Towards a Microscopic Theory of Hydrophobic Solutions

By Derek Y. C. Chan,† D. John Mitchell, Barry W. Ninham*

AND

Bernard A. Pailthorpe

Department of Applied Mathematics, Research School of Physical Sciences, Institute of Advanced Studies, The Australian National University, Canberra, A.C.T. 2600, Australia

The distinguishing features of water and apolar solute molecular potentials responsible for the behaviour of hydrophobic solutions are inferred from a consideration of the thermodynamic properties of bulk water. These molecular properties are built into exactly soluble models in one dimension, and their necessity underlined by a comparison of models which give normal and hydrophobic solution thermodynamics. The form of solute–solvent and solute–solute molecular distribution functions is explored, and used to infer the nature of solute induced structure and the solvent-mediated hydrophobic interaction between apolar molecules in water.

1. INTRODUCTION

No single theory is yet able to account for the properties of bulk water and aqueous solutions of apolar solutes. Attempts to formulate a statistical mechanical theory of aqueous systems usually involve complicated models which do not permit accurate treatment, and the essential physics is obscured by the approximations invoked.

Several clear pathways towards an understanding of hydrophobic solutions can be discerned in the literature. A fundamentalist approach is to construct first a viable model for water, and then to graduate to solution properties. Molecular models of more or less reality can be constructed to mimic the observed properties of water and are already well developed.[1] There are also model calculations for the interaction between " hydrophobic " molecules in water-like solvents.[2] A more pragmatic approach to solutions is to feed in known thermodynamic properties of water as in the scaled particle theory [3-5] or more recently by using the experimental angle-averaged oxygen–oxygen correlation functions of water to characterise its properties.[6] Such theories, while involving one or two adjustable parameters do enjoy a certain measure of success in obtaining numerical agreement with observed solvation and solution properties. Nonetheless, since such approaches have already built in the unique features of water, their capacity to provide an understanding for the properties of hydrophobic solutions at a molecular level is diminished.[7] This is doubly so if it be borne in mind that such theories often necessarily rely on approximate equations of liquid state physics or approximate techniques whose validity is still unclear.

Another class of theories chooses to focus attention on the structured water presumed to surround hydrophobic solutes. This type of approach has its origins

† Queen Elizabeth II Fellow.

in the concept of a (statistical) " iceberg " around apolar solutes. This idea introduced by Frank and Evans,[8] allows one to interpret the high heat capacity as a reflection of the energy needed to " melt down " such " structures ". Examples of attempts to quantify the ill-defined concept of structure are the mixture models of Ben-Naim [9] and of Némethy and Scheraga [10, 11] who approach the problem of hydrophobic interaction by considering the effects of apolar solutes in altering the distribution of molecules in a mixture of ordered and disordered clusters. Much care has been given to the construction of a rigorous definition of the mixture model or quasi-mixtures in terms of molecular distribution functions.[9] The advance represented by the work of these authors is certainly of major importance. However, it is probably fair to say that despite a long history, the status of mixture models is still obscure.

From a statistical mechanical viewpoint the degree of solute-induced solvent structure is well defined and a knowledge of the molecular distribution functions is sufficient to characterise a system completely. There has been a series of recent papers motivated by this philosophy which focuses attention on the calculation and nature of the distribution functions that determine solute-induced solvent structure and solvent-mediated solute–solute interactions for model systems.[12-16] Also extant, and predating such calculations, is a conceptually simple mean field theory which parameterises the same quantities.[17] While such calculations are still quite some way from a complete description of aqueous systems, they help to delineate the interplay between solute/solvent size ratios, strength of molecular potentials, and thermodynamic parameters such as pressure and temperature. From this brief resumé it is clear that the development of a theoretical understanding of hydrophobic solutions has evolved along several disparate but complementary paths. The situation has been reviewed in more detail elsewhere.[18]

Even if refinement of these various approaches provides a precise quantitative description of hydrophobic solution properties there would still remain a large gap to be bridged. What is missing are simple explicit analytic models which capture and exhibit those essentials of the problem at a molecular level which the experimentalist knows intuitively must be at the heart of the matter.[19] The aim of this paper is to attempt just that by (1) isolating which of many possible factors at a molecular level could be primarily responsible for the unusual features of hydrophobic solutions ; and by (2) building exactly soluble models which do illustrate how such factors conspire to produce these features. These models are *one*-dimensional, deliberately so, because exact analytical solutions can be obtained. Any conclusions are not, therefore, affected by approximation methods needed to handle more complex models. The use of one-dimensional models is at first sight absurd and deserves comment. First, a minor observation : far from critical points, all bulk liquid properties are matched by equations reminiscent of, and generalisations of the van der Waals theory, and are therefore independent of dimensionality. More important is the simplicity of one-dimensional models which belies their strength. If the inclusion of any one molecular property in a model is the only such property which can give out hydrophobic-like solution thermodynamics this will constitute strong corroborative evidence that this molecular property plays an overriding determining role in real aqueous systems.

