

Generalized Solvation Heat Capacities[†]

Dor Ben-Amotz*

Department of Chemistry, Purdue University, West Lafayette, Indiana 47907-1393

B. Widom

Baker Laboratory, Department of Chemistry, Cornell University, Ithaca, New York 14853-1301

Received: March 23, 2006; In Final Form: May 12, 2006

The partial molar heat capacity associated with a constant-pressure solvation process is extended to define a total of six generalized solvation heat capacities, each of which contain unique physical information. These arise from all the possible cross derivatives of the reversible heat of solvation (with respect to T and N), each evaluated at either constant pressure or constant volume. The resulting quantities may be interconverted using expressions that depend on the solvent equation of state and the solute partial molar volume. Moreover, contributions to each of the solvation heat capacities arising from the temperature dependence of the solute–solvent interaction energy and the solvent-reorganization energy (at either constant pressure or constant volume) are formally identified. For the self-solvation of a molecule in its own pure fluid, the latter quantities may be extracted directly from experimental data, while for more general solvation processes additional input is required, either from computer simulation or from theoretical approximations. The results are used to experimentally quantify the generalized heat capacities pertaining to the self-solvation of xenon, difluoromethane, n -hexane, and water, as well as the hydration of xenon, cyclohexane, and three hard sphere solutes (of about the same size as water, xenon, and cyclohexane).

1. Introduction

The partial molar heat capacity of a solute represents the change in the heat capacity of the entire system induced by the addition of a solute (at constant pressure). Both the magnitude and sign of this thermodynamic quantity can be remarkably sensitive to intermolecular interactions, particularly in water. For example, hydration heat capacities are typically large and positive for nonpolar solutes but negative for some ions.^{1–3} Although the mechanisms underlying this variability remain a subject of speculation,^{4–12} computer simulations are quite helpful in revealing mechanistic details that would be difficult or impossible to measure experimentally.^{2,13–15} As a result, it is now clear that a remarkably fragile clathrate hydrate like structure forms around methane or rare gas solutes in low-temperature water but disintegrates readily with increasing temperature. This fragility manifests itself experimentally as a hydration entropy that increases strongly with temperature, thus giving rise to a large positive hydrophobic heat capacity. Recent theoretical and simulation studies further imply that hydrophobic hydration depends in a previously unanticipated way on the size of nonpolar groups.^{16,17} More specifically, large nonpolar groups may no longer be capable of supporting clathrate-like water structures and thus induce a dewetting transition, to form a hydration–shell structure resembling that of a vapor–liquid interface. Although the implications of these remarkable predictions have not been extended to partial molar heat capacities, simulation measurements imply that there can indeed be a significant difference between the hydration structure and thermodynamics of small and large hydrophobic groups.^{15,18–21} Here we offer additional perspectives to this discussion, by generalizing the definition of solvation heat capacities, identifying fundamental underlying contributions, and relating the results to experimental self-solvation and hydration processes.

The definition of the partial molar heat capacity, $(\partial C_p/\partial N)_p = [(\partial/\partial N)(\partial H/\partial T)_p]_p$, clearly indicates that two derivatives are to be evaluated at constant pressure. Thus, we suggest that it would be appropriate to use the notation C_{pp} to designate the latter quantity. That also implies that C_{pp} may be viewed as a member of a family of solvation heat capacities, including C_{VV} , C_{PV} , and C_{VP} , each obtained by imposing either a constant volume or a constant pressure constraint when evaluating each of the above derivatives. This procedure may be further generalized to generate a total of six quantities each of which have the same units as the usual partial molar heat capacity but which do not in general have the same magnitudes or even the same signs. Here we report the derivation of thermodynamic identities which may be used to experimentally evaluate each of these generalized heat capacities, C_{ij} . Moreover, we employ a statistical mechanical analysis to identify fundamental underlying intermolecular interaction contributions to each C_{ij} . In some systems all of these contributions can be uniquely determined directly from experimental measurements, while in others such a decomposition requires additional input either from numerical simulation or from theoretical approximation. Although most of the generalized solvation heat capacity results described in this work are apparently new, the relationship between C_{pp} and C_{VV} has been recently discussed.²² However, the latter analysis invoked an approximation which, although apparently quite reasonable, has since been found to have a restricted range of applicability.²² No such approximation is invoked in deriving the exact expressions presented here. However, to facilitate the extraction of solute–solvent and solvent rearrangement contribution to the generalized hydration heat capacities of hydrophobic solutes, we make use of aqueous cavity chemical potentials derived from computer simulation measurements^{4,23} combined with first-order thermodynamic perturbation theory.^{24,25}

[†] Part of the special issue “Charles B. Harris Festschrift”.

The challenges associated with both measuring and predicting partial molar heat capacities stem in large part from the fact that evaluating thermodynamic second derivatives requires extremely accurate experimental, simulation, or theoretical results. As a typical example, reported values for the hydration heat capacity of xenon at room temperature range from 160 to 350, in J/(K mol) units,^{4,13,26–28} with the most reliable experimental values apparently converging to around 230 J/(K mol).²⁹ However, even with such uncertainty it is quite clear that solvation heat capacities are strikingly sensitive to both molecular structure and the thermodynamic constraints imposed during a solvation process. For example, although argon (Ar) and a bromide ion (Br[−]) have quite similar hydration volumes (≈ 29 cm³/mol);^{1,28} the partial molar hydration heat capacity of Ar is ≈ 170 J/(K mol) while that of Br[−] is about -70 J/(K mol).^{1,4,30}

The remainder of this paper is organized as follows. Section 2 presents exact thermodynamic expressions for the newly identified family of generalized solvation heat capacities. In section 3 these are decomposed into intermolecular interaction contributions. The results are applied to experimental self-solvation and hydration processes in section 4, and the conclusions are summarized in section 5. Supplementary thermodynamic expressions pertaining to any solvation or phase transfer process are collected in the Appendix.

2. Generalized Solvation Heat Capacities

The heat capacity of any system is a measure of the temperature change induced by a given reversible heat exchange, δq , between the system and its surroundings. The fundamental equation of thermodynamics implies that $\delta q = T dS = dU + P dV$.³¹ Thus, the heat capacity of a system maintained at constant pressure is, $C_P = (\delta q / \delta T)_P = T(\partial S / \partial T)_P = (\partial H / \partial T)_P$. The corresponding partial molar heat capacity represents the change in C_P produced by adding a solute molecule (N) to the system, at a fixed temperature, pressure, and number of solvent molecules (N_0)

$$C_{PP} \equiv \left(\frac{\partial C_P}{\partial N} \right)_{T,P,N_0} = T \left[\frac{\partial}{\partial N} \left(\frac{\partial S}{\partial T} \right)_P \right]_{T,P,N_0} = \left[\frac{\partial}{\partial N} \left(\frac{\partial H}{\partial T} \right)_P \right]_{T,P,N_0} = T \left[\frac{\partial}{\partial T} \left(\frac{\partial S}{\partial N} \right)_{T,P,N_0} \right]_P = \left[\frac{\partial}{\partial T} \left(\frac{\partial H}{\partial N} \right)_{T,P,N_0} \right]_P = T \left(\frac{\partial s|_P}{\partial T} \right)_P = \left(\frac{\partial h|_P}{\partial T} \right)_P \quad (1)$$

Thus, we may also define C_{VV} as the quantity obtained by performing all of the above partial derivatives at constant volume rather than constant pressure

$$C_{VV} \equiv \left(\frac{\partial C_V}{\partial N} \right)_{T,V,N_0} = T \left[\frac{\partial}{\partial N} \left(\frac{\partial S}{\partial T} \right)_V \right]_{T,V,N_0} = \left[\frac{\partial}{\partial N} \left(\frac{\partial U}{\partial T} \right)_V \right]_{T,V,N_0} = T \left[\frac{\partial}{\partial T} \left(\frac{\partial S}{\partial N} \right)_{T,V,N_0} \right]_V = \left[\frac{\partial}{\partial T} \left(\frac{\partial U}{\partial N} \right)_{T,V,N_0} \right]_V = T \left(\frac{\partial s|_V}{\partial T} \right)_V = \left(\frac{\partial u|_V}{\partial T} \right)_V \quad (2)$$

One may further generalize the above procedure by combining constant pressure and constant volume cross derivatives

$$C_{PV} \equiv \left(\frac{\partial C_P}{\partial N} \right)_{T,V,N_0} = T \left[\frac{\partial}{\partial N} \left(\frac{\partial S}{\partial T} \right)_P \right]_{T,V,N_0} = \left[\frac{\partial}{\partial N} \left(\frac{\partial H}{\partial T} \right)_P \right]_{T,V,N_0} \quad (3)$$

$$C_{VP} \equiv \left(\frac{\partial C_V}{\partial N} \right)_{T,P,N_0} = T \left[\frac{\partial}{\partial N} \left(\frac{\partial S}{\partial T} \right)_V \right]_{T,P,N_0} = \left[\frac{\partial}{\partial N} \left(\frac{\partial U}{\partial T} \right)_V \right]_{T,P,N_0} \quad (4)$$

Notice that C_{PV} and C_{VP} are not equivalent, both because C_P and C_V are physically different quantities and because the two

partial derivatives with respect to N are not equivalent; thus, C_{PV} and C_{VP} are doubly different. Moreover, one may also generate an additional unique pair of cross derivatives by switching the order of differentiation in eqs 3 and 4

$$C_{\bar{P}\bar{V}} \equiv T \left[\frac{\partial}{\partial T} \left(\frac{\partial S}{\partial N} \right)_{T,P,N_0} \right]_V = T \left(\frac{\partial s|_P}{\partial T} \right)_V = \left(\frac{\partial h|_P}{\partial T} \right)_V - \bar{v} \left(\frac{\partial P}{\partial T} \right)_V \quad (5)$$

$$C_{\bar{V}\bar{P}} \equiv T \left[\frac{\partial}{\partial T} \left(\frac{\partial S}{\partial N} \right)_{T,V,N_0} \right]_P = T \left(\frac{\partial s|_V}{\partial T} \right)_P = \left(\frac{\partial u|_V}{\partial T} \right)_P + \bar{v} \left(\frac{\partial P}{\partial T} \right)_V \quad (6)$$

Although the latter quantities may be viewed as members of the former family of generalized solvation heat capacities, the new quantities differ in that they are not expressible as derivatives of either C_P or C_V . On the other hand, like C_{PP} and C_{VV} , but unlike C_{PV} and C_{VP} , the new quantities are expressible in terms of derivatives of the solute chemical potential μ , since $s|_P = -(\partial \mu / \partial T)_P$, $s|_V = -(\partial \mu / \partial T)_V$, $h|_P = (\partial \beta \mu / \partial \beta)_P$, $u|_V = (\partial \beta \mu / \partial \beta)_V$, and $\bar{v} = (\partial \mu / \partial P)_T$ (see Appendix for further details).

