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Excess Entropy in Alcohol−Water Solutions: A Simple Clustering Explanation[†]

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We show that the anomalous negative excess entropy of mixing characteristic of aqueous lower alcohols containing hydrophobic groups is quantitatively consistent with a model exploiting only the experimentally observed molecular-scale segregation of the components across the entire concentration range. The simple model presented here, which uses plausible interatomic distances as its only free parameters, obviates the need to invoke "iceberg" or other water restructuring concepts which, though frequently postulated in explaining the hydrophobic interaction, are unsupported by recent experiments.

Introduction

If two or more liquids are miscible (form a homogeneous mixture when combined), it is well-known that the total entropy of the mixture will be higher than the entropy of the pure components prior to mixing. This can be established[1] simply by noting that if the number of molecules of component j in the mixture is N_j, the volume of the mixture is V, and each component is randomly distributed throughout the volume; the local density per unit volume of component j in the mixture is equal to the mean density of that component, that is, $\rho_j = \bar{\rho}_j = N_j/V$. Hence, the entropy of this ideal mixture is given by

$$S_{id} = -k\sum_j \int_V \bar{\rho}_j \ln \frac{\bar{\rho}_j}{\bar{\rho}} = -kN\sum_j x_j \ln x_j \qquad (1)$$

where $\bar{\rho} = N/V$ is the mean density of all molecules in the mixture and $N = \sum_j N_j$. Since for any mixture the mole fraction of component j, $x_j = N_j/N$, will be less than unity, the entropy given by (1) must always be positive compared to either of the pure components on their own (where $x_j = 1$).

In fact, the measured entropies of mixing molecules with hydrophobic headgroups in water are significantly less than their ideal values.[2] As an example, Figure 1 shows the observed excess entropy for methanol−water solutions as a function of methanol mole fraction.[3] This phenomenon has been the subject of numerous analyses, one of the earliest of which, by Frank and Evans,[2] has had seminal influence on solution theory thinking for over half a century. Fundamentally, Frank and Evans proposed a structural origin for the observed excess entropies and postulated the existence of an "iceberglike" structure forming around the hydrophobic entity in water.
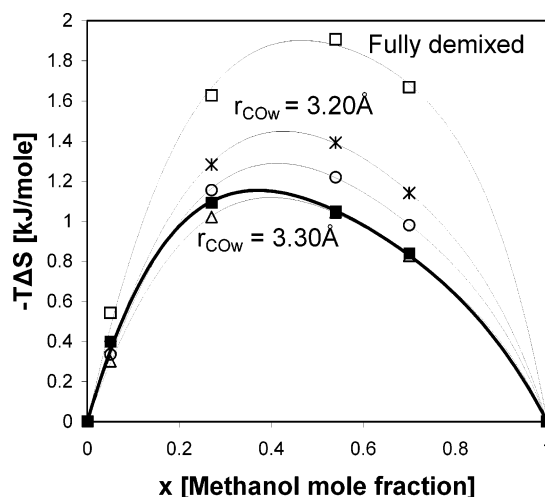

Figure 1. Measured excess entropy (solid squares, bold line),[3] $-T\Delta S_{excess}/N$, for methanol−water solutions as a function of methanol mole fraction at $T = 298$ K. The fully demixed excess entropies (open squares) are calculated according to Table 1. The excess entropies, eq 3 and Table 2, are shown for different values of the parameter used to define the interfacial region between clusters, namely, $r_{CO_w} = 3.20$ Å (asterisks), 3.25 Å (circles), and 3.30 Å (triangles) (criterion A in the text). The lines are fifth-order polynomial fits to the data points as guides to the eye.

Although this notion of enhanced water structure has persisted as a key element in models of the hydrophobic effect, it has not been supported by detailed analysis of its possible forms nor has there been any estimate of the extent of structural enhancement needed to account quantitatively for the observed negative excess entropy or its concentration dependence.

