ELSEVIER

Biophysical Chemistry 51 (1994) 349-357

Biophysical
Chemistry

The entropy of hydration of simple hydrophobic solutes

Michael E. Paulaitis *, Henry S. Ashbaugh, Shekhar Garde

Center for Molecular and Engineering Thermodynamics, Department of Chemical Engineering, University of Delaware, Newark, DE 19716, USA

Received 24 January 1994; accepted 25 February 1994

Abstract

Infinite-dilution partial molar entropies of solvation of simple, monatomic solutes in water are defined in terms of the entropy associated with (1) solute insertion at constant volume and at a fixed position in the solvent, and (2) expansion or contraction of the pure solvent to maintain constant pressure. A statistical mechanical expansion for the entropy of solution in terms of multiparticle correlation functions is applied to this definition to identify three intrinsic contributions to the hydration entropy – solute–solvent pair correlations, rearrangement of solvent in the vicinity of the solute molecule, and expansion or contraction of the pure solvent – which we evaluate for the inert gases in water at 25°C. For the smaller solutes, we find that the solvent reorganization and solvent expansion contributions offset one another such that the entropy of hydration is determined almost exclusively by solute–water pair correlations. The solute–water pair correlation entropy also prevails as the primary factor determining entropies of hydration for the larger solutes; however, solvent reorganization now makes a small, negative contribution to the entropy.

Key words: Partial molar entropy; Hydration; Solute–solvent correlation

1. Introduction

In a recent publication [1] we presented a statistical mechanical expansion for the entropy in terms of multiparticle correlation functions that was used to identify the major contributions to the entropy of hydration of simple monatomic, hydrophobic solutes. Of these contributions, the two-particle solute–water correlation function alone, evaluated via Monte Carlo simulations, was found to account for the large negative entropies and the large positive heat capacities of solvation for methane at infinite dilution in water at room temperature. Contributions to the entropy of hydration due to perturbations in water–water pair correlations were not calculated [2], but were taken to be negligible for solute insertion at constant temperature and pressure [3]. In an extension of these simulation studies [4] we also calculated the contribution of solute–water pair correlations to the entropies of hydration of inert gases and model Lennard-Jones particles. Solute–water pair correlation entropies were found to agree reasonably well with the experimental values for the inert gases, thereby lending support to the notion that solute-induced perturbations in water–water pair correlations do

---

* Corresponding author.

0301-4622/94/$07.00 © 1994 Elsevier Science B.V. All rights reserved
SSDI 0301-4622(94)00055-0

not make significant contributions to the entropy of hydration for these solutions. The model Lennard-Jones solutes were studied for the purpose of characterizing the dependence of the entropy on solute size and the solute–water pair interaction energy. We found that the primary factor determining the solute–water pair correlation entropy was solute size, with the pair interaction energy playing a secondary, but significant role. In addition, we examined two of the key assumptions in our entropy formulation: the decoupling of translational and orientational correlations in the first hydration shell and the neglect of orientational correlations in the second and higher hydration shells. It was estimated that these assumptions impose a limitation of approximately 1 to 2 e.u. in the accuracy of our calculated solute–water pair correlation entropies.

In this work we evaluate contributions to the entropy of hydration for the inert gases at 25°C stemming from perturbations to water–water pair correlations in the presence of the solute, and from the expansion or contraction of pure solvent required to maintain constant pressure. The two contributions are compared with solute–water pair correlation entropies that were calculated previously for these solutions.

2. Thermodynamic relations

Neglecting intramolecular degrees of freedom, the entropy of a polyatomic fluid in the canonical ensemble is derived by a Kirkwood factorization of the N-particle correlation function and substitution into the Gibbs expression for the entropy [5]. The resulting expression is

$$S_N = -\frac{kN}{\rho}\frac{\Omega}{\sigma}\int f_N^{(1)} \ln\left(h^s f_N^{(1)}\right) \mathrm{d}\boldsymbol{p}_1\, \mathrm{d}\boldsymbol{J}_1 - \frac{k\rho^2}{2\Omega^2}\int g^{(2)} \ln g^{(2)}\, \mathrm{d}\boldsymbol{r}^2\, \mathrm{d}\omega^2 + \text{higher order terms} \qquad (1)$$

