Theoretical support to the structural (descriptive) Biochemistry
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Theme: Bioelements and biomolecules. Functional groups and chemical bonds specific for biomolecules.

1. Bioelements and biomolecules

Bioelements

Bioelements are the chemical elements that make up living organisms (C, H, O, N, P, S) and those required in the metabolism (some metals such as Na, Ca, K, Fe, Mg, Zn, non-metals such as Cl, I).

Bioelements can be named as **biogenic elements** - chemical elements that give rise living organism.

Biogenic elements can be divided in **organogenic** and **minerals**.

Organogenic are bioelements which generate organic compounds. These elements are C, H, O, N, and in some cases P and S.

They possess some structural features which have led to their selection as the **organogenic**.

First, the small sizes of atoms and their ability to form from 1 to 4 chemical bonds.

Second, the small sizes of atoms of organogenic elements allow the formation of strong and stable chemical bonds.

The most important organogenic element is carbon. Carbon can form multiple bonds with all organogenic bioelements but also with itself forming straight or branched chains. These chains form the skeleton or backbone of all organic compounds. In the body carbon combining with other organogenic bioelements generates various molecules that will form the structural-functional basis of cells and organism. These molecules are called **biomolecules.**

To **minerals** belong some metals such as Na, K, Ca, Mg, Zn, Mn, Fe, Cu, Cr, V, Mo, and some non-metals such as Cl, I, F, Se, Br.

By their content in the body biolements can be classified as **macroelements** and **microelements**, do not be confused with macronutrients and micronutrients.

Some of macroelements are non-metals such as H, O, C, N, P, C, S, F and some are metals such as Na, K, Ca, Mg.

To the **microelements** refer so-called trace transition metals like manganese, iron, zinc, copper, cobalt, molybdenum etc. They can be essential and non-essential for organism (anthropogenic) as cadmium, lead, aluminum.

General characteristic of the main bioelements that make up the human body

Almost 99% of the weight of the human body is made up of six bioelements **oxygen, carbon, hydrogen, nitrogen, calcium, phosphorus.**

About 0.85% are five bioelements: potassium, sulfur, sodium, chloride and magnesium. All these 11 bioelements may be considered essential for life and are macroelemnts.

The remaining 0.15% is oligo- and microelements that are vital but the role of some of them are not completely understood.

Below are shown two tables indicating the percentage content of bioelements by mass of dry and wet body.

Tab.1. The content of the most abundant elements in the human body (in % of dry mass, without water) (from D. Voet, Biochemistry, 2008)

C	61.7
N	11.0
O	9.3
H	5.7
Ca	5.0
P	3.3
K	1.3
S	1.0
Cl	0.7
Na	0.7
Mg	0.3

Tab.2. Content of the main bioelements in % by their mass in relation to the wet mass of the body, e.g. Oxygen makes up 65% of the wet weight of the human body or 45 kg of a 70 kg adult. (from D. Taylor, The elemental composition of 70 kg 'reference' person, 1995)

Macrobioelements	**%**	**kg**
Oxygen	65	45.5
Carbon	18.5	12.6
Hydrogen	9.5	7
Nitrogen	3.2	2.1
Calcium	1.5	1.05
Phosphorus	1	0.7
Potassium	0.4	0.14
Sulfur	0.3	0.175
Sodium	0.2	0.105
Chlorine	0.2	0.105
Magnesium	0.1	0.035
Microbioelements: boron, chromium, cobalt, cooper, fluorine, iodine, iron, manganese, molybdenum, selenium, silicon, vanadium, zinc	0.85	0.595

The atomic percentage differs from that of the mass, e.g. the number of oxygen atoms in relation to the other elements is 24%, hydrogen 62, carbon 12, nitrogen 1.8, calcium 1 and phosphorus 0.78. Data on weight in percentages % and the number of atoms of bioelements may differ slightly depending on the source.

Macroelements non-metals

Carbon (C)

The carbon makes up 21.15% of the total weight of the human body or 12.6 kg of bwa (*b.w.a.* - **body weight of an adult** of up to 70 kg) and 61.7% of dry weight. It is fundamental organogenic bioelement of all living organisms.

The carbon is the component of proteins, carbohydrates, lipids and other biomolecules.

In some cells and blood is found in the form of bicarbonate ion HCO_3^-. Bicarbonate participates in various biochemical reactions such as biosynthesis of glucose, fatty acids, it is also important in maintaining acid-base balance in the blood.

Nitrogen (N)

Nitrogen makes up 3.1% of total weight (2.1 kg of bwa) and 11% of dry weight of the human body.

It is a main component of amino acids, proteins, nucleic acids.

Also it can be found in the composition of inorganic compounds of vital importance such as nitric oxide NO and ammonium ions or salts of NH_4^+.

Because of its ability to form donor-acceptor bonds it can fix protons - gives the basic properties of proteins, bind some metals in different proteins.

Nitrogen occurs in the body and in the free molecular state as N_2 gas dissolved in the blood as a result of the process of inspiration of atmospheric air. This nitrogen under certain conditions can cause **Caisson disease** (Decompression sickness, divers' disease) a condition arising from dissolved N_2 (gas) coming out of solution into bubbles inside the body. This disease can produce many symptoms, and its effects may vary from joint pain and rashes to paralysis and death.

Oxygen (O)

Oxygen makes up 62% of total body weight (45.5 kg of bwa) and 9.3% of dry weight.

It enters in the composition of proteins, carbohydrates, lipids and many other biomolecules.

It is needed in the process of respiration as oxidant.

Hydrogen (H)

The hydrogen make up 10% of the mass of the body (7 kg of bwa).

In the body it is not found in the free atomic (H) or molecular H_2 state but only in composition of different biomolecules or in ionized state as so called hydrogen proton H^+ (cation).

Hydrogen ions contribute to the acid environment in the body. Their excess can cause a pathological condition called acidosis.

Atomic hydrogen is part of all biomolecules - proteins, carbohydrates, lipids, nucleic acids etc.

It is the main and only source of energy virtually for all living organisms. Hydrogen is extracted from some compounds like glucose, fatty acids and oxidized by oxygen to water to release energy required for organism.

Phosphorus (P)

Phosphorus makes up 0.95% of the weight body (700 g of bwa).