There have been numerous re-examinations of the basic Frank and Evans concept. For example, Lee[4] developed a theory based on Widom's potential distribution method.[5] The changes in thermodynamic quantities when a hydrophobic molecule is solvated are split into two processes, a so-called compensating part in which the net change in the Gibbs free energy is small

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or zero at all temperatures (i.e., the contributions from entropy and enthalpy changes are opposite and equal) and a noncompensating part which is nearly independent of temperature. On the basis of an earlier analysis,[6] Lee then points out that for the special case of insertion of a cavity into water the total free energy change is related directly to the noncompensating part of the entropy change that arises simply from the exclusion zone that has to exist around a cavity. Hence, according to this analysis, the underlying cause of the hydrophobic effect is entropic in nature. Graziano[7] pursues this idea further by showing that the opposite dependencies on solute size of the solvation Gibbs free energy of the noble gases compared with aliphatic hydrocarbons can be explained, at least qualitatively, within an exactly analogous framework. Hummer et al.[8] use an information theoretic approach to calculate the potential of mean force between cavities in water and demonstrate that this has the properties expected of hydrophobic interactions. Guillot and Guissani[9] claim, using computer simulation, to see the melting of the iceberg when a gas−water mixture is heated toward the boiling point. Equally, the excess entropy of simple hydrophobic molecules in water can be understood quantitatively, at least at infinite dilution, within the context of the Pratt−Chandler theory.[10] More recently, Ashbaugh et al.[11] have advanced a thermodynamic theory of hydrophobic hydration which also does not involve any concept of structure enhancement. What is quite clear however is that the iceberg concept is still widely discussed and utilized.[12]

Experimental evidence for any structural enhancement of water near a hydrophobic entity in solution is hard to come by. Several diffraction experiments have apparently seen little or no effect on water structure at low concentrations of alcohol in water.[13] Computer simulations of alcohol in water give a mixed picture: some of the early work[14] apparently supports the Frank−Evans structure enhancement picture, while other simulations[15] seem to contradict the Frank−Evans model. A recent surface-specific vibrational spectroscopy study of water near hydrophobic surfaces[16] has concluded that, if anything, hydrogen bonds tend to be more broken near such surfaces compared to the bulk liquid.

Recent experimental and computational studies have shown that water in the presence of alcohol and other molecules[17,18] tends to form clusters, Figure 2, instead of being randomly mixed, and that these clusters can become large and percolate at certain concentration ranges. This leads us to pose the question of whether the excess entropy in such solutions can be understood in terms of a simple excluded volume argument. In other words, is the inherent molecular-scale segregation in these systems sufficient to explain the observed excess entropy? As long ago as 1942, Flory[19] had already hinted at something along these lines when he wrote the following: "When there is a large heat effect accompanying the mixing of two liquids composed of molecules of ordinary size, the observed entropy of mixing usually deviates considerably from the ideal entropy given by (1) (same as eq 1 in this paper), i.e. the solution is not "regular". Due to differences in the energies of interaction between like and unlike pairs of molecules, distribution of the two species is not random as is assumed in the derivation of (1)."

Excess Entropy of a Fully Demixed and Partly Demixed Solution

To answer this question, we first estimate the excess entropy assuming complete demixing of the two components at the microscopic level; that is, there is everywhere a sharp boundary between water regions and alcohol regions. In this case, the
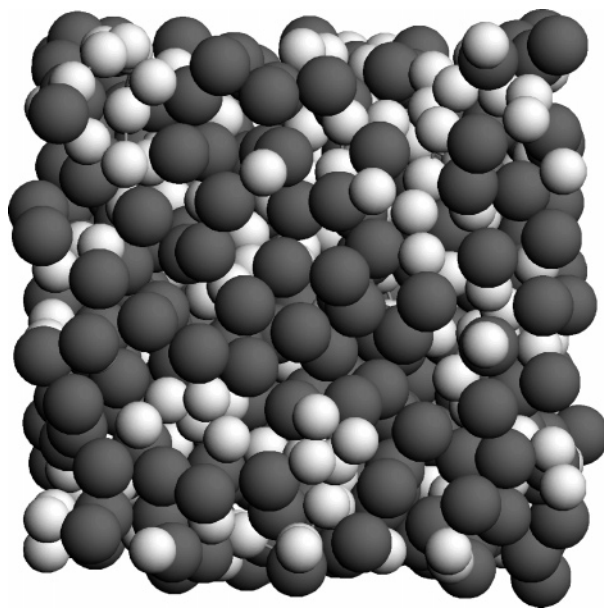

