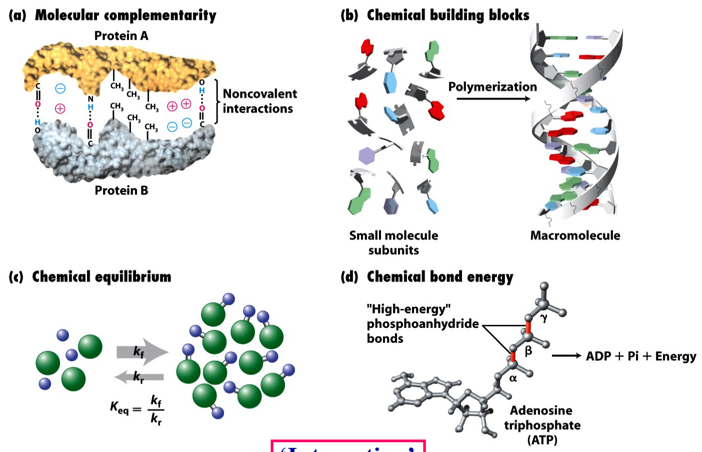
Molecular and Cellular Biology

2. Bio-Chemical Foundations & Key Molecules of a Cell

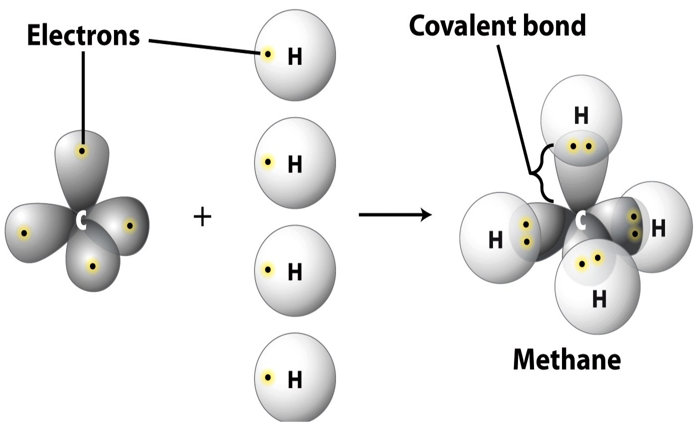
Prof. Dr. Klaus Heese

Cell Function & Chemistry



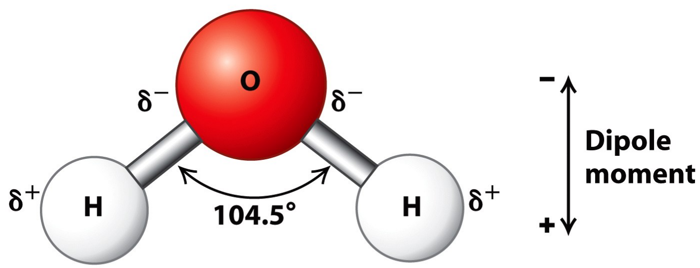
'Interaction'

Molecular Bonds Define Cellular Functions

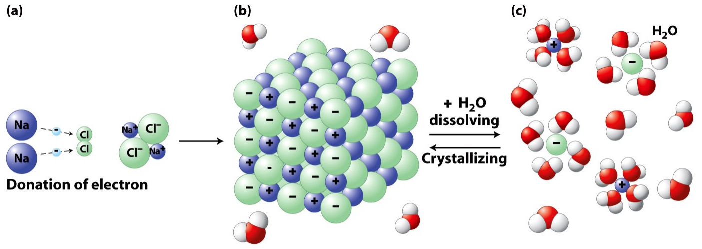


Interactions of single atoms define a molecule which in turn define the cell.
Breaking and synthesizing bonds are the key for cell metabolism and energy.

Water – H_2O

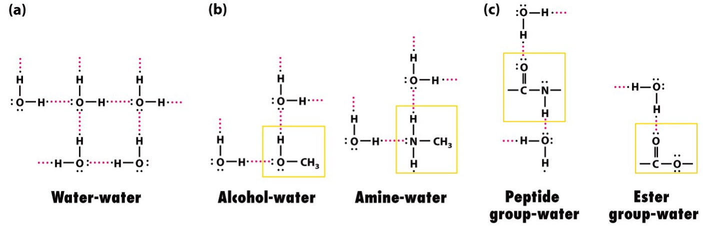


multi-functions of water in chemistry and cell functions

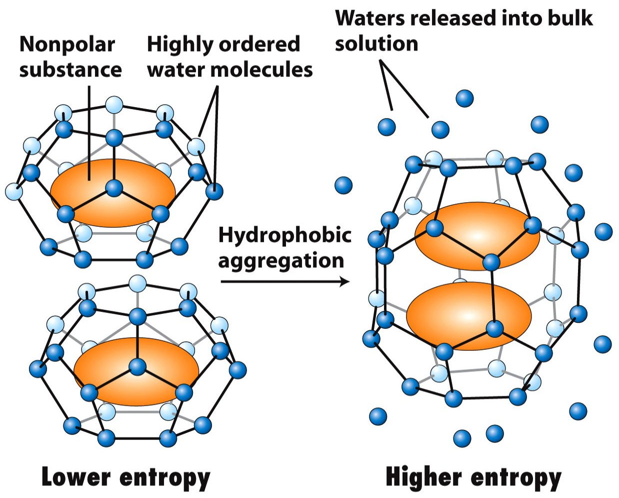


water & ions

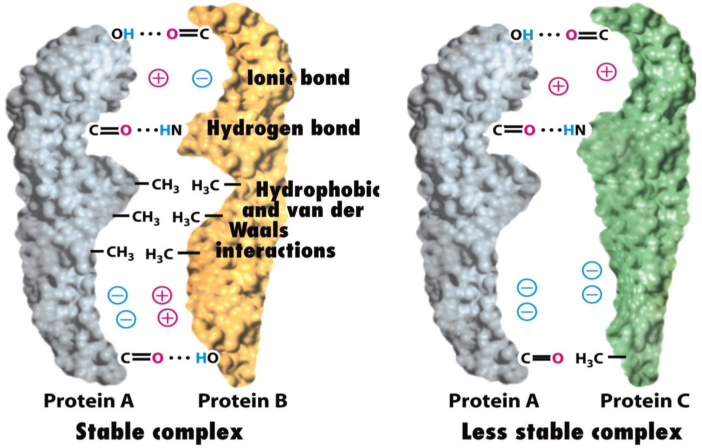
H-bridges defines function of molecules such as proteins



water & van der Waals



H-bridges defines function of molecules such as proteins ---> native protein folding for proper protein action