It is an important component of nucleic acids, proteins - phosphoproteins, lipids - phospholipids and minerals that make up the bone.

Phosphorous occurs mostly in bones and teeth as component of hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$.

Phosphorus is an energy component of biomolecules such as ATP, creatinphosphate, phosphoenolpyruvate.

Phosphorus is also a component of blood buffer systems.

Phosphorus is a nutrient and its daily food needs is 1.3 grams.

Sulfur (S)

The sulfur makes up 0.16% of the weight body (175 g of bwa).

It is component of some amino acids - cysteine and methionine and respectively proteins. Also it is important component of biomolecules such as taurine, coenzyme A, S-adenosylmethionine, and the important to the body vitamins like thiamine (B1) and biotin (H).

Sulfur in the body can be found in inorganic form as sulfate.

Sulfur is a nutrient and its daily food needs accounts for approximately one gram.

Chlorine (Cl)

The amount of chlorine in the human body is about 105 g (0.2%). It in particular occurs in the ionic state as chloride Cl^-.

The blood plasma concentration of chloride ions is 96-105 mmol/L.

Chloride ions are important in the formation of hydrochloric acid HCl which is component of gastric juice.

Chloride ions can be activators of enzymes e.g. salivary amylase and may be involved in transport processes of O_2 and CO_2 in the blood.

The chlorine is important in the synthesis of compounds with bactericidal activity (e.g. hypochlorous acid, HOCl produced by certain white blood cells) and thus has a role in immunity.

Macroelements metals

Sodium (Na)

The content of Na in the body is about 0.08% (60 g of 70 kg bwa).

It is the main extracellular cation.

It is found in ionized form as Na^+, 44% extracellular and 9% intracellular, the rest is stored in the bone tissue.

The concentration of sodium ions in plasma is 132-144 mmol/L.

The daily requirement is 1g (usually we consume 4-7g), the main source is table salt (NaCl).

Sodium is important in maintaining osmotic pressure.

The high concentration of sodium in the blood called **hypernatremia** causes hypertension and edema.

Potassium (K)

The amount of potassium in the body is approximately 0.23% (160 g of 70 kg bwa).

K is the principal intracellular cation (98%).

It is important in muscle contraction, normal functioning of the heart, nerve impulse transmission, activation of enzymes.

The daily intake is 3.2 g.

The plasma concentration is from 3.5 to 5.5 mmol/L, intracellular 115-125 mmol/L.

The low concentration of K in the blood called **hypokalemia**, is observed in adrenal dysfunction (hyperaldosteronism), and is accompanied by disturbances of cardiac function.

Magnesium (Mg)

The content of Mg in the body is 0.27% (25 g).

It is concentrated in considerable amounts (60-65%) in mineralized tissues (dentin, enamel, bones).

It also is contained in large amounts in muscle and liver(7-8 mmol/kg wet weight).

Extracellular magnesium constitutes about 1%. In the cells it occurs in the form of ions Mg^{2+}.

The concentration of magnesium ions in plasma is 0.66–1.07 mmol/L.

Mg is important in the energy processes, it forms complexes with ATP ($MgATP^{2-}$), in the biosynthesis of the protein, the stability of the ribosome.

The daily food requirement is 0.7 g.

Calcium (Ca)

The body content of calcium is 1.4% (1.25 kg). It occurs mainly in the bones and teeth (1kg) mostly in the form of hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$.

In blood and lymph it occurs in free form as Ca^{2+} cation or bound to proteins.

The concentration of calcium ions inside the cells (intracellular) is more than 7000 times lower than in the blood plasma (i.e. at <0.0002 mmol/L, compared with 1.4 mmol/L in the plasma).

Calcium ions are important in blood clotting, muscle contraction, nerve impulse transmission.

The daily requirement is 0.5 g, but must be consumed 1 g because is absorbed only 50%, the rest is excreted as $Ca_3(PO_4)_2$ and $(R\text{-}COO)_2Ca$.

Non-metallic trace elements

Iodine (I)

The content of iodine in the body is about 25 mg (4 • 10-5%).

Occurs in free form as I^- ion around 1%, the rest is found in the composition of thyroid hormones (triiodothyronine and thyroxine).

Iodine is essential for health. In addition to being essential component of the thyroid hormones it is involved in many biochemical processes.

Although most is concentrated in the thyroid gland, it occurs in large quantities in other organs such as salivary glands, brain, cerebrospinal fluid, gastric mucosa, mammary gland, ovary, and eye.

In the brain, it can be found in the choroid plexus, an area where the cerebrospinal fluid is produced, but also in the *substantia nigra*, an area associated with Parkinson's disease.

Iodine is essential for normal growth and development of the organism. Iodine deficiency during intrauterine development and during growth can lead to **cretinism.**

Fluorine (F)

Fluorine in the human body is contained in an amount of about 7 mg (~10^{-5}%).

Fluorine is a component of fluorapatite $Ca_{10}(PO_4)_6F_2$ - tooth enamel mineral substance.

Insufficiency of fluorine contributes to the development of **caries** and excess - to **fluorosis** (dental or generalized).

Bromine (Br)

Bromine content in the body is about 10^{-5}% (7 mg).

His role is not yet fully elucidated. Some studies say that can replace chlorine in some immune processes. As it can be activator of salivary amylase. Large amounts were detected in some endocrine glands e.g. pituitary.

Microelements metals

Chromium (Cr)

The content of Cr in the body is 6 g (0.1%).

Occurs as Cr^{3+}.

It is important in the metabolism of glucose and lipids.

It is involved in the normal functioning of insulin.

Chromium helps maintain the activation or activity of enzymes (kinases) required for insulin signal transduction.

According to some studies, chromium enhances the production of fatty acids and is involved in the metabolism of plasma lipoproteins (HDL and LDL).

Chromium also decreases the level of triglycerides.

Molybdenum (Mo)

The content of Mo in the body is 5 mg.

it is a part of the xanthine oxidase enzyme. It is important in the metabolism of nucleic acids.

Manganese (Mn)

The content of Mn in the body is 12 mg.

It is concentrated in bone (43%), the rest in soft tissues like the kidney, pancreatic, muscle and skin.

Forms complexes with several proteins, nucleic acids, it is necessary for the activity of enzymes involved in the metabolism of carbohydrates, proteins, cholesterol.

