

INTRODUCTION

Historically, each water molecule in the liquid state has been considered to be dynamically hydrogen-bonded in tetrahedral configurations to three or four other water molecules.⁷ Bonds are weak (1.3 to 2.8 kcal/mole) and last only about 10^{-11} seconds but continually tie molecules together in clusters.⁸ The extremely high melting and boiling points of water are considered to be due to this type of hydrogen bonding.⁷ However, recent high-speed studies have provided evidence that, at any instant, water molecules hydrogen bond more strongly together to form trimers in bulk liquid water with two water molecules hydrogen-bonded to a central water molecule.⁹ Molecular orbital calculations back in the 60's and 70's forecast that such a trimer, with a hydrogen-bond length of 2.76 Angstroms, would be the largest hydrogen-bonded unit in liquid water¹⁰ and, in 1972, the trimer and linear tetramer were identified by X-ray scattering on the surface of liquid water.¹¹ However, the nature of hydrogen-bonding within the trimer and ordered elements of hydration which form on non-hydrogen-bonding hydrophobic surfaces remained an open question until 1999 when Dr. Isaacs at Bell Labs concluded, based on X-ray analysis, that hydrogen bonding in ice is "covalent" with a bond-strength of 4.7 and 8.2 kcal/mole.¹² As mentioned above, additional evidence for two different types of hydrogen-bonding between water molecules was provided in 2009 when Professor Stanley, in a detailed mathematical analysis of the properties of liquid water, concluded that liquid water, in the liquid state and on surfaces is composed of two different density-forms of water.⁶

Tetrahedral hydrogen bonding, which is the form on and within thermodynamically-stable forms of natural molecules (including proteins), is based primarily on the dielectric polarity of water molecules and involves the columbic attachment of water molecules together and with other polar molecules at point charges on their surfaces.^{7,8} Distances and angles of bonding vary considerably to provide for thermodynamic stabilization in natural hydrated states.⁷ Covalent hydrogen-bonding, on the other hand, involves the quantized overlap of electron clouds of adjacent water molecules around a central proton - similar to covalent bonding between carbon atoms.¹² Covalent hydrogen bonds are stable at 0°C and below but, in liquid water, the trimer and longer linear elements which form on hydrophobic surfaces and between ions, are unstable and last only about 10^{-12} seconds.¹³

X-ray diffraction from the surface of liquid water at 25°C produces weak peaks for the trimer at 4.5 Angstroms and a linear tetramer at 6.8 Angstroms (2.76A between the oxygens) with a major peak at 2.9 Angstroms for most of the water molecules.¹¹ At 2.9 Angstroms, most of the molecules are far enough apart to permit rotation but close enough for surface charges to draw them into coordinated point-charge hydrogen-bonding and intermittent covalent bonding. Although trimers and tetramers represent only a small fraction of surface water, by forming rapidly and repetitively, they may contribute to the surface tension.

If oil is on the surface of water, surface tension increases and the oil molecules lose freedom. Instead of bending, twisting and turning in the liquid state, oil molecules adjacent to water lose entropy and energy and are forced to align parallel to each other in layers.¹⁶ At the same time, molecular orbital calculations indicate that water molecules at the interface assemble into short covalent linear and cyclic elements parallel to the surface and in preferred orientations.¹⁷ As a water molecule moves from the dynamic liquid state to the surface state and covalently-bonds to two neighbors, it loses about 9 kcal/mole of energy to adjacent water molecules but, as it moves rapidly (by a rotation)¹⁴ back into the liquid state, it absorbs similar quantized units of energy from the surface and drives molecules within that surface toward lower energy and greater order.^{4,15}

Thus, it is the spontaneous and rapid movement of water molecules from ordered covalently-bonded states on hydrophobic and ionically-ordered surfaces to more mobile, higher-energy point-charge states which drives more massive, slower-moving molecules, like those in gasoline and oil, toward lower energy and higher order.^{15,16} In fact, recent studies indicate that movements and energy changes in water molecules adjacent to large ions and ordering surfaces conform to Quantum Mechanics, not Newtonian Physics - they “jump” from one energy-state to the next.¹⁸ Back in 1944, it was Erwin Schrodinger, one of the fathers of Quantum Mechanics, who concluded in his little book, *What is Life?*, that it is this unidirectional movement of energy from natural molecules into water which drove early random molecular systems toward order and life - the opposite direction from what one might expect based on the Second Law of Thermodynamics.¹⁹

Of course, it is this same unidirectional transfer of quantized units of energy from polypeptides to water as they are released from ribosomes, which not only drives folding and assembly but, by repetitively forming in particular orientations on surfaces, may assist in directing assembly and function as well.²⁰ During the earliest phases of molecular evolution, when polypeptides most likely were produced at random, those which could fold spontaneously into thermodynamically-stable forms and release unstable covalently-ordered water, survived - those which could not fold into stable functional forms, were chewed up by lytic enzymes and ribozymes.