where k is Boltzmann's constant, h is Planck's constant, ρ is the number density, $\boldsymbol{r}^N$ the Cartesian coordinates of the N molecules, $\boldsymbol{p}^N$ the linear momenta, ω^N the Euler angles, $\Omega = \int \mathrm{d}\omega$, $\boldsymbol{J}^N$ the angular momenta, σ the symmetry number of the molecules (2 for water), s the number of external degrees of freedom per molecule (6 for nonlinear molecules), $f_N^{(1)}$ the one-particle distribution function, and $g^{(2)}$ the two-particle correlation function. The first term in this expansion is the contribution to the entropy associated with the individual particles and reflects the ability of each particle to occupy any point in the volume of the system. The second term accounts for correlations in the positions and the orientations of pairs of particles. The higher order terms represent correlations that cannot be accounted for by the superposition approximation when the potential energy of the system is described by a general, multi-body potential function. For pairwise additive potentials, these terms represent triplet and higher order correlations expressed in terms of pair correlations [6,7]. Calculation of the triplet and higher order correlations is very difficult to do by simulation. Moreover, it has been shown that keeping only the one- and two-particle terms in the expansion gives an accurate approximation for entropy of Lennard-Jones and hard-sphere fluids at high densities [8–10]. Therefore, we consider the calculation of entropies of hydration on the basis of pair correlations alone.

The entropy of a mixture can likewise be expressed in terms of a multiparticle correlation function expansion. Truncating this expansion at the level of pair correlations, the expression for an aqueous solution containing a monatomic solute is

$$\begin{aligned} S = {} & N_\mathrm{w}\left[\frac{6}{2}k - k\ln\left(\rho_\mathrm{w}\Lambda_\mathrm{w}^3 q_\mathrm{w}^{-1}\right)\right] \\ & + N_\mathrm{s}\left[\frac{3}{2}k - k\ln\left(\rho_s\Lambda_\mathrm{s}^3\right)\right] \\ & - N_\mathrm{w}^2\frac{k}{2V\Omega^2}\int g_\mathrm{ww}\ln g_\mathrm{ww}\,\mathrm{d}\boldsymbol{r}\,\mathrm{d}\omega^2 \\ & - N_\mathrm{s}^2\frac{k}{2V}\int g_\mathrm{ss}\ln g_\mathrm{ss}\,\mathrm{d}\boldsymbol{r} \\ & - N_\mathrm{s}N_\mathrm{w}\frac{k}{V\Omega}\int g_\mathrm{sw}\ln g_\mathrm{sw}\,\mathrm{d}\boldsymbol{r}\,\mathrm{d}\omega, \end{aligned} \qquad (2)$$

where subscripts s, w denote solute and water, respectively; N_w, N_s are the number of molecules; ρ_w, ρ_s are number densities; q_w is the rotational partition function of water; and g_{ww}, g_{sw}, g_{ss} are pair correlation functions. The partial molar entropy at infinite dilution is obtained directly from Eq. (2) by differentiating with respect to N_s at constant T, P, and N_w. Alternatively, solvation at constant pressure can be thought of as a two-step process in which the solute is first dissolved at constant volume and then the solution expands or contracts to re-establish the original pressure. In this case, the partial molar entropy at infinite dilution is given by the standard thermodynamic relation,

$$\bar{S}_s^\infty = \hat{S}_s^\infty + \bar{v}_s^\infty \left(\frac{\partial S}{\partial V} \right)_{T,N_w,N_s=0}, \tag{3}$$

where $\hat{S}_s^\infty$ is the partial specific entropy at infinite dilution, defined below, and $\bar{v}_s^\infty$ is the partial molar volume of the solute at infinite dilution. Eq. (3) is similar to an expression for the partial molar entropy derived by Hildebrand et al. [11] in terms of a partial entropy of mixing at constant *excess* volume. The partial specific entropy is obtained from Eq. (2) by differentiating with respect to N_s at constant T, V, and N_w. In the limit of infinite dilution, this quantity is

$$\begin{aligned}\hat{S}_s^\infty = & \left[\frac{3}{2}k - k \ln\left(\rho_s \Lambda_s^3\right) \right] \\ & - k - k\frac{\rho_w}{\Omega} \int g_{sw} \ln g_{sw} \, \mathrm{d}\boldsymbol{r} \, \mathrm{d}\omega \\ & - \frac{k}{2} \frac{N_w^2}{V\Omega^2} \\ & \times \left(\frac{\partial}{\partial N_s} \int g_{ww} \ln g_{ww} \, \mathrm{d}\boldsymbol{r} \, \mathrm{d}\omega^2 \right)_{T,V,N_w,N_s \to 0}.\end{aligned} \tag{4}$$

The first two terms in this equation are one-particle contributions to the partial specific entropy, the third term is the solute–water pair correlation entropy, and the last term accounts for solvent rearrangement in the vicinity of the solute when the solute is inserted at constant volume. Solute-induced perturbations to water–water pair correlations can make a substantial, negative contribution to the partial specific entropy of hydration. For example, Yu and Karplus [12] show, within the context of the hypernetted chain approximation to an integral equation theory, that this contribution amounts to approximately 25–30% of total entropy of hydration for simple Lennard-Jones solutes in TIP3P water.