In the next section we briefly recapitulate the unusual bulk properties of water and point out how they can be understood from very general considerations in terms of the strong and highly directional hydrogen bonds. In section 3 we shall then construct models which show how these unusual molecular properties of water can conspire with those of apolar solutes to yield hydrophobic solution thermodynamics.

From calculated molecular distribution functions we can infer the degree of solvent structure near " hydrophobic " solutes, as well as the behaviour of such structures in solute–solute interaction. Our results also indicate that extreme care must be exercised in attempting to deduce the nature of the hydrophobic interaction from the low solute mole fraction behaviour of activity coefficients and osmotic pressure.

2. BULK WATER

In searching for an analytic model for hydrophobic solutions, it is essential to determine first how the anomalous bulk properties of water are linked to molecular properties. Of the anomalous bulk properties, especially deserving of recapitulation are: high melting and boiling points; high value of dielectric constant; the minimum in the isothermal compressibility κ_T (at 1 atm) as a function of temperature (for most liquids κ_T is an increasing function of temperature); high value of the heat capacity (around 9 k per molecule compared with 3 k from translational and rotational degrees of freedom); and the density maximum at 1 atm between 0 and 4°C. The structure of most simple liquids is determined primarily by the hard core repulsive part of the intermolecular potential and the attractive tail can be treated as a perturbation. By contrast, in water, because of the strong (quasi-chemical) and highly directional (tetrahedral) nature of the hydrogen bonds between molecules, the attractive part of the intermolecular potential is of comparable importance to, and can even dominate, the hard core repulsion in determining thermodynamic quantities. This loose observation is important to our subsequent theme. It can be made more explicit and illustrated if we consider the conditions necessary for the existence of the density maximum, at constant pressure, in a one dimensional model system.

For a one dimensional fluid with nearest neighbour interactions, the exact equation of state is given by eqn (A1) and (A2). At constant pressure P, the temperature dependence of the density is governed by the form of the enthalpy function $H(x) \equiv Px + u_{11}(x)$, as a function of intermolecular separation. Analysis of eqn (A1) reveals that if the intermolecular potential $u_{11}(x)$ has a hard core at $x = R$ and an energy minimum located at the same position, then, irrespective of the pressure, the system cannot have a density maximum as a function of temperature since $H(x)$ also has a minimum at $x = R$. However, if the minimum of $u_{11}(x)$ is located at a *larger* intermolecular separation than that of the hard core, then the system may exhibit a density maximum at constant pressure provided the enthalpy function $H(x)$ also has an *absolute* minimum at a position away from the hard core in addition to the minimum $x = R$. In water a situation similar to that just posed is brought about by two factors: the strong and highly directional hydrogen bonds which operate effectively at intermolecular separations which are larger than close packed, and the relatively weak dispersion interactions which are effective at smaller separations.

For a brief illustration of this argument for the existence of the density maximum and for the link between this property and the compressibility minimum consider a one-dimensional fluid in which the intermolecular potential is

$$
\begin{aligned}
u(x) &= \infty &,& \quad x < R \\
&= 0 &,& \quad R < x < 2R-a \\
&= -\varepsilon < 0, & & \quad 2R-a < x < 2R \\
&= 0 &,& \quad x > 2R.
\end{aligned} \tag{1}
$$

We note that this potential satisfies the criterion for the existence of a density maximum, namely that the potential minimum is located at a *larger* intermolecular separation than the hard core part of the potential. It is clear from eqn (1) that the

range of this potential permits interaction only between nearest neighbours. From the results given in the Appendix we have calculated the density [eqn (A.1)] and the isothermal compressibility $\kappa_T = \dfrac{1}{\rho}\left(\dfrac{\partial \rho}{\partial P}\right)_T$. The results, showing the characteristic density maximum and compressibility minimum of water, are given in fig. 1. With increasing pressure, the maximum and minimum occur at lower temperatures. This is consistent with the " vanishing " of the density maximum and compressibility minimum in liquid water at high pressures. More detailed calculations on one-dimensional lattice and continuum models as well as two-dimensional interstitial lattice models to illustrate these properties of water may be found in the work of Bell et al.[20, 21] and of Ben-Naim.[9]

To sum up : the distinguishing bulk properties of water due to the strong and highly directional hydrogen bonds can be reflected in a model by a molecular potential whose energy minimum is located away from hard core contact. While other effects such as many-body potentials and molecular asymmetry have not been considered, such factors are common to a number of fluids besides water, which do not have unusual solution thermodynamics. These factors do not therefore appear to be crucial.
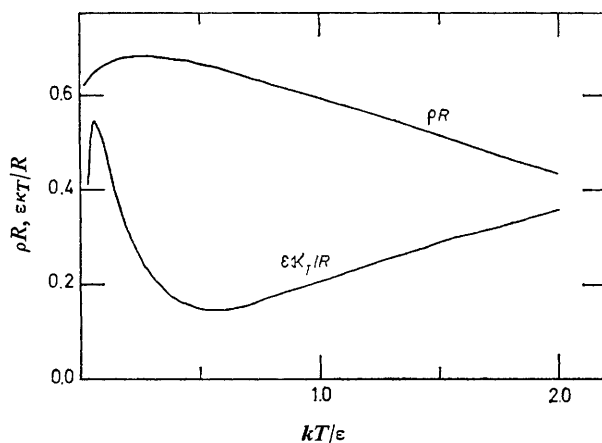

FIG. 1.—Temperature dependence of the density ρ and isothermal compressibility κ_T for a one-dimensional fluid with the molecular potential given by eqn (1). The reduced pressure is $PR/\varepsilon = 1.5$ and the well width is $a/R = 0.4$ and the ordinate scale refers to both curves.