The following thermodynamic identities may be used to evaluate all of the above generalized heat capacities from C_{PP} , along with the solute partial molar volume and solvent equation of state.

$$C_{VV} = C_{PP} - T \left\{ \left(\frac{\partial P}{\partial T} \right)_V \left[\left(\frac{\partial \bar{v}}{\partial T} \right)_P + \left(\frac{\partial \bar{v}}{\partial T} \right)_V \right] + \bar{v} \left(\frac{\partial^2 P}{\partial T^2} \right)_V \right\} \quad (7)$$

$$C_{PV} = C_{PP} - \left(\frac{\partial C_P}{\partial P} \right)_T \left(\frac{\partial P}{\partial N} \right)_{V,T} = C_{PP} - T \bar{v} \left(\frac{\partial^2 V}{\partial T^2} \right)_P \left(\frac{\partial P}{\partial V} \right)_T \quad (8)$$

$$C_{VP} = C_{PP} - T \left(\frac{\partial P}{\partial T} \right)_V \left[\left(\frac{\partial \bar{v}}{\partial T} \right)_P + \left(\frac{\partial \bar{v}}{\partial T} \right)_V \right] \quad (9)$$

$$C_{\bar{P}\bar{V}} = C_{PP} - T \left(\frac{\partial P}{\partial T} \right)_V \left(\frac{\partial \bar{v}}{\partial T} \right)_P \quad (10)$$

$$C_{\bar{V}\bar{P}} = C_{PP} - T \left\{ \left(\frac{\partial P}{\partial T} \right)_V \left(\frac{\partial \bar{v}}{\partial T} \right)_P + \bar{v} \left[\frac{\partial}{\partial T} \left(\frac{\partial P}{\partial T} \right)_V \right]_P \right\} \quad (11)$$

The required equation of state variables may further be expressed in terms of the solvent thermal expansion and compressibility coefficients, $\alpha_P = 1/V(\partial V / \partial T)_P$ and $\kappa_T = -1/V(\partial V / \partial P)_T$, respectively. The solvent's thermal pressure coefficient, $(\partial P / \partial T)_V$, which appears repeatedly in the above expressions, is here given a special symbol.

$$\xi = \left(\frac{\partial P}{\partial T} \right)_V = \frac{\alpha_P}{\kappa_T} \quad (12)$$

The corresponding second derivative may thus be expressed as $(\partial^2 P / \partial T^2)_V = (\partial \xi / \partial T)_V = (\partial \xi / \partial T)_P + \xi (\partial \xi / \partial P)_T$. Moreover, the constant volume temperature derivative of \bar{v} may be expressed in terms of somewhat more commonly encountered derivatives, $(\partial \bar{v} / \partial T)_V = (\partial \bar{v} / \partial T)_P + \xi (\partial \bar{v} / \partial P)_T$. With these identities, the above generalized heat capacity relations may be re-expressed as follows

$$C_{VV} - C_{PP} = -T \left[\left(\frac{\partial \xi \bar{v}}{\partial T} \right)_V + \xi \left(\frac{\partial \bar{v}}{\partial T} \right)_P \right] = -T \left[\left(\frac{\partial \xi \bar{v}}{\partial T} \right)_P + \xi \left(\frac{\partial \xi \bar{v}}{\partial P} \right)_T + \xi \left(\frac{\partial \bar{v}}{\partial T} \right)_P \right] = -T \left[\bar{v} \left[\left(\frac{\partial \xi}{\partial T} \right)_P + \xi \left(\frac{\partial \xi}{\partial P} \right)_T \right] + \xi \left[2 \left(\frac{\partial \bar{v}}{\partial T} \right)_P + \left(\frac{\partial \bar{v}}{\partial P} \right)_T \right] \right] \quad (13)$$

$$C_{PV} - C_{PP} = -T \left(\frac{\bar{v}}{\kappa_T} \right) \left[\alpha_P^2 + \left(\frac{\partial \alpha_P}{\partial T} \right)_P \right] \quad (14)$$

$$C_{VP} - C_{PP} = -T \zeta \left[2 \left(\frac{\partial \bar{v}}{\partial T} \right)_P + \zeta \left(\frac{\partial \bar{v}}{\partial P} \right)_T \right] \quad (15)$$

$$C_{\bar{P}\bar{V}} - C_{PP} = -T \zeta \left(\frac{\partial \bar{v}}{\partial T} \right)_P \quad (16)$$

$$C_{\bar{V}\bar{P}} - C_{PP} = -T \left[\zeta \left(\frac{\partial \bar{v}}{\partial T} \right)_P + \bar{v} \left(\frac{\partial \zeta}{\partial T} \right)_P \right] \quad (17)$$

Experimental solvation heat capacities are often expressed as heat capacity changes associated with a phase transfer process. For example, hydration heat capacities are usually defined as the difference between the partial molar heat capacity of the solute in water and in the vapor phase (both of which are maintained at the same constant pressure).

If the vapor phase is assumed to be ideal (I) then $C_{PP}^I = C_{PV}^I = C_{\bar{V}\bar{P}}^I = C_{VV}^I + k = C_{VP}^I + k = C_{\bar{P}\bar{V}}^I + k$ (where k Boltzmann's constant). Thus, for an ideal solvation process each of the generalized solvation heat capacities become $\Delta C_{ij} = C_{ij} - C_{ij}^I$, and are related as follows to the quantities defined in eqs 1–4 and 13–17 (where the first term on the right-hand-side of the above equality implicitly pertains to the solution phase).

$$\Delta C_{PP} = C_{PP} - C_{PP}^I = C_{PP} - C_{VV}^I - k \quad (18)$$

$$\Delta C_{VV} - \Delta C_{PP} = C_{VV} - C_{PP} + k \quad (19)$$

$$\Delta C_{VP} - \Delta C_{PP} = C_{VP} - C_{PP} + k \quad (20)$$

$$\Delta C_{PV} - \Delta C_{PP} = C_{PV} - C_{PP} \quad (21)$$

$$\Delta C_{\bar{V}\bar{P}} - \Delta C_{PP} = C_{\bar{V}\bar{P}} - C_{PP} \quad (22)$$

$$\Delta C_{\bar{P}\bar{V}} - \Delta C_{PP} = C_{\bar{P}\bar{V}} - C_{PP} + k \quad (23)$$

When heat capacities are expressed in molar rather than molecular units, k should be replaced by $R = kN_A$ (where N_A is Avogadro's number). Note that the above results may also be applied to any phase transfer process, represented as a combination of ideal solvation steps (as further described in the Appendix).

3. Decomposition of Heat Capacities

Although the thermodynamic identities presented in section 2 may be used to experimentally evaluate and interrelate generalized heat capacities, they do not in themselves reveal how these thermodynamic quantities are linked to intermolecular interactions. To obtain some insight into this relationship, one may decompose each of the solvation heat capacities into terms arising from the solute–solvent interaction energy, $\langle \Psi \rangle$, and the solvent reorganization energies at constant pressure, $\Delta \langle \Phi \rangle|_P$, or constant volume, $\Delta \langle \Phi \rangle|_V$ (as further described in the Appendix).²⁴ For example, by combining eqs 1 and 2 above with eqs 36, 42, and 47 of the Appendix, one may obtain the following decompositions of ΔC_{PP} and ΔC_{VV} .

$$\Delta C_{PP} = \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \left(\frac{\partial \Delta \langle \Phi \rangle|_P}{\partial T} \right)_P + P \left(\frac{\partial \bar{v}}{\partial T} \right)_P - k = \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \left(\frac{\partial \Delta \langle \Phi \rangle|_V}{\partial T} \right)_P + \left[\frac{\partial (T \zeta \bar{v})}{\partial T} \right]_P - k \quad (24)$$

$$\begin{aligned} \Delta C_{VV} = & \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_V + \left(\frac{\partial \Delta \langle \Phi \rangle|_V}{\partial T} \right)_V = \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \zeta \left(\frac{\partial \langle \Psi \rangle}{\partial P} \right)_T + \\ & \left(\frac{\partial \Delta \langle \Phi \rangle|_V}{\partial T} \right)_P + \zeta \left(\frac{\partial \Delta \langle \Phi \rangle|_V}{\partial P} \right)_T = \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \zeta \left(\frac{\partial \langle \Psi \rangle}{\partial P} \right)_T + \\ & \left(\frac{\partial \Delta \langle \Phi \rangle|_P}{\partial T} \right)_P + \zeta \left(\frac{\partial \Delta \langle \Phi \rangle|_P}{\partial P} \right)_T - T \left[\left(\frac{\partial \zeta \bar{v}}{\partial T} \right)_P + \zeta \left(\frac{\partial \zeta \bar{v}}{\partial P} \right)_T \right] + \\ & P \left[\left(\frac{\partial \bar{v}}{\partial T} \right)_P + \zeta \left(\frac{\partial \bar{v}}{\partial P} \right)_T \right] \quad (25) \end{aligned}$$

Notice that the above expressions, combined with eqs 13 and 19, imply the following additional identities.

$$\left(\frac{\partial \langle \Psi \rangle}{\partial P} \right)_T + \left(\frac{\partial \Delta \langle \Phi \rangle|_P}{\partial P} \right)_T = -T \left(\frac{\partial \bar{v}}{\partial T} \right)_P - P \left(\frac{\partial \bar{v}}{\partial P} \right)_T \quad (26)$$

$$\left(\frac{\partial \langle \Psi \rangle}{\partial P} \right)_T + \left(\frac{\partial \Delta \langle \Phi \rangle|_V}{\partial P} \right)_T = \bar{v} - T \left[\left(\frac{\partial \bar{v}}{\partial T} \right)_P + \left(\frac{\partial \zeta \bar{v}}{\partial P} \right)_T \right] \quad (27)$$

ΔC_{PV} and ΔC_{VP} may be decomposed by combining eqs 14, 15, and 24.

$$\begin{aligned} \Delta C_{PV} = \Delta C_{PP} - T \left(\frac{\bar{v}}{\kappa_T} \right) \left[\alpha_P^2 + \left(\frac{\partial \alpha_P}{\partial T} \right)_P \right] = & \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \\ & \left(\frac{\partial \Delta \langle \Phi \rangle|_P}{\partial T} \right)_P + P \left(\frac{\partial \bar{v}}{\partial T} \right)_P - T \left(\frac{\bar{v}}{\kappa_T} \right) \left[\alpha_P^2 + \left(\frac{\partial \alpha_P}{\partial T} \right)_P \right] - k = \\ & \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \left(\frac{\partial \Delta \langle \Phi \rangle|_V}{\partial T} \right)_P + \left[\frac{\partial (T \zeta \bar{v})}{\partial T} \right]_P - \\ & T \left(\frac{\bar{v}}{\kappa_T} \right) \left[\alpha_P^2 + \left(\frac{\partial \alpha_P}{\partial T} \right)_P \right] - k \quad (28) \end{aligned}$$

$$\begin{aligned} \Delta C_{VP} = \Delta C_{PP} - T \zeta \left[2 \left(\frac{\partial \bar{v}}{\partial T} \right)_P + \zeta \left(\frac{\partial \bar{v}}{\partial P} \right)_T \right] + k = & \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \\ & \left(\frac{\partial \Delta \langle \Phi \rangle|_P}{\partial T} \right)_P + P \left(\frac{\partial \bar{v}}{\partial T} \right)_P - T \zeta \left[2 \left(\frac{\partial \bar{v}}{\partial T} \right)_P + \zeta \left(\frac{\partial \bar{v}}{\partial P} \right)_T \right] = \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \\ & \left(\frac{\partial \Delta \langle \Phi \rangle|_V}{\partial T} \right)_P + \bar{v} \left[\zeta + T \left(\frac{\partial \zeta}{\partial T} \right)_P \right] - T \zeta \left[2 \left(\frac{\partial \bar{v}}{\partial T} \right)_P + \zeta \left(\frac{\partial \bar{v}}{\partial P} \right)_T \right] \quad (29) \end{aligned}$$