Mn^{2+} is important in bone formation as activator of the enzymes xiyozyltransferase and glycosyltransferase.

Other roles of Mn are: is involved in the synthesis of thyroid and sex hormones, helps to maintain glucose and cholesterol levels in the blood, it is an efficient antioxidant, participates in immune processes, participates in the synthesis of proteins and nucleic acids, facilitates absorption of vitamins B1, C, biotin .

Iron (Fe)

The content of Fe in the body is 5 g (0.007%).
It is a component of hemoglobin, myoglobin, cytochromes.
It is important in biological oxidation (tissue respiration).

Copper (Cu)

The content of Cu in the body is 100 mg, around 30% is concentrated in muscles, and much is contained in the brain.

Metallic copper and its compounds are toxic. Cu ions form complexes with the groups -SH, -NH_2 of protein inactivating them.

It is necessary for the functioning of respiratory chain and generation of energy (ATP synthesis), participates in the synthesis of collagen and elastin.

Zinc (Zn)

The content of zinc in the body is 1.8 g (0.0024%).

In high amount is found in the muscle (65%), bone (20%), liver, red cells, prostate.

It is a component of **carbonic anhydrase** and superoxide dismutase.

It is an osteotropic bioelement.

Vanadium (V)

The content of V in the body is 1 mg.

Vanadium is most frequently found in the kidneys, spleen, lungs, testes and blood.

Its compounds are predominant in blood as vanadate and bound to transferrin as vanadyl.

It is concentrated and stored in bones as vanadate.

Vanadium is involved in haematopoesis, lipid metabolism, bones and teeth metabolism, prevents tooth caries, prevents cardiovascular diseases, has hypoglycemic effects facilitating action of insulin, and may reduce cholesterol scum in the vessels.

Its deficiency is associated with obesity and diabetes.

1.1.2. Biomolecules

Biomolecules are molecules synthesized by the organism for structural (anatomical) and physiological purposes.

They can be divided into **biomacromolecules or biopolymers**, **complex biomolecules** and **biomicromolecules.**

To biopolymers refer proteins, polysaccharides, and nucleic acids. The prefix *poly* indicates that this group of biomolecules is composed of small molecules called **monomers**.

Monomers are linked together by specific chemical bonds to form chains - **polymers**. The prefix *macro* indicates that they have very large dimensions.

To **micromolecules** refers biomolecules of small dimensions such as amino acids, amines, carboxylic acids, monosaccharides, nitrogenous bases.

Complex biomolecules which are not polymers but are made up of several small molecules include lipids and nucleotides.

The structure, physicochemical properties and biomedical role of biomolecules will be analyzed at special topics provided for.

1.2. Functional groups and types of chemical bonds specific for biomolecules

1.2.1 Functional groups

In terms of organic chemistry **functional groups** can be defined as group of atoms of non hydrocarbonic nature (they do not contain repetitive - CH_2 - sequences) as hydroxyl OH, carbonyl CO, carboxyl COOH, amino NH_2, sulfhydryl SH, which may substitute one or more hydrogen atoms from some hydrocarbon, determines membership of the given substance to a certain class, providing at the same time, chemical properties characteristic of that class, e.g. OH for alcohols, CO for aldehydes and ketones, COOH for carboxylic acids, NH_2 for amines etc.

From the biochemical point of view, they can be defined as a group that will determine the specific physicochemical properties of the biomolecules and their biological activity or effect.

Usually biomolecules can contain several types of functional groups, which obviously affects the chemical properties of biomolecules making them capable of participating in various kinds of biochemical reactions or biological processes. An example may be proteins which contain several functional groups which can manifest at the same time the specific properties of organic compounds of different types, as basic or/and acidic properties, or they can be oxidized, reduced, chemically modified (acylated, phosphorylated, glycosylated).

Below are described some functional groups commonly found in various types of biomolecules.

Hydroxyl functional group (- OH)

This functional group is widespread among biomolecules. Although this group in organic chemistry belongs to a specific class of organic compounds such as alcohols and phenols, in biochemistry it is present in various types of biomolecules, not necessarily alcohols.

However, despite being present in different types of biomolecules, it may confer essentially the same physical and chemical properties specific for alcohols and phenols.

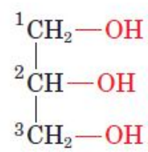
This group is present in amino acids, proteins, carbohydrates, lipids, and in some organic acids, polyalcohols (glycerol). It is a polar functional group and can give biomolecules polar, hydrophilic properties.

OH group is important in the formation of chemical bonds between the bio-molecules such as ester bonds, glycosidic, hydrogen bonds.

It is important to not confuse this group with that present in alkaline bases, e.g. NaOH. In these compounds it can dissociate as hydroxyl ion OH^- giving the environment a basic character, this is not specific to biomolecules. Rather, in some biomolecules in certain circumstances, it behaves like acid.

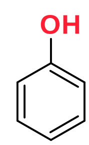
Types of biomolecules in which the hydroxyl group is present

Aliphatic alcohols R-OH



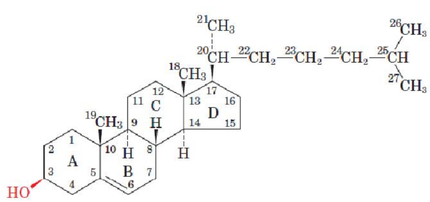
Glycerol (polyalcohol)

Aromatic Alcohols Ar-OH



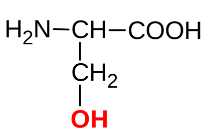
Phenol

Steroidic alcohols (sterols)

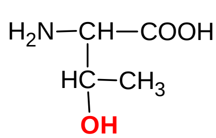


Cholesterol

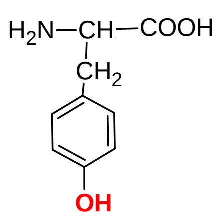
Amino acids (proteins)



Serine

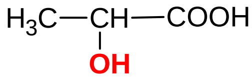


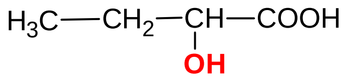
Threonine

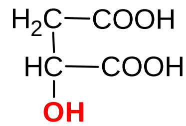


Tyrosine

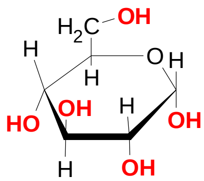
Hydroxy acids


Lactic acid


β-Hydroxybutiric acid

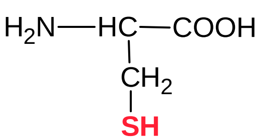

Malic acid

Carbohydrates


Glucose

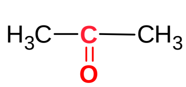
Functional sulfhydryl group (- SH)

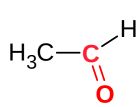
It is the functional group of thiols R-SH, alcohol analogs. It is found in the cysteine amino acid and respective in proteins, in coenzyme A (CoA), glutathione. Participate in disulfide bond formation in some proteins, e.g. insulin.

