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C H A P T E R

2

Water : The Solvent of Life

A striking example of water in both the solid and liquid states. Life as we know it depends on the properties of this simple molecule.

GENERAL CONSIDERATIONS

Water is the mother liquor of all forms of life. It is the vital essence, miracle of Nature, and the great sustainer of life. The essentiality of water for living systems is quite evident as without water, there is no life. The essentiality of water is a continuous reminder of the aqueous origin of life. It was in the solvent water that the chemical reactions of biological processes evolved. All aspects of cell structure and function are adapted to the physical and chemical properties of water. The strong attractive forces between water molecules result in water's solvent properties. A meagre tendency of water to ionize is of utmost importance to the structure and function of biomolecules. The water molecule and its ionization products (H^+ and OH^-) greatly influence the structure, assemblage and properties of all the cellular components, including enzymes and other proteins, nucleic acids and lipids. Water is needed not only for biochemical reactions, but also for transporting substances, across membranes, maintaining body temperature, dissolving waste products for excretion and producing digestive fluids.

Water is the medium in which the first cells arose, and the solvent in which most biochemical transformations take place. The properties of water have shaped the course of evolution and exert a decisive influence on the structure of biomolecules in aqueous solution. Many of the weak interactions within and between biomolecules are strongly influenced by the solvent properties of water. Even water-

insoluble components, such as membrane lipids, interact with each other in ways dictated by the polar properties of water.

No other substance on earth is as abundant as water. It is almost everywhere in air, clouds, oceans, lakes, rivers, springs or glaciers. In the 5 km layer below the sea level on Earth, water is nearly 6 times as abundant as all other substances put together. And, none other occurs in 3 states— solid, liquid and gaseous—at the same time. It is water that had conditioned our climate. The water in oceans, seas and the atmosphere (vapour) acts as an accumulator of heat. In hot weather, it absorbs heat and in cold, it gives up heat; thus, it keeps the planet warm. Without water, our planet would be cooled to subzero temperatures long ago and all forms of life would have perished. It takes 10 litres of water to produce 1 litre of petroleum, 100 litres for 1 kg of paper, 4,500 litres for 1 kg of rice, 4,500 litres for l ton of cement and 20,000 litres to produce 1 ton of steel. This roughly gives us an idea of the extent of water usage. Water has deluded us into believing that it is abundant and in exhaustible. But it is merely an illusion rather than a reality. The volume of water on the earth is about 1,36,00,00,000 cubic kilometres which covers nearly 70% of the earth's surface. The global scenario is that 97% of water is in the sea, 2% locked up in the Arctic and Antarctic oceans, and 1% is fresh water. Of this 1% fresh water, 0.22% is in the underground acquifer and the remaining 0.78% of the world's water fills the rivers, streams, lakes and ponds. No doubt, water is a renewable source but it is finite too. So it has to be used judiciously. The daily water requirement of an average person is as follows :

> 15 litres – for cooking and drinking needs
>
> 35-40 litres – for toilet needs
>
> 65 litres – for bathing, washing, and other sundry needs.

Water accounts for ca 70% or more of the weight of most organisms. In human adults also, total body water accounts for about 70% of the lean body mass. Variations observed are mainly due to differences in fat contents. In obese males, water constitutes a lower percentage of body weight (45–60%) than in lean individuals (55 – 70%). Adult lean females have a low water content (45 – 60%) and the value in infants can be in the range 65 – 75%. Our normal body temperature of 37°C is maintained mainly because water is expelled by lungs and skin. However, a loss of 10% of water in our body is serious; a loss of 20% fatal. In humans, water is not evenly distributed between the two major compartments (intracellular and extracellular) of the body (Table 2–1). In an adult male of 70 kg body weight, 70% of water (*i.e.*, about 30 litres) is found in intracellular fluids. Of this, about 4 litres are found in bones which does not readily participate in fluid exchange. Nearly 30% of water (*i.e.*, about 12 litres) is found in extracellular fluid. Plasma (3 litres), interstitial fluid (8.5 litres) and transcellular fluid (l litre) come under this category.

Table 2–1.   **Water distribution in an adult male of 70 kg body weight**

Compartment	Total body water (in litres)
Intracellular fluids	30
Extracellular fluids	
Plasma	3
Interstitial and lymph	8.5 } 12.5
Transcellular fluid	1

The maintenance of **water balance**, the equilibrium between water intake and output, is a critical aspect of metabolism. An adult in water balance generally takes in and loses about 2.8 litres of water per day in temperate climate and between 3.3 and 7.3 litres per day in tropical climate (Table 2–2). Besides the water obtained from foods and liquids, **metabolic water** is also made available through the oxidation of food in the body. Oxidation of 100 g each of fat, carbohydrate and protein yields 107,

55 and 41g of water, respectively. Water losses occur by evaporation (water vapour in exhaled air and perspiration) and by excretion of urine and feces.

Table 2–2. **Daily water intake and output (or loss) from the human body**

Intake/output	Temperate climate	Tropical climate
Intake		
As liquids	1.5 ⎫	2 – 5 ⎫
In foods	1.0 ⎬ 2.8	1 – 2 ⎬ 3.3 – 7.3
Oxidation of foods	0.3 ⎭	0.3 ⎭
Output (or Loss)		
Urine	1.5 ⎫	1.0 – 1.5 ⎫
Feces	0.1 ⎬ 2.8	0.1 – 0.2 ⎬ 3.3 – 7.3
Evaporation through skin	0.8 ⎫	1.8 – 5.2 ⎫
Evaporation through lung	0.4 ⎭	0.4 ⎭

If the output of water significantly exceeds its intake, **dehydration** occurs due to diarrhea, vomiting, fever and high environmental temperatures. Dehydration is especially serious in young children because their body pool of water is small and hence can be readily depleted. If water accumulates in tissues, then **edema** occurs. Edema is often observed in children suffering from kwashiorkor, a nutritional disease caused by an inadequate intake of protein. In the Carribeans, children with kwashiorkor are called *sugar babies* because of their plump appearance (a deceiving indication of good health).

Water is the most important possession of humanity and keeping in view the importance of the role of water on our planet, NASA has launched a satellite named *Aqua* to study the effect of water in its various forms on climate. The aim is to find whether there are any changes in the pattern of water cycle-climate relationship as a result of human-generated factors. *Aqua* is second in a series of 3 satellites planned by NASA with a view to gathering comprehensive data on Earth and its surroundings. Information gathered by *Aqua* will complement that being gathered by an earlier launched satellite, *Terra*, which concentrates on land mass studies. A third satellite, *Aura*, is to be launched in 2004, which will focus on atmospheric studies. Mission *Aqua* is indeed a commendable initiative of NASA because it concerns water, the magic substance on earth.

CLINICAL IMPLICATIONS - 1

Kwashiorkor is the Bantu word meaning displaced child. This refers to the fact that kwashiorkor appears in infants when they are no longer nursed by their mothers, *i.e.*, are displaced from the breast by the birth of a new baby. Kwashiorkor is a protein malnourishment syndrome that results from a diet adequate in calories but deficient in protein. It is characterized by degeneration of the liver, severe anemia, and inflammation of the skin. Kwashiorkor is especially common among children in industrially-underdeveloped countries where the diet consists primary of a single plant material, as in Indonesia, where rice is the main food, and in parts of Africa and Latin America, where corn (maize) is the principal staple. Worldwide, corn is the second or third largest crop and it is a staple for nearly half the world's malnourished people (For this reason, intense efforts have been directed at breeding stations for producing corn with a higher quality protein. The results have been marvellous; the quality protein maize (QPM) has a protein quality twice that of normal corn and almost equal to milk. If found fit on field trials, it will be good news for the impoverished populations in Mexico and Central America where maize constitutes about 85% of the grain consumed).

Early clinical evidence of protein malnutrition is vague but does include lethargy, apathy or irritability. When well advanced, it results in retarded growth, lack of stamina, loss of muscular tissue, a secondary

immunodeficiency, increased susceptibility to infections, and edema of dependent parts. The child may develop impaired appetite, anorexia, flabbiness of subcutaneous tissue and loss of muscle tone and may show little interest in play or in toys. The liver may enlarge early or late; fatty infiltration is common. Edema usually develops early; failure to gain weight may be masked by edema, which is often present in internal organs before it can be recognized externally in the face and limbs. The affected children are said to have a characteristic "*sugar baby*" *appearance* due to their bloated body. Renal plasma flow, glomerular filtration rate, and renal tubular function are decreased. The heart may be small in early stages, but is usually enlarged later.

