

Water: Structure and Properties

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Water is a major component of all living things. It is anomalous in many of its physical and chemical properties. Some are essential for life while others have profound effects on the size and shape of living organisms, how they work, and the constraints within which they must operate. Many of water's basic physical properties can now be explained, at least semiquantitatively, in molecular and structural terms, although in spite of intense study it remains incompletely understood.

Introduction

Water is the material cause of all things (Thales, 624–546 BC).

Water is a unique, ubiquitous substance that is a major component of all living things. Its nature and properties have intrigued philosophers, naturalists and scientists since antiquity. Water continues to engage the attention of scientists today as it remains incompletely understood in spite of intense study over many years. This is primarily because water is anomalous in many of its physical and chemical properties. Some of water's unique properties are literally essential for life, while others have profound effects on the size and shape of living organisms, how they work, and the physical limits or constraints within which they must operate. This was recognized by Lawrence Henderson in 1913 in his classic and still very readable book, *The Fitness of the Environment: An Inquiry into the Biological Significance of the Properties of Matter*. Since then more has been learned about the structure and properties of water at the molecular level, much of it through spectroscopic and thermodynamic experiments. The more recent discipline of computer simulation has also played a role, having achieved a level of sophistication in the study of water in which it can be used to interpret experiments and simulate properties not directly accessible by experiment. Many of water's basic physical properties can now be explained, at least semiquantitatively, in molecular and structural terms.

Basic physical properties

Selected physical properties of water are given in Table 1. To put these in context, comparison is made to the organic solvents methanol and dimethyl ether, where one and two of the hydrogen atoms are replaced by a methyl group, respectively. Water is a small solvent, occupying about 0.03 nm^3 per molecule in the liquid state at room temperature and pressure, yet it is highly cohesive because of the strong intermolecular interactions (hydrogen

Introductory article

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bonds, or H-bonds) between the oxygen and hydrogen atoms. This is reflected in its high boiling point, the large amount of heat needed to vaporize it, and its high surface tension. Replacement of one or both of the hydrogens dramatically weakens these intermolecular interactions, reducing the magnitude of these quantities. The strong cohesive interactions in water also result in:

- (1) a high viscosity, since for a liquid to flow interactions between neighbouring molecules must constantly be broken; and
- (2) a high specific heat capacity – the ability to store a large amount of potential energy for a given increment in kinetic energy (temperature).

In part water's high specific heat and heat of vaporization relative to other liquids results from its small size. More intermolecular interactions are contained in a given volume of water than comparable liquids. When this is taken into account by expressing the specific heat and heat of vaporization on a molar basis, methanol and water are comparable. The surface tension of water, however, is still anomalously large after accounting for differences in size. Water has one of the highest dielectric constants of any nonmetallic liquid. It also has the remarkable properties of expanding when it is cooled from 4°C to its freezing point, and again when it freezes. Both the expansion of water and its high dielectric constant reflect subtle structural features of liquid water at the molecular level.

Biological relevance of water's physical properties

Water, owing to its high boiling point, exists predominantly in its liquid form in the range of environments where life flourishes, although the other two phases, ice and vapour, play an essential role in shaping the environment. The high specific heat and heat of vaporization of water

Table 1 Selected physical properties of water

Property	Water	Methanol	Dimethyl ether
Formula	H ₂ O	CH ₃ OH	(CH ₃) ₂ O
Molecular weight (g mol ⁻¹)	18	32	46
Density (kg L ⁻¹)	0.998	0.7914	0.713
Boiling point (K)	373	338	248
Molecular volume (nm ³)	0.0299	0.0420	0.107
Volume of fusion (nm ³)	0.0027	Negative	Negative
Liquid density maximum (K)	277	None	None
Specific heat (J K ⁻¹ g ⁻¹)	4.18	2.53	2.37
(J K ⁻¹ mol ⁻¹)	75.2	81.0	109.0
Heat of vaporization (kJ g ⁻¹)	2.3	1.16	0.40
(kJ mol ⁻¹)	41.4	37.1	18.4
Surface tension (mN m ⁻¹)	72.8	22.6	16.4
Viscosity (μPa s)	1002	550	233
Dielectric constant	78.6	33.6	5.0
Dipole moment (Cm × 10 ³⁰) ^a	6.01	5.68	4.34

Values at 293 K unless indicated.