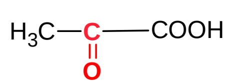

Cysteine

Carbonyl functional group (= C = O)

It is functional group of ketones R_1-CO-R_2 and aldehydes R-CHO. Is present in ketoacids as pyruvic, oxaloacetic, acetoacetic; monosaccharides (aldoses and ketoses).


Acetone


Acetaldehyde


Pyruvic acid

Carboxyl functional group (- COOH)

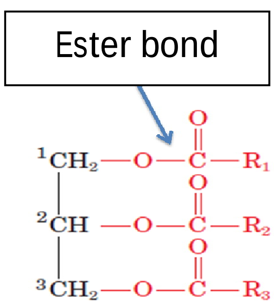
Is the functional group of carboxylic acids R-COOH and is present as additional group in biomolecules such as amino acids, proteins, certain carbohydrates, lipids.

CH_3 - $(CH_2)_n$ – COOH	$H_2N-\underset{\displaystyle R}{\underset{\vert}{CH}}-COOH$
Fatty acid	Amino acid

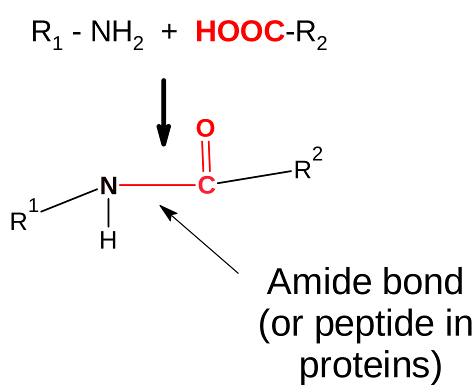
This group gives biomolecules an acidic property. In the body it is in ionized form as carboxylate -COO$^-$.

$$R-COOH \rightleftharpoons R-COO^- + H^+$$

The carboxyl group is involved in the formation of ester bonds (in lipids),

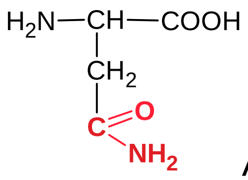


amide bonds in proteins (peptide bond).



Amide functional group (- $CONH_2$)

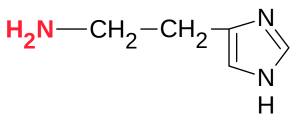
It is a functional group of the amides R-$CONH_2$, is present in biomolecules such as amino acids (asparagine and glutamine) and proteins.



Asparagine

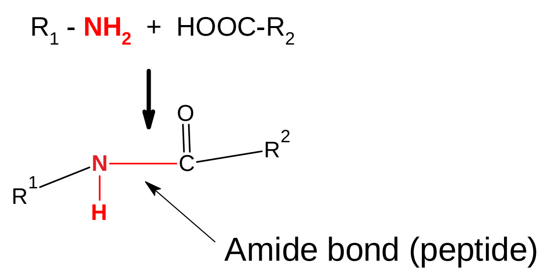
Amino functional group (- NH_2)

It is a functional group of the amines R-NH_2 and is present in biomolecules such as amino acids, proteins, amino sugars, and some lipids, biogenic amines (dopamine, serotonin and histamine).



Histamine

Amino group participates in the formation of amide special bonds – peptide bonds specific to proteins.



Amino group gives compounds basic character, it binds hydrogen ions. In the organism occurs in ionized form as -NH_3^+.

$$R\text{-}NH_2 + H^+ \rightarrow R\text{-}NH_3^+$$

Acyl functional group (- CO-R)

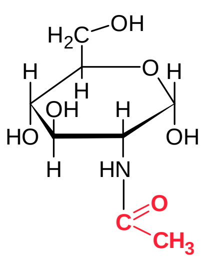
It is not considered functional when bound to the carbon atom.

In the organism it appears as a result of cleavage of OH group from carboxylic acids or aldehydes during biochemical reactions.

It can be linked to the atoms such as sulfur, nitrogen and phosphorus.

It is the functional group of **acylthiols** R_2-CO-S-R_1 e.g. the coenzyme A, where it is connected to sulfur of mercaptoethanol, one of the components of coenzyme A.

The acyl group is present in acylamines R_2-CO-NH-R_1, in amino sugars e.g. N-acetyl glucosamine.



N-acetyl-glucosamine

1.3 Types of chemical bonds

The chemical bonds associated to biomolecules can be divided into two types: **covalent and non-covalent.**

Covalent bonds may be **non-polar, polar, and coordinative or donor-acceptor**.

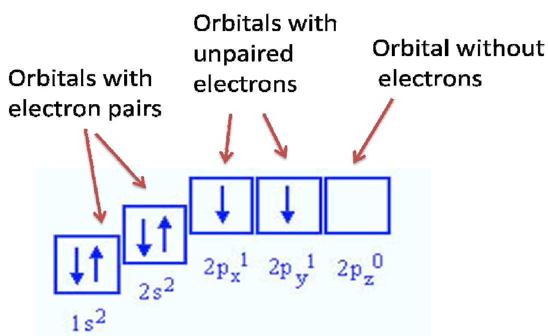
The non-covalent bonds can be ionic, hydrogenic, van der Waals and hydrophobic.