The connection between the partial molar entropy in Eq. (3) and Ben-Naim's standard entropy of solvation [13],

$$\Delta S_s^* = -\frac{\partial \mu_s^{\text{res}}}{\partial T} \tag{5}$$

defined in terms of the residual chemical potential,

$$\mu_s^{\text{res}} = \mu_s - kT \ln \rho_s \Lambda_s^3 \tag{6}$$

is made by equating partial molar entropies. From Eqs. (5) and (6), the partial molar entropy is

$$\begin{aligned}\bar{S}_s &= -\frac{\partial \mu_s}{\partial T} = -\frac{\partial \mu_s^{\text{res}}}{\partial T} - k \ln \rho_s \Lambda_s^3 + kT\alpha + \frac{3}{2}k \\ &= \Delta S_s^* - k \ln \rho_s \Lambda_s^3 + kT\alpha + \frac{3}{2}k,\end{aligned} \tag{7}$$

where α is the thermal expansion coefficient of the solution, Equating Eq. (7) to Eq. (3) gives at infinite dilution,

$$\begin{aligned}\Delta S_s^{*\infty} = & \hat{S}_s^\infty - \left[\frac{3}{2}k - k \ln\left(\rho_s \Lambda_s^3\right) \right] \\ & - \left(kT\kappa_T{}^\circ - \bar{v}_s^\infty\right) \left(\frac{\partial S}{\partial V} \right)_{T,N_w,N_s=0},\end{aligned} \tag{8}$$

where $\kappa_T{}^\circ$ is the isothermal compressibility of pure water. Eq. (8) defines the standard entropy of solvation in terms of two contributions: (1) The entropy associated with inserting the solute into the solvent at constant volume and at a fixed position. This contribution is given by the partial specific entropy of solvation, excluding the one-particle entropy contribution. (2) The entropy associated with expansion or contraction of the pure solvent to maintain the constant pressure. The quantity, $(kT\kappa_T{}^\circ - \bar{v}_s^\infty)$, in the second contribution is defined by the well-known Kirkwood–Buff expression [14],

$$\left(kT\kappa_T{}^\circ - \bar{v}_s^\infty\right) = \int \left[g_{sw}(r) - 1 \right] \mathrm{d}\boldsymbol{r}. \tag{9}$$

It depends directly on solute–water pair correlations, and includes both the excluded volume of the solute and volume changes due to rearrangement of solvent in the vicinity of the solute molecule [15]. It can be thought of as a statistical measure of the fractional excess number of water molecules needed to hydrate the solute at infinite dilution, relative to the uniform, bulk density of pure water [16,17]. If $\bar{v}_s^\infty > kT\kappa_T{}^\circ$, as it is for simple hydrophobic solutes, then this contribution to the entropy of hydration is positive. Therefore, we will refer to it as the solvent expansion entropy. The derivative, $(\partial S/\partial V)_{T,N_w,N_s=0}$, in Eq. (8) is evaluated from Eq. (2) by differentiating with respect to V at constant T and N_w, and then taking the limit, $N_s \to 0$. Substituting this result and the expression for $\hat{S}_s^\infty$ into Eq. (8) gives the standard entropy of solvation in terms of solute–water and water–water pair correlation functions,

$$\begin{aligned}\Delta S_s^{*\infty} = {} & -k - k\frac{\rho_w}{\Omega}\int g_{sw} \ln g_{sw}\, d\boldsymbol{r}\, d\omega \\ & -\frac{k}{2}\frac{N_w^2}{V\Omega^2} \\ & \times\left(\frac{\partial}{\partial N_s}\int g_{ww} \ln g_{ww}\, d\boldsymbol{r}\, d\omega^2\right)_{T,V,N_w,N_s\to 0} \\ & -k\rho_w(kT\kappa_T{}^\circ - \bar{v}_s^\infty) \\ & \times\left(1+\frac{\rho_w}{2\Omega^2}\int g_{ww} \ln g_{ww}\, d\boldsymbol{r}\, d\omega^2\right)_{N_s=0} \\ & +\frac{k}{2}\frac{N_w^2}{V\Omega^2}(kT\kappa_T{}^\circ - \bar{v}_s^\infty) \\ & \times\left(\frac{\partial}{\partial V}\int g_{ww} \ln g_{ww}\, d\boldsymbol{r}\, d\omega^2\right)_{T,N_w,N_s=0}. \end{aligned} \tag{10}$$