^aIn the gas phase.

have important consequences for organisms at the cellular and physiological level, in particular for the efficiency of processes involving heat transfer, temperature regulation, cooling, etc. Viscosity is the major parameter of water that determines how fast molecules and ions can be transported and how rapidly they diffuse in aqueous solution. It thus provides a physical upper limit to the rates of many molecular level events, within which organisms must live and evolve. These include the rates of ion channel conductance, association of substrates with enzymes, binding rates, and rates of macromolecular assembly. It also sets an upper bound to the length scale over which biological processes can occur purely by diffusion. In many cases, for example in enzyme–substrate reactions, evolution has pushed the components of living systems to the limits set by water’s viscosity.

The high surface tension of water is relevant at two levels. First, below a length scale of about 1 mm surface tension forces dominate gravitational and viscous forces, and the air–water interface becomes an effectively impenetrable barrier. This becomes a major factor in the environment and life style of small insects, bacteria and other microorganisms. Second, at the molecular (0.1–100 nm) scale the surface tension plays a key role in water’s solvent properties. The high dielectric constant of water also plays an important role in its action as a solvent. The biological significance of the expansion of water upon cooling below 4°C and upon freezing, though crucial, is largely indirect through geophysical aspects

such as ocean and lake freezing, the formation of the polar ice cap, and in weathering by freeze–thaw cycles.

Molecular Structure and Polarity

The geometry of the water molecule is illustrated in **Figure 1a**. It consists of two O–H bonds of length 0.096 nm at an angle of 104.5°. Other basic properties of water are its size, shape and polarity. Atoms that are not bonded will repel each other strongly if brought close enough that their electron orbitals overlap. At larger distances two atoms attract each other weakly due to an induced dipole-induced dipole (London dispersion) force. The combination of repulsive and attractive interactions is termed the van der Waals interaction. The point at which the repulsive and attractive forces balance is commonly used to define the diameter of an atom, which for oxygen and hydrogen are 0.32 nm and 0.16 nm, respectively. The water molecule is thus approximately spherical. Water is electrically neutral, but because the electronegativity of oxygen is much greater than that of hydrogen the electron distribution is concentrated more around the former, i.e. water is electrically polarized, having a permanent dipole moment of 6×10^{-30} Cm in the gas phase. The dipole moment is even larger (*c.* 8×10^{-30} Cm) in liquid and ice because neighbouring water dipoles mutually polarize each other. A useful way to represent the polarity of a molecule is to assign a partial charge to each atom, so as to reproduce the molecule’s net charge, dipole moment, and possibly higher-order electrical moments (**Figure 1b**). The magnitude

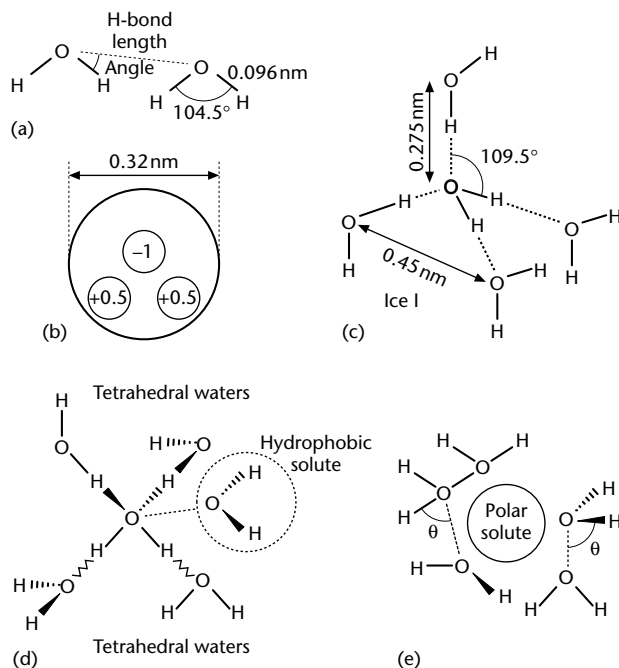


Figure 1 Structure of water. (a) Definition of key lengths and angles. (b) Model of water. (c) Structure of Ice I. (d) Schematic of H bonding structure in liquid water, and in presence of an apolar solute. (e) Schematic of H bonding structure around a positively charged ion of polar atom.

of an atom's partial charge is a measure of its polarity. For water there is about $+0.5$ on each hydrogen, and a charge of opposite sign and twice this magnitude on the oxygen. In contrast, the hydrogens of an apolar molecule such as methane have a partial charge of ≈ 0.1 , and methane's dipole moment is zero. Thus water is a very polar molecule with the ability to make strong electrostatic interactions with itself, other molecules and ions.

