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Biophysical Chemistry 105 (2003) 241–250

Biophysical Chemistry

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Entropy convergence in hydrophobic hydration: a scaled particle theory analysis

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Received 16 September 2002; accepted 1 November 2002

Abstract

The occurrence of entropy convergence in hydrophobic hydration is verified from available experimental thermodynamic data for both noble gases and hydrocarbons. The entropy convergence phenomenon can be reproduced by means of the scaled particle theory, provided that a temperature-dependent hard sphere diameter is used for water molecules. The calculated work of cavity creation shows a non-monotonic temperature dependence with a flat maximum slightly above 100 °C, irrespective of the cavity size. The corresponding cavity entropy changes converge approximately 100 °C, in qualitative agreement with the experimental finding.

Keywords: Entropy convergence; Work of cavity creation; Scaled particle theory; General condition for entropy convergence

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1. Introduction

Two of the most striking features associated with the hydrophobic phenomenon are the large negative entropy change, ΔS, and the large positive heat capacity change, ΔC_p, associated with the transfer of nonpolar molecules into water at room temperature [1–5]. Since the heat capacity change is large and positive, the negative entropy change observed at room temperature will diminish in magnitude at higher temperatures, eventually passing through zero if ΔC_p remains large [4]. The entropy and the heat capacity changes at room temperature are different for different solutes so that one would initially expect that the temperature at which the entropy becomes zero would be different for each different solute. It was Sturtevant [6], who first observed that the ratio, $\Delta S/\Delta C_p$, for transfer from a non-polar liquid phase to water at room temperature was nearly the same for all solutes for which the experimental data were available. This meant that the transfer of a solute species with a large negative ΔS had a large ΔC_p, and that with a small negative ΔS a small ΔC_p, so that the ΔS values for different solute species would tend to converge as the temperature is raised. Sturtevant noted that the value of the $\Delta S/$

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doi:10.1016/S0301-4622(03)00073-5

ΔC_p ratio was such that ΔS for all solutes would nearly converge to zero at 100 °C [6].

In the mean time, Privalov and his colleagues found that the entropy and enthalpy changes upon denaturation of some globular proteins converged at approximately 100 °C, although the values of the enthalpy and entropy at this temperature were not zero [7]. These two sets of observations, one on the small molecule transfer process and the other on globular protein denaturation, remained curious but largely unnoticed features of thermodynamics until Baldwin noticed the connection between these observations [8]. Murphy et al. [9] then found that plots of ΔS vs. ΔC_p, at one temperature, for a series of homologous solute species give straight lines with the same slope but different intercepts for transfer processes from solid to water, from nonpolar liquid to water, and from gas phase to water as well as for the protein denaturation. The fact that these plots were linear implied the existence of a convergence temperature at which the entropy changes converged to the same value for all the compounds. The fact that the slopes were the same for all the processes meant that the entropies converged at the same temperature for each of these processes. The common convergence temperature given by the value of the observed slope was 112 °C [9].

A strong debate arose on the physical meaning of the entropy convergence phenomenon, especially for its potential usefulness to dissect the thermodynamic contributions to globular protein stability [8–16]. At the present, however, the occurrence of entropy convergence for the thermal denaturation of globular proteins is not demonstrated by the current, expanded set of experimental thermodynamic data [17,18]. This is presumably because denaturation is a complex process that involves many temperature-dependent factors other than the hydrophobic effect. There is also the suggestion by Huang and Chandler [19] that the difference in behavior between the small molecule transfer processes and globular protein denaturation processes arises from the length-scale dependent change in the mechanism of hydrophobic effect. On the other hand, the entropy convergence phenomenon is real for the small molecule transfer processes. (See the Section 3 of this paper.) Several authors [12,13] put forward a group additivity approach based on the assumption that the hydrophobic contribution to the entropy change vanishes at the convergence temperature. Other authors [14–16] questioned the validity of the additivity assumption and tried to provide alternative approaches. One of us [11] has shown that the convergence phenomenon will be observed if the entropy is a bilinear function of temperature and a property of the solute species.

More recently, Garde et al. [20] here referred to as GHGPP, provided a more statistical mechanical explanation of the entropy convergence phenomenon for the gas to water transfer (hydration) process. This is based on the expression for the free energy of cavity formation that they obtain by means of the application of the information theory [21]. According to this explanation, entropy convergence in the hydrophobic hydration process directly follows from the small temperature dependence of the isothermal compressibility of liquid water. This conclusion was confirmed by the recent results of Nezbeda on a primitive water model [22].