Similarly, $\Delta C_{\bar{P}\bar{V}}$ and $\Delta C_{\bar{V}\bar{P}}$ may be decomposed either using 16, 17, and 24 or by combining eqs 5, 6, 18, 22, and 23 with eqs 42 and 47 in the Appendix.

$$\begin{aligned} \Delta C_{\bar{P}\bar{V}} = \Delta C_{PP} - T \zeta \left(\frac{\partial \bar{v}}{\partial T} \right)_P + k = & \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \left(\frac{\partial \Delta \langle \Phi \rangle|_P}{\partial T} \right)_P + \\ & (P - T \zeta) \left(\frac{\partial \bar{v}}{\partial T} \right)_P = \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \left(\frac{\partial \Delta \langle \Phi \rangle|_V}{\partial T} \right)_P + \\ & \bar{v} \left[\zeta + T \left(\frac{\partial \zeta}{\partial T} \right)_P \right] = \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_V + \left(\frac{\partial \Delta \langle \Phi \rangle|_V}{\partial T} \right)_V + T \left(\frac{\partial \zeta \bar{v}}{\partial T} \right)_V \quad (30) \end{aligned}$$

$$\begin{aligned} \Delta C_{\bar{V}\bar{P}} = \Delta C_{PP} - T \left[\zeta \left(\frac{\partial \bar{v}}{\partial T} \right)_P + \bar{v} \left(\frac{\partial \zeta}{\partial T} \right)_P \right] = & \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \\ & \left(\frac{\partial \Delta \langle \Phi \rangle|_P}{\partial T} \right)_P + P \left(\frac{\partial \bar{v}}{\partial T} \right)_P - T \left[\zeta \left(\frac{\partial \bar{v}}{\partial T} \right)_P + \bar{v} \left(\frac{\partial \zeta}{\partial T} \right)_P \right] - k = \\ & \left(\frac{\partial \langle \Psi \rangle}{\partial T} \right)_P + \left(\frac{\partial \Delta \langle \Phi \rangle|_V}{\partial T} \right)_P + \zeta \bar{v} - k \quad (31) \end{aligned}$$

4. Results and Discussion

The generalized heat capacities defined by eqs 1–6 each have unique physical significance. C_{PP} and C_{PV} represent changes in

TABLE 1: Pure Liquid Properties (at 0.1 MPa)^a

| liquid | <i>T</i> (K) | ρ (1/nm ³) | α_P (1/K) | κ_T (1/MPa) | $(\partial\alpha_P/\partial T)_P$ $\times 10^3$ (1/K ²) | ζ (MPa/K) | $(\partial\zeta/\partial T)_P$ (MPa/K ²) | $(\partial\zeta/\partial P)_T$ (1/K) |
|--|--------------|--------------------------------|---------------------|-----------------------|--|--------------------|---|---|
| xenon | 162 | 13.57 | 0.00221 | 0.00158 | 1.16 | 1.39 | −0.0130 | 0.00760 |
| | 165 | 13.48 | 0.00224 | 0.00166 | 1.24 | 1.35 | −0.0127 | 0.00771 |
| CH ₂ F ₂ | 137 | 16.53 | 0.00170 | 0.00053 | 0.319 | 3.23 | −0.0284 | 0.00726 |
| | 221 | 14.06 | 0.00228 | 0.00146 | 1.24 | 1.56 | −0.0141 | 0.0084 |
| <i>n</i> -C ₆ H ₁₄ | 178 | 5.32 | 0.00119 | 0.00067 | −0.005 | 1.79 | −0.0135 | 0.00525 |
| | 298 | 4.58 | 0.00140 | 0.00177 | 0.391 | 0.795 | −0.00517 | 0.00566 |
| | 341 | 4.29 | 0.00163 | 0.00272 | 0.665 | 0.597 | −0.00416 | 0.00641 |
| H ₂ O | 274 | 33.42 | −0.00052 | 0.000506 | 1.72 | −0.104 | 0.0339 | 0.00701 |
| | 298 | 33.33 | 0.000256 | 0.000453 | 0.965 | 0.565 | 0.0227 | 0.00394 |
| | 372 | 32.06 | 0.000744 | 0.000488 | 0.557 | 1.52 | 0.00581 | 0.0017 |

^a These data derive from NIST tables of refs 32 and 43. Note that 1 MPa = 1 J/cm³ and so molar volumes in cm³/mol may be multiplied by pressure in MPa to produce energies in J/mol. The temperature range for each liquid extends approximately from the freezing point to the boiling point.

TABLE 2: Solvation Heat Capacities (at 0.1 MPa)^a

| solute | solvent | <i>T</i> (K) | ΔC_{PP} (J/(K mol)) | ΔC_{VV} (J/(K mol)) | ΔC_{PV} (J/(K mol)) | ΔC_{VP} (J/(K mol)) | $\Delta C_{\bar{P}\bar{V}}$ (J/(K mol)) | $\Delta C_{\bar{V}\bar{P}}$ (J/(K mol)) |
|--|--|--------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--|--|
| xenon | xenon | 165 | 24 | 26 | −54 | 10 | 10 | 95 |
| CH ₂ F ₂ | CH ₂ F ₂ | 221 | 45 | 29 | −69 | 19 | 19 | 145 |
| <i>n</i> -C ₆ H ₁₄ | <i>n</i> -C ₆ H ₁₄ | 298 | 51 | 42 | −79 | 16 | 16 | 210 |
| H ₂ O | H ₂ O | 298 | 42 | −85 | −74 | 49 | 49 | −81 |
| Xe | H ₂ O | 298 | 228 | −128 | −67 | 214 | 223 | −97 |
| c-C ₆ H ₁₂ | H ₂ O | 298 | 410 | −356 | −219 | 374 | 392 | −282 |
| $\sigma_{HS} = 0.27$ nm | H ₂ O | 298 | 113 | −26 | −13 | 120 | 120 | −21 |
| $\sigma_{HS} = 0.39$ nm | H ₂ O | 298 | 227 | −112 | −70 | 233 | 233 | −89 |
| $\sigma_{HS} = 0.56$ nm | H ₂ O | 298 | 430 | −422 | −306 | 434 | 434 | −354 |

^a The experimental self-solvation data are derived from NIST tables (refs 32, 43) while those for the hydration of Xe, cyclohexane, and the hard-sphere solutes are obtained from the ORCHYD database (refs 26, 44) combined with the C-EOS and GvdW1 (as described in ref 4 and the Appendix). The only exception is the partial molar volume of cyclohexane in water (and its temperature dependence). In this case the experimental partial molar volume results reported in ref 4 were fit directly to a quadratic function of temperature (from 298 to 424 K) in order to obtain \bar{v} and $(\partial\bar{v}/\partial T)_P$; the pressure derivative of \bar{v} was obtained from ORCHYD (and used to extrapolate the 10 MPa experimental partial molar volumes down to 0.1 MPa).

the total C_P of a fluid induced by adding a single solute either at constant pressure or at constant volume, respectively. Similarly, C_{VV} and C_{VP} represent changes in the total C_V of a fluid induced by adding a single solute either at constant volume or at constant pressure. Moreover, C_{PP}/T and $C_{\bar{P}\bar{V}}/T$ are equivalent to the temperature derivatives of $s|_P$ evaluated at either constant pressure or constant volume, while C_{VV}/T and $C_{\bar{V}\bar{P}}/T$ are equivalent to the temperature derivatives of $s|_V$ evaluated at either constant volume or constant pressure.

Equations 7–11 and 13–17 indicate that both solvent equation of state and solute partial molar thermodynamic quantities are required in order to quantify and interrelate each of the generalized heat capacities. Tables 1 and 2 contain equation of state data for four pure liquids and generalized solvation heat capacities for several self-solvation and hydration processes. The equation of state data in Table 1 span the entire normal liquid range of xenon (Xe), difluoromethane (CH₂F₂), *n*-hexane (*n*-C₆H₁₄), and water (H₂O). The first four rows of Table 2 pertain to self-solvation processes in each of the above four fluids, and the remaining rows pertain to the hydration of Xe, cyclohexane (c-C₆H₁₂) and three hard-sphere solutes whose diameters, σ_{HS} , are close to those of water, xenon, and cyclohexane.

Note that CH₂F₂ has a gas-phase dipole moment of 1.98 D, which is similar to that of water, 1.86 D.³² However, both the bulk properties (Table 1) and self-solvation heat capacities (Table 2) of CH₂F₂ have less in common with water than with the two nonpolar fluids. Other well-known anomalous properties of water include its density maximum at ≈ 4 °C and the associated negative values of α_P at low temperature and strong increase in ζ with temperature (see Table 1)—all of which are

thought to be linked to a latent liquid–liquid phase transition that is buried within the supercooled/superpressed metastable fluid region of the water phase diagram.^{33,34} The self-solvation heat capacities of water also clearly differ from those of other fluids, particularly the negative values of ΔC_{VV} and $\Delta C_{\bar{V}\bar{P}}$ (see Table 2). The latter differences may again be traced to the anomalous thermal expansion properties of water, as $(\partial\zeta/\partial T)_P$ is positive for water and negative for the other fluids, and predominates in both eqs 13 and 17 (we will return to discuss this issue from a different perspective below).

The generalized hydration heat capacities of nonpolar solutes in water differ markedly from those of polar solutes (of which the self-solvation of water is a rather extreme example). The large positive hydration ΔC_{PP} of nonpolar solutes is often cited as a signature of the hydrophobic effect. A particularly informative comparison is that of the self-solvation of water with the hydration of a hard-sphere solute of 0.27 nm diameter (obtained from cavity chemical potential simulations in SPC/E water).^{4,23} Although both solutes are similar in size, the ΔC_{PP} associated with the hydration of the hard sphere is more than twice that of water. The two larger hard spheres listed at the bottom of Table 2, which are similar in size to xenon and cyclohexane, respectively,^{35,36} also have quite similar ΔC_{PP} values to the latter solutes. These results clearly suggest that ΔC_{PP} is relatively insensitive to the cohesive interactions between nonpolar molecules and water but is quite sensitive to solute–solvent hydrogen bonding interactions (as exemplified by the self-solvation of water).