Figure 2. Snapshot of a mixture of methanol (black spheres) and water (white spheres) at a methanol mole fraction of 0.54, as obtained from EPSR simulation of the neutron diffraction data at this concentration. A large percolating cluster of methanol molecules can be seen in the center, with smaller clusters of water molecules below it. In other regions, the water and methanol molecules are better mixed: these would be classified as being in the interfacial region in the present model and therefore treated as randomly mixed.

local density of j molecules, ρ_j, is either $\sim 1/v_j$, where v_j is the molar volume of component j in the pure form, or zero. According to (1), regions of zero density will not contribute to the entropy. Writing $\bar{\rho} = 1/\bar{v}$, where $\bar{v} = \sum_j x_j v_j$ is the mean molar volume of the mixture, then the excess entropy relative to ideal mixing becomes

$$\Delta S = -k\left\{\sum_j \int dV \rho_j \ln\left(\frac{\rho_j}{\bar{\rho}}\right) - N\sum_j x_j \ln x_j\right\} =$$
$$-kN\sum_j x_j \ln\left(\frac{\bar{v}}{x_j v_j}\right) \quad (2)$$

For the pure liquids, the molar volume of water is $v_w \sim 30$ Å^3 at 298 K, while, for methanol, the molar volume is $v_m \sim 68$ Å^3. We assume the values in the mixture are not appreciably different from their pure liquid values.[20] These values can then be used to calculate the excess entropy given by eq 2 and the results compared with the measured excess entropies for methanol−water.

Note that the result (2) makes no reference to the detailed nature of the clustering, nor to any structural changes that may take place in the respective liquids. The only assumption is that there is a sharp boundary between water and alcohol clusters, that is, no mixing at the atomic level. In practice, the interface between alcohol and water regions will be more diffuse, comprising regions in which the two species intermingle via hydrogen bonding, thereby creating the equivalent of the random mixture in this region. These interface regions will therefore contribute little or nothing to the excess entropy. If we assume that of the N_j molecules of type j a fraction f_j are found, by some criterion to be specified, to be interfacial molecules, then the excess entropy function becomes

$$\Delta S = -kN\left\{\sum_j x_j(1 - f_j) \ln\left(\frac{\bar{v}}{v_j}\right) + \sum_j x_j f_j \ln x_j - \sum_j x_j \ln x_j\right\}$$

$$= -kN\sum_j x_j(1 - f_j) \ln\left(\frac{\bar{v}}{x_j v_j}\right) \tag{3}$$

The overall entropy is therefore raised toward the random mixing value, leading to less negative excess entropy.

Application to Neutron Scattering Data on Methanol−Water Mixtures

The neutron diffraction experiments on methanol−water mixtures have already been described in some detail elsewhere,[17] and only the salient features will be described here. In essence, a series of neutron diffraction patterns are recorded for a particular concentration of methanol in water, using different combinations of H and D to highlight either the water−water correlations or the methanol−methanol correlations of the methanol−water correlations. The mole fractions of methanol in water that have been studied so far are $x_m = 0.05$, 0.27, 0.54, and 0.70, as well as of course the pure liquids. These diffraction patterns are then interpreted via a Monte Carlo simulation procedure called empirical potential structure refinement (EPSR) which attempts to make a model of the scattering system. The empirical potential is used to drive the simulated structure factors as close as possible to the experimental values. The result is a set of computational models of the system that are in quantitative agreement with the experimental data.

A fundamental observation from the resulting structures is that at all concentrations the methanol−water mixture appears segregated at the molecular level, as referred to above. Taking the extreme view, if we assume the mixture is fully segregated—no mixing—as in eq 2, the excess entropy of mixing can be calculated directly without further reference to the simulation. The results of doing this are shown in Table 1 and Figure 1. These demonstrate clearly that the qualitative trend of the measured excess mixing entropy is indeed explained by this simple demixing scenario: there is no need to invoke the concept of either the water or methanol adopting a more ordered structure in solution. In fact, the fully demixed entropies are too extreme compared to the measured values, and we need to seek an additional factor to explain the difference.

