LANDMARK UNIVERSITY, OMU-ARAN

BCH 212LECTURE NOTE

INTRODUCTION TO PHYSICAL BIOCHEMISTRY

DEC, '12

LECTURE NOTE FOR BCH 212

Water is essential for life. Life as we know exist because of water, a common component of all biological cells and their extracellular environment. It covers 2/3 of the earth's surface and every living thing is dependent upon it. Water is the most abundant constituent of the human body accounting approximately 60 to 70% of the body mass in a normal adult and it is a major component of many bodily fluids including blood, urine, and saliva. An understanding of water and its properties is important to the study of biochemistry. The macromolecular components of cells—proteins, polysaccharides, nucleic acids, and membranes—assume their characteristics shapes in response to water. Some types of molecules interact extensively with water and as a result are very soluble. Other molecules do not dissolve easily in water and to associate with each other to avoid water. Much of the metabolic machinery of cells has to operate in an aqueous environment because water is an essential solvent as well as a substrate for many cellular reactions.

The physical properties of water allow it to act as a solvent for ionic and other polar substances and the chemical properties of water allow it to form weak bonds with other compounds, including other water molecules. The chemical properties of water are also related to the functions of macromolecules, entire cells and organisms. The Interactions are important sources of structural stability in macromolecule and large cellular reactions. It is important to in mind that mind that water is not just an inert solvent; it is also a substrate for many cellular reaction.

IMPORTANCE OF WATER

1. It is a medium in which body solutes, both organic and inorganic, are dissolved and metabolic reaction take place.

2. It acts as a vehicle for transport of solute.

3. Water itself participates as a substrate and a product in many chemical reactions, e.g. glycolysis, citric acid cycle and respiratory chain.

4 .The stability of subcellular structures and activities of the numerous enzymes are dependent on adequate cell hydration.

5. The abundance of water in cells and tissues of all large multicellular organisms regulate the temperature because of water’s highest latent heat of evaporation.

6. Water acts as a lubricant in the body so as to prevent friction in joints, peritoneum and conjunctiva.

7. Both a relative deficiency and an excess of water impair the function of tissues and organs

THE WATER MOLECULE IS POLAR

A water molecule (H_2O) is V-shaped and the angle between the two covalent (O-H) bonds is 104.5^o. Some important properties of water arise from its angled shape and the intermolecular bonds that it can form. An oxygen atom has eight electrons in the inner shell and six electrons in the outer shell. The outer shell can potentially accommodate four pairs of electrons in one *s* orbital and three *p* orbitals. However, the structure of water and its properties can be better explained by assuming that the electrons in the outer shell occupy four sp^3 hybrid orbitals. Think of these four orbitals as occupying the four corners of tetrahedron that surrounds the central atom of oxygen. Two of the sp^3 hybrid orbitals contain a pair of electrons and the other two each contain a single electron. This means that oxygen can form covalent bonds with other atoms by sharing electrons to fill these single electron orbitals. In water the covalent bonds involve two different hydrogen atoms each of which shares its single electron with the oxygen atoms.

The H-O-H bond angle in free water molecule is 104.5^o but if the electron orbitals were really pointing to the four corners of a tetrahedron, the angle would 109.5^o The usual explanation for this difference is that there is a strong repulsion between the lone electron pairs and this repulsion pushes the covalent bond orbitals closer together, reducing the angle from 109.5^o to 104.5^o.

Oxygen atoms are more electronegative than hydrogen atoms because an oxygen nucleus attracts electron attracts electrons more strongly than the single proton in the hydrogen nucleus. As a result, an uneven distribution of charge occurs within each O-H bond of the water molecule with oxygen bearing a partial negative charge and hydrogen bearing a partial positive charge. This uneven distribution of charge within a bond is known as a dipole and the bond is said to be polar.

The polarity of a molecule depends on the polarity of its covalent bonds and it geometry. The angled arrangement of the polar O-H bonds of water creates a permanent dipole for the molecule. Water and gaseous ammonia are electrically neutral, both molecule are polar. The high solubility of polar ammonia molecules in water is facilitated by strong interactions with polar water molecules. The solubility of ammonia in water demonstrates the principle that “likes dissolves likes”.

HYDROGEN BONDING IN WATER

One of the most important consequences of the polarity of the water molecule is that water molecules attract one another. The attraction between one of the slightest positive hydrogen atoms of one water molecule and the slightest negative electron pairs in one of the sp3 hybrid orbitals produces a hydrogen bond. In a hydrogen bond between two water molecules, the

hydrogen atom remains covalently bonded to its oxygen atom, the hydrogen donor. At the same time, it is attracted to another oxygen atom called the hydrogen acceptor. In effect, the hydrogen atom is being shared (unequally) between the two oxygen atoms. The distance from the hydrogen atom to the acceptor oxygen is about twice the length of the covalent bond.

Water is the only molecule capable of forming hydrogen bonds; these interactions can occur between any electronegative atom and hydrogen attached to another electronegative atom. Hydrogen bonds are much weaker than typical covalent bonds. The strength of hydrogen bonds in water and in solution is estimated to be about 20 kJ mol^{-1}

$$H—O—H + H—O—H \rightarrow O—H\text{-----}O \qquad \Delta H_f = -20 \text{ kJ mol}^{-1}$$

Fig. 1 Hydrogen Bonding

About 20 kJ mol^{-1} of heat is given off when hydrogen-bonded water molecules form in water under standard conditions (standard conditions are 1atm pressure and a temp 25°C). This value is the standard enthalpy of formation (ΔH_f). It means that the change in enthalpy when hydrogen bonds form is about - 20 kJ mol^{-1} per molecule of water. This is equivalent to saying that +20 kJ mol^{-1} of heat energy is required to disrupt hydrogen bonds between water molecules—the reverse of the reaction above. The strength of hydrogen bond is less than 5% of the strength of typical covalent bonds. Hydrogen bonds are weak interactions compared to covalent bonds but their large number is the reason for the stability of liquid water.

Orientation is important in hydrogen bonding. A hydrogen bond is most stable when the hydrogen atom and the two electronegative atoms associated with it (the two oxygen atoms, in the case of water) are aligned, or nearly in line

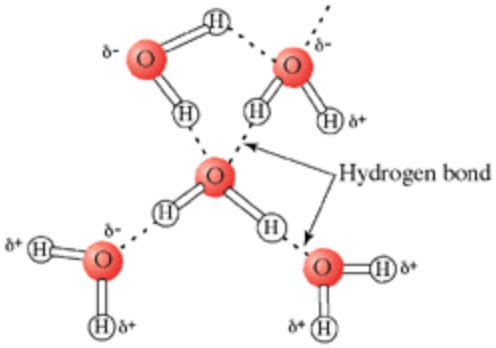


Figure: Hydrogen Bonding in Water

Water molecules are unusual because they can form four O—H—O aligned hydrogen bonds with up to four other water molecules. They can donate each of their two hydrogen atoms to two other water molecules and accept two hydrogen atoms from two other water molecules. Each hydrogen atom can participate in only one hydrogen bond. This tetrahedral lattice structure is responsible for the crystalline structure of ice. In the common form of ice, every molecule of water participates in four hydrogen bonds, as expected. Each of the hydrogen bonds points to the oxygen atom of an adjacent water molecule and these four adjacent hydrogen bonded oxygen atoms occupy the vertices of a tetrahedron. This arrangement is consistent with the structure of water shown in Figure 2, except that the bond angles are all equal (109.5°). This is because the polarity of individual water molecules, which distorts the bond angles, is cancelled by the presence of hydrogen bonds. The ability of water molecules in ice to form four hydrogen bonds and the strength of these hydrogen bonds give ice unusually high melting point because a large amount of energy, in form of heat is required to disrupt the hydrogen bonded lattice of ice. In the transition from ice to water, only some hydrogen bonds are broken. Liquid water has a rapidly changing structure as hydrogen bonds break and new bonds form; the half-life of hydrogen bonds in water is less than $1x\ 10^{-11}$ s. Thus the structure of liquid water is constantly fluctuating with a variety of structures containing many water molecules being constantly formed and changed, this responsible for the fluidity of water. The fluidity of liquid water is primarily a consequence of the constantly fluctuating pattern of hydrogen bonding as hydrogen bonds break and reform.