Monomers

vs

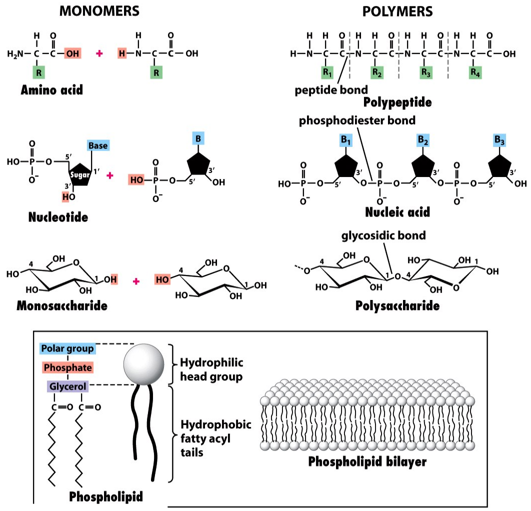
Polymers:

defines

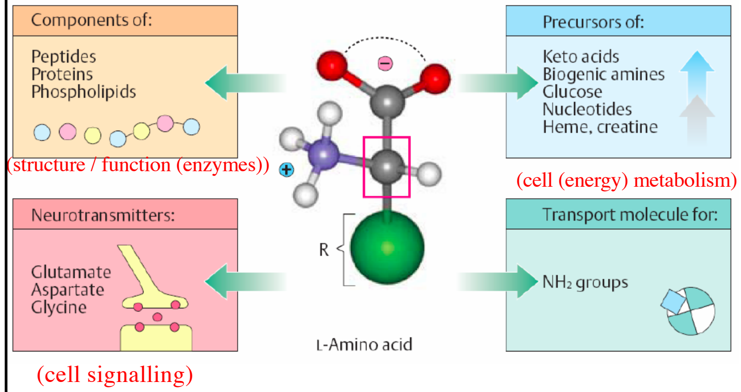
cell feature

&

cell metabolism

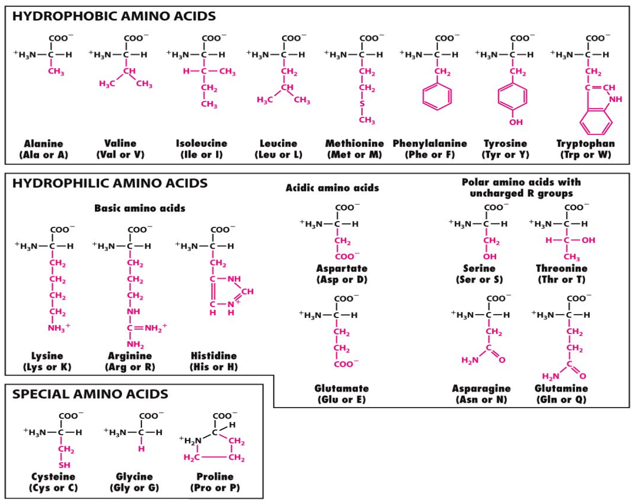


Amino Acids are:

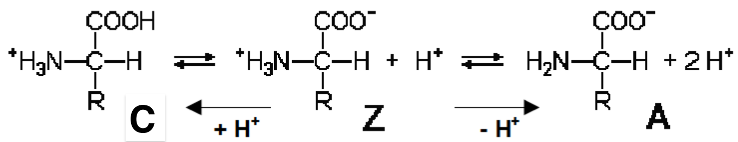


Amino

Acids



Dissociation of Amino Acids



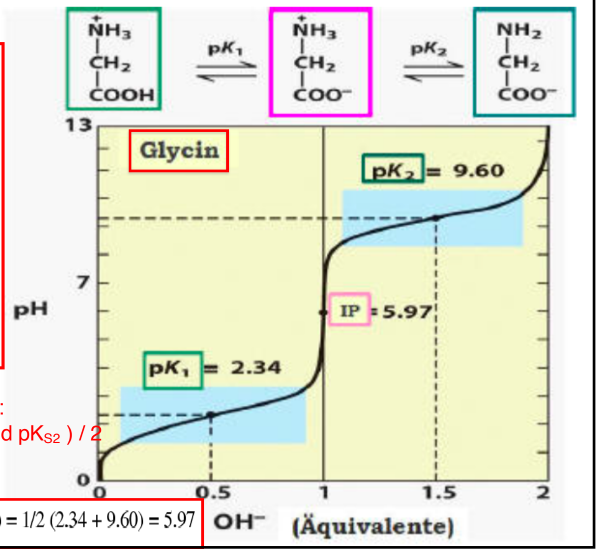
Cation (C) 'Zwitter' (hybrid) Anion (A)

At isoelectric point (pH_{IP}) the AA is neutral and in most cases as 'Zwitter'/hybrid form

In a similar way – each protein has a pH_{IP} where it is neutral (uncharged).

Acid/Basic – buffer features ---> CHM4006

'Titration - curve' of Glycine



Isoelectric point:
pH_{IP} = (pK_{S1} and pK_{S2}) / 2

$pI = 1/2\,(pK_1 + pK_2) = 1/2\,(2.34 + 9.60) = 5.97$

(the value in the basic area will be excluded)

Glu/E: pH(IEP) = $\frac{pK_{S1} + pK_{SR}}{2}$

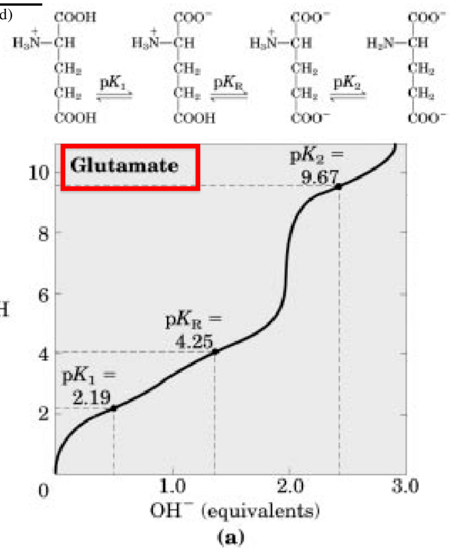
= (2.19+4.25)/2

= 3.22

$pI = 1/2\,(pK_n + pK_{n+1})$

pK_n and pK_{n+1} refer to the specie with the netto-charge = 0; means here, the H+ reaction that makes from the neutral specie a positive specie and the de-H+ reaction that makes from the neutral specie a negative specie.

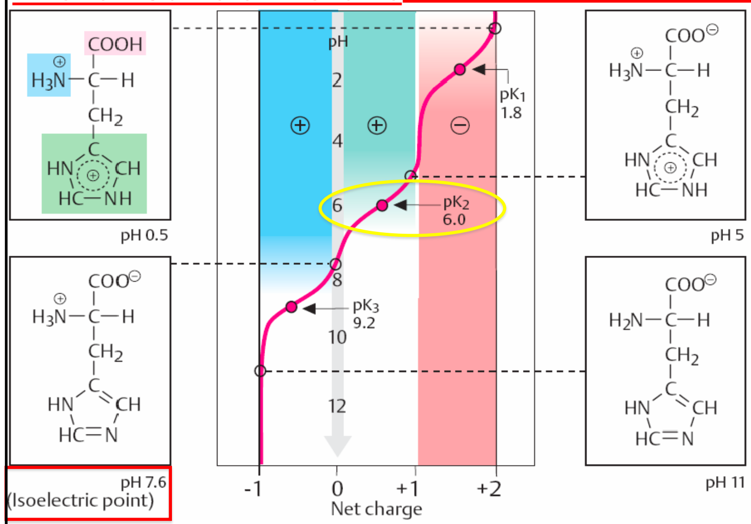
pK_R is the pK value of the side group R



Also here the buffer ranges are from a physiological point of view (pH around 7) not relevant

Titration Curve of Histidine

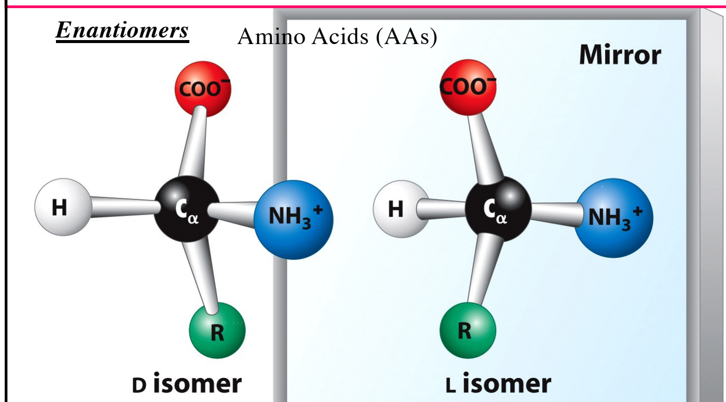
the only AA with a pK in physiological range



(Isoelectric point)

Special feature of molecules that define cell (function) which defines life.

