Chemical Components of Cells

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eLearning in Studienbereichen – MNF – Universität Potsdam

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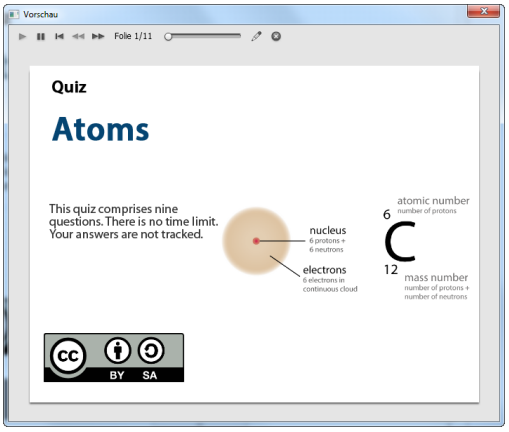
Letzte Überarbeitung: **Februar 2015**.

I. Components of Life

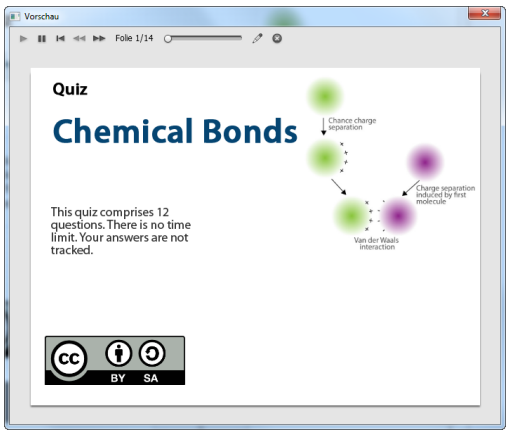
Matter consists of chemical elements. Chemical bonds hold atoms together. Water is essential to all known forms of life. Water is the universal solvent. The hydrophobic effect is the property that nonpolar molecules tend to form intermolecular aggregates (or intramolecular interactions) in an aqueous medium. Amphiphiles form structurally ordered aggregates such as lipid bilayers.

Quizzes

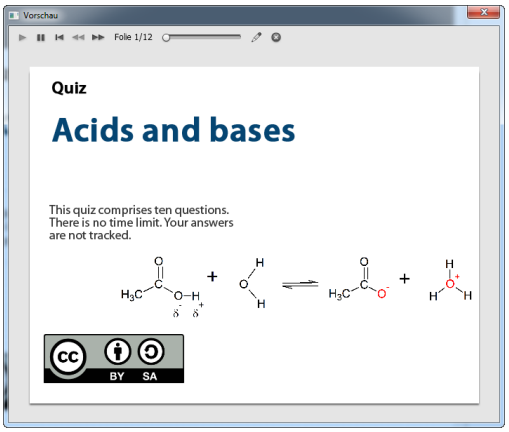
Start this chapter with the quizzes to test for your mastery. You may reattempt the quizzes later to check your progress.



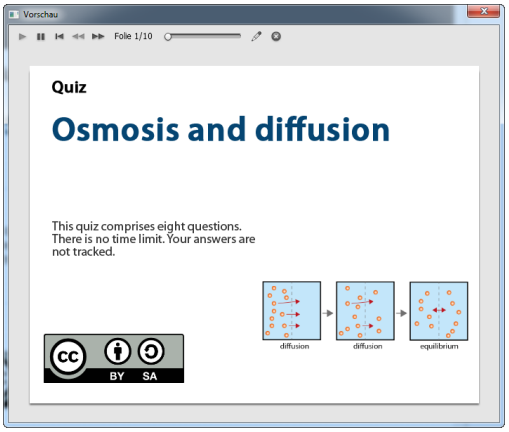
Quiz 1. Atoms. Click to play - HTML5 or Flash (opens new window in your standard web browser).



Quiz 2. Chemical bonds. Click to play - HTML5 or Flash (opens new window in your standard web browser).



Quiz 3. Acids and bases. Click to play - HTML5 or Flash (opens new window in your standard web browser).



Quiz 4. Diffusion and osmosis. Click to play - HTML5 or Flash (opens new window in your standard web browser).

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Matter and elements

Matter is anything that has mass and occupies space. Matter consists of chemical elements.

Chemical elements are compounds which cannot be further divided into other compounds. A chemical element is defined by its **atomic number**, that is, by the number of protons in its nucleus. All atoms of a given element have the same atomic number. This number dictates the chemical properties of the element.

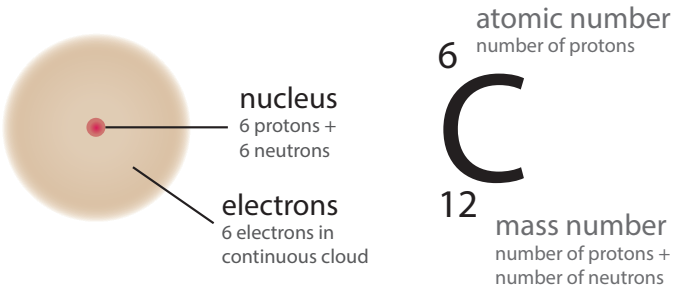

Figure 1. The carbon atom. An atom consists of a nucleus and electron cloud. The positively charged nucleus contains the atom's mass (protons and neutrons). The atomic number indicates the number of protons. The mass number indicates the number of protons and neutrons (each with atomic mass 1). The electrons are considered to have zero mass.

The electric charge carried by each proton is equal and opposite to the charge carried by a single **electron**. The whole atom is electrically neutral, because the number of negatively charged electrons surrounding the nucleus is equal to the number of positively charged protons.

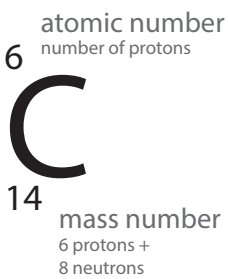

Figure 2. Carbon-14 isotope.

In addition to protons, the positively charged nucleus also consists of **neutrons**, which are electrically neutral and have the same mass as protons. They contribute to the structural stability of the nucleus. If there are too many or too few neutrons, the nucleus may disintegrate by radioactive decay.

An element can exist in several forms called **isotopes**, each isotope having different number of neutrons but the same number of protons.

For more details on elements, atoms, and isotopes see:

IUPAC (2013) Periodic table of the elements (PDF)

UC Davis ChemWiki (2014) Periodic table of the elements (interactive)

GCSE Bitesize Chemistry - The BBC (2014) Atomic structure

Khanacademy (2014) Atomic number, mass number, and isotopes

There are **92** elements which occur naturally (and over 100 known elements), each differing from the others in the number of protons and electrons in its atoms.

Life requires only about **25** chemical elements. Four elements (**carbon, oxygen, hydrogen and nitrogen**) make up **96%** of the living matter. These elements are the buildings blocks of molecules such as carbohydrates, proteins, and nucleic acids.

Phosphate, sulphur, calcium, potassium, magnesium, and iron account for nearly the rest (**4%**) and are required in larger amount by all organisms.

The **trace elements** or **micronutrients** which are needed can differ from organism to organism.

The electrons determine how atoms interact. Atoms with incomplete outer shells have a strong tendency to achieve a completed outermost shell.

This electron exchange can be achieved either by transferring electrons from one

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atom to another (ionic bonds, see page 5) or by sharing electrons between two atoms (covalent bonds, see below).

Chemical bonds

A **chemical bond** is an attractive force that holds atoms together. Chemical bonds are characterized in several ways. An obvious characteristic of a bond is its **strength**. Bond strengths are measured by the energy required to break them (in kilojoules per mole).