In this paper, we study the entropy convergence phenomenon for hydration using the scaled particle theory (SPT), which is an alternative, older statistical mechanical theory [23,24]. We define hydration as the process of transferring a solute molecule from a fixed position in the ideal gas phase to a fixed position in water [2]. The hydration process can be considered to be made of two steps, the cavity formation followed by turning on the attractive potential between the solute and the solvent molecules [4,25]. It has been argued that the entropy change accompanying the second of these two steps is small compared to that of the first step [4,24,25]. Therefore we consider only the cavity formation step in this article, as did GHGPP [20]. We find that the SPT also gives an excellent entropy convergence behavior, with the convergence temperature and the common entropy value at the convergence temperature in qualitative agreement with the experimentally observed values. Hong Qian (personal communication, [26]) also noted that the SPT formulation of entropy change is consistent with the convergence behavior near 100 °C.

Table 1
Estimates of the Gibbs energy cost of cavity creation as a function of temperature in water, for different cavity diameters, calculated by means of the SPT relationship, Eq. (1), using the experimental density of liquid water at 1 atm from Kell [29], and the reported values of the hard sphere diameter

T (°C)	v_1 (cm^3 mol^{-1})	σ_1 (Å)	ξ	ΔG_c[3 Å] (kJ mol^{-1})	ΔG_c[4 Å] (kJ mol^{-1})	ΔG_c[5 Å] (kJ mol^{-1})	ΔG_c[6 Å] (kJ mol^{-1})
0	18.023	2.758	0.367	14.1	22.3	32.5	44.6
25	18.073	2.748	0.362	15.0	23.8	34.7	47.6
50	18.238	2.736	0.354	15.7	24.8	36.1	49.6
75	18.485	2.721	0.344	16.1	25.4	37.0	50.7
100	18.803	2.704	0.332	16.3	25.7	37.3	51.1
125	19.191	2.684	0.318	16.2	25.6	37.1	50.9
150	19.655	2.662	0.303	16.0	25.2	36.5	50.0

The expression ΔG_c[3 Å] means the work to create a cavity of 3 Å diameter.

We search for the common features between these two rather different theoretical approaches (GHGPP and SPT) by means of a general expression for the entropy convergence condition. We suggest that the entropy convergence is observed because of two conditions, (i) that the free energy of cavity formation shows a maximum as a function of temperature and (ii) that the free energy is dominated by a single factor, probably either the surface area or the volume, of the cavity.

2. Methods

The cavity free energy, ΔG_c, was calculated using the following expression from the SPT [23,24],

$$\Delta G_c = RT\left[K_0 + K_1(\sigma_c/\sigma_1) + K_2(\sigma_c/\sigma_1)^2 + K_3(\sigma_c/\sigma_1)^3\right], \quad (1)$$

where $K_0 = -\ln(1-\xi)$; $K_1 = u = 3\xi/(1-\xi)$; $K_2 = u(u+2)/2$; and $K_3 = \xi P v_1/RT$. In these relations R is the gas constant; T is the absolute temperature; ξ is the volume packing density of the pure solvent, which is defined as the ratio of the physical volume of a mole of solvent molecules over the molar volume of the solvent; σ_c is the cavity size, defined as the diameter of the spherical region from which any part of any solvent molecules is excluded; σ_1 is the hard sphere diameter of the solvent molecules; P is the pressure; and v_1 is the molar volume of the solvent.

We used the ambient pressure of 1 atm for P as suggested by other authors [24,27,28]. In addition, we used (a) the experimental values of liquid water density at 1 atm in the temperature range 0–150 °C compiled by Kell [29], and listed in the second column of Table 1 in terms of molar volume and (b) a temperature dependent hard sphere diameter for water molecules. The temperature dependence of σ_1 was obtained in the following manner. Soda [30] determined the σ_1 values of the water molecule that will reproduce the contact density function calculated by means of computer simulations at different temperatures. As expected [23], the σ_1 values determined by Soda slightly decrease on increasing the temperature (e.g. $\sigma_1 = 2.748$ Å at 25 °C and 2.704 Å at 100 °C), because the molecules are more effectively able to penetrate one another's repulsive fields on raising the thermal energy. The σ_1 values over the range 0–150 °C was obtained by a polynomial fitting of Soda's estimates in the 25–100 °C range and by extrapolation to lower and higher temperatures. These values are listed in the third column of Table 1. They agree with those determined by Pierotti [31] and Wilhelm [32] from the analysis of gas solubility measurements over a smaller temperature range. Moreover the σ_1 value at 25 °C, 2.748 Å, is close to the location of the first peak in the oxygen–oxygen radial distribution function of liquid water determined by means of both X-ray and neutron scattering measurements [33–35].

