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H-Densities: A New Concept for Hydrated Molecules

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ABSTRACT

It is common to represent molecules by "ball-and-stick" models that represent static positions of atoms. However, the vibrational states of water molecules involved in hydrogen bonding have wide amplitudes, even in their ground states. Here we introduce a new representation of this wide-amplitude vibrational motion: H-density plots. These plots represent the delocalized zero-point vibrational motion of terminal hydrogen atoms of water molecules weakly bound to other molecules. They are a vibrational analogy to electron densities. Calculations of the H-densities for complexes of water with water, benzene, phenol, and DNA bases are presented. These are obtained using the quantum diffusion Monte Carlo method. Comparisons of measured and calculated rotational constants provide experimental evidence of the new concept.

Introduction

Studying the noncovalent bonds between water molecules and other molecules has become a major area of research.

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New spectroscopic techniques are yielding quantitative information on these hydrogen bonds,¹ and modern methods of theoretical chemistry are being applied to provide a detailed description.² The applications of this research are enormous, ranging from molecular solvation³ to properties of condensed phases⁴ to the structure and function of biomolecules.⁵

Understanding the hydrogen bond presents particular difficulties that are not present in more strongly bound molecular systems. The low frequencies of the intermolecular vibrations means that direct spectroscopic studies of the hydrogen bond must be done in the far-infrared.⁶ In addition, the strong anharmonic nature of the hydrogen bond makes spectral analysis difficult. Indirect spectroscopic studies of the hydrogen bond, through near-infrared or electronic transitions of a suitable hydrated chromophore, are more common.^{7,8} Because the bonding is so weak, reliable theoretical predictions on water-molecule interactions are hard to make, and the strongly anharmonic nature of the intermolecular modes and large vibrational zero-point effects add to the difficulties. Even a simple system such as water dimer has only very recently been treated in a reliable way by the modern methods of theoretical chemistry,⁹ and a complete understanding of the infrared spectrum of water dimer has not yet been achieved. Therefore, describing and understanding water-molecule interactions remains a major challenge.

Using high-resolution spectroscopy to study clusters made from molecules solvated by a selected number of water molecules represents a systematic way of understanding the hydrogen bond. If this can be achieved routinely for hydrated biomolecules, the implications for

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molecular biology will be significant. However, such size-selected experiments are difficult to perform and require producing hydrated clusters in the gas phase. Therefore, theoretical studies are particularly important in understanding and predicting the molecular interactions, structures, and dynamics. Recently there has been some progress in performing detailed spectroscopic experiments on clusters such as indole–water in the gas phase,¹⁰ and much effort is being expended on being able to do similar experiments on more complicated hydrated biomolecules.

The full theoretical treatment of the bound states of a molecule first requires the calculation and construction of a suitable potential energy surface and then needs a quantum mechanical treatment of the nuclear motion to calculate the vibrational–rotational states. There has been a great deal of work proposing potentials for hydrogen-bonded systems¹¹ and using them to describe various properties, but there has been little work on the vibrational dynamics. Conventional descriptions such as normal modes are not appropriate for the intermolecular vibrations, and treatments that can describe the floppy nature of the hydrogen bond are needed.

It is now becoming clear that the vibrational zero-point averaging of the intermolecular bonds in water–molecule interactions has an important influence on the properties of these species. A calculation of the bond dissociation energy, D_0 , requires the vibrational zero-point energy, and, in hydrated clusters, this can often be as much as one-third of the well depth of the intermolecular potential.¹² In addition, molecular properties of clusters containing water molecules are very sensitive to the wide amplitude of the anharmonic vibrations involving hydrogen atoms, and tunneling effects are also prevalent.¹³ Indeed, the amplitudes can be so large that a conventional classical “ball-and-stick” description of water–molecule interactions is not appropriate, and a delocalized “vibrational probability density” picture is required, similar to what is used to describe densities of electrons in molecules. Here we introduce a new concept—the H-density—which is a plot of the probability density associated with the vibration of hydrogen atoms in a hydrated cluster. We emphasize that this is a more accurate way of portraying hydrated molecules than just drawing a molecular structure.

