Glossary - *Biochemistry* *(Intro)*

Alosteric Effect: Are interactions b/w spatially distinct sites; i.e.: a conformational change induced by the binding of a molecule to one site in a protein that alters other sites of the same protein (a molecular switch for receiving, integration, and transmission of signals); as in the case of hemoglobin, phospho-fructokinase, and ribonucleotide reductase;

Glycosidic Bond: A type of covalent bond that links sugar units together in a polysaccharide.

Fischer Representation: A two-dimensional representation of the molecule in which the C-atoms are aligned in a linear fashion, usually in a open-chain manner.

Haworth Projection: In such a projection, the C-atoms in the ring (furan, pyran) are not explicitly shown. The approximate plane of the ring is perpendicular to the plane of the paper, with the heavy lone on the ring projecting toward the reader.

Anomers: The C-1 carbon of a sugar ring (either pyranose or furanose form) to which the -OH group is attached;

a-form: α designates that the hydroxyl group attached to a C-1 is below the plane of the ring;

a-bond: The bond emerging from a C-1 carbon lies below the plane of the ring;

b-form: β designates that the hydroxyl group attached to a C-1 is above the plane of the ring;

b-bond: The bond emerging from a C-1 carbon lies above the plane of the ring;

(1-4): The anomeric C atom where the glycosidic bonding between mono-saccharides occurs; in this particular case b/w the C-1 of the first and the C-4 of the second mono-saccharide.

Hydrid Ion: Commonly a byproduct of oxidation processes; it consists of a H-nucleus and two electrons (**:**H^-)

Isomer: One of two or more compounds that contain the same number of the same atoms in different arrangements.

Geometrical I.: Atoms have the same partners but in different arrangements in space; such isomers cannot be interconverted w/o breaking a chemical bond;

e.g.: ClHC=CHCl as *cis*- (w/ dipol moment) and *trans*-(w/o dipole moment) dichlorethylene

Stereo-I.: Atoms have the same partners but in different arrangements in space; the letters D- and L- designate the absolute configuration of the asymmetrical orientation of ^{2}C: H-C-OH

- **Optical** I.: Stereoisomeric compounds that are non-superimposable mirror images;
  e.g.: *cis*- and *trans*-2-butene

Structural I.: Molecules that have the same molecular formula, but different structure;

e.g.: CH_3-O-CH_3 is a structural isomeric to CH_3-CH_2-OH

Maxwell-Boltzmann Speed Distribution: Displays the most probable spectrum of molecular speeds available to the system at a particular temperature; e.g. molecular oxygen has an average speed of 200[m/s] at 73[K], whereas it increases to about 400[m/s] at 273[K] (compare Brownian motion); see chemistry - gas.

Prosthetic Group: The tightly bound, non-protein portion of an enzyme but essential for its function; they differ from coenzymes in that they are more firmly attached (usually permanently) to the enzyme protein; e.g.: the heme group present in cytochromes.

Schiff Base: A nucleophile attacks a carbonyl group to form a tetrahedral intermediate which dehydrates afterwards generating the Schiff Base; serves as an e^--sink and is considered a potent e^- acceptor.

Substitution Reaction: A reaction in which an atom (or a group of atoms) replaces an atom in the original molecule; or in complexes; reaction typical of alkanes in which the displacement atom is a hydrogen atom.

Heterologic SR.: The atoms replaced, deprives the remaining molecule of electrons;

Homoligic SR.: The electrons are evenly shared b/w the trunk and the atom removed;

Nucleophilic SR.:

- N-SR of **1st Order**:
- N-SR of **2nd Order**:

Pauli Exclusion Principle: No two electrons in an atom can have the same four quantum numbers.

Glossary - *Biochemistry* *(Carbohydrates - Sugars)*

Asymmetry: Stereoisomer.

Carbohydrate: A compound that of the general formula $C_m(H_2O)_n$, although small deviations from this general formula are often encountered; they include starches, cellulose, and sugars like:
Fructose = fruit sugar (ketone) $C_6H_{12}O_6$
Glucose (aldehyde) $C_6H_{12}O_6$
Ribose (?) $C_5H_{10}O_5$
Deoxyribose (?) $C_5H_{10}O_4$
Sucrose $C_{12}H_{22}O_{11}$

Saccharide: Sugar units that are known as Mono-, Di-, or Poly-saccharides;

Mono-S.: Simple carbohydrates, aldehydes or ketones (see biochem-HC) with only two or more OH-groups $(CH_2O)_n$; e.g.: *triose* with n = 3, $(C_3H_6O_3)$ like aldose (R-CHO) or ketose (R-CO-R); see table below;

- *Pentoses* and *hexoses* of aldehydes react with alcohol to form a hemiacetal (hexagonal ring = *pyranose*); they usually adopt a typical chair-like conformation, to a lesser extent a boat-like conformation; e.g.:
  D-Glucose ($C_6H_{12}O_6$) + alcohol → α-D-Glucopyranose (a ring form of glucose)
  D-Glucose ($C_6H_{12}O_6$) + alcohol → β-D-Glucopyranose (a ring form of glucose)
- *Pentoses* and *hexoses* of ketones react with alcohol to form a hemiketal (pentagonal ring = *furanose*); they bend into a tyoical envelop-like conformation; e.g.:
  D-Fructose ($C_6H_{12}O_6$) + alcohol → α-D-Fructofuranose (a ring form of fructose)

Di-S.: When monosaccharides are warmed in an acid medium (HCl) containing an alcohol (methanol), the H^+ of the acid facilitates the removal of the -OH group by protonating the anomeric carbon atom (dehydration reaction); e.g.: hexose → acidic, alcoholic medium → glycosidic bonding of hexose **+ H_2O**

- Sucrose is obtained by joining a glucose with a fructose unit:
  D-**Gluco**pyranose + D-**Fructo**furanose → α-D-Glucopyranosyl-(1-2)-β-D-Fructofuranoside + H_2O
- Lactose is obtained by joining a galactose with a glucose unit:
  D-**Galacto**pyranose + D-**Gluco**pyranose → α-D-Galactopyranosyl-(1-4)-β-D-Glucopyranose + H_2O
- Maltose is obtained by joining two glucose units together:
  D-**Gluco**pyranose + D-**Gluco**pyranose → α-D-Glucopyranosyl-(1-4)-α-D-Glucopyranose + H_2O

with the numbers in parenthesis indicating the anomeric C atom where the glycosidic bonding occurs.

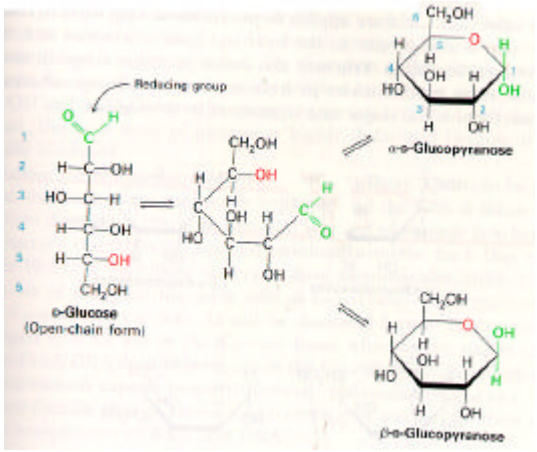
Poly-S.: A chain of many saccharide units, such as glucose, covalently linked together; e.g.:

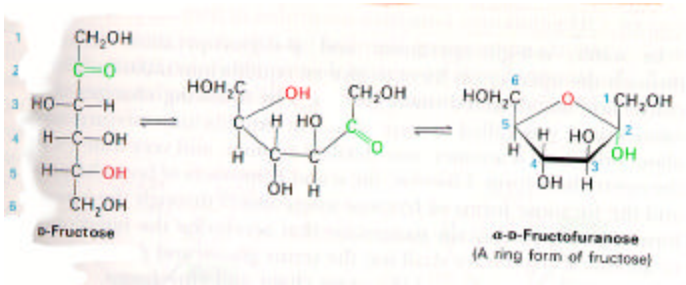
- Glycogen, a very large, branched polymer of glucose residues, where the main chain is joined together by α-1,4 glycosidic bonds, whereas the side chains are joined together by α-1,6-glycosidic bonds.
- Starch either in the form of Amylose (the unbranched form of α-1,4 linkages) and Amylopectin the branched form with α-1,6 linkage per thirty α-1,4 linkages.
- Cellulose, an indigestible polysaccharide for humans; an unbranched polymer of glucose residues joined by β-1,4 linkages. The β-configuration allows cellulose to form very long straight chains.
- Chitin, which consists of N-acetylglucosamine residues in β-1,4 linkage. Chitin is like cellulose except that the substituent at C-2 is an acetylated amino group instead of a hydroxyl group.

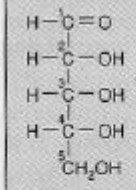
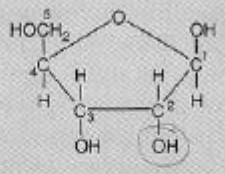
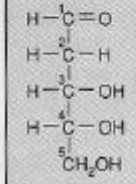
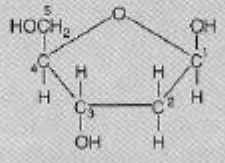
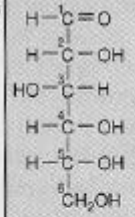
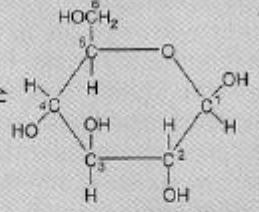
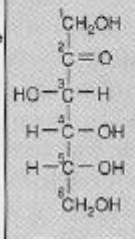
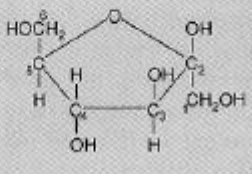
Stereoisomer: Isomers in which atoms have the same partners arranged differently in space (see biochem-HC); in which the letters D- and L- designate the absolute configuration of the asymmetrical orientation of C-2: H-C-OH; e.g.: D-aldose or L-aldose;

Stereochemical relations of D-aldoses and D-ketoses (linear Fischer representation)

	D-stereoisomer of aldose		L-stereoisomer of ketose	
triose n = 3, $(C_3H_6O_3)$	D-glyceraldehyde		Dihydroxyacetone	
tetrose with n = 4, $(C_4H_8O_4)$	D-Erythrose	D-Threose	D-Erythrulose	
pentose with n = 5, $(C_5H_{10}O_5)$	D-Ribose D, Arabinose	D-Xylose D-Lyxose	D-Ribulose	D-Xylulose
hexose with n = 6, $(C_6H_{12}O_6)$	D-Allose D-Altrose D-Glucose D-Mannose	D-Gulose D-Idose D-Galactose D-Talose	D-Psicose D-Fructose	D-Sorbose D-Tagatose





Sugar	Open chain	Ring	Significance
Pentoses Ribose			Sugar-phosphate backbone of RNA
Deoxyribose			Sugar-phosphate backbone of DNA
Hexoses Glucose			Energy source; cell walls
Fructose			Energy source; fruit sugar; soft-drink sweetener

Glossary - *Biochemistry* *(Hydrocarbons)*

Functional Group: Is a group of atoms that is largely responsible for the chemical behavior of the parent molecule.

