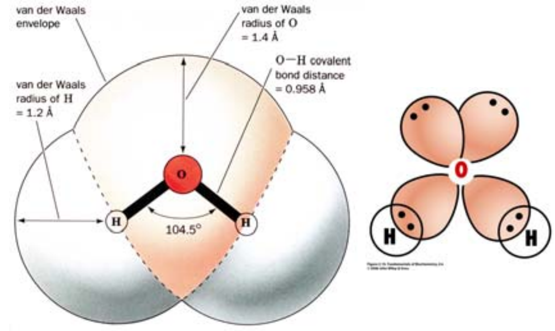
Comprehensive Exam Review
12/03/2009

Structure & Properties of Water

Bent geometry, O-H bond length of 0.958Å
Can form Hydrogen bonds



Henderson - Hasselbalch equation

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

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

Take (-)Log of each $pH = -\log K + \log\frac{[A^-]}{[HA]}$

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

The 6 step approach

1. Write the Henderson + Hasselbalch equation.
2. Write the acid base equation
3. Make sure either an H^+ or OH^- is in the equation.
3. Find out what you are solving for
4. Write down all given values.
5. Set up equilibrium conditions.
6. Plug in H + H equation and solve.

What is the pH of a solution of that contains 0.1M CH_3COO^- and 0.9 M CH_3COOH?

1) pH = pK + Log $\frac{[A^-]}{[HA]}$

2) $CH_3COOH \longleftrightarrow CH_3COO^- + H^+$

3) Find pH

4) pK = 4.76 A^- = 0.1 M HA = 0.9 M

5) Already at equilibrium

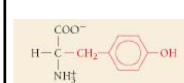
6) X = 4.76 + Log $\frac{0.1}{0.9}$

Log 0.111 = -.95 X = 4.76 + (-.95) X = 3.81

Amino Acids

You must know Table 4.1 p76-77:

Their names
Their structure
Their three letter code
Their one letter code



Tyrosine, Tyr, Y, aromatic, hydroxyl

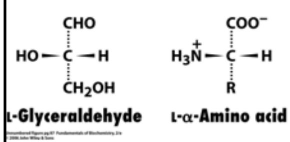
The Fischer Convention

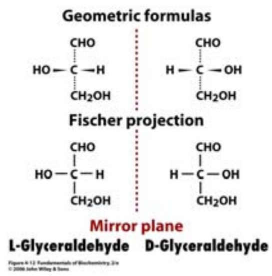
Absolute configuration about an asymmetric carbon