Dermatitis is common. Darkening of the skin appears in irritated areas but not in those exposed to sunlight, a contrast to the situation in pellagra. Dyspigmentation (either hyper- or hypo-) may occur in these areas after desquamation (shedding of epithelial tissues, chiefly of the skin) or may be generalized. Thus, characteristic scaly erythematous rashes develop on the skin. The hair is often sparse, dry, thin, brittle, and hypopigmented (reddish-brown) with "*flag sign*" (alternating bands of black and brown hair). A decrease in the concentration of serum albumin is the most characteristic change. Bone growth is usually delayed. Growth hormone (GH) secretion may be enhanced. Stupor (partial unconsciousness), comma and death may ultimately follow.

PHYSICAL PROPERTIES OF WATER

The physical properties of water differ markedly from those of other solvents. For example, water as a hydride of oxygen (H_2O) has a higher melting point, boiling point, heat of vapourization and surface tension than do the comparable hydrides of sulfur (H_2S) and nitrogen (NH_3) and most other common liquids (Table 2–3). These unusual properties are a consequence of strong attractions between adjacent water molecules, which give liquid water great internal cohesion.

Table 2–3.   **Some physical properties of water and other common liquids**

Substance	Melting point, °C	Boiling point, °C	Heat of vapourization, cal/g	Heat capacity, cal/g	Heat of fusion, cal/g	Surface tension	Dielectric constant
Water	0	100	540	1,000	79.7	72.8	80
Methanol	– 98	65	263	0.600	22	–	33
Ethanol	– 117	78	204	0.581	24.9		
Propanol	– 127	97					
Butanol	– 90	117					
Acetone	– 95	56	125	0.528	23	23.7	21.4
Butane	– 135	0.5					
Hexane	– 98	69					
Chloroform	– 63	61	59	0.226		27.1	5.1
Benzene	6	80	94	0.500	30	28.9	2.3
Hydrogen sulfide	– 85	– 60	132	–	16.7		
Ammonia	– 78	– 33	327	1.120	84		
Hydrofluoric acid	– 92	19	360	–	54.7		

The vapourization of ice is called *sublimation* and the vapourization of a liquid is called *evaporation*. Both processes occur more rapidly as the temperature increases. However, evaporation occurs most frequently when water is heated above its boiling point, 100°C at sea level. Evaporation involves considerable amount of heat; 536 cal are needed to overcome the attraction between water molecules and to convert 1 g of water at 100°C into vapour. Heat lost at the point of evaporation returns at the point of condensation (the conversion from vapour to liquid). Such phenomena play a major role in meteorological cycles and the evaporative cooling of organisms.

Seawater behaves somewhat diferently. **Seawater** is defined as water with a minimum salinity of 24.7 0/00 (0/00 = parts per thousand). It's density, or rather its specific gravity ralative to that of an equal volume of pure water (sp. gra. = 1) at atmospheric pressure, is correlated with salinity. At 0°C, the density of sea water increases at a lower temperature and decreases at higher temperatures. No definite freezing point exists for seawater. Ice crystals begin to form at a temperature that varies with salinity. As pure water freezes out, the remaining unfrozen water becomes more salty, which further lowers its freezing point. If the temperature decreases further, a solid block of ice crystals and salt ultimately forms.

In humans, about 60% of red blood corpuscles (RBCs) and 92% of blood plasma are water. About 75% of most other tissues comprises of water; the only exceptions are such relatively inert tissues as hair, nails and the solid portion of bones. Water is also a principal constituent of the environment in which organisms thrive. Water has some unusual properties of physiological importance. These are described below :

1. Expansion on freezing. Most substances decrease in volume (and hence increase in density) as their temperature decreases. But in case of water, there is a temperature at which its density exceeds that at higher or lower temperatures. This temperature is 4 °C. In fact, water just above the freezing point is heavier than water at the freezing point. Therefore, it moves towards the bottom, freezing begins at the surface and the bottom is last to freeze. Organisms living at the bottoms of fresh-water lakes are, hence, protected from freezing. It may, however, be concluded that :

(*a*) While almost all substances contract on cooling, water expands. If water could contract on cooling, it would have become heavier and would have sunk. Thus, all water on earth would gradually have become ice.

(*b*) When temperature of water is raised above 0 °C, its volume decreases upto 4 °C and thereafter increases. Water thus has the minimum volume and hence the maximum density of 1.00 at 4 °C. The volume of water at 4 °C increases either on heating or cooling it.

(*c*) While all substances increase in volume when they are melted, the volume of ice decreases when melted : volume of 1g of ice is 1.09 cc but when it melts into water, it occupies only 1cc.

(*d*) Frozen water is less dense than liquid water.

2. Uniquely high surface tension. Like a stretched membrane, the surface of a liquid tends to contract as much as possible. This phenomenon is called *surface tension*. Water has the highest surface tension (of 72.8) of any known liquid. And it is the reason why water rises to unusually high levels in narrow capillary tubes. This has great significance in physiology.

3. Uniquely high heat capacity. There occurs a smaller temperature rise in water as compared to most other substances, when a given amount of heat is applied. Thus, water acts as a temperature buffer. It maintains its temperature more successfully than most other substances. We may, thus, say that has a high heat capacity (1,000 cal/g).

4. High solvent power. Water is a solvent for a great number of molecules which form ionized solutions in water. It may, thus, be called a universal solvent which facilitates chemical reactions both outside of and within biological systems.

Table 2–4 lists some of the unique features of water.

Table 2–4.   **Water and its features**

Property	Chemistry	Result
1. Universal solvent	Polarity	Facilitates chemical reactions
2. Adheres and is cohesive	Polarity; hydrogen bonding	Serves as transport medium
3. Resists changes in temperature	Hydrogen bonding	Helps keep body temperature constant
4. Resists change of state (from liquid to ice and from liquid to steam)	Hydrogen bonding	Moderates earth's temperature
5. Less dense as ice than as liquid water	Hydrogen bonding changes	Ice floats on water
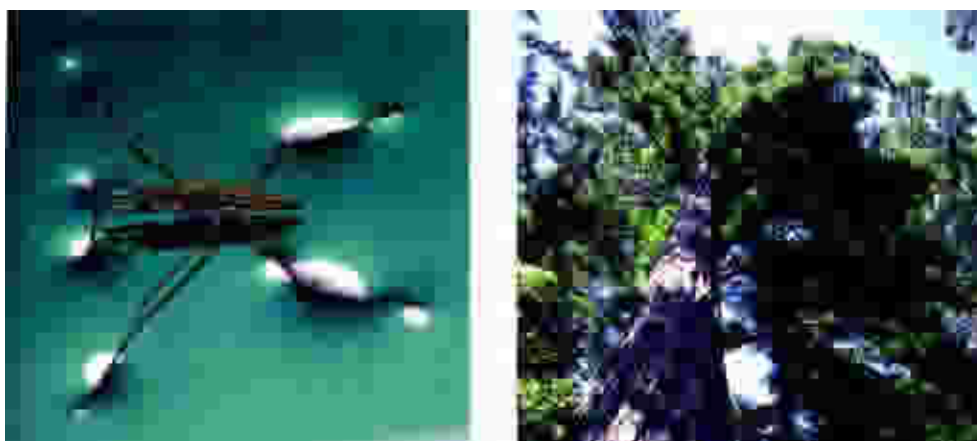
(*a*)   (*b*)

Fig. 2-1. Cohesion among water molecules

(*a*) Cohesion among water molecules allows water striders to skate across the surface of still waters.

(*b*) In giant redwoods, cohesion holds water molecules together in continuous strands from the roots to the topmost leaves even 100 meters above the ground.

It is due to the cohesive property of water molecules that allows water striders to skate across the surface of still waters and empowers giant redwoods to raise water about 100 metres above the ground (Fig. 2-1).

