cancellation of these quantities would mean that the molar free energy of any pure fluid is zero, which is clearly untenable.

The difference between the present results and the conclusions of refs 53–56 is a question of physical interpretation. In various statistical mechanical derivations, the solvent reorganization energy appears in the expressions for both the solvation energy and entropy but cancels out in the expression for the free energy.^{33,61} However, the solvent–solvent energy is implicit in the Boltzmann factors that determine the ensemble averages. The fact that a term does not contribute *formally* to the free energy in one theory does not mean that it does not contribute *physically* and that it cannot appear explicitly in a different theory.

In the test particle approach the expression for the excess chemical potential contains an ensemble average over the unperturbed solvent, whereas the expressions for the energy and entropy also contain averages over the system after solute insertion.^{53,61} On the basis of this, Ben-Naim argued that the free energy depends on the *structure* of the solvent and not on *structural changes* in the solvent. However, insertion probability actually depends on both the average structure and the structural fluctuations of the solvent. Of course, fluctuations and changes are related: what is a structural *fluctuation* in the pure solvent becomes a structural *change* after solute insertion. Thus, structural “changes” implicitly make their contribution to the free energy in the test particle method. Further, mixture-type ideas of solvent structure^{54–56} are a rather limited definition of structure.⁶²

Ashbaugh and Paulaitis,¹⁵ using the same correlation expansion for the entropy that is used here, argued that the solvent reorganization energy and entropy exhibit complete cancellation. They used Mayer cluster expansions of the correlation functions and showed that energy–entropy cancellation holds up to third order in density. However, this does not constitute a proof that cancellation will hold at liquidlike densities. Further, in the test particle analysis the authors performed at liquidlike densities the definition of solvent reorganization entropy in that analysis may not necessarily correspond to the definition based on the change in the solvent–solvent correlation functions (eq 9). Cancellation of the solvent reorganization energy and entropy in the low-density limit is also obtained in the present work. In the low density limit $G = \exp(-u/kT)$ and it is easy to show that

$$\Delta E_{\text{ww}} - T\Delta S_{\text{ww}} + (PV)^{\text{ex}} = -\frac{1}{2}E_{\text{sw}} + \frac{1}{2}TS_{\text{sw}} + \frac{kT((P/\rho kT) - 1)}{kT} = 0 \quad (47)$$

if the virial expansion for the pressure is used, truncated at the second term. However, complete cancellation does not take place at higher densities.

In the pure simple systems studied here use has been made of the accurate EOS of these systems for (a) evaluation of the liberation contributions and (b) calculation of reliable values of the excess energy and entropy. Since such information is not available for most practical systems of interest, the validity of the results obtained will have to be confirmed by comparison to free energy simulations and experiment. In addition, liberation terms in such systems are negligible and, if wanted, could be estimated using the experimental compressibility for the solvent. The following paper presents applications of the present

method to infinitely dilute HS and LJ mixtures of varying size ratio. Application to methane in water will be presented in a forthcoming publication.

Appendix A

Here we show that the two descriptions for the mixture of $N_s = 1$ solute and N_w solvent molecules, the homogeneous description (eqs 6 and 7 with $N_s = 1$ and $\rho_s \rightarrow 0$) and the inhomogeneous one (eqs 19 and 20) are equivalent. In the inhomogeneous description the solute is not considered part of the system whose energy and entropy are written down but merely provides the external field. Therefore, the kinetic energy ($3/2 kT$) and the ideal entropy of the solute ($5/2 k - k \ln(\rho_s \Lambda_s^3)$) do not appear in eqs 19 and 20. For the same reason, the solute–solvent excluded volume term ($\int (-G_{sw} + 1) d\mathbf{r}$) does not appear in the inhomogeneous entropy expression. However, the lack of this term is compensated by the fact that the solvent densities appearing in the ideal solvent entropy terms in the two equations are different; ρ_w is N_w/V , whereas ρ_w^∞ is the asymptotic value of the conditional pair density equal to $N_w/(V_0 + \kappa KT) = N_w/(V - V_{ex})$, where V is the volume of the mixture and V_0 the volume of the pure solvent before solute insertion. Thus, the difference in the ideal solvent entropy terms in eqs 7 and 20 is

$$-kN_w \ln \frac{\rho_w^\infty}{\rho_w} = -k\rho_w V \ln \left(1 - \frac{V_{ex}}{V}\right) \xrightarrow{V \rightarrow \infty} k\rho_w V_{ex} = k\rho_w \int (1 - G_{sw}) d\mathbf{r} \quad (A1)$$

When this extra term is taken into account, the solute–solvent entropy in the inhomogeneous and homogeneous expressions become identical. The difference between ρ_w and ρ_w^∞ is negligible in the solute–solvent terms of eqs 6, 7, 19, and 20 because they multiply a quantity of $\mathcal{O}(1)$.