In addition to the solute–water pair correlation entropy and the contribution associated with solvent rearrangement due to solute insertion at constant volume, the two additional contributions to the entropy of hydration appearing in this equation reflect solvent expansion, in the absence of perturbations in water–water pair correlations, and solvent reorganization due to changes in solvent density as it expands to maintain constant pressure. In what follows, we will consider the magnitude of these contributions for inert gases in water at 25°C.

3. Calculations

The solute–water pair correlation entropy is

$$S_{sw} = -\frac{k(N-1)}{V\Omega}\int g_{sw}^{(2)} \ln g_{sw}^{(2)}\, d\boldsymbol{r}\, d\omega. \tag{11}$$

By assuming the following factorization of the pair correlation function [1]

$$\begin{aligned} g_{sw}^{(2)}(r, \theta, \phi, \chi) &= g_{sw}(r)\cdot g(\theta, \chi, \phi) \text{ for } r \leqslant r_{sh}, \\ g_{sw}^{(2)}(r, \theta, \phi, \chi) &= g_{sw}(r) \text{ for } r \geqslant r_{sh}, \end{aligned} \tag{12}$$

where g_{sw} is the orientationally averaged radial distribution function and r_{sh} is defined as the radius of first hydration shell, we can separate the solute–water pair correlation entropy into a translational and an orientational contribution:

$$\begin{aligned} S_{sw} = {} & -\frac{k(N-1)}{V}\int g_{sw} \ln g_{sw}\, d\boldsymbol{r} \text{ (translational)} \\ & -\frac{k(N-1)V_i}{V\Omega}\int g(\theta, \chi, \phi) \\ & \cdot \ln\{g(\theta, \chi, \gamma)\}\, d\omega \text{ (orientational)}. \end{aligned} \tag{13}$$

For spherically symmetric solutes, the orientational correlation function will be uniform with respect to the third Euler angle, ϕ. The angle θ is defined as that between the dipole vector of water and the solute–water oxygen axis, and χ describes rotation around the water dipole vector [1].

The first integral in Eq. (13) is evaluated over the entire volume of the fluid. However, g_{sw} is only calculated up to a finite cutoff distance in simulations. We have shown [4] that the correction for this long-range behavior is

$$S_{corr} = k\rho_w\int [g_{sw}(r) - 1]\, d\boldsymbol{r}, \tag{14}$$

where the integration is performed up to the distance for which the radial distribution function is calculated in the simulation.

Table 1
Lennard-Jones parameters for the inert gases

	σ (Å)	ϵ (kcal/mol)
helium [a]	2.55	0.02
neon [a]	2.78	0.069
argon [b]	3.401	0.2339
krypton [b]	3.624	0.317
xenon [b]	3.935	0.433
radon [c]	4.36	0.576

[a] Ref. [31]. [b] Ref. [32]. [c] Ref. [33].

The radial and orientational distribution functions were calculated using Jorgensen's BOSS Monte Carlo simulation program [18]. For these simulations, one particle is inserted in a box of water molecules pre-equilibrated at 25°C. Then, depending on solute size, one or two water molecules showing the highest energy of interaction with the solute are deleted. Constant NVT simulations for the mixture are then performed at 25°C. Individual simulations consisted of 5 million or more configurations for equilibration and 60 million configurations for sampling. The TIP4P model for water [19] was used in all simulations. The inert gases were modeled as Lennard-Jones particles with the parameters listed in Table 1. The uncertainties in these parameters have been discussed previously [4]. The solute–water pair correlation entropy was calculated from Eq. (13), using the long-range correction in Eq. (14), with the radial distribution function numerically integrated up to 8 Å for the smaller solutes and up to 10.5 Å for the larger ones. The orientational distribution function was integrated numerically as described elsewhere [1]. Results for the inert gases in water at 25°C are given in the first three columns of Table 2.