Putting all this together, one can picture a water molecule as a slightly sticky sphere of radius 0.32 nm in which two positive charges of $+1/2$ and a negative charge of -1 are embedded at the hydrogen and oxygen atomic centres respectively (Figure 1b). Many of liquid water's properties, including its cohesiveness, its high heat of vaporization, dielectric constant and surface tension can be explained with this simple molecular model. Other properties such as the temperature dependence of the density need a more sophisticated model that includes water's flexibility, polarizability and quantum mechanical effects.

Dielectric Constant

The dielectric constant is a measure of how easily a material is polarized by an electric field relative to vacuum. It is defined by the magnitude of the dielectric polarization (dipole moment per unit volume) induced by a unit field. Water has nearly 80 times the dielectric constant of

vacuum, and it is an order of magnitude more polarizable than most organic solvents. The dielectric constant of a polar liquid such as water depends on four major factors: the permanent dipole moment of the molecule, the density of dipoles, how easily they can reorient in response to a field, and how cooperative this reorientation is. Water has a high dipole moment, it is small so there are a large number of dipoles per unit volume, and in the liquid state they are easily and rapidly (within 10 ps) reoriented. In addition, because water is extensively H bonded, the polarization response is cooperative: water molecules cannot simply reorient independently of their neighbours. They effectively reorient in groups of about three. Finally, there is a small contribution to the dielectric constant (*c.* 2–3) from the polarizability and flexibility of water. All these factors explain the very high dielectric constant of water. Decreasing the temperature increases the dielectric constant since it reduces the randomizing thermal fluctuations that oppose dipole alignment by an electrostatic field. Interestingly, the static dielectric constant of water continues to increase through the freezing point. The high dielectric constant of ice (Table 2) demonstrates the importance of the cooperative effect of dipole reorientation, although the time scale of reorientation is six orders of magnitude longer.

Ionization

Because the O–H bond of water is strongly polarized, the electron density around the hydrogen atom is very low and the O–H bond is rather weak compared with most covalent bonds. Thermal fluctuations in the liquid often (every 20 μ s or so) result in sufficient further polarization of the O–H bond that the hydrogen nucleus can dissociate as a proton, or H^+ ion. Water being an excellent solvent for ions, it can solvate the resulting OH^- and H^+ ions, the latter primarily as H_3O^+ . As a consequence dissociated water has a relatively long lifetime of about 100 μ s in pure water before recombination. The spontaneous ionization of water is characterized by a dissociation constant, derived using eqn [1].

$$\frac{[H^+][OH^-]}{[H_2O]} = 1.82 \times 10^{-16} \text{ mol L}^{-1} \quad [1]$$

With a water concentration of 55.6 mol L^{-1} , the concentration of H^+ at 25°C in pure water is $1.0 \times 10^{-7} \text{ mol L}^{-1}$ and thus it has a pH of $-\log_{10}([H^+]) = 7$. The hydrogen ion is highly mobile in liquid water, diffusing about five times more rapidly than water itself (Table 2). Remarkably, the mobility of a proton in ice is higher still, clearly demonstrating that proton transport occurs not so much by movement of a single proton, but by a hopping mechanism between H-bonded waters, whereby a water molecule accepts a proton on one side, and releases a proton on the other side. Since the lifetime of an individual

Table 2 Selected physical properties of liquid water and ice

	Liquid (293 K)	Ice I (269 K)
Coordination number	4.7	4
Dipole moment (Cm $\times 10^{30}$)	8.0–8.7	8.7–9.4
Polarizability (nm)	0.144	0.144
Static dielectric constant	78.6	93
Ionization constant (mol L $^{-1}$)	1.82×10^{-16}	3.8×10^{-22}
Dissociation rate (s $^{-1}$)	2.5×10^{-5}	3×10^{-9}
Dielectric relaxation time	9.5 ps	10 μ s
Molecular reorientation time	10 ps	10 μ s
Molecular translation time	20 ps	10 μ s
H $_3$ O $^+$ lifetime	1 ps	0.1 ps
H-bond lifetime	1 ps	–
Diffusion constant (m 2 s $^{-1}$)		
H $_2$ O	2×10^{-9}	3.9×10^{-15}
H $^+$	9×10^{-9}	2×10^{-8}
Coordination water exchange time		
Around water	1 ps	–
Around a typical ion	1–10 ns	–

