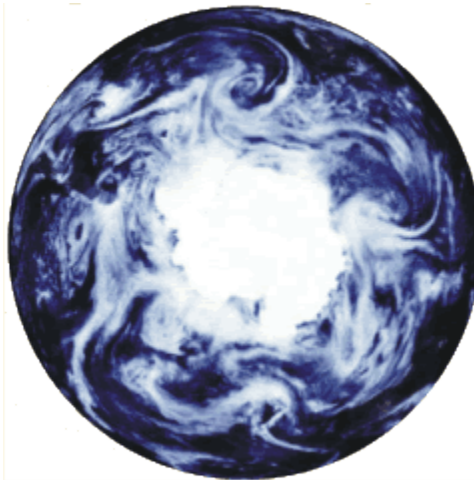


# Water and life

- ▼ Can life exist without water?
- ▼ Consequences of changes in water's hydrogen bond strength
- ▼ Estimating the effect of changes in water hydrogen bond strength
- ▼ Effect of water hydrogen bond strength on melting and boiling point
- ▼ Effect of hydrogen bond strength on the temperature of maximum density
- ▼ Effect of water hydrogen bond strength on kosmotropes and chaotropes
- ▼ Effect of water hydrogen bond strength on its dissociation
- ▼ Effect of water hydrogen bond strength on biomolecule hydration
- ▼ Effect of water hydrogen bond strength on its other physical properties
- ▼ Conclusions concerning water and life



## Can life exist without water? <sup>a</sup>

Water and life are closely linked. This has been recognized throughout history by civilizations and religions and is still the case with scientists today [1011]. Liquid water is required for life to start and for life to continue. No enzymes work in the absence of water molecules. No other liquid can replace water. We are very fortunate, therefore, that our planet is so well endowed. Water is a common material in the Universe, being found as widely dispersed gaseous molecules and as amorphous ice in tiny grains and much larger asteroids, comets and planets, but water needs particularly precise conditions to exist as a liquid as it does on Earth. It is most likely that this water arrived from multiple sources, such as comets and asteroids, somewhat after solid planet Earth was formed [1015].

The development of life required this water. How exactly this was achieved, is a question that has interested many since well before the early experiments producing amino acids from simpler molecules by electric discharge in aqueous systems [1016]. More recently, various theories have been propounded but without a consensus except for the key involvement of liquid water [1017].

Water possesses particular properties that cannot be found in other materials and that are required for life-giving processes (but see also [1153]). These properties are brought about by the hydrogen-bonded environment particularly evident in liquid water [1423]. Hydrogen bonds are roughly tetrahedrally and arranged such that when strongly formed the local clustering expands, decreasing the density. Such low density structuring naturally occurs at low and supercooled temperatures and gives rise to many physical and chemical properties that evidence the particular uniqueness of liquid

water. If aqueous hydrogen bonds were actually somewhat stronger, then water would behave similar to a glass, whereas if they were weaker then water would be a gas and only exist as a liquid at sub-zero temperatures.

The quantitative and qualitative consequences of strengthening or weakening of the hydrogen bond in water are considered here. It is found that if the hydrogen bond strength was slightly different from its natural value then there may be considerable consequences for life. Water would not be liquid on the surface of Earth at its average temperature if the hydrogen bonds were as little changed as 7% stronger or 29% weaker. The temperature of maximum density naturally occurring at about 4 °C would disappear if the hydrogen bonds were just 2% weaker. Major consequences for life are found if the hydrogen bonds did not have their natural strength. Even very slight strengthening of the hydrogen bonds may have substantial effects on normal metabolism. Water dissociation becomes much less evident if the hydrogen bonds are just a few percent stronger but pure water contains considerably more H<sup>+</sup> ions if they are few percent weaker. The important alkali metal ions Na<sup>+</sup> and K<sup>+</sup> lose their distinctive properties if the hydrogen bonds are 11% stronger or 11% weaker respectively. Hydration of proteins and nucleic acids depends importantly on the relative strength of the biomolecule-water interactions as compared with the water-water hydrogen bond interactions. Stronger water hydrogen bonding leads to water molecules clustering together and so not being available for biomolecular hydration. Generally, the extended denatured forms of proteins become more soluble in water if the hydrogen bonds become substantially stronger or weaker. If the changes in this bonding are sufficient, present natural globular proteins cannot exist in liquid water. [[Back to Top](#) ▲]

