Final Exam Review
(4/28/11)

Lecture note excerpt covering all lectures

Chapter 2

Gibbs Free Energy (G)

The **Free Energy (G)** change of a spontaneous process is negative

Free energy is defined as follows: $G = H - TS$
Normally, we are interested in the change in free energy so the following equation is more useful: $\Delta G = \Delta H - T\Delta S$
For a spontaneous process, $\Delta G < 0$.

If the **ΔG is < 0**, the process is called **exergonic**
If the **ΔG is > 0**, the process is called **endergonic**
If the **ΔG is = 0**, the process is called **equilibrium**

ΔS	ΔH	ΔG = ΔH - TΔS
+	-	All favorable at all temperatures spontaneous
-	-	Enthalpy favored. Spontaneous at temperatures **below** $T = \frac{\Delta H}{\Delta S}$
+	+	Entropy driven, enthalpy opposed. Spontaneous at Temperatures **above** $T = \frac{\Delta H}{\Delta S}$
-	+	Non-spontaneous

Equilibrium Constants

- Relationships between concentration and free energy
- $\Delta G^0 = -RT \ln K_{eq}$, where ΔG^0 is the free energy change in the standard state, R is the gas constant 8.3145 J/K-mol

$$aA + bB \leftrightarrow cC + dD$$

$$\Delta G = \Delta G^0 + RT \ln\left(\frac{[C]^c[D]^d}{[A]^a[B]^b}\right)$$

At equilibrium, $\Delta G=0$ so $\Delta G^0 = -RT \ln K_{eq}$ 

$$K_{eq} = \frac{[C]_{eq}^c[D]_{eq}^d}{[A]_{eq}^a[B]_{eq}^b} = e^{-\Delta G^0/RT}$$ 

Chapter 4 - Amino Acids

The building blocks of proteins

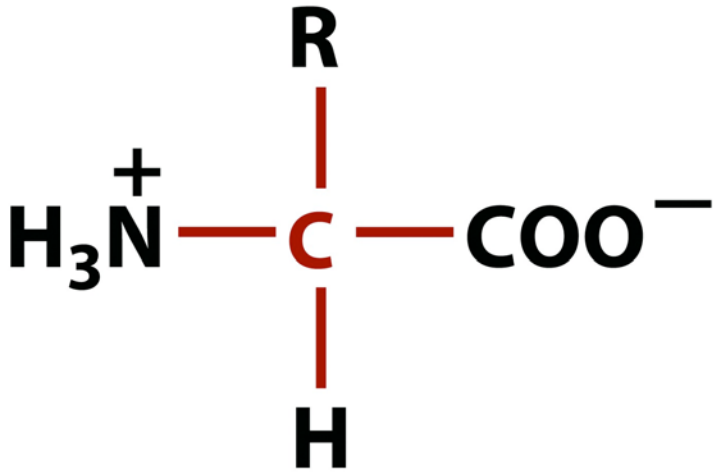


Figure 4-2 Fundamentals of Biochemistry, 2/e
© 2006 John Wiley & Sons

$pK_1 \approx 2.2$ while $pK_2 \approx 9.4$, pK_R for R group pK's

In the physiological pH range, both NH_2 and COOH are completely ionized.

They can act as either an acid or a base.

They are Zwitterions, molecules having charged groups of opposite polarity.