The main aim of this Account is to communicate to a wider audience the importance of vibrational zero-point averaging and the need for a vibrational probability density description of hydrogen atoms in hydrated molecules. We do this by reporting calculations for a range of increasingly complex systems, from pure water clusters, to hydrated methanol, benzene, and phenol, and to the interaction of water with DNA bases. We also compare in detail with available experimental data to emphasize the reliability of the theoretical treatment.

Intermolecular Vibrations and the Hydrogen Bond

To describe vibrational states of hydrated molecules, a general and robust method is needed for solving the

Schrödinger equation for the bound-state nuclear motions from appropriate potential energy surfaces. Several studies have demonstrated the inadequacies of the harmonic normal mode approximation for the intermolecular modes of water–molecule systems,¹⁴ and an alternative method is needed. Diffusion Monte Carlo (DMC) is a way of solving the Schrödinger equation for the ground state of a multidimensional system.¹⁵ It exploits an analogy between the time-dependent Schrödinger equation and the diffusion equation. Since the diffusion equation describes a random walk, a random walk algorithm can thus be devised to solve the Schrödinger equation. In its simplest form, this approach gives only the vibrational ground-state energy, wave function, and properties, but this is appropriate for comparison with high-resolution spectroscopy measurements done on molecular beams prepared at very low temperatures.

The accuracy of calculations of vibrational states is always crucially dependent on the quality of the potential energy surface. For small water clusters, sophisticated potentials have been constructed that include many-body induction interactions together with quite accurate water–water pair interactions.¹⁶ For more complicated hydrated molecules, the potentials are not so accurate and are based on empirical forms that have been built to reproduce a variety of experimental and theoretical data.¹⁷ These potentials do contain realistic terms for the short-range repulsions and long-range attractive interactions. However, comparisons with experiment often show these potentials to work surprisingly well,¹⁸ and thus the predictions made with them should be reasonable if not highly accurate. There has also been considerable recent progress in applying good *ab initio* methods to hydrogen-bonded systems,¹⁹ although this approach only normally provides harmonic frequencies which, as has been emphasized, are not normally sufficient for water–molecule interactions.

The DMC method was first applied to calculations of molecular electronic structure,¹⁵ but it recently has had significant applications to the vibrational states of weakly bound molecules.^{14,20} It exploits the linearity of the diffusion equation in Cartesian coordinates and number of particles and is readily applicable to systems with many degrees of freedom. The algorithm is very simple, just involving a random walk of atomic coordinates. The wave function is represented by a cloud of configurations weighted by the potential energy surface. No differentiation or integration is needed in the simulations. For weakly bound molecules, a rigid-body version of DMC is very useful which involves random rotations and translations of the monomer molecules making up a cluster.²¹ This assumes that the high-frequency intramolecular vibrations of water and the host molecule can be decoupled from the low-frequency intermolecular vibrations. This rigid-body approach is used in the calculation of the results presented here, although it should be stressed that DMC does apply to intramolecular vibrations also.

In much of this article we will discuss DMC calculations of rotational constants as these are related to molecular

structure, are extracted from measured microwave and infrared spectra, and illustrate clearly the importance of vibrational averaging effects. The results presented also illustrate the crucial role of vibrational zero-point energy (VZPE) in determining the relative stability of weakly bound clusters. However, it is important to point out that other useful molecular properties, such as dipole moments, can also be calculated with this approach.²²

One-Particle Densities

The DMC simulation provides a simple and efficient way of calculating the wave function for any particle of the quantum system under investigation. Indeed, a numerical representation of the wave function can be readily obtained by binning the weight of the configuration into a grid element whose coordinates match the position of the particle of interest. In this way, it is possible to obtain, at the end of the simulation, the one-particle wave function $|\phi_p\rangle$ of the particle p as a three-dimensional function in coordinate space $\phi_p(x,y,z)$. Accordingly, once the wave function is known, it is possible to calculate the probability density for the particle to occupy a given position in space from

$$\rho_p(x,y,z) = |\phi_p(x,y,z)|^2$$

This calculation can be performed simultaneously for each particle present in the system, and n different probability densities $\rho_{p_1}, \rho_{p_2}, \dots, \rho_{p_n}$ are obtained which describe the probability of finding a given particle in a given volume element.