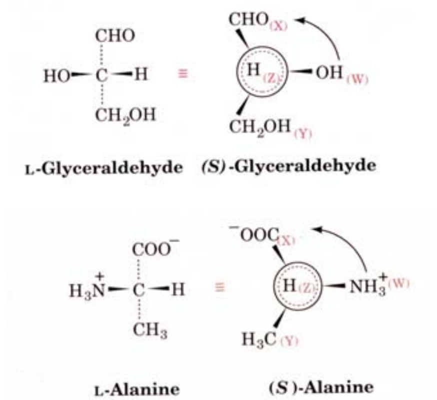
related to glyceraldehyde

(+) = D-Glyceraldehyde

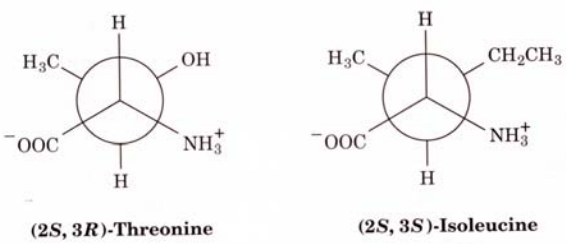
(-) = L-Glyceraldehyde





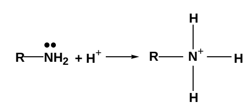


Newman Projection Threonine and Isoleucine

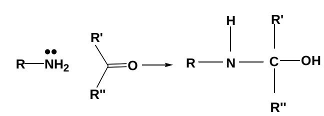


Nucleophiles

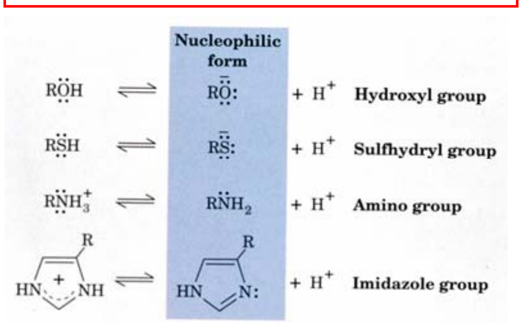
Basic reaction of amine

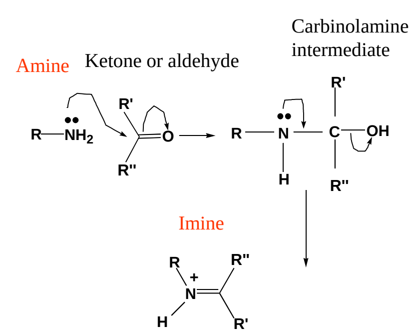


Nucleophilic reaction of an amine



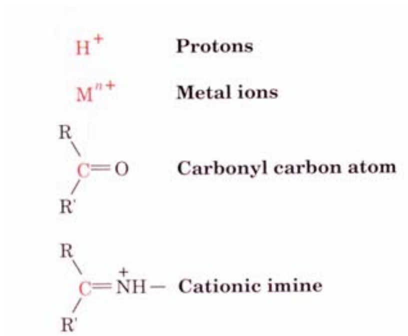
Biologically important nucleophiles

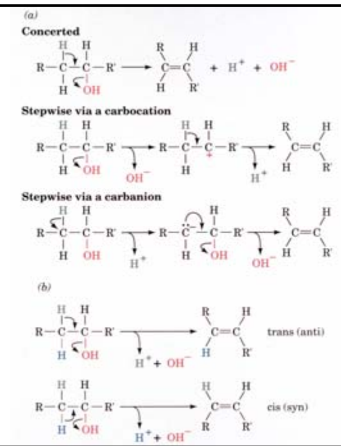


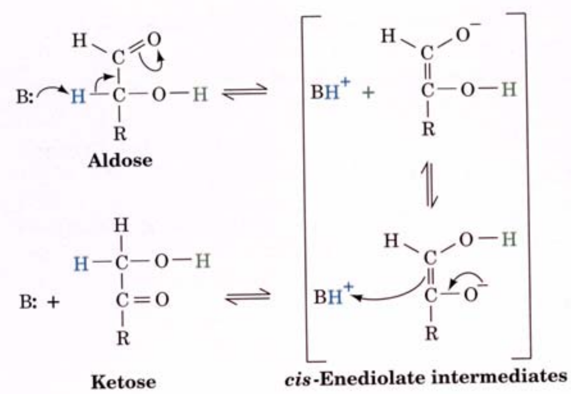


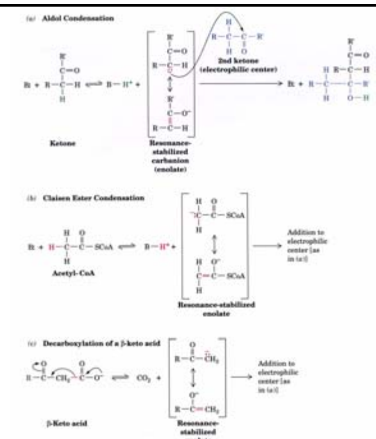
Movement of an electron pair from a position and pointing to the electron deficient center attracting the pair.