Enantiomers Amino Acids (AAs)

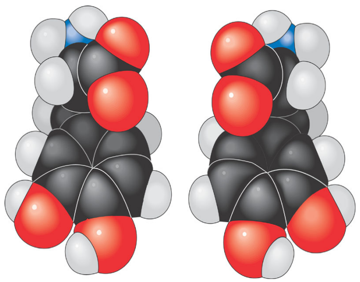


AAs: only L-form is proteinogen

Enantiomers are chiral molecules that are *mirror images* of one another. Furthermore, the molecules are *non-superimposable* on one another. This means that the molecules cannot be placed on top of one another and give the same molecule.

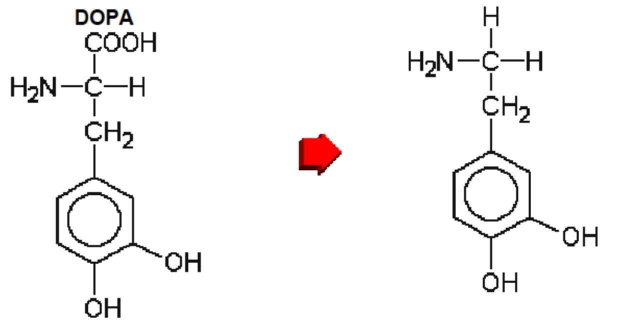
Enantiomers

– are important in the pharmaceutical industry



L-Dopa
(effective against Parkinson's disease)

D-Dopa
(biologically inactive)



Dopamine
catecholamine

neurotransmitter

---> Parkinson Disease

TABLE 2-1 Bonding Properties of Atoms Most Abundant in Biomolecules

ATOM AND OUTER ELECTRONS	USUAL NUMBER OF COVALENT BONDS	TYPICAL BOND GEOMETRY
H·	1	—H
·Ö·	2	O
·S̈·	2, 4, or 6	S
·N̈·	3 or 4	N
·P̈·	5	P
·Ċ·	4	C

TABLE 2-2 Common Functional Groups and Linkages in Biomolecules

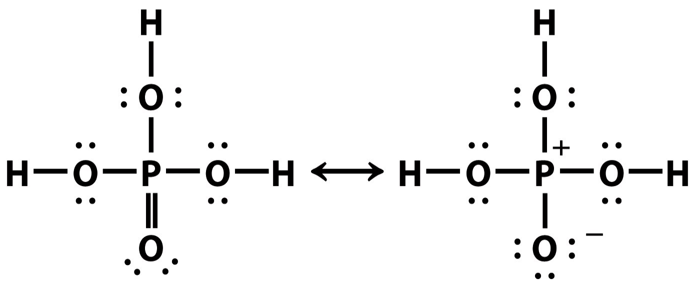
FUNCTIONAL GROUPS

—OH Hydroxyl (alcohol)	—C(=O)—R Acyl (triacylglycerol)	—C(=O)— Carbonyl (ketone)	—C(=O)—O⁻ Carboxyl (carboxylic acid)
—SH Sulfhydryl (Thiol)	$—NH_2$ or $—NH_3$ Amino (amines)	—O—P(=O)(O⁻)—O⁻ Phosphate (phosphorylated molecule)	—O—P(=O)(O⁻)—O—P(=O)(O⁻)— Pyrophosphate (diphosphate)

LINKAGES

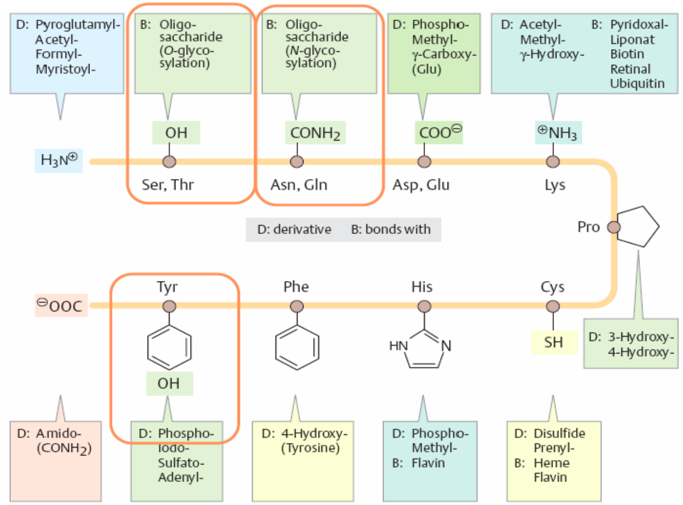
—C—O—C(=O)— Ester	—C—O—C— Ether	—N—C(=O)— Amide

Phosphate (groups/bonds) – Energy & Enzymes & DNA

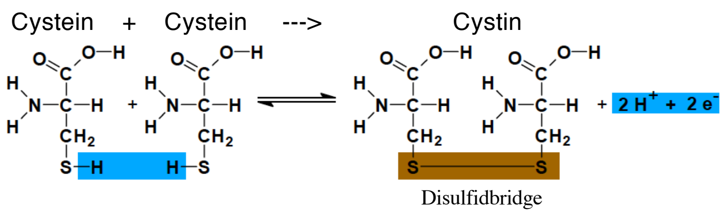


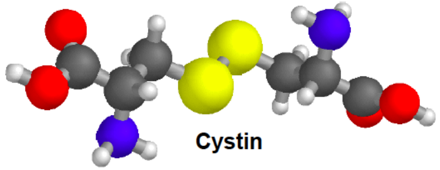
Energy: ATP
Enzymes: kinases and phosphatase
DNA: A, T, C, G (linked via P)

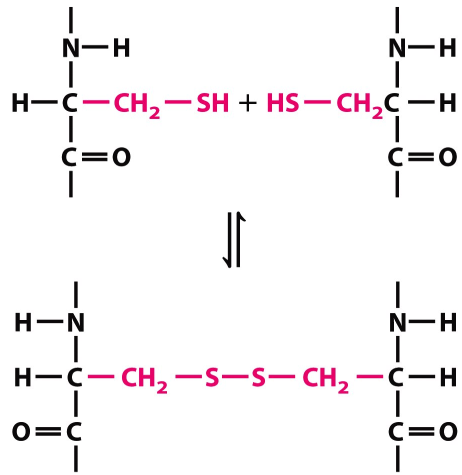
Post-translational modifications of Amino Acids