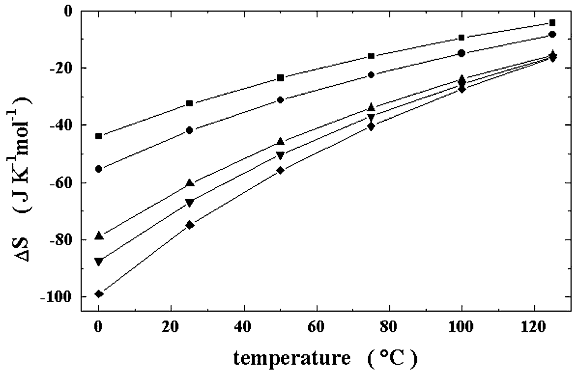

Fig. 1. Plot of ΔS vs. temperature for He (squares), Ne (circles), Ar (up triangles), Kr (down triangles) and Xe (diamonds). The data are from Ref. [36], after correction for the Ben-Naim standard.

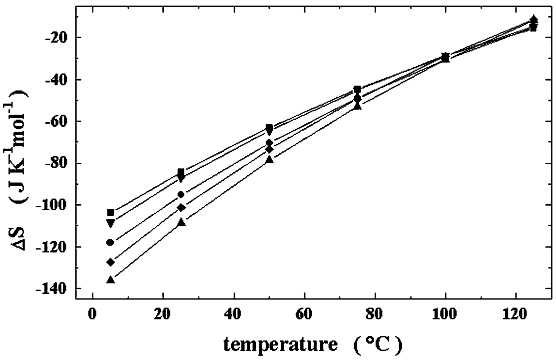

Fig. 2. Plot of ΔS vs. temperature for ethane (squares), propane (circles), butane (up triangles), benzene (down triangles) and toluene (diamonds). The data are from Ref. [37].

The ΔS_c values were calculated by numerical differentiation of the ΔG_c values with respect to temperature.

3. Results

3.1. Experimental data

As a reference for comparison, we present here the experimental data on the entropy convergence collected from the literature. The temperature dependence of hydration entropy change, ΔS, for noble gases [36] is shown in Fig. 1, and for ethane, propane, *n*-butane, benzene and toluene [37] in Fig. 2. Excluding He and Ne, ΔS for the rare gases appear to converge at approximately 130 °C while those for the hydrocarbons converge in the temperature range of 100–110 °C. The entropy values at the convergence temperature are approximately -15 and -25 J K^{-1} mol^{-1}, respectively.

If the heat capacity change, ΔC_p, is assumed to be constant, the entropy change can be written as

$$\Delta S = \Delta C_p \ln(T/T^*) + \Delta S^*, \qquad (2)$$

where T^* is the convergence temperature and ΔS^* is ΔS at T^*. Therefore, if ΔS for a series of solute species is plotted against ΔC_p at one experimental temperature, a straight line will be obtained, as indicated in the Section 1. Such a plot was referred to as the MPG entropy plot after the names of the authors who first made such plots [11]. The convergence temperature and the value of ΔS at the convergence temperature can be obtained from the slope and intercept, respectively, of such a plot. Murphy et al. [9] obtained $T^* = 121$ °C and $\Delta S^* = -11$ J K^{-1} mol^{-1} (after correction for the different standard state used) from such a plot using the ΔS and ΔC_p data for the hydration of noble gases and alkanes at room temperature. Fig. 3 shows a

