Water

From a biological standpoint, water has many distinct properties that are critical for the proliferation of life that set it apart from other substances. It carries out this role by allowing organic compounds to react in ways that ultimately allows replication. All known forms of life depend on water. In the human body around 70% of the fat free mass consists of water. Water is vital both as a solvent in which many of the body's solutes dissolve and as an essential part of many metabolic processes within the body. Metabolism is the sum total of anabolism and catabolism. In anabolism, water is removed from molecules (through energy requiring enzymatic chemical reactions) in order to grow larger molecules (e.g. starches, triglycerides and proteins for storage of fuels and information). In catabolism, water is used to break bonds in order to generate smaller molecules (e.g. glucose, fatty acids and amino acids to be used for fuels for energy use or other purposes). Water is thus essential and central to these metabolic processes.

Water is also central to photosynthesis and respiration. Photosynthetic cells use the sun's energy to split off water's hydrogen from oxygen. Hydrogen is combined with CO_2 (absorbed from air or water) to form glucose and release oxygen. All living cells use such fuels and oxidize (burn) the hydrogen and carbon to capture the sun's energy and reform water and CO_2 in the process (cellular respiration).

Water as a catalyst

Water is also central to acid-base neutrality and enzyme function. An acid, a hydrogen ion (H^+, that is, a proton) donor, can be neutralized by a base, a proton acceptor such as hydroxide ion (OH^-)to form water. Water is considered to be neutral, with a pH (the negative log of the hydrogen ion concentration) of 7. Acids have pH values less than 7 while bases have values greater than 7. Stomach acid (HCl) is useful to digestion. However, its corrosive effect on the esophagus during reflux can temporarily be neutralised by ingestion of a base such as aluminum hydroxide to produce the neutral molecules water and the salt aluminum chloride. Human biochemistry that involves enzymes usually performs optimally at water's neutral pH of 7, stomach enzymes however, such as trypsin, have evolved to work optimally in a much more acidic enviroment.

Water as a solvent

Water is also a good solvent due to its polarity. When an ionic or polar compound enters water, it is surrounded by water molecules (Hydration). The relatively small size of water molecules typically allows many water molecules to surround one molecule of solute. The partially negative dipole ends of the water are attracted to positively charged components of the solute, and vice versa for the positive dipole ends.

In general, ionic and polar substances such as acids, alcohols, and salts are relatively soluble in water, and non-polar substances such as fats and oils are not. Non-polar molecules stay together in water because it is energetically more favorable for the water molecules to hydrogen bond to each other than to engage in van der Waals interactions with nonpolar molecules.

An example of an ionic solute is table salt; the sodium chloride, NaCl, separates into Na^+ cations and Cl^- anions, each being surrounded by water molecules. The ions are then easily transported away from their crystalline lattice into solution. An example of a nonionic solute is table sugar. The water dipoles make hydrogen bonds with the polar regions of the sugar molecule (OH groups) and allow it to be carried away into solution.

The solvent properties of water are vital in biology, because all biochemical reactions take place only within aqueous solutions.

Acid dissociation constant

An acid dissociation constant, K_a, (also known as acidity constant, or acid-ionization constant) is a quantitative measure of the strength of an acid in solution. It is the equilibrium constant for a chemical reaction known as dissociation in the context of acid-base reactions. The equilibrium can be written symbolically as:

$$\mathrm{HA} \rightleftharpoons \mathrm{A}^- + \mathrm{H}^+$$

where HA is a generic acid that dissociates by splitting into A^-, known as the conjugate base of the acid, and the hydrogen ion or proton, H^+, which, in the case of aqueous solutions, exists as a solvated hydronium ion. In the example shown in the figure, HA represents acetic acid, and A^- the acetate ion. The chemical species HA, A^- and H^+ are said to be in equilibrium when their concentrations do not change with the passing of time. The dissociation constant is usually written as a quotient of the equilibrium concentrations (in mol/L), denoted by [HA], $[A^-]$ and $[H^+]$:

$$K_\mathrm{a} = \frac{[\mathrm{A}^-][\mathrm{H}^+]}{[\mathrm{HA}]}$$

Due to the many orders of magnitude spanned by K_a values, a logarithmic measure of the acid dissociation constant is more commonly used in practice. The logarithmic constant, pK_a, which is equal to $-\log_{10} K_a$, is sometimes also (but incorrectly) referred to as an acid dissociation constant:

$$\mathrm{p}K_\mathrm{a} = -\log_{10} K_\mathrm{a}$$

The larger the value of pK_a, the smaller the extent of dissociation at any given pH (see Henderson–Hasselbalch equation). A weak acid has a pK_a value in the approximate range −2 to 12 in water. Acids with a pK_a value of less than about −2 are said to be strong acids; a strong acid is almost completely dissociated in aqueous solution, to the extent that the concentration of the undissociated acid becomes undetectable. pK_a values for strong acids can, however, be estimated by theoretical means or by extrapolating from measurements in non-aqueous solvents in which the dissociation constant is smaller, such as acetonitrile and dimethylsulfoxide.

Amino acid pKa values

pKa values of amino acid side chains play an important role in defining the pH-dependent characteristics of a protein. The pH-dependence of the activity displayed by enzymes and the pH-dependence of protein stability, for example, are properties that are determined by the pKa values of amino acid side chains.

The pKa values of an amino acid side chain in solution is typically inferred from the pKa values of model compounds (compounds that are similar to the side chains of amino acids). (*See Amino acid for the pKa values of all amino acid side chains inferred in such a way.) The table below lists the model pKa values that are normally used in a protein pKa calculation.*

Amino Acid	**pKa**
Asp	3.9
Glu	4.3
Arg	12.0
Lys	10.5
His	6.08
Cys	8.28
Tyr	10.1

Protein pKa calculations

In computational biology, **protein pKa calculations** are used to estimate the pKa values of amino acids as they exist within proteins. These calculations complement the pKa values reported for amino acids in their free state, and are used frequently within the fields of molecular modeling, structural bioinformatics, and computational biology.

The effect of the protein environment

When a protein folds, the titratable amino acids in the protein are transferred from a solution-like environment to an environment determined by the 3-dimensional structure of the protein. For example, in an unfolded protein an aspartic acid typically is in an environment which exposes the titratable side chain to water. When the protein folds the aspartic acid could find itself buried deep in the protein interior with no exposure to solvent.

Furthermore, in the folded protein the aspartic acid will be closer to other titratable groups in the protein and will also interact with permanent charges (e.g. ions) and dipoles in the protein. All of these effects alter the pK_a value of the amino acid side chain, and

pK_a calculation methods generally calculate the effect of the protein environment on the model pKa value of an amino acid side chain.

Typically the effects of the protein environment on the amino acid pK_a value are divided into pH-independent effects and pH-dependent effects.

pKa calculation methods

Determining pKa values from titration curves

From the titration curve of protonatable group, one can read the so-called pK_a which is equal to the pH value where the group is half-protonated.