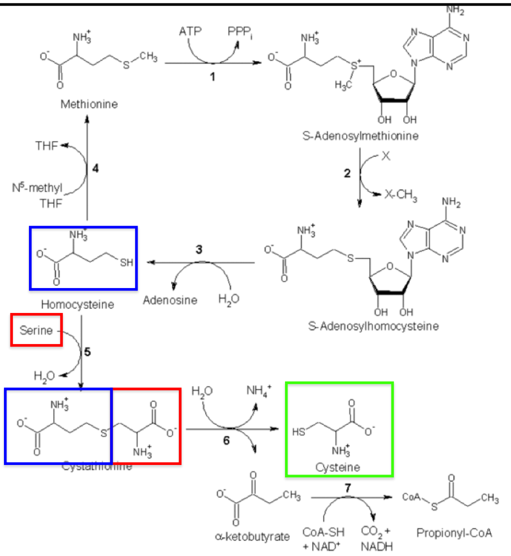


Disulfid (S-) -bridges



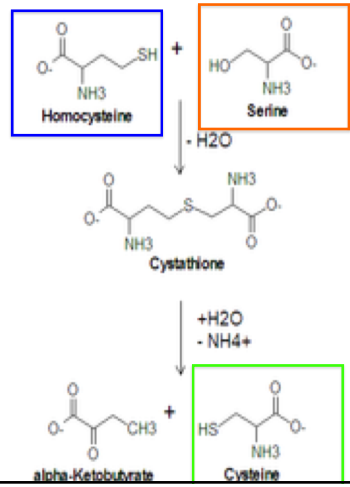


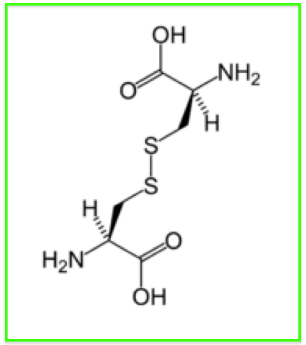




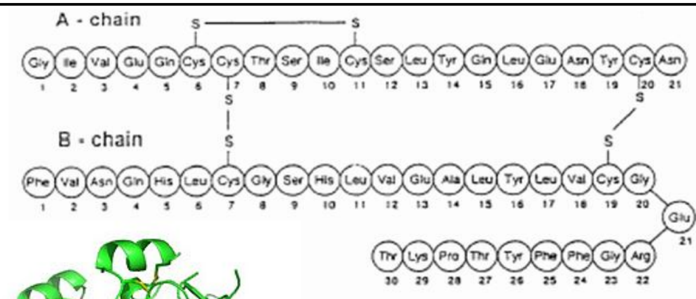
http://en.wikipedia.org/wiki/Homocysteine

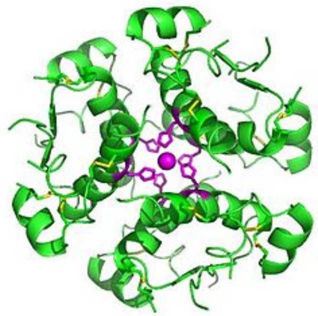
http://en.wikipedia.org/wiki/Cysteine





Cystine (shown here in its neutral form), two cysteines bound together by a disulfide bond.

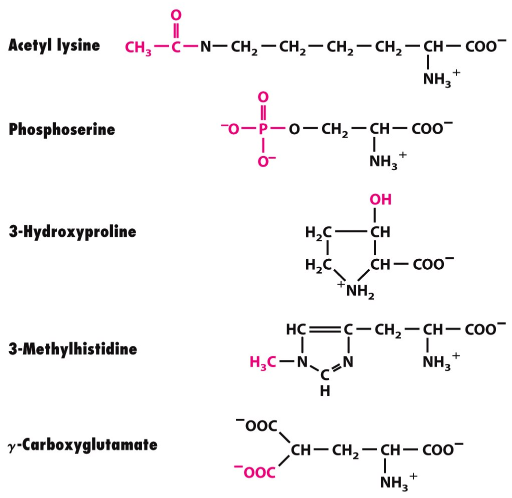




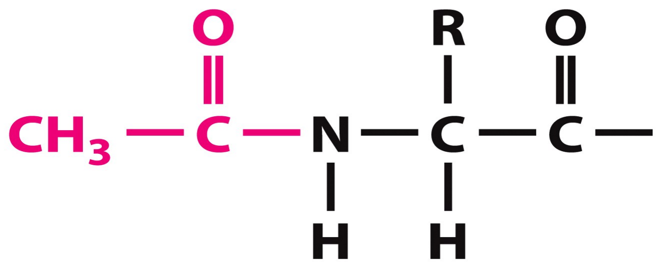
Insulin

(controls blood glucose level)

http://reddymed.com/insulin.htm



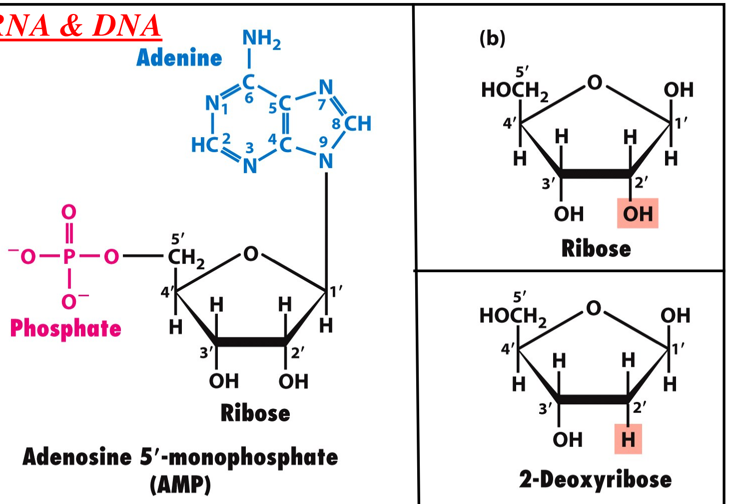
Controlling protein activities …



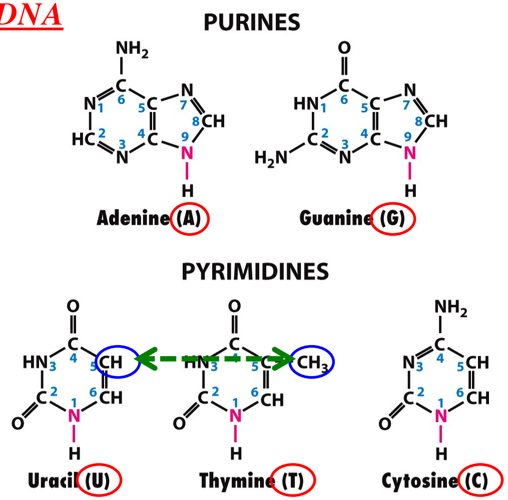
Acetylated N-terminus

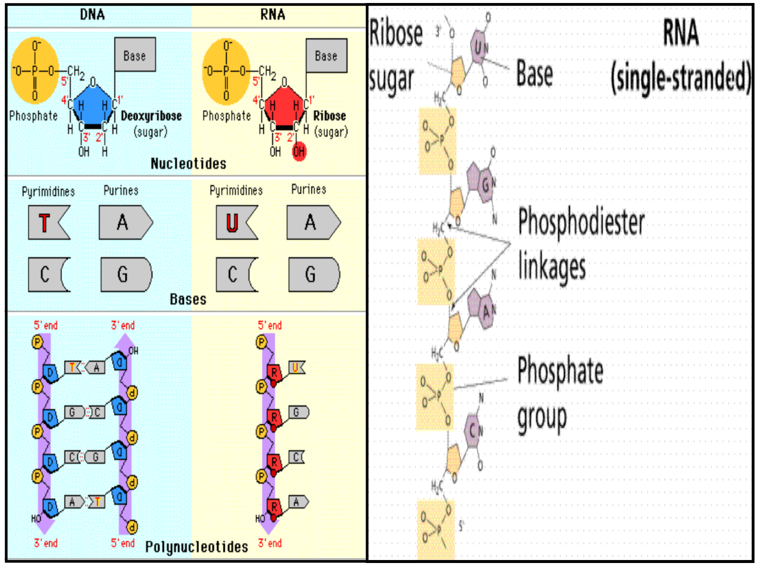
also: acetylation of genes ---> gene activation:
in contrast: gene methylation ---> gene silencing

RNA & DNA

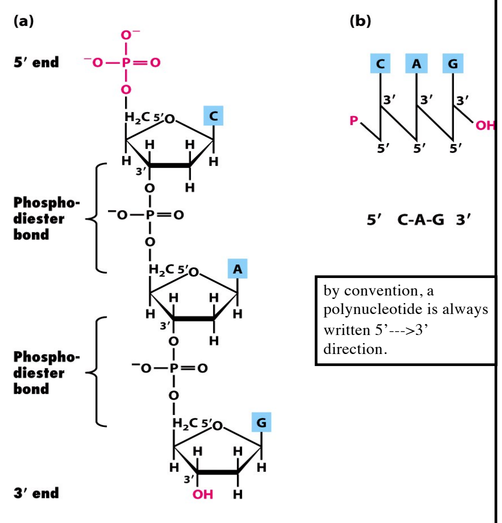


RNA & DNA





Alternative representations of a nucleic acid strand illustrating its chemical directionality.



by convention, a polynucleotide is always written 5'--->3' direction.