STRUCTURE OF WATER MOLECULE

In a water molecule (Figs. 2–2 and 2–3*a*, 3*b*), each hydrogen atom shares an electron pair with the oxygen atom. The geometry of the water molecule is dictated by the shapes of the outer electron orbitals of the oxygen atom, which are similar to the bonding orbitals of carbon. These orbitals describe a rough tetrahedron, with a hydrogen atom at each of the two corners and unshared electrons

at the other two. The H—O—H bond angle is 104.5°, 5° less than the bond angle of a perfect tetrahedron which is 109.5°; the nonbonding orbitals of the oxygen atom slightly compress the orbitals shared by hydrogen.

The oxygen nucleus attracts electrons more strongly than does the hydrogen nucleus (*i.e.*, the proton); oxygen is more electronegative. The sharing of electrons between H and O is therefore unequal; the electrons are more often in the vicinity of the oxygen atom than of the hydrogen. This unequal electron sharing creates two electric dipoles in the water molecule, one along each of the H—O bonds. The oxygen atom bears a partial negative charge (δ^-), and each hydrogen a partial positive charge (δ^+). The resulting electrostatic attraction between the oxygen atom of one water molecule and the hydrogen of another water molecule (Fig. 2–3c) constitutes a **hydrogen bond.**
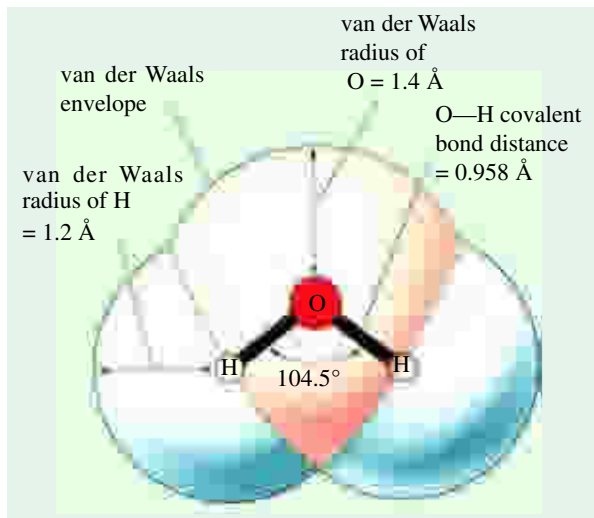
Fig. 2–2. The Structure of a water molecule

The outline represents the van der Waals envelope of the molecule (where the attractive components of the van der Waals interactions balance the repulsive components). the skeletal model of the molecule indicates its covalent bonds. The H – O – H bond angle is 104.5°. Both hydrogen atoms carry a partial positive charge and the oxygen a partial negative charge, creating a dipole.
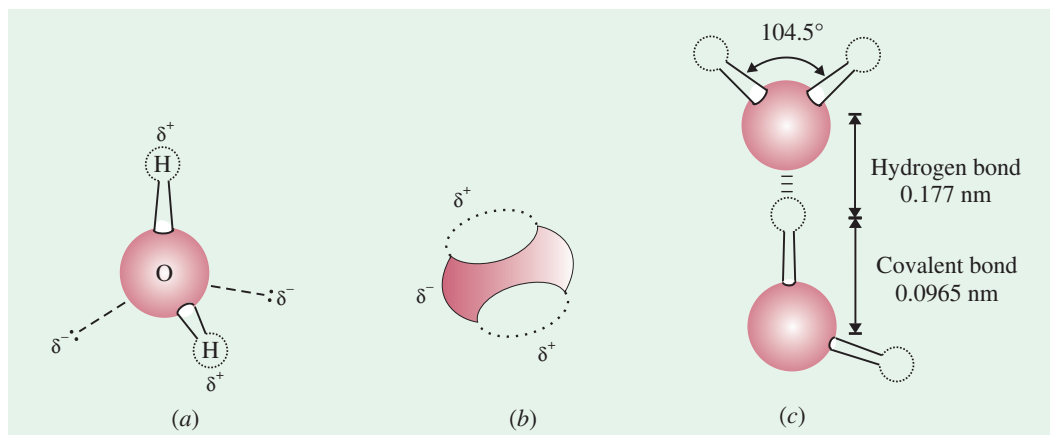

Fig. 2–3. The dipolar nature of the water molecule

A. Ball-and-stick model (dashed lines represent the nonbonding orbitals). There is nearly tetrahedral arrangement of the outer shell electron pairs around the oxygen atom; the two hydrogen atoms have localized partial positive charges and the oxygen atom has two localized partial negative charges.

B. Space-filling model.

C. Two water molecules joined by a hydrogen bond (designated by 3 thick horizontal lines) between the oxygen atom of the upper molecule and a hydrogen atom of the lower one. Hydrogen bonds are longer and weaker than covalent O — H bonds.

Polarity of water. Knowing the electronegativity of 2 atoms allows one to predict whether a bond between them will be covalent or ionic. The larger the difference in electronegativities of 2 atoms, the more likely they are to form an ironic rather than a covalent bond. Sodium and chlorine, for

example, have a large difference is electronegativities and hence form ionic bonds. Carbon and nitrogen, on the contrary, have similar, moderate electronegativities and they usually form covalent bonds.

Even in a covalent bond, however, atoms may not share electrons equally. When atoms differ in electronegativity, they do not share electrons equally. Instead, the diffuse clouds of shared electrons tilt toward the more electronegative atoms. In a water molecule, for example, an oxygen atom shares electrons with 2 hydrogen atoms. But the shared electrons are more concentrated around the oxygen nucleus than around the 2 hydrogen nuclei (Fig. 2-4). Consequently, the oxygen atom has a slight negative charge and the 2 hydrogen atoms have a slight positive charge.
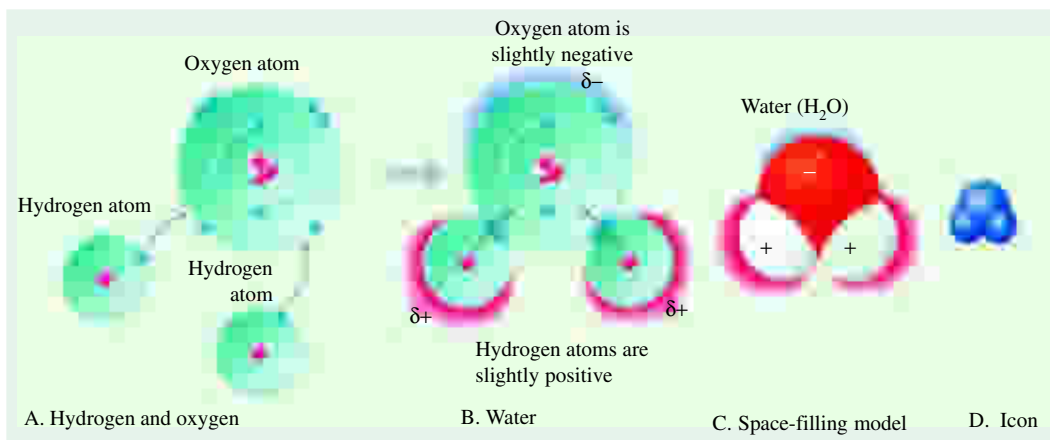
Fig. 2-4. The polarity of water

A. Two atoms of hydrogen and one atom of oxygen share electrons in two covalent bonds to form a molecule of water. **B.** Because the oxygen atom is more electronegative than the hydrogen atoms, the electrons spend more time hovering around the oxygen end of the water molecule. As a result, the oxygen end has a slightly negative charge, while the hydrogens have a slight positive charge. Such a partial charge, less than one full electron, is symbolized by δ. **C.** Space-filling model of water molecule. **D.** Icon for water.