Amino	$-NH_2$
Bromo	-Br
Chloro	-Cl
Fluro	-F
Hydroxyl	-OH (alcohols)
Iodo	-I
Nitro	$-NO_2$
Vinyl	$-CH=CH_2$

Alcohol: All alcohols contain the hydroxyl group, **-OH**, usually formed as a byproduct by the fermentation of sugars or starch; e.g.:
Methyl alcohol = methanol CH_3-OH
Ethyl-alcohol = ethanol C_2H_5-OH
Ethyl-2-alcohol = ethylene glycol C_2H_4-$(OH)_2$
Propyl-alcohol = propanol C_3H_7-OH
benzene-alcohol = phenol C_6H_5-OH

- **Primary** A.: Aldehydes with CO-groups; with two possible oxidation levels;
- **Secondary** A.: Ketone, carbon groups with one oxidation level;
- **Tertiary** A.: with no oxidation level at all

Aldehydes: Compounds with a carbonyl functional group and the general formula **RCHO**, where R is an H-atom, an alkyl, or an aryl group; can be converted from alcohols; their functional group is =C=O and differing from ketones only one H-atom is bonded to the C-atom; e.g.:
formaldehyde $H_2C=O$
Amines: Organic bases that have the functional group **-NR_2**, where R may be H, an alkyl group, or an aryl group;
amide ion NH_2^-
ethylamine CH_3-CH_2-NH_2
aniline (benzene C_6H_5- + -NH_2)
Aryl Group: A group of atoms equivalent to a benzene ring or a set of fused benzene rings, less 1H atom.
Carboxylic Acid: An usually weak acid that contains the carboxyl group **-COOH** (react easily with alcohol to form pleasant smelling esters) e.g.:
Acetic acid CH_3-COOH
Benzoic acid C_6H_5-COOH
Butric acid CH_3-$(CH_2)_2$-COOH
Citric acid COH-COOH-$(CH_2$-$COOH)_2$
Formic acid H-COOH
Glycine NH_2-CH_2-COOH
Oxalic acid HOOC-COOH
Ether: An organic compound containing the **R-O-R'** linkage, where R and R' are alkyl and/or aryl groups; formed by the condensation reaction of alcohols; highly explosive (in air tend to form peroxides) e.g.:
dimethyl-ether CH_3-O-CH_3
Esters: An organic compound containing the **R-O-R'** linkage, where R and R' are alkyl and/or aryl groups; used in the perfume industry, flavoring agents and as well as in DNA and RNA, ATP, cAMP, NADP, etc.; e.g.:
banana: 3-methylbuthyl acetate CH_3-$COOCH_2$-CH_2-$CH_2(CH_3)_2$
orange: octyl acetate CH_3-COOCH-CH_3-C_6H_{13}
apple: methyl butyrate CH_3-CH_2-CH_2COOCH_3
thioester: substitution of O with S;
Ketone: Compounds with a corbonyl functional group and the general formula **RR'CO**, where R and R' are alkyl and/or aryl groups; be converted from alcohols; their functional group is =C=O and differing from aldehydes, no H-atom is bonded to the C-atom; e.g.:
acetone $(H_3C)_2C=O$

Hydrocarbons: These molecules mainly consist of two elements, Hydrogen and Carbon.

Alipathic HC: Do not contain a benzene group, or benzene ring;

- **Alkanes**: HC's with the general formula C_nH_{2n+n}, where n = 1, 2, 3, ...; e.g.: first 6 linear alkanes:

methane (CH_4);	CH_4	C_1
ethane (C_2H_6);	CH_3-CH_3	C_2
propane (C_3H_8);	CH_3-CH_2-CH_3	C_3
butane and isobutane(C_4H_{10});	CH_3-$(CH_2)_2$-CH_3	C_4
pentane (C_5C_{12});	CH_3-$(CH_2)_3$-CH_3	C_5
hexane (C_6C_{14})	CH_3-$(CH_2)_4$-CH_3	C_6

- **Alkyl Groups**: When an H-atom is removed from alkanes; e.g.:

methyl (CH_3);	-CH_3
ethyl (C_2H_5);	-CH_2-CH_3
propyl (C_3H_7);	-CH_2-CH_2-CH_3
butyl and isobutyl (C_4H_9);	-CH_2-$(CH_2)_2$-CH_3

- **Alkenes**: HC's that contain one or more carbon-carbon double bonds (C=C); they have the general formula C_nH_{2n}, where n = 2, 3, 4, ...

methylene (CH_2)	HC=CH w/ one free bonding for each C atom
ethylene (C_2H_4)	$H_2C=CH_2$
propylene (C_3H_6)	H_3C-CH=CH_2 (2-propylene)
butene (C_4H_8)	CH_2=CH-CH_2-CH_3 (1-butene)
pentene (C_5H_{10})	CH_3-CH_2-CH_2-CH=CH_2 (5-pentene)
hexene (C_6H_{12})	CH_3-CH_2-CH=CH-CH_2-CH_3 (3-hexene)

- **Alkynes**: HC's that contain one or more carbon-carbon triple bonds (C≡C); they have the general formula C_nH_{2n-2}, where n = 2, 3, 4, ...

methyne (CH_3)	
propyne (C_3H_5)	CH_3-C°C-H (2-propyne)
butyne(C_4H_7)	HC≡C-CH_2-CH_3 (1-butene)
pentyne (C_5H_9)	CH_3-CH_2-CH_2-C°CH (5-pentyne)
hexyne (C_6H_{11})	CH_3-CH_2-C°C-CH_2-CH_3 (3-hexyne)

- **Cycloalkanes**: Alkanes whose atoms are joined in rings; with the general formula C_nH_{2n}, where n = 3, 4, 5,....

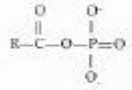
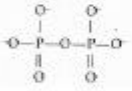
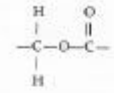
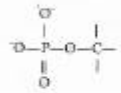
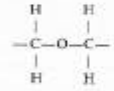
cyclopropane (C_3H_6);	-CH_2-CH_2-CH_2-	C_3 - triangular
cyclobutane (C_4H_8);	-CH_2-CH_2-CH_2-CH_2-	C_4 -squared
cyclopentane (C_5C_{10});	-CH_2-CH_2-CH_2-CH_2-CH_2-	C_5 - pentagonal
cyclohexane (C_6H_{12})	-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-	C_6 - hexagonal

Aromatic HC: Contain one or more benzene rings; each ring consists of **6** C-atoms attached via a *double bond* on one and a *single bond* on the other side, typically forming the C_6 -ring; C_6H_6

Ethyl + benzene	C_6H_5 - CH_2-CH_3 (ethylbenzene)
Chlor + benzene	C_6H_5 - Cl (chlorobenzene)
Amino + benzene	C_6H_5 - NH_2 (aminobenzene)

Nomenclature: Hydrocarbon molecules are denoted by their number of C-atoms embedded in a molecule; the C-atoms are numbered along the longest C-chain, with the initial C_1 closest to the C-atom bearing the substituted group; e.g.: a C_4-linear chain equivalent to butane-body with a CH_3 attached to 2^{nd} C = 2-methylbutane;

Important functional groups and their reactions

Functional group	Name	Typical reactions
	Aldehyde	Functional group of reducing sugars such as glucose
	Alcohol	Lipids, carbohydrates
 (R = H, alkyl, or aryl)	Amine	Formation of ammonium salts with acids
	Acid anhydride	Energy metabolism, for example, acetyl phosphate
	Phosphoanhydride	Energy metabolism, for example, ATP
	Carbon-carbon double bond	Addition reactions with halogens, hydrogen halides, and water; hydrogenation to yield alkanes
	Carbon-carbon triple bond	Addition reactions with halogens, hydrogen halides; hydrogenation to yield alkenes and alkanes
	Carbonyl	Reduction to yield alcohols; oxidation of aldehydes to yield carboxylic acids
	Carboxyl	Esterification with alcoholic reaction with phosphorus pentachloride to yield acid chlorides
	Carboxylic acid	Organic, amino, and fatty acids
	Ester	Lipids of Bacteria and Eukarya, amino acid attachment to tRNAs
 (R = alkyl or aryl)	Ester	Hydrolysis to yield acids and alcohols
	Phosphate ester	Nucleic acids, DNA and RNA
	Ether	Lipids of Archaea, sphingolipids
 (X = F, Cl, Br, I)	Halogen	Exchange reactions: $CH_3CH_2Br + KI \longrightarrow CH_3CH_2I + KBr$
	Hydroxyl	Esterification (formation of an ester) with carboxylic acids; oxidation to aldehydes, ketones, and carboxylic acids
	Keto	Pyruvate, citric acid cycle intermediates
	Thioester	Energy metabolism, biosynthesis of fatty acids

Glossary - *Biochemistry* *(DNA and RNA)*

CAP: Catabolite Activator Protein, an alosteric protein which binds first to a cAMP (cyclic adenosine monophosphate) before it can dock onto the DNA, enabling the RNA polymerase to join it, triggering the mRNA synthesis.

DNA (deoxyribonucleic acid, since this sugar lacks the O-atom at the 2-C-position): A double chain of linked nucleotides; composed of a base, purine or pyrimidine, and a phosphate group, PO_3^-, having deoxyribose as their sugars) ; the fundamental substance of which genes are composed (see genetics for image);
in **eukaryota**: DNA wrapped around histones, forming nucleosomes on solenoids; i.e. chromosomes.
in **prokaryota**: DNA is circular and supercoiled, do not have chromatin (histones etc.).
DNA **Double Helix**: Two right-handed interlocking helixes, constituting a B-DNA type helix, joined by hydrogen bonds between the pairs purine-pyrimidine bases (A pairs w/ T and G w/ C); together 2nm in diameter. The helical structure makes a 360° twist after each 10 residues of each chain; i.e.: 3.4nm.
The **major Groove** 1.2nm wide and slightly deeper then the **minor Groove**, 0.6nm wide; these result due to the non-glycosidic bonding of opposing pairs of the centrally located purine and pyrimidine pairs and the phosphate-sugar backbone on the outside.
DNA **Sequence**: The linear assembly of purine-pyrimidine nucleotides (A pairs w/ T and G w/ C) along a DNA strand.