Covalent bonds

Covalent bonds are very strong. They are formed when two atoms share a pair of electrons.

In covalent bonds, electrons are shared.

Metals do not hold on to electrons with enough strength to participate in covalent bonding. The great majority of covalent bonds will form between two non-metals. Covalent compounds are called **molecules**.

Strong bonds almost never fall apart at physiological temperatures. This is why atoms united by covalent bonds always belong to the same molecule.

The free energy – expressed as ΔG – accompanying the formation of covalent bonds from free atoms such as hydrogen or oxygen is very large and negative (-200 to -450 kJ).

The **sharing of a single electron pair** (sharing of two valence electrons) is termed a **single bond**. For example, the molecule **methane** (Figure 3) has four covalent bonds, one between carbon and each of the four hydrogens. Carbon contributes an electron, and hydrogen contributes an electron.

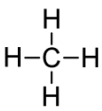

Figure 3. Methane has four single bonds.

When two pairs of electrons (four valence electrons) are shared, a **double bond** results. Examples are oxygen gas and ethylene (Figure 4).

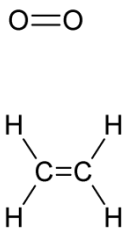

Figure 4. Oxygen molecule and ethylene.

Carbon and hydrogen atoms are usually not shown explicitly in skeletal formulas of an organic compound (Figure 5).

Figure 5. The ethylene molecule. C and H atoms are not shown explicitly.

Double bonds are stronger and shorter than single bonds and have a characteristic effect on the three-dimensional geometry of molecules containing them. A double bond prevents the rotation of one part of a molecule relative to the other around the bond axis.

Many molecules contain bonds that are intermediate in character between single and double bonds (**partial double bonds**).

For example, proteins are chains of amino acids held together by peptide bonds. Peptide bonds are formed when the carboxyl group of one amino acid reacts with the amino group of another amino acid.

The steric restriction of double bonds and partial double bonds has a major impact on the structure of macromolecules such as proteins and nucleic acids.

For example, the partial double-bond character of the peptide bond results in the inability of the bond to rotate, and this constrains the conformation of the peptide backbone.

Triple bonds are known, wherein three pairs (six valence electrons total) are shared. An example is nitrogen gas (Figure 6).

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N≡N

Figure 6. Nitrogen (N_2) molecule.

Polarity of covalent bonds

Polarity means unequal sharing of electrons. When the atoms joined by a covalent bond belong to different elements, the atoms attract the shared electrons to different degrees.

The atoms differ in a property called **electronegativity**. Electronegativity is a chemical property which describes the power of an atom to attract electrons towards itself.

Elecronegativity is a relative value:

0 < EN < 4.0.

Examples:

H: 2.20; C: 2.55; N: 3.04; O: 3.44; F: 3.98

Hydrogen bonds (see page 7) are the result of electrostatic attraction caused by the uneven distribution of electrons within covalent bonds.

For more details on electronegativity see:

Khanacademy (2014) Electronegativity

UC Davis ChemWiki (2014) Electronegativity

Ionic bonds

An ionic bond is formed when electrons are donated by one atom to another.

Ionic bonds are most likely to be formed by atoms that have one or two electrons in their unfilled outer shell or are just one or two electrons short of acquiring a filled outer shell.

Metals will lose electrons fairly readily, they tend not to gain electrons. In contrast, the atoms designated as non-metals have high electron affinities. They will gain electrons.

Ionic bonds are also regarded as strong bonds. However, ionic compounds do not exist as molecules. In the solid state, ionic compounds are in crystal lattices containing cations and anions.

Ionic bonding is a type of **electrostatic interaction**.

An **ion** is an atom or group of bonded atoms which have lost or gained one or more electrons, making them negatively or positively charged. A negatively charged ion, which has more electrons than protons is known as an **anion**. A positively-charged ion, which has fewer electrons than protons, is known as a **cation** (example NaCl, see Figure 7).

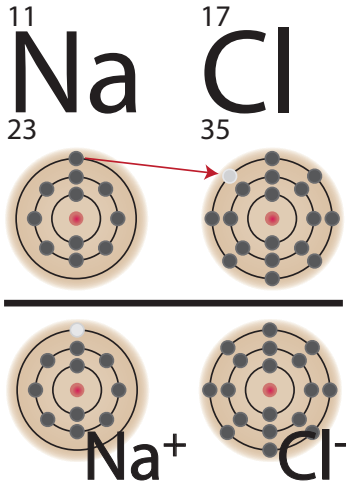

Figure 7. NaCl. Sodium has one valence electron in its outermost shell. In ionized form it is commonly found with one lost electron, as **Na^+**. Chlorine has seven valence electrons. In ionized form it is commonly found with one gained electron, as **Cl^-**. The overall effect in table salt, NaCl, is electrical neutrality. The electronegativity of Na and Cl is 0.93 and 3.16, respectively.

Many **organic molecules** possess ionic groups that contain one or more units of net positive or negative charge. Examples are the negative phosphate groups (e.g. of DNA and RNA), and the negative carboxyl group (COO^-) and positive amino group (NH_3^+) of amino acids.

In many cases, either an inorganic cation like Na^+, K^+ or Mg^{2+} or an inorganic anion like Cl^- or SO_4^{2-} neutralizes the charge of ionized organic molecules.

Ionic substances dissolve readily in water. In aqueous solution, cations and anions are usually surrounded by shells of water molecules and so do not directly

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bind to oppositely charged groups.

Thus, electrostatic bonds are usually not of primary importance in determining the molecular shapes of organic molecules such as proteins in water.

Weak chemical bonds

Weak bonds (or better: interactions) are easily broken, and when they exist singly, they exist fleetingly. Weak bonds represent intermolecular forces and are constantly made and broken at physiological temperatures.

Weak binding forces are effectively only when the interacting surfaces are close.

This proximity is possible only when the molecular surfaces have complementary structures. Weak interactions play a fundamental role in structural biology, polymer science, surface science etc. Only when present in ordered groups do weak bonds last a long time. For example, the secondary protein structures such as the α helix and the β sheets, and the tertiary structure of proteins are stabilized by a multitude of weak interactions.

Furthermore, weak bonds are particularly important for **short contacts** between molecules (e.g. in signalling pathways or in enzyme-substrate interactions).

Three main types of weak bonds are relevant for biological systems:

1. Van der Waals bonds.
2. Hydrophobic bonds (better described as hydrophobic effect).
3. Hydrogen bonds.

Van der Waals bonds

Van der Waals forces are non-covalent forces. Van der Waals bonding arises from a **non-specific attractive force** originating when two atoms come close to each other.

It is not based on the existence of permanent charge separations, but rather on the **induced fluctuating charges** caused by the nearness of molecules (Figure 8). It therefore operates between all types of molecules, nonpolar as well as polar. It depends heavily on the distance between the interacting groups.

Although van der Waals attractions are individually very weak, they can become important when two macromolecular surfaces fit very close together, because many atoms are involved. Van der Waals forces are an effective binding force at physiological temperatures only when several atoms in a given molecule are bound to several atoms in another molecule. Then the energy of interaction is greater than the dissociating tendency resulting from random thermal movements.

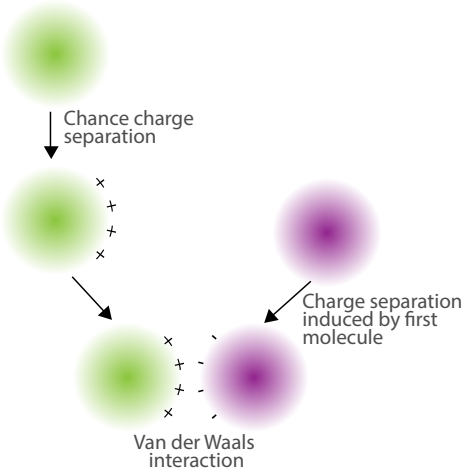

Figure 8. Van der Waals interaction.