Molecules that have uneven distributions of electrical charge are said to be **polar**, since they have positive and negative poles in the same way that a magnet has 2 poles (Fig. 2-4). When a polar molecule, such as water, comes close to an ion or to another polar molecule, its negative pole points toward the other molecule's positive pole, and its positive pole toward a neighbouring negative pole. Molecules with approximately uniform charge distributions are said to be **nonpolar.**

Hydrogen bonds between water molecules. When a hydrogen atom attaches to a highly electronegative atom such as oxygen or nitrogen, the resulting covalent bond is polar. In this case, the hydrogen atom acquires a slight positive charge. Such a hydrogen atom can then participate in a hydrogen bond–a weak interaction to a negatively-charged atom in another molecule (Fig. 2-5). The most common hydrogen bonds are those between water molecules, but other hydrogen bonds also play a critical role in the structure of proteins and DNA.
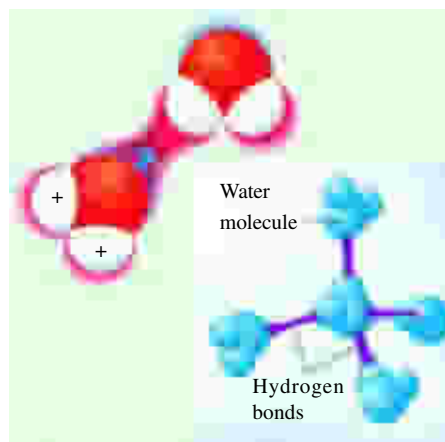
Hydrogen bonds are weaker than covalent bonds.

Fig. 2-5. Hydrogen bonds betweeen water molecules

The hydrogen atoms of one water molecule are attracted to the oxygen atoms of another water molecule.

The hydrogen bonds in liquid water have a **bond energy** (the energy required to break a bond) of only about 20 kJ/mol, as compared to 460 kJ/mol for the covalent O—H bond. At room temperature, the thermal energy of an aqueous solution (*i.e.*, the kinetic energy resulting from the motion of individual atoms and molecules) is of the same order as that required to break hydrogen bonds. When water is heated, the resulting temperature increase causes the faster motion of individual water molecules. Although at any given time, most of the molecules in liquid water are hydrogen-bonded, the lifetime of each hydrogen bond is less than 1×10^{-9}s. Nevertheless, the very large number of hydrogen bonds between molecules confers great internal cohesion on liquid water.
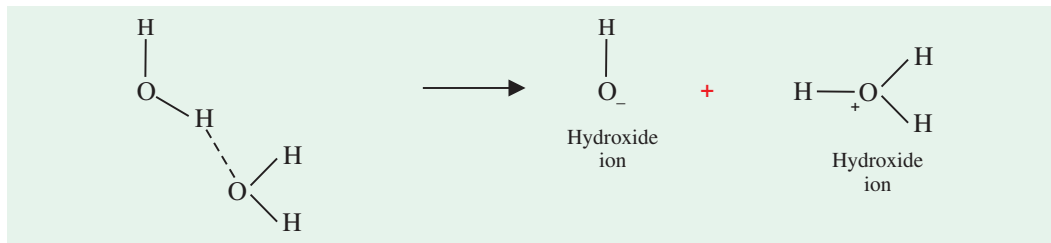

Fig. 2–6. **Formation of hydronium ion**

Water itself has a slight tendency to ionize and can act both as a weak acid and as a weak base. When it acts as an acid, it releases a proton to form a **hydroxyl ion.** When it acts as a base, it accepts a proton to form a **hydronium ion.** Most protons in aqueous solutions exist as hydronium ions.

The hydrogen atoms in a few molecules are occasionally lost to neighbouring water molecules (Fig. 2–6), giving rise to hydrated proton, called a hydronium ion, H_3O^+ and a *hydroxide ion*, OH^-. All protons in water are hydrated to some extent, but is unnecessary to write them as such. The symbol H^+ refers to any proton in water irrespective of its degree of hydration.

WEAK INTERACTIONS IN AQUEOUS SOLUTIONS

A. Hydrogen Bonding Between Water Molecules

The nearly tetrahedral arrangement of the oxygen electrons (bond angle 104.5°) allows each water molecule to form hydrogen bonds with 4 neighbouring water molecules. At any moment in liquid water at room temperature, each water molecule forms hydrogen bonds with an average of 3.4 other water molecules (Fig. 2–7). The water molecules are in continuous motion in the liquid state, hence hydrogen bonds are constantly and swiftly being broken and formed.
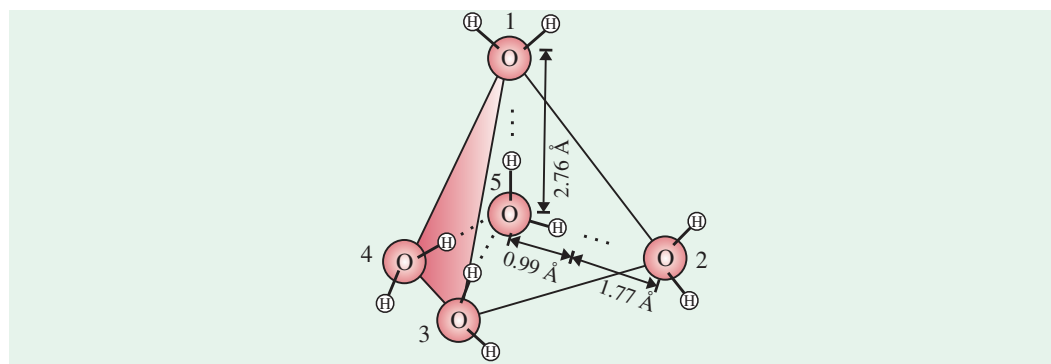

Fig. 2–7. Tetrahedral hydrogen bonding of a water molecule, in ice

Molecules 1, 2 and 5 are in the plane of the paper with molecule 3 above and molecule 4 below the plane. Molecules 1, 2, 3 and 4 are positioned at the corners of a regular tetrahedron.

In ice, however, each water molecule is fixed in space and forms hydrogen bonds with 4 other water molecules to produce a regular lattice structure (Fig. 2–8). Much thermal energy is needed to

break the large number of hydrogen bonds in such a lattice and this is the reason for a relatively high melting point of water. When ice melts or water evaporates, heat is taken up by the system :
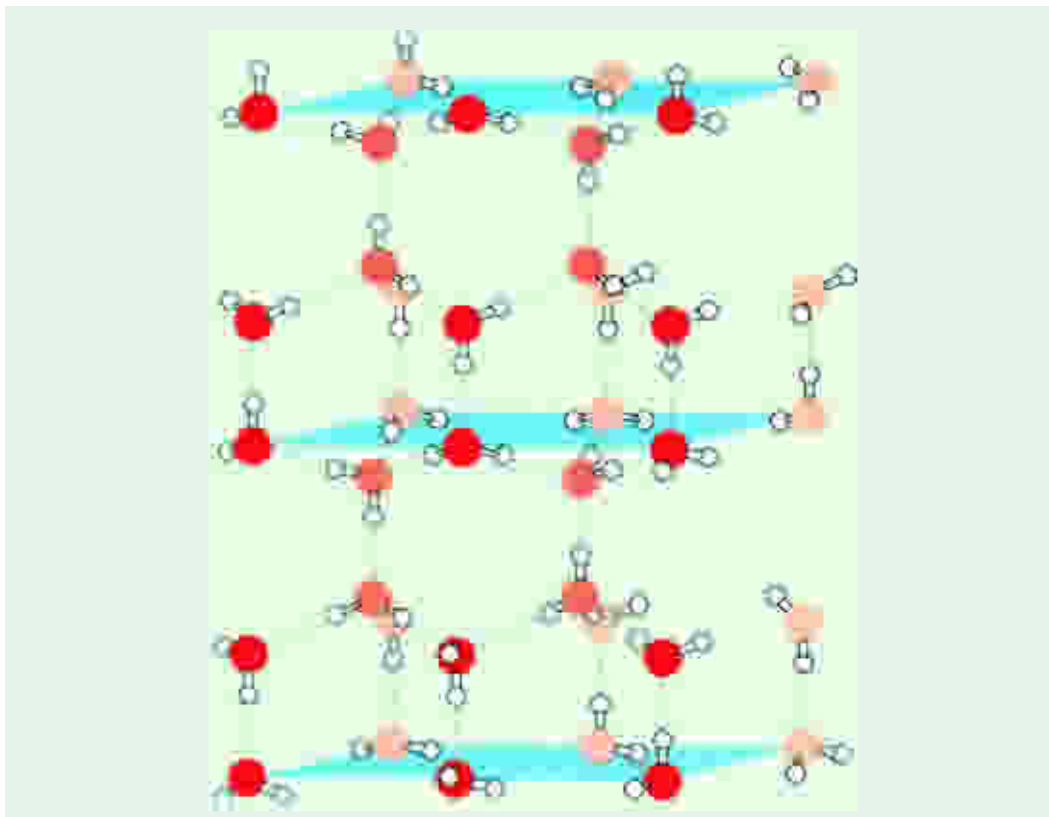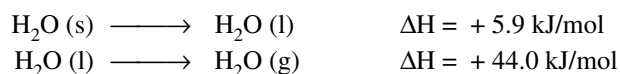

Fig. 2–8. The structure of ice

The tetrahedral arrangement of the water molecules is a consequence of the roughly tetrahedral disposition of each oxygen atom's sp^3- hybridized bonding and lone pair orbitals Oxygen and hydrogen atoms are represented, respectively, by red and white spheres, and hydrogen bonds are indicated by dashed lines. Note the open structure that gives ice its low density relative to liquid water.