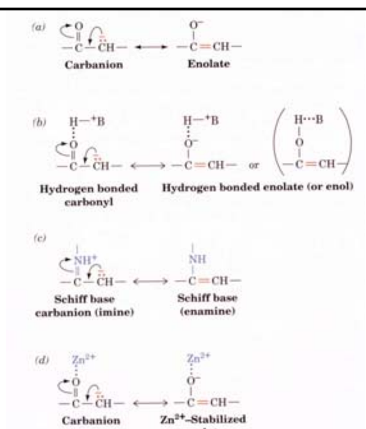
Common biological electrophiles











Group transfer reactions

Y: + A—X ⟶ Y—A + X:

Acetyl group transfer

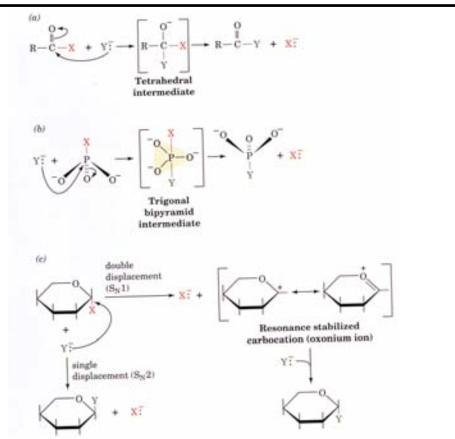
- Nucleophile attack on an acyl carbonyl to form a tetrahedral intermediate
- Peptide bond hydrolysis

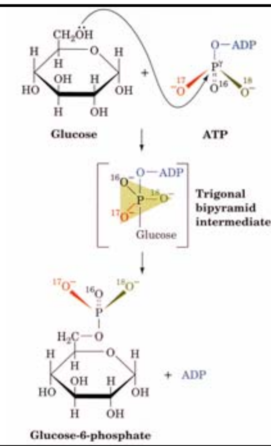
Phosphoryl group transfer

- nucleophile attack on a phosphate to yield a trigonal bipyramid intermediate
- Kinase reactions involving transfer of phosphate from ATP to organic alcohols

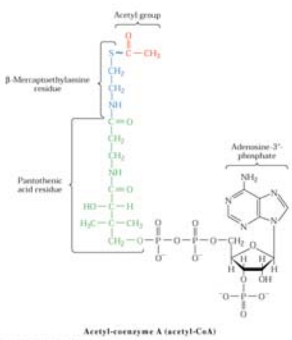
Glycosyl group transfers

- substitution of one group at the C1 carbon of a sugar for another





Thioesters (Acetyl-coenzyme A)



High energy compound

Carrier of acetyl and acyl groups

Can be used to drive exogenic processes

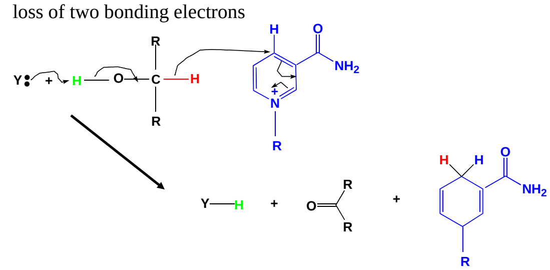
e.g. GTP from GDP

Oxidations and reductions

Oxidation : Loss of Electrons

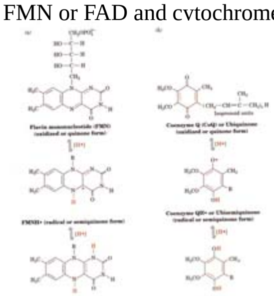
Reduction: Gain of Electrons

Many redox reactions involve the breaking of a C-H bond and the loss of two bonding electrons



Electron transfer reactions to oxygen undergo transfer of one electron at a time (Pauli exclusion principle)

Oxidations to oxygen from NADH require two electron steps to be changed to one electron steps. Stable radical structures like FMN or FAD and cvtochromes are involved.



Reduction of NAD+ to NADH

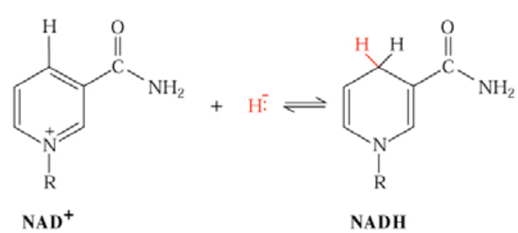


Figure 13-10. Reduction of NAD+ to NADH.