There also exists a powerful **van der Waals repulsive force**, which comes into play at even shorter distances. This repulsion is caused by the overlapping of the outer electron shells of the atoms involved.

The van der Waals attractive and repulsive forces balance at a certain distance specific for each type of atom.

For more details on Van der Waals forces see:

UC Davis ChemWiki (2014) Van der Waals forces

IUPAC Compendium of Chemical Terminology (1994) Van der Waals forces

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Hydrogen bonds

This type of bond always involves a hydrogen atom, thus the name. Hydrogen bonds are a relatively strong form of intermolecular attraction.

The typical hydrogen bond is stronger than van der Waals forces, but weaker than covalent or ionic bonds. Hydrogen bonds are much more specific than van der Waals bonds, since they demand the existence of molecules with complementary donor hydrogen and acceptor groups.

Hydrogen bonds, unlike van der Waals bonds, are **highly directional**. In the strongest bonds, the hydrogen atom points directly at the acceptor atom. If it points more than 30° away, the bond energy is much less.

Hydrogen bonds are always formed between **pairs of groups**, with one of them (often C=O or C=N-) containing the negative end of a dipole and the other providing the proton.

Hydrogen bonds are the result of electrostatic attraction caused by the uneven distribution of electrons within covalent bonds. A hydrogen bond exists between an **electronegative atom** (oxygen in case of water) and a **hydrogen** bonded to another electronegative atom (oxygen of another molecule in case of water).

Thus, a hydrogen bond is formed between a covalently bound donor hydrogen atom with some positive charge and a negatively charged, covalently bound acceptor atom (Figure 9).

Examples of hydrogen bonds

Hydrogen bonds can occur between molecules (intermolecularly), or within different parts of a single molecule (intramolecularly).

Intramolecular bonding is partly responsible for the secondary, tertiary, and quaternary structures of proteins and nucleic acids. Hydrogen bonds also help enzymes bind to their substrates, help antibodies bind to their antigen, help transcription factors bind to each other and to bind DNA.

For more details on hydrogen bonds see:

UC Davis ChemWiki (2014) Hydrogen bonding

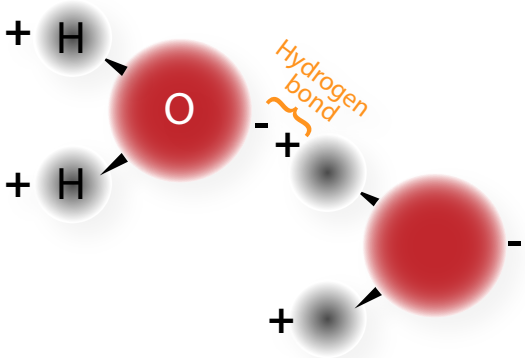

Figure 9. Hydrogen bond between two water molecules. The bonding electrons of the O-H bonds of water molecules are attracted more tightly to the oxygen atom than to the hydrogen atoms. A small positive charge is left on the hydrogen and a small negative charge on the oxygen.

Water

Water is essential to all known forms of life. Water is the **universal solvent**, dissolving many types of substances.

Substances that will mix well and dissolve in water (e.g. salts) are known as **hydrophilic** (water-loving) substances, while those that do not mix well with water (e.g. fats and oils), are known as **hydrophobic** (water-fearing) substances.

The energy of hydrogen bonds per atomic group is much greater than that of van der Waals contacts. Thus, molecules will form hydrogen bonds in preference to van der Waals contacts.

Polar organic molecules such as sugars, organic acids and amino acids, which contain a large number of groups that form excellent hydrogen bonds (e.g. =O or -OH), are soluble in water (i.e. are hydrophilic).

Every group that is capable of forming a hydrogen bond is able to form hydro-

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gen bonds with water. While the insertion of such groups into a water lattice breaks water-water hydrogen bonds, it results simultaneously in the formation of hydrogen bonds between the polar organic molecule and water. These alternative arrangements, however, are not usually as energetically satisfactory as the water-water arrangements, so that even the most polar molecules ordinarily have only **limited solubility**.

Water is 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 to form glucose and release oxygen. All living cells use such fuels and oxidise the hydrogen and carbon and reform water and CO_2 in the process termed cellular respiration.

Acids and bases

In a molecule possessing a highly polar covalent bond between a hydrogen and another atom, the hydrogen atom almost entirely has given up its electron to the companion atom. The hydrogen atom exists as an almost naked positively charged hydrogen nucleus, a proton (H^+).

When this molecule is dissolved in water the proton will be attracted to the partial negative charge on the O atom of an adjacent water molecule.

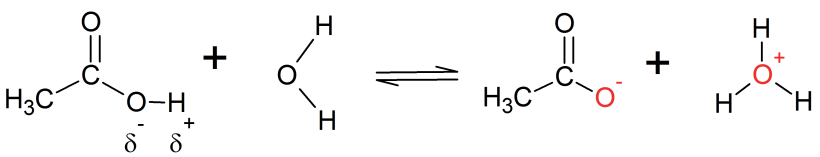

Figure 10. Acetic acid (CH_3COOH) donates a proton to H_2O. The acetate ion (CH_3COO^-) is the conjugate base of acetic acid, CH_3COOH.

The proton dissociates from its original partner and associates with the oxygen atom of the water molecule generating a hydronium ion (H_3O^+). Such a substance that can donate protons is termed an acid (Figure 10). The higher the concentration of H_3O^+, the more acidic is the solution.

Under this definition, in every acid-base reaction,

$$HA + H_2O \leftrightarrow H_3O^+ + A^-$$

an **acid** (*HA*) reacts with a base (H_2O) to form the **conjugated base** of the acid (A^-) and the conjugate acid of the base (H_3O^+).

The above acid dissociation reaction is characterized by its equilibrium constant which, for acid-base reactions, is known as a dissociation constant. The dissociation constant quantifies the tendency of a compound or an ion to dissociate.

The **acid dissociation constant**, K_a, is the equilibrium constant for the reaction in which a weak acid is in equilibrium with its conjugate base in aqueous solution.

$$K = \frac{[H_3O^+][A^-]}{[HA][H_2O]}$$

$$K_a = K[H_2O] = \frac{[H_3O^+][A^-]}{[HA]}$$

Quantities in square brackets symbolize the molar concentrations of the indicated substances.

Since in dilute aqueous solutions the water concentration is essentially constant (**55.6 M**), this term is customarily combined with the dissociation constant, which then takes the form mentioned above.

The strength of an acid is specified by its dissociation constant. A strong acid completely ionizes in solution. For strong acids K_a is high and for weak acids it is low.

pK_a

Since the values of K_a vary by many orders of magnitude it is customary to use

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as a measure of the acid strength **pK_a**.

This is the negative logarithm of K_a:

pK_a = - log K_a

For very strong acids pK_a is less than zero, while very weak acids have pK_a values as high as 15 or more. Examples:

- log 10.000 = - 4

- log 0.0001 = + 4

The opposite of an acid is a **base**.

A base is a substance that can accept protons. A base raises the concentration of hydroxyl (OH^-) ions. Because an OH^- ion combines with a H_3O^+ ion, an increase in the OH^- concentration causes a decrease in the concentration of H_3O^+, and vice versa.