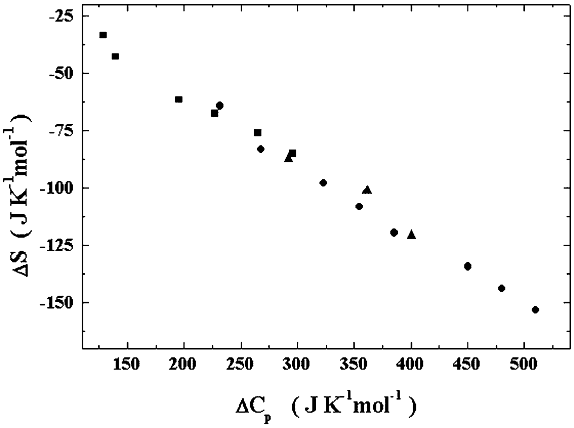

Fig. 3. Plot of ΔS vs. ΔC_p at 25 °C for noble gases (squares), aliphatic hydrocarbons (circles), benzene, toluene and *c*-hexane (triangles). The data for noble gases and aliphatic hydrocarbons are from Ref. [38], after correction for the Ben-Naim standard. The data for benzene and toluene are from Ref. [37]; those for *c*-hexane are from Ref. [39].

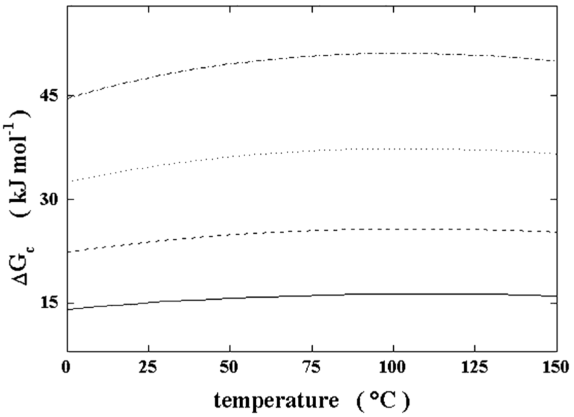

Fig. 4. Plot of ΔG_c vs. temperature in water for different cavity diameters. The ΔG_c values are calculated by means of SPT using the experimental density of liquid water and considering σ_1 temperature-dependent (for more details, see text and Table 1). The cavity diameters are $\sigma_c = 3$, 4, 5 and 6 Å, respectively, from the bottom to top.

similar plot using a different dataset for the hydration of noble gases and aliphatic hydrocarbons [38] and including the new data for the hydration of benzene and toluene [37] and cyclohexane [39]. The 17 points are again well represented by a linear relationship ($r = -0.9959$), from which one obtains $T^* = 132 \pm 3$ °C and $\Delta S^* = 2.4 \pm 2.4$ J K^{-1} mol^{-1}. Use of other datasets [36,40–42] gives values that are intermediate between these two sets of values. The difference between the T^* and ΔS^* values determined from the MPG plot and those that were determined directly from the temperature-dependence of ΔS can be attributed mainly to the temperature dependence of the heat capacity change.

3.2. Results from the SPT calculation

The cavity free energies, ΔG_c, were calculated for different cavity diameters, $\sigma_c = 3$, 4, 5 and 6 Å, over the temperature range 0–150 °C. The calculated values are given in Table 1 and plotted in Fig. 4. They are positive and large at all temperatures and show a broad maximum at slightly above 100 °C for all cavity sizes. A qualitatively similar result was obtained by Guillot and Guissani [43], using the test particle insertion method coupled with molecular dynamics simulations, and by GHGPP [20], using both the test particle insertion method and an information theory model. A second-degree polynomial fitting gives $T_{\max} \cong 109$, 107, 104, and 103 °C for $\sigma_c = 3$, 4, 5 and 6 Å, respectively. The slight decrease of $T_{\max}$ on increasing the cavity diameter was obtained also by GHGPP from their computer simulations [20]. The shape of the ΔG_c curves resembles that of the experimental ΔG for the hydration of noble gases and small hydrocarbons [44], although the calculated curves are shifted upward due to the neglect of the solute–solvent van der Waals interaction.

Above calculations were made using the σ_1 values that change with temperature as shown in Table 1. Although σ_1 decreases by less than 0.1 Å over the range 0–150 °C, this decrease is required in order to obtain the ΔG_c maximum in the given temperature range. If σ_1 is fixed at 2.75 Å independent of temperature, ΔG_c proves to be a monotonically increasing function over the entire range 0–150 °C (data not shown).