Electron transfer reactions

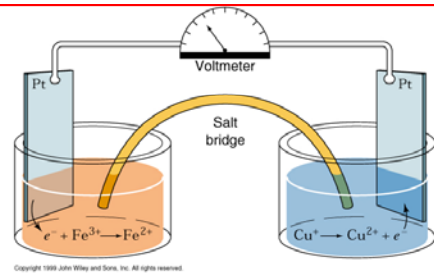
$$A_{ox}^{n+} + B_{red} = A_{red} + B_{ox}^{n+}$$

$$\Delta G = \Delta G^{0} + RT\ln\left[\frac{A_{red}}{A_{ox}^{n+}}\right]\left[\frac{B_{ox}^{n+}}{B_{red}}\right]$$

Half-cell reactions either donate or accept electrons

Electron donor (reducing agent)

Electron acceptor (oxidizing agent)



Nernst Equation- electromotive force -EMF- reduction potential

Work is non -pressure volume work or

$\Delta G = -w' = -w^{elec}$

$W^{elec} = nF\Delta E$

or

$\Delta G = -nF\Delta E$

$$\Delta E = \Delta E^{o} - \frac{RT}{nF}\ln\left(\frac{[A_{red}]}{[A_{ox}^{n+}]}\frac{[B_{ox}^{n+}]}{[B_{red}]}\right)$$

F = Faraday constant = 96,485 Coulombs per mole of electrons

ΔE^0 = standard reduction potential or midpoint potential

Measuring potentials

$$A_{ox}^{n+} + ne^- \leftrightarrow A_{red} \quad \text{and} \quad B_{ox}^{n+} + ne^- \leftrightarrow B_{red}$$

$$E_A = E_A^0 - \frac{RT}{nF}\mathrm{Ln}\frac{[A_{red}]}{[A_{ox}^{n+}]}$$

$$\boxed{\Delta E^{o} = E^{o}_{(e\text{-}acceptor)} - E^{o}_{(e\text{-}donor)}}$$

However, there is no absolute potential to reference!

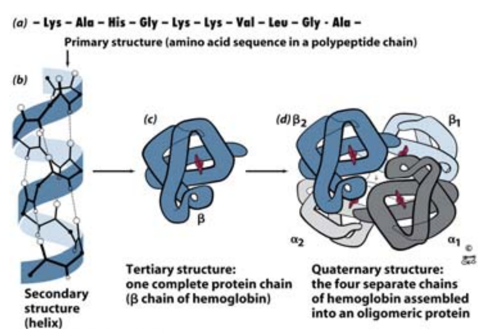
$$2H^{+} + 2e^{-} \leftrightarrow H_2(g)$$

At equilibrium and in contact with a platinum electrode and at 1 M H^+ and STP this is defined as zero potential. At pH of 7.0 this is -0.421 V = $E^{o\prime}$. Prime means that it is at pH 7.0.

Every thing is referenced to this potential

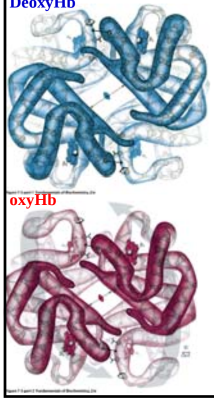
See Table in FOB pg 473 for standard potentials

Example of each level of protein structure



Hemoglobin structure

DeoxyHb



oxyHb

β-monomers are related by 2-fold symmetry (same is true for α)

Note changes in structure:

between β-monomers – see big double-headed arrows

at points of contact – see small arrows

Binding of the O_2 on one heme is more difficult but its binding causes a shift in the α1-β2 (& α2-β1) contacts and moves the distal His E7 and Val E11 out of the oxygen's path to the Fe on the other subunit. This process increases the affinity of the heme toward oxygen.

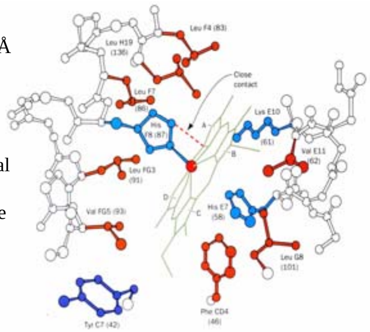
The α1-β2 contacts have two stable positions .