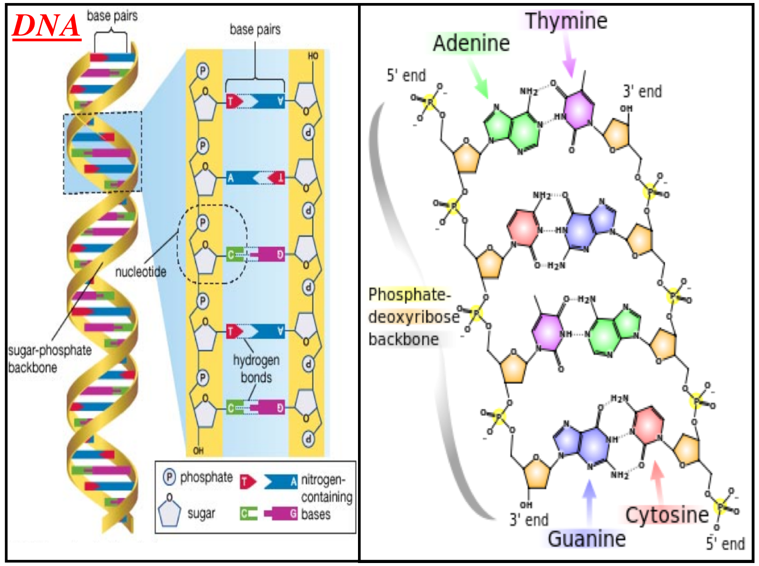
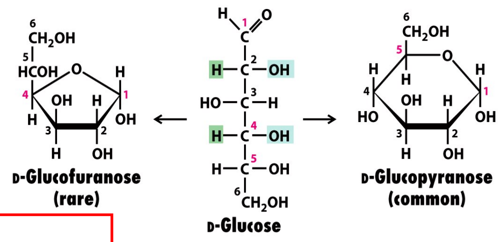
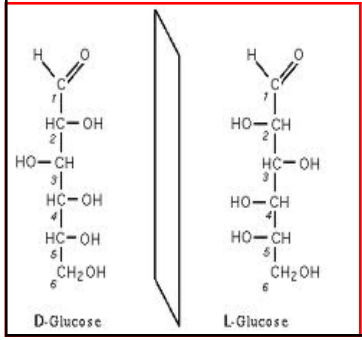


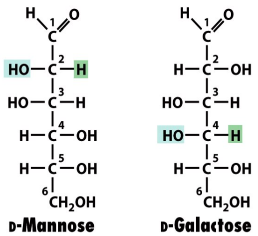
TABLE 2-3 Terminology of Nucleosides and Nucleotides

BASES		PURINES: ADENINE(A)	PURINES: GUANINE(G)	PYRIMIDINES: CYTOSINE(C)	PYRIMIDINES: URACIL(U) THYMINE(T)
Nucleosides	in RNA	Adenosine	Guanosine	Cytidine	Uridine
	in DNA	Deoxyadenosine	Deoxyguanosine	Deoxycytidine	Deoxythymidine
Nucleotides	in RNA	Adenylate	Guanylate	Cytidylate	Uridylate
	in DNA	Deoxyadenylate	Deoxyguanylate	Deoxycytidylate	Deoxythymidylate
Nucleoside monophosphates		AMP	GMP	CMP	UMP
Nucleoside diphosphates		ADP	GDP	CDP	UDP
Nucleoside triphosphates		ATP	GTP	CTP	UTP
Deoxynucleoside mono-, di-, and triphosphates		dAMP, etc.	dGMP, etc.	dCMP, etc	dTMP, etc.

Cell Metabolism & Energy

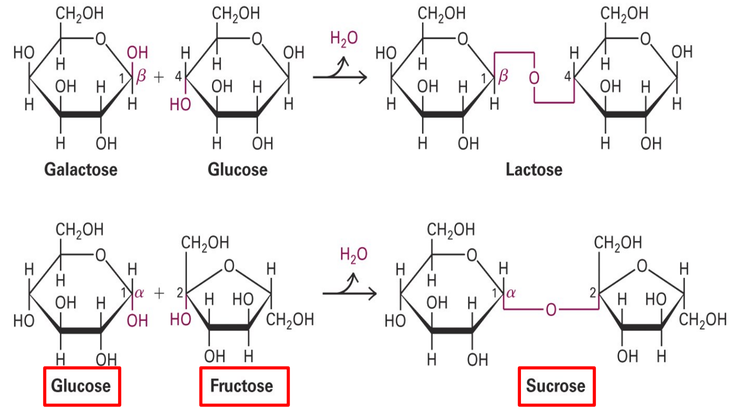






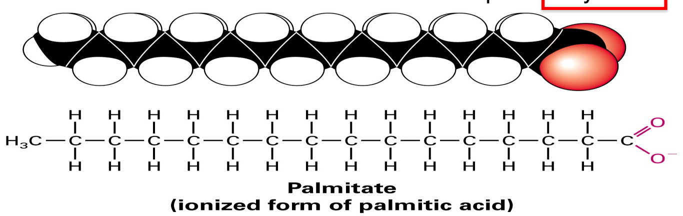
Cell Metabolism & Energy

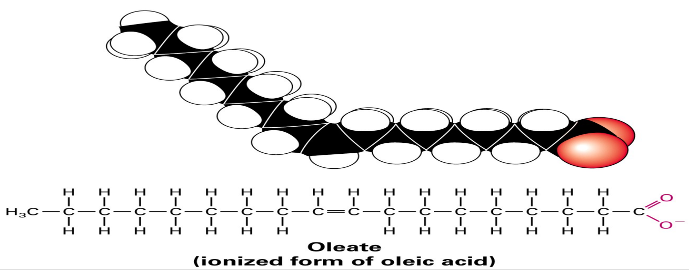
Di-Saccharides Lactose and Sucrose



Lipids – Cell Membrane and Cell Metabolism etc

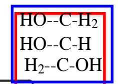
The effect of a double bond on the shape of fatty acids

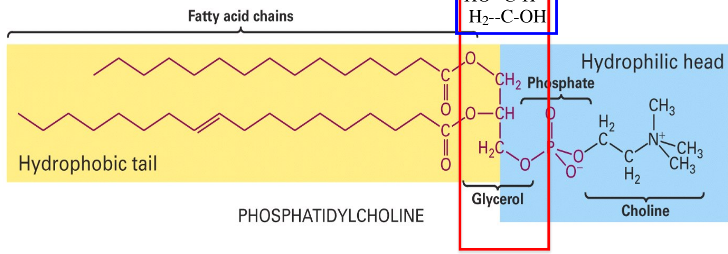




Fatty Acids & Lipids

Phosphatidylcholine, a typical phosphoglyceride



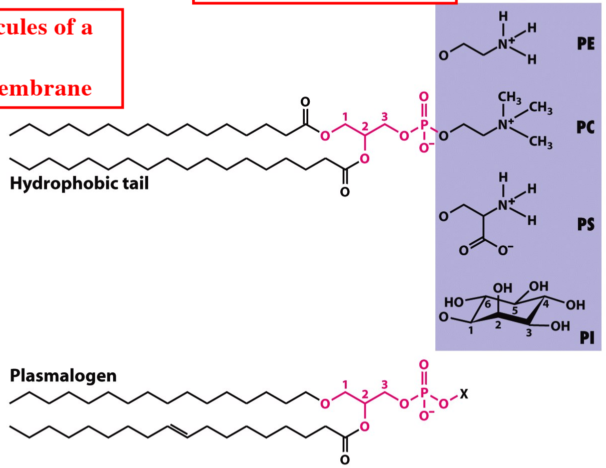


All phosphoglycerides are amphipathic – having a hydrophobic tail (yellow) and a hydrophilic head (blue) in which glycerol is linked via a phosphate group to an alcohol. Either of or both the fatty acyl side chains in a phosphoglyceride may be saturated or unsaturated. In phosphatidic acid (red), the simplest phospholipid, the phosphate is not linked to an alcohol.