To see the correspondence between the homogeneous and inhomogeneous expressions for the solvent–solvent terms, we need the connection between the inhomogeneous PCF and the homogeneous three-particle correlation function. The probability of finding two particles at \mathbf{r}, \mathbf{r}' in the inhomogeneous system (given that the “source” particle is at the origin) is

$$\rho(\mathbf{r}) \rho(\mathbf{r}') g_{ww}^{\text{inh}} = \rho_w^2 g_{sw}(\mathbf{r}) g_{sw}(\mathbf{r}') g_{ww}^{\text{inh}}(\mathbf{r}, \mathbf{r}') = \rho_w^2 G_{sw}(\mathbf{r}) G_{sw}(\mathbf{r}') g_{ww}^{\text{inh}}(\mathbf{r}, \mathbf{r}') \quad (A2)$$

This probability in the homogeneous system is given by the triplet correlation function

$$\rho_w^2 g_{sww}^{(3)}(\mathbf{0}, \mathbf{r}, \mathbf{r}') \quad (A3)$$

Therefore

$$g_{sww}^{(3)}(\mathbf{0}, \mathbf{r}, \mathbf{r}') = g_{sw}(\mathbf{r}) g_{sw}(\mathbf{r}') g_{ww}^{\text{inh}}(\mathbf{r}, \mathbf{r}') \quad (A4)$$

Using the definition of $\delta g^{(3)}$ (eq 1), we also see that

$$g_{ww}^{\text{inh}}(\mathbf{r}, \mathbf{r}') = g_{ww}(\mathbf{r}, \mathbf{r}') \delta g^{(3)}(\mathbf{0}, \mathbf{r}, \mathbf{r}') \quad (A5)$$

The homogeneous expressions for the solvent–solvent energy and entropy in eqs 6 and 7 are obtained by substituting eqs A4 and A5 into eqs 19 and 20 using the CE identities

$$g_{ww} = 1/V \int g_{sww} d\mathbf{r}_s \quad \rho_w^\infty \int G_{sw} d\mathbf{r} = N_w \quad (A6)$$

For the entropy, the inhomogeneous two-particle term gives rise

to the homogeneous two-particle and the logarithmic three-particle term:

$$-1/2 k \rho_w^2 \int g_{sww}^{(3)} \ln \delta g^{(3)} d\mathbf{r} d\mathbf{r}' \quad (A7)$$

To obtain perfect correspondence between the two approaches, we could replace $g_{ww}^{\text{inh}} \ln g_{ww}^{\text{inh}}$ in eq 20 by $g_{ww}^{\text{inh}} \ln g_{ww}$.

Appendix B

Here we perform an alternative calculation of the liberation term using an explicit expression for the long range value of $\delta g^{(3)}$. For an infinitely dilute mixture of s in w ($N_s = 1$), the limiting value of the conditional density of s given the position of a solvent molecule is

$$\rho_s g_{sw} \rightarrow 1/(V - V_{ex}) \quad (B1)$$

where V_{ex} is the solute–solvent excluded volume ($\int (1 - G_{sw}) d\mathbf{r}_s$) and $\rho_s = 1/V$. Therefore, to order $\mathcal{O}(1/V^2)$, the limiting value of g_{sw} is

$$g_{sw} \rightarrow \frac{1}{1 - V_{ex}/V} = 1 + \frac{V_{ex}}{V} + \frac{V_{ex}^2}{V^2} \quad (B2)$$

Similarly, the conditional density of s given the position of two solvent particles is

$$\rho_s g_{slww} \rightarrow 1/(V - V_{ex2}) \quad (B3)$$

where $V_{ex2} = \int (1 - G_{s|ww}) d\mathbf{r}_s$ is the excluded volume between the solute and two solvent molecules (a function of the distance between the solvent molecules). Therefore,

$$g_{slww} \rightarrow 1 + \frac{V_{ex2}}{V} + \frac{V_{ex2}^2}{V^2} \quad (B4)$$

Since

$$g_{s|ww} = g_{sw} g_{sw} \delta g^{(3)} \quad (B5)$$

the long-range behavior of $\delta g^{(3)}$ in the limit of s being far from two solvent molecules can be deduced from eqs B2 and B4:

$$\delta g^{(3)} \rightarrow 1 + \frac{V_{ex2} - 2V_{ex}}{V} + \frac{(V_{ex2} - V_{ex})^2}{V^2} \quad (B6)$$