The solvent expansion entropy is calculated using the thermodynamic identity,

$$\left(\frac{\partial S}{\partial V}\right)_{T,N_\mathrm{w},N_\mathrm{s}=0}=\left(\frac{\partial P}{\partial T}\right)_{V,N_\mathrm{w},N_\mathrm{s}=0} \tag{15}$$

and the thermal expansion coefficient and isothermal compressibility for pure water [20]. Partial molar volumes for the inert gases at infinite dilution were estimated from a corresponding states correlation based on Kirkwood–Buff solution theory [21] and the measured partial molar volume for argon at infinite dilution in water [22]. The characteristic volume of the solute is required in this correlation and was taken to be the atomic volume ($\pi\sigma^3/6$) of each gas. The results are given in the fourth column of Table 2.

4. Discussion

The total calculated entropies of hydration in column 5 of Table 2 are obtained from

$$\Delta S_\mathrm{s}^{*\infty}|_\mathrm{calc}=-k-k\frac{\rho_\mathrm{w}}{\Omega}\int g_\mathrm{sw}\ln g_\mathrm{sw}\,\mathrm{d}\boldsymbol{r}\,\mathrm{d}\omega+\left(kT\kappa_T{}^\circ-\bar{v}_\mathrm{s}^\infty\right)\left(\frac{\partial P}{\partial T}\right)_{V,N_\mathrm{w},N_\mathrm{s}=0}, \tag{16}$$

which excludes the contribution due to solute-induced perturbations in water–water pair correlations. It can be seen from these results that the sum of the calculated contributions in each case agrees quite well with the experimental value of the entropy of hydration. In addition, the calcu-

Table 2
Comparison of hydration entropies of the inert gases at 25°C. All values in e.u. (1 e.u. = 1 cal/mol K)

	Trans. corr.	Orient. corr.	Pair corr. entropy	Solvent expansion	Total calc.	Experimental [a]		
helium	−4.6	−3.0	−7.6	+2.5	−7.1	−8.0,		−7.8
neon	−6.2	−4.1	−10.3	+2.9	−9.4	−10.1,	−10.8,	−10.0
argon	−10.5	−6.2	−16.7	+4.2	−14.5	−14.7,	−15.6,	−14.4
krypton	−11.4	−7.0	−18.4	+4.7	−15.7	−16.3,	−16.8,	−16.0
xenon	−13.4	−7.3	−20.7	+5.5	−17.2	−17.4,	−19.6,	−17.8
radon	−16.0	−8.6	−24.6	+6.6	−20.0	−18.2,		

[a] First and second columns from ref. [34]; third column from ref. [35] after change of standard states.

lated results reproduce reasonably well the observed increase in magnitude of the entropy with increasing solute size. The primary factor determining the large negative entropies of hydrophobic hydration is the solute-water pair correlation entropy. This observation is consistent with those made recently by Rashin and Bukatin [23] who calculated entropies of hydration on the basis of solute-water pair correlations using a continuum model for water. The solvent expansion entropy also makes a significant contribution to the entropy of hydration. In light of the work of Yu and Karplus [12], however, we expect the entropy associated with solute-induced perturbations to water-water pair correlations to compensate, at least in part, for the solvent expansion entropy. The calculation of this contribution to the entropy on the basis of molecular simulations is a formidable task. Water-water pair correlations are of higher dimensionality than the solute-water pair correlations we have evaluated, and solute-induced perturbations to water-water orientational correlations will most likely be limited to the first hydration shell [24], and as such, will involve a relatively small number of water molecules. Therefore, the determination of translational and orientational water-water pair correlation functions will require inordinately long simulations and probably additional approximations before they can be properly evaluated.

Alternatively, the magnitude of this contribution to the entropy of hydration can be estimated. If we make the reasonable assumption that solvent rearrangement due to solute-insertion at constant volume is primarily an excluded volume effect, then the two solvent reorganization contributions to the entropy will offset one another to an extent that depends on the magnitude of the excluded volume of the solute relative to its infinite-dilution partial molar volume. Pratt and Pohorille [15] calculated the infinite-dilution partial molar volume for a hard spherical cavity of subatomic size in water and found that the excluded volume is approximately two and one-half times the partial molar volume. The physical reason for this large difference is the high packing efficiency of water molecules in the vicinity of the solute [25]. We have calculated $\bar{v}_s^\infty$ for methane in water