In the biochemical literature the strength of a base is nearly always given by the pK_a of the conjugate acid. **Strong bases** have weak conjugate acids with **high pK_a** values, while **weak bases** have strong conjugate acids with **low pK_a** values.

pH

p = negative log of a quantity

pH = negative log of hydrogen ion concentration

Water is an **amphoteric substance**. It can react as either an acid or base.

$$H_2O + H_2O \leftrightarrow H_3O^+ + OH^-$$

As above, the constant $[H_2O]$ = 55.6 M can be incorporated into the dissociation constant to yield the expression for the ionization constant of water:

$$K = \frac{[H_3O^+][OH^-]}{[H_2O]^2}$$

$$K_w = K[H_2O]^2 = [H_3O^+][OH^-]$$

$$= 10^{-14}\, mol^2 / l^2$$

The value of K_w at 22°C is $10^{-14} M^2$. Pure water must contain equimolar amounts of H^+ and OH^- so that

$$[H_3O^+] = [OH^-] = \sqrt{K_w} = 10^{-7}\, M$$

If $[H^+]$ is greater than this value, $[OH^-]$ must be correspondingly less and vice versa. Solutions with **$[H^+] = 10^{-7}$ M** are said to be **neutral**, those with **$[H^+] > 10^{-7}$** are said to be **acidic**, those with **$[H^+] < 10^{-7}$** are said to be **basic**.

$$[H_3O^+] = 10^{-7} : neutral$$
$$[H_3O^+] < 10^{-7} : basic$$
$$[H_3O^+] > 10^{-7} : acidic$$

The values of $[H^+]$ for most solutions are inconveniently small and difficult to compare. A more practical quantitiy is the **pH**:

$$pH = -\log[H_3O^+]$$

The pH of pure water is 7.0, whereas acidic solutions have pH < 7.0 and basic solutions have pH > 7.0.

$$pH = 7.0 : neutral$$
$$pH > 7.0 : basic$$
$$pH < 7.0 : acidic$$

Buffers

Buffered solutions resist change in its pH even when a strong acid or strong base is added to it. Buffers stabilize a solution's pH.

A mixture of a **weak acid (HA)** and of **its conjugate base (A^-)** constitutes a **buffer** with resists changes in pH.

Since the properties of biological substances vary significantly with small changes in pH, they require environments in which the pH is insensitive to additions of acids or bases. Therefore, biological fluids are heavily buffered.

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The pH of the blood

The pH of the blood is closely controlled at pH 7.4. Even slight deviations are critical (Table 1).

Table 1. Acid-base homeostasis. The ending 'emia' means in the blood.

Term	Explanation
Acidemia	arterial blood pH < 7.35
Acidosis	process that lowers arterial blood pH to < 7.35
Alkalemia	arterial blood > 7.45
Alkalosis	process that raises arterial blood pH to > 7.45

Phosphate ions and many biological molecules, such as proteins (e.g., hemoglobin), nucleic acids, and lipids, as well as numerous small organic molecules, bear multiple acid-base groups that are effective as buffer components in the physiological pH rage.

The regulation of blood pH, however, happens via the control of the ratio of HCO_3^- (bicarbonate) to CO_2 (carbon dioxide). This is termed the bicarbonate buffering system.

An increase of the partial pressure of CO_2 causes the formation of H_2CO_3 (carbonic acid). The carbon dioxide - carbonic acid equilibrium is catalyzed by the enzyme carbonic anhydrase. Carbonic acid releases a proton and blood pH decreases. The blood becomes more acidic.

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

CO_2 can be exhaled via the lung. Thus, breathing shifts the reaction to the left such that fewer hydrogen ions are free.

An increase of HCO_3^- also lowers the blood pH. The bicarbonate ion can be excreted in the urine.

Thus, the lung and the kidneys play pivotal roles in the control of the bicarbonate buffering system.

Henderson-Hasselbalch equation

Buffers are often added to maintain a constant pH in biochemical research. The equation is useful for estimating the pH of a buffer solution and finding the equilibrium pH in acid-base reactions.

The **relationship** between the **pH** of a solution and the **concentrations** of an **acid** and its **conjugate base** can be derived as given below. The equation indicates that the p*K* 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.

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] and [A^-]. It is maximal when pH = p*K* and decreases rapidly with a change in pH from that point.

$$K_a = K[H_2O] = \frac{[H_3O^+][A^-]}{[HA]}$$

$$[H_3O^+] = K_a\left(\frac{[HA]}{[A^-]}\right)$$

$$pH = -\log K_a + \log\left(\frac{[A^-]}{[HA]}\right)$$

$$= pK_a + \log\left(\frac{[A^-]}{[HA]}\right)$$

Hydrophobic effect

Fats and other materials whose molecules consist largely of nonpolar groups have a low solubility in water and a high solubility in nonpolar solvents. Hydrocarbons, which contain many C-H bonds, are especially unpolar and hydrophobic. In **unpolar molecules** the electronegativity of elements is similar or identical.

The hydrophobic effect is the major driving force for the folding of globular proteins and the formation of membranes and micelles from aqueous solution. In addition, the hydrophobic effect is im-

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portant in the partitioning of proteins into membranes.

The hydrophobic effect is the property that nonpolar molecules tend to form **intermolecular aggregates** (or **intramolecular interactions**) in an aqueous medium.

The term hydrophobic effect emphasizes the fact that nonpolar groups will try to arrange themselves so that they are not in contact with water molecules.

Two components are relevant (Figure 11).

1. Water has the strong tendency to exclude nonpolar groups. There is a very strong attraction of water molecules for one another via hydrogen bonds. In other words, water forces hydrophobic groups together in order to minimize the disruptive effects on the hydrogen-bonded water network.

2. The nonpolar compounds bind to each other via van der Waals attractive forces.

For more details on the hydrophobic effect see:

UC Davis ChemWiki (2014) Hydrophobic interactions

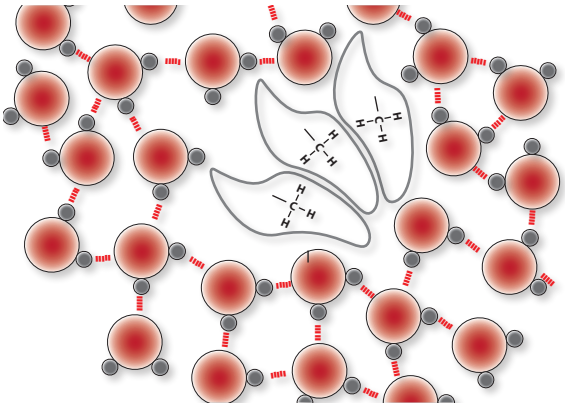

Figure 11. Hydrophobic effect. Water excludes nonpolar groups.

The hydrophobic effect is entropy-driven

Pure water molecules adopt a structure which maximizes entropy (S) (like any compounds tend to maximise entropy). A hydrophobic molecule will disrupt this high-entropy structure and decrease entropy, because it creates a 'cavity' as it is unable to interact with the water molecules.

When more than one 'cavity' is present, the surface area of disruptions is high, meaning that there are fewer free water molecules. To counter this, the water molecules push the hydrophobic molecules together and form a structure around them which will have a **smaller surface area** than the total surface area of the cavities. This maximizes the amount of free water and thus the entropy.

Amphiphiles

Most biological molecules have **both polar** (or ionically charged) **and nonpolar segments and are therefore simultaneously hydrophilic and hydrophobic**.

An example are fatty acids (Figure 12). Such molecules are said to be **amphiphilic** (or, synonymously, amphipathic).