1.3.1 Covalent bonds

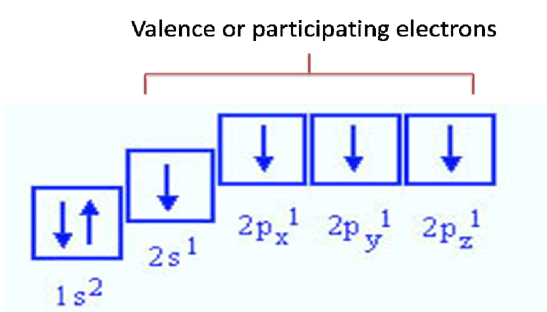
Covalent bonds appear as a result of interaction between atoms of (bio)elements and are defined as electrostatic attraction between a pair of electrons shared by the two atoms, being involved their nuclei. In other words, an electron of one atom pairs with an electron of another atom of the same or different kind.

It is known, that in atoms to be energetically stabile, their energetic levels must be filled with electrons. Except to inert gases, all the elements have their energetic levels incomplete, hence the tendency of atoms to combine with each other in order to complete their energetic levels with electrons. As a result covalent bonds form.

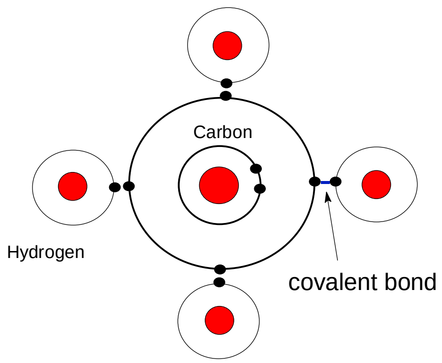
Below, as example is illustrated arrangement of the carbon electrons on energetic levels, the last being incomplete. It contains two unpaired electrons and a free orbital.



In organic molecules and respective biomolecules, the carbon atom is in excited state, an electron from $2s^2$ orbital pass to free $3p_z^0$ orbital (see figure above) as a result apier 4 orbitals with one unpaired electron on which (see figure below). These unpaired electrons will participate in the formation of covalent bonds. These electrons are called **valence** or **participating electrons,** and in the case of carbon atom, it can form



to 4 covalent bonds, for example, in the molecule of methane (CH_4) shown below.



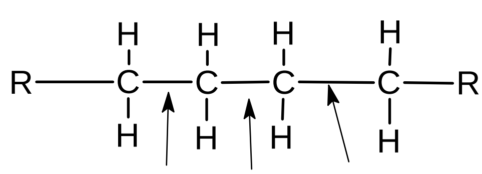
Sharing of electrons allows each atom to form a more stable electron configuration. In the chemical formulas, a covalent bond often is represented by a line between atoms.

Covalent bonds are very strong, for example, to break the C-C, C-H or C-O bonds is needed a large amount of energy, usually between 300 and 400 kJ/mol.

Depending on what kind of atoms (the degree of electronegativity) will participate in the formation of covalent bonds they can be: **non-polar** and **polar** and a special covalent bond called **coordinative** or donor-acceptor.

Non polar covalent bond

This bond is formed between atoms of the same or very close electronegativity. Each atom puts in common one electron. The pair of electrons is shared equally by the two atoms. For example, bonds between carbon atoms wich form the hydrocarbon chains (-CH2-CH2-CH2-CH2-) of the biomolecules.

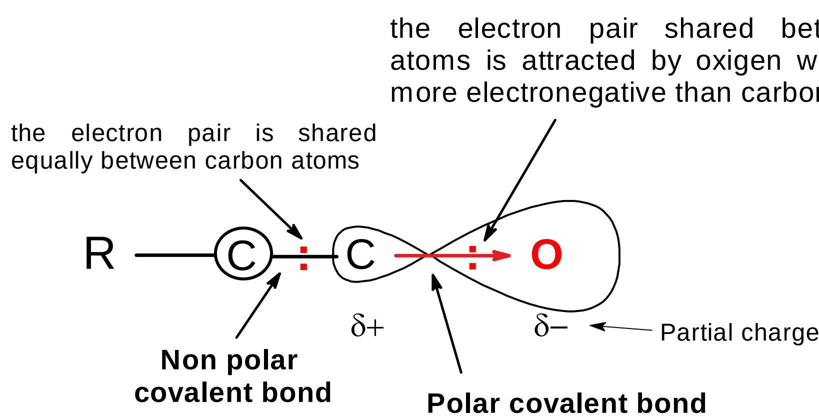


non polar covelent bonds

The presence of non polar covalent bonds in a biomolecule gives extra rigidity and makes it more inert chemically, more stable, that is very important especially for those biomolecules that have a structural role, for example lipids in biological membranes.

Polar covalent bond

This bond is formed between different kinds of non-metallic atoms of bioelements having different electronegativity. Although each atom put together one electron to form bond, electron pair formed is attracted by the more electronegative atom. For example the C-O, C-N, C-S bonds are polar. Oxygen, nitrogen and sulfur are more electronegative than carbon and they will attract the electron pair. As a result, these atoms become partially charged negative (because of electron partially attracted from carbon) and carbon atom becomes partially charged positive (because of its nucleus charged partially positive) (see the picture below).



Difference between non-polar and polar covalent bonds

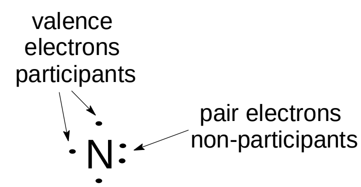
These bonds confer biomolecules a high degree of chemical reactivity, being more amenable to be broken during metabolic processes.

Coordinative or donor-acceptor covalent bond

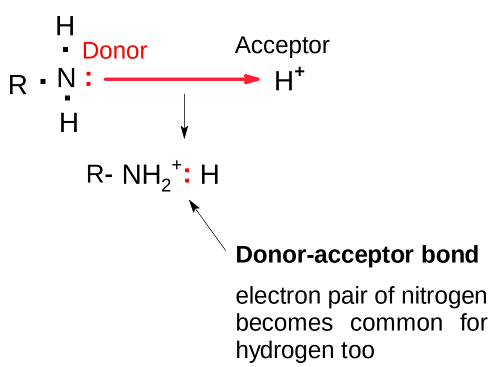
It is a special case of the covalent bond in which both electrons necessary to form the bond come from the same atom. In other words, covalent bond formation involves non participating electrons (pair) of the same atom.

The atom wich "donates" electron pair is called the **donor**, and the atom wich ''accepts'' is called acceptor.