H $_3$ O $^+$ ion is ≈ 1 ps, about five orders of magnitude shorter than the lifetime of dissociated water, many hopping events occur before recombination. This lifetime is also shorter than the molecular translation time, again indicating that direct diffusion of the H $_3$ O $^+$ cannot account for the high proton mobility. The ionization constant of water is orders of magnitude higher than that of most organic solvents. Water's unique ability to ionize easily and to solvate OH $^-$ and H $^+$ ions allows it to partake in OH $^-$ and H $^+$ exchange with many polar solutes. Water can donate its H $^+$ to a base, or accept (solvate) H $^+$ from an acid. Acid–base and proton exchange reactions are pervasive in biology, occurring in protein folding, protein binding, enzyme catalysis, ion pumping, ion channel reactions, bioenergetic pathways, synthesis of ATP, and in the chemiosmotic mechanisms of energy transduction, to name a few. Communication of a biological signal or transmission of energy via protons is also extremely rapid due to the facile ionization of water and the high proton mobility.

Hydrogen Bonding

Water structure

Water exists in three phases: vapour, liquid and ice, the last of which has at least nine known forms. For biological phenomena, the most important is the liquid phase. It is useful, however, when describing its structure to use the simplest form of ice, Ice I, as a reference. The structures of

both are dominated by the hydrogen-bonding interaction. The hydrogen bond (H-bond) is a strong bond formed between a polar hydrogen and another heavy atom, usually carbon, nitrogen, oxygen or sulfur in biological molecules. In the gas phase the strength of an H bond between two waters is 22.7 kJ mole $^{-1}$, although in liquids and solids its strength is greatly dependent on geometry and the surrounding molecules. It is sometimes characterized as intermediate between ionic and covalent bonds in character, although its energy as a function of the length and angle can be quite accurately described by a Coulombic interaction between the partial atomic charges on the hydrogen, the heavy atom it is covalently attached to, and the oxygen, nitrogen, carbon or sulfur atom with which it is making the H-bond.

Ice I is a tetrahedral lattice where each water makes H-bonds to four other waters, which lie equidistant from each other at the vertices of a regular tetrahedron with edge lengths of 0.45 nm (**Figure 1c**). The H-bonds are 0.275 nm long measured from oxygen to oxygen, and linear (0° H-bond angle; **Figure 1a**). The H-bonding pattern of ice is symmetrical: each water makes two donor H bonds with its hydrogen atoms, and two acceptor H-bonds with the hydrogen atoms of neighbouring waters. The 2–2 H-bonding symmetry is an important feature of water. Combined with an H–O–H bond angle very close to the ideal tetrahedral angle of 109.5° , and with the tendency for the four neighbouring waters to repel each other electrostatically, it is sufficient to explain the tetrahedral H-

bonding pattern of Ice I and the persistence of the tetrahedral pattern in liquid water.

A different way of describing the structure of Ice I is to count up the number of neighbours each water has as a function of distance. Starting at the central water depicted in **Figure 1c** and moving out, the first four neighbours are found at a distance of 0.275 nm. The next set is encountered at 0.45 nm: 12 waters that are H-bonded to the first four neighbours. Continuing out, shells of water are encountered at discrete distances. The resulting radial distribution function (rdf) is characteristic of a crystalline solid, and consists of discrete peaks (**Figure 2**). The number of waters in the first peak defines the ‘coordination’ number, which in Ice I is four. Liquids do not have a single structure since the molecules are in constant motion but the rdf is an extremely useful way to describe their average structure. **Figure 2** shows the rdf for liquid water obtained either from X-ray scattering experiments or computer simulations using the water model in **Figure 1b**. The rdf for liquids is normalized to one so that the value at any point is the average number of waters found at that distance relative to the number expected if the distribution of water molecules were completely random, i.e. if there were no structure.