The density of most substances increases upon freezing as molecular motion slows and tightly packed crystals form. Water expands as the temperature drops below $4^{o}C$. This expansion is caused by the formation of the more open hydrogen –bonded ice crystal in which the water molecule.

Two additional properties of water are related to its hydrogen-bonding characteristics—its specific heat and it heat of vaporization. Relatively large amount of heat is required to raise the temperature of water because each water molecule participates in multiple hydrogen bonds that must be broken in order for the kinetic energy of the water molecule to increase. The abundance of water in the cells and tissues of all large multicellular organisms means that temperature

fluctuations within the cells are minimized. This feature is of critical biological importance since the rates of most biochemical reactions are sensitive to temperature.

HYDROGEN BONDS AND OTHER WEAK INTERACTIONS INFLUENCE BIOLOGICAL MOLECULE

Biochemists are concerned not just with strong covalent bonds that define chemical structure but with the weak forces that act under relatively mild physical conditions. The structures of most biological molecules are determined by the collective influence of many individually weak interactions. The weak electrostatic forces that interest biochemists include ionic interaction, hydrogen bonds and *van der waal* forces.

The strength of association of ionic groups of opposite charge depends on the chemical nature of the ions, the distance between them and the polarity of the medium. In general, the strength of the interaction between two charged groups (i.e., the energy required to completely separate in the medium of interest) is less than the energy of a hydrogen bond.

The non-covalent associations between neutral molecules, collectively known as *van der -waals* forces, arises from electrostatic interaction among permanent or induced dipoles (the hydrogen bond is a special kind of dipolar interaction). Interactions among permanent dipoles such as carbonyl groups are much weaker than ionic interactions. A permanent dipole also induces a dipole moment in a neighboring group by electrostatically distorting it electron distribution. Such dipole induced interactions are generally much weaker than dipole-dipole interaction.

Higher orders of protein structures are stabilized primarily- and often exclusively – by noncovalent interactions. Principal among these are hydrophobic interactions that drive most hydrophobic amino acids side chains into the interior of the proteins, shielding them from water. Other significant contributors include hydrogen bonds and salt bridges between the carboxylate of aspartate

Water is an excellent Solvent

The polar character of water makes it an excellent solvent for polar and ionic materials, which are said to be hydrophilic. On the other hand, nonpolar substances are virtually insoluble in water and are consequently described as hydrophobic. Water is an excellent solvent for both ionic compound (e.g., NaCl) and low molecular weight nonionic polar compounds (e.g., sugar and alcohol). Ionic compounds are soluble because water can overcome the electrostatic attraction between ions through solvation of the ions. Nonionic polar compounds are soluble because water molecules can form hydrogen bonds to polar groups (e.g., -OH).

Amphipathic compounds which contain both large non polar hydrocarbon chains (hydrophobic groups) and polar or ionic groups (hydrophilic groups) may associate with each other in

submicroscopic aggregations called micelles. Micelles have hydrophilic (water liking) groups on their exterior (bonding with solvent water), and hydrophobic water (water disliking) groups clustered in their interior. They occur in spherical, cylindrical or ellipsoidal shapes. Micelles structures are stabilized by hydrogen bonding with water, by van der waals attractive forces between hydrocarbon groups in the interior and by energy of hydrophobic reactions. As with hydrogen bonds, each hydrophobic interaction is very weak but many such interactions result in formation of large stable structures.

Hydrophobic interaction plays a major role in maintaining the structure and functions of cell membranes, the activity of proteins, the anesthetic action of non-polar compound such as chloroform and nitrous oxide, the absorption of digested fats and the circulation of hydrophobic molecules in the interior of micelles in blood plasma.

Polar solvents such as water weaken the attractive forces between oppositely charged ions (such as Na^+ and Cl^-) and can therefore hold the ions apart. (In nonpolar solvents, ions of opposite charge attract each other so strongly that they coalesce to form a solid salt.) An ion immersed in a polar solvent such water attracts the oppositely charged ends of the solvent dipoles. The ion is thereby surrounded by one or more concentric shells of oriented solvent molecules. Such ions are said to be solvated or, when water is the solvent, to be hydrated.

The bond dipoles of uncharged polar molecules make them soluble in aqueous solutions for the same reasons that ionic substances are water soluble. The solubility's of polar and ionic substances are enhanced when they carry functional groups, such as hydroxyl (OH), carbonyl (C=O), carboxylate (COO^-), or ammonium (NH_3^+) groups, that can form hydrogen bond with water. Indeed, water soluble biomolecules such as proteins, nucleic acids and carbohydrates bristle with just such groups. Nonpolar substances, in contrast, lack hydrogen bonding donor and acceptor groups.

BONDS IN BIOLOGICAL SYSTEM

3. **Nonpolar or Hydrophobic Bond**. Many amino acids (like alanine, valine, leucine, isoleucine, Methionine, tryptophan, phenylalanine and tyrosine) have the side chains or R groups which are essentially hydrophobic, i.e., they have little attraction for water molecules in comparison to the strong hydrogen bonding between water molecules. Such R groups can unite among themselves with elimination of water to form linkages between various segments of a chain or between different chains. This is very much like the coalescence of oil droplets suspended in water. The association of various R groups in this manner leads to a relatively strong bonding. It also serves to bring together groups that can form hydrogen bonds or ionic bonds in the absence of water. Each type linkage, thus, helps in the formation of the other; the hydrophobic bonds being most efficient in this aspect. The hydrophobic bonds also play important role in other protein

interactions, for example, the formation of enzyme-substrate complexes and antibody- antigen interactions.

1**. Disulfide Bond (-S-S-)**. In addition to the peptide bond, a second type of covalent bond found between amino acid residues in proteins and polypeptides is the disulfide bond, which is formed by the oxidation of the thiol or sulfhydryl (-SH) groups of two cysteine residues to yield a mole of cystine, an amino acid with a disulfide bridge . In generalized form, the above reaction may be written as:

$$2R—SH + 1/2\ O_2 \rightleftharpoons R—S—S—R + H_2O$$

Insulin is another excellent example where two peptide chains are linked together by 2 disulfide bonds. The presence of an internal disulfide bond in the glycyl (or A) chain between residues 6 and 11 is noteworthy.

4. Ionic or Electrostatic Bond or Salt linkage or Salt Bridge. Ions possessing similar charge repel each other whereas the ions having dissimilar charge attract each other. For example, divalent cations like magnesium may form electrostatic bonds with 2 acidic side chains. Another instance of ionic bonding may be the interaction between the acidic and basic groups of the constituent amino acids shown at the bottom of Fig. 9−13. The R groups of glutamic acid and aspartic acid contain negatively charged carboxylate groups, and the basic amino acids (arginine, histidine, and lysine) contain positively charged amino groups in the physiological pH range. Thus, these amino acids contribute negatively charged and positively charged side chains to the polypeptide backbone. When two oppositely charged groups are brought close together, electrostatic interactions lead to a strong attraction, resulting in the formation of an electrostatic bond. In a long polypeptide chain containing a large number of charged side chains, there are many opportunities for electrostatic interaction. Intramolecular ionic bonds are rather infrequently used in the stabilization of protein structure but when they are so used, it is often with great effect. In fact, ionized groups are more frequently found stabilizing interactions between protein and other molecules. Thus, ionic bonds between positively charged groups (side chains of lysine, arginine and histidine) and negatively charged groups (COO − group of side chain of aspartic and glutamic acids) do occur. These ionic bonds, although weaker than the hydrogen bonds, are regarded as responsible for maintaining the folded structure (or the tertiary structure) of the globular proteins.