3. HYDROPHOBIC SOLUTIONS

We commence discussion of the properties of hydrophobic solutions with a summary of relevant thermodynamic quantities. The chemical potential or partial free energy of a solute molecule (species 2) in a solution with a solute mole fraction X_2 at temperature T and pressure P is $\mu_2(X_2, P, T)$. Adopting as the reference state that of pure unmixed solvent and solute molecules at the same P and T, the partial free energy of mixing is

$$\Delta\mu_2(X_2, P, T) = \mu_2(X_2, P, T) - \mu_2(1, P, T). \tag{2}$$

However it will be convenient to use excess quantities, that over and above values for ideal solutions, denoted by the superscript E :

$$\Delta\mu_2^E(X_2, P, T) = \Delta\mu_2(X_2, P, T) - \Delta\mu_2^{\text{ideal}}(X_2, P, T). \tag{3}$$

Other quantities of interest are the partial excess enthalpy ΔH_2^E, entropy ΔS_2^E, heat capacity at constant pressure $\Delta C_{P_2}^E$ and the partial volume change ΔV_2^E:

$$\Delta \mu_2^E = \Delta H_2^E - T \Delta S_2^E$$

$$\Delta S_2^E = -\frac{\partial}{\partial T}(\Delta \mu_2^E)_P$$

$$\Delta C_{P_2}^E = \frac{\partial}{\partial T}(\Delta H_2^E)_P \qquad (4)$$

$$\Delta V_2^E = \frac{\partial}{\partial P}(\Delta \mu_2^E)_T.$$

We now briefly contrast the difference between normal and hydrophobic solutions in terms of these excess quantities. We shall confine our discussion to the limit of infinite dilution $X_2 \rightarrow 0$. By normal solutions we mean those mixtures of simple liquids which have been most studied in the literature. Concerning these there is general agreement that at least their thermodynamic properties are well understood. Examples are mixtures of inert gases, non-polar hydrocarbon, and mixtures of polar solutes and solvents. For normal solutions the enthalpy ΔH_2^E and the entropy ΔS_2^E have the same sign and so give opposing contributions to the free energy. However one always has $|\Delta H_2^E| > |T\Delta S_2^E|$ so that $\Delta \mu_2^E$ is dominated by and has the same sign as ΔH_2^E. Both $\Delta C_{P_2}^E$ and ΔV_2^E are small and can be of either sign.[7]

On the other hand, hydrophobic solutions (aqueous solutions of apolar solutes) are characterised by a large and positive excess free energy of mixing that is due to a large negative entropic contribution. The enthalpy is small and can be of either sign. The accepted interpretation of this phenomenon by Frank and Evans [7, 8] is that hydrophobic solutes can induce extensive " structuring " of surrounding water molecules with a consequent large entropy change upon solution. Due to the rather open structure of bulk water, molecules in the vicinity of apolar solutes with which they only interact *via* weak dispersion forces can, while still retaining the hydrogen bonds, rearrange to form solvent cages in some way reminiscent of the ice like crystalline hydrates of noble gases and small hydrocarbon molecules.[23] This picture is further supported by the large positive values of the heat capacity of $\Delta C_{P_2}^E$ which reflect the energy needed to " melt down " such a structured solvent. The large negative value of ΔV_2^E indicates that in dilute solutions at least, water molecules near apolar solutes rearrange to more efficient packing configurations.

Note that scaled particle theory,[3, 4] which is exact for very small and very large solutes, assumes that for very large solutes the solvation energy is just the interfacial energy, γ, times the solute surface area. But since $\partial \gamma / \partial T < 0$, the entropy of solution of any large solute in water is positive, opposite to that for small solutes, and since $\gamma > 0$ the enthalpic contribution must again dominate as in normal solutions. With all other things equal, the solution properties of apolar solutes must revert to normal as the solute size increases. We shall illustrate these points with some model calculations in the next section.

4. MODEL CALCULATIONS

For reasons discussed in the Introduction, we now examine the interplay between the solute–solvent and solvent–solvent intermolecular potential as well as solute/solvent size ratio on the thermodynamic behaviour of dilute solutions using a one-dimensional model. Effects upon the solvent–solute and solute–solute correlation

functions will also be given. Initially we consider for simplicity, only nearest neighbour interactions for solute and solvent particles of the same size.