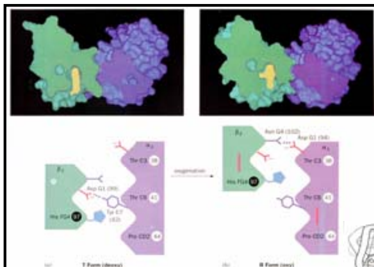
These contacts, which are joined by different but equivalent sets of hydrogen-bonds that act as a binary switch between the T (deoxy) and the R (oxy) states

The positive cooperativity of O_2 binding to Hb

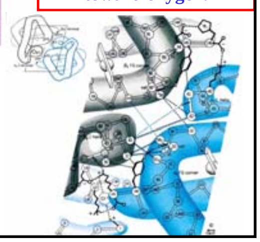
The effect of the ligand-binding state of one heme on the ligand-binding affinity of another.

The Fe iron is about 0.6 Å out of the heme plane in the deoxy state. When oxygen binds it pulls the iron back into the heme plane. Since the proximal His F8 is attached to the Fe this pulls the complete F helix like a lever on a fulcrum.





Binding causes a shift in the α1-β2 contacts and moves the distal His E7 and Val E11 out of the oxygen's path to the Fe on the other subunit. This process increases the affinity of the heme toward oxygen.



The **α1-β2 contacts have two stable positions with different but equivalent sets of hydrogen bonds to act as binary switch between the T and the R states**

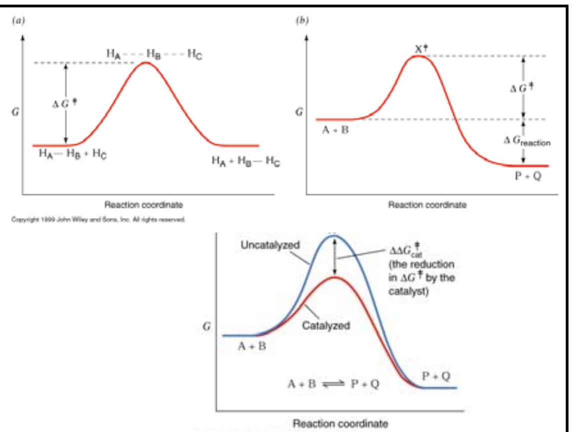
General Properties of Enzymes

- **Increased reaction rates sometimes 10^6 to 10^{12} increase**

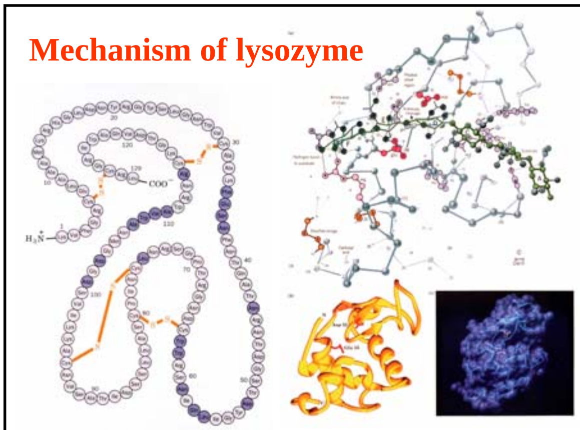
  Enzymes do not change ΔG between the reactants and products.

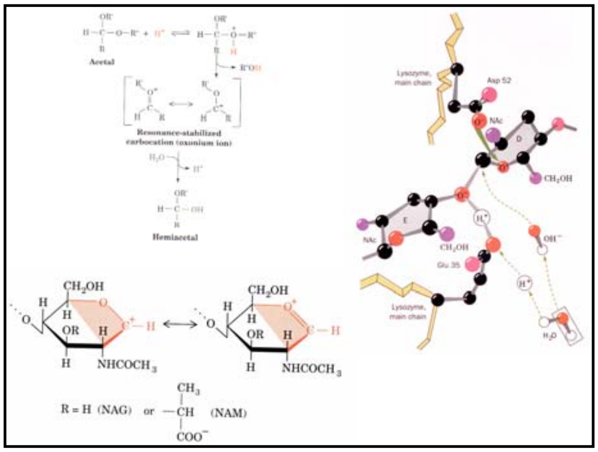
  They increase reaction rates (catalysts).