(After Pauling, LC, 1960)

$$H_2O \text{ (s)} \longrightarrow H_2O \text{ (l)} \qquad \Delta H = +5.9 \text{ kJ/mol}$$
$$H_2O \text{ (l)} \longrightarrow H_2O \text{ (g)} \qquad \Delta H = +44.0 \text{ kJ/mol}$$

B. Hydrogen Bonding Between Water and Solute Molecules

Hydrogen bonding is not unique to water. They readily form between an electronegative atom (usually oxygen or nitrogen) and a hydrogen atom covalently bonded to another electronegative atom in the same or another molecule (Fig. 2–9). However, hydrogen atoms covalently bonded to carbon atoms (which are not electro-negative), do not participate in hydrogen bonding. The distinction explains why butanol ($CH_3 CH_2 CH_2 CH_2.OH$) has a relatively high boiling point of 117°C in contrast to butane ($CH_3 CH_2 CH_2 CH_3$) which has a boiling point of only –0.5°C. Butanol has a polar hydroxyl group and, hence, can form hydrogen bonds with other butanol molecules.

Uncharged but polar biomolecules such as sugars dissolve readily in water because of the stabilizing effect of the many hydrogen bonds that form between the hydroxyl groups or the carbonyl oxygen of the sugar and the polar water molecules. Alcohols, aldehydes and ketones all form hydrogen
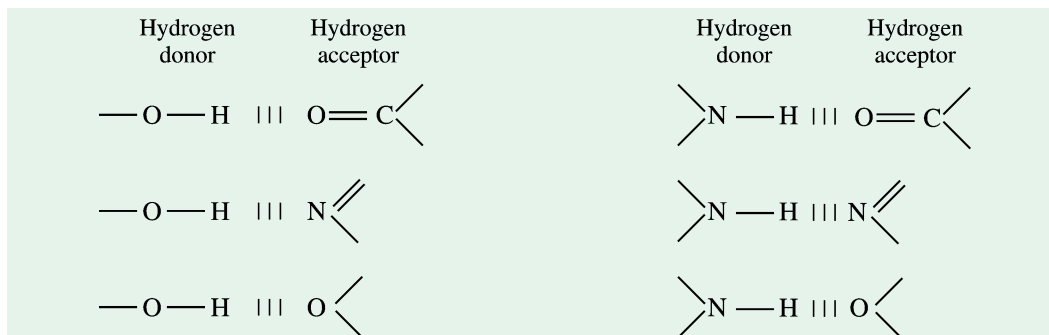
Fig. 2–9. Common types of hydrogen bonds

Note that in biological systems, the electronegative atom (*i.e.*, the hydrogen acceptor) is usually oxygen or nitrogen. The distance between two hydrogen-bonded atoms varies from 0.26 to 0.31 nm.

bonds with water, as do compounds containing N—H bonds (Fig. 2–10), and the molecules containing such groups tend to be soluble in water.
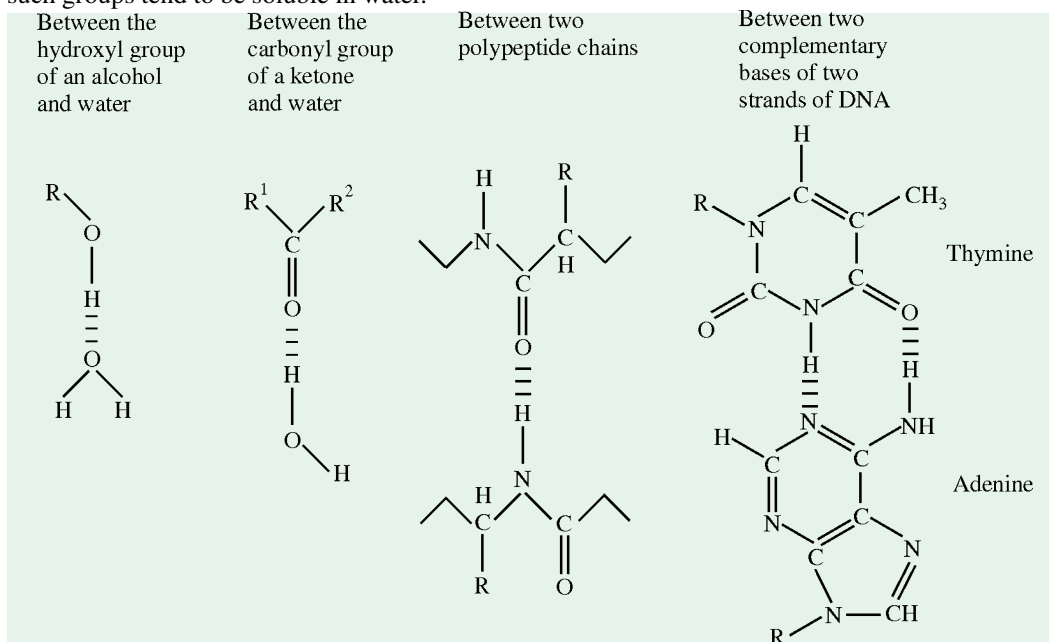

Fig. 2–10. Some hydrogen bonds of biological importance

Hydrogen bonds are strongest when the bonded molecules are oriented to maximize electrostatic interaction. This happens when the hydrogen atom and the two atoms that share it are in a straight line (Fig. 2–11). *Hydrogen bonds are, thus, highly* directional and are capable of holding two hydrogen-bonded molecules or groups in a specific geometric arrangement.
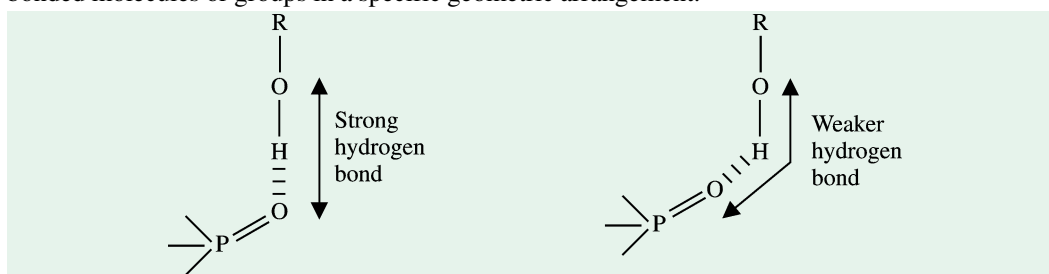

Fig. 2–11. Directionality of the hydrogen bond

The attraction between the partial electric charges is greatest when the three atoms involved (in this case, O, H and O) lie in a straight line.

C. Interaction Between Water and Charged Solutes

Water is a polar solvent. It readily dissolves most biomolecules, which are generally charged or polar compounds (Table 2–5). Compounds that dissolve readily in water are **hydrophilic** (*hudor*[G] = water; *philic*[G] = loving). In contrast, nonpolar solvents (such as chloroform and benzene) are poor solvents for polar biomolecules, but readily dissolve nonpolar biomolecules such as lipids and waxes.