2. **Hydrogen Bond (>CO.....HN<)**. When a group containing a hydrogen atom, that is covalently-bonded to an electronegative atom, such as oxygen or nitrogen, is in the vicinity of a second group containing an electronegative atom, an energetically favourable interaction occurs which is referred to as a hydrogen bond. The formation of a hydrogen bond is due to the tendency of hydrogen atom to share electrons with two neighbouring atoms, esp., O and N. For example, the carbonyl oxygen of one peptide bond shares its electrons with the hydrogen atom of another peptide bond. Thus,

THE HYDROPHOBIC EFFECT IN WATER

When a nonpolar substance is added to an aqueous solution, it does not dissolve but instead is excluded by the water. The tendency of water to minimize its contact with hydrophobic molecules is termed the hydrophobic effect. Many large molecules and molecular aggregates, such as proteins, nucleic acids, and cellular membranes, assume their shapes at least partially in response to hydrophobic effect.

Consider the thermodynamics of transferring a nonpolar molecule from an aqueous solution to a nonpolar solvent. In all cases, the free energy change is negative, which indicates that such transfers are spontaneous processes. Interestingly, these transfer processes are either endothermic (positive ΔH) or isothermic ($\Delta H = 0$); that is, it is enthalpically more or less equally favorable for nonpolar molecules to dissolve in water as in nonpolar media. In contrast, the entropy change (expressed as $-T\Delta S$) is large and negative in all cases. Clearly, the transfer of a hydrocarbon from an aqueous medium to a nonpolar medium is entropically driven (i.e., the free energy change is mostly due to an entropy change).

Entropy, or "randomness" is a measure of the order of a system. If entropy increases when a nonpolar molecule leaves an aqueous solution, entropy must decrease when the molecule enters water. This decrease in entropy when a nonpolar molecule is solvated by water is an experimental observation, not a theoretical conclusion. Yet the entropy changes are too large to reflect only the changes in the conformations of the hydrocarbons. Thus the entropy changes must arise mainly from some sort of ordering of the water itself.

The hydrophobic effect, which causes nonpolar substances to minimize their contacts with water, is the major determinant of native protein structure. The aggregation of nonpolar side chains in the molecules that would otherwise form ordered "cages" around the hydrophobic groups. Aggregation of the nonpolar molecules increases the entropy of the system, since the number of water molecules required to hydrate the aggregated solute is less the number of water molecule required to hydrate the dispersed solute molecules. This increase in entropy accounts for the spontaneous aggregation of nonpolar substances in water.

Colligative properties

The colligative properties of a solvent depend on the concentration of solute particles. These properties include freezing point depression, vapor pressure depression, osmotic pressure and boiling point elevation. The freezing point of

Osmotic pressure is a measure of the tendency of water molecule to migrate from a dilute to a concentrated solution through a semipermeable membrane. The migration of water molecules to is termed osmosis

WATER MOVES BY OSMOSIS AND SOLUTES MOVE BY DIFFUSION

The fluid inside cells and surrounding cells in multicellular organisms is full of dissolved substances ranging from small inorganic ions to huge molecular aggregates. The concentrations of these solutes affect water's colligative properties, the physical properties that depend on the concentration of dissolved substances rather than on their chemical features.

Osmosis occurs when two solutions of different concentrations are separated by a membrane which will selectively allow some species through it but not others. Then, material flows from the less concentrated to the more concentrated side of the membrane. A membrane which is selective in the way just described is said to be **semipermeable**. Osmosis is of particular importance in living organisms, since most living tissue is semipermeable in one way or another.

In biological systems, the semi permeability relies on a set of solute transporters and channels. The cell membrane is formed of a lipid bilayer with polar head groups facing out, and nonpolar hydrocarbon tails in the middle of the membrane. The consequence is that charged and polar substances cannot cross the membrane. In general, these membranes are impermeable to large and polar molecules, such as ions, proteins, and polysaccharides, while being permeable to non-polar and/or hydrophobic molecules like lipids as well as to small molecules like oxygen, carbon dioxide, nitrogen, nitric oxide, etc. Permeability depends on solubility, charge, or chemistry, as well as solute size. Water molecules travel through the plasma membrane, tonoplast membrane (vacuole) or protoplast by diffusing across the phospholipid bilayer via aquaporins (small trans membrane proteins similar to those in facilitated diffusion and in creating ion channels). Osmosis provides the primary means by which water is transported into and out of cells. The turgor pressure of a cell is largely maintained by osmosis, across the cell membrane, between the cell interior and its relatively hypotonic environment.

Aquaporins are membrane proteins which allow water, but no other molecule, not even H_3O^+ to pass through. For other solutes and ions, there exist specific transporters, some which allow a solute to diffuse down a natural gradient, and others which actively pump ions or other solutes in or out of the cell. These transporters, pumps and channels can be gated and regulated as well, allowing a cell to respond to varying osmotic conditions. Osmosis also is the net movement of solvent molecules through a partially permeable membrane into a region of higher solute concentration, in order to equalize the solute concentrations on the two sides. It may also be used to describe a physical process in which any solvent moves, without input of energy, across a semipermeable membrane (permeable to the solvent, but not the solute) separating two solutions

of different concentrations. Although osmosis does not require input of energy, it does use kinetic energy and can be made to do work.

Osmosis can be explained using the concept of thermodynamic free energy: the less concentrated solution contains more free energy, so its solvent molecules will tend to diffuse to a place of lower free energy in order to equalize free energy. Since the semipermeable membrane only allows solvent molecules to pass through it, the result is a net flow of water to the side with the more concentrated solution. Assuming the membrane does not break, this net flow will slow and finally stop as the pressure on the more concentrated side lessens and the movement in each direction becomes equal: this state is called dynamic equilibrium.

Osmosis can also be explained using the notion of entropy, from statistical mechanics. A system that has two solutions of different concentrations separated by a semipermeable membrane has less entropy than a similar system having two solutions of equal concentration. The system with the differing concentrations is said to be more ordered, and thus has less entropy. The second law of thermodynamics requires the presence of an osmotic flow that will take the system from an ordered state of low entropy to a disordered state of higher entropy. Thermodynamic equilibrium is achieved when the entropy gradient between the two solutions becomes zero.

The tendency for osmotic flow to occur from a solvent to a solution is usually measured in terms of what is called the osmotic pressure of the solution, symbol Π. This osmotic pressure is not a pressure which the solution itself exerts but is rather the pressure which must be applied to the solution (but not the solvent) from outside in order to just prevent osmosis from occurring. The osmotic pressure is defined to be the pressure required to maintain equilibrium, with no net movement of solvent. Osmotic pressure is a colligative property, meaning that the osmotic pressure depends on the molar concentration of the solute but not on its identity.

CHEMICAL PROPERTIES OF WATER

Water is not just a passive component of the cell or extracellular environment. By virtue of its physical properties, water defines the solubilities of other substances. Similarly, water's chemical properties determine the behavior of other molecules in solution.

IONIZATION OF WATER

As H_2O is the medium of biological systems one must consider the role of this molecule in the dissociation of ions from biological molecules. Water is essentially a neutral molecule but will ionize to a small degree. This can be described by a simple equilibrium equation:

H_2O <——> $H^+ + OH^-$

There is actually no such thing as a free proton (H+) in solution. Rather, the proton is associated with a water molecule as a hydronium ion, H_3O^+.

$$2H_2O\ (l) \rightleftharpoons H_3O^+(aq) + OH^-(aq)$$

The other product of water's ionization is the hydroxide ion, OH^-. The proton of a hydronium ion can jump more rapidly to another water molecule and then to another. Proton jumping is also responsible for the observation that acid-base reactions are among the fastest reactions that take place in aqueous solution.