The calculated cavity ΔS values are given in Table 2 and plotted in Fig. 5. In line with experimental data, they are negative and large and increase in magnitude with the cavity size at room temperature. All increase markedly with temperature, but at different rates so that they converge tightly at approximately 100 °C, where $\Delta S \cong -4$ J K^{-1} mol^{-1}, nearly independent of the cavity size. The convergence temperature is at the low end of the range of experimentally observed T^* values. The fact that ΔS^* is negative is in qualitative agreement with the experimental findings, although its magnitude is somewhat smaller (-4 J K^{-1} mol^{-1} vs. -15 and -25 J K^{-1} mol^{-1} from Figs. 1 and 2). Part of the discrepancy can be attributed to the neglect of the entropy contribution from the solute–water interaction, which should be small but a negative quantity [4]. The fact that SPT gives too weak a temperature-dependence of the heat capacity change [4] would also contribute to the difference between the calculated and observed values of both ΔS^* and T^*. One of us [11] suggested that ΔS^* should be given approximately by the temperature derivative of the free energy for inserting a mathematical point in water, which in Ben-Naim standard is given by

$$\Delta G_c(\sigma_c = 0) = -RT\ \ln(1-\xi). \quad (3)$$

$\Delta S(\sigma_c = 0)$ is -0.7 J K^{-1} mol^{-1} at 110 °C and -0.3 J K^{-1} mol^{-1} at 132 °C, using the ξ values listed in the fourth column of Table 1. The ΔS^* value calculated from the temperature-dependence of ΔS is similar to these values.

4. Discussion

We have shown that the application of SPT using the experimental density of liquid water and considering the slight temperature dependence of the hard sphere diameter of water molecules produces cavity ΔS values that tightly converge near the experimentally observed convergence temperature. The ΔS value at the convergence temperature, ΔS^*, is negative, consistent with the experimental data. Its magnitude is smaller than the experimental value, but at least part of the difference was expected since the calculation ignores the contribution from the solute–solvent van der Waals interaction. It is near the ΔS values for inserting a mathematical point, which also does not have the van der Waals interaction with the solvent.

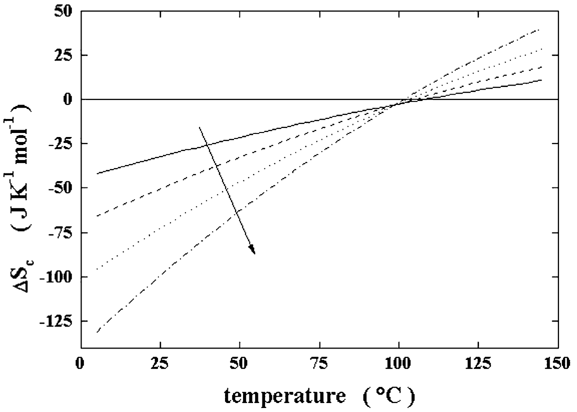

Fig. 5. Plot of $\Delta S_c = -(\partial \Delta G_c/\partial T)$ vs. temperature in water for different cavity diameters. The arrow indicates entropy curves for cavities with diameter of 3, 4, 5 and 6 Å, respectively. The convergence temperature is close to 100 °C (Table 2).

One of us [11] has shown that entropy convergence will be observed if ΔS is a bilinear function of temperature T and a characteristic property of the solute X. However, the expression for the entropy change upon cavity formation as given by the SPT is not obviously linear in T or X. Hong Qian (personal communication, [26]) wrote ΔG_c of SPT in the form of

$$\Delta G = a_g(T)X + b_g(T), \quad (4)$$

where $X = \sigma_c^2$, ignoring the linear and the cubic terms in σ_c, and then showed that the temperature derivative of $a_g(T)$ would become zero at the experimentally observed T^*. Our calculations show that this is indeed the main mechanism of entropy convergence by SPT, but that the linear term does give a small effect (see below). GHGPP [20] showed that their expression of the cavity free

Table 2

Estimates of the cavity entropy change as a function of temperature for different cavity diameters, calculated by means of the second-degree polynomial fitting of the numbers from local numerical differentiation of the ΔG_c functions calculated using Eq. (1) from SPT

T (°C)	ΔS_c[3 Å] (J K^{-1} mol^{-1})	ΔS_c[4 Å] (J K^{-1} mol^{-1})	ΔS_c[5 Å] (J K^{-1} mol^{-1})	ΔS_c[6 Å] (J K^{-1} mol^{-1})
0	−44.3	−70.0	−101.7	−139.4
25	−32.3	−50.4	−72.7	−99.2
50	−21.4	−32.7	−46.5	−62.8
75	−11.5	−16.8	−23.0	−30.3
95	−4.3	−5.3	−6.2	−7.1
98	−3.34	−3.66	−3.85	−3.80
100	−2.7	−2.6	−2.3	−1.7
125	5.1	9.8	15.7	23.1
150	11.80	20.3	31.0	44.1

The expression ΔS_c[3 Å] means the entropy change to create a cavity of 3 Å diameter. According to these estimates $T^* = 98$ °C.

energy from information theory produces entropy convergence by writing their free energy essentially in the form of Eq. (4) (see below).