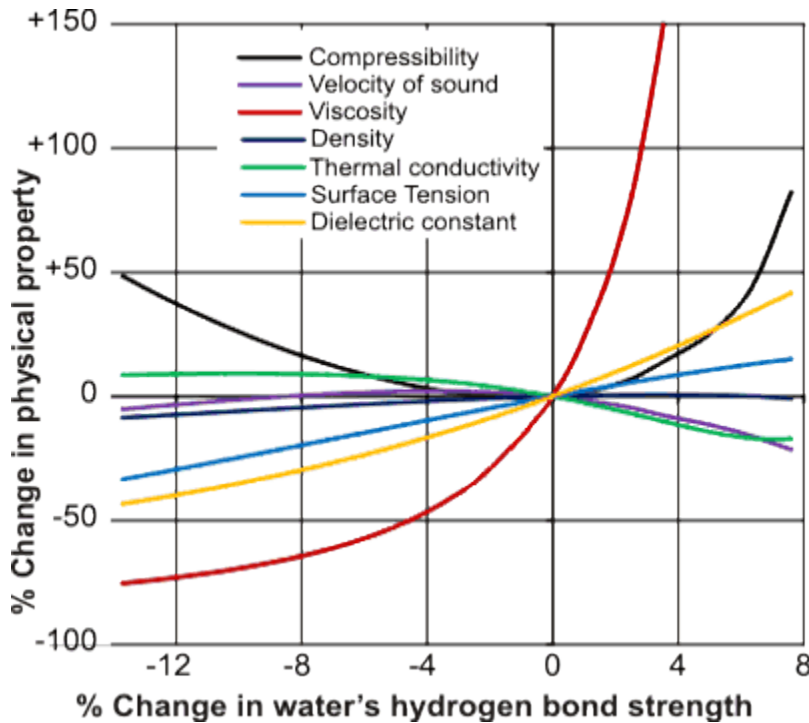
### Consequences of changes in water's hydrogen bond strength

How much variation in water's hydrogen bond is acceptable for life to exist? A superficial examination gives the range of qualitative effects as indicated below.

Consequences of changes in water's hydrogen bond strength	
Water hydrogen bond strength	Main consequence
No Hydrogen-bonding at all	No life
Hydrogen bonds slightly weaker	Life at lower temperatures
No change	Life as we know it
Hydrogen bonds slightly stronger	Life at higher temperatures
Hydrogen bonds very strong	No life

Intriguingly, liquid water acts in subtly different manners as circumstances change, responding to variations in the physical and molecular environments and occasionally acting as though it were present as more than one liquid phase. Sometimes liquid water is free flowing whilst at other times, in other places or under subtly different conditions, it acts more like a weak gel. Shifts in the hydrogen bond strength may fix water's properties at one of these extremes to the detriment of processes requiring the opposite character. Evolution has used the present natural responsiveness and variety in the liquid water properties such that it is now required for life as we know it. DNA would not form helices able to both zip and unzip without the present hydrogen bond strength. Enzymes would not possess their 3-D structure without it, nor would they retain their controlled flexibility required for their biological action. Compartmentalization of life's processes by the use of membranes with subtle permeabilities would not be possible without water's intermediate hydrogen bond strength.

In liquid water, the balance between the directional component of hydrogen bonding and the isotropic van der Waals attractions is finely poised. Increased strength of the hydrogen bond directionality gives rise to ordered clustering with consequential effects on physical parameters tending towards a glass-like state, whereas reducing its strength reduces the size and cohesiveness of the clusters with the properties of water then tending towards those of its isoelectronic neighbors methane and neon, where only van der Waals attractions remain.



Shown opposite (and below) are variations in water's physical properties with changes in its hydrogen bond strength.<sup>b</sup>

Quite small percentage changes in the strength of the aqueous hydrogen bond may give rise to large percentage changes in such physical properties as melting point, boiling point, density and viscosity. Some of these potential changes may not significantly impinge on life's processes, (*e.g.* compressibility or the speed of sound) but others are of paramount importance.

Although in most cases, weakening or strengthening of the hydrogen bond strengths cause contrary effects on the physical properties, this is not always the case if the hydrogen bond strength tends towards high or low extremes.

Effect of hydrogen bond strength on water's physical properties		
Property	Change on H-bond strengthening	Change on H-bond weakening

Melting point	Increase	Decrease
Boiling point	Increase	Decrease
State, at ambient conditions on Earth	→ Solid glass	→ Gas
Adhesion	Decrease	Decrease
Cohesion	Increase	Decrease
Compressibility	Increase	Decrease
Density	Decrease	Increase
Dielectric constant	Increase	Decrease
Diffusion coefficient	Decrease	Increase
Enthalpy of vaporization	Increase	Decrease
Glass transition	Increase	Decrease
Ionization	Decrease	Increase → Decrease
Solubility, hydrophile	Decrease	Decrease
Solubility, small hydrophobe	Increase	Decrease → Increase
Specific heat	Increase	Decrease
Surface tension	Increase	Decrease
Thermal conductivity	Decrease	Increase → Decrease
Viscosity	Increase	Decrease

Adhesion and hydrophilic solubility both decrease on hydrogen bond strengthening due to increased water-water interactions reducing water's ability to bind to the hydrophilic or molecular surface. On hydrogen bond weakening, they both decrease due to the reduced water-surface or water-solute interactions. Strong hydrogen bonding eases the formation of expanded cavities as evidenced in the clathrate ices, and which can accommodate small hydrophobic molecules, so increasing their solubility. However, such small hydrophobic molecules will also be more easily dissolved when weak hydrogen bonding allows more facile cavity formation to allow their entry into solution. [[Back to Top](#) ▲]

### Estimating the effect of changes in water hydrogen bond strength

Clearly, estimates of the physical consequences, due to variations in the hydrogen bond strength, may vary from one method to another but the data above indicates that relatively small changes in hydrogen bond strength may have some relatively large effects. Strengthening hydrogen bonding has particularly important effects on viscosity and diffusion as indicated by the large changes occurring in supercooled normal water.