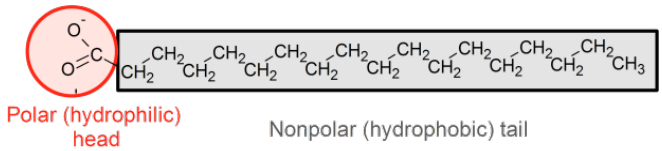

Figure 12. Fatty acids have both polar and nonpolar groups.

Water tends to hydrate the hydrophilic portion of an amphiphile, but it also tends to exclude its hydrophobic portion. Therefore, **amphiphiles form structurally ordered aggregates**.

Such aggregates may take the form of **micelles**, or may arrange themselves to form bilayered sheets or vesicles in which the polar groups face the aqueous face (**lipid bilayer**).

The lipid bilayer is the universal basis of membrane structures, and its properties are responsible for the general properties of cell membranes.

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Diffusion and osmosis

Diffusion is the net movement of atoms, ions, and molecules from a region of a high concentration to a region of a lower concentration (Figure 13).

Diffusion is the basis of passive transport down an unequal distribution of particles, or concentration gradient, in cells.

A concentration gradient of particles is an energy-rich condition because free energy is minimized when all concentrations are equal.

If the concentration of [A] outside the membrane is greater than that inside, ΔG for the transfer of A from outside to inside will be negative and the spontaneous net flow of A will be inward. If [A] is greater inside than outside, ΔG is positive and an inward net flow of A will not occur spontaneously.

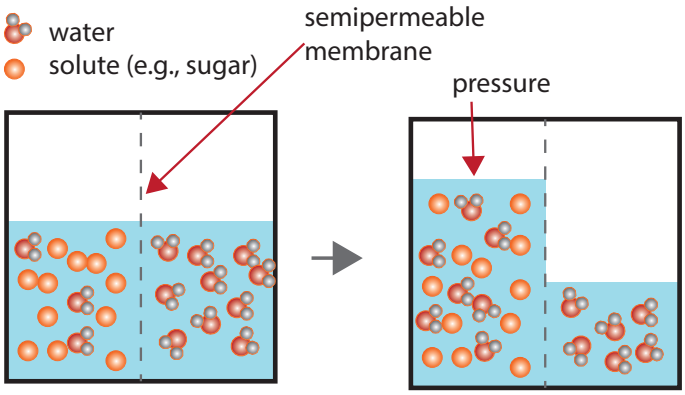

Figure 14. Movement of solvent (water) across a semipermeable membrane. Osmotic pressure builds up until no net movement of solvent takes place. The osmotic pressure depends on the molar concentration of the solute.

For more details on diffusion and osmosis see:

Khanacademy (2014) Diffusion and osmosis

GCSE Bitesize Science - The BBC (2014) Diffusion and osmosis

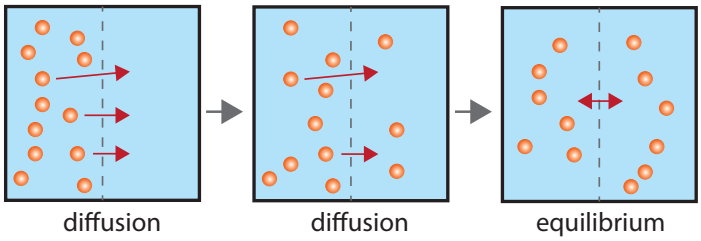

Figure 13. Movement of particles in a solution.

Osmosis is the net movement of solvent molecules such as water through a partially permeable (or semipermeable) membrane into a region of higher solute concentration (Figure 14).

Biological membranes have specialized water channels termed aquaporins that facility the movement of water.

Animal cells continuously pump out unwanted solutes to maintain the osmitoc equilibrium. Plant cells have tough cell walls that balance the osmotic pressure created by the solutes in the cell and thereby limit the flux of water into the cell.

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Biological membranes

Membranes function to organize biological processes by compartmentalizing them. The primary purpose of cell membranes is the physical separation of the intracellular components from the extracellular environment.

The cell, the basic unit of life, is essentially defined by its enveloping **plasma membrane**. The cell membrane is also termed plasma membrane or plasmalemma (in plants).

In eukaryotes, many **subcellular organelles**, such as nuclei, mitochondria, chloroplasts, the endoplasmic reticulum, and the Golgi apparatus, are likewise membrane bounded.

Lipid bilayer

Biological membranes consist of a thin layer of **amphipathic lipids** which spontaneously arrange so that the hydrophobic "tail" regions are shielded from the surrounding polar fluid, causing the more hydrophilic "head" regions to associate with the cytosolic and extracellular faces of the resulting bilayer. This forms a lipid bilayer containing the cellular components (Figure 13).

Lipid bilayers are impermeable to ionic and polar substances. To penetrate a lipid bilayer, a solute molecule must shed its hydration shell and become solvated by the bilayer's hydrocarbon core. Such a process is highly unfavourable for polar molecules.

The permeabilities of substances increase with their solubilities in nonpolar solvents.

The arrangement of hydrophilic and hydrophobic heads of the lipid bilayer prevents hydrophilic solutes from passively diffusing across the band of hydrophobic tail groups, allowing the cell to control the movement of these substances via transmembrane protein complexes such as pores and gates.

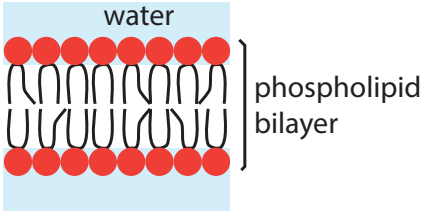

Figure 13. Phospholipid bilayer. Biological membranes are composed largely of phospholipids. In an aqueous environment, the hydrophobic tails of the fatty acids form a lipid bilayer.

Cell membranes are **asymmetrical**. They present a different face to the interior of the cell than they show to the exterior. The two halves of the bilayer often include different phospholipids and glycolipids. Glycolipids are located mainly in the plasma membrane and the sugar groups are exposed to the exterior of the cell. The glycolipid molecules get their sugar groups in the Golgi apparatus.

Fluid mosaic model

Lipids are highly mobile in the plane of the bilayer (**lateral diffusion**). The bilayer is a **two-dimensional fluid** in which the hydrocarbon chains undergo rapid motions.

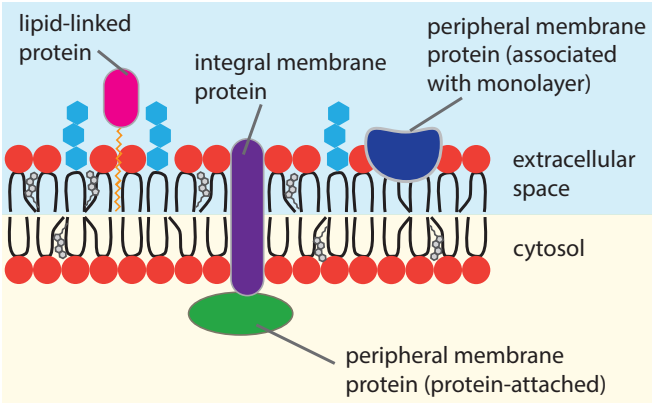

Figure 14. Plasma membrane. Phospholipids (red head groups) and glycolipids (blue head groups) are distributed assymetrically in the plasma membrane. Cholesterol (grey) is distributed equally in both monolayers and stiffens membranes. Integral membrane proteins traverse the lipid bilayer and interact extensively with the hydrocarbon region of the bilayer. Peripheral membrane proteins are associated with the membrane in different ways, e.g., protein-attached, lipid-linked, or anchored to the cytosolic surface (monolayer-associated).

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Most membrane functions (apart from the role as a permeability barrier) are carried out by **membrane proteins** (Figure 14). All membrane proteins have a specific orientation, which is crucial for their function.