Fatty Acids & Lipids

Molecules of a Biomembrane

Phosphoglycerides

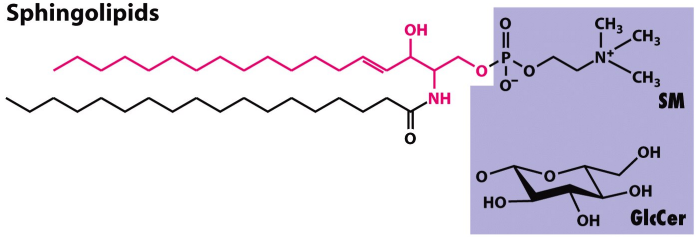


PC = phosphatidylcholine; PE = phosphatidylethanol; PS = phosphatidylserine; SM = sphingomyelin; PI = phosphoinositol

Molecules of a Biomembrane

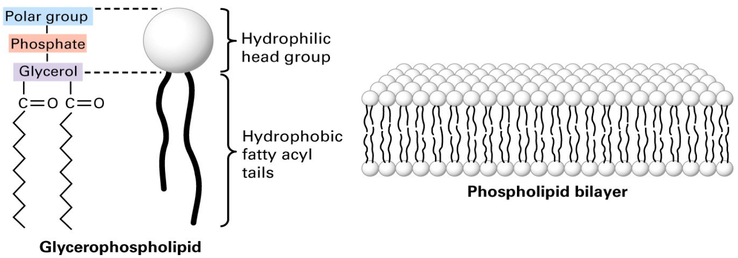
Fatty Acids & Lipids

Sphingolipids

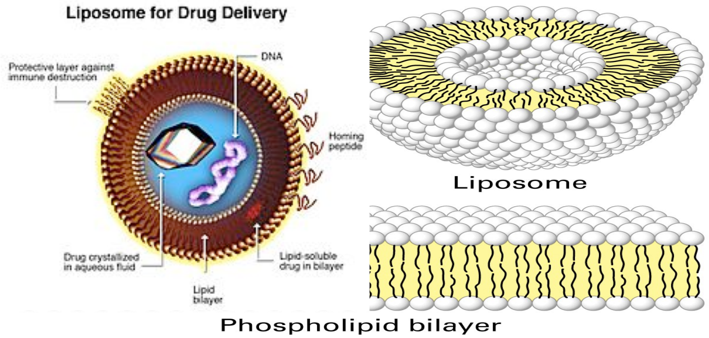


PC = phosphatidylcholine; PE = phosphatidylethanol; PS = phosphatidylserine; SM = sphingomyelin; PI = phosphoinositol

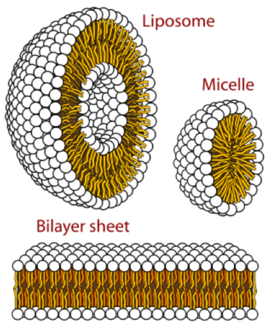
Essential Cell Membrane Molecules



Cross-sectional views of the three structures formed by phospholipids in aqueous solutions

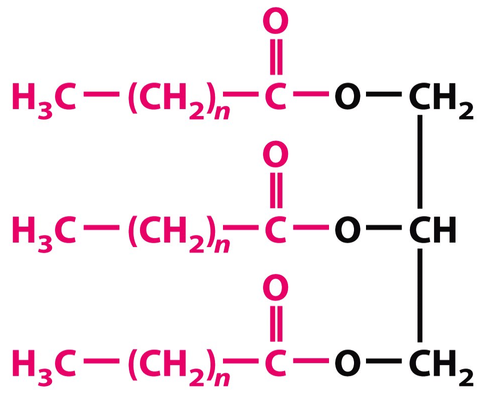


The white spheres depict the hydrophilic heads of the phospholipids, and the squiggly black lines (in the yellow regions) represent the hydrophobic tails. Shown are a spherical micelle with a hydrophobic interior composed entirely of fatty acyl chains; a spherical liposome,



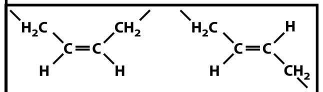
A micelle is an aggregate of surfactant molecules dispersed in a liquid colloid

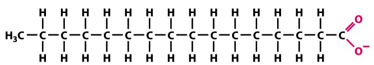
Micelles are approximately spherical in shape.



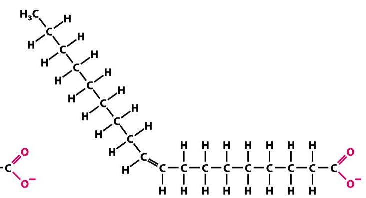
Triacylglycerol

Fatty Acids





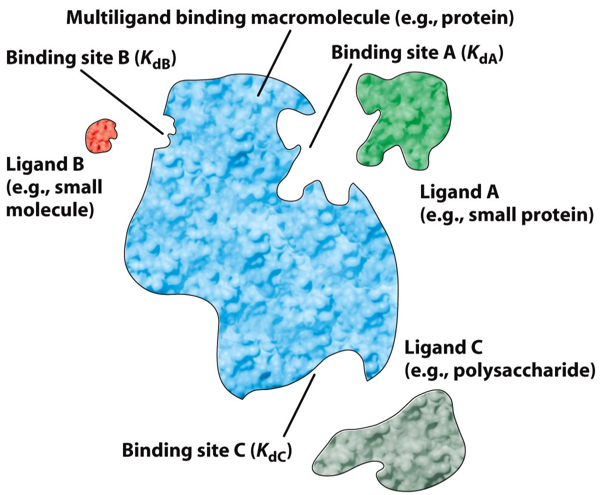
Palmitate
(ionized form of palmitic acid)



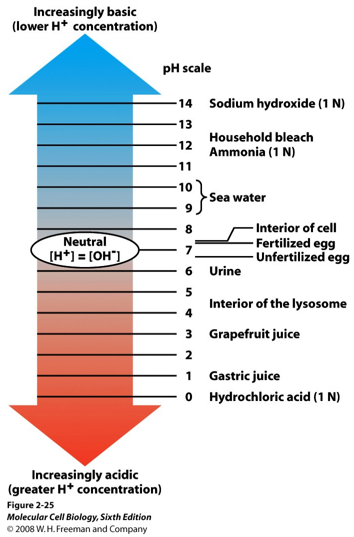
Oleate
(ionized form of oleic acid)