The broad overlapping peaks decaying away to a constant value of one at large distances is characteristic of a liquid. The first peak or hydration shell indicates that there is a high probability that two waters will be separated by about 0.25–0.30 nm, the range of H-bonding distances. Beyond 0.3 nm there is a dip since waters at this distance are likely to overlap with those in the first shell, then there is a smaller peak at 0.45 nm, which is the remains of the

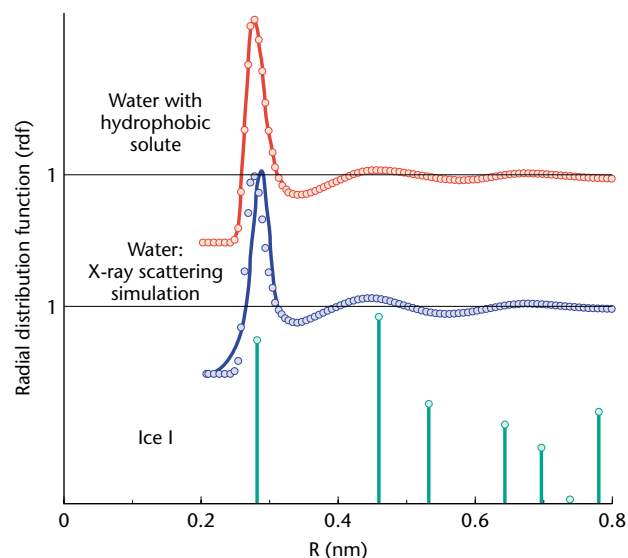


Figure 2 Radial distribution functions (rdf) of Ice I (bottom), pure water (middle), and water around a hydrophobic solute (top). Lines, measured; circles, computer simulation.

second layer seen in the Ice I structure. The area under the first peak gives the coordination number of water at 25°C as 4.7. This is somewhat higher than for Ice I, indicating that the lattice structure has partially collapsed, and each water on average makes an H bond to more than four waters. Organic solvents typically have coordination numbers of 6 or higher, so by comparison water has an ‘open’ structure. Experiments and computer simulations show that the open structure results from the high degree of angular ordering in liquid water. **Figure 3** shows the probability distribution of H-bond angles made by each water to its 4.7 neighbours. It is bimodal, and should be contrasted with the H-bond angle distribution for Ice I, which is a single peak at 0°. In liquid four of the H bonds are approximately linear (mean angle of about 12°), and very close to their length in Ice I. This indicates that much of the tetrahedral structure of Ice I persists in liquid water, albeit in a distorted form (**Figure 1d**). The H-bond to the additional neighbour(s) is more distorted, with an average angle of about 52°, since these neighbours have to sit in a face of the tetrahedron formed by the primary hydration waters.

The open tetrahedral structure is also responsible for the anomalous temperature dependence of water density. Water contracts upon melting, and continues to contract until it reaches a temperature of 4°C, above which it expands like most liquids. In the contraction phase the collapse of the open tetrahedral structure due to increasingly bent H-bonds outweighs the normal tendency for materials to expand because the molecules become further apart.

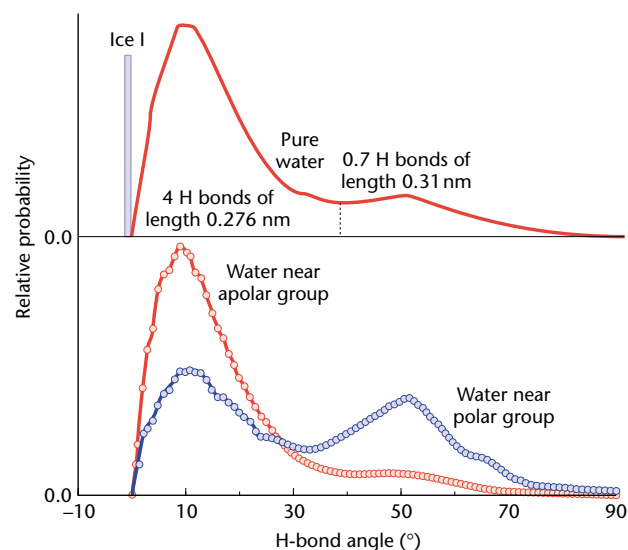


Figure 3 Hydrogen bond angle probability distribution for Ice I and pure water (top), and for water around solutes (bottom).