Proteins constitute about 50% of the mass of plasma membranes. The fluid mosaic model postulates that integral proteins resemble "icebergs" floating in a two-dimensional lipid "sea" and that these proteins diffuse laterally in the lipid matrix unless their movements are restricted by associations with other cell components.

In contrast to the high mobility in the plane of the bilayer, the transfer of a lipid molecule across a bilayer, a process termed transverse diffusion or a **flip-flop**, is an extremely rare event. This is because a flip-flop requires the polar head group of the lipid to pass through the hydrocarbon core of the bilayer.

Membrane transport

Biological membranes regulate the composition of the intracellular medium by controlling the flow of molecules and ions into and out of the cell. Cell membranes are **selectively permeable** and able to regulate what enters and exits the cell.

Small unpolar molecules such as CO_2 and O_2 can simply diffuse across membranes. The transfer of the vast majority of compounds such as ions, charged molecules, and large molecules depends on membrane transport proteins that span the lipid bilayer.

Channels and transporters can carry out **passive transport**, or facilitated diffusion (Figures 15, 16). Ions and molecules flow from high concentration to low concentration so as to equilibrate their concentration gradient.

Active transport allows transport of ions and molecules from low concentration to high concentration, i.e., against their concentration gradient. Such an endergonic process muss be coupled to a exergonic process such as ATP hydrolysis to make it happen. Examples include coupled transporters (Figure 17) and ATP-driven pumps (Figure 18).

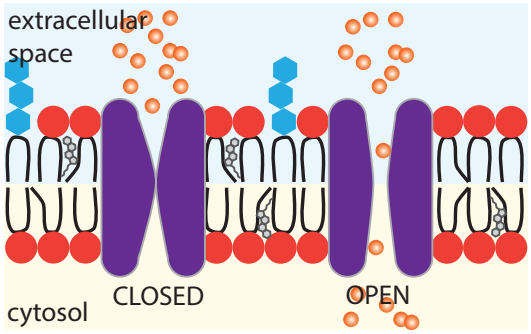

Figure 15. Passive transport by channels. An ion or molecule that has the proper size and electrical charge can slip through an open channel.

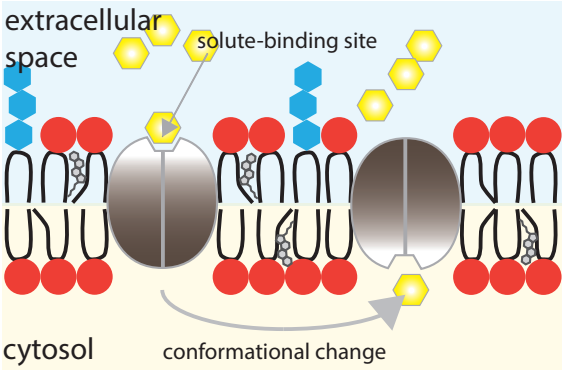

Figure 16. Passive transport by a transporter. Transporter proteins bind only those molecules or ions that fit into a binding site. Changing its conformation allows transfer of the compound.

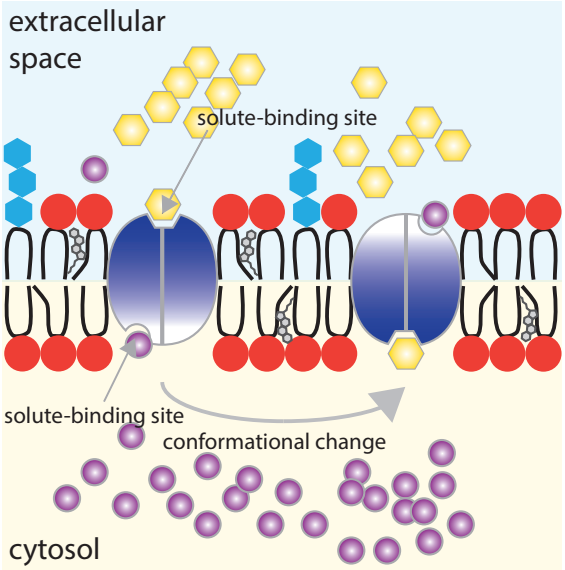

Figure 17. Antiporter proteins couple the

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uphill transport of one solute to the downhill transport of another. Symporter proteins couple the endergonic transport of one solute with the exergonic transport of another solute in the same direction (not shown). The first solute is transported against its concentration gradient (uphill), the second solute is transported with its concentration gradient (downhill).

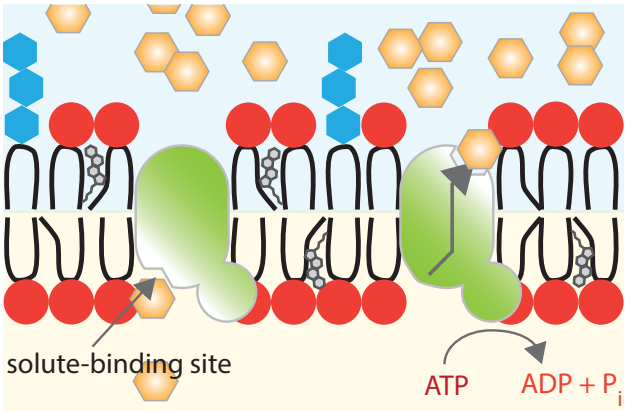

Figure 18. ATP-driven pumps couple the endergonic (uphill) transport to the exergonic hydrolysis of ATP.

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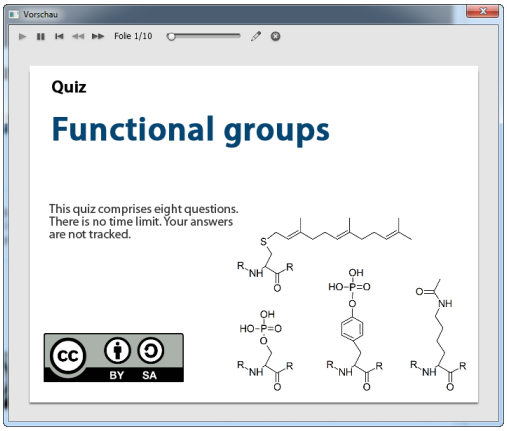
II. Chemical groups

Carbon is the basis of the chemistry of all known life. Organic compounds are molecules with carbon in them. Carbon has the ability to form long, indefinite chains with interconnecting C-C bonds. Functional groups are specific groups of atoms within molecules that are responsible for the characteristic chemical reactions of those molecules.

Quiz

Start this chapter with the quiz to test for your mastery. You may reattempt the quiz later to check your progress.



Quiz 1. Functional groups. Click to play - HTML5 or Flash (opens new window in your standard web browser).

Carbon

Living matter consists of a relatively small number of elements. C, H, O, N, P, and S, all of which form covalent bonds, comprise 92% of the dry weight of living matter.

Carbon (**C**) is the basis of the chemistry of all known life. Organic compounds are molecules with carbon in them. The predominance of carbon in living matter is a result of its tremendous **chemical versalitity** compared with all the other elements.

Organic chemistry is the study of chemical compounds consisting primarily of carbon and hydrogen. The original definition of "organic" chemistry came from the misperception that these compounds were always related to life processes, but this is not the case.

The most common carbon-12 isotope has six positively charged protons and six neutrally charged neutrons in its nucleus, as well as six negatively charged electrons in the surrounding electron cloud. To become stable, carbon will form four covalent bonds with other atoms to fill the outer shell.

Only five elements, boron (**B**), carbon (**C**), nitrogen (**N**), silicon (**Si**), and phosphorus (**P**), have the capacity to make three or more bonds each.