EFFECTS OF INTERMOLECULAR POTENTIALS

Given a nearest neighbour interaction potential $u_{ij}(x)$ between species i and j at separation x, the partial excess free energy of the solute at infinite dilution is known to be [24]

$$\Delta\mu_2^E(0, P, T) = -kT \ln (F_{12}^2/F_{11}F_{22}) \tag{5}$$

where

$$F_{ij} = \int_0^\infty \exp\{-[u_{ij}(x)+Px]/kT\}\, \mathrm{d}x. \tag{6}$$

The corresponding enthalpic contribution to the excess free energy is

$$\Delta H_2^E = 2h_{12} - h_{11} - h_{22} \tag{7}$$

with

$$h_{ij} = F_{ij}^{-1} \int_0^\infty [u_{ij}(x)+Px] \exp\{-[u_{ij}(x)+Px]/kT\}\, \mathrm{d}x. \tag{8}$$

The " volume " change upon solution is

$$\Delta V_2^E = 2V_{12} - V_{11} - V_{22} \tag{9}$$

where

$$V_{ij} = F_{ij}^{-1} \int_0^\infty x \exp\{-[u_{ij}(x)+Px]/kT\}\, \mathrm{d}x. \tag{10}$$

For calculations, we choose potentials of the form

$$\begin{aligned}
u_j(x) &= \infty && x < R \\
&= -A_{ij}/x^2 && R < x < 2R \\
&= 0 && x > 2R
\end{aligned} \tag{11}$$

where R is the hard core size of the particle and the x^{-2} distance dependence mimics that of a one-dimensional array of parallel plates interacting under dispersion forces with the coefficients A_{ij} identified as Hamaker constants.[25]

The effects of varying the pressure and interaction parameters on the thermodynamic behaviour of the solution are summarised in table 1.

If A_{12} is less than but not too close to $\frac{1}{2}(A_{11}+A_{12})$ one finds that $\Delta\mu_2^E$, ΔH_2^E, ΔS_2^E and ΔV_2^E are all positive and $\Delta C_{P_2}^E$ is negative (case 1). Conversely when A_{12} is greater than but not too close to $\frac{1}{2}(A_{12}+A_{12})$ (case 2) all the above inequalities are reversed. For both cases $|\Delta H_2^E| > |\Delta\mu_2^E|$ and $|\Delta H_2^E| > T|\Delta S_2^E|$. In other words, the change in enthalpy opposes that in entropy but the former still dominates—similar to the behaviour in normal solutions. Further, at high pressures we also have $|\Delta H_2^E| \gg T|\Delta S_2^E|$, reminiscent of regular solutions. When the interactions between all species in the mixture are similar, $A_{12} \approx \frac{1}{2}(A_{11}+A_{22})$, various possibilities arise. Of special interest is the case when the enthalpy almost vanishes and all the thermodynamic quantities obey the same inequalities as those of a hydrophobic solution (cf. table 1, case 3). It is interesting to note that the Hamaker constants for the rather, small dispersion interaction due to electronic correlations in water + hydrocarbon systems also satisfies case 3.[25] However, unlike hydrophobic solutions the magnitudes of the non-vanishing terms in case 3 are much smaller than those in case 1 or 2.

For case 3 varying the temperature or pressure changes the thermodynamic inequalities to those of case 1 or 2. When A_{11} and A_{22} are widely different (by a factor of 2 say) but A_{12} is still the arithmetic mean, the thermodynamic inequalities again become more like those of case 1 or 2. We remark parenthetically that case 2 is not allowed if interactions are due to dispersion forces [for dispersion forces $A_{12} < \frac{1}{2}(A_{11}+A_{22})$ always].

TABLE 1.—TYPICAL THERMODYNAMIC INEQUALITIES OF NEAREST NEIGHBOUR ONE-DIMENSIONAL SOLUTIONS AT INFINITE DILUTION. (SEE TEXT FOR DISCUSSION).

(A) Effects of molecular potential

	thermodynamic properties
case (1) $A_{12} < \frac{1}{2}(A_{11}+A_{22})$	$\Delta\mu_2^E, \Delta H_2^E, \Delta S_2^E, \Delta V_2^E > 0, \Delta C_{P_2}^E < 0$
case (2) $A_{12} > \frac{1}{2}(A_{11}+A_{22})$	$\Delta\mu_2^E, \Delta H_2^E, \Delta S_2^E, \Delta V_2^E < 0, \Delta C_{P_2}^E > 0$
case (3) $A_{12} \approx \frac{1}{2}(A_{11}+A_{22})$	$\Delta S_2^E, \Delta V_2^E < 0, \Delta\mu_2^E, \Delta C_{P_2}^E > 0, \Delta H_2^E \approx 0$

(B) Effect of pressure [cases (1) and (2) only]

high pressure $PR/kT > 1$	$\begin{cases} |\Delta H_2^E| \gg T|\Delta S_2^E| \\ \Delta V_2^E, \Delta C_{P_2}^E \text{ small} \end{cases}$
low pressure $PR/kT < 1$	$\begin{cases} |\Delta H_2^E| \approx T|\Delta S_2^E| \\ |\Delta H_2^E| \gg |\Delta\mu_2^E| \end{cases}$