It is possible to investigate the effect that changes in hydrogen bonding strength of water make in its properties by examination of the actual properties of water or other molecules with different hydrogen bond strength. However, different methods, materials or conditions have weaknesses in their utility. The possibilities for examining the effects of varying hydrogen bond strengths are:

- Changing the physical environment of water such as temperature or pressure and examining the consequential changes in the physical parameters, if assumed solely due to the variation

in the hydrogen bond strength. However, varying the temperature also changes the heat energy content and some compensation may be required to negate effects other than hydrogen bond strength changes, such as density effects. Also, changing the pressure increases density and reduces hydrogen bond lengths, which increases hydrogen bond strength, but also bends the bonds so reducing their tetrahedrality. A simple way of assessing the average hydrogen bond strength is the enthalpy of evaporation calculated from the difference in the enthalpy of the liquid and gaseous phases [540].

- Modeling water as an equilibrium mixture of low-density and high-density clusters (for example, [23]) and examining the consequences of hydrogen bond strength variation on the cluster equilibrium with resultant effects on the physical properties. This concept has been shown to explain qualitatively and quantitatively most anomalies of liquid water. The free energy change for the equilibrium between dense and less dense clusters is very small due to compensation between enthalpic and entropic effects. Just a small shift in the enthalpic component, due to changes in hydrogen bond energy may shift the equilibrium position decisively one way or the other.
- Examine the physical properties of the isotomers of water, HDO or D<sub>2</sub>O. These have apparently stronger hydrogen bonds than H<sub>2</sub>O due to their reduced van der Waals core consequent upon nuclear quantum effects. The hydrogen bond strength differences met using this method are small.
- Examine the physical properties of the hydrides of neighboring elements, NH<sub>3</sub>, HF or H<sub>2</sub>S, which possess differing hydrogen bond strengths. The hydrogen bond strength differences encountered by this method are rather large.

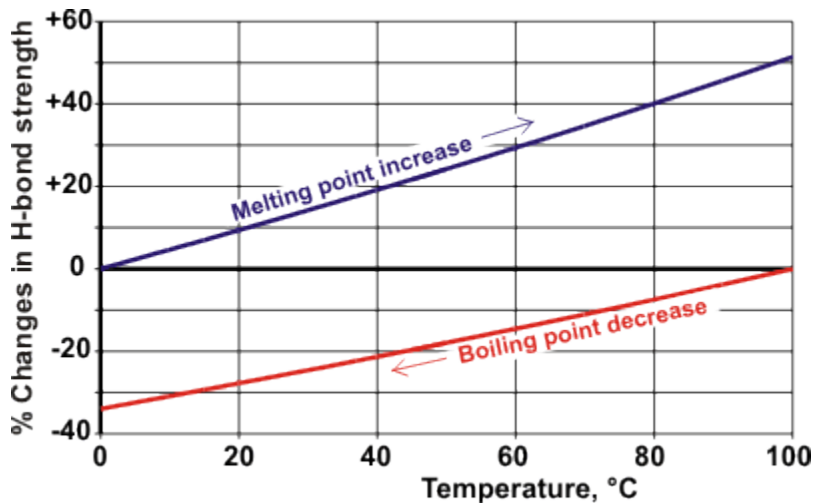
In the following discussion the effects of varying hydrogen bond strength on individual physical properties, and the consequences for life, are initially independently discussed without regard to other changes that might also be occurring at the same time, such as changes in the physical state of water. [[Back to Top ▲](#)]

### **Effect of water hydrogen bond strength on melting and boiling point**

In ice, all water molecules participate in four hydrogen bonds (two as donor and two as acceptor) and are held relatively static. In liquid water, some of the weaker hydrogen bonds must be broken to allow the molecules to move around. The large energy required for breaking these bonds must be supplied during the melting process and only a relatively minor amount of energy is reclaimed from the change in volume. The free energy change ( $\Delta G = \Delta H - T\Delta S$ ) must be zero at phase changes such as the melting or boiling points. As the temperature of liquid water decreases, the amount of hydrogen bonding increases and its entropy decreases. Melting will only occur when there is sufficient entropy change to compensate for the energy required for the bond breaking. The low entropy (high organization) of liquid water causes this melting point to be high. If the hydrogen bond strength (that is, enthalpy change) in water is raised then the melting point must rise for the free energy change to stay zero.