DNA **Mutation**: (L. mutare, to change) A permanent change in chemical structure, organization, or amount of DNA; produces a gene or a chromosome set differing from the wild type, resulting in a faulty protein (loss or gain of function; gains and selection are the tools of evolution); e.g.: UV-radiation (*Xerodermy pigmentosum*), etc.

DNA **Packing**: In Eukaryota;
Histone: A type of basic protein that forms the unit around which DNA is coiled in the nucleosomes of eukaryotic chromosomes, allowing extreme long DNA molecules to be packed into a cell nucleus. **h1** (stabilizing solenoid, in between every nucleosome) **h2, h2a, h2b, h3, h4** (form the octameric core).
Gyrase: En energy-transducing enzyme; it converts free energy of ATP into torsional energy for supercoiling;
Nucleosome: The basic unit of eukaryotic chromosome structure; a ball of eight histone molecules wrapped around by two coils of DNA; it is the main protagonist in packing the DNA strand; can easily be disturbed by UV-exposure (easily absorbs wavelengths of about 260nm)
Scaffold: The central framework of a chromosome to which the DNA solenoid is attached as loops; composed largely of topoisomerase.
Solenoid Structure: The packed arrangement of DNA in eukaryotic nuclear chromosomes produced by coiling the continuos string of nucleosomes.
Supercoil: A closed double stranded DNA molecule that is twisted on itself in prokaryotes. Kinking of specific base sequences allows bending of discrete sites; packaging is even further increased by the slightly twisted base pairs, they are not co-planar.
Negatively Supercoiling: Allows a more compact packing than a relaxed twisted DNA circle, by twisting the DNA helix in itself again.
Topoisomerase: Enzyme unwinding the tightly coiled DNA arrangement, for DNA-replication (see below).

DNA **Replication**:
Semiconservative Replication: The established model of DNA replication in which each double-stranded molecule is composed of on parental strand and one newly polymerized strand; i.e.: parental strand determines the sequence of the complimentary strand (after Meselson and Stahl). DNA synthesis is mediated by several enzymes (see below);

- In prokaryota: Starts at a special site named oriC and ending at the opposed terminus of the circular DNA.
- In eukaryota: Occurs in the S-phase of the cell-cycle (part of interphase); there many Ori-sites allow simultanous replication.
  DNA **Topoisomerase**: Enzyme unwinding the tightly coiled DNA arrangement, for DNA-replication. It catalyzes a 3-step process: cleavage of one or both strands of DNA, passing of a segment of DNA through this breakage and resealing of the broken ends

Replication Fork: The point at which the two strands of DNA are separated to allow replication of each strand moving from the 3' to the 5' end of the parental sense (coding, upper or + strand), see polymerase.

- **Lagging Strand**: The strand that is synthesized apparently in the 3' to 5' direction, by ligating short fragments synthesized individually in the 5' to 3' direction (see okazaki fragments).

- **Leading Strand**: The strand that is made in the 5' to 3' direction by continuos polymerization at the 3' growing tip.
- **Okazaki Fragments**: Each of the short discontinued segments in the 3'-5'direction of the lagging strand made by DNA polymerase-III - about 1500 bases in eu-, 150 bases in prokaryota.

Helicase: An ATP-driven enzyme actively involved in the separation of the complimentary nucleotides of DNA; i.e.: separates the double helix into separate parental strands at roomtemperature, which would otherwise take a min. temperature of 90°C.

Ligase: An ATP-driven enzyme that can rejoin a broken phosphodiester bond in a nucleic acid, primarily used in the lagging strand to bond Okazaki fragments together (3' with 5' terminus), as well as bonding strands after the repair of mismatched bases.

Polymerase: Various enzymes that synthesizes new DNA strands (from 5' to 3') involved in the polymerization (formation) of large molecules out of monomeric units (building blocks), using a DNA template.

- **P.-I**: (Kronberg enzyme) A polypeptide chain (protein) consisting of a large fragment (Klenow) and a small fragment, that catalyzes chain growth in the 5'-3' direction, removes mismatched bases, degrades double stranded DNA; monomeric units like dTTP (**d**esoxy**T**hymine**T**ri**P**hosphate), dATP, dCTP, dGTP, dTTP, dUTP (in RNA only) are added to the newly synthesized strand (mediated by Mg^{2+} ions): dNTP, deoxyriboNucleoside TriphosPhate
  $(DNA)_{n\ residues} + dNTP \leftrightarrow (DNA)_{n+1} + PP_i$ PP_i, pyrophosphate group
  DNA-P-I adds deoxyribonucleotides to the 3'OH terminus of the preexisting DNA chain (primer); i.e.: a nucleophilic attack of the 3'-OH terminus of that primer on the innermost P-atom of a dNTP; this does take place only if the base on the incoming nucleotide is complementary to the base of the template strand. It also is capable of removing mismatched nucleotides of the newly synthesized strand; i.e.: proofreads and repairs.
- **P.-II**: Structural genes for proteins are transcribed by polymerase II; it is also required in DNA repair.
- **P.-III**: A protein in the form of an asymmetric dimer with a shorter arm for the leading strand and a longer arm for the lagging strand (Okazaki fragments); i.e.: a holoenzyme consisting of various subunits; designed to grasp its template and not let it go until it has been completely replicated by pol-I; it also cut out introns and splice exons.

Polymerase Chain Reaction (PCR): A method used to amplify a specific DNA sequence in vitro by repeated cycles of synthesis using specific primers and DNA polymerase.

Primase: This specializes RNA polymerase joins the prepriming complex in a multisubunit assembly called primosome.

Primer: A short RNA nucleic chain (polynucleotide) required to recognize the origin in DNA replication and to allow binding of nascent DANN, 1^{st} nucleotide (covalently bonded) during DNA polymerase. The Primer is again excised at a later stage of replication. The reason for using RNA- rather than DNA-Polymerase are:

- DNA polymerase I tests the correctness of the preceding base pair before forming a new phoshpodiester bond; RNA polymerase does not doe this;
- The use of RNA polymerase to initiate DNA synthesis is also plausible from an evolutionary viewpoint; RNA was probably present long before DNA emerged.

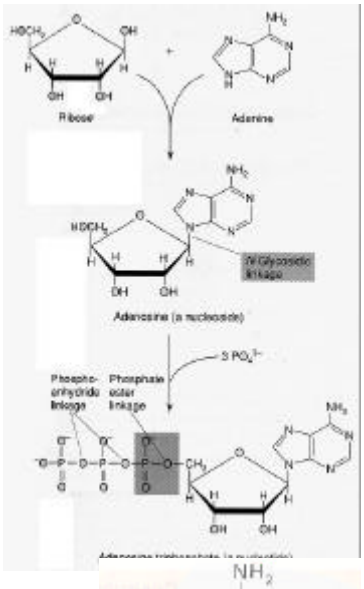
DNA-**Types**: Currently three separate forms are known:

A-DNA: A right-handed double helix made up of antiparallel strands held together by base paring. The helix is wider and shorter than the B-form, and its base pairs are tilted rather than normal to the helix axis; this form of helix is fond in the RNADNA hybrids and in the hairpin of tRNA.

B-DNA: Right-handed double helix denominated by a major (1.2nm) and a minor groove (0.6nm); these arise due to the glycosidic bonds of base pairs which are not diametrically opposite each other; the resulting slightly twisted arrangement allows kinking (bent at discrete sites) which makes this form of DNA the perfect type to be packed in a supercoiled manner into the nucleus of cells.

Z-DNA: A left-handed sequence of hexanucleotides hold together by base pairs; the phosphates of the backbone zigzags; this form is found in short oligonucleotides that have alternating sequences pyrimidines and purines;

Nucleoside: A purine or pyrimidine base bounded to a sugar.
Nucleotide: A purine or pyrimidine base bounded to a sugar and a phosphate ester; the basic single unit of nucleic acid composed of a PO_4^{2-}- and a 5-C sugar (either deoxy / ribose)-group and a purine / pyrimidine attached to it.

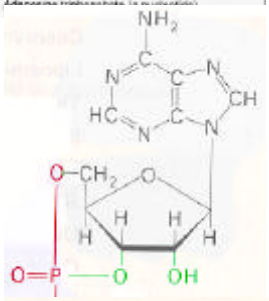


Phosphate Groups: High-energy phosphate compounds in the sense that much free energy is released when they are hydrolyzed.

- **ATP**: **A**denosine**T**ri**P**hosphate, a molecule consisting of adenine, ribose sugar, and 3-P groups. ATP can transfer energy from one molecule to another. ATP hydrolyzes to form ADP by releasing energy.
- ADP - Adenosine Di Phosphate, the de-energized state of ATP;
- AMP - Adenosine Mono Phosphate, the lowest energy state of ATP;

  $$\text{Energy charge} = \frac{[ATP] + \frac{1}{2}[ADP]}{[ATP] + [ADP] + [AMP]}$$

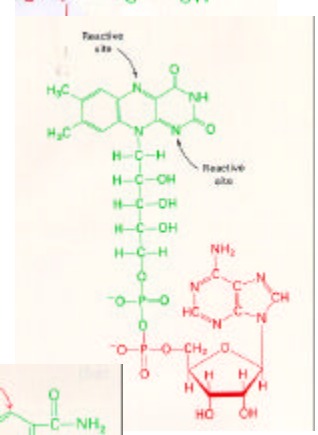
  accepting values of "0",all AMP and "1", all ATP;
  Anabolic Pathway: ATP-consuming;
  Catabolic Pathway: ATP-generating;
- **dATP, dCTP, dGTP, dTTP**, are activated precursors to enable chain elongation in DNA synthesis;
- **cAMP** (cyclic AMP): A ubiquitous cyclic nucleotide (adenosine 3`5`-cyclic monophosphate) produced from ATP by the enzymatic action of adenylate cyclase; important cellular regulatory agent that acts as the second messenger for many hormones and transmitter as a signal amplificator or in blood coagulation.
- **GTP**: **G**uanosine**T**ri**P**hosphate, high energy molecule similar to ATP that participates in several energy-requiring processes, i.e. peptide bond formation; as with ATP, GTP can acquire the lower energy levels as GDP and GMP.