The global probability density of the system is written as a sum of the one-particle densities,

$$\rho_{\text{tot}} = \sum_i \rho_{p_i}$$

To gain insights into the structure of the ground-state solution of the system, it is convenient to partition the total density into mass-selected densities. Indeed, it is often useful to know the probability of finding any particle of a given mass in a determined volume of space, rather than having to analyze the density for each particle separately. In our partitioning scheme, we construct the one-particle density for the k particles with identical mass m_i :

$$\rho_{m_i} = \sum_k \rho_{p_k}$$

This function then allows the regions of high probability density of particles of mass m_i to be represented by a three-dimensional isosurface defined by

$$\rho_{m_i} \geq \epsilon$$

where ϵ is the limit probability, usually set to 0.01, to obtain a 99.9% likelihood surface. This process can be repeated for each mass of the particles present in the system and is identical with the usual one-particle density function in the case of a single particle.

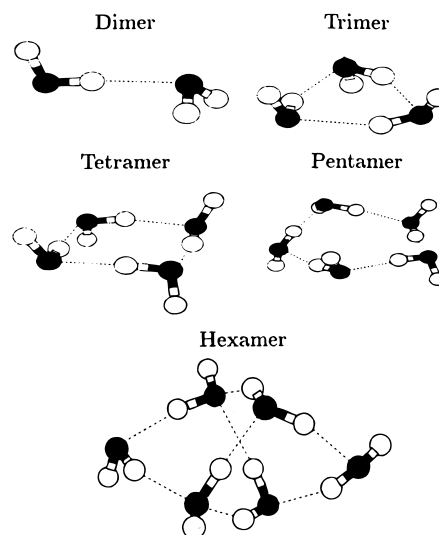


FIGURE 1. Schematic description of the ground states of water clusters $(\text{H}_2\text{O})_n$ ($n = 2-6$).²⁰

Table 1. Rotational Constants for Water Clusters

water cluster	rot. const (MHz)	potential minimum ²⁰	DMC ²⁰	expt ^{6,23}
trimer (H_2O) ₃	A	6886	5676	5796
	B	6769	5676	5796
	C	3507	3316	
tetramer (D_2O) ₄	A	3713	3063	3080
	B	3713	3063	3080
	C	1901	1583	
pentamer (D_2O) ₅	A	2150	1739	1750
	B	2110	1739	1750
	C	1102	849	
hexamer (H_2O) ₆ (cage)	A	2345	2136	2164
	B	1195	1096	1131
	C	1145	1043	1069

Plots of these *vibrational* probability densities have strong analogies to the diagrams conventionally used to display *electron* probability densities. Here we give several examples of the plots for hydrogen atoms, the H-densities, calculated for hydrated molecules with the monomers treated as rigid bodies. These plots for water molecules attached to other molecules are a more accurate representation than atoms having fixed positions and illustrate clearly the particularly wide amplitudes of hydrogen atoms not taking part directly in hydrogen bonding.

Water Clusters

Figure 1 shows schematic classical descriptions of the ground states of the water clusters $(\text{H}_2\text{O})_n$ ($n = 2-6$). For the trimer, tetramer, and pentamer, the clusters form rings with the O atoms being close to planar and the hydrogen bonds essentially being equivalent.²⁰ For the water hexamer with $n = 6$, the lowest energy structure is not a ring and has a nonplanar cage form.²³ In this isomer of the hexamer there are eight hydrogen bonds, with two being formed across the cage. Table 1 compares rotational constants A , B , and C , calculated with DMC for these water clusters, with experiment.²⁰ Theoretical rotational constants obtained by pure classical minimization of the potential are also shown, and these results do not include