Table 2–5. **Some examples of polar, nonpolar and amphipathic biomolecules**

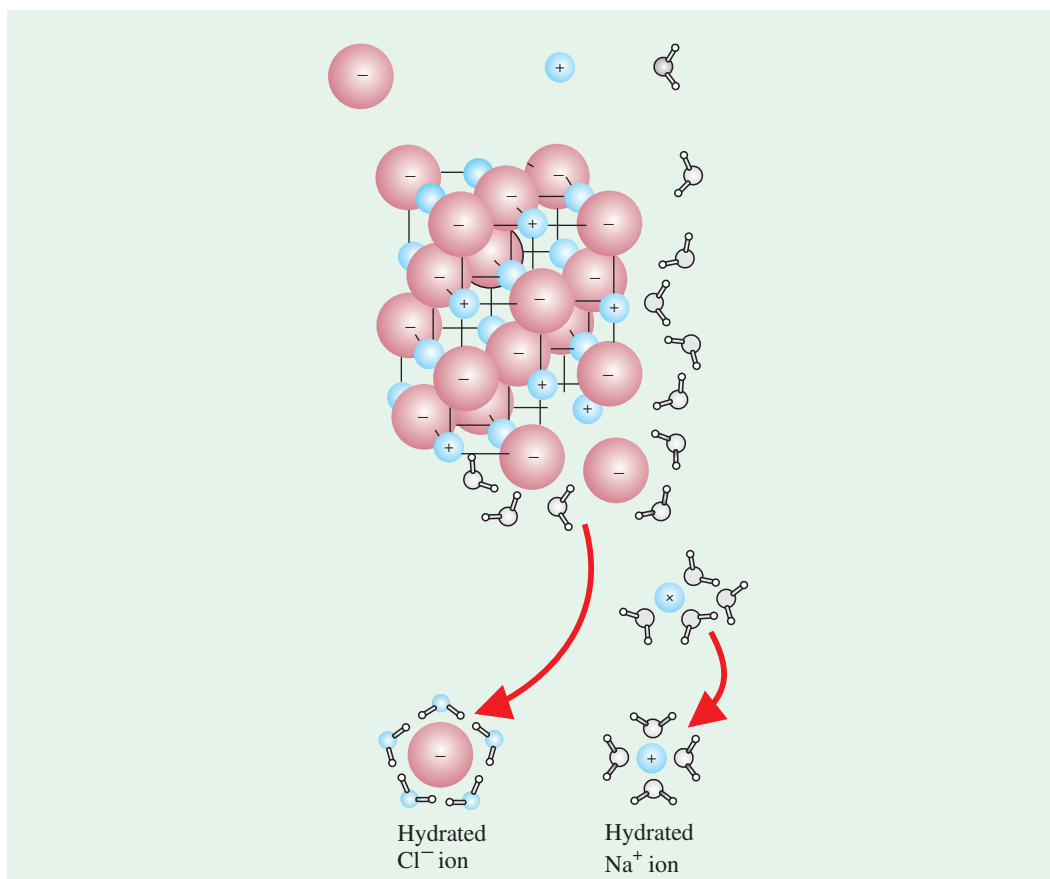| *Biomolecule*	*Ionic form at pH 7*
Polar	
Glucose	
Glycine	$^+NH_3$—CH_2—COO^-
Aspartic acid	^-COO—CH_2—CH—COO^- with $^+NH_3$ on CH
Lactic acid	CH_3—CH—COO^- with OH
Glycerol	$HOCH_2$—CH—CH_2OH with OH
Nonpolar	
Typical wax	$CH_3(CH_2)_7$—CH=CH—$(CH_2)_6$—CH_2—C(=O)—O—CH_2—$(CH_2)_7$—CH=CH—$(CH_2)_7$—CH_2—CH_3
Amphipathic	
Phenylalanine	—CH_2—CH—COO^- with $^+NH_3$
Phosphatidylcholine	

Hydrated
Cl⁻ ion

Hydrated
Na⁺ ion

Fig. 2–12.   Interaction between water and crystalline salts such as NaCl

Note that water dissolves many crystalline salts by hydrating their component ions (in this case, Na$^+$ and Cl$^-$ ions).

(Adapted fro*m AL Lehninger, DL Nelson and MM Cox, 1993*)

Water dissolves salts such as NaCl by hydrating and stabilizing the Na$^+$ and Cl$^-$ ions, weakening their electrostatic interactions and thus counteracting their tendency to associate in a crystalline lattice. In fact, the NaCl crystal lattice is disrupted as water molecules cluster about the Cl$^-$ and Na$^+$ ions. The ionic charges are, thus, partially neutralized and the electrostatic attractions necessary for lattice formation are weakened. As a result, the Na$^+$ and Cl$^-$ ions leaving the crystal lattice acquire far greater freedom of motion (Fig. 2–12). The resulting increase in the entropy (a measure of the degree of randomness or disorder of a system) of the system is largely responsible for the ease of dissolving the salt in water.

D. Interaction Between Water and Nonpolar Gases

The biologically important gases CO_2, O_2 and N_2 are nonpolar. In the diatomic molecules O_2 and N_2, electrons are shared equally by both atoms. In CO_2, each $C = O$ bond is polar, but the two dipoles are oppositely directed and cancel each other (Table 2–6). The movement of these molecules from the disordered gas phase into aqueous solution constrains their motion and therefore represents a decrease is entropy. As a consequence, these gases are very poorly soluble in water. Some organisms have water-soluble carrier proteins (such as hemoglobin and myoglobin) that facilitate the transport of oxygen. Carbon dioxide gas forms carbonic acid (H_2CO_3) in aqueous solution, and is transported in that form. Two other gases, NH_3 and H_2S, also have biological roles in some organisms. These gases are polar and dissolve easily in water.

Table 2–6.   **Solubilities of some gases in water**

Gas	Structure*	Polarity	Solubility in water (g/L)	Temperature (°C)
Nitrogen	N≡N	Nonpolar	0.018	40
Oxygen	O=O	Nonpolar	0.035	50
Carbon dioxide	O=C=O	Nonpolar	0.970	45
Ammonia	(H, H, H, N)	Polar	900	10
Hydrogen sulfide	(H, H, S)	Polar	1,860	40

* The arrows represent electric dipoles; there is a partial negative charge (δ^-) at the head of the arrow, a partial positive (δ^+; not shown here) at the tail.

E. Interaction Between Water and Nonpolar Compounds

When water is mixed with a hydrocarbon such as benzene or hexane, two phases form: neither liquid is soluble in the other. Shorter hydrocarbons such as ethane have small but measurable solubility in water. Nonpolar compounds such as benzene, hexane and ethane are **hydrophobic** (*hudor*[G] = water; *phobic*[G] = hatred) as they are unable to undergo energetically favourable interactions with water molecules. In fact, they interfere with the hydrogen bonding among water molecules. All solute molecules or ions dissolved in water interfere with the hydrogen bonding of some water molecules in their immediate vicinity, but polar or charged solutes (such as NaCl) partially compensate for the lost hydrogen bonds by forming new solute-water interactions. The net change in enthalpy (the heat content of the reacting system) for dissolving these solutes is usually small. Hydrophobic solutes offer no such compensation. Addition of water to such solutes may hence result in a small gain of enthalpy; the breaking of hydrogen bonds requires the addition of energy to the system. Furthermore, dissolving hydrophobic solutes in water results in a measurable decrease in entropy.

Amphipathic compounds contain regions that are polar (or charged) and regions that are nonpolar (Table 2–5). When amphipathic compounds are mixed with water, the two regions of the solute molecule experience conflicting tendencies: the polar or charged, hydrophilic region interacts favourably with the solvent and tends to dissolve whereas the nonpolar hydrophobic region has the opposite tendency, to avoid contact with the water. The nonpolar regions of the molecules cluster together to present the smallest area to the solvent, and the polar regions are arranged to maximize their interaction with the aqueous solvent. These stable structures of amphipathic compounds in water, called **micelles**, may contain hundreds or thousands of molecules. The forces that hold the nonpolar regions of the molecules together are called **hydrophobic interactions.**

Many biomolecules are amphipathic (Table 2–5): proteins, pigments, the sterols and phospholipids of membranes and certain vitamins all have polar and nonpolar surface regions. Structures composed of these molecules are stabilized by hydrophobic interactions among the nonpolar regions. Hydrophobic interactions among lipids and between lipids and proteins, are the most important determinants of structure in biological membranes; also hydrophobic interactions between nonpolar amino acids stabilize the 3–'D' folding patterns of proteins.