- **Milder reaction conditions**
- **Great reaction specificity**
- **Can be regulated**

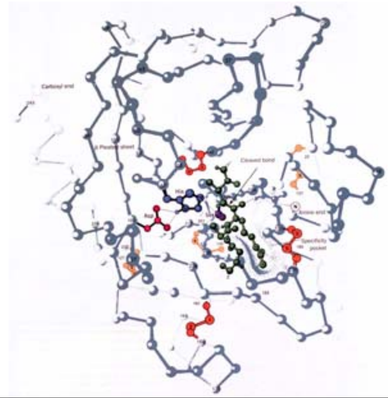


Mechanism of lysozyme

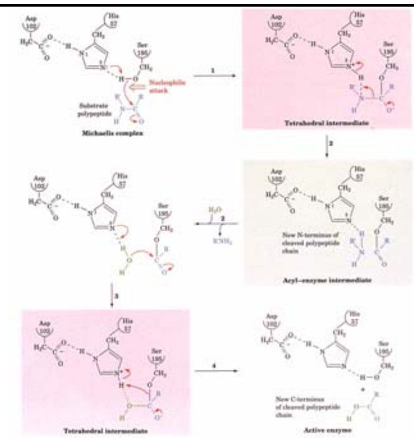




Serine proteases

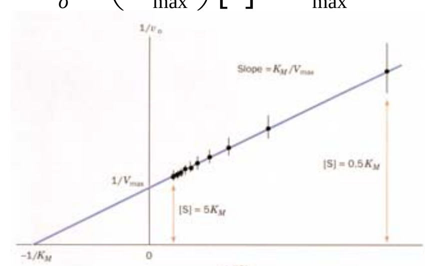


Bovine
Trypsin



Enzyme Kinetics: The double reciprocal plot

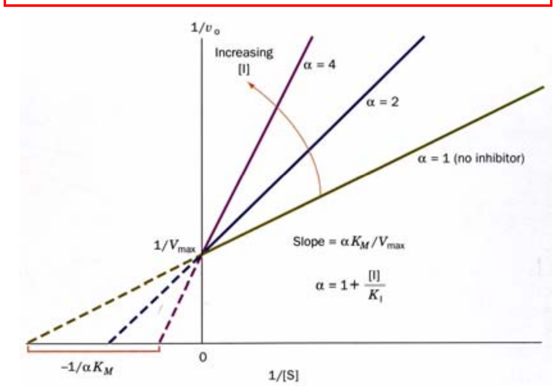
$$\frac{1}{v_o} = \left(\frac{K_M}{V_{max}}\right)\frac{1}{[S]} + \frac{1}{V_{max}}$$



Competitive Inhibition

$$\begin{array}{l} E \;+\; S \;\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}}\; ES \;\xrightarrow{k_2}\; P \;+\; E \\ + \\ I \\ K_I \Big\updownarrow \\ EI \;+\; S \;\longrightarrow\; \text{NO REACTION} \end{array}$$

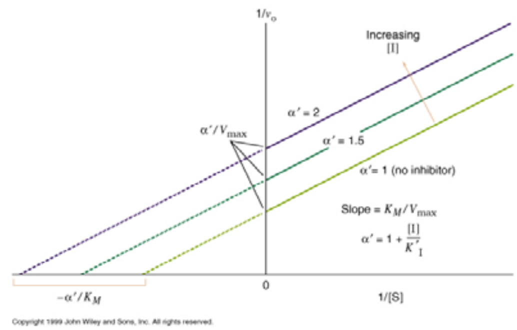
Competitive Inhibition: Lineweaver-Burke Plot