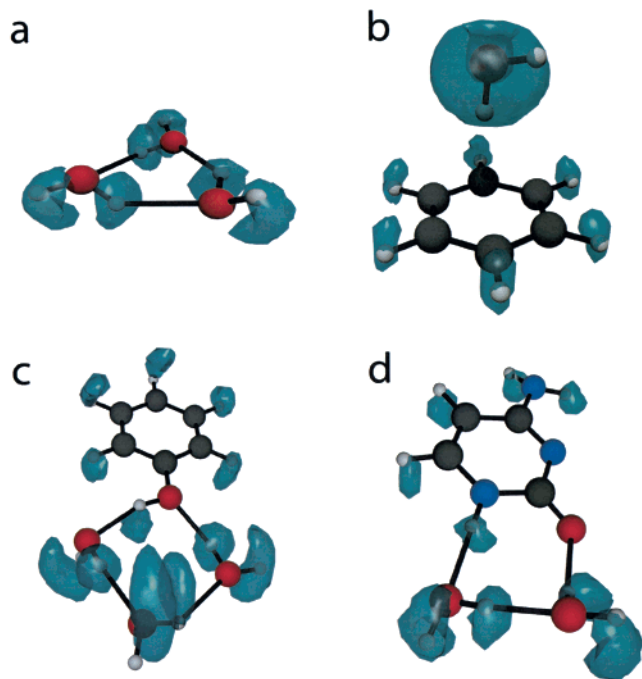


FIGURE 2. Plots of the H-densities for (a) $(\text{H}_2\text{O})_3$, (b) benzene- H_2O , (c) phenol- $(\text{H}_2\text{O})_3$, and (d) cytosine- $(\text{H}_2\text{O})_2$.

the quantum mechanical averaging over the vibrational ground state. It can be seen that vibrational averaging is essential to get rotational constants close to the experimental results. Therefore, pure classical minimization of potentials is insufficient for modeling these properties of water clusters. Note the significant decrease of the rotational constants which indicates the lengthening of the bonds that results from vibrational averaging over a strongly anharmonic potential of a weakly bound molecule.

An analysis of the H-densities in water trimer reveals interesting features which are transferable to other hydrogen-bonded clusters (Figure 2a). Where we expect a hydrogen bond between two water molecules, we see a concentration of the H-density, which corresponds to a localized proton between the two oxygen atoms. This is very much in accord with the classical picture of a hydrogen bond. However, in the case of free hydrogen atoms, where a classical approach would expect OH bonds to point either above or below the plane of the hydrogen-bonded ring, the H-density shows a strong delocalization effect. The H-density covers both up and down positions, removing any asymmetry to give rotational constants appropriate for a symmetric top molecule, in agreement with the experimental data (Table 1).²⁵ We can, therefore, distinguish two types of hydrogen atoms in the ground vibrational state of the water trimer: a “classical” localized atom which maintains the hydrogen bond, and a delocalized “quantum” atom which does not participate directly in the intermolecular bonding and has a wide amplitude motion.

The effects of zero-point vibrational energy are particularly acute for the water hexamer $(\text{H}_2\text{O})_6$, where it determines the structure of the lowest energy isomer.²³

Figure 3 shows calculated structures and energies of the various isomers of water hexamer. Pure classical minimization of the potential used gives a prism geometry as the isomer with lowest energy, but calculation of the vibrational zero-point energy gives the cage geometry as the lowest energy isomer. This has been confirmed by high-resolution spectroscopy in the far-infrared region, and only the cage isomer gives rotational constants close to experiment (see Table 2).²³ The energy ordering of isomers of larger clusters is very sensitive to the potential energy surface, but these results clearly show that it is crucial to perform an accurate calculation of the vibrational zero-point energy for any realistic comparison with experiment.

Figure 4 shows the average O–O bond length plotted against the number of water molecules n in the pure water cluster $(\text{H}_2\text{O})_n$.²⁰ It is seen that there is a significant decrease of the O–O distance as n is increased for clusters with cyclic structures. Comparison of the O–O distances obtained by classical minimization of the potential and by DMC once again emphasizes the importance of vibrational averaging in these systems. However, for the water hexamer with $n = 6$, the cage structure has a somewhat larger O–O distance which is closer to that obtained for liquid water at 25 °C.²⁶ For this reason, the cage water hexamer has been called “the smallest water droplet”.²⁷ In the case of the cage form of water hexamer, there are eight hydrogen bonds, which contrasts with the six obtained for a water hexamer with a cyclic structure. Two of these hydrogen bonds across the cluster are very weak, the other six are also slightly weaker than those for the cyclic structure, and there is a corresponding lengthening of the O–O bond.