Hydrogen bonding between water and polar solutes also causes some ordering of water molecules but the effect is less significant than with nonpolar solutes.

F. Van der Waals Interactions

van der Waals interactions (named after J. D. van der Waals) are weak, nonspecific, interatomic attractions and come into play when any two uncharged atoms are 3 to 4 Å apart. Though weaker and less specific than electrostatic and hydrogen bonds, van der Waals interactions are no less important in biological systems. The basis of a van der Waals bond is that *the distribution of electronic charge around an atom changes with time.*
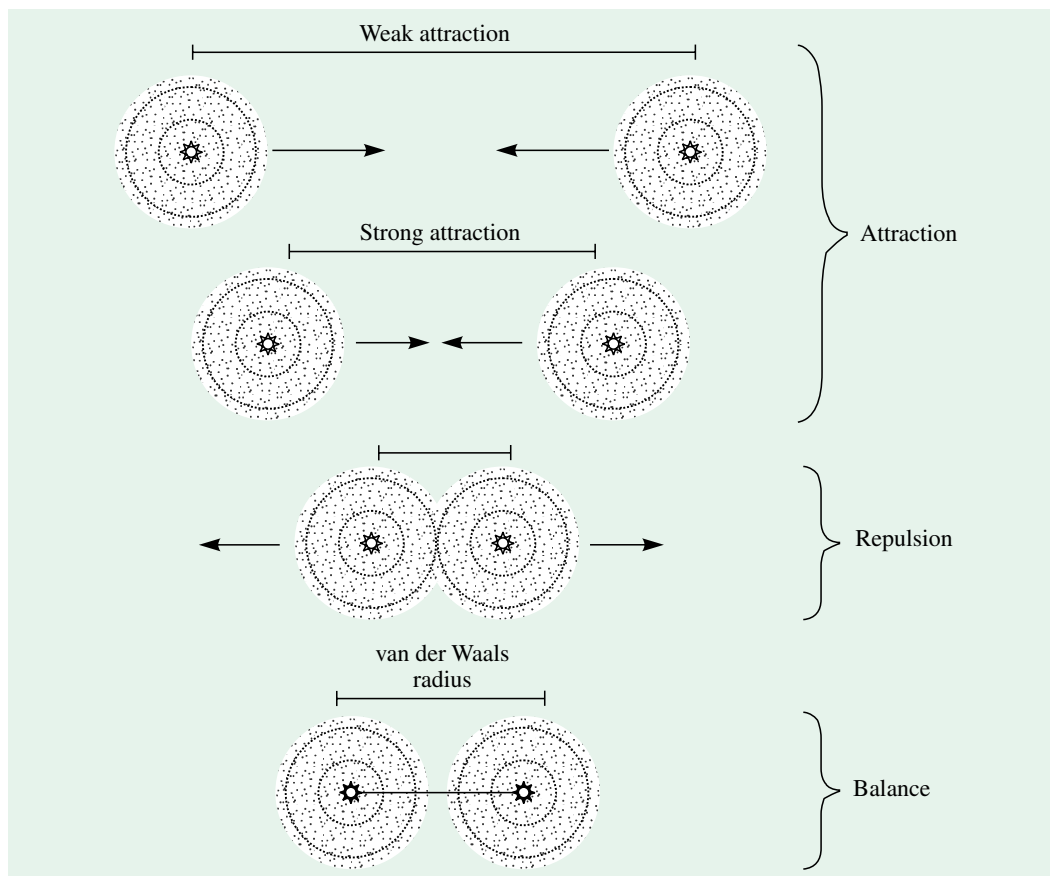

Fig. 2–13. **Schematic of van der Waals forces of attraction, repulsion and balance between two atoms**

All types of molecules exhibit van der Waals forces which arise from the attraction of the bound electrons of one atom for the nucleus of another. When two atoms are far apart, there is a very weak attraction which becomes stronger as the atoms move closer together (Fig. 2–13). However, if the atoms move close enough for their outer electron shells to overlap, then a force of repulsion ocurs. At a certain distance, defined as the *van der Waals contact radius*, there is a balance between the forces of attraction and those of repulsion. Each type of atom has a specific van der Waals contact radius (Table 2–7). At this point of balance, the two atoms are separated by the *van der Waals contact distance* (Fig. 2–14). The contact distance between an oxygen and carbon atom, for example, is 3.4 Å which is obtained by adding 1.4 and 2.0 Å, the contact radii of the O and C atoms, respectively.

Table 2–7.   **van der Waals contact radii of atoms and group**

Atom/Group	*Radius (in Å)*
H	1.2
O	1.4
N	1.5
S	1.85
P	1.9
C	2.0
CH_3	2.0
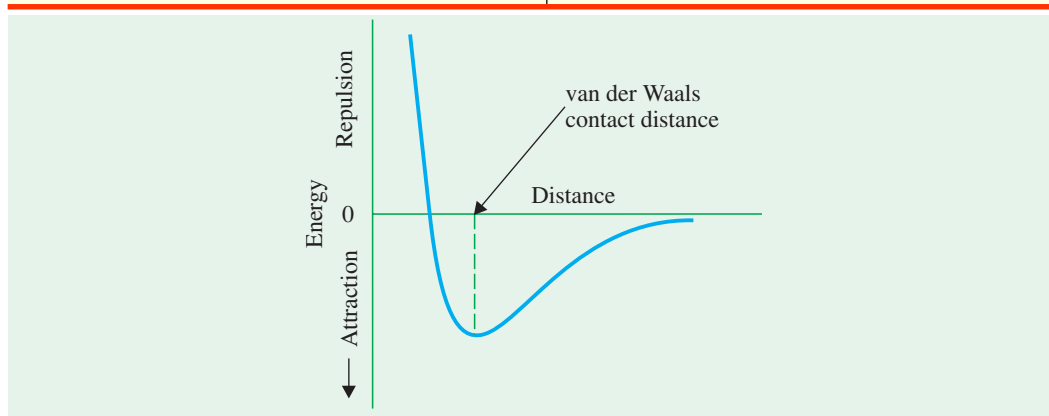
Fig. 2–14. Energy of a van der Waals interaction as a function of the distance between two atoms

The van der Waals bonding energy between two average atoms is very small, *i.e.*, about 1 kcal/ mol, which is only slightly greater than the average thermal energy (0.6 kcal/mol) of molecules at room temperature. It is considerably weaker than a hydrogen or electrostatic bond, which is in the range of 3 to 7 kcal/mol. The Energy of a most favourable or the van der waals contact distance. The energy rises rapidly owing to electron-electron repulsion as the atoms move closer together than this distance.

Table 2–8.   **Strengths of bonds common in biomolecules**

Type of bond	*Bond dissociation energy (kJ/mol)*	*Type of bond*	*Bond dissociation energy (kJ/mol).*
Single bonds		**Double bonds**	
O—H	461	C = O	712
H—H	435	C = N	615
P—O	419	C = C	611
C—H	414	P = O	502
N—H	389	**Triple bonds**	
C—O	352	N ≡ N	930
C—C	348	C ≡ C	816
S—H	339	**Noncovalent bonds or interactions**	
C—N	293	Hydrogen bonds	
C—S	260	van der Waals forces	
N—O	222	Hydrophobic bonds	4–20
S—S	214	Ionic interactions	

Since van der Waals interactions are very week, it is customary to call them as a force rather than a bond. The crystalline compounds possessing these forces are very soft and have low melting points. In fact, the more symmetrical the molecule, the greater are the *van der Waals forces*. These forces are greater for compounds than for atoms and moleculles of elements.

ROLE OF NONCOVALENT INTERACTIONS

The noncovalent interactions described above (hydrogen bonds and ionic interactions among charged groups and hydrophobic interactions and van der Waals interactions among nonpolar groups) are much weaker than covalent bonds (Table 2–8). The input of about 350 kJ of energy is required to break a mole (6×10^{23}) of C—C single bonds, and of about 410 kJ to break a mole of C—H bonds, but only 4-8 kJ is sufficient to disrupt a mole of typical van der Waals interactions (Table 2–9).