Using the long-range value of $\delta g^{(3)}$ (eq B6), the last integral in eq 27 becomes

$$1/2 V \rho_w^2 \int (\delta g^{(3)} - 1) g_{ww}^\circ u_{ww} d\mathbf{r} = 1/2 \rho_w^2 \int (V_{ex2} - 2V_{ex}) g_{ww}^\circ u_{ww} d\mathbf{r} \quad (B7)$$

where $g_{ww} = g_{ww}^\circ$ when the solute is identical to the solvent. The result for the entropy is similar:

$$-1/2 k V \rho_w^2 \int [g_{ww}^{\text{inh}} \ln g_{ww}^{\text{inh}} - g_{ww}^{\text{inh}} + 1] - [g_{ww}^\circ \ln g_{ww}^\circ - g_{ww}^\circ + 1] d\mathbf{r} = -1/2 k \rho_w^2 \int (V_{ex2} - 2V_{ex}) g_{ww}^\circ \ln g_{ww}^\circ d\mathbf{r} \quad (B8)$$

The two types of expressions for the long-range contribution (eqs B7 and B8 vs eqs 28 and 29) are equivalent by virtue of the relationship between the triplet correlation function and the

TABLE 5: Self-Consistent Calculation of Liberation Entropy for the Hard-Sphere Fluid^a

1	2	3	4	5	6
ρ^*	ΔS_{ww}^{cor}	$-\rho^* \kappa k T s^{(2)}$	$\int \Delta(g \ln g - g)$	$1/2 \rho^* s^2 V_{ex}^2$	tot ΔS_{ww}
0.1	0.036	0.139	-0.025	0.057	0.21
0.3	0.24	0.197	-0.020	0.250	0.67
0.5	0.65	0.169	0.064	0.376	1.26
0.7	1.60	0.128	0.071	0.452	2.25
0.9	3.42	0.098	0.081	0.490	4.09

^a 2. The correlation contribution to the solvent reorganization entropy. 3. One contribution to the liberation entropy (last term of eq 26). 4. The other liberation contribution, eq B8 and the first term of eq B12 ($\Delta = V_{ex2} - 2V_{ex}$). 5. The second term in eq B12. 6. Total solvent reorganization entropy, the sum of columns 2–5. Should be compared to $-s^{(2)}$ in Table 1. All values in k units.

isothermal density derivative of the PCF:^{50,51}

$$\frac{1}{G_{12}} \frac{\partial G_{12}}{\partial \rho} \rho \kappa k T = \int (G_{13} - 1)(G_{23} - 1) d\mathbf{r}_3 + \int G_{13} G_{23} (\delta G^{(3)} - 1) d\mathbf{r}_3 \quad (\text{B9})$$

which, using the compressibility equation, can be rewritten as

$$\frac{1}{G_{12}} \frac{\partial G_{12}}{\partial \rho} \rho \kappa k T = \int [G_{13} G_{23} \delta G^{(3)} - 1] d\mathbf{r}_3 - 2\kappa k T + 2/\rho = -(V_{ex2} - 2V_{ex}) \quad (\text{B10})$$

Equations B7 and B8 have the advantage of giving self-consistent results. That is, the KSA that is employed in the calculation of the correlation terms is also employed for the calculation of V_{ex2} in eq B8.

As mentioned in Appendix A, the solvent–solvent term in the inhomogeneous entropy expression corresponds to the homogeneous solvent–solvent term plus the homogeneous logarithmic three-particle term ($\int g^{(3)} \ln g^{(3)}$). Exact correspondence to the homogeneous two-particle term is obtained if this term is subtracted from the results. The value of this contribution at long range can be calculated knowing the asymptotic behavior of $\delta g^{(3)}$ in the CE (eq B6) and it is:

$$-1/2 \kappa \rho_w^2 \int g_{ww}^o \left(1 + \frac{V_{ex2} - 2V_{ex}}{V} + \frac{(V_{ex2} - V_{ex})^2}{V^2} \right) \times \left(\frac{V_{ex2} - 2V_{ex}}{V} + \frac{(V_{ex2} - V_{ex})^2}{V^2} \right) d\mathbf{r} d\mathbf{r}' \quad (\text{B11})$$

The term $\mathcal{Q}(1/V^2)$ contributes only for large distances between the solvent molecules, where $V_{ex2} = 2V_{ex}$. The final result is

$$-1/2 \kappa \rho_w^2 \int g_{ww}^o (V_{ex2} - 2V_{ex}) d\mathbf{r} - 1/2 \kappa \rho_w^2 V_{ex}^2 \quad (\text{B12})$$

The first term in eq B12 was found to largely compensate with the term in eq B8, therefore they are listed together in Table 5. The second term varies from 0 (low density limit) to $-1/2 \kappa$ (incompressible fluid limit). The calculation of V_{ex2} was done using the KSA ($G_{s|ww} = G_{sw} G_{sw}$).