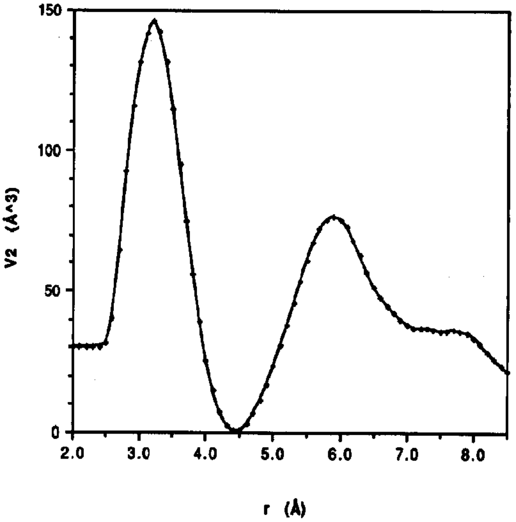

Fig. 1. Calculated partial molar volume at infinite dilution for methane in water at 25°C and 1 atm as a function of intermolecular separation.

at 25°C and 1 atm using the following form of the Kirkwood-Buff expression and the radial distribution function for pure water and the solute-water radial distribution function evaluated by Monte Carlo simulations.

$$\rho_w \bar{v}_s^\infty = 1 + \rho_w \int \left[g_{ww}{}^\circ(r) - 1 \right] \mathrm{d}\boldsymbol{r} - \rho_w \int \left[g_{sw}(r) - 1 \right] \mathrm{d}\boldsymbol{r}. \qquad (17)$$

The results are given in Fig. 1. A striking feature of this plot is the large variation in $\bar{v}_s^\infty$ for $r < 7.5$ Å. It appears, however, that $\bar{v}_s^\infty$ asymtotically approaches a value of 36.5 Å^3 between 7-8 Å before drifting downward at larger separations due to periodic box size effects in the simulation. The excluded volume contribution to the partial molar volume corresponds to the first maximum in this plot, and is approximately four times the value for $\bar{v}_s^\infty$. This difference is even greater than that observed by Pratt and Pohorille, and is evidently due to the expected higher packing efficiency of water around a solute of atomic size [4]. Thus, for methane in water at 25°C, we estimate the solvent reorganization entropy for solute insertion at constant volume to be four times that for solvent expansion.

Table 3
Calculated solvation expansion entropy contributions to the hydration entropies of the inert gases at 25°C. (All values in e.u.)

	Total solvent expansion	Solvent expansion neglecting reorgan.	Solvent reorgan. contribution
helium	+2.5	+1.6	+0.9
neon	+2.9	+1.9	+1.0
argon	+4.2	+2.7	+1.5
krypton	+4.7	+3.0	+1.7
xenon	+5.5	+3.5	+2.0
radon	+6.6	+4.3	+2.3

If the two solvent reorganization contributions had offset one another exactly, Eq. (16) would become,

$$\Delta S_s^{*\infty} = -k - k\frac{\rho_w}{\Omega}\int g_{sw}\ln g_{sw}\,\mathrm{d}\boldsymbol{r}\,\mathrm{d}\omega - k\rho_w(kT\kappa_T^{\circ} - \bar{v}_s^{\infty}) \times \left(1 + \frac{\rho_w}{2\Omega^2}\int g_{ww}\ln g_{ww}\,\mathrm{d}\boldsymbol{r}\,\mathrm{d}\omega^2\right)_{N_s=0}. \quad (18)$$

The last term in this equation is the solvent expansion entropy in the absence of solvent reorganization, which we evaluate as the product of $\rho_w(kT\kappa_T^{\circ} - \bar{v}_s^{\infty})$ and the molar entropy of pure liquid water at 25°C [26]. The results of this calculation for the inert gases are shown in Table 3. About two-thirds of the solvent expansion entropy can be attributed to this contribution, and thus solvent reorganization due to solvent expansion will contribute approximately +1–2 e.u. to the entropy of hydration depending on solute size. For the smaller solutes in Table 3, if solvent reorganization due to solute insertion is three times this value, we find that this contribution to the entropy of hydration will more or less cancel the total solvent expansion entropy. For the larger solutes, however, solvent reorganization due to solute insertion will contribute an additional −1 or 2 e.u. to the entropy of hydration if we take this contribution to be four times the solvent reorganization contribution due to solvent expansion.