Table 2–9. **Some weak interactions among biomolecules in aqueous solvent**

Weak interaction		Stabilization energy (kJ/mol)
Hydrogen bonds Between neutral groups	$\rangle C = O \cdots H - O -$	8 – 21
Between peptide bonds	$\rangle C = O \cdots H - N \langle$	8 – 21
Ionic interactions Attraction	$-^+NH_3 \rightarrow \leftarrow ^-O - C -$ (O double bond C)	42
Repulsion	$-^+NH_3 \longleftrightarrow H_3N^+ -$	≈ – 21
Hydrophobic interactions	$CH_3 \quad CH_3 \quad CH_3 \quad CH_3$ CH ... CH2	4 – 8
van der Waals interactions	Any two atoms in close proximity	4

Hydrophobic interactions are similarly weak, and ionic interactions and hydrogen bonds are only a little stronger; a typical hydrogen bond can be broken by the input of about 20 kJ/mol. In aqueous solvent at 25°C, the available thermal energy is of the same order as the strength of these weak interactions. Consequently, hydrogen bonds and ionic, hydrophobic and van der Waals interactions are continuously formed and broken.

Although these 4 types of interactions are individually weak relative to covalent bonds, the cumulative effect of many such interactions in a protein or nucleic acid can be very significant. For example, the noncovalent binding of an enzyme to its substrate may involve several hydrogen bonds and one or more ionic interactions, as well as hydrophobic and van der Waals interactions. The formation of each of these weak bonds contributes to a net decrease is free energy; this binding free energy is released as bond formation stabilizes the system.

The most stable (native) structure of most macromolecules is that in which weak-bonding possibilities are maximized. The folding of a single polypeptide or polynucleotide chain into its 3-dimensional shape is determined by this principle. The binding of an antigen to a specific antibody depends on the cumulative effects of many weak interactions. The energy released when an enzyme binds noncovalently to its substrate is the main source of catalytic power for the enzyme. The binding of a hormone or a neurotransmitter to its cellular receptor protein is the result of weak interactions.

ROLE OF WATER IN LIFE

A saying goes, 'there is no life without water'. Life and water are inextricably connected (Fig. 2-15). Life probably originated in water. Wherever life is found, there is water; and wherever liquid water is found, there is life. Water makes up more than 70% of the material of living organisms themselves and covers more than 75% of Earth's surface. It is the medium in which most cells are constantly bathed and the major component of cells themselves. Not only do most biochemical reactions occur in water, but water itself participates in many biochemical reactions.

Fig. 2-15. Essentiality of water to organisms

Killer whale (*Orcinus orca*) spend their entire lives in the ocean.

REFERENCES

1. **Dick DAT :** Cell Water. *Butterworth Publishers, Inc., Stoneham, M.A. 1966*.

2. **Edsall JT, Wyman J :** Water and Its Biological Significance. *In Biophysical Chemistry. Vol.1. Academic Press, Inc., New York. 1958*.

3. **Eisenberg D, Kauzmann W :** The Structure and Properties of Water. *Oxford University Press, New York, 1969*.

4. **Franks R (editor) :** Water : A Comprehensive Treatise. *Vol. 4. Plenum Press, New York. 1975*.

5. **Franks R, Mathias SF (editors) :** Biophysics of Water. *John Wiley and Sons, Inc., New York. 1982*.

6. **Henderson LJ :** The Fitness of Environment. *Beacon Press, Boston, MA. 1927. [Reprinted, 1958.]*

7. **Pullman A, Vesilescu V, Packer L (editors) :** Water and Ions in Biological Systems. *Plenum Press, New York. 1985.*

8. **Rupley JA, Gratton E, Careri G :** Water and glubular proteins. *Trends Biochem. Sci.* **8:** *18, 1983.*

9. **Snoeyink VL, Jenkins D :** Water Chemistry. *John Wiley and Sons, New York. 1980.*

10. **Stillinger FH :** Water revisited. *Science.* **209:** *451–457, 1980.*

11. **Symons MCR :** Water structure and reactivity. *Acc. Chem. Res.* **14:** *179–187, 1981.*

12. **Wiggins PM :** Role of water in some biological processes. *Microbiol. Rev.* **54 :** *432–449, 1990.*

PROBLEMS

It is very difficult to learn something well without somehow participating in it. The chaper-end problems are therefore an asset of any textbook. This book contains few problems in each chapter which are of regurgitory type. Rather they are designed to make one think and to offer insights not discussed in the text. The difficulties in solving these problems range from those that require only a few moments reflection to those that might take an hour or more of concentrated effort to work out.

1. In a hospital laboratory, a 10.0 mL sample of gastric juice, obtained several hours after a meal, was titrated with 0.1 M NaOH to neutrality ; 7.2 mL of NaOH was required. The patient's stomach contained no ingested food or drink, thus assume that no buffers were present. What was the pH of the gastric juice ?

2. One common description of the pK_a of an acid is that it represents the pH at which the acid is half ionized, that is, the pH at which it exists as a 50 : 50 mixture of the acid and the conjugate base. Demonstrate this relationship for an acid HA, starting from the equilibrium-constant expression.

3. The amino acid glycine is often used as the main ingredient of a buffer in biochemical experiments. The amino group of glycine, which has a pK_a of 9.6, can exist either in the protonated form ($—NH_3^+$) or as the free base ($—NH_2$) because of the reversible equilibrium

   $$R—NH_3^+ \rightleftharpoons R—NH_2 + H^+$$

   (*a*) In what pH range can glycine be used as an effective buffer due to its amino group ?

   (*b*) In a 0.1 m solution of glycine at pH 9.0, what fraction of glycine has its amino group in the $—NH_3^+$ form ?

   (*c*) How much 5 m KOH must be added to 1.0 L of 0.1 M glycine at pH 9.0 to bring its pH to exactly 10.0 ?

   (*d*) In order to have 99% of the glycine in its $—NH_3^+$ form, what must the numerical relation be between the pH of the solution and the pK_a of the amino group of glycine ?

4. Catechols substituted with long-chain alkyl groups are the components of poison ivy and poison oak that produce the characteristic itchy rash.
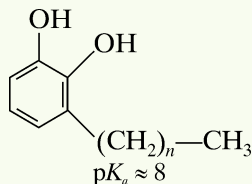
If you were exposed to poison ivy, which of the treatments below would you apply to the affected area ? Justify your choice.

(*a*) Wash the area with cold water.

(*b*) Wash the area with dilute vinegar or lemon juice.

(*c*) Wash the area with soap and water.

(*d*) Wash the area with soap, water, and baking soda (sodium bicarbonate).

5. Aspirin is a weak acid with a pKa of 3.5.
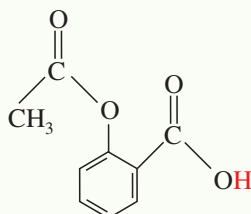
It is absorbed into the blood through the cells lining the stomach and the small intestine. Absorption requires passage through the cell membrane, which is determined by the polarity of the molecule: charged and highly polar molecules pass slowly, whereas neutral hydrophobic ones pass rapidly. The pH of the gastric juice in the stomach is about 1.5 and the pH of the contents of the small intestine is about 6. Is more aspirin absorbed into the bloodstream from the stomach or from the small intestine ? Clearly justify your choice.

6. Why can we blow a bubble with soap water but not with plain water ?

7. Why does ice melt when salt is sprinkled on it ?

8. Why is salt not soluble in oil but soluble in water ?

9. When a piece of paper is wet with water, it tears off easily. But the same paper if soaked in oil doesn't lose strength. Why ?

10. Why does the water film move away when we touch a wet surface ?

11. Why does water wet the glass while mercury does not ?

12. Why does ice melt but wax harden when subjected to pressure ?

13. Why are ice cubes preferred to water at 0°C to cool a soft drink ?

14. When glucose is added and stirred, the water feels cooler. Why ?

15. How can hydrogen, a combustible, and oxygen, a supporter of combustion when combined in the form of water extinguish fire ?

16. Why is snow white although water of which it is made up of is transparent ?

17. Why is water liquid but hydrogen sulfide a gas ?

18. Why is sea water salty ?

19. How do fishes survive in frozen lakes ?

20. Why do we feel thirsty ?

21. How is water purified ?