The ionization (dissociation) of water is described by an equilibrium expression in which the concentration of the parent substance is in the denominator and the concentration of the dissociated products are in the numerator.

This equilibrium can be calculated as for any reaction:

$$K_{eq} = \frac{[H^+][OH^-]}{[H_2O]}$$

Because the concentration of the dissociated H_2O is so much larger than the concentrations of its component ions, it can be considered constant and incorporated into K to yield an expression for the ionization of water,

$$K_w = [H^+][OH^-]$$

The value of K_w, the ionization constant of water is 10^{-14} at 25^0C.

This term is referred to as the ion product. In pure water, to which no acids or bases have been added:

$K_w = 1 \times 10^{-14}\ M^2$

As K_w is constant, if one considers the case of pure water to which no acids or bases have been added:

$[H^+] = [OH^-] = 1 \times 10^{-7}$ M

Pure water must contain equimolar amount of H^+ and OH^-, Solutions with $[H+] = 10^{-7}$ M are said to be neutral, those with $[H+] > 10^{-7}$ are said to be acidic, and those with $[H+] < 10^{-7}$ are said to be basic. Most physiological solutions have hydrogen ion concentrations near neutrality. For example the human blood is normally slightly basic with $[H+] = 4.0 \times 10^{-8}$ M.

A more practical quantity, which was devised in 1909 by Søren Sørenson is known as the pH:

$pH = – \log [H^+] = \log 1/[H+]$

The higher the pH, the lower is the H+ concentration; the lower the pH, the higher is the H+ concentration.

Acid-Base Reaction

Johannes Bronsted and Thomas lowry formulated general definition of acid and base, an acid is a substance that can donate protons and a base is a substance that can accept protons. Under this

$$HA + H_2O \ <\!\!\longrightarrow H_3O^+ + A^-$$

A Bronsted acid (HA) react with Bronsted base (H_2O) to form the conjugate base of the acid (A^+) and the conjugate acid of the base (H_3O^+).

$$HA \ <\!\!\longrightarrow H^+ + A^-$$

Accordingly, the acetate ion (CH_3COO^-) is the conjugate base of acetic acid (CH_3COOH) and the ammonium ion (NH_4^+) is the conjugate acid of ammonia (NH_3)

Gilbert Lewis described a lewis acid as a substance that can accept an electron pair and a Lewis base as a substance that can donate an electron pair.

pK_a

Acids and bases can be classified as proton donors and proton acceptors, respectively. This means that the conjugate base of a given acid will carry a net charge that is more negative than the corresponding acid. In biologically relevant compounds various weak acids and bases are encountered, e.g. the acidic and basic amino acids, nucleotides, phospholipids etc.

Weak acids and bases in solution do not fully dissociate and, therefore, there is an equilibrium between the acid and its conjugate base. This equilibrium can be calculated and is termed the **equilibrium constant = K_a**. This is also sometimes referred to as the dissociation constant as it pertains to the dissociation of protons from acids and bases.

In the reaction of a weak acid:

$HA <\!\!\longrightarrow A^- + H^+$

the equilibrium constant can be calculated from the following equation:

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

As in the case of the ion product:

$pK_a = -\log K_a$

Therefore, in obtaining the –log of both sides of the equation describing the dissociation of a weak acid we arrive at the following equation:

$$-\log K_a = -\log \frac{[H^+][A^-]}{[HA]}$$

Since as indicated above $-\log K_a = pK_a$ and taking into account the laws of logrithms:

$$pK_a = -\log[H^+] - \log \frac{[A^-]}{[HA]}$$

$$pK_a = pH - \log \frac{[A^-]}{[HA]}$$

From this equation it can be seen that the smaller the pK_a value the stronger is the acid. This is due to the fact that the stronger an acid the more readily it will give up H^+ and, therefore, the value of [HA] in the above equation will be relatively small.

BUFFERS

A buffer solution is one that resists a change in pH on the addition of acid (H+) or base (OH−), more effectively than an equal volume of water. Most commonly, the buffer solution consists of a mixture of a weak Brönsted acid and its conjugate base; for example, mixtures of acetic acid and sodium acetate or of ammonium hydroxide and ammonium chloride are buffer solutions. A buffer system consists of a weak acid (the proton donor) and its conjugate base (the proton acceptor). As an example, a mixture of equal concentrations of acetic acid and acetate ion, found at the midpoint of the titration curve, is a buffer system. The titration curve of acetic acid has a relatively flat zone extending about 0.5 pH units on either side of its midpoint pH of 4.76. In this zone, there is only a small change in pH when increments of either H+ or OH − are added to the system. This relatively flat zone is the buffering region of the acetic acid-acetate buffer pair. At the midpoint of the buffering region, where the concentration of the proton donor (acetic acid) exacts equals that of the proton acceptor (acetate), the buffering power of the system is maximal, i.e., its pH changes least on addition of an increment of H+ or OH − The pH at this point in the titration curve of acetic acid is equal to its pKa. The pH of the acetate buffer system does change slightly when a small amount of H^+ or OH^- is added, but this change is very small compared with the pH change that would result if the sameamount of H^+(or OH^-) were added to pure water or to a solution of the salt of a strong acid and strong base, such as NaCl, which have no buffering power. Each conjugate-acid-base pair has a characteristic pH zone in which it is an effective buffer. The $H_2PO_4^-$/ HPO_4^{2-}pair has a pKa of 6.86 and thus can serve as a buffer system near pH 6.86; the NH_4^+/NH_3 pair, with a pKa of 9.25, can act as a buffer near pH 9.25.

