Hydrophobic solvation of nonspherical solutes

Lawrence R. Pratt

Department of Chemistry, University of California, Berkeley, California 94720

David Chandler

School of Chemical Sciences, University of Illinois, Urbana, Illinois 61801
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The theory of hydrophobic effects presented by Pratt and Chandler is generalized to include nonpolar solutes which are distinctly aspherical. The theory is used to study the solvation of simple aspherical hydrocarbon solutes in liquid water. The radial solvation of each component of diatomiclike solutes is studied as a function of their separation, or bond length. From these results it is found that when the bond length is large enough that one water molecule can fit between the apolar pair, the radial solvation of each is the same as that when the bond length approaches infinity. The solvation of the various sites of the homologous series methylene, ethane, propane, and n-butane is also studied, and effects of the geometrical structure of the solutes on their solvation is discussed.

I. INTRODUCTION

The structure of solvent water around apolar solutes in aqueous solution has long been recognized as a primary feature of hydrophobic effects. In general this structure must be expected to depend on the special characteristics of the interactions between solute and solvent molecules. Examples of such characteristics of apolar solute molecules are their size and shape. In a previous paper, we proposed a molecular theory which makes direct verifiable predictions about the radial structure of the solvent water near spherical apolar solutes. That theory applies to such spherical solutes as the atomic rare gases, and also to nearly spherical molecules such as methane. In the present work we extend our theory so that we are able to study directly the solvent structure around apolar but distinctly aspherical solutes in aqueous solution.

The theoretical tools which are employed in this generalization are the same ones which have been successfully used in studying the structure of nonassociated liquids composed of highly aspherical molecules. We view an aspherical molecular solute as a collection of spherical (extended atom) interaction sites held together by chemical bonding forces. Intramolecular distribution functions which describe the solute molecular structure are introduced, and the goal of the theory is to yield intermolecular atom—atom correlation functions. In the present work these correlation functions describe the radial solvation by water of the atomic constituents of the solute molecule, for example, the solvation of a methyl group in solute molecules such as ethane and propane. The atom—atom intramolecular correlation functions which we study are directly proportional to the angularly averaged local solvent density at the solvated surface. Thus, throughout this paper we occasionally refer to relative changes in these correlation functions as changes in solvation of the spherical components of the solute molecules.

This extension of our theory provides additional basic information with which to develop a microscopic understanding of hydrophobic effects. For example, it is clear that a practical theory of the solvation of a methyl group in an ethane solute gives conditional information about three-body correlations in the solution. This is because the theory has to take cognizance of the intramolecular correlation between two methyl groups in predicting preferred locations of a third molecule (water). Thus, we can consider a solute molecule with the general dimer structure, vary the bond length, and inquire whether there are special values for the bond length which yield unusual structural enhancement of the solvation. This type of information about three-body correlations also makes possible a thorough investigation of the role of slowly varying dispersion forces in hydrophobic correlations. We take up this latter problem in a subsequent article.

In the next section we develop the necessary theoretical results. Section III then presents numerical applications of our theory to diatomiclike solutes, of which ethane is one example, and also to larger hydrocarbons.

Probably the most direct tests of the predictions of our theory can be obtained from computer simulations of aqueous solutions. Unfortunately these computer simulation data do not seem to be presently available. Geiger et al. and Pangali et al. have used computer simulation techniques to study the solvation of pairs of spherical solutes in water. However, the structural properties reported by these groups are appropriate to the case in which the solute molecules are not bound together. Pangali et al. did use a harmonic binding force between the two solutes in order to bias their Monte Carlo sampling in an efficient way. The non-rigidity of the resulting bond between the solute pair can be simply included in our theory. But the data collected by Pangali et al. does not yield the distribution of water outside a spherical constituent of a diatomic molecule because their method of collecting data removed the bias introduced by the harmonic binding force. Indeed, if their simulation were carried out long enough, the ensemble averages studied by Pangali et al. should be independent of the harmonic force between the solutes, and should approach the radial distribution of water outside a free spherical solute. Since the solvation results reported by these authors do depend on the harmonic binding force,
their results must change systematically if their simulation is lengthened. Thus a direct comparison between our results and those of Pangali et al. is not meaningful here.