The results in Table 2 indicate that the magnitudes and signs of other generalized solvation heat capacities, ΔC_{ij} , often differ quite significantly from ΔC_{PP} . However, some ΔC_{ij} values are

TABLE 3: Intermolecular Interaction Contributions to ΔC_{PP} (at 0.1 MPa)^a

| solute | solvent | T (K) | \bar{v} (cm ³ /mol) | $[\partial(T\zeta\bar{v})/\partial T]_P$ (J/(K mol)) | $(\partial\langle\Psi\rangle/\partial T)_P$ (J/(K mol)) | $(\partial\Delta\langle\Phi\rangle _P/\partial T)_P$ (J/(K mol)) | $(\partial\Delta\langle\Phi\rangle _V/\partial T)_P$ (J/(K mol)) |
|--|--|---------|-------------------------------------|---|--|---|---|
| Xe | Xe | 165 | 44.7 | −11 | 64 | −32 | −21 |
| CH ₂ F ₂ | CH ₂ F ₂ | 221 | 42.8 | −33 | 106 | −53 | −20 |
| <i>n</i> -C ₆ H ₁₄ | <i>n</i> -C ₆ H ₁₄ | 298 | 131.6 | −54 | 120 | −60 | −6 |
| H ₂ O | H ₂ O | 298 | 18.2 | 133 | 100 | −50 | −183 |
| Xe | H ₂ O | 298 | 45.8 | 351 | 5 ^b | 231 ^b | −120 ^b |
| c-C ₆ H ₁₂ | H ₂ O | 298 | 98.3 | 747 | 12 ^b | 406 ^b | −341 ^b |
| $\sigma_{HS} = 0.27$ nm | H ₂ O | 298 | 19.6 ^c | 145 ^c | 0 ^c | 121 ^c | −24 ^c |
| $\sigma_{HS} = 0.39$ nm | H ₂ O | 298 | 46.4 ^c | 342 ^c | 0 ^c | 235 ^c | −107 ^c |
| $\sigma_{HS} = 0.56$ nm | H ₂ O | 298 | 115.1 ^c | 849 ^c | 0 ^c | 438 ^c | −411 ^c |

^a See footnote *a* of Table 2. ^b Obtained by combining experimental ΔC_{PP} and $\Delta u|_P$ data with first-order perturbation theory (GvdW1) using eq 57, as described in the Appendix and refs 4 and 24. More specifically, the GvdW1 mean field coefficients for Xe/H₂O and c-C₆H₁₂/H₂O are $a = 624 \pm 15$ J nm³/mol and $a = 1428 \pm 30$ J nm³/mol, respectively, and the hard-sphere diameters of Xe, c-C₆H₁₂, and H₂O are $\sigma = 0.393$ nm, $\sigma = 0.564$ nm, and $\sigma_w = 0.27 \pm 0.01$ nm, respectively (where the error bars in a derive from the uncertainty in σ_w). ^c Obtained from the water cavity equation of state (C-EOS), as described in the Appendix and ref 4.

TABLE 4: Other ΔC_{ij} Intermolecular Contributions (at 0.1 MPa)^a

| solute | solvent | T (K) | $(\partial\bar{v}/\partial T)_P$ (cm ³ /(K mol)) | $(\partial\bar{v}/\partial P)_T$ (cm ³ /(MPa mol)) | $(\partial\langle\Psi\rangle/\partial T)_V$ (J/(K mol)) | $(\partial\Delta\langle\Phi\rangle _V/\partial T)_V$ (J/(K mol)) | $(\partial\langle\Psi\rangle/\partial P)_T$ (J/(MPa mol)) |
|--|--|---------|--|--|--|---|--|
| Xe | Xe | 165 | 0.1001 | −0.0733 | 20 | 7 | −33 |
| CH ₂ F ₂ | CH ₂ F ₂ | 221 | 0.0976 | −0.0623 | 39 | −10 | −43 |
| <i>n</i> -C ₆ H ₁₄ | <i>n</i> -C ₆ H ₁₄ | 298 | 0.1848 | −0.2300 | 33 | 9 | −109 |
| H ₂ O | H ₂ O | 298 | 0.00463 | −0.0088 | 99 | −184 | −3 |
| Xe | H ₂ O | 298 | 0.079 | −0.050 | 0 ^b | −128 ^b | −9 ^b |
| c-C ₆ H ₁₂ | H ₂ O | 298 | 0.157 | −0.096 | 0 ^b | −356 ^b | −22 ^b |
| $\sigma_{HS} = 0.27$ nm | H ₂ O | 298 | 0.005 ^c | −0.009 ^c | 0 ^c | −26 ^c | 0 ^c |
| $\sigma_{HS} = 0.39$ nm | H ₂ O | 298 | 0.012 ^c | −0.021 ^c | 0 ^c | −112 ^c | 0 ^c |
| $\sigma_{HS} = 0.56$ nm | H ₂ O | 298 | 0.029 ^c | −0.052 ^c | 0 ^c | −422 ^c | 0 ^c |

^a See footnote *a* of Table 2. ^b Obtained by combining experimental and first order (GvdW1) perturbation theory, as described in the Appendix and footnote *b* of Table 3. ^c Obtained from the cavity equation of state (C-EOS), as described in the Appendix and ref 4.

very similar, or even exactly equal, to each other. For example, it is necessarily the case that $\Delta C_{VP} = \Delta C_{\bar{V}P}$ for any self-solvation process. This is because $\Delta C_{\bar{V}P} - \Delta C_{VP} = (\partial\bar{v}/\partial T)_P + \zeta(\partial\bar{v}/\partial P)_T = (\partial\bar{v}/\partial T)_V$, which vanishes identically for any self-solvation process. For more general solvation processes one might expect $(\partial\bar{v}/\partial T)_V \approx 0$ to remain a good approximation. However, given the experimental difficulties associated with measuring $(\partial\bar{v}/\partial T)_V$ directly—or measuring both $(\partial\bar{v}/\partial T)_P$ and $(\partial\bar{v}/\partial P)_T$ sufficiently accurately—the general validity of the prior approximation remains an open question. Notice that neither $(\partial\bar{v}/\partial T)_P$ nor $(\partial\bar{v}/\partial P)_T$ are available for hard spheres in water, as the only available hard sphere hydration \bar{v} values are those recently obtained by Floris from simulations performed at $T = 298$ K and $P = 0.1$ MPa (in TIP4P water).³⁷ Thus, we have chosen to approximate the $(\partial\bar{v}/\partial T)_P$ and $(\partial\bar{v}/\partial P)_T$ values of hard spheres in water by assuming that their partial molar volumes have the same thermal expansion and compressibility coefficients as that of pure water, which also implies that $(\partial\bar{v}/\partial T)_V = 0$. This approximation is not expected to introduce significant error as the resulting thermodynamic and heat capacity predictions are relatively insensitive to these derivatives (since the derivatives of ζ typically play a more significant role than those of \bar{v}). For example, the ΔC_{ij} values obtained from ΔC_{PP} ⁴ for the largest hard-sphere solute (with $\sigma_{HS} = 0.56$ nm) would change by less than 10% if the corresponding $(\partial\bar{v}/\partial T)_P$ and $(\partial\bar{v}/\partial P)_T$ values were assumed to be the same as the extrapolated experimental values for c-C₆H₁₂ (see Table 4).

The generalized solvation heat capacities are clearly quite sensitive to the chemical nature of the solute and solvent molecules. Understanding this sensitivity requires quantifying intermolecular interaction contributions to ΔC_{ij} . For self-solvation processes, one can independently identify solute–solvent, $\langle\Psi\rangle$, and solvent reorganization, $\Delta\langle\Phi\rangle$, contributions

to ΔC_{ij} , by making use of eq 56 in the Appendix. For more general solvation processes $\langle\Psi\rangle$ and $\Delta\langle\Phi\rangle$ cannot be obtained from experimental measurements without additional input from simulation and/or theoretical approximations. In analyzing the hydration heat capacities of nonpolar solutes, we have combined the cavity equation of state (C-EOS) of water⁴ with first-order perturbation theory (GvdW1)²⁴ to determine $\langle\Psi\rangle$ (see Appendix for details). Since $\langle\Psi\rangle$ is found to contribute relatively insignificantly to ΔC_{PP} for hydrophobic solvation processes (as further discussed below), the approximations inherent in our use of the C-EOS and GvdW1 should not significantly affect the accuracy of our results.

Note that for both self-solvation and more general solvation processes, $\langle\Psi\rangle$ and $\Delta\langle\Phi\rangle$ represent physically quite different energies, as $\langle\Psi\rangle$ is the direct interaction energy between the added (solute) molecule and the surrounding (solvent) molecules, while $\Delta\langle\Phi\rangle$ represents the change in the solvent–solvent interaction energy induced by adding the solute. An additional contribution to ΔC_{PP} comes from the temperature derivative of $T\zeta\bar{v}$ (see eq 24), which clearly also depends on solute–solvent interactions via the partial molar volume of the solute. However, \bar{v} primarily reflects the size (van der Waals volume) of the solute while $\langle\Psi\rangle$ and $\Delta\langle\Phi\rangle$ are more sensitive to solute–solvent cohesive interactions (and are also strongly solute size dependent).

The way in which each of the above quantities contribute to ΔC_{PP} may be inferred from the results in Table 3. Note that eq 24 indicates that the sum of the temperature derivatives of $\langle\Psi\rangle$ and $\Delta\langle\Phi\rangle|_P$ is essentially equivalent to $\Delta C_{PP} + R$ (in molar units), since $P(\partial\bar{v}/\partial T)_P$ is negligible at ambient pressure. Thus, the results in Table 3 indicate that for all the self-solvation processes both $\langle\Psi\rangle$ and $\Delta\langle\Phi\rangle|_P$ contribute significantly to ΔC_{PP} . On the other hand, for the hydration of nonpolar solutes ΔC_{PP} is determined almost entirely by $\Delta\langle\Phi\rangle|_P$. In other words, these

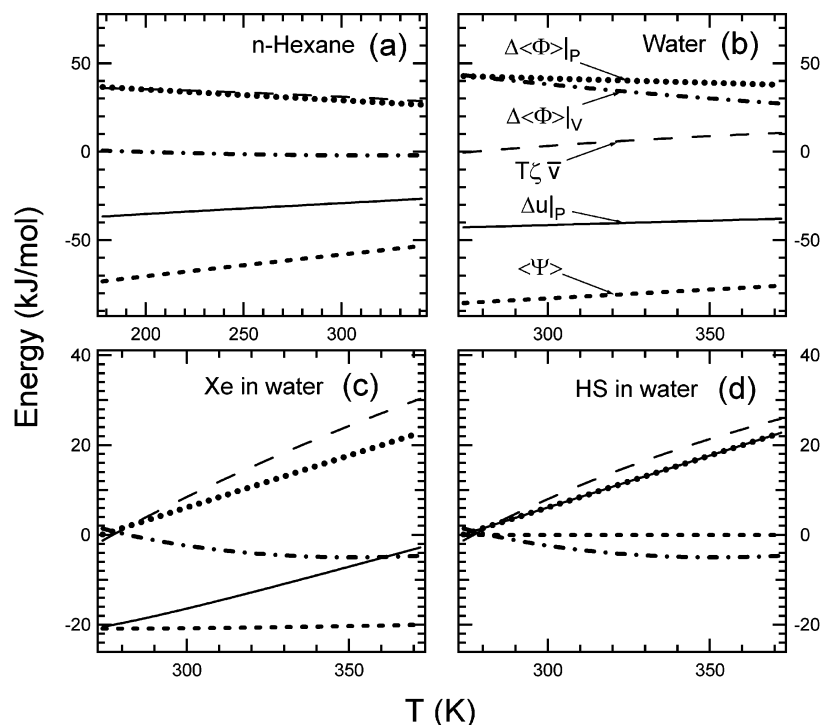


Figure 1. The partial molar solvation energy, $u|_P \approx h|_P$, solute-solvent interaction energy, $\langle \Psi \rangle$, and solvent reorganization energies, $\Delta\langle \Phi \rangle|_P$ and $\Delta\langle \Phi \rangle|_V$, as well as $T\zeta\bar{v}$ are plotted as a function of temperature (at $P = 0.1$ MPa). The four panels represent results for (a) the self-solvation of *n*-hexane, (b) the self-solvation of water, (c) the hydration of Xe, and (d) the hydration of a hard-sphere that is similar in size to Xe.