At the temperature of the phase change, this free energy is zero, so on melting (solid  $\rightarrow$  liquid)  $\Delta H_m = T_m\Delta S_m$  and on vaporization (liquid  $\rightarrow$  gas)  $\Delta H_v = T_v\Delta S_v$ . In order to calculate the hydrogen bond strength, it is assumed that the entropy changes, during the phase changes, remain constant with respect to the temperature range. The enthalpy change required to equal the temperature times this entropy change is regarded as the hydrogen bond strength required at the melting point. Thus, the percentage increase in the hydrogen bond strength is given by  $100 \times (T\Delta H_m/T_m - \Delta H_T) / \Delta H_T$  where  $\Delta H_T$  is the bond enthalpy at temperature T and  $\Delta H_m$  is the bond enthalpy at its normal melting point  $T_m$ . There is considerable hydrogen bonding in liquid water resulting in high cohesion that prevents water molecules from being easily released from the water's surface. Consequentially, the vapor pressure is reduced and water has a high boiling point. Using similar argument to that

used above for melting point, the percentage reductions in the hydrogen bond strength that result in lower boiling points are given by  $100(T \Delta H_v / T_v - \Delta H_T) / \Delta H_T$ , where  $\Delta H_v$  is the bond enthalpy at its normal boiling point  $T_v$  under one atmosphere pressure.



Opposite shows how the bond strength increases affect the melting point and how bond strength decreases affect the boiling point. The resulting relationship shows that water would freeze at the average surface temperature of Earth (15 °C) with a 7% strengthening in water's hydrogen bond or it would boil on a 29% weakening. At our body temperature (37 °C) the strengthening required for freezing is 18% and the weakening required to turn water into steam is 22%. The melting and boiling points of other liquids shows that these values are reasonable.

D<sub>2</sub>O has a melting point almost 4 °C higher than H<sub>2</sub>O with bond strength 2% higher, which values fit on the melting point line above. Hydrogen sulfide, which does form hydrogen bonds with strong bases but is poor proton donor, has a boiling point of -60 °C with intermolecular interactions only 20% of that of water [1018]. Hydrogen fluoride and hydrogen cyanide both possess hydrogen bond interactions slightly greater than 50% of that of water and boil at 20 °C and 26 °C respectively.

[[Back to Top](#) ▲]

### Effect of hydrogen bond strength on the temperature of maximum density

The high density of liquid water is due mainly to the cohesive nature of the hydrogen-bonded network. This reduces the free volume and ensures a relatively high-density, compensating for the partial open nature of the hydrogen-bonded network. It is usual for liquids to expand when heated, at all temperatures. However, at 4 °C water expands on heating or cooling. The density maximum is brought about by the opposing effects on increasing temperature, causing (a) structural collapse of the tetrahedral clustering evident at lower temperatures so increasing density, and (b) thermal expansion, creating extra space between unbound molecules, so reducing density.

As expanses of water are cooled, stratification of water occurs that depends on density. In freshwater lakes, the densest water is that at about 4 °C. This water sinks to the bottom circulating its contained oxygen and nutrients. Further cooling causes the surface temperature to drop towards 0 °C but has no immediate effect on deep-water temperatures which remain at 4 °C. When the surface water reaches 0 °C it may rapidly freeze, as only molecules at the surface have to be cooled further. The ice forms an insulating layer over the liquid water underneath and so slows down any

further surface cooling. The water at the bottom of ice-covered lakes remains at 4 °C throughout the winter so preserving animal and plant life there. In spring the warming rays of the sun melt the surface Ice layer first. Seawater behaves differently as the salt content lowers the temperature of maximum density below its freezing point and the maximum density is no longer observed. As seawater density increases with pressure, due to depth, convection only involves about the top hundred meters. A major part of this must be cooled to the freezing point (-2 °C) before salt-water surface Ice may form.

There would be clear consequences for aquatic life if the temperature of maximum density was not observed in freshwater lakes and rivers. Cooling would result in most of the water being at 0 °C before ice formation is initiated. Such changes in hydrogen bond strength would not significantly affect the low density of ice, which would still float on water. However, subsequent ice formation may give rise to slushy ice formation without a well-formed insulating upper surface layer of ice. More ice would form, however, due to the lack of the insulation and this ice would take far longer to thaw, as additionally more water would have to warm first. Much larger volumes of the fresh water would thus be affected and the greater ice formation may more easily reach the bottom of shallow lakes. The resultant situation would have both positive and negative consequences for the aquatic life as any remaining liquid surface would allow favorable surface gas exchange but there would be less liquid water. The end result for life, due to the loss of this density maximum, would therefore be important but not overwhelmingly life-threatening, except for shallow lakes.

The weakening of the hydrogen bond strength required to remove the maximum density property may be estimated in a number of ways. A 2% decrease in the hydrogen bond energy reduces the maximum density by the 4 °C required. The decrease calculated from the cluster equilibrium of Wilse Robinson [56, 409], where the free energy change between their proposed water clusters is zero close to 0 °C, also agrees with this value. D<sub>2</sub>O has a raised temperature of maximum density (11.185 °C) due to its stronger hydrogen bonds but if this bond strengthening is used as an estimate of that required to lower the temperature of maximum density of H<sub>2</sub>O below 0 °C, this also requires a hydrogen bond energy weakening close to 2%. [[Back to Top ▲](#)]