We see then that by adjusting intermolecular potentials and external conditions, one can almost obtain hydrophobic-like thermodynamics. However when various thermodynamic quantities satisfy the required " hydrophobic " inequalities (case 3, table 1), the entropic contribution to the excess energy, $T|\Delta S_2^E|$, is very small ($\sim 0.2\,kT$/particle) compared with " normal " one-dimensional solutions ($\sim 2\,kT$/particle). This is because when the solute size is bigger than or equal to a solvent particle, the introduction of a solute particle between two solvent molecules " breaks up " a solvent–solvent " bond " and replaces it by two solute–solvent " bonds ". This does not allow the solvent particles to maintain their interaction while accommodating a solute particle, as is possible in aqueous solutions. Next we move on to consider the effects of smaller solutes which will allow solvents on either side of the solute to interact. A similar model which allows for the formation of solvent n-mers has been put forward by Lovett and Ben-Naim [26] to study solute effects in a mixture model of water.

EFFECTS OF SOLUTE SIZE

(i) THERMODYNAMICS

Consider a one-dimensional solution in which the solute particle size R_2 is less than that of the solvent particles R_1. This allows for the possibility of solvent particles on either side of the solute to interact. In this way, we can study the effects of the ability of water molecules to form " pseudo-clathrates " or solvent cages around small solutes upon solution thermodynamics. This is the only property which this one-dimensional model has in common with water.

In order to exhibit analytically the thermodynamics of this model, we choose as the solvent–solvent interaction the square well potential

$$
\begin{aligned}
u_{11}(x) &= \infty & x &< R_1 \\
&= -\varepsilon & R_1 &< x < 2R_1 \\
&= 0 & x &> 2R_1.
\end{aligned} \tag{12}
$$

The solute–solvent interaction is treated as a hard core repulsion

$$\begin{aligned} u_{12}(x) &= \infty \qquad x < \tfrac{1}{2}(R_1 + R_2) \\ &= 0 \qquad\ x > \tfrac{1}{2}(R_1 + R_2). \end{aligned} \tag{13}$$

Note that this choice for the solute–solvent potential is a severe test of the solute size effect on solution thermodynamics since no allowance is made for " adjustments " in the solute–solvent potential as in the previous example.

The thermodynamics of this model is straightforward. Eqn (5) for the partial excess free energy of the solute at infinite dilution is generalized to

$$\Delta\mu_2^E(0, P, T) = -kT \ln (F_{121}/F_{11}F_{22}), \tag{14}$$

where F_{121} is a configurational integral corresponding to the solvent–solute–solvent complex shown in fig. 2 :

$$F_{121} = \int_0^\infty dx \int_0^x dy \exp \{-[u_{12}(y) + u_{11}(x) + u_{12}(x-y) + Px]/kT\}. \tag{15}$$

When the solute size becomes equal to or bigger than that of the solvent particle, the presence of a solute breaks up a solvent–solvent " bond " and the quantity F_{121} factorizes : $F_{121} = F_{12}^2$, to give the earlier result. Eqn (12)-(15) give

$$\Delta\mu_2^E(0, P, T)$$
$$= -kT \ln\left\{\frac{1 - [1 - \exp(-\beta\varepsilon_{11})]\{1 + \beta P(R_1 - R_2)\exp[-\beta P(R_1 - R_2)]\}}{1 - [1 - \exp(-\beta\varepsilon_{11})]\exp(-\beta P R_1)}\right\} \tag{16}$$

where $\beta = 1/kT$. This model is capable of giving hydrophobic-like thermodynamics ($T\Delta S_2^E \ll 0$, $T|\Delta S_2^E| \gg H_2^E$, large $\Delta C_{P_2}^E$, etc.). Typical results are given in table 2 for
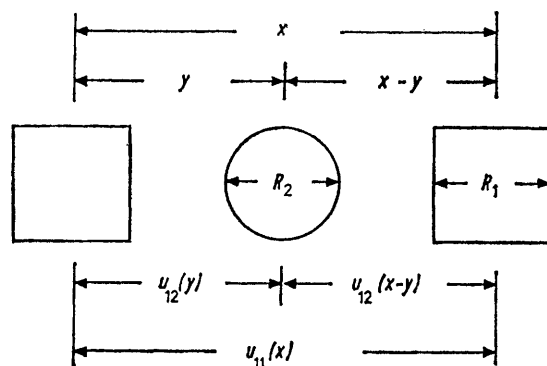

FIG. 2.—Solvent–solute–solvent complex of a pseudo-clathrate model where $u_{11}(x)$ is the solvent–solvent potential and $u_{12}(x)$ is the solute–solvent potential, cf. eqn (15).

the case $R_2/R_1 = 0.6$. Results from the nearest neighbour one-dimensional model ($R_2/R_1 = 1$) which exhibit normal solution properties are included for comparison. At higher temperatures the solution properties revert to normal behaviour again ($|\Delta H_2^E| \gg T|\Delta S_2^E|$, etc.). The experimental hydrophobic effect also vanishes at elevated temperatures.