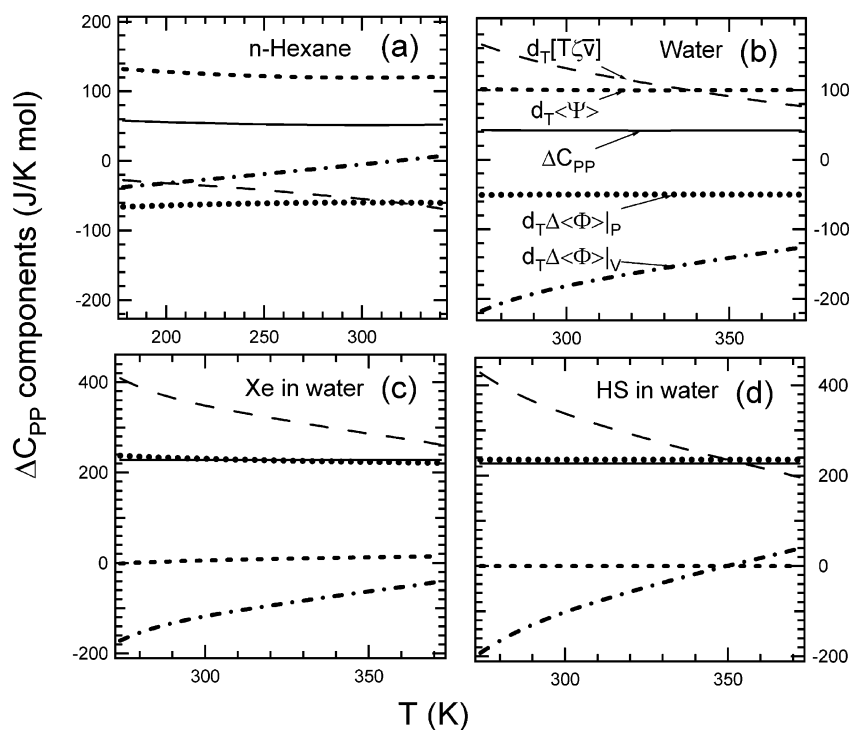


Figure 2. The partial molar heat capacity, ΔC_{PP} , and its components (each of which are temperature derivatives of the quantities in Figure 1) are plotted as a function of temperature. The notation $d_T(\dots)$ is used to represent temperature derivatives evaluated at constant pressure, $(\partial \dots / \partial T)_P$.

results make it clear that the characteristically large positive hydrophobic heat capacities predominantly derive from the strongly temperature-dependent reorganization energy of water around nonpolar solutes.

The first equality in eq 25, combined with the GvdW1 approximation, implies that $\Delta C_{VV} = (\partial \Delta\langle \Phi \rangle|_V / \partial T)_V$ for the hydration of hydrophobic solutes. Thus, the GvdW1 approximation implies that the experimental ΔC_{VV} of hydrophobic solutes also derives from the energetics of water reorganization.

To better understand the significance of the above results, it is useful to consider the temperature-dependent plots in Figures 1 and 2. Note that all the quantities in the last three columns of Table 3 are temperature derivatives and so are equivalent to the slopes of the corresponding curves in Figure 1. The curves in Figure 2 show how parameters in Table 3 vary with temperature. In other words, the curves in Figure 2 represent the temperature dependence of the slopes of the curves in Figure 1. Inspection of Figure 1 makes it clear that the sign of $\langle \Psi \rangle$ is

typically negative, which reflects the fact that solute–solvent interactions are predominantly cohesive (attractive). However, the magnitude of $\langle\Psi\rangle$ varies greatly from one solution to another. For example, $\langle\Psi\rangle$ is much more negative for the self-solvation of water than for the solvation of Xe in water (and is necessarily exactly equal to zero for the solvation of a hard sphere in water). Heat capacities are only sensitive to the temperature derivative of $\langle\Psi\rangle$, not its magnitude. The $\langle\Psi\rangle$ results in Figure 1b show that the temperature derivative of $\langle\Psi\rangle$ is positive for the self-solvation of water, which indicates that the cohesive interaction energy of water molecules decreases significantly with increasing temperature. For the hydration of nonpolar solutes, the temperature derivative of $\langle\Psi\rangle$ is much smaller, which explains why the corresponding contribution of $\langle\Psi\rangle$ to ΔC_{PP} is relatively insignificant. On the other hand, the temperature derivative of $\Delta\langle\Phi\rangle_P$ is quite large and positive for the hydration of nonpolar solutes and is nearly equivalent to ΔC_{PP} , as clearly evidenced by the similarity of the solid and dotted curves in parts c and d of Figure 2.

One of the more subtle and intriguing features of the results shown in Figures 1 and 2 is the difference between the constant-volume solvent reorganization energies, $\Delta\langle\Phi\rangle_V$, in different solutions. These reorganization energies represent the change in the average solvent–solvent interaction energy induced by the addition of a solute at fixed volume. Notice that there is no change in the average number density of the solvent in any such constant-volume solvation process. Thus, if cohesive solvent–solvent interactions were describable by the van der Waals mean field approximation, then $\Delta\langle\Phi\rangle_V$ would necessarily vanish identically (because this approximation implies that configuration averaged cohesive energy depends only on the average molecular number density). This prediction is remarkably consistent with the experimental self-solvation of *n*-hexane, for which both $\Delta\langle\Phi\rangle_V$ and its temperature derivative are nearly zero, as shown in Figures 1a and 2a. On the other hand, for the self-solvation of water, Figures 1b and 2b indicate that both $\Delta\langle\Phi\rangle_V$ and its temperature derivative have considerable magnitudes. This should not be surprising given that the cohesive (hydrogen bonding) interactions in water are not expected to conform to the van der Waals mean field approximation. What is perhaps more surprising is the fact that the magnitudes of $\Delta\langle\Phi\rangle_V$ are again quite small for the hydration of nonpolar and hard sphere (HS) solutes, as illustrated in parts c and d of Figure 1. In other words, the rearrangement of water molecules which takes place around xenon (or a hard sphere of similar size) occurs in such a way that very little water–water hydrogen bonding energy is sacrificed (at constant volume). However, although $\Delta\langle\Phi\rangle_V$ is relatively small, it has a significant temperature derivative, particularly at low temperature, as illustrated in parts c and d of Figure 2.

It is also interesting to note that eq 36 implies that $\Delta\langle\Phi\rangle_V \approx \Delta\langle\Phi\rangle_P - T\zeta\bar{v}$. The latter two quantities have different physical significance, and typically also opposite signs. The quantity $-T\zeta\bar{v}$, which is usually negative, reflects the energy change associated with compression of the solvent induced by adding a solute at constant volume. In other words, it is equivalent to the energy change which would be produced if the pure solvent were compressed by an amount equal to the solute's partial molar volume. Thus, $\Delta\langle\Phi\rangle_P$ clearly represents that portion of $\Delta\langle\Phi\rangle_V$ which is not associated with solvent compression. Moreover, $\Delta\langle\Phi\rangle_P$ is typically positive, which implies that the solute-induced rearrangement of solvent molecules (other than bulk compression) generally leads to a loss of solvent–solvent cohesion. These relationships also help explain the apparent

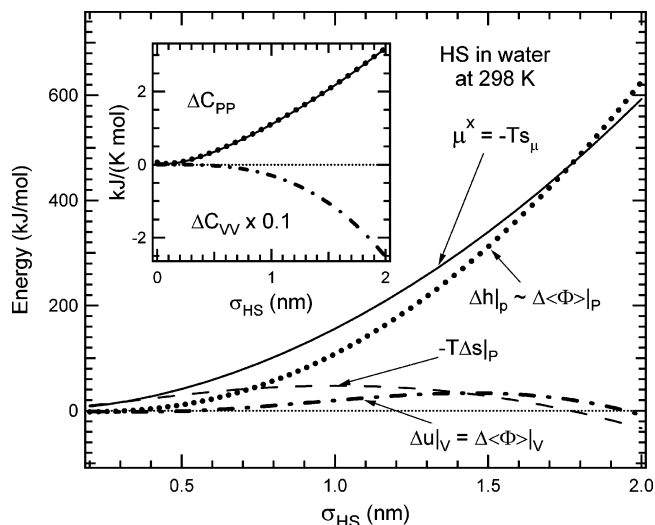


Figure 3. The hydration chemical potential, μ^* , enthalpy, $h|_P$, and entropy, $s|_P$, of hard-sphere solutes are plotted as a function of σ_{HS} at $T = 298$ K and $P = 0.1$ MPa. The hydration enthalpy differs by approximately $RT \approx 2.4$ kJ/mol from the constant-volume water reorganization energy, $\Delta\langle\Phi\rangle_P$, while the corresponding constant-volume reorganization energy, $\Delta\langle\Phi\rangle_V$, is much smaller in magnitude. The inset shows the corresponding hydration heat capacities ΔC_{PP} and ΔC_{VV} (note that these are in kJ rather than J units, and ΔC_{VV} is 10 times larger than it appears).

mirror symmetry between the temperature derivatives of $\Delta\langle\Phi\rangle_V$ and $T\zeta\bar{v}$ that is evident in Figure 2. In other words, since $\Delta\langle\Phi\rangle_P$ is virtually temperature independent, the derivatives of $\Delta\langle\Phi\rangle_V$ and $T\zeta\bar{v}$ mirror each other.

The decomposition of generalized solvation heat capacities can also clarify the significance of the negative values of ΔC_{VV} and $\Delta C_{\bar{V}P}$ for hydration processes (including the self-solvation of water). The first equality in eq 25 indicates that ΔC_{VV} may be expressed as the sum of the constant-volume temperature derivatives of $\langle\Psi\rangle$ and $\Delta\langle\Phi\rangle_V$, whose values are given in Table 4. These make it clear that the predominant contribution to ΔC_{VV} comes from the large negative temperature derivative of $\Delta\langle\Phi\rangle_V$. Also note that comparison of the hydration results shown in Tables 3 and 4 indicate that the constant-pressure and constant-volume temperature derivatives of $\Delta\langle\Phi\rangle_V$ are similar in magnitude (as are the corresponding derivatives of $\langle\Psi\rangle$). Thus, eq 31 implies that the primary difference between ΔC_{VV} and $\Delta C_{\bar{V}P}$ derives from the extra $\zeta\bar{v}$ term. Although the latter quantity is usually positive, it is typically not sufficiently large to overcome the negative reorganization energy contribution, and thus $\Delta C_{\bar{V}P}$ remains negative.