An example may be the bond between the nitrogen atom of the amino group and the hydrogen cation (proton). The nitrogen atom on the last energetic level has 5 electrons three of which are unpaired and are **participants** in the formation of covalent bonds, two electrons form pair, and are **non-participants**.

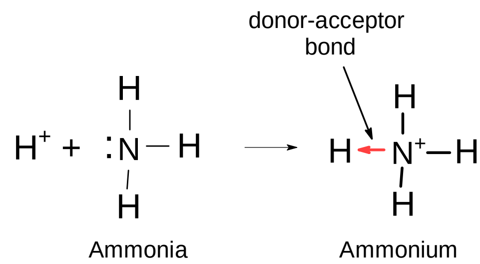


In the amino group unpaired electrons of nitrogen form covalent bonds, one with carbon and two with hydrogen, the electron pair do not participate in the formation of covalent bonds but can participate in formation of donor-acceptor bond being offered (donated) to an atom that possess a free orbital without electrons, for example to the cation of hydrogen. In fact, nitrogen offers one electron that hydrogen lacks to form a normal covalent bond. The amino group takes on a positive charge because of the hydrogen proton that attracting electron from nitrogen gives nitrogen a positive charge. This acquired positive charge becomes common for the entire amino group (see below diagram).



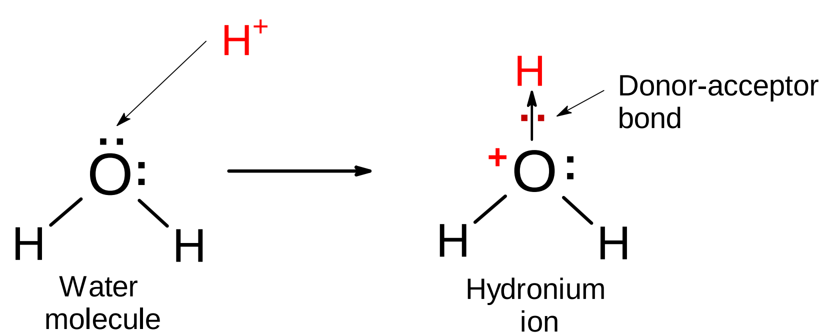
Nitrogen can donate electron pair to metals having free orbitals, for example to iron in hemoglobin. Other examples of donor-acceptor bonds formation can be formation of ammonium ion NH_4^+ and H_3O^+ hydronium ion. Both ions play an important role in the living body. Namely the formation mechanism of these ions, entail a need to specify in more details the biological significance of donor-acceptor bond.

Ammonium ion is formed when the molecule of ammonia NH_3 comes into contact with a hydrogen ion H^+ originating from the acid or water. Ammonia nitrogen is the donor and hydrogen ion is acceptor. Because of positively charged hydrogen ion ammonium ion becomes whole charged positive. Ammonium ion contains 3 covalently polar bonds N-H and one donor-acceptor N → H.



Ammonia is very toxic gas for the body. It is formed in some biochemical processes. Because of the ability of the nitrogen atom to form donor-acceptor bond, ammonia quickly interacts with hydrogen cations turning into ammonium ions, which are less toxic and can easily be removed from the body. Another example is the bonding of hydrogen cations by the imidazole nitrogen of histidine in hemoglobin. This contributes to the maintenance of normal hydrogen ions concentration in the blood and respectively the blood pH.

Hydronium ion, H_3O^+ are formed when the water molecule H_2O, in wich the oxygen atom has 2 nonpaticipating pairs of electrons, comes into contact with a hydrogen ion H^+ derived from an acid or another water molecule. Oxygen is a donor of pair of electrons and hydrogen ion is an acceptor. Because of positively charged hydrogen ion whole hydronium ion becomes positive. The hydronium ion contains 2 polar covalent bonds O-H and one donor-acceptor O → H (see reaction below)



1.3.2 Non-covalent bonds or interactions

Interactions between biomolecules (or between different parts of a biomacromolecule) are governed by a variety of weak links called **non-covalent bonds**. These links can occur between atoms of certain functional groups both within a biomolecule or between different biomolecules. Non-covalent bonds are not dependent on share electrons, but rather on attractive electric forces between atoms of biomolecules. These bonds are weak; their formation released very little energy - 4 to 20 kJ/mol that is why they can be easily broken and reformed. This feature allows non-covalent bonds to mediate the dynamic interactions between different biomolecules in the cell. Even if these bonds are weak individually, being numerous their forces are additive. Taken together, they provide considerable stability to biomolecules e.g. bonds that stabilize the double helix of DNA or tridimensional organization of protein molecules. They are also important in various biological processes in which biomolecules are interlinked specific and transitional e.g. hormone-receptor complex formation, antigen-antibody. Depending on how biomolecules interact with each other and what kind of forces governing these interactions can be distinguished several categories of non-covalent interactions: **van der Waals forces, electrostatic** and **hydrophobic interactions**.

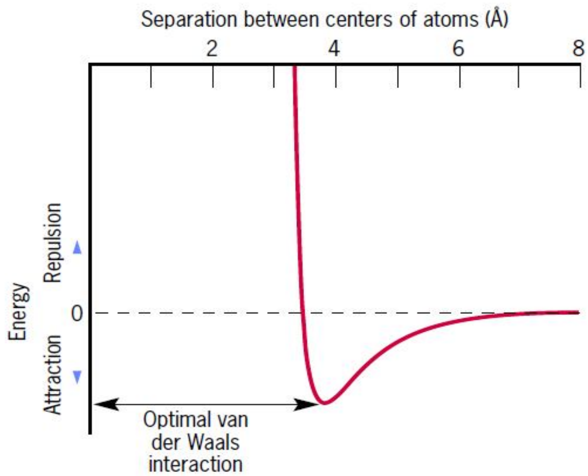
A. van der Waals forces

Van der Waals interactions or van der Waals forces are relatively weak forces of attraction or repulsions between neutral molecules, atoms. They were named after Dutch scientist Johannes Diderik van der Waals.

These forces are caused by correlations in the fluctuating polarizations of nearby particles (molecules, atoms)and tendency of particles to form electric dipoles, in line with each other and transmitting polarization to neighboring particles.