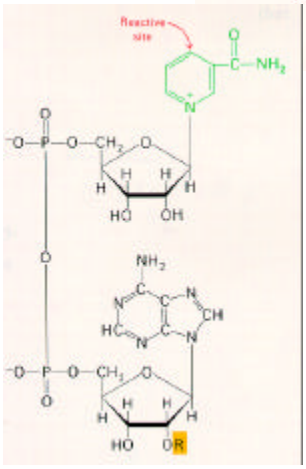
Adenine Dinucleotides: Major electron carrying compounds in the oxidation of fuel molecules;

- **FAD**: **F**lavin**A**denine**D**ineucleotide, a coenzyme formed by the condensation of riboflavin phosphate and adenylic acid; performs an important function in electron transport (oxidation of fuel molecules) and as a prostethic group for some enzymes.

FADH - intermediate to $FADH_2$; only one site of the isoalloxazine ring is occupied;
$FADH_2$ - isoalloxazine ring can occupy $2e^-$ and $2H^+$;



- **NAD**: **N**icotinamid**A**denine**D**inucleotide, a coenzyme which is widely distributed in living organisms, participating in many enzymatic reactions; made up of adenine, nicotinamide, and two molecules each of d-ribose and phosphoric acid; it functions as an electron acceptor in many of the oxidation reactions of respiration
  NAD^+ - oxidized form; is a major electron acceptor in the oxidation of fuel molecules (respiratory chain); with the reactive part the pyridine ring on top.
  NADH - reduced form of NAD^+; in the oxidation process accepts a H-ion and two electrons, which are equivalent to a hydride ion; R = H-ion;
  $NADP^+$ - oxidized form, a coenzyme that functions as an electron acceptor in many of the reduction reactions of biosynthesis; similar in structure to NAD^+ except that it contains an extra phosphate; R = PO_3^--ion.
  It is exclusively used as an e-donor in reductive biosynthesis, whereas NADH is oxidized by the respiratory chain to generate ATP.



RNA (ribonucleic acid): A single stranded nucleic acid similar to DNA but having ribose as its sugar (contains a OH-group at the 2-c position) and uracil rather than thymine as one of the bases; RNA is used as a working copy of the original DNA strand; RNA is less stable than DNA (for protein-, polypeptide chain synthesis see biochem.-AA).

mRNA (messenger RNA, constituting for 5% of total RNA): An RNA molecule transcribed from the DNA of a gene, and from which a protein is translated by the action of ribosomes.

- Capping of mRNA (methylation -CH_2 of the N^+ site of guanine or adenosine) is executed at the 5' terminus of the nascent mRNA to protect the 5'ends from phosphatase and nuclease activities; caps enhance the translation by eukaryotic protein-synthesizing system.
- Poly-A tail at the 3' terminus, is not encoded by the DNA; it increases the effectiveness of mRNA as a template in protein synthesis and protects mRNA from nuclease activities.

rRNA (ribosomal RNA, 80% of total RNA) A class of small (21 different proteins + an extra RNA molecule) and large (34 different proteins + 2 extra RNA molecules) subunit-RNA molecules, coded in the nuclear organizer, that have an integral role in ribosome structure and function. Eukaryotic and prokaryotic mRNA (incl their subunits) just differ slightly in their molecular weight.

tRNA: (transfer RNA, 15% of total RNA): Small cloverleaf (schematic; skeletal model is L-shaped) adapter molecules that bear specific amino acids (at the 3'-end =CCA) to the ribosome during translation. All tRNA must interact in nearly the same way (common structural features) therefore must fir into the A, P, E sites of rRNA. The amino acid is inserted into the growing polypeptide chain when the anticodon of the tRNA pairs with a codon on the mRNA being translated. The attachment of the amino acid to the specific tRNA is catalyzed by specific *aminoacetyl-tRNA-synthetases* (activation enzymes), this process requires the presence of the AA and an ATP:

$$\text{amino acid} + \text{ATP tRNA} + H_2O \leftrightarrow \text{aminoacyl-tRNA} + \text{AMP} + PP_i \text{ (exergonic)}$$

Mismatches of AA with the mediating tRNA are excluded by hydrolytic functions of the synthethase (at a perfect match AMP is released according to the formula stated above).

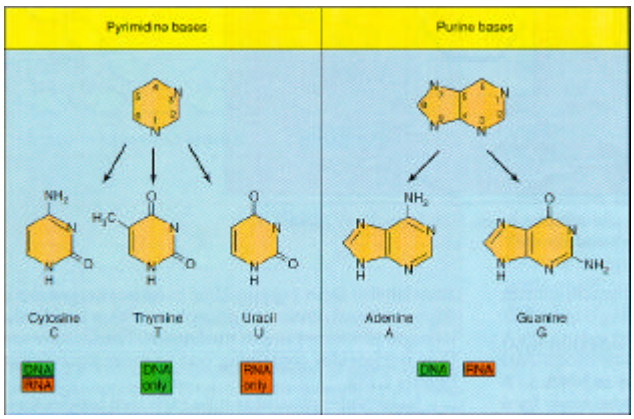
Common features of tRNA:

- tRNA is usually 73 to 93 ribonucleotides long;
- 5' terminus of tRNA is phosphorylated; usually pG
- base sequence at the 3' terminus of tRNA is CCA (the activated amino acid attaches to the 3'-OH group of the terminal adenosine);
- about half the nucleotides in tRNAs are base-paired (double helices); 5 groups of bases are not paired:
  i) 3'-CCA terminal region;
  i) the TψC-loop (derived from the name ribothymine-pseudouracil-cytosine);
  i) the *extra arm* made of some extra residues;
  i) the DHU loop containing several dihydrouracil residues and
  i) the anticodon loop, consisting of seven bases with the following sequence:
  pyrimidine-pyrimidine-X-Y-Z-modified purine-variable base

RNA Polymerase: Enzyme that catalyzes the synthesis of an RNA strand from a DNA template (does not require a primer, i.e. a core enzyme and the sigma factor - together form the holoenzyme). RNA polymerase is under control of cAMP and CAP; transcription is hindered (starvation) if only few glucose molecules are present whereas many glucose molecules degrade cAMP, facilitating transcription ("stop 'n go" mechanism). Synthesis of RNA (transcription) starts with initiation, elongation, and termination; transcription is based on the non-coding or complementary DNA strand, which makes the synthesized RNA identical to the coding strand (except for the uracil-base).

- **Promoter** (Initation): The site on DNA where RNA polymerase binds and begins transcription, i.e.: a regulator region just shortly off the 5' end of a gene. RNA polymerase itself is unable to start transcription at promoter site, rather it needs the σ-subunit to make this holoenzyme complete and to make the promoter site recognizable. Once found, RNA polymerase unwinds the template DNA by nearly 2 turns.
- **Transcription Bubble** (Elongation): During elongation of the RNA transcript, duplex DNA is unwound at the forward end of RNA polymerase and rewound at its rear end.
- Termination: A stop signal in the form of a hairpin loop followed by several uracil residues.
- **Rho-Factor**: Protein factor of prokaryota required to recognize certain transcription termination signals.
- **Sigma Subunit**: Enables RNA-pol to recognize promoter sites.

Purine: A type of double CN-ring base.
Adenine: Pairs with thymine.
Guanine: Pairs with cytosine.
Pyrimidine: A type of single CN-ring base.
Cytosine: Pairs with guanine.
Thymine: Pairs with adenine; in DNA only.
Uracil: In place of thymine (found in RNA only) that pairs with Adenine.



Splicing: The reaction that removes introns and joins together exons in eukaryotic RNA.
Exon: Any non-intron section of the coding sequence of a gene (in eukaryota only); exons spliced together constitute the mRNA and are translated into proteins (compare intron).
Intron (Gk. intervening sequence): A segment of largely unknown function (non-coding) within a gene of eukaryota which is initially transcribed but is not found in the functional mRNA - cut out (compare exon).

- **Self splicing** introns: A ribosome OH-group attacks a 5' splice site. The newly formed 3'-OH terminus of the upstream exon then attacks the 3' splice site to form a phosphodiester bond with the downstream exon.
- **Splicosome catalyzed** splicing: Splicing of mRNA precursors is carried out by splicosomes, which consist of small nuclear robonucleoprotein particles (snRNPs). Splice sites are specified by sequences at ends of introns and by a branch site near their 3' end. The 2'-OH of an A in the branch site attacks the 5' splice site to forma lariat intermediate. The newly generated3'-OH terminus of the upstream exon then attacks the 3' splice site to become joined to the downstream exon.

Template: A molecular "mold" that shapes the structure or sequence of another molecule; e.g. the nucleotide sequence of DNA acts as a template to control the nucleotide sequence of RNA during transcription.

Glossary - *Biochemistry* *(Aminoacids and Proteins)*

Amino Acid: A peptide; the basic building block of proteins or polypeptides equipped w/ a carboxyl group COOH, an amino group NH_2, a H-atom and a distinctive R-group.

Acidic AA: Have a negative and hydrophilic (Asp, Glu) or neutral but hydrophilic side chains (Asn, Gln).