For the larger solutes, the impact of solvent reorganization on the entropy of solvation is more pronounced in water than it is, for example, in typical nonpolar solvents precisely because the solvent expansion entropy of water is attenuated. Water is characterized by a low value of $(\partial P/\partial T)_{V,N}$ compared to most nonpolar solvents [27], and on a molecular level, liquid water has a larger fractional free volume compared to the hard-sphere liquid, but this free volume is distributed such that the confirgurational entropy of water is lower [28]. The results also suggest that solvent rearrangement contributions to the entropy of hydration will be even more prominent for larger solutes. Indeed, such contributions are essential for describing the density profile of water near interfaces [29]. Solvent reorganization contributions could also be implicated in the effect of elevated temperatures on hydrophobic phenomena. Indeed, we now expect that the deviations from experiment we have observed in our calculations of hydration entropies for methane at elevated temperatures [1,3] may, in part, be attributed to solvent reorganization.

Acknowledgement

We are indebted to Dr. Lawrence Pratt for numerous valuable discussions. This work is supported by the National Science Foundation (Grant BCS9210401) and a National Science Foundation Fellowship for HSA (Grant GER9253850).

References

[1] T. Lazaridis and M.E. Paulaitis, J. Phys. Chem. 96 (1992) 3847.

[2] D.E. Smith, B.B. Laird and A.D.J. Haymet, J. Phys. Chem. 97 (1993) 5788.

[3] T. Lazaridis and M.E. Paulaitis, J. Phys. Chem. 97 (1993) 5789.

[4] T. Lazaridis and M.E. Paulaitis, J. Phys. Chem. 98 (1994) 635.

[5] D.C. Wallace, J. Chem. Phys. 87 (1987) 2282.

[6] T. Morita and K. Hiroike, Progr. Theoret. Phys. 25 (1961) 537.

[7] C. De Dominicus, J. Math Phys. 3 (1962) 983.

[8] B.B. Laird and A.D.J. Haymet, Phys. Rev. A 45 (1992) 5680.

[9] I. Borzsák and A. Baranyai, Chem. Phys. 165 (1992) 227.
[10] A.B Schmidt, J. Chem. Phys. 99 (1993) 4225.
[11] J.H. Hildebrand, J.M. Prausnitz and R.L. Scott, Regular and related solutions (Van Nostrand Reinhold, New York, 1970) p. 80.
[12] H.-A. Yu and M. Karplus, J. Chem. Phys. 89 (1988) 2366.
[13] A. Ben-Naim, J. Phys. Chem. 82 (1978) 792.
[14] J.G. Kirkwood and F.P. Buff, J. Chem. Phys. 19 (1951) 774.
[15] L.R. Pratt and A. Pohorille, Proc. EBSA Workshop on Water–Biomolecule Interaction (1992).
[16] P.G. Debenedetti, Chem. Eng. Sci. 9 (1987) 2203.
[17] S. Kim and K.P. Johnston, IEC Res. 26 (1987) 1206.
[18] W.L. Jorgensen, BOSS version 2.8 (Yale University, New Haven, 1989).
[19] W.L. Jorgensen, J. Chandrasekhar, J.D. Madura, R.W. Impey and M.L. Klein, J. Chem. Phys. 79 (1983) 926.
[20] R.C. Weast, CRC Handbook of Chemistry and Physics, 64th Ed. (CRC Press, Boca Raton, 1983).
[21] S.W. Brelvi and J.P. O'Connell, AIChE J. 18 (1972) 1239.
[22] E.W. Tiepel and K.E. Gubbins, J. Phys. Chem. 76 (1972) 3044.
[23] A.A. Rashin and M.A. Bukatin, J. Phys. Chem. 98 (1994) 386.
[24] A.H. Narten, J. Chem. Phys. 56 (1972) 5681.
[25] B.K. Lee, Biopolymers 24 (1985) 813.
[26] S.I. Sandler, Chemical and engineering thermodynamics (Wiley, New York, 1989) App. III.
[27] J.H. Hildebrand, J.M. Prausnitz and R.L. Scott, Regular and related solutions (Van Nostrand Reinhold, New York, 1970) App. 6.
[28] A. Pohorille and L.R. Pratt, J. Am. Chem. Soc. 112 (1990) 5066.
[29] G. Hummer and D.M. Soumpasis, Phys. Rev. E 19 (1994), in press.
[30] P.L. Privalov and S.J. Gill, Pure Appl. Chem. 61 (1989) 1097.
[31] J.O Hirschfelder, C.F. Curtiss and R.B. Bird, Molecular theory of gases and liquids (Wiley, New York, 1954).
[32] L. Verlet and J.-J. Weis, Mol. Phys.24 (1972) 1013.
[33] G.A. Miller, J.Phys. Chem. 64 (1960) 163
[34] A. Ben-Naim, Solvation thermodynamics (Plenum Press, New York, 1987).
[35] D. Krause Jr., B.B. Benson, J. Soln. Chem. 18 (1989) 823.