Effect of solutes

Solutes perturb the structure of water, primarily in the solute's first hydration shell (the layer of water in contact with the solvent), with a lesser effect on more distant waters. **Figure 2** shows the rdf for liquid water around the hydrophobic (water-avoiding) solute tetramethyl ammonium. There is a slight sharpening of the distribution caused by an increase in the first peak height and a decrease in the first dip. This is indicative of increased ordering of water in the first hydration shell, but the effect is not large. The rdf of liquid water is dominated by the size and packing of the water, i.e. by the van der Waals interactions, and these are relatively insensitive to the presence of the solute. In contrast, solutes have a large effect on the angular structure of water (**Figure 3**). Apolar solutes and groups shift the bimodal distribution of water–water H-bond angles towards the more ice-like, linear form, effectively increasing the ordering of water by decreasing the less ordered population of H-bonds. These solutes lack the ability to make strong electrostatic interactions with water, and they interact primarily through the van der Waals potential. Their effect is essentially geometric: they tend to displace the more weakly H-bonded facial water in the coordination shell (**Figure 1d**), thus reducing the population of more bent H-bonds. Ions and polar solutes and groups have the opposite effect. They shift the distribution of water–water H-bond angles towards the more bent form. This is a consequence of the strong electrostatic interactions they can make with water. Water dipoles tend to align towards or away from the atoms with large atomic partial charges, consequently distorting the water–water H-bond (**Figure 1e**).

Hydrophobic and Hydrophilic Interactions: Water as a Solvent

Perhaps water's most important biological role is as a solvent. It can dissolve a remarkable variety of important molecules, ranging from simple salts through small molecules such as sugars and metabolites to very large molecules such as proteins and nucleic acids. In fact water is sometimes called the universal solvent. Practically all the molecular processes essential to life – chemical reactions, association and binding of molecules, diffusion-driven encounters, ion conduction – will only take place at significant rates in solution, hence the importance of water's solvent properties. Equally important as water's abilities as a good solvent is its differential effect as a solvent – the fact that it dissolves some molecules much better than others. **Figure 4** shows the relative solubilities in water of a selection of solutes that are of biological importance or are building blocks of biologically important macromolecules. The solubilities range over 50 orders of magnitude! The high end includes ions and charged

amino acids such as arginine, and aspartic acid. These solutes are hydrophilic (water-loving). This category also includes some other neutral amino acids such as asparagine, the peptide backbone of proteins, the phosphate-sugar backbone of nucleic acids, sugars and lipid head-groups. At the low solubility end are aliphatic amino acids such as leucine, the aromatic amino acids such as phenylalanine, and the hydrocarbon 'tails' of lipids. These solutes are hydrophobic. Other solutes such as nucleic acid bases and the amino acid tryptophan have intermediate solubility, and cannot be simply classified as hydrophobic or hydrophilic.

Physical basis of solvation

The logarithm of the solubility of a solute is proportional to the thermodynamic work, or hydration free energy (ΔG^{hyd}) necessary to transfer it into water from a reference solvent (here cyclohexane). High water solubility corresponds to a negative (favourable) ΔG^{hyd} , low solubility to a positive ΔG^{hyd} (work must be performed to dissolve the solute). ΔG^{hyd} is directly related to the properties of the solute, the water, and the strength of interactions between water and solvent. It is here that the high surface tension and dielectric constant of water are crucial. The surface tension is the work necessary to create a unit area of water–vacuum interface (units of force per unit length are equivalent to energy per unit area). Work is necessary since interactions must be broken to bring water from the interior to the surface. Hydrating a solute can be divided into two steps:

- creation of a solute-shaped cavity in water, which requires work to be done against the surface tension of water;
- placing the solute in the cavity, which involves interactions of the solute with water molecules and restructuring of the water.

The first step always opposes dissolution of any solutes. If the interactions between the solute and water are weak, as they are for apolar solutes and groups, the cavity term dominates and the solubility will be low. The cavity term drives aggregation of apolar molecules to reduce the surface area in contact with solvent. This is known as the hydrophobic effect. In contrast, when a polar or ionic solute is dissolved in water the electric field from the solute's partial atomic charges induces a large polarization (reorientation) of the water dipoles resulting in an attractive electrostatic field (the reaction field) back at the solute. This results in a high solubility – a consequence of water's high dielectric constant, and the reason it can dissolve a wide range of ionic and polar solutes.