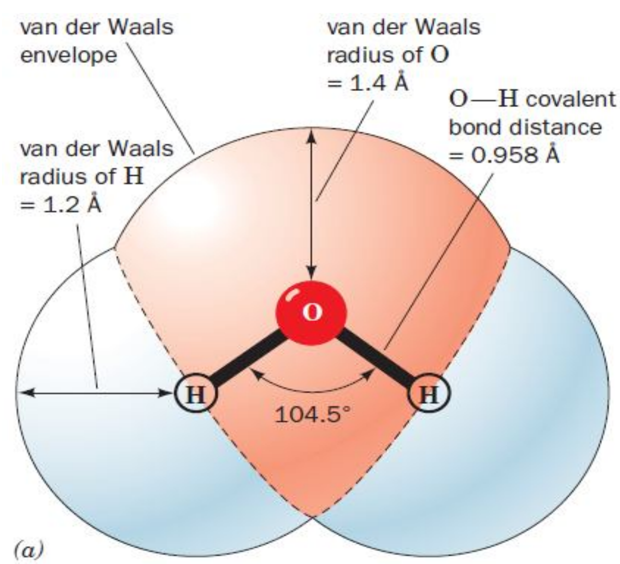
Each molecule has a range of electromagnetic action, the length of which varies depending on the type of atoms that make it up and on the orientation of molecule itself. Unbound free atoms have such range too. This range is called **van der Waals radius** (R_{vdw}).

Van der Waals radius indicates the electromagnetic fields of molecules or atoms that enable their mutual attraction up to a certain distance from which begin to act repulsion forces (see the diagram below).



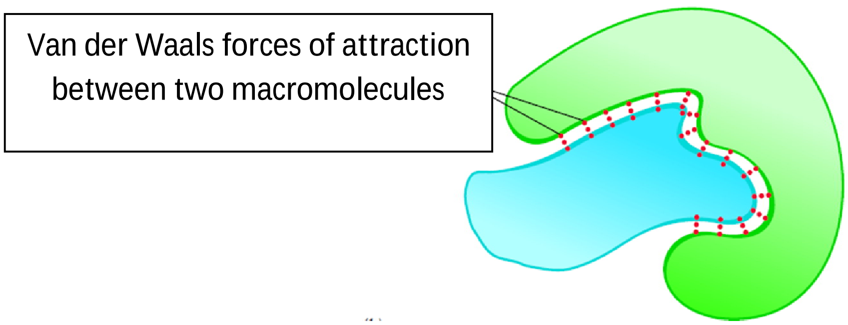
Å – Ångström=10^{-10}m

In other words, R_{vdw} indicates the effective area of a molecule or atom which can provide a contact to other atoms or molecules without the formation of chemical bonds. Within this area van der Waals forces act. The figure below illustrates the structure of the water molecule where is shown the length of covalent bonds between atoms of O and H and their van der Waals radius.



From the picture we can see that each atom has its R_{vdw} length. Due to these variations in length and orientation of molecule the dipole moments are created which will contribute to the attraction between molecules, but only up to distance corresponding to Rvdw. To overcome the van der Waals forces of repulsion is required to spend more energy than they possess. In this case the molecules get closer to each other and form chemical bonds.

Van der Waals attraction forces are important in biological systems. They contribute to the contacts of the various biomacromolecule for example in the formation of quaternary structure of the proteins - the association of several polypeptide chains into a functional protein molecule. Although these forces are very weak, their energy being 0.4 to 1.3 kJ/mol, they are numerous and acts additive.



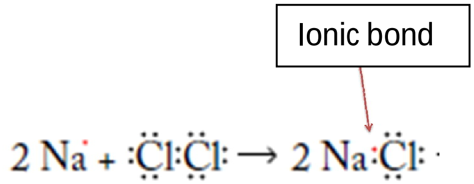
B. Electrostatic Interactions

These interactions may occur in biomolecules and between biomolecules as a result of electrostatic attraction between their ionized atoms or those who possess partial electric charge. In this category can be distinguished two types of non-covalent bonds: **ionic and hydrogen**.

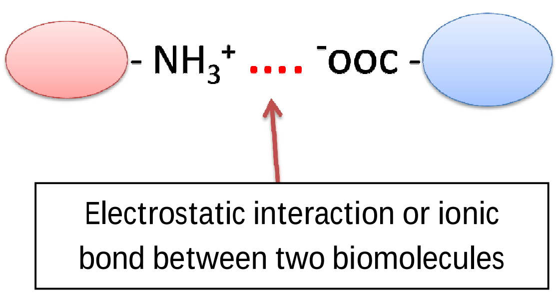
Ionic bonds

These bonds involve electrostatic attraction between oppositely charged ions e.g. Na^+ and Cl^- or biomolecules possessing oppositely charged functional groups e.g. $-NH_3^+$ and $-COO^-$. In fact, the thru ionic bonds form as a result of interactions of the atoms with very different electronegativity, e.g. Na^+ and Cl^- in NaCl crystals (table salt). Chlorine is more electronegative than Na and during interaction, chlorine completely takes an electron from Na, as a result chlorine gains an extra electron turning into negatively charged ion Cl^-

(anion) and Na losing completely its electron turning into positively charged ion Na^+ (cation). As a result, they will attract each other creating ionic bond.



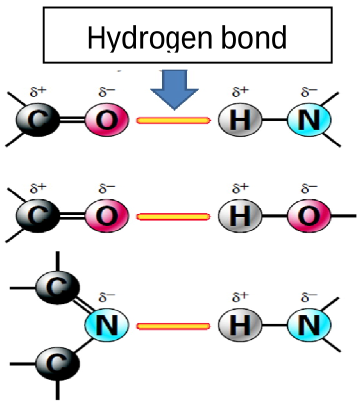
This bond is stronger than the covalent, but in contact with water it breaks easily due to the phenomenon of dissociation. In the case of biomolecules, already ionized and which possess positive or negative charged atoms or both, ionic bonding occurs as a result of electrostatic attraction between them. For example, amino group $-NH_3^+$ positively ionized generated by donor-acceptor mechanism will interact electrostaticaly with carboxylate group $-COO^-$ generated as a result of disociation. Therefore in biochemistry ionic bonds are often called electrostatic interactions or salt bridges. Ionic bonds can be intermolecular or intramolecular.