Dramatic hydration shell restructuring (dewetting) is expected to occur around hard-sphere solutes that are larger than about 1 nm in diameter.^{4,16,17,38} Although the degree to which dewetting takes place around hydrocarbons and proteins remains a subject of debate,^{20,21} both theoretical predictions and simulation results leave no doubt that such restructuring does occur in water around large cavities (hard-sphere solutes) under ambient conditions. The C-EOS may be used to quantify the thermodynamic signatures of dewetting around hard-sphere solutes, as illustrated in Figure 3.⁴ This shows how the excess chemical potential, $\mu^* = kT \ln\langle e^{+\beta\Delta\Psi}\rangle = -Ts_\mu$, as well as its partial molar enthalpic, $\Delta h|_P = \Delta\langle\Phi\rangle_c|_P - kT$, and entropic, $-T\Delta s|_P = -Ts_\mu - \Delta\langle\Phi\rangle_c|_P + kT$, components depend on solute diameter, σ_{HS} (at $T = 298$ K and $P = 0.1$ MPa). These results are obtained using eqs 34, 47, and 48, keeping in mind that $\langle\Psi\rangle = \epsilon_\mu = 0$ for a hard-sphere solute. Notice that the chemical potential is essentially equivalent to $-T\Delta s|_P$ for small σ_{HS} , while

at large σ_{HS} it becomes predominantly enthalpic, as predicted theoretically and observed in recent simulations.^{16,38} The diameter at which $\Delta h|_p$ and $-T\Delta s|_p$ cross, $\sigma_{\text{HS}} \approx 0.75$ nm or $R_c = (\sigma_{\text{HS}} + \sigma_w)/2 \approx 0.5$ nm, is slightly larger than that observed in simulations performed at a metastable negative pressure (tension) of ≈ -100 MPa. Although direct simulation of the crossover at 0.1 MPa is hampered by numerical noise,³⁸ the C-EOS predictions in Figure 3 are likely to be robust as they are assured self-consistency with accurate temperature-dependent cavity chemical potential and surface tension results.⁴

Another interesting feature in Figure 3 is the diameter at which $\Delta s|_p$ crosses zero, which indicates that the entropy of water is unchanged when a hard sphere of ≈ 1.8 nm diameter ($R_c \approx 1$ nm) is dissolved at constant pressure. Hydration of smaller hard spheres is accompanied by a decrease in the entropy of water while for larger hard spheres the entropy of water increases (relative its bulk value), consistent with the formation of a looser (more vaporlike) hydration shell. Figure 3 also shows that the constant-volume reorganization energy, $\Delta\langle\Phi\rangle_{c|v}$ (dot-dashed curve), remains small in comparison with $\Delta\langle\Phi\rangle_{c|p}$ (dotted curves) for all of the hard-sphere solutes in this figure. However, the temperature derivative of $\Delta\langle\Phi\rangle_{c|v}$, which dictates the magnitude of ΔC_{VV} , is invariably more significant, particularly for large solutes. The inset graph in Figure 3 shows how $\Delta C_{PP} \approx (\partial\Delta\langle\Phi\rangle_{c|p}/\partial T)_p$ and $\Delta C_{VV} = (\partial\Delta\langle\Phi\rangle_{c|v}/\partial T)_v$ depend on σ_{HS} . The almost perfect equivalence of the solid and dotted curves in the inset demonstrate that the temperature derivatives of $\Delta h|_p$ (solid curve) and $\Delta\langle\Phi\rangle_{c|p}$ (dotted curve) are virtually identical, and thus the partial molar heat capacity of all hard-sphere solutes is dictated by the constant-pressure reorganization energy of water. Notice that ΔC_{VV} is invariably negative and only becomes larger in magnitude than ΔC_{PP} near the diameter at which $\Delta h|_p$ and $-T\Delta s|_p$ cross. At larger diameters ΔC_{VV} becomes much larger in magnitude than ΔC_{PP} . Comparison of the second equalities in eqs 24 and 25, as well as eq 27, indicates that the largest contribution to the difference between ΔC_{PP} and ΔC_{VV} comes from the temperature derivative of $T\zeta v$, which scales roughly with as the cube of σ_{HS} , and is also approximately equal to the difference between the temperature derivatives of $\Delta\langle\Phi\rangle|_p$ and $\Delta\langle\Phi\rangle|_v$ (both evaluated at constant pressure).

5. Conclusions

The generalized solvation heat capacities identified in this work, ΔC_{ij} , complement and extend the usual partial molar solvation (or hydration) heat capacity, which in our notation is ΔC_{PP} . The exact expressions presented in section 2 may be used to evaluate each ΔC_{ij} from ΔC_{PP} given data pertaining to the equation of state of the pure solvent and the partial molar volume of the solute. The influence of intermolecular solute-solvent and solvent-reorganization energies on each ΔC_{ij} may be identified using the exact statistical mechanical expressions presented in section 3 (and the Appendix). For self-solvation processes the latter decomposition may be performed entirely using experimental data, while for more general solvation processes additional theoretical and/or simulation input is required. For the hydration of nonpolar solutes, we have combined first-order perturbation theory (GvdW1)²⁴ with the aqueous cavity equation of state (C-EOS)⁴ to extract intermolecular contributions to ΔC_{ij} . The accuracy of the results is assured by the fact that only the solute-solvent interaction energy, $\langle\Psi\rangle$, is obtained with the aid of the GvdW1 approximation and $\langle\Psi\rangle$ contributes relatively insignificantly to ΔC_{ij} for

nonpolar hydration processes. More importantly, our results indicate that for nonpolar solutes, ΔC_{PP} is determined almost entirely by the large positive temperature derivative of the constant-pressure water reorganization energy, $\Delta\langle\Phi\rangle|_p$. Similarly, the corresponding ΔC_{VV} values are determined entirely by the temperature derivative of constant-volume water reorganization energy, $\Delta\langle\Phi\rangle|_v$. On the other hand, for self-solvation processes (including the hydration of a water molecule) the positive sign of ΔC_{PP} is dictated by the positive temperature derivative of $\langle\Psi\rangle$ rather than the smaller negative reorganization energy contribution (see Table 3). Thus, we have established that *quite different intermolecular interaction mechanisms underly the observed hydration heat capacities of polar and nonpolar molecules.*

The most difficult to find (or measure) experimental parameters that are required to interconvert ΔC_{ij} values are the temperature and pressure derivatives of the solute partial molar volume, \bar{v} . (A notable exception is the interconversion of ΔC_{PP} and ΔC_{PV} , which does not require derivatives of \bar{v} .) For self-solvation processes all of the required quantities may be obtained directly from the equation of state of the solvent. In other cases, if the derivatives of \bar{v} are lacking, the following approximations may prove to be useful: $(\partial\bar{v}/\partial T)_p \approx \bar{v}\alpha_p$, $(\partial\bar{v}/\partial P)_T \approx \bar{v}\kappa_T$, and $(\partial\bar{v}/\partial T)_v \approx 0$ (where α_p and κ_T pertain to pure solvent). We have used the first two approximations to estimate the derivatives of \bar{v} for hard-sphere solutes in water. However, the experimentally derived partial molar volumes of xenon and cyclohexane in water (see Table 4) suggest that the thermal expansion and compressibility of nonpolar solutes may be significantly larger than that of water itself (and thus the first two of the above approximations may prove to be lower bound estimates when applied to nonpolar hydration processes). The third approximation also appears to be inconsistent with experimental nonpolar hydration results (see Table 2), as ΔC_{VP} and $\Delta C_{\bar{P}V}$ would be precisely identical if $(\partial\bar{v}/\partial T)_v = 0$. Given the difficulties associated with accurately measuring derivatives of \bar{v} , we suggest that the accuracy (or inaccuracy) of each of the above approximations remains to be determined. However, since the obtained ΔC_{ij} values are relatively insensitive to the derivatives of \bar{v} , the numerical values of the results in Tables 1–4 (and Figures 1–3) are not likely to be significantly affected by such experimental uncertainties.

It is important to keep in mind that all of the hydrophobic hydration results in Tables 3 and 4 and Figures 1–3 are contingent on our use of the C-EOS and GvdW1 approximations to extract solute-solvent and water-reorganization contribution from experimentally measured quantities. The latter approximations imply, for example, that ΔC_{PP} is approximately temperature independent, while some experimental measurements imply that hydrophobic hydration heat capacities may decrease with temperatures over the normal liquid range.³ However, critical comparisons of results from various laboratories also suggest that the temperature variation of ΔC_{PP} is small compared to experimental uncertainty.^{29,30}

Acknowledgment. Support for this work from the National Science Foundation is gratefully acknowledged.

Appendix: Phase Transfer Thermodynamics

Consider a process in which a molecule is transferred from one phase (γ) to another phase (ω). At equilibrium, the ratio of the solute number densities, ρ , in the two phases is equivalent

to the phase partitioning equilibrium constant, or Ostwald coefficient, L

$$L \equiv \frac{\rho_\omega}{\rho_\gamma} = e^{-\beta\Delta\mu^*} \quad (32)$$

The chemical potential difference, $\Delta\mu^* = \mu(\rho^*; \omega) - \mu(\rho^*; \gamma)$, pertains to the transfer of a solute which has the same number density (concentration) in the two phases, $\rho_\omega = \rho_\gamma = \rho^*$ (and $\beta = 1/kT$ is the usual thermal coefficient). Thus, $\Delta\mu^*$ represents the chemical potential change associated with transferring a single solute from the γ to the ω phase. Moreover, since the solute's translational degrees of freedom are unaltered by such a transfer process, $\Delta\mu^*$ is also equivalent to the reversible work associated with transferring a *stationary* solute between the two phases, each of which are independently held at constant volume and temperature throughout the transfer process.^{28,24} Equivalently, $\Delta\mu^*$ represents the chemical (non- PV) reversible work associated with transferring such a solute between the two phases, each of which are maintained at constant pressure and temperature.

If γ is an ideal gas and ω is water, then $\Delta\mu^*$ is equivalent to the solute's excess chemical potential in the aqueous phase, μ^\times (defined such that the solute number densities are the same in the ideal gas and solution phase).²⁴ Alternatively, if ω is the pure solute liquid (and γ is again assumed to be an ideal gas), then $L = \rho kT/P$, where ρ and P are the liquid's number density and vapor pressure. A more general phase transfer process may be expressed as a combination of such ideal solvation processes. Thus, all of the thermodynamic functions associated with any solvation or phase-transfer process may be obtained from experimental measurements of L (or equivalently $\Delta\mu^*$) and its derivatives with respect to T and/or P .^{4,24,28}

The potential distribution theorem relates the excess chemical potential to the average Boltzmann factor associated with the change in the total energy of the system induced by attempting to insert a solute ("test particle") into a preequilibrated fluid.^{39,40} More specifically, the total configuration energy of the system may be expressed as, $U^\times = \Phi + \Psi$, where Φ represents the interaction energy of the molecules in the pure solvent and Ψ represents the change in energy induced by adding the solute to the fluid in a given (fixed) configuration. Note that such a decomposition does not require assuming that the intermolecular potential functions are pairwise additive.²⁴ The potential distribution theorem implies that

$$\beta\mu^\times = -\ln\langle e^{-\beta\Psi} \rangle_{N=0} \quad (33)$$

where the subscript ($N = 0$) indicates that the average is evaluated over the equilibrium configurations of the *pure solvent* (in the absence of the solute).^{39,40} An alternative inverse expression relates μ^\times to an average pertaining to the removal of a solute from an initially *equilibrated solution* (containing the solute).^{24,40}

$$\beta\mu^\times = +\ln\langle e^{+\beta\Psi} \rangle = \beta\langle\Psi\rangle + \ln\langle e^{+\beta\delta\Psi} \rangle \quad (34)$$

$$= \beta(\epsilon_\mu - Ts_\mu) \quad (35)$$

The variable $\delta\Psi \equiv \Psi - \langle\Psi\rangle$ represents the deviation (fluctuation) of the solute-solvent interaction energy from its average value. Thus, $\epsilon_\mu = \langle\Psi\rangle$ is the *average* solute-solvent interaction energy and $s_\mu = -k \ln\langle e^{+\beta\delta\Psi} \rangle$ is the entropy associated with solute-solvent energy *fluctuations* (both evaluated over equilibrium configurations of a system containing the solute). Also

notice that $\ln\langle e^{+\beta\delta\Psi} \rangle$ is necessarily positive (and so s_μ is negative), while $\langle\Psi\rangle$ is usually (but not necessarily) negative.²⁴

One may additionally identify the solute-induced changes in the solvent-solvent interaction energy as, $\Delta\langle\Phi\rangle \equiv \langle\Phi\rangle - \langle\Phi\rangle_{N=0}$, where the latter two quantities represent the average energies of the pure solvent evaluated over configurations pertaining to a system either with or without a solute molecule, respectively. This solvent reorganization energy also depends on external constraints in the sense that $\Delta\langle\Phi\rangle|_V \equiv \langle\Phi(T,V)\rangle - \langle\Phi(T,V)\rangle_{N=0}$ is not in general equivalent to $\Delta\langle\Phi\rangle|_P \equiv \langle\Phi(T,P)\rangle - \langle\Phi(T,P)\rangle_{N=0}$, even when $\langle\Phi(T,V)\rangle_{N=0}$ and $\langle\Phi(T,P)\rangle_{N=0}$ are assumed to pertain to the same thermodynamic state (i.e., the same temperature and average number density).