The simulated molecular ensembles can help here, as we can define a criterion to say whether a water molecule is "bonded" to a methanol molecule, and vice versa, and use this to calculate the fraction of interfacial molecules to use in eq 3. Methanol clusters are identified in the simulation by the requirement that any two carbon atoms separated by 5.6 Å or less are assumed to be in the same cluster; this is the position of the first minimum in the carbon−carbon radial distribution function. Likewise, two water molecules are assumed to be in the same cluster if their oxygen atoms are 3.5 Å or less apart. To estimate the fraction of molecules in the interfacial region, three different criteria have been adopted.

The first (A) is based on the carbon to water oxygen distance, r_{CO_w}, the second (B) is based on either the methanol oxygen to water hydrogen distance, r_{OH_w}, or the methanol hydroxyl hydrogen to water oxygen distance, r_{HO_w}, and the third (C) is based on either the CO_w distance, the OH_w distance, *or* the HO_w distance. Criterion A therefore represents a general specification for the distance of approach of a water molecule to a methanol molecule for the two molecules to be assigned to the interfacial region, whereas criterion B refers specifically to water hydrogen

TABLE 1: Negative Excess Entropy of Methanol−Water Solutions on the Basis of a Simple Model That Assumes All of the Molecules of Each Component Occur in Completely Segregated Clusters of the Same Density as Their Pure Liquid Counterparts, eq 2[a]

x_m	$\bar{v}$ (Å^3)	$\bar{v}/x_m v_m$	$\bar{v}/x_w v_w$	$-T\Delta S_{excess}/N$ (kJ/mol)	experiment[3] (kJ/mol)
0.00	30.0		1.000	0.000	0.000
0.05	31.9	9.382	1.119	0.542	0.399
0.27	40.3	2.193	1.838	1.626	1.092
0.54	50.5	1.376	3.661	1.906	1.050
0.70	56.6	1.189	6.289	1.667	0.840
1.00	68.0	1.000		0.000	0.000

[a] These are the entropy values which would occur if the fluids were fully demixed and therefore represent limiting values. Note that these calculated values make no reference to the detailed arrangement of molecules in the liquids, either before or after mixing. For the present calculation and measurements, $T = 298$ K.

TABLE 2: Estimated Surface Fractions and Modified Negative Excess Entropy of Methanol−Water Solutions, eq 3, after Correcting for the Fraction of Methanol, f_m, and Water, f_w, Molecules That Occur in the Interfacial Regions of the Respective Clusters[a]

r_{CO_w} (Å)		methanol mole fraction			
		0.050	0.270	0.540	0.700
3.20	f_m	0.572	0.355	0.239	0.166
	f_w	0.042	0.143	0.279	0.349
	$-T\Delta S_{excess}/N$	0.373	1.282	1.391	1.140
3.25	f_m	0.694	0.475	0.322	0.224
	f_w	0.058	0.202	0.372	0.454
	$-T\Delta S_{excess}/N$	0.335	1.154	1.219	0.980
3.30	f_m	0.798	0.593	0.405	0.285
	f_w	0.077	0.268	0.466	0.553
	$-T\Delta S_{excess}/N$	0.301	1.020	1.044	0.826

[a] The surface fractions are determined by looking for methanol−water pairs where the C−O$_w$ distance, r_{CO_w}, is at or below the value specified. In these calculations, $T = 298$ K.

bonding to the methanol molecule, either through the water hydrogen atom or the methanol hydrogen atom. Criterion C is a combination of these two criteria. Specific distances that were tried for criterion A are 3.20, 3.25, and 3.30 Å for r_{CO_w}, for criterion B are 1.75, 1.80, and 1.85 Å for both r_{OH_w} and r_{HO_w}, and for criterion C are 1.70, 1.75, and 1.80 Å for both r_{OH_w} and r_{HO_w}, with r_{CO_w} set to 3.1 Å. All three sets of distances are close to or slightly below the position of the first peak in the corresponding radial distribution functions, indicating that the overall thickness of the interfacial region is roughly the same as the mean separation of a pair of molecules of different kinds. Table 2 shows the surface fractions and derived excess entropies for criterion A, while the excess entropies derived from criteria A−C using eq 3 are shown in Figures 1 and 3, respectively.