### **Effect of water hydrogen bond strength on kosmotropes and chaotropes**

Ions cause considerable changes to the structuring of water. The difference in their effects depends on the relative strength of ion-water and water-water interactions. Ionic chaotropes are large singly charged ions, with low charge density (for example, SCN<sup>-</sup>, H<sub>2</sub>PO<sub>4</sub><sup>-</sup>, HSO<sub>4</sub><sup>-</sup>, HCO<sub>3</sub><sup>-</sup>, I<sup>-</sup>, Cl<sup>-</sup>, NO<sub>3</sub><sup>-</sup>, NH<sub>4</sub><sup>+</sup>, Cs<sup>+</sup>, K<sup>+</sup>, (NH<sub>2</sub>)<sub>3</sub>C<sup>+</sup> (guanidinium) and (CH<sub>3</sub>)<sub>4</sub>N<sup>+</sup> (tetramethylammonium) ions) that exhibit weaker interactions with water than water with itself and thus interfere little in the hydrogen bonding of the surrounding water. Small or multiply-charged ions, with high charge density, are ionic kosmotropes (for example, SO<sub>4</sub><sup>2-</sup>, HPO<sub>4</sub><sup>2-</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup>, Li<sup>+</sup>, Na<sup>+</sup>, H<sup>+</sup>, OH<sup>-</sup> and HPO<sub>4</sub><sup>2-</sup>). Ionic kosmotropes exhibit stronger interactions with water molecules than water with itself and therefore are capable of breaking water-water hydrogen bonds. If the water-water hydrogen bond energy were to increase, the kosmotropic ions would become chaotropic and if the water-water hydrogen bond energy were to decrease, chaotropic ions would become kosmotropic. At present, the biologically important ions Na<sup>+</sup> and K<sup>+</sup> lie on opposite sides of the chaotropic/kosmotropic divide, facilitating many cellular functions by virtue of their differences. If they both had similar aqueous characteristics, cellular membrane function would have had to evolve differently and it is difficult to suppose how this might occur with the present natural availability of the ions.

The different characteristics of the intracellular and extracellular environments manifest themselves particularly in terms of restricted diffusion and a high concentration of chaotropic inorganic ions and kosmotropic other solutes within the cells, both of which encourage intracellular low density water structuring. The difference in concentration of the ions is particularly apparent between

Na<sup>+</sup> (intracellular 10 mM, extracellular 150 mM) and K<sup>+</sup> (intracellular 159 mM, extracellular 4 mM); Na<sup>+</sup> ions creating more broken hydrogen bonding beyond their inner hydration shell and preferring a high aqueous density whereas K<sup>+</sup> ions prefer a lower density aqueous environment. The interactions between water and Na<sup>+</sup> are stronger than those between water molecules, which in turn are stronger than those between water and K<sup>+</sup> ions.

The hydration enthalpies for Na<sup>+</sup> and K<sup>+</sup> are known to be -413 kJ mol<sup>-1</sup> and -331 kJ mol<sup>-1</sup> [1019], straddling the kosmotrope/chaotrope divide. Using the mildly chaotropic Cl<sup>-</sup> ion, with hydration enthalpy -363 kJ mol<sup>-1</sup>, as a marker, the division point between these ion types may be estimated as close to halfway between the K<sup>+</sup> and Na<sup>+</sup> hydration enthalpies (-372 kJ mol<sup>-1</sup>). The changes in the water hydrogen bond energy required to convert the chaotrope K<sup>+</sup> to a kosmotrope is thus estimated as 331/372 = 11% weakening and for converting the kosmotrope Na<sup>+</sup> to a chaotrope is 413/372 = 11% strengthening.

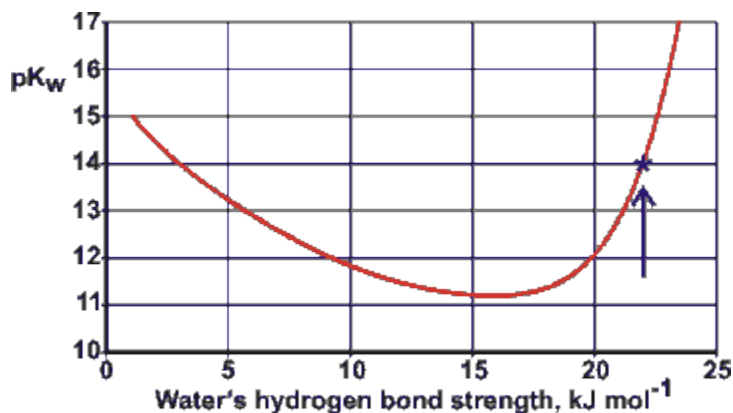
The consequences of changes to the properties of Na<sup>+</sup> and K<sup>+</sup> ions in aqueous environments are difficult to quantify but are clearly far reaching. There is no cation that could easily replace K<sup>+</sup> inside cells as the more chaotropic alkali metal cations Rb<sup>+</sup> and Cs<sup>+</sup> are rare and NH<sub>4</sub><sup>+</sup> is toxic and little different from K<sup>+</sup> as a chaotrope. Although other ions could replace Na<sup>+</sup> as a cationic kosmotrope, Li<sup>+</sup> is rare and divalent ions (for example, Mg<sup>2+</sup>) may cause other effects, such as chelation. Life as we know it could not exist without the present balance between Na<sup>+</sup> and K<sup>+</sup> ions. The weakening of hydrogen bond strength shifting K<sup>+</sup> to become chaotropic either would cause K<sup>+</sup> ions to remain outside cells with consequences on the cell membrane potential or would cause intracellular water to be too disorganized to support present intracellular processes. [Back to Top ▲]

### Effect of water hydrogen bond strength on its dissociation

No amount of liquid water contains only H<sub>2</sub>O molecules due to self-dissociation producing hydroxide and hydrogen ions.