The difference between the solvent reorganization energies at constant pressure and constant volume is equal to the energy change associated with expanding the volume of the pure solvent by an amount that is equal to the partial molar volume of the solute.^{4,24}

$$\Delta\langle\Phi\rangle|_P - \Delta\langle\Phi\rangle|_V = (T\zeta - P)\bar{v} \quad (36)$$

Note that $(T\zeta - P)$ is equivalent to the internal pressure $(\partial U/\partial V)_T$ of the pure solvent, and the solute partial molar volume, \bar{v} , corresponds to the volume change produced by adding a single solute to a solvent held at constant pressure

$$\bar{v} \equiv \left(\frac{\partial V}{\partial N}\right)_{T,P,N_0} \quad (37)$$

Similarly, we define \bar{p} as the pressure change produced by adding a solute to a system held at constant volume

$$\bar{p} \equiv \left(\frac{\partial P}{\partial N}\right)_{T,V,N_0} \quad (38)$$

The above two quantities are closely related to each other

$$\bar{p} = \frac{\bar{v}}{V\kappa_T} \quad (39)$$

Notice that the above relation implies that \bar{p} must vanish in the macroscopic ($V \rightarrow \infty$) limit, although \bar{v} need not. In an ideal gas system $\bar{v}^I = kT/P$ and $\bar{p}^I = kT/V$, and so $\Delta\langle\Phi\rangle|_P = \Delta\langle\Phi\rangle|_V = 0$. This also implies that the following changes in \bar{v} and \bar{p} are associated with the transfer of a solute from an ideal gas to a fluid at either constant pressure or volume, respectively

$$\Delta\bar{v} = \left(\frac{\partial V}{\partial N}\right)_{T,P,N_0} - \left(\frac{\partial V}{\partial N}\right)_{T,P,N_0}^I = \bar{v} - \frac{kT}{P} \quad (40)$$

$$\Delta\bar{p} = \left(\frac{\partial P}{\partial N}\right)_{T,V,N_0} - \left(\frac{\partial P}{\partial N}\right)_{T,V,N_0}^I = \bar{p} - \frac{kT}{V} \quad (41)$$

The above notation implies that the first term on the left-hand side of each equation pertains to the fluid phase (ω) while the second term pertains to the ideal gas phase ($\gamma = I$). We employ this notational convention throughout this paper whenever describing such ideal solvation processes.

The following expressions represent the energy, entropy, and enthalpy changes associated with an ideal constant-volume solvation process:

$$\Delta U|_V = \left(\frac{\partial U}{\partial N}\right)_{T,V,N_0} - \left(\frac{\partial U}{\partial N}\right)_{T,V,N_0}^I = \left(\frac{\partial\beta\mu}{\partial\beta}\right)_V - \left(\frac{\partial\beta\mu}{\partial\beta}\right)_V^I = \langle\Psi\rangle + \Delta\langle\Phi\rangle|_V \quad (42)$$

$$T\Delta s|_V = T\left[\left(\frac{\partial S}{\partial N}\right)_{T,V,N_0} - \left(\frac{\partial S}{\partial N}\right)_{T,V,N_0}^I\right] = -T\left[\left(\frac{\partial \mu}{\partial T}\right)_V - \left(\frac{\partial \mu}{\partial T}\right)_V^I\right] = -kT \ln\langle e^{\beta\delta\Psi}\rangle + \Delta\langle\Phi\rangle|_V = Ts_\mu + \Delta\langle\Phi\rangle|_V \quad (43)$$

$$\Delta h|_V = \left(\frac{\partial H}{\partial N}\right)_{T,V,N_0} - \left(\frac{\partial H}{\partial N}\right)_{T,V,N_0}^I = \Delta u|_V + V\Delta\bar{p} = \langle\Psi\rangle + \Delta\langle\Phi\rangle|_V + \frac{\bar{v}}{\kappa_T} - kT \quad (44)$$

The Helmholtz free energy change associated with such an ideal constant-volume solvation process is equivalent to the solute's excess chemical potential, which may in turn be used to evaluate the associated Gibbs free energy change

$$\Delta a|_V = \mu^\times = \left(\frac{\partial A}{\partial N}\right)_{T,V,N_0} - \left(\frac{\partial A}{\partial N}\right)_{T,V,N_0}^I = \Delta u|_V - T\Delta s|_V = \langle\Psi\rangle + kT \ln\langle e^{\beta\delta\Psi}\rangle \quad (45)$$

$$\Delta g|_V = \Delta u|_V - T\Delta s|_V + V\Delta\bar{p} = \mu^\times + \frac{\bar{v}}{\kappa_T} - kT = \langle\Psi\rangle + kT \ln\langle e^{\beta\delta\Psi}\rangle + \frac{\bar{v}}{\kappa_T} - kT \quad (46)$$

When an ideal solvation process is carried out at constant pressure the following partial molar solvation enthalpy, entropy, and energy are obtained

$$\Delta h|_P = \left(\frac{\partial H}{\partial N}\right)_{T,P,N_0} - \left(\frac{\partial H}{\partial N}\right)_{T,P,N_0}^I = \left(\frac{\partial \beta\mu}{\partial \beta}\right)_P - \left(\frac{\partial \beta\mu}{\partial \beta}\right)_P^I = \langle\Psi\rangle + \Delta\langle\Phi\rangle|_P + P\bar{v} - kT = \langle\Psi\rangle + \Delta\langle\Phi\rangle|_V + T(\zeta\bar{v} - k) \quad (47)$$

$$T\Delta s|_P = T\left[\left(\frac{\partial S}{\partial N}\right)_{T,P,N_0} - \left(\frac{\partial S}{\partial N}\right)_{T,P,N_0}^I\right] = -T\left[\left(\frac{\partial \mu}{\partial T}\right)_P - \left(\frac{\partial \mu}{\partial T}\right)_P^I\right] = -kT \ln\langle e^{\beta\delta\Psi}\rangle + \Delta\langle\Phi\rangle|_P + P\bar{v} - kT = -kT \ln\langle e^{\beta\delta\Psi}\rangle + \Delta\langle\Phi\rangle|_V + T(\zeta\bar{v} - k) \quad (48)$$

$$\Delta u|_P = \left(\frac{\partial U}{\partial N}\right)_{T,P,N_0} - \left(\frac{\partial U}{\partial N}\right)_{T,P,N_0}^I = \Delta h|_P - P\Delta\bar{v} = \langle\Psi\rangle + \Delta\langle\Phi\rangle|_P = \langle\Psi\rangle + \Delta\langle\Phi\rangle|_V + (T\zeta - P)\bar{v} \quad (49)$$

In this case the partial molar solvation Gibbs free energy is equal to the solute's excess chemical potential, and this may in turn be used to evaluate the partial molar Helmholtz solvation free energy

$$\Delta g|_P = \mu^\times = \left(\frac{\partial G}{\partial N}\right)_{T,P,N_0} - \left(\frac{\partial G}{\partial N}\right)_{T,P,N_0}^I = \Delta h|_P - T\Delta s|_P = \Delta u|_P + P\Delta\bar{v} - T\Delta s|_P = \langle\Psi\rangle + kT \ln\langle e^{\beta\delta\Psi}\rangle = \langle\Psi\rangle - Ts_\mu \quad (50)$$

$$\Delta a|_P = \mu^\times - P\Delta\bar{v} = \left(\frac{\partial A}{\partial N}\right)_{T,P,N_0} - \left(\frac{\partial A}{\partial N}\right)_{T,P,N_0}^I = \langle\Psi\rangle + kT \ln\langle e^{\beta\delta\Psi}\rangle - P\bar{v} + kT = \langle\Psi\rangle - Ts_\mu - P\bar{v} + kT \quad (51)$$

The quantity $\zeta\bar{v}$ appears frequently in expressions which relate constant-pressure and constant-volume solvation thermodynamic functions, as illustrated by the following identities

$$\zeta\bar{v} = s|_P - s|_V = \Delta s|_P - \Delta s|_V + k \quad (52)$$

$$= \frac{1}{T}(h|_P - u|_V) = \frac{1}{T}(\Delta h|_P - \Delta u|_V) + k \quad (53)$$

$$= \left(\frac{\partial h|_P}{\partial T}\right)_V - T\left(\frac{\partial s|_P}{\partial T}\right)_V = \left(\frac{\partial \Delta h|_P}{\partial T}\right)_V - T\left(\frac{\partial \Delta s|_P}{\partial T}\right)_V + k \quad (54)$$

$$= T\left(\frac{\partial s|_V}{\partial T}\right)_P - \left(\frac{\partial u|_V}{\partial T}\right)_P = T\left(\frac{\partial \Delta s|_V}{\partial T}\right)_P - \left(\frac{\partial \Delta u|_V}{\partial T}\right)_P + k \quad (55)$$

It is important to note that eqs 47–51 pertain to experimental solvation processes (rather than to the transfer of a stationary solute). Also notice that, although the vapor is assumed to be an ideal gas, eqs 47–51 may also be used to evaluate the thermodynamic functions associated with any experimental phase transfer process. More specifically, any such process may be expressed as a combination of ideal solvation processes. Moreover, although the above expressions pertain to the solvation (phase transfer) of a single solute molecule, they are not restricted to the infinite dilution limit, as the solvent may itself be composed of molecules of the same type as the solute (or any arbitrary mixture of components).