Only these elements can form chains of covalently linked atoms that can also have side chains. B, N, Si, and P are unsuitable as the basis of a complex chemistry.

The other elements are either metals, which tend to form ions rather than covalent bonds; noble gases, which are essentially chemically inert; or atoms such as H or O that can each make only one or two covalent bonds.

Carbon compounds

Carbon exhibits remarkable properties. Different forms include the hardest natural substance (diamond) and one of the softest substances (graphite) known.

Carbon has a great affinity for bonding with other small atoms, including other carbon atoms, and is capable of forming multiple stable covalent bonds with such atoms. Most forms of carbon are comparatively unreactive under normal conditions.

Carbon has the ability to form long, indefinite chains with interconnecting C-C bonds.

Carbon compounds include:

- Gasoline is a liquid mixture consisting mostly of hydrocarbons.
- Amino acids are the building blocks of

proteins.

- DNA is a long polymer of simple units called nucleotides, with a backbone made of sugars and phosphate atoms.
- Lipids are any hydrophobic naturally-occurring molecules.
- Carbohydrates are compounds with the chemical formula $C(H_2O)_n$, where *n* is any number of three or greater. Sucrose ("sugar") and starch are examples.
- There also are completely synthetic carbon compounds, such as the nanoparticles.

Functional groups

Functional groups are specific groups of atoms within molecules that are responsible for the characteristic chemical reactions of those molecules.

The same functional group will undergo the same or similar chemical reactions regardless of the size of the molecule it is a part of.

- Functional groups are hydrophilic and increase the solubility of organic compounds in water.
- Functional groups are attached to the carbon backbone of organic molecules.
- Functional groups determine the characteristics and chemical reactivity of molecules. Functional groups are far less stable than the carbon backbone and are likely to participate in chemical reactions.
- Functional groups provide specific properties to molecules. For example, the sexual hormones **testosterone** and **estradiol** are structurally very similar. However, the small difference in their structures confers significant differences in the development and morphology of animals.

Hydroxyl group

Hydroxyl stands for a molecule consisting of an oxygen atom and a hydrogen atom connected by a covalent bond.

When the oxygen atom is linked to a larger molecule the hydroxyl group is a functional group (–OH). An **alcohol** is any organic compound in which a hydroxyl group is bound to a carbon atom.

The oxygen atom has a high electronegativity (attracts electrons), therefore, the hydroxyl group is **polar** and attracts water molecules. Organic compounds with hydroxyl groups show an increased solubility in water (i.e. are more hydrophilic).

The most common alcohol is **ethanol**, which is created by **fermentation** of fruits or grains with yeast (Figure 1).

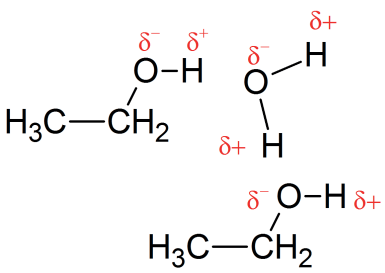


Figure 1. Ethanol is a simple alcohol. The polar hydroxyl group forms hydrogen bonds with water.

Chemical reactions of alcohols

Alcohols form **esters** in a condensation reaction between an alcohol and a carboxylic acid in a reaction known as esterification (Figure 2).

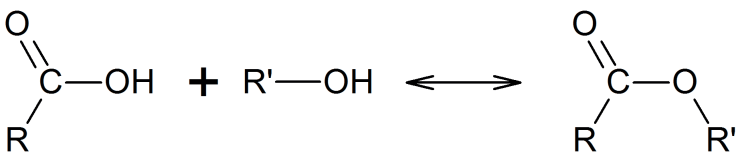


Figure 2. A carboxylate ester derived from a carboxylic acid and an alcohol.

Primary alcohols can be **oxidized** either to aldehydes (R-CHO) or to carboxylic acids (R-COOH). The oxidation of secondary alcohols gives a ketone.

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Carbonyl group

A carbonyl group is a functional group composed of a carbon atom double-bonded to an oxygen (C=O).

Oxygen is more electronegative than carbon and thus pulls electron density away from carbon to increase the bond's polarity. The carbonyl carbon becomes **electrophilic**, and thus more reactive with nucleophiles.

Electron-deficient compounds are called electrophiles (electron lovers). They may be positively charged, contain an unfilled valence electron shell, or contain an electronegative atom. Biologically important electrophiles are protons, metal ions, the carbon atom of carbonyl groups, and cationic imines. Electrophilic reagents participate in chemical reactions by accepting an electron pair.

Eletron-rich compounds are called **nucleophiles** (nucleus lovers). They are negatively charged or contain unshared electron pairs that easily form covalent bonds with electron-deficient centers.

Biologically important nucleophilic groups include amino, hydroxyl, imidazole, and sulhydryl groups. Nucleophilic reagents form chemical bonds to the electrophile by donating the bonding electrons.

See also:

UC Davis ChemWiki (2014) Chapter 8: Nucleophilic substitution reactions, part I

A carbonyl group characterizes different types of compounds. An **aldehyde** ('alcohol dehydrogenated') is an organic compound containing a terminal carbonyl group (Figure 3).

A **ketone** is the functional group characterized by a carbonyl group (C=O) linked to two other carbon atoms. A ketone can be generally represented by the formula $\mathbf{R_1(CO)R_2}$.

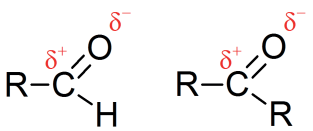

Figure 3. The aldehyde (left) and keto group (right) have polar C-O bonds.

In the presence of an acid catalyst the ketone is subjected to so-called **keto-enol tautomerism**. Keto-enol tautomerism refers to the chemical equilibrium between a keto form and an enol (Figure 4).

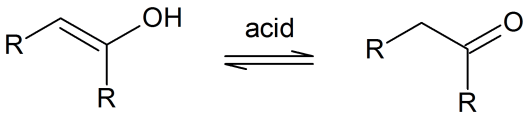

Figure 4. Enol form (left) and keto form (right).

The keto-enol tautomerism is important in several areas of biochemistry. The enol and keto forms are said to be tautomers of each other. The interconversion of the two forms involves the movement of a proton and the shifting of bonding electrons. The keto form predominates at equilibrium for most ketones, but the enol form is important for some reactions.

Carboxyl group

Carboxylic acids also represent a type of carbonyl group. Its structure is composed of one carbon atom attached to an oxygen atom by a double bond and to a hydroxyl group by a single bond (Figure 5).

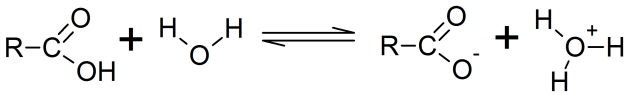

Figure 5. The carboxylic acid group is much more acidic than an alcohol group.

Carboxylic acids show a much higher **acidity** in comparison to, for example, alcohols. The acidity of a carboxylic acid can be explained by **resonance effects**.

Both the carboxyl group (with proton) and the carboxylate anion (which lost a proton) are stabilized by resonance, but the stabilization of the anion is much greater than that of the neutral function.

The carboxyl group (or carboxy group)

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is present in amino acids and fatty acids. Numerous organic acids are also characterized by the carboxyl group, e.g. malic acid, pyruvic acid, lactic acid and citric acid.

Amino group

The amino group is a functional group found in all amines and amino acids. The amino group acts as a base, a group that can accept protons.

Amino acids are named for the amino group. Glycine is the simplest amino acid (Figure 6).