Aliphatic AA: Amino acids in which the shorter side chains are hydrophilic (Ala, Gly, Pro,) whereas the long side chains gradually become hydrophobic, the more C-atoms it contains (Ile, Leu, Val); they do not have benzene rings. Attention, Proline differs slightly in structure;

Aliphatic hydroxylic AA: Amino acids with highly hydrophilic side chains (Ser, Thr);

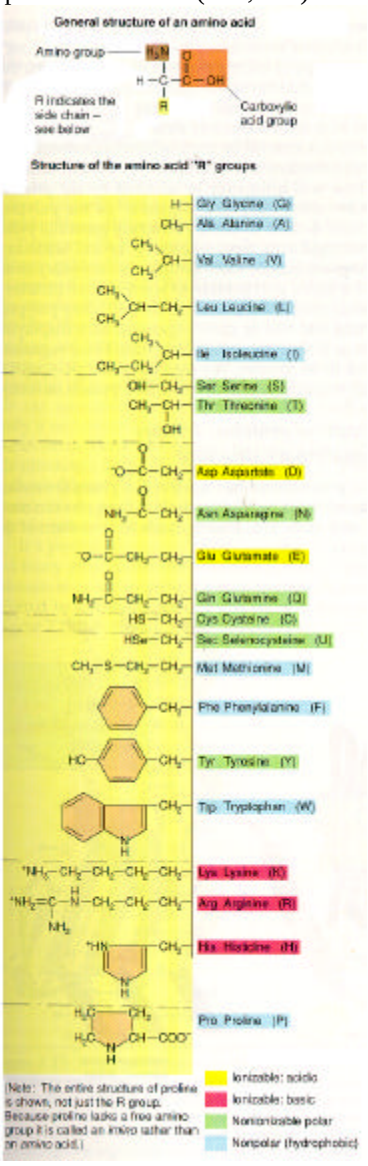
Aromatic AA: Side chain w/ a phenyl (benzene) ring attached to a methylene (-CH_2-) group (Phe, Trp, Tyr); highly hydrophobic;

Basic AA: Positively charged and highly hydrophilic side chain (Arg, Lys, His);

Sulfuric side chain: Hydrophobic sidechain (Cys, Met);

Nomenclature w/ triplet base sequences of mRNA:

Ala (alanine):	GCU GCC GCA GCG	nonpolar (alipatic)
Arg (arginine):	CGU CGC CGA CGG AGA AGG	basic (charged-ionizable)
Asn (asparagine):	AAU AAC	polar (nonionizable)
Asp (aspartic acid):	GAU GAC	acid (charged-ionizable)
Cys (cysteine):	UGU UGC	polar (nonionizable) + SH-tail
Gln (glutamine):	CAA CAG	polar (nonionizable)
Glu (glutamic acid):	GAA GAG	acid (charged-ionizable)
Gly (glycine):	GGU GGC GGA GGG	nonpolar
His (histidine):	CAU CAC	basic (charged-ionizable)
Ile (isoleucine):	AUU AUC AUA	nonpolar (alipatic)
Leu (leucine):	UUA UUG CUU CUC CUA CUG	nonpolar (alipatic)
Lys (lysine):	AAA AAG	basic (charged-ionizable)
Met (methionine):	AUG	**Start** + SCH_3-tail
	UAA UAG UGA	**Stop**
Phe (phenylaline):	UUU UUC	nonpolar (aromatic)
Pro (proline):	CCU CCC CCA CCG	nonpolar
Ser (serine):	UCU UCC UCA UCG AGU AGC	polar (nonionizable) + OH-tail
Thr (threonine):	ACU ACC ACA ACG	polar (nonionizable) + OH-tail
Trp (tryptophan):	UGG	nonpolar (aromatic)
Tyr (tyrosine):	UAU UAC	polar (nonionizable) + OH-tail
Val (valine):	GUU GUC GUA GUG	nonpolar (alipatic)



AA-Biosynthesis: AA are made from intermediates of the CAC andother major pathways. Humans can't make 9 of the set out of 20 - the essential AA (His, Iso, Leu, Lys, Met, Phe, Thre, Try, Val) which should be covered by food.

AA-Degradation: The strategy of amino acid degradation is to form major metabolic intermediates that can be converted into glucose or be oxidized by the CAC (citric acid cycle). The deamination of some AA is easily achieved by splitting the NH_4^+ from the main molecule, whereas in others a complicated mechanism mediated by NADH and arginase.

Urea Cycle: Arginine is hydrolyzed to urea $CO(NH)_2$ to urea and ornithine by arginase. Argininosuccinate synthethase then catalyzes the condensation of citrulline and asparate. Synthesis of argininosuccinate is driven by the cleavage of ATP into AMP and pyrophosphate and by subsequent hydrolysis. Finally argininosuccinase cleaves argininosuccinate again into arginine and fumarate (see biochem. - metabolism).

Bonds b/w AA: A link between two amino acids in which a byproduct is released (always endothermic);

Disulfide B.: A disulfide bridge is formed from the sulfohydryl groups (-SH) of cysteine residues yielding a cystine residue releasing a H_2 molecule.

Peptide B.: A type of a *rigid* and *planar* covalent bond (b/w the C and N atoms - there is a large degree of rotational freedom about these bonds on either side of the rigid peptide bond), joining amino acids in a polypeptide (also known as amide bond).The bonding of the α-carboxyl group of one amino acid to the α-amino group of another amino acid; in which a H_2O molecule is released; hence the biosynthesis of peptide bonds requires an input of free energy, whereas their hydrolysis is thermodynamically downhill.

Peptide Unit: A unit of a rigid planar array of N, H, C, and a O-atom;

Polypetide B.: Several amino acids linked together by peptide bonds determining the primary structure;

- **Dipeptide**: Two amino acids joined together;
- **Tripeptide**: Three amino acids joined together to form a linear chain;
- **Tetrapeptide**: Four amino acids joined together to form a linear chain;
- **Pentapeptide**: Five amino acids joined together to form a linear chain;
- **Polypeptide**: A linear chain of many amino acids (backbone) joined together by peptide bonds, with distinctive but variable side chains (depending upon the AA involved in the polypeptide).

Chaperon: A group of proteins that help other proteins fold or refold from a partially denaturated state; i.e.: disulfide-bonds are established which are the main structural holdfasts in proteins.

Coenzymes: Bound rather loosely to enzymes, and a single coenzyme molecule may associate with a number of different enzymes at different times during growth. They serve as intermediate carriers of small molecules from one enzyme to the other; most coenzymes are derivatives of vitamins; see biochem. - metablolism.

Enzyme: Usually a protein functioning as a catalyst in living organisms, which promotes *specific* reactions or groups of reactions; i.e.: lowers activation energy without being consumed or affected by the process w/o altering reaction equilibria.

Active Site: The portion of an enzyme that is directly involved in binding substrate(s).

Substrate: The molecule undergoing reaction with an enzyme.

Task of E. in humans:

- Enzymatic catalysis: Enzymes exhibit enormous catalytic power - increase by at least millionfold;
- Transport and storage: as in the case of hemoglobin transports oxygen, myoglobin stores it in muscles, etc.
- Coordinated motion: As in muscle contraction accomplished by the sliding motion of actin and myosin.
- Mechanical support: As in the case of collagen, provides stiffness and strength (fibrous protein).
- Immune protection: Antibodies that recognize and combine w/ surface proteins of viruses, etc.
- Generation and Transmission of nerve impulses: Response of nerve cells to specific stimuli are mediated by receptor proteins, like rhodopsin or chlorophyll in plants.
- Control of growth and differentiation: Repressor and growth proteins control the expression of genomes; hormones like insulin and thyroid stimulating hormones; serve as sensors to control flow of energy and matter.

Enzyme Kinetics: An enzyme E combines with a substrate S to form an ES complex, with a rate constant k_1.The ES complex can dissociate again (k_2), or it can proceed to form product P, wit a rate constant k_3:

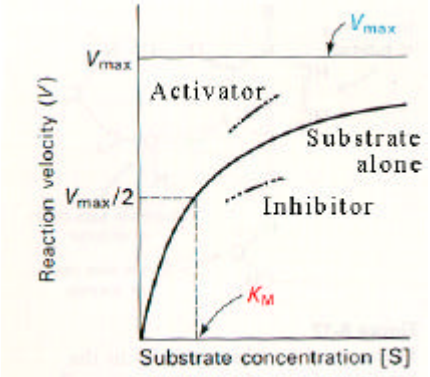
$E + S \underset{\leftarrow k_2 \leftarrow}{\rightarrow k_1 \rightarrow} ES \rightarrow k_3 \rightarrow E + P$ k_x, rate of reaction [varies]

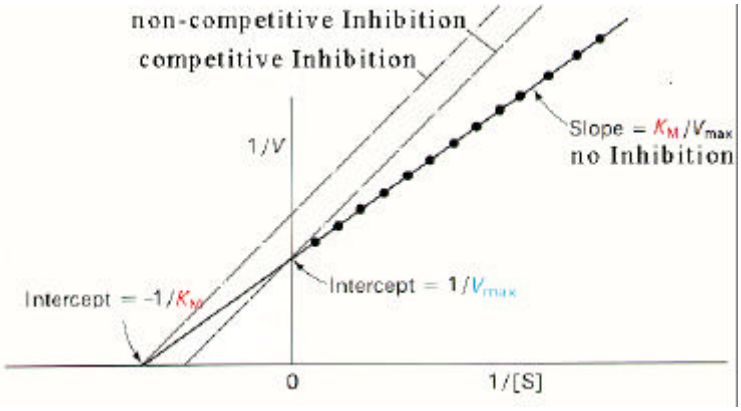
Michelis-Menten EQ: $V = V_{max} \frac{[S]}{[S] + K_M} = k_3 \cdot [ES] \frac{[S]}{[S + K_M]}$ [x], concentration [mol/L]

k_3, turnover constant

Michaelis-constant $K_M = \frac{k_2 + k_3}{k_1}$ K_M, Michaelis constant [mol/L] = reaction taking place at 50%

When $[S] = K_M$, then $V = V_{max}/2$; thus, K_M is equal to the substrate concentration at which the reaction rate is half its maximal value; when $k_3 << k_2$ then K_M equals the strength of the [ES] complex, consequently:
$>K_M$, weak ES-bond
$<K_M$, strong ES bond





Inhibition of Enzyme Activity: Is brought about by small molecules and ions; serves as a major control mechanism in biological systems; drugs and toxic agents have similar effects:
Irreversible Inhibitor: Tightly bound to the target enzyme (either covalently or non-covalently). Therefore, dissociates very slowly; e.g.: nerve gas DIPF on AChe;
Reversible Inhibitor: Characterized by a rapid dissociation of the enzyme-inhibitor complex. These feedback loops are necessary to control the product concentration; i.e: halt production when sufficient product material is available. This effect can either be:

- Competitive I.: The enzyme can either bind substrate (ES-complex) or inhibitor (EI-complex); a competitive inhibitor diminishes the rate of catalysis by reducing the proportion of enzyme molecules bound to a substrate; this effect can be overcome by a sufficiently high concentration of substrate.
- Noncompetitive I.: (alosteric reconfirmation) Inhibitor and substrate can bind simultaneously to an enzyme, forming an ESI-complex; a noncompetitive inhibitor acts by decreasing the turnover number, or is needed to activate the enzyme; this can't be overcome by increased concentration of substrate.
- Ping-Pong mechanism: Substrates bound to an enzyme (mediator) but the products released; itself is a substrate to be used for another [ES] complex (acetyl CoA carboxylase).
- Alosteric enzymes rather follow a sigmoidal path (as in the case of hemoglobin) than a hyperbolic path as indicated by enzyme kinetics; therefore, do not obey it!
  A. Activator: Shifts the conformational equilibrium towards the relaxed (R) state, stabilizing the R-state.
  A. Inhibitor: Shifts the conformational equilibrium towards the tense (T) state, stabilizing the T-state.