A self-solvation process is one in which the solute and solvent are molecules of the same type (and so may be viewed as an extreme example of a nondilute solvation process). A number of additional exact thermodynamic relations apply only to such processes. For example, the following important sequence of identities hold for any self-solvation process

$$\Delta u|_P = \frac{U}{N} - \frac{U^I}{N} = \frac{1}{2}\langle\Psi\rangle = -\Delta\langle\Phi\rangle|_P \quad (56)$$

The first equality is a special case of a standard thermodynamic relation pertaining to any constant-pressure self-solvation thermodynamic function. An elegant derivation of the second equality may be found in the Appendix of a paper by Sanchez et al.,⁴¹ and the third equality follows from eq 49. Thus, for a self-solvation process it is a simple matter to evaluate the solute–solvent interaction energy $\langle\Psi\rangle$ and solvent constant-pressure solvent reorganization energy $\Delta\langle\Phi\rangle|_P$. Moreover, the solute partial molar volume pertaining to a self-solvation process is simply related to the inverse of the solvent number density, $\bar{v} = 1/\rho$, and so eq 36 implies that $\Delta\langle\Phi\rangle|_V = \Delta\langle\Phi\rangle|_P + (P - T\zeta)/\rho$.

For a more general solvation process it is unfortunately not possible to determine either $\langle\Psi\rangle$ or $\Delta\langle\Phi\rangle$ by purely experimental means. In other words, determining the latter quantities requires additional input from computer simulations and/or theoretical approximations. For example, a computer simulation performed on a system composed of molecules with two-body additive potentials may readily be used to evaluate (approximate) the direct solute–solvent interaction energy, $\langle\Psi\rangle$, and then eq 49 combined with the experimental value of $\Delta u|_P$, may be used to infer the value of $\Delta\langle\Phi\rangle|_P$.

Alternatively, thermodynamic perturbation theory may be used to predict the relationship between $\langle\Psi\rangle$ and $\Delta u|_P$, given simulation measurements of the cavity size distribution in pure solvent.⁴ For example, the cavity equation of state (C-EOS) of water (derived from experimental and simulation data)⁴ may be used to accurately predict water reorganization energies, $\Delta\langle\Phi\rangle|_V$ and $\Delta\langle\Phi\rangle|_P$, associated with the formation of spherical cavities of any radius (over the entire normal liquid temperature range). Given these reorganization energies, one may use first-order perturbation theory (GvdW1)²⁴ to approximate $\langle\Psi\rangle \approx -a\rho$ (where a is the van der Waals mean field coefficient and ρ is

the number density of pure water)⁴ at 298 K using

$$\langle \Psi \rangle \approx \Delta u|_P - \Delta \langle \Phi \rangle_{c|P} = \Delta u|_P - \Delta \langle \Phi \rangle_{c|V} + (P - T\zeta)\bar{v} \quad (57)$$

and evaluate the derivatives of $\langle \Psi \rangle$ using $(\partial \langle \Psi \rangle / \partial T)_P = \alpha \rho \alpha_P$, $(\partial \langle \Psi \rangle / \partial P)_T = -\alpha \rho \kappa_T$, and $(\partial \langle \Psi \rangle / \partial T)_V = 0$. The cavity radii, R_c , used to obtain $\Delta \langle \Phi \rangle_{c|V}$ and $\Delta \langle \Phi \rangle_{c|P}$ values from the C-EOS are $R_c = (\sigma + \sigma_w)/2$, where σ and σ_w are the effective hard sphere diameters of the solute and water, respectively. The σ values of xenon and cyclohexane are in this work obtained from the equation of state of the corresponding pure fluids,³⁵ while $\sigma_w \approx 0.27 \pm 0.01$ nm is assumed, as this is representative of the range of water core diameters used in previous scaled particle theory and hydrophobic hydration studies.^{4,23,25,42} Having thus obtained experimentally derived estimates of $\langle \Psi \rangle$ and its derivatives, the first equalities in eqs 24 and 25 are used to obtain $(\partial \Delta \langle \Phi \rangle|_P / \partial T)_P$ and $(\partial \Delta \langle \Phi \rangle|_V / \partial T)_P$ from experimental values of ΔC_{PP} , ΔC_{VV} , ζ , \bar{v} , T , and P . This is the procedure which we have used to obtain the Xe and cyclohexane hydration results in Tables 3 and 4 and Figures 1 and 2 (see the notes in Table 3 for further details).

Although the above procedure relies on the GvdW1 approximation, the uncertainty in the results is expected to be no greater than that of the experimental ΔC_{ij} values. This is because the GvdW1 approximation is only used to obtain $\langle \Psi \rangle$ values, and the resulting $(\partial \langle \Psi \rangle / \partial T)_P$ contributions to ΔC_{PP} are very small (see Table 3). Thus, our use of the GvdW1 approximation is not expected to significantly affect the obtained $(\partial \Delta \langle \Phi \rangle|_P / \partial T)_P$ and $(\partial \Delta \langle \Phi \rangle|_V / \partial T)_P$ values. It is also important to point out the difference between the above procedure and that used in a recent GvdW1 analysis of rare gas hydration thermodynamics.⁴ In the latter study the GvdW1 approximation was used to predict both $\langle \Psi \rangle$ and $(\partial \Delta \langle \Phi \rangle|_V / \partial T)_P$, while here the latter quantity is obtained from $\langle \Psi \rangle$ and the experimental ΔC_{PP} . In other words, the results in Tables 3 and 4 are derived as directly as possible from experimental measurements.

References and Notes

- (1) Hedwig, G. R.; Hakin, A. W. *Phys. Chem. Chem. Phys.* **2004**, *6*, 4690.
- (2) Gallagher, K. R.; Sharp, K. A. *J. Am. Chem. Soc.* **2003**, *125*, 9853.
- (3) Tanford, C. *The Hydrophobic Effect: Formation of Micelles and Biological Membranes*, 2nd ed.; Wiley: New York, 1980. Graziano, G.; Lee, B. *J. Phys. Chem. B* **2005**, *109*, 8103. Krause, D.; Benson, B. B. *J. Sol. Chem.* **1989**, *18*, 823. Fernandez-Prini, R.; Crovetto, R. *J. Phys. Chem. Ref. Data* **1989**, *18*, 1231.
- (4) Ben-Amotz, D. *J. Chem. Phys.* **2005**, *123*, 184504. Implementation of the C-EOS requires using β in mol/kJ units and R_c in nm units on the right-hand-side of eq A2.
- (5) Bhimalapuram, P.; Widom, B. *Physica A* **2001**, *298*, 229.
- (6) Southall, N. T.; Dill, K. A. *J. Phys. Chem. B* **2000**, *104*, 1326.
- (7) Lazaridis, T. *Acc. Chem. Res.* **2001**, *34*, 931.
- (8) Ashbaugh, H. S.; Truskett, T. M.; Debenedetti, P. G. *J. Chem. Phys.* **2002**, *116*, 2907.
- (9) Eads, C. D. *J. Phys. Chem. B* **2002**, *106*, 12282.
- (10) Chatterjee, S.; Ashbaugh, H. S.; Debenedetti, P. G. *J. Chem. Phys.* **2005**, *123*.
- (11) Cooper, A. *Biophys. Chem.* **2005**, *115*, 89.
- (12) Graziano, G. *Phys. Chem. Chem. Phys.* **1999**, *1*, 1877.
- (13) Paschek, D. *J. Chem. Phys.* **2004**, *120*, 10605.
- (14) Rick, S. W. *J. Phys. Chem. B* **2003**, *107*, 9853.
- (15) Shimizu, S.; Chan, H. S. *Proteins* **2002**, *49*, 560.
- (16) Chandler, D. *Nature* **2005**, *437*, 640.
- (17) Lum, K.; Chandler, D.; Weeks, J. D. *J. Phys. Chem. B* **1999**, *103*, 4570.
- (18) Cheng, Y. K.; Rossky, P. J. *Nature* **1998**, *392*, 696.
- (19) Huang, X.; Margulis, C. J.; Berne, B. J. *J. Phys. Chem. B* **2003**, *107*, 11742.
- (20) Zhou, R.; Huang, X.; Margulis, C. J.; Berne, B. J. *Science* **2004**, *305*, 1605.
- (21) Ashbaugh, H. S.; Pratt, L. R.; Paulaitis, M. E.; Cloherty, J.; Beck, T. L. *J. Am. Chem. Soc.* **2005**, *127*, 2808.
- (22) Widom, B.; Bhimalapuram, P.; Koga, K. *Phys. Chem. Chem. Phys.* **2003**, *5*, 3085. We take this opportunity to correct an error in the entries ΔS_v^* , ΔE_v , and $(\Delta C_v)_v$ in Table 1 of this reference. The first of eq 19, the first of eq 20 and eq 21 of this reference, which led to the incorrect entries in that Table 1, are in error. The remaining entries are correct.
- (23) Ashbaugh, H. S.; Pratt, L. R. *Rev. Mod. Phys.* **2006**, *78*, 159.
- (24) Ben-Amotz, D.; Rainery, F.; Stell, G. *J. Phys. Chem. B* **2005**, *109*, 6866.
- (25) Pratt, L. R.; Chandler, D. *J. Chem. Phys.* **1977**, *67*, 3683.
- (26) Plyasunov, N. V.; Plyasunov, A. V.; Shock, E. L. *Int. J. Thermophys.* **2004**, *25*, 351. Plyasunov, A. V.; Plyasunova, N. V.; Shock, E. L. "The database for the thermodynamic properties of neutral compounds in the state of aqueous solution," Department of Geological Sciences, Arizona State University: Tempe, AZ, 2005 (<http://webdocs.asu.edu/>).
- (27) Crovetto, R.; Fernandez-Prini, R.; Japas, M. L. *J. Chem. Phys.* **1982**, *76*, 1077.
- (28) Ben-Naim, A. *Solvation Thermodynamics*; Plenum Press: New York, 1987.
- (29) Battino, R. *Krypton, Xenon and Radon*; Solubility Data Series, Vol. 2; Pergamon Press: New York, 1979.
- (30) Battino, R. *Argon*; Solubility Data Series, Vol. 4; Pergamon Press: New York, 1980.
- (31) Callen, H. B. *Thermodynamics and an Introduction to Thermostatistics*, 2nd ed.; John Wiley and Sons: New York, 1985.
- (32) Lemmon, E. W.; McLinden, M. O.; Huber, M. L. NIST Standard Reference Database 23, Version 7.0, 2002.
- (33) Debenedetti, P. G.; Stanley, H. E. *Phys. Today* **2003**, *56*, 40.
- (34) Paschek, D. *Phys. Rev. Lett.* **2005**, *94*, 217802.
- (35) Ben-Amotz, D.; Herschbach, D. R. *J. Phys. Chem.* **1990**, *94*, 1038.
- (36) Ben-Amotz, D.; Willis, K. G. *J. Phys. Chem.* **1993**, *97*, 7736.
- (37) Floris, F. M. *J. Phys. Chem. B* **2004**, *108*, 16244.
- (38) Rajamani, S.; Truskett, T. M.; Garde, S. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 9475.
- (39) Widom, B. *J. Chem. Phys.* **1963**, *39*, 2808.
- (40) Widom, B. *J. Phys. Chem.* **1982**, *86*, 869.
- (41) Sanchez, I. C.; Truskett, T. M.; in't Veld, P. J. *J. Phys. Chem. B* **1999**, *103*, 5106.
- (42) Pierotti, R. A. *Chem. Rev.* **1976**, *76*, 717.
- (43) Lemmon, E. W.; Perkins, A. P.; McLinden, M. O.; Friend, D. G. NIST Standard Reference Database 12, Version 5.0, 2000.
- (44) Plyasunov, A. V.; O'Connell, J. P.; Wood, R. H.; Shock, E. L. *Fluid Phase Equilib.* **2001**, *183*, 133.