Methanol–Water

The methanol–water dimer exhibits a new feature, not found in pure water clusters, in which the hydrogen bond can be donated by the H–O group of methanol (MW) or by a H–O group of water (WM) as shown in Figure 5. Pure classical minimization of the potential energy gives the water–donor isomer with by far the lowest energy. However, DMC calculations show that the vibrational zero-point energies of these two isomers are very different and brings the total energies of the vibrational ground states of these two isomers very close together.²⁸ Furthermore, the rotational constants of these two isomers are so similar that only a detailed study with deuterated species can distinguish between them.²⁹ This indicates once again the importance of having the most accurate methods to calculate vibrationally averaged rotational constants and properties for hydrogen-bonded systems.

Benzene–Water

The benzene–water dimer is particularly interesting as the “ π ” hydrogen bond between H_2O and benzene is directed toward the center of the benzene ring. Figure 2b shows the calculated H-density of benzene–water.¹⁸ This figure clearly shows the wide-amplitude nature of the free hydrogen atom of H_2O , which is completely delocalized

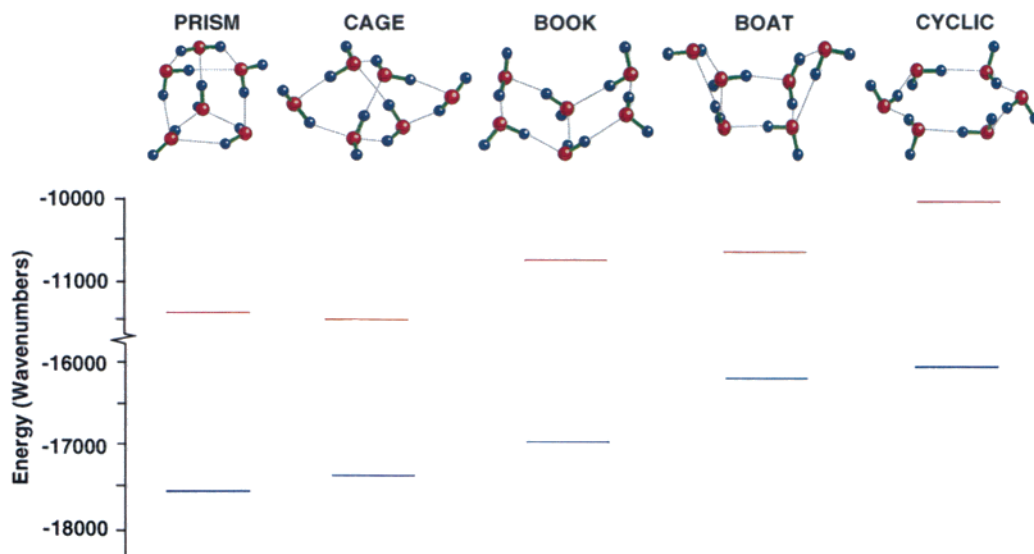


FIGURE 3. DMC calculations of the stabilities of the five lowest energy water hexamer structures.²³ Values of D_e (lower line) and D_0 (upper line) are shown for each isomer. Note that the cage structure has a D_e smaller than that for the prism structure by 213 cm^{-1} , whereas the D_0 calculations give a cage structure more stable than that of the prism by 62 cm^{-1} .

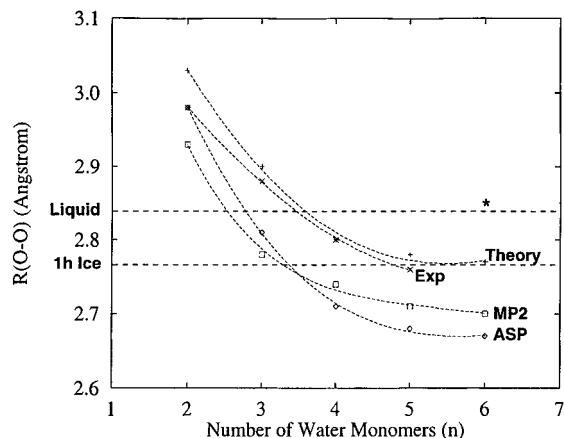


FIGURE 4. Average O–O separation for the cyclic structures as a function of cluster size.²⁰ “Theory” refers to the DMC computations,²⁰ while no vibrational averaging is done in the MP2 ab initio calculations or the results indicated for the “ASP” potential,¹⁶ which was used in the DMC simulations. “Exp” refers to the experimental results deduced from far-infrared spectroscopy.^{6,23} The star for water hexamer corresponds to the value for the three-dimensional cage structure.