Lysozyme: An glycosidase enzyme which cleaves the polysaccharide component of cell walls in certain bacteria; usually those composed of NAG (N-acteylglucosamine) and NAM (N-acetylmuramate); it hydrolyzes the β-1,4-glycosidic bond between C-1 of NAG and C-4 of NAM (consumes a H_2O molecule for each bond broken; endergonic). It best works at pH of around 5, i.e.: when glutamic acid (35) is unionized and asparate (52) is ionized.

Prosthetic Group: The tightly bound, nonprotein portion of an enzyme but essential for its function; they differ from coenzymes in that they are more firmly attached (usually permanently) to the enzyme protein; e.g.: the heme group present in cytochromes.

Protein: (Gk. Proteios, primary) A complex organic compound composed of many (about 100) aminoacids joined together by peptide bonds, initiating w/ the amino residue H_3N-terminal and terminating w/ the carboxyl residue COO^--terminal(see polypeptide chain).

Protein Structure: Folding of the protein structure is achieved with the help of Chaperones. Protein function arises from conformation, which is the 3D arrangement of atoms in a structure.

- **Primary** S.: The sequence of amino acids, forming a polypeptide chain (determines folding).
- **Secondary** S.: Spiral (alpha-helix) or zigzag (beta-sheet) arrangement of a polypeptide chain.

Alpha Helix: A tightly coiled polypeptide main inner-chain forming the inner part of the rod, and the side chains extended outward in a helical array; the helical is stabilized by H-bonds b/w the NH and CO groups of the same main strand; the α-helix found in proteins is *right*-handed.

Beta pleated Sheet: A fully extended polypeptide chain stabilized by H-bonds b/w NH and CO groups od different polypeptide strands (of parallel oriented strands);

- **Tertiary** S.: The folding or coiling of the secondary structure to form a globular molecule originating from a single gene;
- **Quartiary** S.: A protein constructed of more than one globular molecules; i.e.: originating from different genes;

P. **Synthesis**: The flow of genetic information usually directed from the DNA to a protein by the activity of tRNA rRNA, and mRNA synthesized themselves from DNA; splicing of exons, capping and tailing; transportation into cytoplasm; translation from mRNA into polypeptide chain.

- One gene one enzyme: Each gene regulates the production of only one enzyme;
- One gene one polypeptide chain: Synthesis of each polypeptide chain is regulated by a different gene. Once the mRNA has settled onto the promoting site of the mRNA (Shine del Garno sequence), a $tRNA^{MET}$ (loaded with MET) clicks into the P-site (peptidyl) of the rRNA (the only one capable to do so) which currently settles at the AUG-codon of the mRNA. At the point of attachment the subsequent tRNA with the matching anticodon is slipped into the A-site(aminoacyl) of the ribosomal complex. As the complex moves along the mRNA strand, a tRNA linked to its particular amino acid fits into the first place and the first $tRNA^{MET}$ is released (Exit-site), leaving behind its amino acid, now enzymatically linked to the second amino acid by a peptide bond. The process continues dictated by the DNA from which the RNA was transcribed until the STOP-codon is reached. This triggers the release of the polypeptide chain and the separation of the ribosomal subunits from the mRNA; see biochem - DNA, RNA.

Special Proteins: Globin, a protein belonging to the myoglobin-hemoglobin family .

- **Chlorophyll**: (Gk. chloros, green + phyllon, leaf) The green pigment of plant cells, which is the receptor of light energy in photosynthesis; a tetrapyrrole ring structure on top with 4 internally placed N-atom, itself facing towards the centrally located Mg-atom; the entire complex is attached to a hydrophobic $C_{20}H_{39}$ phytol tail, which anchors the molecule into the photosynthetic thylakoid membrane; see table below.
- **Cytochrome**: Proteins with an iron-containing poryphyrin ring prosthetic groups (heme) attached to them. They undergo oxidation and reduction through loss or gain of a single electron by the iron atom at the center of the cytochrome: Cytochrome-Fe^{2+} ↔ cytochrome-Fe^{3+} + e^-

Heme Group: An iron protophyrine portion of many respiration pigments $C_{34}H_{33}O_4N_4FeOH$; four of the 6 valence electron are shared by the neighboring N's, whereas the remaining two are left for the distal and proximal histidine molecules.

- **Hemoglobin** HG: (Gk. hemo, blood) The oxygen carrying pigment of the erythrocytes, formed by the developing erythrocyte in bone marrow. It is a complex protein composed of four heme groups and four globin polypeptide chains. They are designated as α, β, γ, δ in an adult (embryonic HG is different), and each is composed of several hundred amino acids.

Each of these subunits houses a hydrophobic pocket, stuck together at these pockets, consistuting a molecule 4 times the size of myoglobin.

$HG(O_2)_n \leftrightarrow HG + nO_2$

Equilibrium constant $K = [HG][O_2]^n / [HG(O_2)_n]$

→, 1st order reaction

←, 2nd order reaction

[x], concentration in [mol/L]

Allosteric Effect: The O_2 affinity on an "empty" hemoglobin increases, because fewer salt bridges need to be broken (postage stamp analogy). The conformational change is brought about by the contacting regions of the 4 HG subunits denoted as $\alpha_1\beta_1$ and $\alpha_2\beta_2$. These two pairs are twisted to each other by 90°, allowing

a rotational angle of 15° according to the deoxigenated (T = taut) or oxigenated (R = relaxed) form. The $\alpha_1\beta_2$ contacting region is designed to act as a switch b/w these alternative structures. Thus, a structural change (oxigenation) w/n the subunit is translated into a changed interface b/w subunits, resulting in a slightly doomed porphyrine ring.

Bohr-Effect: A change in hemoglobin-oxygen affinity due to a change in pH. The presence of higher levels of CO_2 ($CO_2 + H_2O \leftrightarrow HCO_3^- + H^+$) in the capillaries of metabolic active tissue promotes the release of O_2 from hemoglobin.

BPG (2,3-biphosphoglycerate or DPG) binds to HG and lowers its oxygen affinity; it is present in adults in the same molar concentration than HG is; it is needed to unload the oxygen in the capillaries by binding to the deoxiginated form (not to the oxiginated form); it is strictly controlled by the Bohr effect. BPG lowers the O_2-affinity of HG by a factor of 26, which is essential in enabling HG to unload O_2 in tissue capillaries; BPG is stereochemically complementary to the central cavity formed by the 4 HG subunits; i.e.: 1BPG binds to one HG, this stabilizes the quartiary structure by crosslinks in the β-chains. The CO-terminals of BPG form 8 saltbridges which must be broken during oxigenation.

Cooperative effect: Binding at one heme facilitates the binding of O_2 at the other hemes on the same tetramer; conversely, the unloading of O_2 at one heme facilitates the unloading of O_2 at the others (heme groups communicate w/ each other), thus the cooperative binding of O_2 by HG enables it to deliver 1.83 times more oxygen than w/o it.

- **Flavoprotein**: Proteins containing a derivative of roboflavin; the flavon portion, which is the prosthetic group that is alternately reduced as it accepts H-atoms and oxidizes when electrons are passed on. It is commonly found in the electron transport chain during the synthesis of ATP. Riboflavin, also called vitamin B_2, is a required growth factor for some organisms.
- **Myoglobin**: (Gk. myo, muscle) An iron containing protophyrin-globin complex found in muscle; serves as a reservoir for oxygen and gives some muscles their red or pink color; the oxygen binding site allows the attachment of a distal and proximal histidine molecule. MG has a far higher O_2-affinity at low partial pressures than HG. $\rightarrow$, 1st order reaction
  $MGO_2 \leftrightarrow MG + O_2$ $\leftarrow$, 2nd order reaction
  Equilibrium constant $K = [MG][O_2] / [MGO_2]$ [x], concentration in [mol/L]
- **Phycobiliosome**: A large protein found in cyanobacteria and some red algae; they are bound in the outer face of thylakoid membranes, where they serve as light-absorbing antennas (for green and yellow hues) to funnel exitation energy into the reaction centers of photosystem II

Reading Frame: The codon sequence that is determined by the reading nucleotides in groups of three from some specific start codon, read consecutively in one direction; the grammar of DNA.

ORF (open reading frame): A section of a sequenced piece of DNA that begins with a start codon and ends with a stop codon; it is presumed to be the coding sequence of a gene.

Ramachandran Plot: Displays the values of ϕ and ψ

ϕ: Angle of rotation at the bond b/w the N and the α-C-atom;

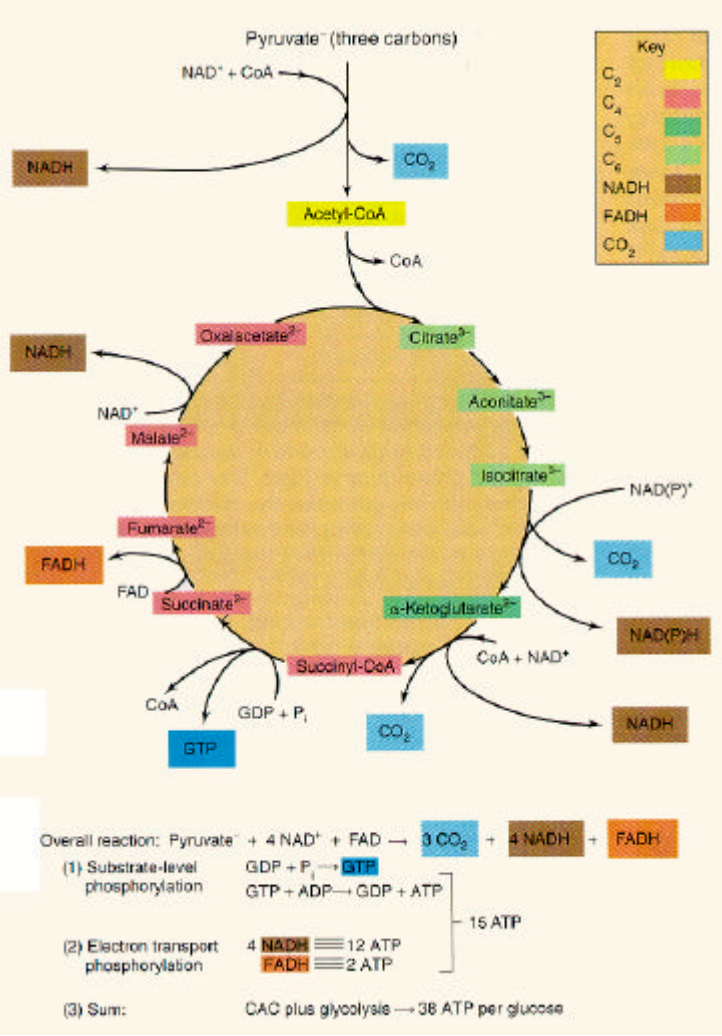
ψ: Angle of rotation at the α-C-atom and carbonyl atom;

Shine-Del-Garno Sequence: A 3-9 nucleotide long sequence preceding the start-region (AUG) of mRNA (see protein synthesis, transcription)

Glossary - *Biochemistry* *(Metabolism)*

Anaplerotic Reaction: (Gk. anapleros, to fill up) Synthesis of oxalacetate form pyruvate by carboxylase (see CAC).