II. THEORY

In Ref. 1, we described the hydrophobic solvation of spherical apolar solutes, denoted generically by the symbol A. The solvent water is identified by the symbol W. The theory presented in Ref. 1 has two principal ingredients. The first is the measured structure and equation of state of pure liquid water. This information is to be employed to study the correlations and thermodynamic properties of the spherical solutes in solution. The second ingredient is the integral equation approximations which use this empirical information about the pure solvent to compute AW and AA pair correlations. The approximations are guided by requiring that they give reliable results when applied to systems with non-associated molecular solvents. On the basis of these considerations we proposed and studied the integral equations

\begin{align}
K_A(r) &= 1 - h_{AW}(r) - c_{AW}(r) + \beta_{AW} c_{AW} h_{AW}(r), \\
K_W(r) &= 1 - h_{AW}(r) - c_{AW}(r) + \beta_{AW} c_{AW} h_{AW}(r), \\
c_{AW}(r) &= 0, \quad r > c_{AW}, \\
h_{AW}(r) &= 0, \quad r < c_{AW}.
\end{align}

Here M = A or W, the length c_M is the van der Waals diameter characterizing the spherical interaction between A and M, and the h_{AW}(r) are the usual radial distribution functions associated with a spherical solute A. The notation a+b(r) indicates a convolution integral

\[ a + b(r) = \int df(r')b(|r - r'|). \]

The measured properties of the pure solvent enter these equations through the quantities \( \rho_w \) and \( h_{AW}(r) \). The density of pure liquid water is \( \rho_w \), and

\[ h_{AW}(r) = \text{oxygen-oxygen radial distribution for pure liquid water}. \]

Equations (1) can be viewed as defining the direct correlation functions \( c_{AW}(r) \). From this point of view Eqs. (2) make an approximate closure of Eqs. (1).

The more general theory employed in the present work has the same principal ingredients. It is constructed by altering the form of the Ornstein-Zernike (OZ)-like equations (1) to allow for the influence of intramolecular correlations. This is done in such a way that the theory gives reliable results when it is applied to nonassociated molecular solvents. In particular, we use OZ-like equations patterned after the RISM integral equation:

\begin{align}
\tilde{h}_A(r) &= \omega_A r c_{AW}(r) + \rho_c c_{AW} h_{AW}(r), \\
\tilde{h}_W(r) &= \omega_A r c_{AW}(r) + \rho_c c_{AW} h_{AW}(r), \\
\end{align}

The Greek letters index the extended atom groups in the solute molecule, summation over repeated Greek subscripts is implied, and the \( \omega_A(r) \) are intramolecular correlation functions for the solute:

\[ \omega_A(r) = 1 - \delta_{Av}(r) + (1 - \delta_{Av})\delta(r - r^+ + r^0) \]

where \( r^+ \) denotes the position of site \( \alpha \) in the solute molecule and angular brackets indicate the equilibrium ensemble average. Equations (4) then replace Eqs. (1). Again Eqs. (2) can be viewed as approximate closure relations for Eqs. (4). Equations (3) and (4) can then be solved numerically. The particular numerical method we have employed is based on the diagrammatic series which is equivalent to the solution of these integral equations. These cluster graphs are ordered and summed according to a slight modification of the chain recursion method of Dale and Friedman. The algorithm is embodied in the following equations:

\begin{align}
\tilde{h}_A^{(1)}(r) &= \delta_{Av}(r) h_{AW}(r) - \frac{1}{1 - \beta_{AW} h_{AW}(r)}, \\
\tilde{h}_W^{(1)}(r) &= \frac{1}{1 - \beta_{AW} h_{AW}(r)}, \\
\tilde{h}_A^{(2)}(r) &= \tilde{h}_A^{(1)}(r) - \frac{1}{1 - \beta_{AW} h_{AW}(r)}, \\
\tilde{h}_W^{(2)}(r) &= \tilde{h}_W^{(1)}(r) - \frac{1}{1 - \beta_{AW} h_{AW}(r)}, \\
\end{align}

These equations are used to calculate the \( \tau_M^{(N)} \) sequentially, by starting with (0c) and (0d) and employing fast Fourier transform techniques with the recursion relations (4a) and (4b). In the present approximations we have found that the sum \( \tau_M^{(N)} \) converges monotonically to within 10^-8 of its limit for all \( r > \tau_w \) when \( N = 50 \).

III. RESULTS

A. Diatomic solutes and ethane

One simple class of apolar molecular solutes are those with a diatomic A_2 structure. We will model the ethane molecule with a structure of this sort. If the intramolecular bond is rigid, and has a length \( l \), then

\[ \omega_{12}(r) = \delta(r - l)/4\pi l^2. \]

For ethane we would assume that the methyl (methane) particles have a van der Waals radius of \( \tau_w = 3 \delta_{Av} = 1.85 \text{ Å} \) and

\[ l = 1.54 \text{ Å}. \]

Equations (2) and (4) can then be straightforwardly solved to yield \( \tilde{g}_{AW}(r) \) which describes the solvation of the methyl group in ethane. However, as mentioned above, it is of interest to consider how the solvation of these pair of spherical groups changes when their bond length is varied. Therefore, for the purposes of this section, we define

\[ \tilde{g}_{AW}(r|l) = \text{radial distribution of water around a methane site in a diatomic molecule with rigid bond length \( l \).} \]