Table 2. Calculated and Experimental Rotational Constants A , B , and C for the Isomers of Water Hexamer (H_2O)₆ (in MHz)²³

geometry	calculated (DMC)		
	A	B	C
cyclic	1211	1211	598
book	1798	1078	802
boat	1733	1125	1054
prism	1607	1355	1256
cage	2136	1096	1043
experiment ²³	2164	1131	1069

over angular motions in two perpendicular directions and gives a nearly spherical H-density. This results in the rotational constants for benzene–water having the form appropriate for a symmetric top, in contrast to the asymmetric-top geometry found by pure classical mini-

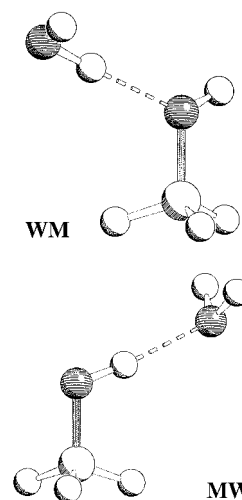


FIGURE 5. Two isomers for methanol–water.

Table 3. Rotational Constants (in MHz) for D_2O –Benzene

	A	B	C
DMC ³⁰	2845	2029	2029
experiment ³¹	2842	1906	1906

mization.^{18,30} This effect of vibrational averaging of the intermolecular motion has also been confirmed experimentally,³¹ and Table 3 compares the theoretical and experimental rotational constants for benzene– D_2O . It can be seen that only the results obtained after vibrational averaging are close to experiment. Once again, the rotational constants calculated with pure classical minimization of the potential are not in accord with experiment and do not have the form of a symmetric top.

Phenol–Water

Given the clear effects of vibrational averaging and delocalization of the intermolecular water vibrations in water

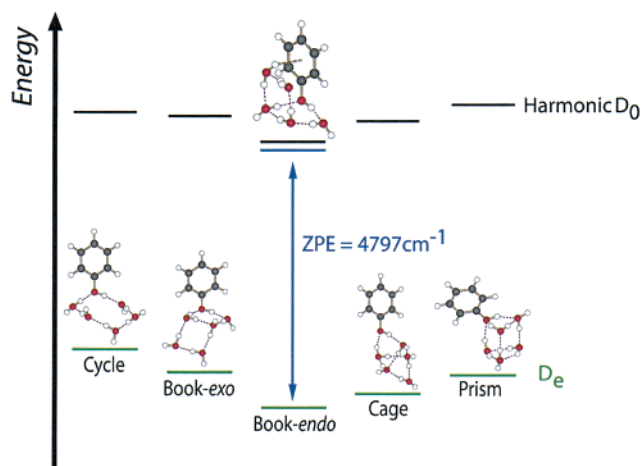


FIGURE 6. Schematic diagram of isomers of phenol–(H₂O)₅. Also shown are the harmonic corrections to the energies and the anharmonic energy obtained by DMC for the book-*endo* isomer with a π hydrogen bond.³²

clusters and benzene–water, it is no surprise that they are important also in the clusters of water with phenol. Here there are three types of hydrogen bonds: the water donor and phenol donor, similar to the two types found in methanol–water, and the π -hydrogen bond of the type found in water–benzene. These clusters show some similarities to pure water clusters in that the phenol–(H₂O)_n clusters have essentially planar geometries for $n = 2$ –4, while the geometries for $n = 5$ are three-dimensional.³² However, the geometry of the lowest-energy isomer for phenol–(H₂O)₅ is still in doubt.