However, trimer-formation may be responsible for another critical property of water. As pure liquid water cools, mean bonding distances the molecules decrease and density increases until the temperature reaches 4°C - then density decreases as the temperature is lowered on down to 0°C. Although this decrease in density has been attributed to the presence of pseudo-forms of ice, pure water in a clean glass container can be cooled to as much as 30 degrees below zero C without crystallizing.⁷ On the other hand, if the water is in contact with a surface in which the atoms are in hexagonal arrangements, similar to those in ice, crystallization occurs immediately at 0°C. Thus, the two-dimensional forms in ice cannot be present - instead, the decrease in the density of water as it approaches 0°C most likely is produced by an increase in the frequency of trimer formation. By forming spontaneously as a more ridged linear element, it extends and orders point-charge hydrogen-bonding of water molecules around it and decreases the local density. If pure water is carefully cooled below 0°C, the frequency of linear element formation and viscosity continue to increase until, at -40°C, crystallization occurs immediately to yield a form of ice called “cubic”²¹ in which all of the molecules are in linear elements and covalently-linked at a distance of 2.75Angstroms.²²

Cubic ice is called the “kinetic” product of crystallization because it forms most rapidly as electron orbitals overlap a central proton.²³ However, it is unstable at atmospheric pressure and, as it warms to 0°C, isomerizes to the thermodynamically more-stable “hexagonal” form in which the molecules are in both linear and non-linear forms at covalent distances of 2.75A to 2.84A²²

Although the structural order of water on proteins, nucleic acids and carbohydrates is displayed by proton magnetic resonance as the doublet peaks of ice rather than the singlets of liquid water,²⁴ lipid and ionic surfaces within natural molecules are so dynamic and the order in water so localized and fleeting, that it has been impossible to visualize its precise spatial structure. However, ultra-high-speed crystallographic analysis of water on the ridged hydrophobic surface of graphite by the late Professor Zewail and his group at CIT has displayed surface water as linearly-ordered hexagonal layers with cubic patterning between the layers - the same as in cubic ice.²⁵

Thus, as polypeptides emerge from ribosomes, the probability is high that water forms short-lived covalent linear elements of hydration on hydrophobic surfaces and between charge centers and that it is this unstable covalent surface water which, in leaving to increase the energy and entropy of hydration, drives those regions into coils and beta-sheets.¹⁵ At the same time, it is dynamic point-charge hydrogen-bonding of surface water to small peptides (like glycine and serine) in polypeptide chains which permit sufficient mobility in chains to permit ordering regions to combine and form lower energy, thermodynamically more-stable assemblies.^{2,4}

As water-soluble proteins form, most peptides with hydrocarbon side chains are left in the center forming an anhydrous core while most of them on the surface hydrogen bond with water at angles which disrupt coordinated hydration order to increase stability and solubility. However, ordering peptides, which are held in selective positions on the surface, induce the formation of dielectric covalent linear elements to direct substrate and regulator molecules into binding sites.²⁰ In fact, as enzyme and receptor sites open and close in response to the dynamics of surface water, covalent linear elements of hydration must likely form within those spaces.²⁶ Half-lives of those elements are too brief to achieve thermodynamic equilibria but, if substrates or regulator molecules (with analogous dimensions and binding properties) are drawn into the sites and adjust angles and distances of bonding to achieve thermodynamic stability, proteins shift into active conformations and perform their vital functions.²⁰ Based on this concept of surface hydration, it should come as no surprise that most regulator molecules, like hormones and neurotransmitters, mimic the dimensions and hydrogen-bonding properties of transient quantized linear elements of hydration.²⁰

Indeed, it is unfortunate that surface water, although extremely important for natural structure and function, is never displayed. For example, the classical structure of DNA is never displayed as hydrated but the X-ray crystallographic pattern, which was used by Watson and Crick to construct their helical model was obtained by Rosalind Franklin by spraying a crystalline sample with water.²⁷ Only if surrounded by at least 13 water molecules per base pair, does DNA adopt the helical structure which has become the logo for modern molecular biology.²⁸ Only by transiently-forming linear elements of six to seven water molecules between the anionic oxygens of surface phosphates across the wide groove and three to four across the narrow groove to delocalize the high negative charge, is the structure stabilized in the B form.²⁸ Dehydration converts it into the A Form which does not exist in nature.

For the past century, attention of the scientific community has been directed to the identification of structure for natural molecules - now it is time to reveal that it is surface water which not only provides for spontaneity and order in function but provided the quantized spatial criteria for the selection of the molecules of life.²⁰

Although tetrahedral hydrogen bonds can vary in lengths and angles in thermodynamically-stable states, a standard hydrogen-bond length of 2.76Å and angle of 109.5° (as found by molecular orbital calculations and in trimers and tetramers on the surface of liquid water at 25°C)^{8,10} are used in this article to fill spaces and stabilize molecules in short-lived transition states.

Companion web sites, www.proteinhydration.com and www.molecularcreation.com, provide more detailed information on surface hydration as well as a description of the role it may have played in the evolution of natural molecules.