Uncompetitive Inhibition

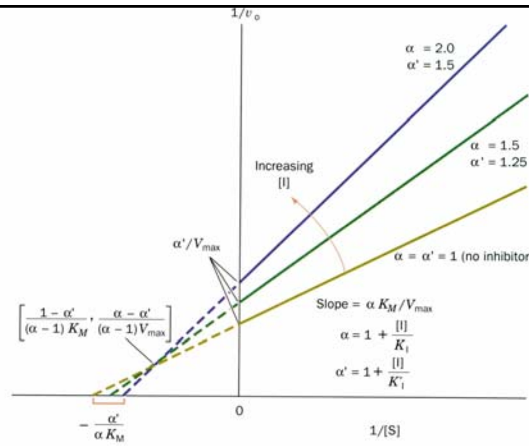
$$
\begin{array}{l}
E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} P + E \\
\qquad\qquad\quad\; + \\
\qquad\qquad\quad\; I \\
\qquad\qquad\quad K_I' \Big\Updownarrow \\
\qquad\qquad\quad\; ESI \longrightarrow \text{NO REACTION}
\end{array}
$$

Uncompetitive Inhibition: Lineweaver-Burke Plot



Mixed inhibition

$$
\begin{array}{ccc}
E + S & \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} & ES \xrightarrow{k_2} P + E \\
+ & & + \\
I & & I \\
K_I \Big\Updownarrow & & K_I' \Big\Updownarrow \\
EI & & ESI \longrightarrow \text{NO REACTION}
\end{array}
$$

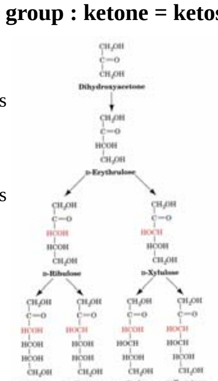


Monosaccharides (D-aldoses)

Carbohydrates are classified as to the nature of the carbonyl group : ketone = ketose aldehyde = aldose

$2^{(n-3)}$ stereoisomers of ketoses

c.f. $2^{(n-2)}$ stereoisomers of aldoses

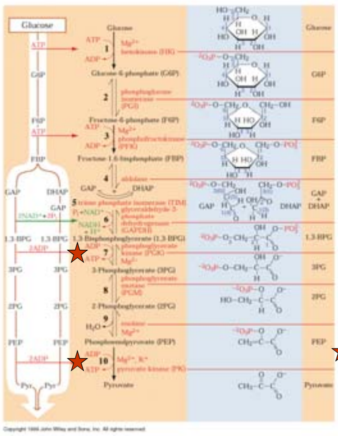


Triose

Tetrose

Pentose

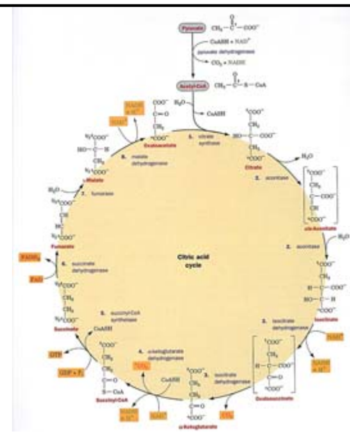
Hexose



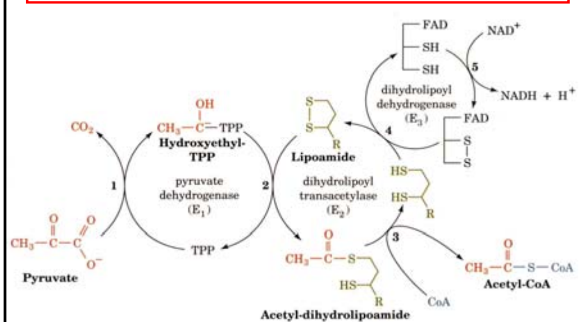
Glycolysis Review

- Stage I: Energy investment (rxns. 1-5), glucose phosphorylated and cleaved to yield 2 G3P and consumes 2 ATP
- State II: Energy recovery (rxns. 6-10), G3P converted to pyruvate with generation of 4 ATP
- Net profit of 2 ATP per glucose

Glucose + 2NAD$^+$ + 2ADP +2P*i* $\rightarrow$ 2NADH + 2pyruvate + 2ATP + $2H_2O$ + 4H$^+$



The five reactions of the pyruvate dehydrogenase multi enzyme complex



Comprehensive Exam

Tuesday December 15, 11:00 AM – 2:00 PM