One further quantity that is of interest is the behaviour of the solvent chemical potential at low solute mole fractions. We write

$$\Delta\mu_1^E(X_2, P, T) = \Delta\mu_1^E(0, P, T) + BX_2^2 + \ldots, \tag{17}$$

TABLE 2.—COMPARISON OF THERMODYNAMIC PROPERTIES OF CLATHRATE AND NEAREST NEIGH-
BOUR ONE-DIMENSIONAL MODELS AT INFINITE DILUTION ($\beta PR_1 = 1.0$, ENERGIES ARE IN UNITS
OF kT)

	clathrate model $R_2/R_1 = 0.6$	nearest neighbour model $R_2/R_1 = 1$
$\Delta\mu_2^E(0, P, T)$	2.09	3.55
ΔH_2^E	0.06	4.52
$T\Delta S_2^E$	−2.03	0.97
$\Delta V_2^E/R_1$	−0.77	0.57
$\Delta C_{P_2}^E/k$	4.87	0.59
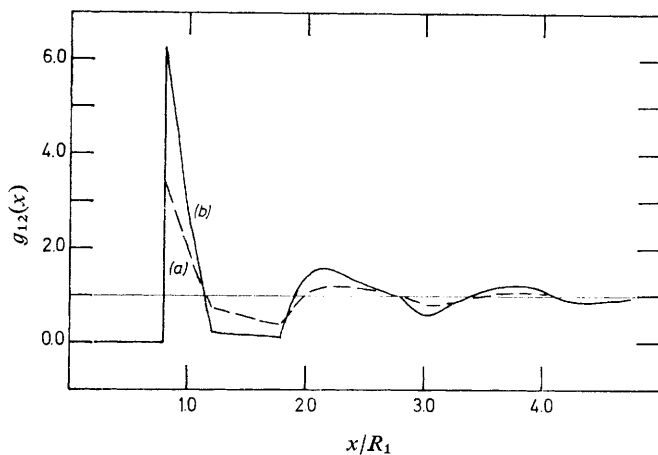
FIG. 3.—Solvent–solute pair distribution function $g_{12}(x)$ at reduced pressure $PR_1/kT = 1.0$, solute/
solvent size ratio $R_2/R_1 = 0.6$ and solvent–solvent potential well depth $\varepsilon/kT = $ (a) 2.0 (normal
solution thermodynamics), (b) 4.0 (hydrophobic solution thermodynamics), cf. eqn (12) and (13).
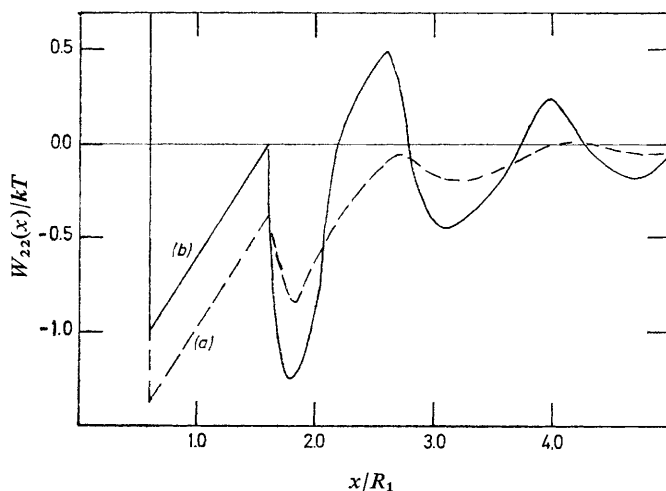

FIG. 4.—Solute–solute potential of mean force $W_{22}(x) = -kT \ln g_{22}(x)$ at reduced pressure $PR_1/
kT = 1.0$, solute/solvent size ratio $R_2/R_1 = 0.6$ and solvent–solvent potential well depth $\varepsilon/kT = $ (a)
2.0 (normal solution thermodynamics), (b) 4.0 (hydrophobic solution thermodynamics).

where the coefficient B is

$$B = \tfrac{1}{2}(F_{12}^2/F_{121} - 1). \tag{18}$$

It is easy to see that for our square well fluid, B is always negative, a situation at variance with that of hydrophobic solutions.[27] When only nearest neighbour interactions are possible ($R_2 \geqslant R_1$), B vanishes since $F_{121} = F_{12}^2$. This is a direct consequence of the lack of connectivity in one-dimensional models.

Nevertheless, with this simple calculation, we have illustrated the importance of the ability of water to form solvent cages in giving rise to typical hydrophobic solution thermodynamics. In one dimension, the formation of such cages is only possible if the solute is smaller than the solvent; this is an artifact of the model. In three dimensions, where a number of solvent molecules can cooperate to form solvent cages, the restriction on solute/solvent size ratio will be such that the interaction energies between solvent molecules forming the solvent cages should not differ appreciably from those of molecules in bulk. We have deliberately chosen the simplest solvent–solvent potential [eqn (12)] to illustrate our ideas and to demonstrate the minimum requirements needed to give hydrophobic solution thermodynamics. The use of more complicated solvent–solvent potentials, e.g., eqn (1) or an extension to include next nearest neighbour interactions, will in no way alter our conclusions.