Discussion

It is clear that this simple device, which involves three or four adjustable parameters, is readily able to explain the observed excess entropies both quantitatively and qualitatively, without the need to invoke restructuring arguments on either the water or the solute. The calculations rely on the fact that the system is clustered, and the result will depend on the size and shape of the clusters, since a few large clusters of globular shape would give rise to relatively few interfacial molecules and more negative excess entropy, whereas sheetlike clusters or a large number of small clusters would have a much higher percentage of surface molecules, leading to less negative excess entropy. Therefore, the nature of the clustering has a direct
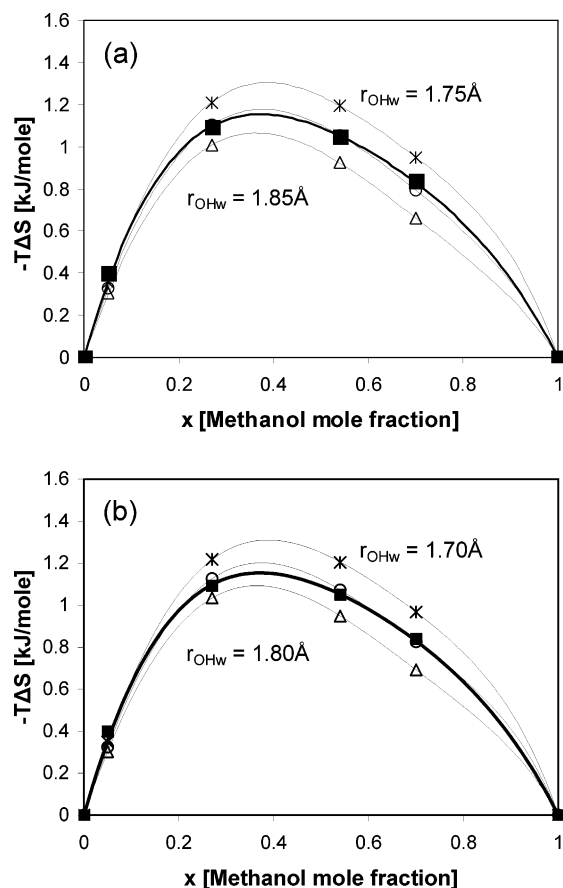
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Figure 3. Calculated excess entropies, eq 3, for different values of the parameters used to define the interfacial region between clusters: (a) (criterion B in the text) separation of either a methanol oxygen atom from a water hydrogen atom, r_{OH_w}, or a methanol hydroxyl hydrogen atom from a water oxygen atom, r_{HO_w}; (b) (criterion C in the text) separation of either a methanol carbon from a water oxygen atom ($r_{CO_w} = 3.1$ Å in this case), a methanol oxygen atom from a water hydrogen atom, r_{OH_w}, or a methanol hydroxyl hydrogen atom from a water oxygen atom, r_{HO_w}. For part a, both r_{OH_w} and r_{HO_w} are respectively 1.75 Å (asterisks), 1.80 Å (circles), and 1.85 Å (triangles). For part b, both r_{OH_w} and r_{HO_w} are respectively 1.70 Å (asterisks), 1.75 Å (circles), and 1.80 Å (triangles). The lines are fifth-order polynomial fits to the data points as guides to the eye. The experimental values are also shown (solid squares, bold line).[3]

impact on the observed excess entropy. At the same time, the values of the adjustable parameters needed to give the best representation of the excess entropy data turn out to be closely related to the observed separation distances between particular atoms in the solution.