As can be seen in Table 5, if the liberation terms are calculated self-consistently and the long-range logarithmic three-particle term is subtracted, the total solvent reorganization entropy is in excellent agreement with $-s^{(2)}$. Only at the highest density a deviation of 4% is observed.

The energy results for the perturbed hard spheres are shown in Table 6. At high density, eq B7 gives values significantly larger than those expected from the density derivative of the

TABLE 6: Self-Consistent Calculation of Liberation Energy for Perturbed Hard-Sphere Fluid^a

1	2	3	4	5
ρ^*	ΔE_{ww}^{cor}	$-\rho \kappa k T e^{ex}$	$\int \Delta g u$	tot ΔE_{ww}
0.1	0.17	0.37	0.019	0.559
0.3	1.22	0.54	0.069	1.829
0.5	2.82	0.44	0.047	3.307
0.7	4.42	0.24	0.157	4.817
0.9	4.80	0.03	1.376	6.206

^a 2. The correlation contribution to the solvent reorganization energy. 3. One contribution to the liberation energy, last term of eq 25. 4. The other liberation contribution calculated from eq B7 ($\Delta = V_{ex2} - 2V_{ex}$). 5. Total solvent reorganization energy, the sum of columns 2, 3, and 4. Should be compared to $-e^{ex}$ in Table 2. All values in kT units. No long-range corrections included.

TABLE 7: Self-Consistent Calculation of the Liberation Entropy for the Lennard-Jones Fluid^a

1	2	3	4	5	6	7
ρ^*	T^*	ΔS_{ww}^{cor}	$-\rho^* \kappa k T s^{(2)}$	$\int \Delta(g \ln g - g)$	$1/2 \rho^* s^2 V_{ex}^2$	tot ΔS_{ww}
0.1	1.2	-0.69	0.951	-1.715	1.770	0.316
0.5	1.4	-0.13	0.989	0.284	0.012	1.155
0.85	0.88	2.57	0.060	0.313	0.482	3.425

^a 3. The correlation contribution to the solvent reorganization entropy. 4. One contribution to the liberation entropy, last term of eq 26. 5. The other liberation contribution, eq B8 and first term of eq B12. 6. The second term in eq B12. 7. Total solvent reorganization entropy, the sum of columns 3–6. Should be compared to $-s^{(2)}$ in Table 3. All values in k units.

TABLE 8: Self-Consistent Calculation of Liberation Energy for the Lennard-Jones Fluid^a

1	2	3	4	5	6
ρ^*	T^*	ΔE_{ww}^{cor}	$-\rho^* \kappa k T e^{(2)}$	$\int \Delta g u$	tot ΔE_{ww}
0.1	1.2	-1.38	2.017	0.060	0.697
0.5	1.4	0.41	2.019	-0.040	2.389
0.85	0.88	5.33	0.121	1.089	6.540

^a 3. The correlation contribution to the solvent reorganization energy. 4. One contribution to the liberation energy, last term of eq 25. 5. The other liberation contribution, eq B7. 6. Total solvent reorganization energy, the sum of columns 3–5. Should be compared to $-e^{ex}$ (PY) in Table 4. All values in kT units.

RDF (Table 2). This is probably due to overestimation of the structure of the function $V_{ex2} - 2V_{ex}$ by the KSA. When the KSA is used in both the calculation of ΔS_{ww}^{cor} and V_{ex2} , the total solvent reorganization energy calculated is in close agreement with the expected value, $-e^{ex}$.

Similar results are obtained for the LJ systems. Use of eqs B7 and B8 and subtraction of the long-range logarithmic three-particle contribution for the entropy (eq B12) gives values for the solvent reorganization energy and entropy in good agreement with $-e^{ex}$ and $-s^{(2)}$. The solvent reorganization energy is very accurate for all three thermodynamic states and the solvent reorganization entropy exhibits only a 4% deviation from $-s^{(2)}$ at the highest density.

Thus, the deviations of the calculated solvent reorganization terms from $-e^{ex}$ or $-s^{(2)}$ are due to the KSA and the inclusion of the homogeneous logarithmic three-particle term in the inhomogeneous two-particle term for the entropy. When the liberation terms are calculated self-consistently (using the KSA) and the long-range logarithmic term is subtracted, very good agreement is obtained with the expected values.

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