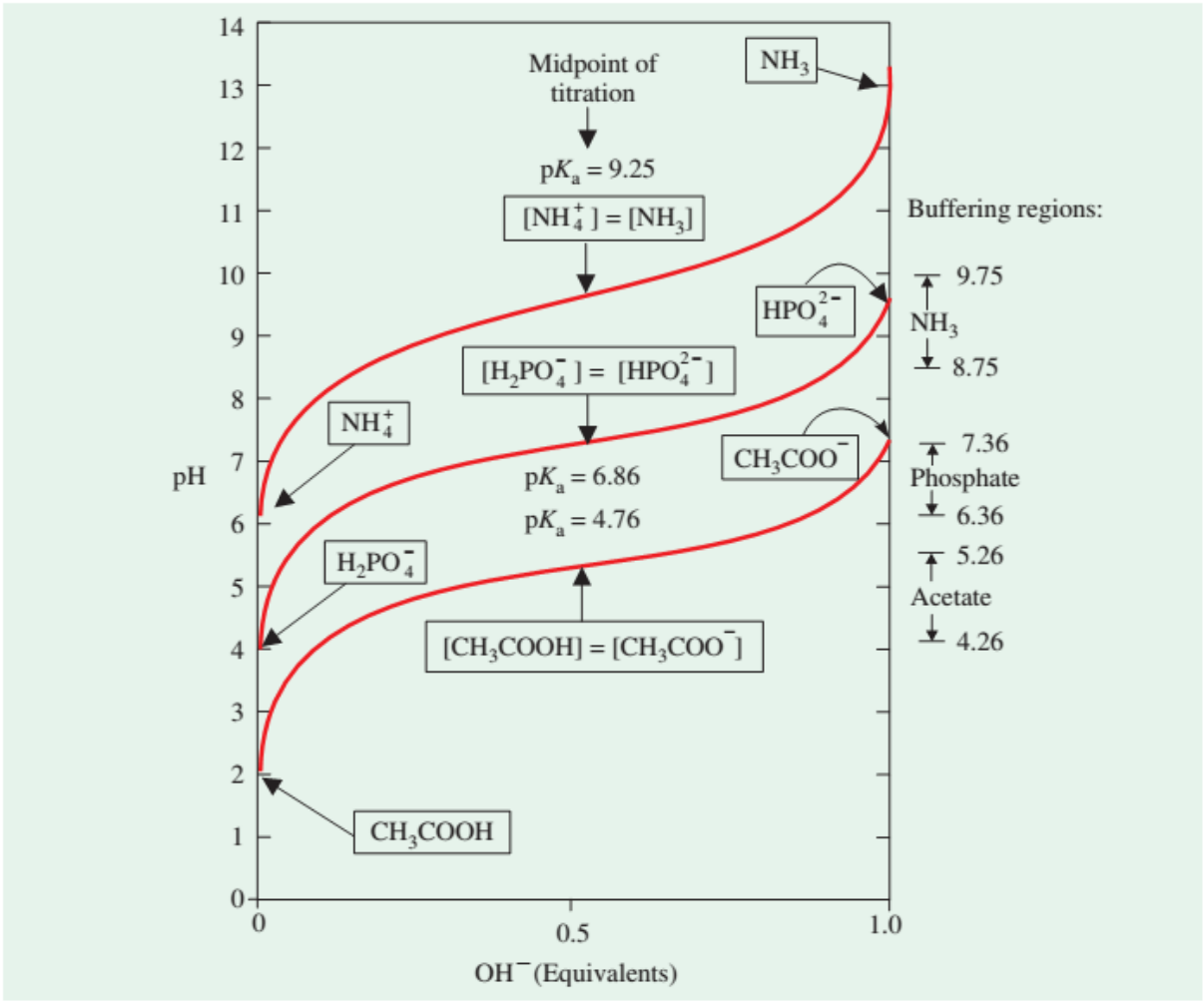


Fig. 3–6. Comparison of the titration curves of 3 weak acids, CH_3COOH, $H_2PO_4^-$ and NH_4^+

Henderson−Hasselbalch Equation

The quantitative relationship among pH, buffering action of a mixture of weak acid with its conjugate base, and the pK_a of the weak acid is given by a simple expression called Henderson-Hasselbalch Equation. The titration curves of acetic acid, $H_2PO_4^-$and $NH4^+$ have nearly identical shapes, suggesting that they all point towards a fundamental law or relationship. This is actually the case. The shape of the titration curve of any weak acid is expressed by Henderson−Hasselbalch equation. This equation is simply a useful way of restating the expression for the dissociation constant of an acid. For the dissociation of a weak acid HA into $H^+$and A^-, the Henderson−Hasselbalch equation can be derived as follows:

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

1. Rearrange the K_a equation to solve for $(H^+]$:

$$[H^+] = K_a \frac{[HA]}{[A^-]}$$

2. Convert to logarithmic functions:

$$\log [H^+] = \log K_a + \log \frac{[HA]}{[A^-]}$$

3. Make the expression negative (or multiply by −1):

$$-\log [H^+] = -\log K_a - \log \frac{[HA]}{[A^-]}$$

4. Substitute pH for $-\log [H^+]$ and pK_a for $-\log K_a$

$$\text{pH} = pK_a - \log \frac{[\text{HA}]}{[\text{A}^-]}$$

5. Now, to remove the minus sign, invert the last term, i.e., −log [HA]/[A]−to obtain HendersonHasselbalch equation :

$$\text{pH} = pK_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$$

The equation is expressed more generally as:

$$\text{pH} = pK_a + \log \frac{[\text{proton acceptor}]}{[\text{proton donor}]}$$

This equation fits the titration curve of all weak acids and enables one to deduce a number of important quantitative relationships. Henderson-Hasselbalch equation is of great predictive value in protonic equilibria as illustrated below:

A. When [A−] = [HA] or when an acid is exactly half neutralized: Under these conditions,

$$\text{pH} = pK_a + \log \frac{[\text{A}^-]}{[\text{HA}]} = pK_a + \log \frac{1}{1} = pK_a + 0 = pK_a.$$

Therefore, at half neutralization, pH = pK_a. The equation, thus, shows why the pK_a of a weak acid is equal to the pH of the solution at the midpoint of its titration.

B. When the ratio [A−]/[HA] = 100 to 1 :

$$\text{pH} = pK_a + \log \frac{[\text{A}^-]}{[\text{HA}]} = pK_a + \log \frac{100}{1} = pK_a + 2$$

C. When the ratio [A−]/[HA] = 1 to 10 :

$$\text{pH} = pK_a + \log \frac{[\text{A}^-]}{[\text{HA}]} = pK_a + \log \frac{1}{10} = pK_a + (-1)$$

If the equation is evaluated at several ratios of [A–] / [HA] between the limits 10^3 and 10^{-3}, and the calculated pH values plotted, the result obtained describes the titration curve for a weak acid.

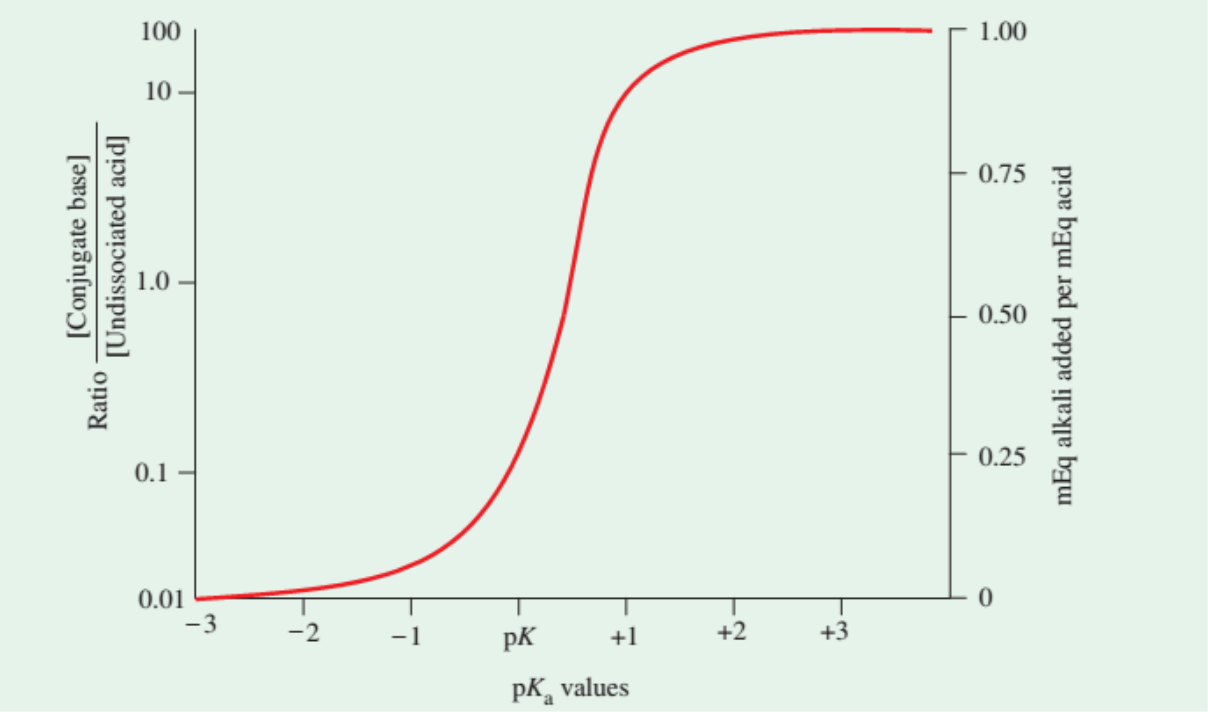


Fig. 3–7. General form of a titration curve calculated from the Henderson-Hasselbalch equation

BIOLOGICAL BUFFER SYSTEMS

Almost every biological process is pH-dependent; a small change in pH produces a large change in the rate of the process. This is true not only for the many reactions in which the H+ ion is a direct participant, but also for those in which there is no apparent role for H+ ions. The enzymes and many of the molecules on which they act, contain ionizable groups with characteristic pK_a values. The protonated amino ($-NH_3^+$) and carboxylic groups of amino acids and the phosphate groups of nucleotides, for example, function as weak acids; their ionic state depends upon the pH of the solution in which they are dissolved. Cells and organisms maintain a specific and constant cytosolic pH, keeping biomolecules in their optimal ionic state, usually near pH 7. In multicelled organisms, the pH of the extracellular fluids (blood, for example) is also tightly regulated. Constancy of pH is achieved primarily by biological buffers: mixtures of weak acids and their conjugate bases. The table below shows some important buffering systems of body fluids which help maintaining pH. A certain amount of many of these is usually present in the body and cellular fluids, and so the maintenance of a constant pH depends on a complex system.