Ionic bonds formed in biological systems are much weaker than those formed between inorganic ions due to the presence of water which constantly tends to destabilize them. Only in depth of biomacromolecules, for example in proteins, where water does not enter, they are more durable and have an important role in structural-functional organization of biomolecules. Thus, ionic bonds participate in stabilizing the three-dimensional tertiary and quaternary structure of proteins, they are important in the formation of complexes between different proteins, protein-nucleic acid complexes, e.g. positively ionized histones form ionic bonds with negatively ionized DNA.

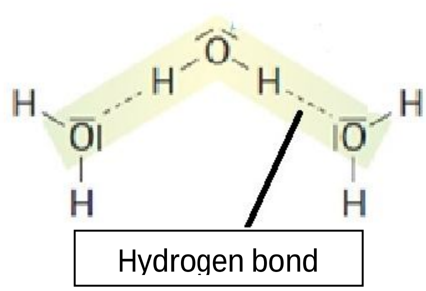
Hydrogen bonds

The **hydrogen bond** is the electrostatic or dipole-dipole attraction between polar molecules, occuring when the partially positively charged hydrogen atom bound to an atom with a higher electronegativity, such as nitrogen or oxygen, presents attraction to another nearby electronegative atom of the same molecule or another (see figure).

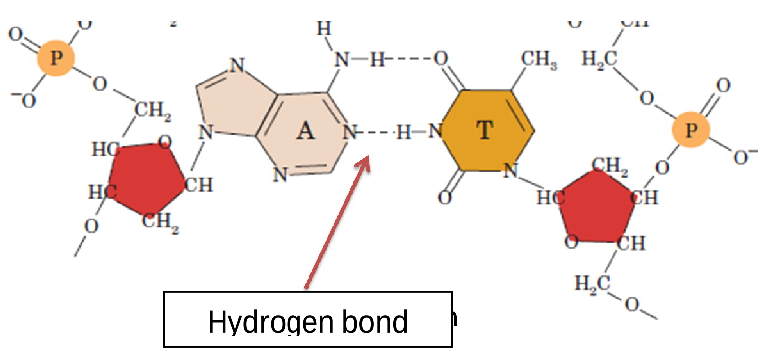


This type of bonding can occur intermolecular, ie between different molecules or intramolecular, ie between components of a single molecule. The hydrogen bond is stronger than van der Waals interaction, but is weaker than ionic or covalent bonds. The energy of formation of this bond is 10-40 kJ / mol.

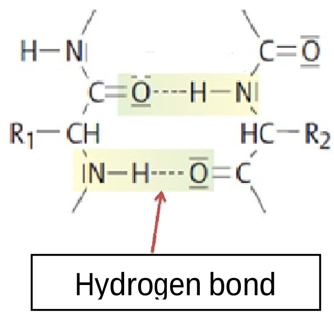
This bond is present both in inorganic compounds, such as water,



as well as biomolecules such as DNA,



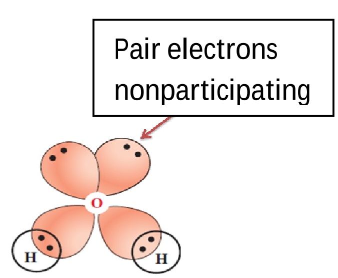
or proteins.



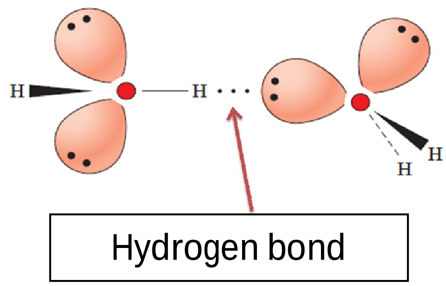
The mechanism of formation of the hydrogen is as follows. In the case where a hydrogen atom is bound covalently to an electronegative atom, O or N, the pair of electrons shared is more shifted to the nucleus of the electronegative atom, leaving the hydrogen atom with a partly positive charge (δ +), as a result, positively charged nucleus of hydrogen atom may aprouch enough at a distance of 0.18 nm to an electron pair of another electronegative atom of another molecule or other part of the same molecule, as a result will apier a weak interaction - **hydrogen bond**. In general, a hydrogen bond can be represented as A ---- DOH, where DOH is a weak acidic group "donor" such as OH, NH, or sometimes, SH, and A is a weakly basic atom " acceptor " , such as O, N or occasionaly S. Structuraly hydrogen bonds are symbolized as H --- A, where H is hydrogen atom and A is an acceptor atom. Their length is shorter by at least 0.05 nm than calculated van der Waals distance, i.e. the maximum distance between two nearby free unbound atoms. In water, for example, the length of the hydrogen bond O --- H is 0.18 nm to 0.26 nm (2.6 Å), corresponding to the van der Waals distance.

To form hydrogen bond is necessary to realise a small amount of energy sufficient to overcome the van der Waals forces of rejection, it occurs when an atom more electronegative than hydrogen through its attractive forces will overcome the forces of van der Waals rejection of the hydrogen atom. As a result, the atoms become close enough to each other to form the bond.

The figure below illustrates the structure of the water molecule where are shown pairs of nonparticipating electrons of oxygen that will contribute to hydrogen bonding.



These electrons will act as a weak base that will attract partly positively charged hydrogen from another water molecule (see picture below)



Hydrogen bonds play an important role in biological systems. Although they are individually weak, being numerous their strength is additive so they participate in the stabilization of the three dimensional structure of proteins and DNA.

C. Hydrophobic interactions

Hydrophobicity (from the Greek Hidros - water, phobos - fear) in chemistry, biochemistry, is a physical property of the molecules to reject to link water. Hydrophobicity is specific to nonpolar molecules, i.e. those molecules (organic and inorganic) which atoms do not have large differences in electronegativity. For example, hydrocarbon chains consisting only of carbon and hydrogen atoms that are nonpolar and they will tend to repel water molecules, as a result these chains can associate (stick) with each other, a phenomenon called **hydrophobic interaction**. These interactions are important in stabilizing the three-dimensional structures of proteins and nucleic acids (DNA). In these biomacromolecules hydrophobic interactions occur in those sectors of the molecule were concentrated many hydrocarbon side chains such as methyl, ethyl, propyl etc. which will exclude water. Hydrophobic interactions can be inter- and intramolecular.

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