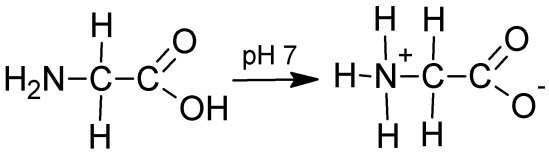

Figure 6. The simple amino acid glycine is a so-called zwitterion under neutral pH. It has a positive charge at the amino group and a negative charge at the carboxylic acid group.

Amines are organic compounds that contain nitrogen as the key atom. Structurally amines resemble ammonia wherein one or more hydrogen atoms are replaced by organic substituents.

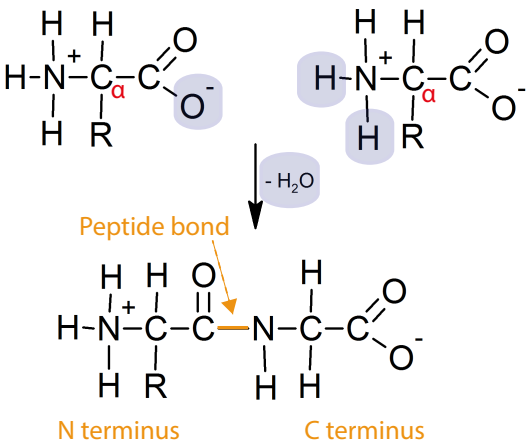

Figure 7. Peptide bond. The carboxyl group of an amino acid reacts with the amino group of another amino acid, causing the release of a molecule of water.

Amino acids are a varied class of molecules which are characterized by a carboxylic acid group and an amino group, both linked to the same carbon atom called the α-carbon. Proteins are polymers of amino acids joined head-to-tail in a long chain (Figure 7).

Sulfhydryl group

The sulfhydryl group is composed of a sulphur atom and a hydrogen atom (-SH). A **thiol** is a compound that contains a thiol (or sulhydryl) group.

The chemistry of thiols is related to the chemistry of alcohols. For example, thiols form thioethers and thioesters, which are analogous to ethers and esters. In contrast to the hydroxyl group, an S-H bond is practically **nonpolar** covalent due to the small electronegativity difference between sulphur and hydrogen.

Thiols show little association by hydrogen bonding, with both water molecules and among themselves. They have lower boiling points and are less soluble in water and other polar solvents than alcohols of similar molecular weight.

Disulfide bond

A disulfide bond is a single covalent bond derived from coupling of thiol groups. The linkage is also called a **disulfide bridge**.

When the thiols of two cysteine residues are brought near each other in the course of protein folding, an oxidation reaction can create a **cystine** unit with a disulfide bond (R-S-S-R, Figure 8).

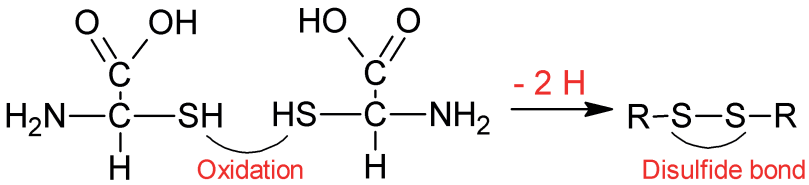

Figure 8. Disulfide bonds are formed between the thiol groups of cysteine residues.

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Disulfide bonds can contribute to a protein's tertiary structure, and play an important role in the folding and stability of some proteins, usually proteins secreted to the extracellular medium. The disulfide bond holds two portions of the proteins together, biasing the protein towards the folded topology (Figure 9).

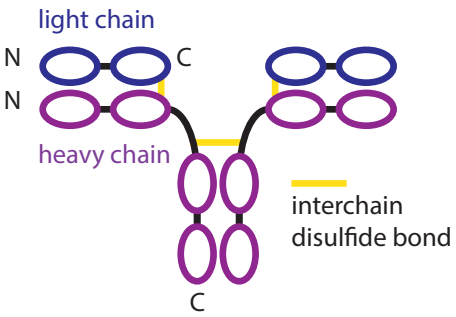

Figure 9. Immunoglobulin G structure. IgG consists of two kinds of polypeptide chains, the light chain (blue) and heavy chain (purple). Each light chain is linked to an heavy chain by a disulfide bond.

Phosphate group

The **phosphate ion** is an ion with the empirical formula PO_4^{3-} (Figure 10). It consists of a central phosphorus atom surrounded by four identical oxygen atoms. The phosphate ion predominates in basic conditions. The phosphate carries a negative three formal charge.

The phosphate ion is the conjugate base of the **monohydrogenphosphate** ion, HPO_4^{2-}. Monohydrogenphosphate is prevalent in weakly basic conditions and is the conjugate base of $H_2PO_4^-$, the **dihydrogen phosphate** ion, which is most common in weakly acid conditions.

In strongly acid conditions, H_3PO_4, **phosphoric acid**, is the main form. Phosphoric acid is the conjugate acid of dihydrogen phosphate.

Phosphate esters can form between a posphate and a free hydroxyl group (e.g., of the amino acids serine, threonine, and tyrosine). Phosphoryl groups are often attached to proteins in this way.

Phosphoanhydride bonds are high-energy bonds found in molecules such as ATP (Figure 11).

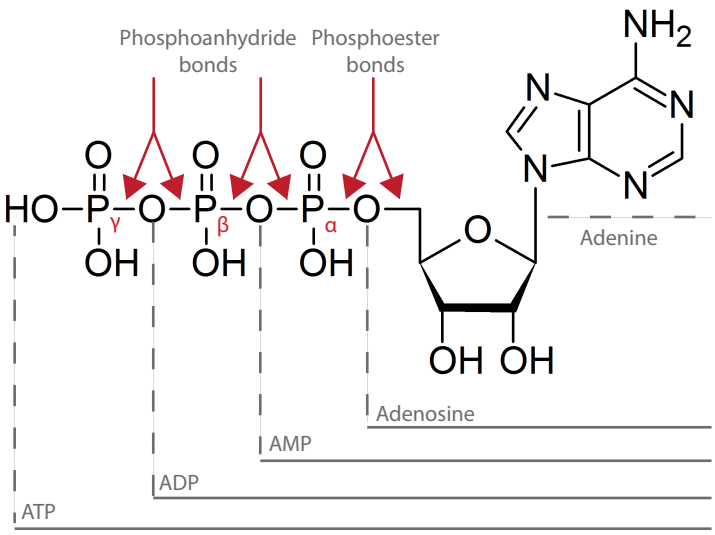

Figure 11. Adenosine triphosphate (ATP). ATP is called the energy currency of the cell.

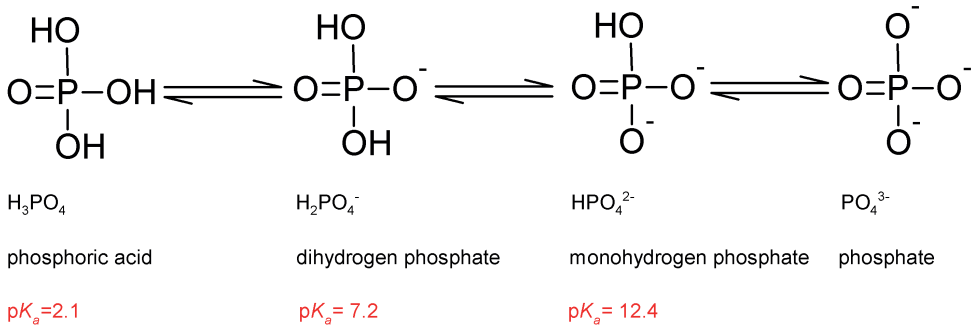

Figure 10. Depending on the pH, phosphate can exist in four forms.

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