Table 3–5. Body fluids and their principal buffers

Body fluids	*Principal buffers*
Extracellular fluids	Biocarbonate buffer Protein buffer
Intracellular fluids	Phosphate buffer Protein
Erythrocytes	Hemoglobin buffer

1. The Phosphate Buffer System

This system, which acts in the cytoplasm of all cells, consists of $H_2PO_4^-$ as proton donor and HPO_4^{2-} as proton acceptor:

$$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$$

The phosphate buffer system works exactly like the acetate buffer system, except for the pH range in which it functions. The phosphate buffer system is maximally effective at a pH close to its pKa of 6.86, and thus tends to resist pH changes in the range between 6.4 and 7.4. It is, therefore, effective in providing buffering power in intracellular fluids. Since the concentration of phosphate buffer in the blood plasma is about 8% of that of the bicarbonate buffer, its buffering capacity is much lower than bicarbonate in the plasma. The concentration of phosphate buffer is much higher in intracellular fluid than in extracellular fluids. The pH of intracellular fluids (6.0 −6.9) is nearer to the pKa of the phosphate buffer. Therefore, the buffering capacity of the phosphate buffer is highly elevated inside the cells and the phosphate is also effective in the urine inside the renal distal tubules and collecting ducts.

2. The Bicarbonate Buffer System

This is the main extracellular buffer system which (also) provides a means for the necessary removal of the CO_2 produced by tissue metabolism. The bicarbonate buffer system is the main buffer in blood plasma and consists of carbonic acid as proton donor and bicarbonate as proton acceptor:

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

The pH of a bicarbonate buffer system depends on the concentration of H2CO3and HCO_3^-, the proton donor and acceptor components. The concentration of H_2CO3, in turn, depends on the concentration of dissolved CO_2, which, in turn, depends on the concentration or partial pressure of CO_2 in the gas phase. With respect to the bicarbonate system, a $[HCO3^-]$ / $[H_2CO_3]$ ratio of 20 to 1 is required for thepH of blood plasma to remain 7.40.

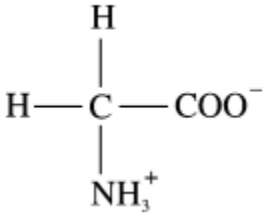
3. The Protein Buffer Systems

The protein buffers are very important in the plasma and the intracellular fluids but their concentration is very low in cerebrospinal fluid, lymph and interstitial fluids. The proteins exist as anions serving as conjugate bases (Pr^-) at the blood pH 7.4 and form conjugate acids (HPr) accepting H^+. They have the capacity to buffer some H2CO3 in the blood.

$$H_2CO_3 + Pr^- \rightleftharpoons HCO_3^- + HPr$$

4. The amino acids buffer system

This system also operates in humans. Amino acids contain in their molecule both an acidic (−COOH) and a basic ($-NH_2$) group. They can be visualized as existing in the form of a neutral zwitterion in which a hydrogen atom can pass between the carboxyl and amino groups. The glycine may, thus, be represented as:



By the addition or subtraction of a hydrogen ion to or from the zwitterion, either the cation or anion form will be produced:

$$\underset{\text{Cation form}}{{}^+H_3N{-}CH_2{-}COOH} \xleftarrow{+H^+} \underset{\text{Zwitterion}}{{}^+H_3N{-}CH_2{-}COO^-} \rightleftharpoons \underset{\text{Anion form}}{H_2N{-}CH_2{-}COO^-} + H^+$$

Thus, when OH^- ions are added to the solution of amino acid, they take up H^+ from it to form water, and the anion is produced. If H^+ions are added, they are taken up by the zwitterion to

produce the cation form. In practice, if NaOH is added, the salt $H_2N\text{-}CH_2\text{-}COONa$ would be formed H^+ and the addition of HCl would result in the formation of amino acid hydrochloride, $Cl\text{-}H\text{ -}H_3N\text{-}CH_2\text{-}COOH$, but these substances would ionize in solution to some extent to form their corresponding ions. Hemoglobin and plasma proteins act as buffers in a similar way.Amino acids differ in the degree to which they will produce the cation or anion form. In other words, a solution of an amino acid is not neutral but is either predominantly acidic or basic, depending on which form is present in greater quantity. For this reason, different amino acids may be used as buffers for different pH values, and a mixture of them possesses a wide buffer range.

5. The Hemoglobin Buffer Systems

These buffer systems are involved in buffering CO_2 inside erythrocytes. The buffering capacity of hemoglobin depends on its oxygenation and deoxygenation. Inside the erythrocytes, CO_2 combines with H_2O to form carbonic acid (H_2CO_3) under the action of carbonic anhydrase. At the blood pH 7.4, H_2CO_3dissociates into H^+ and $HCO_3^-$and needs immediate buffering. Oxyhemoglobin (HbO_2^-), on the other side, loses $O_2$to form deoxyhemoglobin (Hb^-) which remains undissociated (HHb) by accepting $H^+$from the ionization of H_2CO_3. Thus, Hb^- buffers H_2CO_3 in erythrocytes :

$$HbO_2^- \rightleftharpoons Hb^- + O_2$$
$$Hb^- + H_2CO_3 \rightleftharpoons HHb + HCO_3^-$$

Some of the HCO_3^- diffuse out into the plasma to maintain the balance between intracellular and plasma bicarbonates. This causes influx of some Cl^- into erythrocytes along the electrical gradient produced by the HCO_3^- outflow (chloride shift). $HHbO_2$, produced in lungs by oxygenation of HHb, immediately ionizes into H^+ and HbO_2^-. The released hydrogen ions (H^+) are buffered by HCO_3^- inside erythrocyte to form H_2CO_3 which is dissociated into H_2O and CO_2 by carbonic anhydrase. CO_2 diffuses out of erythrocytes and escapes in the alveolar air. Some HCO_3^- return from the plasma to erythrocytes in exchange of Cl^- and are changed to CO_2 .

$$HHb + O_2 \rightleftharpoons HHbO_2 \rightleftharpoons HbO_2^- + H^+$$
$$HCO_3^- + H^+ \rightleftharpoons H_2CO_3 \rightleftharpoons H_2O + CO_2$$

THERMODYNAMICS

Thermodynamics is the study of energy in systems, and the distribution of energy among components. In chemical systems, it is the study of chemical potential, reaction potential, reaction direction, and reaction extent. If we know the energy changes associated with a reaction or process, we can predict the equilibrium concentrations. We can also predict the direction of a reaction provided we know the initial concentrations of reactants and products. The thermodynamic quantity that provides this information is the Gibbs free energy.

FREE ENERGY

The energy actually available to do work (utilizable) is known as free energy. The Gibbs free energy change (ΔG) for a reaction is the difference between the free energy of the products and of the reactants. The overall Gibbs free energy change has two components known as the enthalpy change (ΔH, the change in heat content) and the entropy change (ΔS, the change in randomness). A biochemical process may generate heat or absorb it from the surroundings. Similarly, a process may occur with an increase or a decrease in the degree of disorder, or randomness, of the reactants.

$$\Delta G = \Delta H - T\Delta S$$

Starting with an initial solution of reactants and products, if the reaction proceeds to produce more products, then ΔG must be less than zero ($\Delta G < 0$). In chemistry terms, we say that the reaction is spontaneous and energy is released. When ΔG is greater than zero ($\Delta G > 0$), the reaction requires external energy to proceed and it will not yield more products. In fact more reactants will accumulate as the reverse reaction is favored. When ΔG equals zero ($\Delta G = 0$), the reaction is at equilibrium; the rate of the forward and reverse reactions are identical and the concentrations of the products and reactant no longer change.