This dissociation of water is followed by the utilization of further water molecules to ease the movement of the ions throughout the liquid. Such functions are key to biological processes and do not arise to a significant extent in any non-aqueous liquid except hydrogen fluoride. Aqueous dissociation depends on both H<sub>3</sub>O<sup>+</sup> and OH<sup>-</sup> formation and their physical separation to prevent the rapid reverse reaction reforming H<sub>2</sub>O. H<sub>3</sub>O<sup>+</sup> and OH<sup>-</sup> formation is greater when the hydrogen bonds are strongest whereas ionic separation requires the hydrogen bond networks connecting the ions to be weak in order to prevent the ions reforming water.



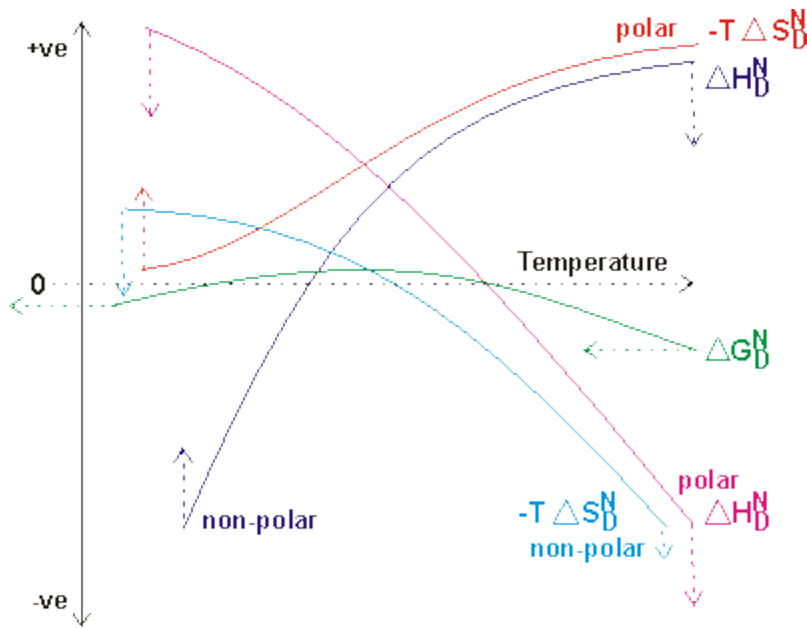


Thus, both strong and weak hydrogen bonding lead to lesser dissociation (see opposite showing the variation of the  $pK_w (= -\text{Log}_{10}(K_w))$  with the hydrogen bond strength of water). The data is calculated from the variation with temperature of the  $pK_w$  and enthalpy of vaporization. Water at 25 °C has a  $pK_w$  of about 14 as indicated on the right hand side of the graph. Changes in hydrogen bond strength between water molecules alter its degree of dissociation.

Strengthened hydrogen bonding increases the (Grotthuss) rate of transfer of these ions in electrical fields but slows down their diffusion otherwise. Acid strength of biomolecular groups is determined by the competition between the biomolecules and water molecules for the hydrogen ions. The strength by which the water molecules hold on to the hydrogen ion depends on their hydrogen bonding strength as a distributor of the charge. Biomolecular ionization, therefore, also depends on hydrogen bond strength. Since all biological processes have dependence on charge, a completely new evolutionary perspective is required if water dissociation is suppressed by water hydrogen bond strengthening. At intermediate hydrogen bond strength, dissociation increases, reducing the pH of neutral solutions. The acidity ( $pK_a$ ) of biomolecular groups, such as phosphate, also shows complex behavior with decreasing water hydrogen bond strength and often produces a  $pK_a$  minimum. Here, there are opposite effects of (a) reduced dielectric, at lower hydrogen bond strength, reducing ionic separation so tending to increase the  $pK_a$  and (b) increased water reactivity, also at lower hydrogen bond strength, increasing hydration effects and enabling the dissociation, so tending to reduce the  $pK_a$ . [[Back to Top](#) ▲]

### **Effect of water hydrogen bond strength on biomolecule hydration**

Water is critical, not only for the correct folding of proteins but also for the maintenance of this structure. The free energy change on folding or unfolding is due to the combined effects of both protein folding/unfolding and hydration changes. Contributing enthalpy and entropy terms may, however, individually be greater than the equivalent of twenty hydrogen bonds but such changes compensate each other leaving a free energy of stability for a typical protein as just equivalent to one or two hydrogen bonds. There are both enthalpic and entropic contributions to this free energy that change with temperature and so give rise to the range of stability for proteins between their hot and cold denaturation temperatures.