Generally, the sufficient condition for observing convergence can be stated as follows: If there is a temperature at which

$$(\partial\Delta S/\partial X)_{\mathrm{Xexp}}=0, \tag{5}$$

where Xexp is the value of X of a typical solute in the series, then ΔS will be maximally independent of X at this temperature. This is clearly also a necessary condition for convergence since, if ΔS converges at a temperature T^*, then ΔS is independent of X at that temperature by definition. This condition applies also in the case where convergence is accurately observed only for a few solutes whose X is near Xexp, but defocuses when X deviates from Xexp.

It can be easily shown that, if ΔS is a bilinear function of T and X, there is always a temperature at which the condition of Eq. (5) is satisfied. In this case, the condition is satisfied for all X, which means that the convergence will be perfect, i.e. ΔS will have the same value at T^* for all solute species. More generally, when ΔS is a linear function of X only,

$$\Delta S=a_{\mathrm{s}}(T)X+b_{\mathrm{s}}(T), \tag{6}$$

convergence will be observed if there is a temperature at which $(\partial\Delta S/\partial X)=a_{\mathrm{s}}(T)=0$. This will be the case if the free energy is in the form of Eq. (4) and $a_{\mathrm{g}}(T)$ shows a maximum (or a minimum) at some T, since $a_{\mathrm{s}}=-\partial a_{\mathrm{g}}/\partial T=0$ at this T. This is the basic mechanism of entropy convergence proposed by GHGPP [20], in which $a_{\mathrm{g}}(T)$ is proportional to $T\rho^2$ and $X=\upsilon^2/\sigma_{\mathrm{n}}^2$ where ρ, υ and σ_{n} are the number density of water, the cavity volume, and the fluctuation (standard deviation from the mean) of the number of water molecules in volume υ, respectively. Blurring of convergence occurs because b_{g} and b_{s} mildly depend on cavity volume and σ_{n} mildly depends on temperature.

In the case of SPT, ignoring the negligibly small cubic term, we have

$$\Delta G_{\mathrm{c}}=g_0(T)+g_1(T)+\sigma_{\mathrm{c}}+g_2(T)\sigma_{\mathrm{c}}^2, \tag{7}$$

and

$$\Delta S=s_0(T)+s_1(T)\sigma_{\mathrm{c}}+s_2(T)\sigma_{\mathrm{c}}^2, \tag{8}$$

where g_0, g_1 and g_2 are RTK_0, RTK_1/σ_1 and RTK_2/σ_1^2, respectively, and $s_{\mathrm{i}}=-\partial g_{\mathrm{i}}/\partial T$ for $i=0$, 1 and 2. The convergence condition is given by

$$\partial\Delta S/\partial\sigma_{\mathrm{c}}=s_1(T)+2s_2(T)\sigma_{\mathrm{c}}=0 \tag{9}$$

This condition will obtain if $s_1(T)$ and $s_2(T)$ become simultaneously zero at some temperature. For example $s_1(T)$ may be always small, as assumed by Qian, in which case Eq. (8) is in the form of Eq. (6) and convergence will obtain at the temperature at which $s_2(T)=0$. However, calculations show that $s_1(T)$ passes through zero at approximately 134 °C and is small but not negligible at 94 °C at which $s_2(T)$ is zero. Condition (Eq. (9)) will also obtain if $s_1(T)$ and $s_2(T)$ are nearly linear functions of T, which ensures that $s_1(T)+2s_2(T)\sigma_{\mathrm{c}}$ will go through zero at some T. In this case, the convergence temperature will depend on σ_{c}, which means that sharp focusing occurs for a limited range of σ_{c} values. The $s_1(T)$ and $s_2(T)$ functions from the SPT are indeed nearly linear functions of T, as can be expected from the fact that ΔG_{c} is a nearly quadratic function of T. The σ_{c} dependence of the convergence is weak because, when σ_{c} is 5 Å, the convergence occurs at approximately 100 °C, which is near the temperature at which $s_2(T)$ is zero. The calculated ΔS values are essentially the same for all cavity sizes in the range of 3–7 Å (Table 2), which covers the size range of most of the noble gas and small hydrocarbon molecules for which the experimental data are available.