A series of linked processes, such as the reactions of a metabolic pathway in a cell, usually proceeds only when associated with an overall negative Gibbs free energy change. Biochemical reactions or processes are more likely to occur, both to a greater extent and more rapidly, when they are associated with an increase in entropy and a decrease in enthalpy.

If we know the Gibbs free energy of every product and every reactant, it would be a simple matter to calculate the free energy change for a reaction by using:

$$\Delta G_{reaction} = \Delta G_{products} - \Delta G_{reactants}$$

What we need are some standard values of ΔG that can be adjusted for concentration. These standards are the Gibbs free energy changes measured under certain conditions. By convention, standard conditions are $25^{o}C$ (298K), 1 atm standard pressure, and 1.0 M of all products and reactants. In most biochemical reaction, the concentration of H^{+} is important, and this is

indicated by the pH. The standard condition for biochemistry reactions is pH = 7.0, which correspond to 10^{-7} M H^+ (rather than 1.0 M as for other reactants and products). The Gibbs free energy change under these standard conditions is indicated by the symbol $\Delta G^{o'.}$

The actual Gibbs free energy is related to its standard free energy by

$$\Delta G_A = \Delta G_A^{o'} + RT \ln [A]$$

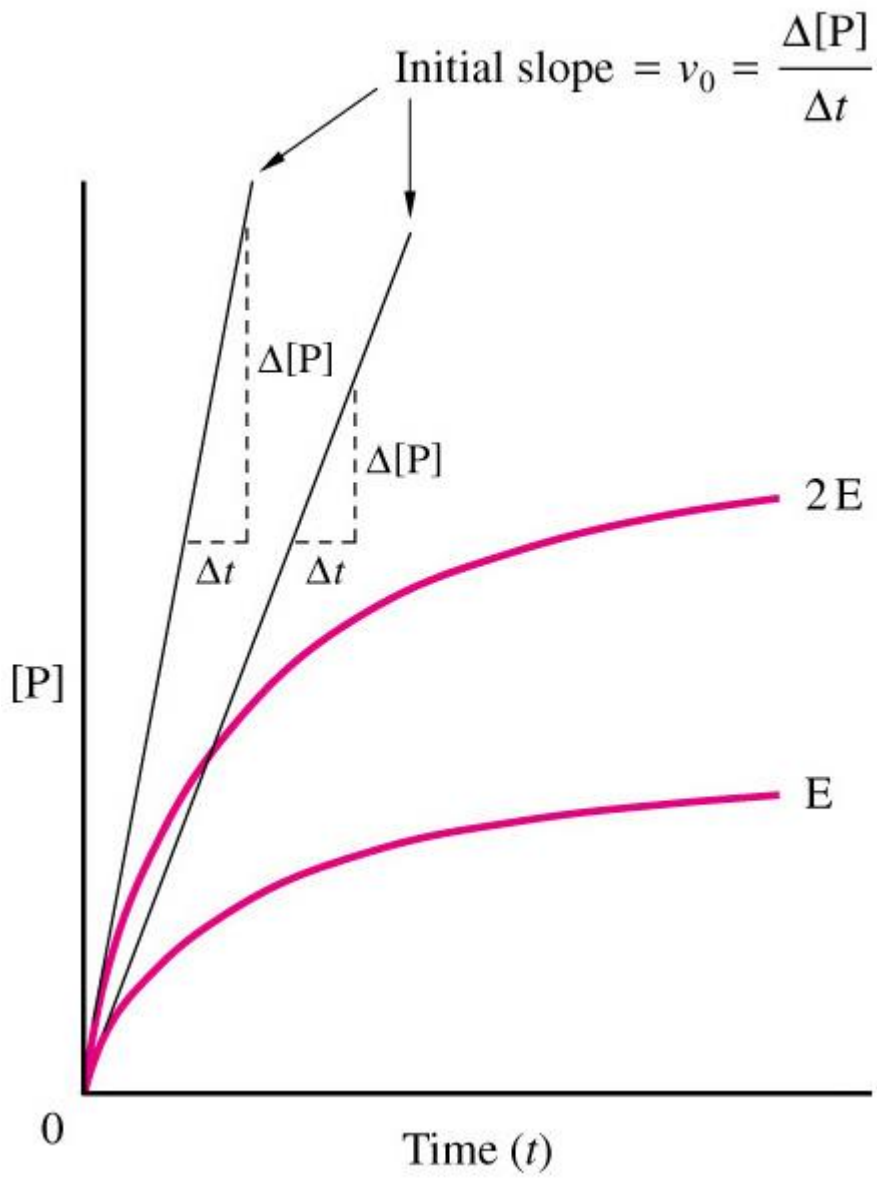
Where R is the universal gas constant ($8.315 kJ^{-1}$) and T is the temperature in kelvin. The term RTln[A] is sometimes given as 2.303 RTlog[A].

CHEMICAL KINETICS

Kinetic experiments examine the relationship between the amount of product (P) formed in a unit time ($\Delta[p]/\Delta t$) and the experimental conditions under which the reaction take place. The basis of most kinetic measurements is the observation that the rate, or velocity (v), of a reaction varies directly with the concentration of each reactant. This observation is expressed in a rate equation. For example the rate equation for the non- enzymatic conversion of substrate (S) to product in an isomerization reaction is written as

$$\Delta[p]/\Delta t = v = k[s]$$

The rate equation reflects the fact that the velocity of a reaction depends on the concentration of the substrate ([s]). The symbol k is the rate constant and indicates the speed or efficiency of a reaction. Each reaction has a different rate constant. The units of the rate constant for a simple reaction are $s^{-1.}$.



As a reaction proceeds, the amount of product ([p]) increases and the amount of substrate ([s]) decreases. An example of the progress of several reactions is shown in graph above. The velocity is the slope of the progress curve over a particular interval of time. The shape of the curves indicates that the velocity is decreasing over time as expected since the substrate is being depleted.

OXIDATION-REDUCTION REACTIONS

Oxidation-reduction reactions are central to the supply of biological energy. In an oxidation-reduction (redox) reaction, electrons from one molecule are transferred to another. Oxidation is the loss of electrons: a substance that is oxidized will have fewer electrons when the reaction is complete. Reduction is the gain of electrons: a substance that gains electrons in a reaction is reduced. Oxidation and reduction reactions always occur together. One substrate is oxidized and the other is reduced. An oxidizing agent is a substance that causes an oxidation-it takes electrons from the substrate that it oxidized. Thus, oxidizing agents gain electrons (i.e., they are reduced). A reducing agent is a substance that donates electrons (and is oxidized in the process).

Oxidation can take several forms, such as removal of hydrogen (dehydrogenation), addition of oxygen, or removal of electrons. Dehydrogenation is the most common form of biological oxidation. Oxidoreductases (enzymes that catalyze oxidation-reduction reactions) represent a large class of enzymes and dehydrogenases (enzymes that catalyze removal of hydrogen) are a major subclass of oxidoreductases.

Most dehydrogenations occur by C-H bond cleavage producing a hydride ion (H^-). The substrate is oxidized because it loses the electrons associated with the hydride ion. Such reactions will be accompanied by a corresponding reduction where another substrate gains electron by reacting with the hydride ion. The dehydrogenation of lactate is an example of removal of hydrogen. In this case the oxidation of lactate is coupled to the reduction of the coenzyme NAD^+.

The nicotinamide coenzymes play a role in many oxidation-reduction reactions. They assist in the transfer of electrons to and from metabolite. The oxidized forms, NAD^+ and $NADP^+$, are electron deficient and the reduced forms, NADH and NADPH carry an extra pair electron in the form of a covalently bound hydride ion.