Criteria B and C, based as they are on the hydrogen bonding between water and methanol, seem to give the best overall agreement in the concentration dependence of the excess entropy. This is not unreasonable given that the primary driver behind the observed clustering is believed to be the readiness of water molecules to form hydrogen bonds with the methanol hydroxyl group (and so as a consequence push the methyl groups closer together, forming methanol clusters). What is very clear from these results, and distinct from earlier models, is that there is at no point any reference to the detailed arrangement of either the water or methanol components: the observed excess entropies can be attributed entirely to the segregation of alcohol and water at the molecular level, without reference to their respective intermolecular structures.

It will be readily apparent that the excess entropy values derived from our model structures, as shown in Figures 1 and

3, are rather sensitive to the chosen values of the cutoff distances, r_{CO_w}, r_{OH_w}, and r_{HO_w}. The values that give a good fit are physically reasonable ones. There is however no independent method of estimating these distances, other than those values that give agreement with experimental excess entropies. Indeed, the notion here that there is a sharp boundary between mixed and unmixed regions of the solution is probably too simplistic, since in practice there would be a continuous change of entropy from the inside of a cluster to the mixing region between clusters. The effects of assuming a continuous boundary between regions of mixed and unmixed fluids might be the subject for a future study, but the point that is made here is that the observed excess entropy does not *need* to imply extra structure, as many previous studies have assumed.

The method adopted here is closely analogous to the original proposals of Flory and Huggins,[19,21] who developed a general theory for the free energy of polymers in solution, using an expression for the entropy of mixing like eq 1. However, they argue that for polymer solutions volume fractions rather than the mole fractions used here are needed to describe the excess entropy, to account for the vastly different volume ratio between polymer and solvent molecule. Indeed, eq 10.1 of Flory[19] appears to be closely replicated by our eq 2, except for a change of sign, caused by his assumption of "randomly entangled (liquid state) polymer molecules", which gives rise to increased entropy for the polymer solution *above* the ideal mixture values. For polymers, the molar fraction of the polymer can be orders of magnitude smaller than the solvent, so the ideal entropy of mixing would be almost zero, even though the polymer occupies much of the volume of the solution. In our small molecule limit, where the molar volumes are much more similar, we expect to see reduced entropy compared to the ideal value because ultimately two molecules cannot occupy the same space. It is noteworthy that Frank and Evans[2] do not appear to refer to the Flory−Huggins concept, even though it has direct relevance to the problem of excess entropy in mixtures of molecules.

In the Flory−Huggins theory, the enthalpy of mixing is assumed to arise from an interaction between the polymer and solvent, with an interaction parameter to be determined for each particular solute and solvent pair. The present work does not discuss enthalpy and free energy but concentrates only on the entropy term. Whether such an extension of the present model to calculate the free energy of mixing can be achieved rests on developing a reliable measure of the enthalpy of mixing. This turns out to be difficult to do accurately with computer simulation, since it involves the cancellation of large numbers− loss of like−like interactions offset by the gain in like−unlike interactions−and therefore requires accurate knowledge of the interaction potentials between different molecule pairs. In their simulations of methanol and water, Ferrario et al.[22] achieve reasonable estimates for the enthalpy of mixing, but it is doubtful this can be repeated in an EPSR simulation, which concentrates primarily on structure. It is also worth noting that even if the hydrogen bonding in our computer simulation model had been switched off, there would still have been a (reduced) degree of clustering observed, arising from the packing of nonoverlapping molecules. Hence, the mixing entropy will never reach its ideal value so long as atoms and molecules do not overlap. A separate paper exploring this in more detail, and the effect of temperature and pressure on the entropy, is in preparation.

Conclusion

In summary, the present simple analysis demonstrates that excess negative entropy and its concentration dependence can

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be explained quantitatively as a direct consequence of the observed tendency of water and alcohol to segregate at the molecular level. The amount of excess entropy is controlled by the width of the interfacial layer between clusters, which, on the basis of the present calculations, is about the diameter of one molecule in thickness or less. In a sense therefore, the proposal by Frank and Evans[2] that the cause of the excess entropy is structural in origin is correct, but there is no need to invoke "enhanced" or iceberglike water structure to explain it.

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