CAC: **C**itric **A**cid **C**ycle (also Krebs or tricarboxylic acid cycle) A series of eight major reactions following glycolysis, in which acetate residues within mitochondria are degraded to CO_2 and NADH.
Under aerobic conditions, the generation of energy (ATP, NADH, $FADH_2$) from glucose is the oxidative decarboxylation of pyruvate to form acetyl CoA:
pyruvate + CoA + NAD^+ → (irreversible) → acetylCoA + CO_2 + NADH
This activated acetyl unit is the completely oxidized to CO_2 by the CAC; this cycle is the final common pathway for the oxidation of fuel molecules (amino acids, fatty acids and carbohydrates).
AcetylCoA + oxalacetate (C-4) → Citrate (C-6) → isomerized → isocitrate (still a 6-C-unit);
isocitrate → oxidative decarboxylation → α-ketoglutarate (5-C) + CO_2 → succinylCoA (4-C) + CO_2;
succinylCoA → succinate (C-4) + CoA + GTP → fumarate (C-4) → hydrated →malate (still C-4);
malate → oxidized → oxaloacetate
In the course of the cycle, 2 of the six C's are oxidized to CO_2 and oxalacetate is regenerated - thus literally making the series of reaction a cycle. Each turn around the cycle uses up one acetyl group and regenerates one molecule of oxalacetate, which is then ready to begin the Krebs cycle again. In the course of these steps, some of the energy released by the oxidation of the C atoms is used to convert ADP to ATP (one molecule per cycle), and some is used to convert NAD^+ to NADH (three molecules per cycle). In addition, some of the energy is used to reduce a second electron carrier - the coenzyme FAD. One molecule of $FADH_2$ is formed from FAD in each turn of the cycle. Oxygen is not directly involved in the Krebs cycle; the electrons and protons removed in the oxidation of C are all accepted by NAD^+ and FAD; the reduced e^--carrier ($FADH_2$, NADH) are subsequently oxidized by the electron transport chain to generate 9ATP molecules (+1 w/n the CAC); i.e.: the rate of CAC depends on the need for ATP:

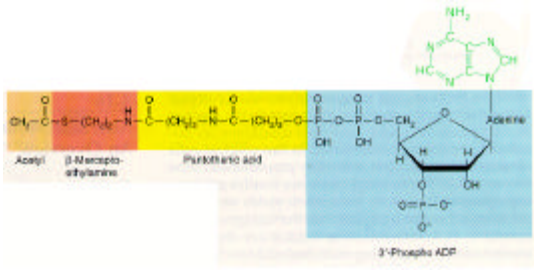


- Citrate: $(CH_2)_2$ CHO CO_2^- $(CO_2^-)_2$
- *cis*-Aconitate: CH_2 CH $C_2O_2^-$ $(CO_2^-)_2$
- Isocitrate: COH_2CH_2 $C_2HO_2^-$ $(CO_2^-)_2$
- α-Keto-glutarate: $CO(CH)_2(CO_2^-)_2$
- Succinyl-CoA: CoA-S-$O(CH_2)_2CO_2^-$
- Succinate: $(CH_2)_2(CO_2^-)_2$
- Fumarate: $(CH)_2(CO_2^-)_2$
- L-Malate: $C_3H_2O(CO_2^-)_2$
- Oxalacetate: $C_3H_4O(CO_2^-)_2$ an anaplerotic reaction (Gk. to fill up)

oxalacetate + acetylCoA + $3NAD^+$ + FAD + GDP + P_i + $2H_2O$ →
→ oxalacetate + $2CO_2$ + 3NADH + $FADH_2$ + GTP + $2H^+$ + CoA

Coenzyme: A nonprotein organic molecule that combines with an apoenzyme to form the functioning holoenzyme; it aids in enzyme-catalyzesd reactions, often by acting as an electron carrier (donor or acceptor);

- **CoA**: A derivative of panthothenic acid to which acetate becomes attached to form acetyl CoA (activated form; A = acetylation).
- **acetyl**COA: Is an universal carrier of acyl groups (R-CO-) which are linked to CoA by a thioester bond (S-) bond; acetylCoA has a higher acetyl group transfer potential, just as ATP carries an activated phosphate group: acetylCoA + $H_2O \rightarrow$ acetate + CoA + H^+
  Foodstuff (fats, polysaccharides, proteins) are broken down into smaller units which than are degraded to acetylCoA:
  pyruvate + TPP (carbanion) → addition compound + CO_2 → hydroxyethyl-TPP
  hydroxyethyl-TPP + lipoamide → carbanion of TPP +acetyllipoamide
  acetyllipoamide + HS → dihydrolipoamide + acetylCoA
- For **ATP**, **FAD**$^+$, **NAD**$^+$, see biochemistry - DNA-RNA.



Electron Transport Chain: see proton gradient.

Energy Harvest: The aerobic pathway breaks down glucose to CO_2 and H_2O, consumes O_2 as a final electron acceptor, and produces a total of 36 ATP per molecule of glucose.

Glycolysis: (Gk. glyk, sweet; lysis, dissolution) A series of reactions in the cytoplasms of a cell, that converts glucose to pyruvate w/ the concomitant production of a small amount of ATP (for details see glycolysis):
$C_6H_{12}O_6 + 2ADP + 2P_i + 2NAD^+ \rightarrow 2C_3H_4O_3 + 2ATP + 2NADH + 2\ H^+ + 2H_2O$

Krebs Cycle: A series of eight major reactions following glycolysis, in which acetate residues within mitochondria are degraded to CO_2 and NADH (for details see CAC):
acetylCoA + $3NAD^+ + FAD + GDP + P_i + 2H_2O \rightarrow 2CO_2 + 3NADH + FADH_2 + GTP + 2H^+ + CoA$

Electron Transport Chain: The energy bucket brigade - the voltage gradient across the mitochondrial wall, drives electrons along with hydrogen ions to the oxygen to generate water (for details see proton gradient):
$1/2O_2 + NADH + H^+ \rightarrow H2O + NAD^+$

Fatty Acid: A molecule with a carboxylic group at one end (hydrophilic) and a long hydrocarbon tail at the other (hydrophobic). FA are components of many lipids.

FA Oxidation:

Glycolysis: (Gk. glyk, sweet; lysis, dissolution) Embden-Mayerhof Pathway - a series of reactions that converts glucose to pyruvate w/ the concomitant production of a small amount of ATP (highly exergonic). Pyruvate is then shuttled into the cells. The series of reactions does not require the presence of oxygen to occur.
(Step 1-3: endergonic preparatory reactions; step 4-9: oxidative reactions; reduction reaction: see pyruvate)

1. Glucose is phosporylated by ATP to glucose-6-phosphate (G6P, a high energy-yielding reaction):
   $C_6H_{12}O_6$ (Glucose) + ATP → (hexokinase) → $C_6H_{11}O_6PO_3^{2-} + ADP + H^+$
2. G6P itself is further processed to fructose-6-phosophate (F6P, a pentose-ring):
   $C_6H_{11}O_6PO_3^{2-} \leftrightarrow$ (phosphogluco-isomerase) $\leftrightarrow C_6H_{11}O_6PO_3^{2-}$
3. finally F6P is altered to fructose-1,6-biphosphate (F1,6BP)
   $C_6H_{11}O_6PO_3^{2-} + 2ATP \leftrightarrow$ (phosphofructokinase) $\leftrightarrow C_6H_{10}O_6(PO_3^{2-})_2 + 2ADP + H^+$
4. Cleavage step: the pentose sugars split into 2 interconvertible 3-C molecules:

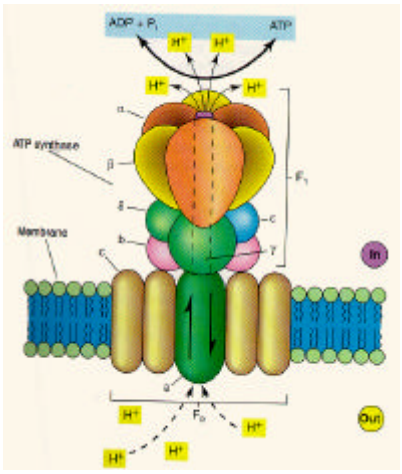
   $C_6H_{10}O_6(PO_3^{2-})_2$ (F1,6BP)
   ↓ (aldolase) ↓
   dihydroacetonephosphate $C_3H_5O_3(PO_3^{2-})$ ↔ glyceraldehyde-3-phosphate (G3P) $C_3H_5O_3(PO_3^{2-})$
5. G3P is oxidized (removal of H^+) to obtain 1,3-biphoglycerate (1,3DPG)
   $C_3H_5O_3(PO_3^{2-}) + P_i + NAD^+ \leftrightarrow$ (DG3-dehydrogenase) $\leftrightarrow C_3H_4O_4(PO_3^{2-})_2 + NADH + H^+$
6. the bond energy of 1,3DPG charges a ADP molecule whilst degrading to a 3-phosphoglycerate (3PG):
   $C_3H_4O_4(PO_3^{2-})_2 + ADP \leftrightarrow$ (glycerate-3-phosphate kinase) $\leftrightarrow C_3H_4O_4(PO_3^{2-}) + ATP$
7. the remaining phosphate group in 3PG is transferred from the 3-C to the 2-C position (2PG):
   $C_3H_4O_4(PO_3^{2-}) \leftrightarrow$ (phosphoglycero mutase) $\leftrightarrow C_3H_4O_4(PO_3^{2-})$
8. A water molecule is ripped of the 2PG to yield a phosphophenolpyruvate (PPP):
   $C_3H_4O_4(PO_3^{2-})$ (2PG) → (enolase) → $C_3H_2O_3(PO_3^{2-}) + H_2O$
9. PPP degenerates to pyruvate by charging another ADP molecule:
   $C_3H_2O_3(PO_3^{2-}) + ADP \rightarrow$ (pyruvate kinase) → $2CH_3\text{-}CO\text{-}COO^- + ATP$