Discussion to the paper by M.E. Paulaitis, H.S. Ashbaugh and S. Garde

Comments

By B.K. Lee

(1) If one ignores the term due to the change in the water–water correlation, the expression for the partial specific entropy, Eq. (4), does not depend on how much structure the pure water had *before* the insertion of the solute. However, since the partial molar entropy is equal to the *change* in entropy upon addition of a solute molecule, should one not expect it to depend on the structure of the solvent before, as well as after, the insertion?

A minor point – why is this entropy called the partial specific entropy? I thought that the term "specific" indicated that the quantity was per weight. The entropy of Eq. (4) appears more like the contant-volume partial molar entropy.

(2) When $v_s^\infty > kT\kappa_T^0$, the solvent expansion entropy is simply the second term in Eq. (3). This is the entropy change upon expansion of the $(N+1)$ molecule system from p' to p^0, where p^0 is 1 atm and p' is the pressure of the system after insertion of the solute under constant volume condition. This term arises from the fact that the system gets compressed if the solute is inserted under the constant volume condition and that the release of this pressure by volume expansion is accompanied by a change in entropy. Therefore this term should be used only when the g_{sw} function in Eq. (4) refers to that in the compressed system with high pressure. However, in the simulation that was used to obtain g_{sw}, one or two water molecules were deleted from the system upon solute insertion. This will effectively lower the pressure and the system is more like that obtained after a constant-pressure insertion rather than a constant-volume insertion. Therefore, in order to obtain the proper g_{sw} function to use in conjuction with Eq. (4), does it not seem more reasonable to insert the solute without deleting any solvent molecules? A related question has to do with the accuracy of the simulation calculation. Does the result of the calculation change upon removal or addition of a few water molecules when the system contains probably a few hundred molecules? (By the way, the number of solvent molecules in the system should be stated somewhere.) If the calculation is insensitive (and it can be made to be infinitely insensitive, simply by increasing the size of the system), does it not indicate that the error of the calculation is probably at least of the same magnitude as the "solvent expansion entropy" term?

Responses by M.E. Paulaitis to Comments

To B.K. Lee

(1) The partial specific entropy should take into account the change in the structure of water from pure water to a perturbed state corresponding to solute insertion at constant volume, so in fact, one cannot ignore the term in our Eq. (4) for the change in water–water pair correlations. However, the change in water structure, and therefore the properties of pure water before insertion, are also accounted for in the third term in Eq. (4), the term for the solute–water pair correlation entropy. Indeed, it is this term that makes the major contributions to solute-induced perturbations in water structure.

The partial molar entropy has a rigorous thermodynamic definition (see, for example, ref. [26] in our paper). It is the derivative of the entropy with respect to the number of moles of one component, holding temperature, pressure, and all other components mole numbers constant. Thus, a constant-volume partial molar entropy would be internally inconsistent. The expression, partial specific entropy, is used by us to denote that this quantity is obtained by holding volume rather than pressure constant when taking the derivative of the entropy. In fact, we really differentiate with respect to number of molecules, not moles, but of course, this is a trivial matter of a factor of Avogadro's constant.

(2) Ideally, one should follow the fate of the $g_{sw} \ln g_{sw}$ integral in Eq. (4) through both steps of the two-step process described in our paper. Thus, if we had evaluated this integral from a simulation in which the solute was inserted at constant volume, as you suggest, we would then need to add to this result another term to account for the change in the integral due to the change in volume. We actually evaluated the $g_{sw} \ln g_{sw}$ integral from a simulation in which the solute was inserted at constant pressure. Therefore, we have accounted for the effect of both steps in the solvation process on the $g_{sw} \ln g_{sw}$ integral.

The solute–water pair correlation functions we obtain from simulations are, in fact, substantially different-depending on whether the solute is inserted at constant pressure or constant volume and this is due to the finite size of the system. However, we indeed do not expect the difference between the partial molar and partial specific entropies to become negligible as we increase the number of water molecules in the system to infinity. This is obvious from Eq. (3).

[1] T. Lazaridis and M.E. Paulaitis J. Phys. Chem. 97 (1993) 5789.