DISTRIBUTION FUNCTIONS

We now go on to examine the way in which solute–solvent and solute–solute distribution functions vary in the one-dimensional model when the system exhibits either normal or hydrophobic-like thermodynamic behaviour. In fig. 3 we exhibit the temperature dependence of the solute–solvent pair distribution function $g_{12}(x)$ for the clathrate model which can have hydrophobic-like properties [cf. table 2]. In fig. 4 we exhibit the solute–solute potential of mean force $W_{22}(x) = -kT \ln g_{22}(x)$ where $g_{22}(x)$ is the solute–solute pair distribution function. Expressions for these quantities are given in the Appendix.

From the figures we can see that when hydrophobic-like thermodynamics prevail, the solvent molecules are more structured around the solute as indicated by the higher first peak in $g_{12}(x)$. In the same regime, the potential of mean force $W_{22}(x)$ has a minimum at the position where the solutes are separated by one solvent particle, rather than at contact. This suggests that solutes prefer to retain the surrounding solvent cage during interaction. This is a simple illustration of the observation that the process of two solutes coming into " contact " is not just a simple reversal of the process of solution.[7, 22]

Finally from the results of this one-dimensional pseudo-clathrate model consider what information can be deduced from the mole fraction dependence of thermodynamic quantities such as the excess solute chemical potential and the second osmotic virial coefficient B_2^* about the nature of the solute–solute interaction. For $PR_1/kT = 1.0$, $\varepsilon/kT = 4$ and $R_2/R_1 = 0.6$ we find that [cf. eqn (17) and (18)]

$$B = -3.3 \tag{19}$$

while the second osmotic virial coefficient is

$$
\begin{aligned}
B_2^*/R_1 &= -\frac{1}{2R_1} \int_0^\infty [g_{22}(x) - 1]\, dx \\
&= \frac{1}{2}\frac{R_2}{R_1} - \frac{1}{2R_1} \int_{R_2}^\infty [g_{22}(x) - 1]\, dx \tag{20} \\
&= -0.38.
\end{aligned}
$$

For the one-dimensional model, B is always negative, thus nothing can be deduced from the sign of this coefficient about the form of the solute–solute potential of mean force W_{22}. The second osmotic virial coefficient B_2^* always contains a positive contribution from the hard core part of $g_{22}(x)$. Even if this contribution is known, it is almost impossible to deduce the complicated form of W_{22} (*cf.* fig. 4) since B_2^* is only a weighted integral of the solute–solute potential of mean force. It is clear that little detailed information about solute–solute interaction can be inferred from such thermodynamic measurements.

5. CONCLUSION

We have attempted to exhibit the relation between the properties of water and apolar solutes and the unusual thermodynamic properties of dilute aqueous solutions of apolar solutes. This has been done through the use of simple solute models. The density maximum at atmospheric pressures as well as the compressibility minimum can be understood in terms of the low density tetrahedral crystalline structure favoured by the strong hydrogen bonds. Similarly the characteristic thermodynamic properties of hydrophobic solutions can be traced back to two factors: (*a*) the similarity between the electronic polarizabilities of water and most small apolar solutes results in a small contribution from dispersion interactions to the enthalpy of solution; (*b*) the open nature of the liquid water structure facilitates the possibility for water molecules around apolar solutes to rearrange to form solvent cages while still maintaining the hydrogen bonds between the solvents. This again results in a small change in enthalpy but a large change in entropy. Estimation of the effect of this mechanism using one-dimensional " pseudo-clathrate " models confirms this picture. From this model calculation we also seen the relative stability of such solvent cages during solute–solute interaction through the study of solute–solute distribution functions. We emphasize that it is very difficult to deduce information about the nature of the solute–solute interaction by studying the mole fraction dependence of solvent chemical potentials or second osmotic virial coefficients. Such information can only come about by considering molecular distribution functions. Finally we remark that extension of the clathrate model to the more realistic potentials, eqn (1) or (11), does not alter our conclusions.

APPENDIX

We give a summary of the formulae needed to compute distribution functions in one-dimensional models. The partition function of a one-dimensional N particle system with nearest neighbour interactions can be written as a $(N+1)$ fold convolution. This problem is easily soluble if one takes the Laplace transform of the partition function with the pressure as the transformed variable or equivalently work in the isobaric ensemble.

For a one-component system with nearest neighbour potential $u_{11}(x)$ the equation of state is known to be [28] ($\beta = 1/kT$)

$$\frac{B'_{11}(\beta P)}{B_{11}(\beta P)} = -\frac{1}{\rho} \tag{A.1}$$

where

$$B_{11}(\alpha) = \int_0^\infty e^{-\alpha x} e^{-\beta u_{11}(x)} \, dx \tag{A.2}$$

and ρ is the number density, P the pressure and the prime in eqn (A.1) denotes a differentiation with respect to the argument.