Thus, according to SPT, the entropy convergence is obtained because $s_1(T)$ and $s_2(T)$ are nearly linear functions of T, or equivalently because $g_1(T)$ and $g_2(T)$ are nearly quadratic functions of T. The convergence is obtained despite the fact that the free energy is a quadratic function of $X=\sigma_{\mathrm{c}}$, although the sharpness of the convergence depends on the linear term being small compared to the quadratic term near the convergence temperature. This contrasts with the explanation offered by GHGPP, which depends on the free energy being a nearly linear function of υ^2/σ_n^2, which they show is nearly independent of temperature.

Why do two seemingly very different theories produce a similar entropy convergence behavior? One common feature between the two explanations is the requirement that the temperature dependence of ΔG_c will have a maximum. One can imagine expressing the ΔG_c function as a polynomial in σ_c, which is the only property of the solute when it is a cavity, with coefficients that are mainly quadratic with respect to temperature. Such a function will show an entropy convergence, the sharpness of which will depend on how much one of the terms in the polynomial dominates over others, in terms of the dependency on σ_c, near the convergence temperature. In SPT, the term that dominates is clearly the σ_c^2 term. It is likely that υ^2/σ_n^2 in the GHGPP theory is related to σ_c^3 [45,46]. Thus, although the dominant solute property X is area in the case of SPT but probably volume in the GHGPP theory, the mechanism by which convergence is produced is rather similar for the two theories. It is possible that the free energy of cavity formation depends both on the area and the volume for the cavity sizes of common hydrocarbon solute molecules [45]. Besides, in the limited range of solute sizes that we are considering, the volume-dependence and surface area-dependence are nearly indistinguishable.

In any case, it is clear that the Gaussian behavior of the microscopic number density fluctuation, a central feature in the GHGPP theory [20], is not needed for entropy convergence. Recently, Garde and Ashbaugh [47] constructed an isotropic model of water, termed HGS after Head-Gordon and Stillinger [48], which is constrained to have the same density and oxygen–oxygen radial distribution function of the SPC water model [49] at different temperatures, but without hydrogen bonds. Molecular-scale density fluctuations in this liquid are distinctly non-Gaussian, but the temperature dependence of ΔG_c is non-monotonic, leading to the occurrence of a sharp entropy convergence [47]. GHGPP also emphasize the fact that σ_n is nearly independent of temperature. σ_n is related to the compressibility of the solvent, which is indeed only weakly dependent on temperature for water. However, the temperature independence of σ_n is also not needed for the entropy convergence. For example, if σ_n^2 were given by $f(T)\upsilon$, convergence will still be observed even when $f(T)$ is a strong function of temperature, as long as the combination $T\rho^2/f(T)$ shows a maximum.

An insight into the temperature dependence of ΔG_c can be obtained by examining the SPT expression of ΔG_c, Eq. (1). It consists of two factors. The RT factor, accounting for the kinetic energy of solvent molecules bombarding the cavity surface [23], increases linearly with temperature. The factor in square brackets is equal to the logarithm of the number of solvent molecules in contact with the cavity of given size and account for the partitioning of empty space in a liquid with given ξ and σ_1 values [23,25]. This term decreases with temperature because both the density of a liquid and the size of its molecules decrease on increasing temperature. For nonpolar liquids this latter term is dominant, leading to a monotonic decrease of ΔG_c with temperature [4,39,50]. In the case of water, however, the density and the molecular size decrease only slightly over the range 0–150 °C (Table 1), leading to a trade-off between the two terms in Eq. (1), which produces the flat maximum above 100 °C. The fact that the balance is delicate is indicated by the fact that, even though σ_1 decreases by less than 0.1 Å over the range 0–150 °C, this decrease is essential in order to obtain the ΔG_c maximum in this temperature range.

In conclusion, it has been shown that a suitable application of SPT is able to reproduce the occurrence of entropy convergence in hydrophobic hydration. The only input data for the SPT calculations are the experimental water density at each temperature and a temperature dependent hard sphere diameter for water molecules. In particular, the information on the compressibility of water, which was suggested to be important by GHGPP, was not needed. We have also presented a general condition for observing entropy convergence. It is suggested that entropy convergence occurs because the free energy of cavity formation in water goes through a maximum at approximately 100 °C for cavity sizes corresponding to common small solute molecules.

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