Thus \( g_{AW}(r|l = 1.54 \text{ Å}) \) gives us again the result appropriate to ethane. Typical results for \( \tilde{g}_{AW}(r|l) \) are shown in Fig. 1. It can be seen that if the bond length is fairly small, \( l < \tau_w \), the presence of the attached second methyl group disrupts the first solvation shell of the first methyl group. In that case, sol-
vent density is shifted from the neighborhood of the first peak of \( g_{w}^{E}(r) \) to the region of the first minimum. The solvent density around a methyl group in ethane is somewhat less layered than the solvent density around a methane molecule. By inspection of the integral equation, we note that as \( l \to \infty \) the solvation of these methyl groups approaches that of the free methane molecule in solution. This is also the case for \( l = 0 \). In both of these cases the solvation of such a methyl group is not disrupted at all by the presence of the second member of the pair. In fact for the largest bond length represented in Fig. 1, which is \( l = 6.4 \, \text{Å} = r_{\text{a}} + r_{\text{v}} \), the \( g_{w}^{E}(r)/l = 0 \) is everywhere within a few percent of \( g_{w}^{E}(r) \). Thus as far as the radial

**FIG. 1.** Radial distribution of water (W) around a methane particle in a (Me)$_2$ dimer with rigid bond length \( l \) in aqueous solution at 25°C and 1 atm pressure. When \( l = 1.54 \, \text{Å} \) this (Me)$_2$ solute provides a realistic model of an ethane molecule.

**FIG. 2.** Comparison of radial distribution of water (W) around primary methyl groups in ethane and propane solutes with that around methane in aqueous solution at 25°C and 1 atm pressure.

**FIG. 3.** Comparison of radial distribution of water (W) around interior (methylene) groups of propane and \( \text{trans} \) n-butane dissolved in liquid water at 25°C and 1 atm.

solvation of these methyl (methane) groups are concerned separation by one water molecule is sufficient to achieve the solvation appropriate to a free methane molecule.

**B. Larger hydrocarbons**

By consideration of larger alkanes we can use our theory to study the way in which solvation of an end methyl group depends on the solute size. The next simplest alkane is propane. There are two different \( g_{w}^{E}(r) \) correlation functions for propane: an exterior methyl-water \( g_{w}^{E}(r) \), and an interior methylene-water \( g_{w}^{E}(r) \). There are also two \( \omega_{\text{w}}^{E} \), \( \alpha^{E} \gamma^{E} \):

\[
\omega_{11}(r) = 5(r - l_{11})/4r_{11}^{2}
\]
\[
\omega_{13}(r) = 5(r - l_{13})/4r_{13}^{2}
\]

The bond length \( l_{11} = 1.54 \, \text{Å} \), \( l_{13} \) is fixed by \( l_{12} \) and the tetrahedral angle to be 2.52 Å. Typical results for \( g_{w}^{E}(r) \) are shown in Fig. 3 compared to those obtained for free methane, and for ethane. As should have been expected the presence of additional methyl and methylene groups further diminishes the density in contact with the end methyl group. This type of change in solvation of a primary methyl with changes in the size of the solute is expected to decrease as the size of the solute increases through a given homologous series. By extending these calculations to (rigid) \( \text{trans} \) n-butane solutes, we find only slight changes in the methyl-water \( g_{w}^{E}(r) \). At contact, \( r = 3.2 \, \text{Å} \), \( g_{w}^{E}(r) \) is raised by \( 4\% \), and at the first minimum, \( r = 5.0 \, \text{Å} \), \( g_{w}^{E}(r) \) is lowered by \( 9\% \) for the trans n-butane relative to propane. Thus the radial structure of the solvation of these methyl groups is primarily sensitive to near neighbor intramolecular correlations.

Although the radial solvation of the end methyl groups in propane and \( \text{trans} \) n-butane is very similar, the solvation of the methylene (interior) groups is appreciably different for these species. This is shown in Fig. 3. It is interesting to note that the change in going from propane to \( \text{trans} \) n-butane is in the same direction but significantly larger than the change \( g_{w}^{E}(r) \) in going from ethane to propane. This can be seen by comparing Figs. 2 and 3. The solvation of the interior sites of the
n-butane molecule thus depend on the intramolecular correlation between the two exterior sites of the solute molecule. To show this more directly Fig. 4 compares the \( g_{\text{H}_{2}O}(r) \) for trans \( n \)-butane with that for gauche \( n \)-butane. Since the interior methylene sites are more exposed when the molecule is in the gauche conformation than when it is in the trans conformation, the density of solvent next to the methylene groups is expected to be larger for the gauche species. This is in fact borne out in Fig. 4.

Finally, we note that the difference in the solvation of interior methylene sites and exterior methyl sites can be observed by comparing the \( g_{\text{H}_{2}O}(r) \) and \( g_{\text{H}_{2}O}(r) \) for propane given in Figs. 2 and 3. Again the exterior sites are more exposed and thus are more strongly solvated.

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