Electrochemical cell

Test

1. Describe the hydrogen bonding in water

This is a chemical bond between hydrogen and an electronegative atom such as oxygen, chlorine etc. The attraction between one of the slightest positive hydrogen atoms of one water molecule and the slightest negative electron pairs in one of the sp3 hybrid orbitals produces a hydrogen bond. In a hydrogen bond between two water molecules, the hydrogen atom remains covalently bonded to its oxygen atom, the hydrogen donor. At the same time, it is attracted to another oxygen atom called the hydrogen acceptor. In effect, the hydrogen atom is being shared (unequally) between the two oxygen atoms. The distance from the hydrogen atom to the acceptor oxygen is about twice the length of the covalent bond. The distance from the hydrogen atom to

the acceptor oxygen is about twice the length of the covalent bond. Water is the only molecule capable of forming hydrogen bonds; these interactions can occur between any electronegative atom and hydrogen attached to another electronegative atom. Hydrogen bonds are much weaker than typical covalent bonds. The strength of hydrogen bonds in water and in solution is estimated to be about 20 kJ mol^{-1}. The strength of hydrogen bond is less than 5% of the strength of typical covalent bonds. Hydrogen bonds are weak interactions compared to covalent bonds but their large number is the reason for the stability of liquid water. Water molecules are unusual because they can form four O—H—O aligned hydrogen bonds with up to four other water molecules. They can donate each of their two hydrogen atoms to two other water molecules and accept two hydrogen atoms from two other water molecules. Each hydrogen atom can participate in only one hydrogen bond.

H—O—H + H—O—H → O—H-----O ΔH_f = -20 kJ mol^{-1}

Hydrogen Bonding

2. What are osmosis and its advantages in a biological system?

Osmosis occurs when two solutions of different concentrations are separated by a membrane which will selectively allow some species through it but not others. Then, material flows from the less concentrated to the more concentrated side of the membrane. A membrane which is selective in the way just described is said to be **semipermeable**. Osmosis is of particular importance in living organisms, since most living tissue is semipermeable in one way or another. Osmosis also is the net movement of solvent molecules through a partially permeable membrane into a region of higher solute concentration, in order to equalize the solute concentrations on the two sides. It may also be used to describe a physical process in which any solvent moves, without input of energy, across a semipermeable membrane (permeable to the solvent, but not the solute) separating two solutions of different concentrations. Although osmosis does not require input of energy, it does use kinetic energy and can be made to do work.

The tendency for osmotic flow to occur from a solvent to a solution is usually measured in terms of what is called the osmotic pressure of the solution, symbol Π. This osmotic pressure is not a pressure which the solution itself exerts but is rather the pressure which must be applied to the solution (but not the solvent) from outside in order to just prevent osmosis from occurring. The osmotic pressure is defined to be the pressure required to maintain equilibrium, with no net movement of solvent. Osmotic pressure is a colligative property, meaning that the osmotic pressure depends on the molar concentration of the solute but not on its identity.

3. Using Henderson Hasselbalch equation describe buffering and its advantage in a biological system.

   Henderson-Hasselbalch equation: the relationship between the pH of a solution and the concentrations of an acid and its conjugate base by rearranging:

   $[H^+] = K([H^+]/[A^+]$

   Taking log of both side of the equation (above)

$$pH = pK_a + \log\frac{[A^-]}{[HA]}$$

   It should be obvious now that the pH of a solution of any acid (for which the equilibrium constant is known, and there are numerous tables with this information) can be calculated knowing the concentration of the acid, HA, and its conjugate base $[A^-]$. This equation indicates that the pK of an acid is numerically equal to the pH of the solution when the molar concentrations of the acid and its conjugate base are equal.

   At the point of the dissociation where the concentration of the conjugate base $[A^-]$ = to that of the acid [HA]:

   $pH = pK_a + \log[1]$

   The log of 1 = 0, Thus, at the mid-point of a titration of a weak acid:

   $pK_a = pH$

   In other words, the term pK_a is that pH at which an equivalent distribution of acid and conjugate base (or base and conjugate acid) exists in solution. The **Henderson-Hasselbalch equation** is often used by chemists and biologists to calculate the pH of a buffer.

4. What is hydrophobic effect?

When a nonpolar substance is added to an aqueous solution, it does not dissolve but instead is excluded by the water. The tendency of water to minimize its contact with hydrophobic molecules is termed the hydrophobic effect. Many large molecules and molecular aggregates, such as proteins, nucleic acids, and cellular membranes, assume their shapes at least partially in response to hydrophobic effect. The hydrophobic effect, which causes nonpolar substances to minimize their contacts with water, is the major determinant of native protein structure. The aggregation of nonpolar side chains in the molecules that would otherwise form ordered “cages” around the hydrophobic groups. Aggregation of the nonpolar molecules increases the entropy of

the system, since the number of water molecules required to hydrate the aggregated solute is less the number of water molecule required to hydrate the dispersed solute molecules. This increase in entropy accounts for the spontaneous aggregation of nonpolar substances in water.

5. What is pH?

$pH = – \log [H^+] = \log 1/[H+]$

The higher the pH, the lower is the H+ concentration; the lower the pH, the higher is the H+ concentration.

$[H^+] = [OH^-] = 1 \times 10^{-7}$ M

Pure water must contain equimolar amount of H^+ and OH^-, Solutions with $[H+] = 10^{-7}$ M are said to be neutral, those with $[H+] > 10^{-7}$ are said to be acidic, and those with $[H+] < 10^{-7}$ are said to be basic. Most physiological solutions have hydrogen ion concentrations near neutrality. For example the human blood is normally slightly basic with $[H+] = 4.0 \times 10^{-8}$ M.

3. Buffer is a solution that resist the change in pH as result of change in hydrogen or hydroxyl ion concentration. The ability of a buffer to resist pH changes with added acid or base is directly proportional to the total concentration of the conjugate acid-base pair, $[HA] + [A^-]$. It is maximal when pH = pK and decreases rapidly with a change in pH from that point. When $[HA] = [A^-]$, the pH of the solution is relatively insensitive to the addition of strong base or strong acid. Such a solution, which is known as an acid-base buffer, is resistant to pH changes because small amounts of added H^+ or OH^-, respectively, react with A^- or HA present without greatly changing the value of $\log ([A^-]/[HA])$.

4. Water is a ‘universal solvent’

The polar character of water makes it an excellent solvent for polar and ionic materials, which are said to be hydrophilic. On the other hand, nonpolar substances are virtually insoluble in water and are consequently described as hydrophobic. Polar solvents such as water weaken the attractive forces between oppositely charged ions (such as Na^+ and Cl^-) and can therefore hold the ions apart. (In nonpolar solvents, ions of opposite charge attract each other so strongly that they coalesce to form a solid salt.) An ion immersed in a polar solvent such water attracts the oppositely charged ends of the solvent dipoles. The ion is thereby surrounded by one or more concentric shells of oriented solvent molecules. Such ions are said to be solvated or, when water is the solvent, to be hydrated.

6b. water is not the only polar solvent. Oxygen atoms are more electronegative than hydrogen atoms because an oxygen nucleus attracts electron attracts electrons more strongly than the single proton in the hydrogen nucleus. As a result, an uneven distribution of charge occurs within each O-H bond of the water molecule with oxygen bearing a partial negative charge and

hydrogen bearing a partial positive charge. This uneven distribution of charge within a bond is known as a dipole and the bond is said to be polar. The polarity of a molecule depends on the polarity of its covalent bonds and it geometry. The angled arrangement of the polar O-H bonds of water creates a permanent dipole for the molecule. Water and gaseous ammonia are electrically neutral, both molecule are polar. The high solubility of polar ammonia molecules in water is facilitated by strong interactions with polar water molecules. The solubility of ammonia in water demonstrates the principle that “likes dissolves likes”.