The presence of solute–solvent complexes such as that shown in fig. 2 requires straight-forward extension of known methods.[28] The expressions for the solute–solvent and solute–solute distribution functions are:

$$g_{12}(x) = -\frac{zB'_{11}(\beta P) e^{-\beta Px}}{C_{121}(\beta P, \beta P)} \mathscr{L}^{-1}\left\{\frac{C_{121}(s, \beta P)}{1 - zB_{11}(s)}\right\} \tag{A.3}$$

$$g_{22}(x) = -\frac{B'_{11}(\beta P) e^{-\beta Px}}{[C_{121}(\beta P, \beta P)]^2} \mathscr{L}^{-1}\left\{[B_{12}(\beta P)]^2 B_{22}(s) + \frac{z[C_{121}(s, \beta P)]^2}{1 - zB_{11}(s)}\right\} \tag{A.4}$$

where the operator $\mathscr{L}^{-1}\{\ \}$ denotes inverse Laplace transform with respect to the variable s and

$$C_{121}(a, b) = \int_0^\infty dx \int_0^\infty dy \, e^{-ax} e^{-by} \exp\left\{-\beta[u_{12}(y) + u_{12}(x) + u_{11}(x+y)]\right\} \tag{A.5}$$

$$B_{ij}(\alpha) = \int_0^\infty dx \, e^{-\alpha x} \exp\left\{-\beta u_{ij}(x)\right\}, \qquad i, j = 1, 2 \tag{A.6}$$

where $u_{12}(x)$ and $u_{22}(x)$ are the solute–solvent and solute–solute potential respectively. The fugacity z is given by

$$z^{-1} = B_{11}(\beta P). \tag{A.7}$$

[1] R. O. Watts, *Chem. Phys.*, 1977, **26**, 367 and references quoted therein.
[2] V. G. Dashevsky and G. N. Sarkisov, *Mol. Phys.*, 1974, **27**, 1271.
[3] F. H. Stillinger, *J. Solution Chem.*, 1973, **2**, 141.
[4] R. A. Pierotti, *J. Phys. Chem.*, 1965, **69**, 281.
[5] A. Ben-Naim and R. Tenne, *J. Chem. Phys.*, 1977, **67**, 627.
[6] L. R. Pratt and D. Chandler, *J. Chem. Phys.*, 1977, **67**, 3683.
[7] F. Franks, in *Water: A Comprehensive Treatise* (Plenum, London, 1975), vol. 4.
[8] H. S. Frank and M. W. Evans, *J. Chem. Phys.*, 1945, **13**, 507.
[9] A. Ben-Naim, *Water and Aqueous Solutions* (Plenum, London, 1974), and references therein.
[10] G. Némethy and H. A. Scheraga, *J. Chem. Phys.*, 1962, **36**, 3382, 3401.
[11] G. Némethy and H. A. Scheraga, *J. Phys. Chem.*, 1962, **66**, 1773.
[12] D. Ronis, E. Martina and J. M. Deutch, *Chem. Phys. Letters*, 1977, **46**, 53.
[13] D. J. Mitchell, B. W. Ninham and B. A. Pailthorpe, *J.C.S. Faraday II*, 1978, **74**, 1098, 1116.
[14] D. J. Mitchell, B. W. Ninham and B. A. Pailthorpe, *J. Colloid Interface Sci.*, 1978, **64**, 194.
[15] D. Y. C. Chan, D. J. Mitchell, B. W. Ninham and B. A. Pailthorpe, *Mol. Phys.*, 1978, **35**, 1669.
[16] D. Y. C. Chan, D. J. Mitchell, B. W. Ninham and B. A. Pailthorpe, *Chem. Phys. Letters*, 1978, **56**, 533.
[17] S. Marčelja, D. J. Mitchell, B. W. Ninham and M. J. Sculley, *J.C.S. Faraday II*, 1977, **73**, 630.
[18] D. Y. C. Chan, D. J. Mitchell, B. W. Ninham and B. A. Pailthorpe, in *Water: A Comprehensive Treatise*, ed. F. Franks (Plenum, London, 1978), vol. 6.
[19] See for example, F. Franks, *Water: A Comprehsnsive Treatise* (Plenum, London, 1972), vol. 1.
[20] G. M. Bell, *J. Math. Phys.*, 1969, **10**, 1753.

[21] G. M. Bell and H. Salouta, *Mol. Phys.*, 1975, **29,** 1621.

[22] F. Franks, *Water : A Comprehensive Treatise* (Plenum, London, 1973), vol. 2.

[23] D. W. Davidson, in *Water : A Comprehensive Treatise*, ed. F. Franks (Plenum, London, 1973), vol. 2.

[24] D. Henderson and P. J. Leonard, *Physical Chemistry : Advanced Treatise*, ed. H. Eyring (Academic, N.Y., 1971), vol. 8B.

[25] B. W. Ninham and V. A. Parsegian, *J. Chem. Phys.*, 1970, **52,** 4578 ; 1970, **53,** 3398.

[26] R. Lovett and A. Ben-Naim, *J. Chem. Phys.*, 1969, **51,** 3108.

[27] J. J. Kozak, W. S. Knight and W. Kauzmann, *J. Chem. Phys.*, 1968, **48,** 675.

[28] E. H. Lieb and D. C. Mattis, *Mathematical Physics in One Dimension* (Academic, N.Y., 1966).

(PAPER 8/673)