TABLE 2-4 Fatty Acids That Predominate in Phospholipids

COMMON NAME OF ACID (IONIZED FORM IN PARENTHESES)	ABBREVIATION	CHEMICAL FORMULA
SATURATED FATTY ACIDS		
Myristic (myristate)	C14:0	$CH_3(CH_2)_{12}COOH$
Palmitic (palmitate)	C16:0	$CH_3(CH_2)_{14}COOH$
Stearic (stearate)	C18:0	$CH_3(CH_2)_{16}COOH$
UNSATURATED FATTY ACIDS		
Oleic (oleate)	C18:1	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$
Linoleic (linoleate)	C18:2	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$
Arachidonic (arachidonate)	C20:4	$CH_3(CH_2)_4(CH{=}CHCH_2)_3CH{=}CH(CH_2)_3COOH$

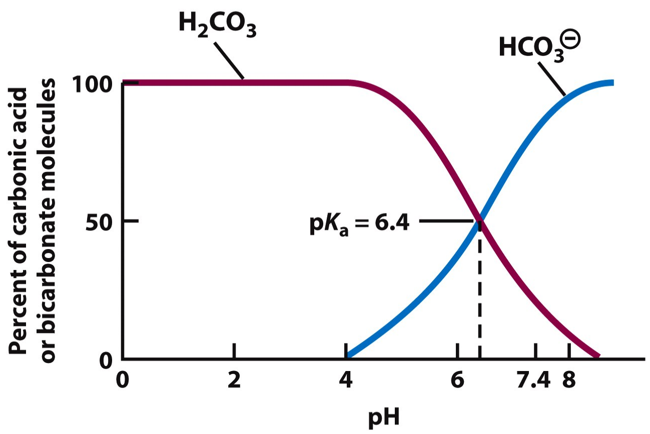


pH

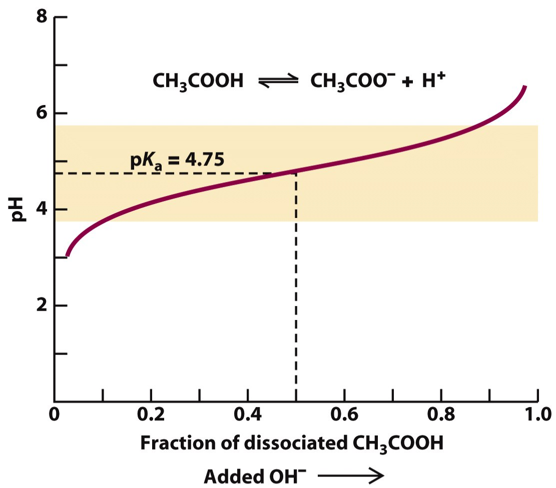


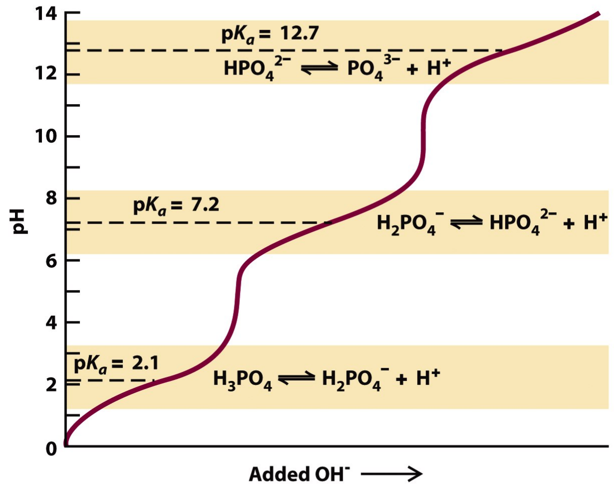
Buffers

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



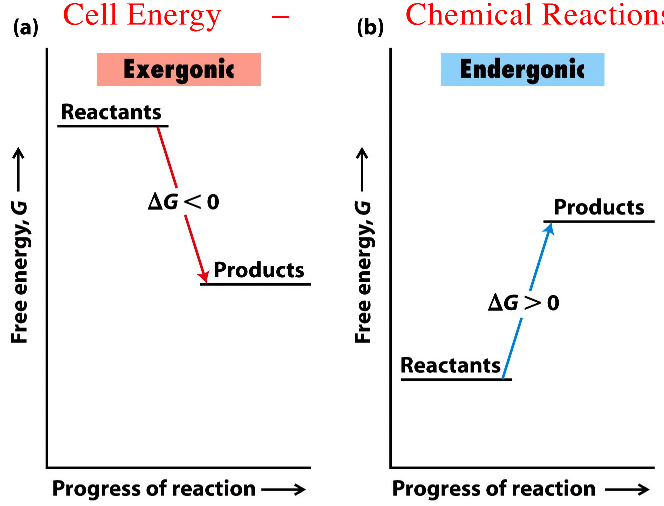
O_2 / CO_2 transport (respiration)



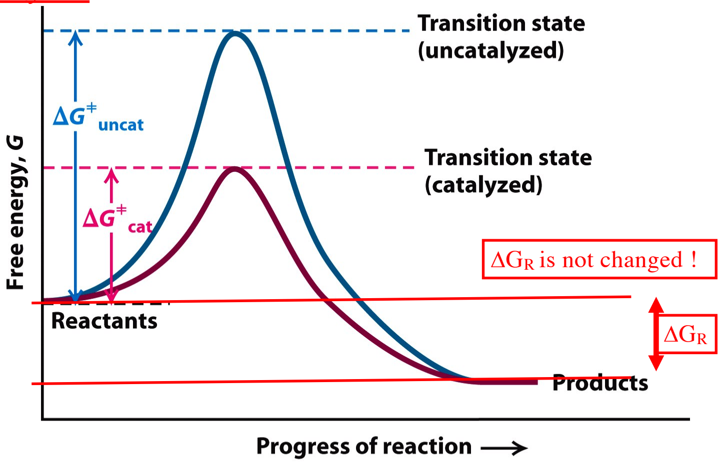


PO4: ATP, DNA, Proteins (cell signalling)

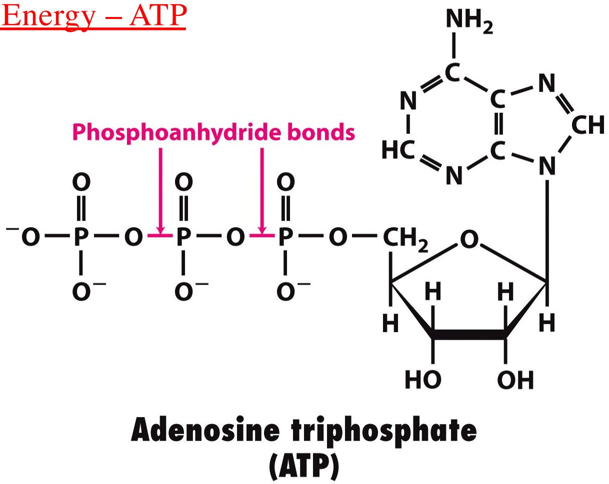
Cell Energy – Chemical Reactions



Enzymes

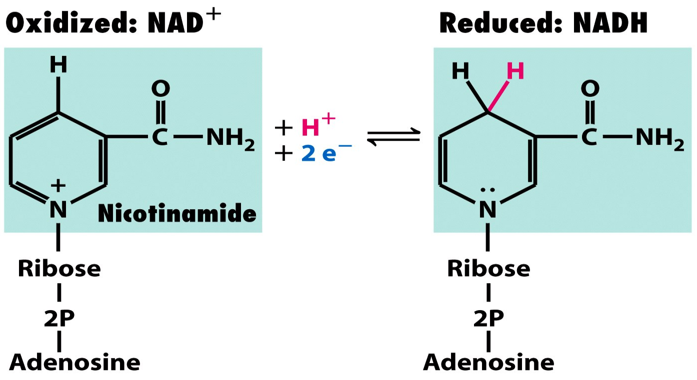


Cell Energy – ATP



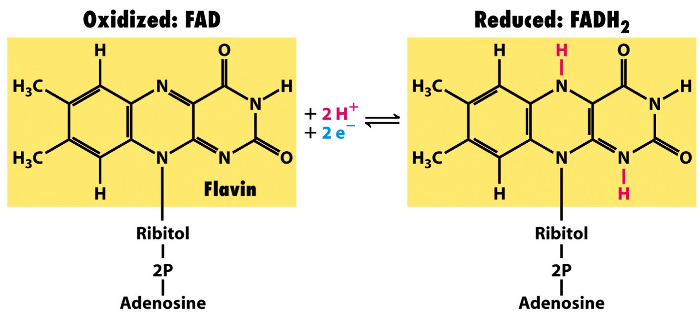
Cell Metabolism, Energy & Red-Ox-Reactions

e⁻ carrier:



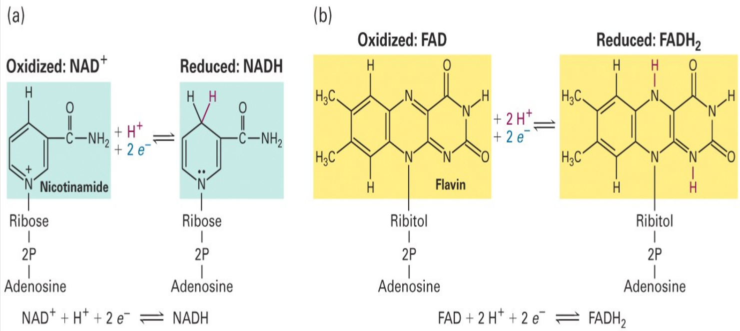
$$NAD^+ + H^+ + 2e^- \rightleftharpoons NADH$$

e⁻ carrier:



$$FAD + 2H^+ + 2e^- \rightleftharpoons FADH_2$$

The Electron Carrying co-enzymes NAD⁺ and FAD



(a) NAD⁺ (nicotinamide adenine dinucleotide) is reduced to NADH by addition of two electrons and one proton simultaneously. In many biological redox reactions (e.g., succinate to fumarate), a pair of hydrogen atoms (two protons and two electrons) are removed from a molecule. One of the protons and both electrons are transferred to NAD⁺; the other proton is released into solution. (b) FAD (flavine adenine dinucleotide) is reduced to $FADH_2$ by addition of two electrons and two protons. In this two-step reaction addition of one electron together with one proton first generates a short-lived semiquinone interemediae (not shown), which then accepts a second electron and protons.

A few universal carriers collect electrons from the stepwise oxidation of various substrates

Cellular oxidation of a nutrient occurs via stepwise reactions (pathways) for efficient energy transduction.

NAD⁺, NADP⁺, FAD, and FMN are universal reversible electron carriers (as coenzymes of various enzymes).

NAD and NADP are dinucleotides able to accept/donate a hydride ion (with 2e⁻) for each round of reduction/oxidation.

NAD (as NAD⁺) usually acts in oxidations and NADP (as NADPH) in reductions.

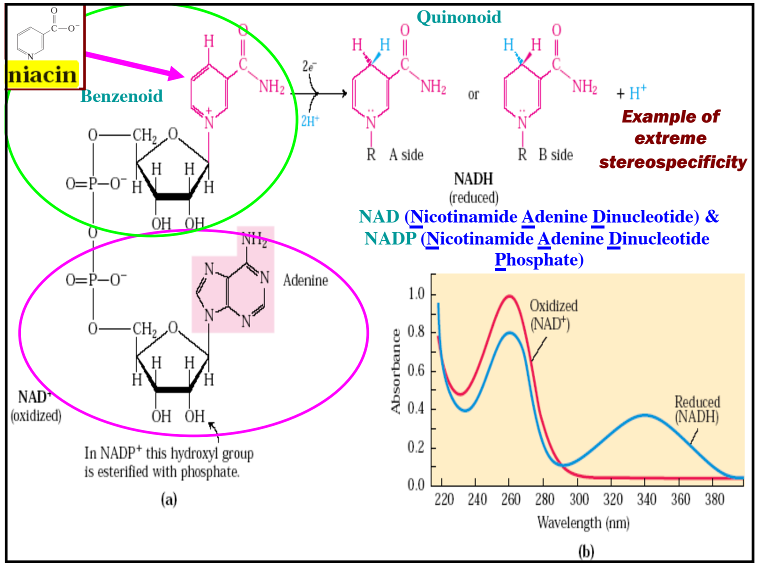
In each specific NAD- or NADP-containing dehydrogenase, the hydride ion is added/taken stereospecifically from one side (A or B) of the nicotinamide ring (*example of extreme stereospecificity*).

FAD or FMN is able to accept/donate one or two electrons (as hydrogen atom), with absorption maximum for the oxidized and reduced forms being 570 nm and 450 nm respectively (*they also act in such light receptor proteins as cryptochromes and photolyases*).

NAD and NADP can easily diffuse out of the enzymes, but FMN and FAD are tightly bound to the enzymes (thus being called *prosthetic groups*, and the complex proteins being called *flavoproteins*).

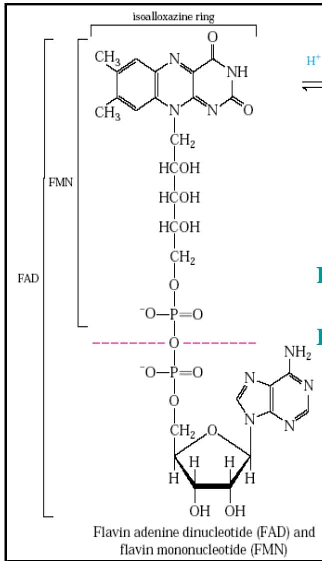
NADH and $FADH_2$ will be further oxidized via the respiratory chain for ATP production.

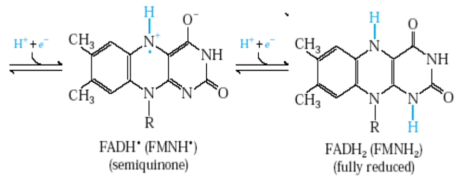
ADP is commonly present in all these universal electron carriers (as well as in Coenzyme A and ATP).



Example of extreme stereospecificity

NAD (Nicotinamide Adenine Dinucleotide) & NADP (Nicotinamide Adenine Dinucleotide Phosphate)





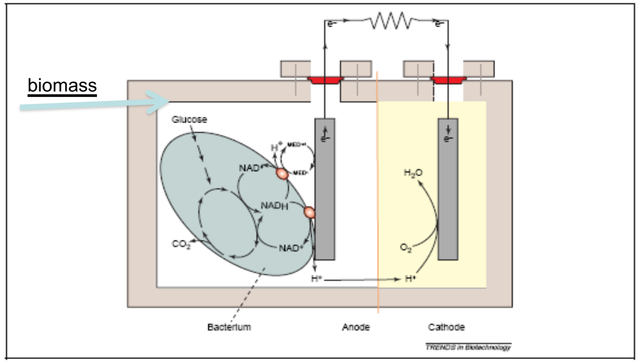
FMN (Flavin mononucleotide)

and

FAD (Flavin Adenine Dinucleotide)

***E'°* of FAD/FMN often differs in different flavoproteins, which are often complex and contain other inorganic ions to help electron transfer.**

Microbial fuel cells (MFCs)



Electrons flow from an anode through a resistor to a cathode where electron acceptors are reduced. Protons flow across a proton exchange membrane (PEM) to complete the circuit.

Essential Bio-Engineering-related Bio-Molecules