In phenol–(H₂O)_n clusters the π hydrogen bond, seen in H₂O–benzene, is not as strong as the normal hydrogen bond for n up to 4. However, with $n = 5$, an isomer with a π hydrogen bond is predicted theoretically to have an energy similar to those of the π hydrogen bonds of other isomers (see Figure 6).³³ It is possible, therefore, that low-temperature samples of phenol–(H₂O)₅ include the isomer with the π hydrogen bond structure. The wide-amplitude nature of the intermolecular modes of the water monomers once again ensures a very large total vibrational zero-point energy in these clusters.

The similarity of the monocyclic clusters of phenol–(H₂O)_n to the pure water clusters is also reflected in their H-density plots (see Figure 2c). Indeed, the hydrogen atoms in phenol–(H₂O)₃ possess the same features as the ones seen in the water trimer. Again, by analyzing the H-density, we find two types of hydrogen atoms: a group of localized hydrogen atoms which form the strong hydrogen-bonded cycle and the free OH groups which oscillate between two minima. Note that, according to the H-density, the phenyl group is also delocalized, which is recognized as typical of a nonbonded group belonging to a hydrogen-bonded ring.

Water–Biomolecules

It is of interest to see if the findings on delocalized vibrational motion for water clusters and the clusters of

water with benzene and phenol also transfer to hydrated molecules of biological interest. Ab initio calculations and DMC simulations have been done on the interaction of water with the DNA bases cytosine and thymine,³⁴ and also on the related biomolecules uracil and indole.³⁵ Such calculations on indole–water are particularly important, as electronic spectroscopy experiments have been done which have given the bond dissociation energy D_0 .¹⁰ Measurement of this important quantity is rather rare in weakly bound clusters of water bound to organic molecules, and the vibrational zero-point energy correction is crucial for a detailed comparison of theory with experiment. For example, in indole–water we calculate a D_0 to be 1787.8 cm^{−1} (with a VZPE correction included of 334 cm^{−1}). This compares quite well with the experimental D_0 of 1693 cm^{−1}.¹⁰

Cytosine has several sites appropriate for hydrogen bonding with water, and the isomer of cytosine–water with lowest energy has two hydrogen bonds, with an overall bond strength nearly twice that of phenol–water. It is, therefore, of interest to see if clusters of more than one water molecule with cytosine follow the pattern of shapes seen for pure water clusters and phenol–water.

Figure 2d shows a plot of the H-densities for the minimum energy structure of two water molecules bound to the DNA base cytosine. The equilibrium structure of the lowest energy isomer of cytosine–(H₂O)₂ has a cyclic shape, rather similar to that of water trimer shown in Figure 2a. Once again, there is a clear wide-amplitude motion in the vibrations of the free OH bonds of the water molecules not involved directly in hydrogen bonding. Thus, even in the hydration of DNA bases such as cytosine, which have H₂O bond energies about twice as large as those for water–phenol, the H-density description is still relevant.

Conclusions

The aim of this Account has been to demonstrate that quantum averaging of the intermolecular vibrational motion of molecules involved in hydrogen bonding is important in understanding the structure and dynamics of hydrated molecules. In addition, we have aimed to show that vibrational probability densities are a useful pictorial representation of these clusters. Diffusion Monte Carlo simulations are a general and useful way for calculating the vibrational probability densities. The H-densities, plots of vibrational densities of hydrogen atoms, show particularly large amplitudes.

Vibrational densities of excited states have not been presented here. They are not obtained easily from the DMC approach, although there has been some progress in this direction.¹⁴ Since vibrationally excited states illustrate a wider amplitude in their motion than ground states and are more sensitive to anharmonicity, the concept of H-densities will be even more relevant. Thus, extension of methods to calculate H-densities for excited vibrational states and for finite temperatures will be an important development.

The vibrational densities have already been useful in explaining observed rotational constants in clusters such as water trimer and water–benzene. As they describe the wide-amplitude motion of hydrogen atoms they will also be useful in rationalizing other structural observations, such as those made by diffraction techniques. The wide-amplitude motion of the hydrogen atoms might influence the ability of other molecules to approach particular functional groups with which the water molecules interact. Therefore, it is likely that the H-density plots will have useful applications in rationalizing reactive events involving hydrated organic molecules or biomolecules. Just as electron densities have proven to be very useful for understanding chemical properties, H-densities are a useful addition to the visualization techniques used for describing the properties of clusters and hydrated molecules.

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