The free energy on going from the native (N) state to the denatured (D) state is given by:

$$\Delta G_N^D = \Delta H_N^D - T\Delta S_N^D$$

The overall free energy change ( $\Delta G_N^D$ ) depends on the combined effects of the exposure of the interior polar and non-polar groups and their interaction with water, together with the consequential changes in the water-water interactions on  $\Delta G_N^D$ ,  $\Delta S_N^D$  and  $\Delta H_N^D$  (see opposite). Denaturation is only allowed when  $\Delta G_N^D$  is negative; the rate of denaturation is then dependent on the circumstances and may be fast or immeasurably slow. The lines are meant to be indicative only. The length and direction of the arrows indicate the changes consequent upon weakening of water's hydrogen bond strength.

The enthalpy of transfer of polar groups from the protein interior into water is positive at low temperatures and negative at higher temperatures [150]. This is due to the polar groups creating their own ordered water, which generates a negative enthalpy change due to the increased molecular interactions. Balanced against this is the positive enthalpy change as the pre-existing water structure and the polar interactions within the protein both have to be broken. As water naturally has more structure at lower temperatures, the breakdown of the water structure makes a greater positive contribution to the overall enthalpy at lower temperatures. Weakening of water's hydrogen bonds reduces the enthalpy of transfer of polar groups at all temperatures as less energy is required to break down water's structure.

In contrast, the enthalpy of transfer of non-polar groups from the protein interior into water is negative below about 25 °C and positive above [150]. At lower temperatures, non-polar groups enhance pre-existing order such as the clathrate-related structures [270], generating stabilization energy but this effect is lost with increasing temperature, as any pre-existing order is also lost. At higher temperatures, the creation of these clathrate structures requires an enthalpic input. Thus, there is an overall positive enthalpy of unfolding at higher temperatures. An equivalent but alternative way of describing this process is that at lower temperatures the clathrate-type structure optimizes multiple van der Waals molecular interactions whereas at higher temperatures such

favorable structuring is no longer available. The extent of these enthalpy changes with temperature is reduced if water's hydrogen bonds are weakened, as the enthalpy change is raised at low temperatures and decreased at higher temperatures.

At ambient temperature, the entropies of hydration of both non-polar and polar groups are negative [151] indicating that both create order in the aqueous environment. However these entropies differ with respect to how they change with increasing temperature. The entropy of hydration of non-polar groups increases through zero with increasing temperature, indicating that they are less able to order the water at higher temperatures and may, indeed, contribute to its disorder by interfering with the extent of the hydrogen-bonded network. Also, there is an entropy gain from the greater freedom of the non-polar groups when the protein is unfolded. In contrast, the entropy of hydration of polar groups decreases, becoming more negative with increasing temperature, as they are able to create ordered hydration shells even from the more disordered water that exists at higher temperatures. Weakening of water's hydrogen bonds raises the entropic cost due to polar group hydration, as there is less natural order in the water to be lost.

Overall, protein stability depends on the balance between these enthalpic and entropic changes. For globular proteins, the free energy of unfolding is commonly found to be positive between about 0 °C and 45 °C. It decreases through zero when the temperature becomes either hotter or colder, with the thermodynamic consequences of both cold and heat denaturation. The hydration of the internal non-polar groups is mainly responsible for cold denaturation as their energy of hydration (that is,  $-\Delta H_N^D$ ) is greatest when cold. Thus, it is the increased natural structuring of water at lower temperatures that causes cold destabilization of proteins in solution. Heat denaturation is primarily due to the increased entropic effects of the non-polar residues in the unfolded state. The

temperature range for the correct folding of proteins ( $\Delta G_N^D$  above) shifts towards lower temperatures if water's hydrogen bonds are weaker and towards higher temperatures if they are stronger. Typically, if the strength of the hydrogen bond increased equivalent to the difference in strength between 0 °C and 100 °C (that is, raised cold denaturation) or decreased equivalent to the difference in strength between 45 °C and 0 °C (that is, lowered heat denaturation) then present proteins would not be stable in aqueous solution. The shifts required may be calculated from the enthalpy and entropy of water to be a 51% increase or an 18% weakening in water's hydrogen bond strength.

As the degree of interaction between water molecules and biological molecules and structures depends on a competition for the water's hydrogen bonding between the molecules and water itself, such processes would change on varying the water-water hydrogen bond strength. Increasing strength causes water to primarily bond with itself and not be available for the hydrating structuring of proteins or DNA, or for dissolving ions. On the other hand, if the water-water hydrogen bond strength reduces then the information exchange mechanisms operating within the cell, such as hydrogen-bonded water chains within and between proteins and DNA, will become non-operational. Evolutionary pressures might be expected to compensate for only some of these effects. [[Back to Top ▲](#)]