In summary, the solubility is determined by two major contributions:

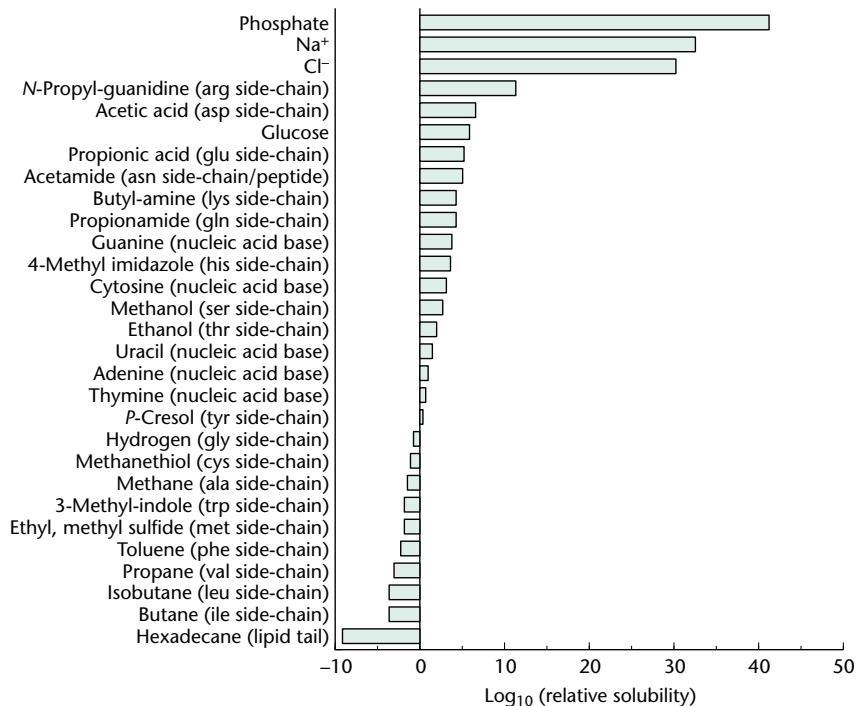


Figure 4 Solubilities of selected solutes in water, expressed as \log_{10} of the solubility ratio between water and the apolar solvent cyclohexane.

- The cavity contribution, which is unfavourable and approximately proportional to area of the solute or solute group(s) exposed to water.
- The electrostatic contribution, which depends on the strength of the reaction field induced in water. This in turn depends on the magnitude of the partial atomic charge, the dielectric constant of water, and how near the atomic charge is to the water (i.e. the atom's radius, and whether it is buried or exposed to solvent).
- formation of macromolecular complexes such as multimeric proteins, protein–nucleic acid assemblies and membrane protein–lipid assemblies;
- specific binding and recognition of molecules with complementary apolar surface groups.

Solvation of polar groups acts in a reverse fashion to the hydrophobic effect in the above processes: there is a strong driving force to keep the ionic and polar portions of proteins, lipids and nucleic acids on the surface in contact with water. This is also the reason that the low dielectric lipid tail region of membranes is impervious to ions, a key property of biological membranes.

The delicate balance between polar and apolar solvation forces contributes to a remarkable fidelity and accuracy of self-assembly. For example, related proteins of different sequence but with conserved patterns of amino acid hydrophobicity/hydrophilicity can adopt structures that are similar to 0.1 nm or better tolerance.

Role of solvation

Many biological macromolecules, such as proteins, nucleic acids and lipids, contain both hydrophilic and hydrophobic groups. Water's differential ability to solvate the different groups produces a driving force for them to adopt structures or self-assemble in ways where the hydrophilic groups are exposed to water and the hydrophobic groups are sequestered from water. This is a major factor in the folding, assembly and maintenance of precise, complex three-dimensional structures of proteins, membranes, nucleic acids and protein–nucleic acid assemblies. For example, the hydrophobic effect promotes:

- formation of a buried apolar core of amino acids in protein folding;
- helix formation in nucleic acids through base stacking;
- formation of lipid membranes with an apolar lipid tail region;

Further Reading

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