Overall reaction: $C_6H_{12}O_6 + 2ADP + 2P_i + 2NAD^+ \rightarrow 2C_3H_4O_3 + 2ATP + 2NADH + 2\ H^+ + 2H_2O$
splitting of F1,6BP yield two successor molecules, therefore steps 5-9 have to be doubled;

Gluco-Neogenesis: The process of self-synthesized glucose by some organisms (like plants) which are not able to directly obtain hexose as a primary source of energy (backwards running glycolytic pathway); starting w/ pyruvate originating from glycolysisor lactate and alanine originating in muscles.
Many cells need NADPH for reductive biosynthesis and nucleic acid. In these cases, ribose-5posphate is converted into glyceraldehyde-3-phosphate and fructose-6-phosphate by transketolase and transaldolase; the net result of these reactions is the formation of 2 hexoses and one triose from 3 pentoses:
Transaldolase: Transfers a 3-C unit; $C_7 + C_3 \leftrightarrow C_4 + C_6$ or $C_5 + C_4 \leftrightarrow C_3 + C_6$
Transketolase: Transfers a 2-C unit $C_5 + C_5 \leftrightarrow C_3 + C_7$

Glycogen: A highly branched D-glucose polymer found in animals stored in an energy rich macro-molecule. Most of the glycogen are linked by α-1,4-glycosidic bonds (linear), with branches at about every 10^{th} residue by a α-1,6-glycosidic bond (branched).
Amylose (starch) is found instead in plants, a linear non-branched chain of glucose molecules bonded together by α-1,4-glycosidic bond.
Glycogendegradation: $glycogen_{n+1} + Pi \rightarrow glycogen + glucose\text{-}1\text{-}phosphate$
Glycogensynthesis:
$Glucose\text{-}6\text{-}phosphate + ATP + glycogen_n + H_2O + UTP \rightarrow glycogen_{n+1} + ADP + 2P_i + UTP$
UTP (UridineTriPhosphate) and UDP (UridineDiPhosphate) are activated forms of glucose.

Phosporylation: (Gk. phosphorous, bringing light) A reaction in which phosphate is added to a compound; e.g.: the formation of ATP from ADP.
Oxidative P.: The process in which ATP is formed as a result of the transport of electron from NADH or $FADH_2$ to O_2 by a series of electron carriers (e-transport chain, major source of ATP in aerobic organisms). OP generates 26 of the 30 molecules of ATP that are formed when glucose is completely oxidized to $CO_2 + H_2O$. The flow of energy (e^-) from NADH or $FADH_2$ to O_2 through protein complexes located in the inner membrane of mitochondria leads to the pumping of protons (H^+) out of the mitochondrial matrix, generating a proton motive force (pH-gradient), with the exterior acidic (+) and the interior basic (-).
ATPase: (the F_0F_1 ATPase complex) The F_0 portion is an integral membrane protein; the F_1 portion contains three copies of α-, and three β-subunits and is bound to F_0 via subunits γ, δ, and ε. The synthesis of ATP from ADP and P_i occurs spontaneously at the catalytic site on a β-subunit of the F_1, due to tight binding of ATP to this site. Proton movement through F_0, driven by the proton-motive force, promotes the catalytic synthesis of ATP by causing the bound ATP to be released; this frees up the site for the binding of ADP and P_i, which, in turn, spontaneously combine to form another tightly bound ATP; the entire process is osmotically coupled.



Site of ATP synthesis:

- Chloroplasts: (photo-phosoporylation) Formation of ATP from ADP (PSI), NADPH from $NADP^+$ (PSII) as energy carriers and inorganic phosphate.
  PS II: (photosystem II) A series of noncovalently bondend complex intrinsic polypeptides; associated with three peripheral (extrinsic) polypeptides, thought to aid in binding of Ca^{2+} and Cl^-, both of which are essential for photolysis of water.
  The P_{680} core complex (LIGHT HARVESTING COMPLEX-II) receives red light energy by inductive resonance *chlorophyll a* and *b* molecules, producing a strong oxidant (oxidizes water) and a weak reductant:
  $2H_2O \rightarrow (E_{light} = h \cdot f) \rightarrow O_2 + 4H^+ + 4e^-$
  f, frequency [s^{-1}] [Hz]
  h, plank's c. $6.63 \cdot 10^{-34}$ [J·s]
  The increasing H^+ concentration (low pH causes an electrochemical proton gradient) within the lumen of the thylakoid is used to synthesize ATP, when H^+ tunnels back out to the stroma through the integral coupling factors (CF's): $ADP + P_i \rightarrow (H^+) \rightarrow ATP$
  PS I: (potosystem I) Even though it uses (far) red light independently, PSII recruits electrons originally released by the PSII H_2O-lysis mediated via the cytochrome complex. This reaction causes cytochrome to transport H^+ ions across the membrane from the stroma into the thylakoid membrane (further decrease of internal pH). Two large polypeptides bind the reaction center P_{700}, some *chlorophyll a* molecules and three

electron carriers ($NADP^+$) called phylloquinone and a Fe-S group. The PSI core complex receives light by inductive resonance from *chlorophyll a* and *b* molecules formed to an other antenna system (LIGHT HARVESTING COMPLEX-I). The strong reductant produced by PSI reduces $NADP^+$, to NADPH, which is released into the stroma: f, frequency [s^{-1}] [Hz]

$2NADP^+ + 2H^+ \rightarrow (E_{light} = h \cdot f) \rightarrow 2NADPH$ h, plank's c. $6.63 \cdot 10^{-34}$ [J·s]

- Flagellar Motor: Flagellar motor of *E. coli* powered by the proton gradient; since rotor and stator are constituted by 16 proton-units each, a 360° turn requires a release of $256H^+$.
- Mitochondria: (oxidative phosphorylation) They contain the respiratory assembly, the enzymes of the CAC, and the enzymes of the FA oxidation. Integral proteins (ATPase) with their head (F_1) reaching out into the matrix and the base (F_0) reaching through the membrane into the intermambrane space.

F_1 consists of 5 polypetides, it is the catalytic protein responsible for the interconversion of ATP and ADP + P_i. F_0 is integrated in the membrane and consists of 3 polypeptides in several copies. It is responsible for channeling protons across the membrane. As protons enter, the dissipation of the proton motive force drives ATP synthesis from ADP + P_i, drives the extrusion of protons to the cell exterior; with every exported ATP, there is a net export of one electron out as well. Thus, ATP synthase is *reversible* in this action.

The final energy yield from one molecule of glucose in a Mitochodrium can be summarized as:

Glycolysis: $2ATP + 4ATP_{\text{ from 2NADH}}$ = 6ATP

Pyruvate → acetyl-CoA: 2x3ATP = 6ATP

CAC: $(1ATP + 9ATP_{\text{ from 3NADH}} + 2ATP_{\text{ from 1FADH2}}) \times 2 = 24ATP$, net yield 36ATP

Phosporylation **in Plants**: According to the <u>light-independent reaction</u>, CO_2 fixation is achieved by the following:

C_3 P.: (<u>Calvin cycle</u>) Enzymatically mediated photosynthetic reactions of <u>shade-plants</u> during which CO_2 is attached to ribulose, a C_5-sugar (RuBP, a CO_2 acceptor is the most abundant proteins of plants, up to 16% of the entire mass),

$$6CO_2 + 12NADPH + 12H^+ + 18ATP \rightarrow 1glucose + 12NADP^+ + 18ADP + 18P_i + 6H_2O$$

C_4 P.: Sun-loving plants with <u>spatial separation</u> of C-fixation: Photosynthesis in chloroplasts of mesophyll cells, synthesis of sugars and starch in the bundle sheath; due to spatial separation no competition between O_2 and CO_2, hence no photorespiration.

CAM P.: (Crassulacean Acid Metabolism) A variant of the C_4 pathway; characteristic of most succulent, slow-growing, desert-plants; e.g.: cacti. <u>Temporal separation</u>: CO_2 fixation at night (dark reaction), photosynthesis during the day (light reaction).

Proton Gradient: The energy bucket brigade - the voltage gradient across the mitochondrial wall, drives electrons along with hydrogen ions to the oxygen to generate water:

$1/2O_2 + NADH + H^+ \rightarrow H2O + NAD^+$

Protons are pumped out of the mitochondrial matrix as electrons are passed down the electron transport chain, which forms part of the inner mitochondrial membrane. The inward movement of protons down the electron gradient as they pass back across the inner membrane through the ATP synthase complex provides energy for synthesis of ATP from ADP and phosphate. Progressing down the electron transport chain, a water molecule as a byproduct is released for every three ATP's formed. As more protons are accumulated at the intermembrane space, a high pH is found there, whereas a low pH is present within the matrix.

Pyruvate: The end-product of glycolysis; the reduction reaction of pyruvate can yield lactate, ethanol and CO_2 as observed in fermentation processes or acetylCoA, water and CO_2 as in the case of aerobic respiration.

Ethanol: Is formed from pyruvate in yeast and several other microorganisms:

$CH_3\text{-}CO\text{-}COO^- + H^+ \rightarrow C_2H_4O$ (acetylaldehyde) + CO_2

$C_2H_4O + H^+ + NADH \leftrightarrow C_2H_5OH$ (ethanol)

Lactate: It is formed by various microorganisms, but also occurs in the cells of higher organisms when there is a shortage of oxygen; as in muscles during exercise:

$CH_3\text{-}CO\text{-}COO^- + H^+ + NADH \leftrightarrow$ (lactate dehydrogenase) $\leftrightarrow C_3H_4O_2OH$ (L-lactate) + NAD^+

Quinone: Highly hydrophobic molecules involved in electron transport. Some quinones are related to vitamin K, a growth factor in higher animals. Like flavoproteins, quinones serve as H-atom acceptors and electron donors in the electron transport chain during the synthesis of ATP.

Ubiquinone: Also known as coenzyme Q or ubiquinol, has a long hydrophobic tail and is the most common e^--carrying molecule in mitochondrial membrane.

Hydroquinone: The protonized (charged) form of ubiquinone.

Urea Cycle: Arginine is hydrolyzed to urea $CO(NH_2)_2$ and ornithine by arginase; an externally supplied carbonyl donor (carbonyl phosphate $H_2N\text{-}CO\text{-}PO_3^{2-}$ forms with ornithine citrulline, which along w/ asparate becomes arginino-succinate. Arginino-succinase cleaves it into arginine and fumarat; arginine is then reintroduced into the UC.