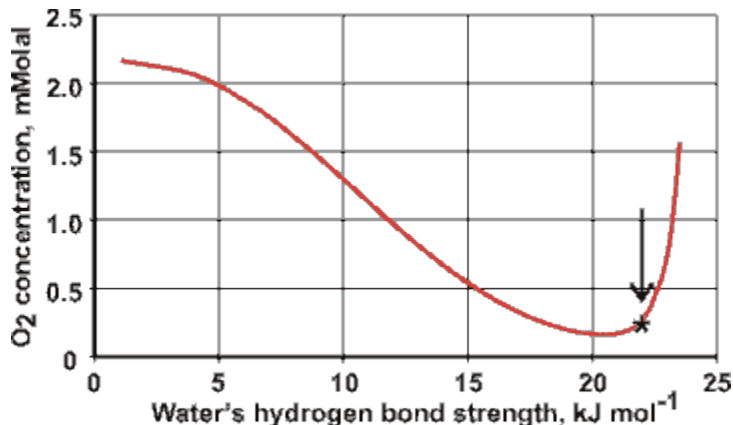
### **Effect of water hydrogen bond strength on its other physical properties**

Changes in water's hydrogen bond strength are expected to affect many of water's physical properties (as above). Some of these alterations only make insignificant changes to whether water can act as the medium for life. Pressure dependent properties such as compressibility have unimportant consequences as we live under relatively constant pressure. Some physical properties such as the speed of sound or refractive index impinge little on life's processes. Other physical

properties change relatively little, such as surface tension, but even such small changes may affect some processes. Without strong hydrogen bonding, there would not be the cohesion necessary for trees to manage to transport water to their tops.

Viscosity is particularly affected on strengthening of water's hydrogen bonds, increasing ten-fold from the value at 37 °C for an increase in hydrogen bond strength of only 8%. An alternative calculation using the Wilse Robinson equilibrium model [69] gives the higher value of 30% hydrogen bond strengthening required to shift the equilibrium temperature sufficiently to achieve this viscosity alteration. However, comparing the data from D<sub>2</sub>O shows a 23% increase in viscosity at 25 °C, or 34% at 0 °C, for only a 2% increase in hydrogen bond strength showing the major effect of hydrogen bonding on the viscosity. As diffusivity varies inversely with viscosity, molecular movements slow down as viscosity increases. This would be expected to have consequences for the speed with which life processes could proceed.

Although D<sub>2</sub>O only has 2-3% stronger hydrogen bonds than H<sub>2</sub>O as calculated from their enthalpy of evaporation, it has crucial effects on mitosis and membrane function. In most organisms it is toxic, causing death at high concentrations. It may be assumed however that life generally could adapt to its use as found for some microorganisms.



The solubility of gaseous oxygen and carbon dioxide are important features of life's processes. In particular, the solubilities increase steeply as the hydrogen bond strength increases from its natural value (see opposite for the dependence of the solubility of oxygen ([1020], at atmospheric pressure and composition) on water's hydrogen bond strength (ambient conditions are indicated).

Carbon dioxide solubility shows greater sensitivity due to the complex equilibria involved. However, its main behavior is an even steeper rise in solubility at high hydrogen bond strengths than that for oxygen; showing a four-fold increase (using data from [1021]) for a 5% hydrogen bond strengthening at 37 °C. The full consequences of these changes are complex and difficult to assess. Oxygen concentrations cannot be lowered below the threshold necessary for complex circulatory life (~0.1 mM, [1022]). With higher oxygen solubility, circulatory animals would be capable of being larger but more efficient anti-oxidant detoxification pathways would be necessary. Nevertheless, it is likely that life could adapt to these changes. [Back to Top ▲]

## Conclusions

The major effects of changes to water's hydrogen bond strength are summarized below, where they are considered individually. It is apparent that small changes of a few percent would not be threatening to life in general but changes in excess of 10% (equivalent to just 2 kJ mol<sup>-1</sup>) may cause

a significant threat. The overall conclusion to be drawn is that water's hydrogen bond strength is poised centrally within a narrow window of its suitability for life.

<b>Effect of H-bond strength on water's physical properties</b>	
<b>% Change in H-bond strength</b>	<b>Effect at 37 °C</b>
Decrease 29%	Water boils
Decrease 18%	Most proteins heat denature
Decrease 11%	K <sup>+</sup> becomes kosmotropic
Decrease 7%	pK <sub>w</sub> up 3
Decrease 5%	CO <sub>2</sub> 70% less soluble
Decrease 5%	O <sub>2</sub> 27% less soluble
Decrease 2%	No density maximum
No change	No effect
Increase 2%	Significant metabolic effects
Increase 3%	Viscosity increase 23%
Increase 3%	Diffusivity reduced by 19%
Increase 5%	O <sub>2</sub> 270% more soluble
Increase 5%	CO <sub>2</sub> 440% more soluble
Increase 7%	pK <sub>w</sub> down 1.7
Increase 11%	Na <sup>+</sup> becomes chaotropic
Increase 18%	Water freezes
Increase 51%	Most proteins cold denature

[[Back to Top](#) ▲]

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### Footnotes

<sup>a</sup> This page is based upon the paper [1023]. [[Back](#)]

<sup>b</sup> The hydrogen bond strength data is calculated using the enthalpy of evaporation with the base temperature 37 °C and assuming two hydrogen bonds per molecule. The physical property data for the same temperature is then used. [[Back](#)]

Source:<http://www1.lsbu.ac.uk/water/life.html>