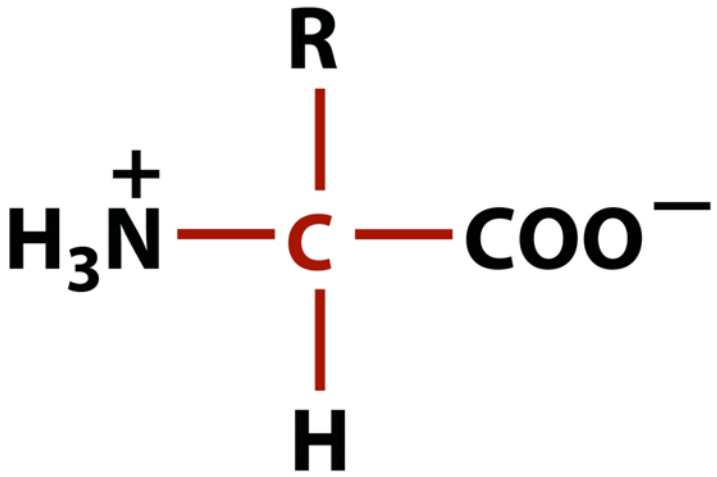


Figure 4-2 Fundamentals of Biochemistry, 2/e
© 2006 John Wiley & Sons

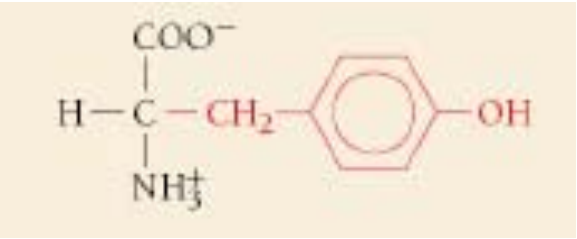
- Please carefully note the charged ends (termini).
- At physiological pH, the ends of an amino acid are charged.
- Certain “R” groups will also be charged at pH 7.

- Backbone of an amino acid is composed of the N, Cα, and C.
- Amino acid structures and sequences are written from left to right, starting with the N-terminus (amino) and finishing with the C-terminus (carboxyl)
- The thing that differentiates each amino acid is the “R” group
- Cα is chiral, except in Gly

Amino Acids

You must know:

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



Tyrosine, Tyr, Y, aromatic, hydroxyl

Classification and Characteristics of Amino Acids

R polarity: three main categories to describe amino acids:

1) Non polar "hydrophobic" nine in all
Glycine, Alanine, Valine, Leucine, Isoleucine, Methionine, Proline, Phenylalanine and Tryptophan

2) Uncharged polar, six in all
Serine, Threonine, Asparagine, Glutamine, Tyrosine, Cysteine

3) Charged polar, five in all
Lysine, Arginine, Glutamic acid, Aspartic acid, and Histidine

Key to structure

(1) Non-polar

Glycine (Gly, G)

Alanine (Ala, A)

Valine (Val, V)

Leucine (Leu, L)

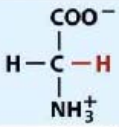
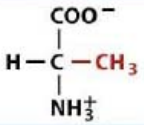
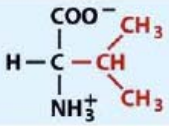
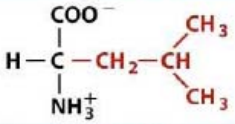
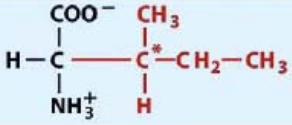
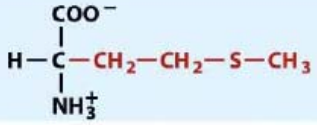
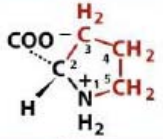
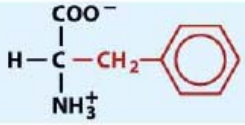
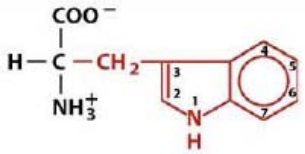
Isoleucine (Ile, I)

Methionine (Met, M)

Proline (Pro, P)

Phenylalanine (Phe, F)

Tryptophan (Trp, W)

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula[a]	Residue Mass (D)[b]	Average Occurrence in Proteins (%)[c]	pK_1 α-COOH[d]	pK_2 α-NH_3^+[d]	pK_R Side Chain[d]
Amino acids with nonpolar side chains						
Glycine Gly G		57.0	7.2	2.35	9.78	
Alanine Ala A		71.1	7.8	2.35	9.87	
Valine Val V		99.1	6.6	2.29	9.74	
Leucine Leu L		113.2	9.1	2.33	9.74	
Isoleucine Ile I		113.2	5.3	2.32	9.76	
Methionine Met M		131.2	2.2	2.13	9.28	
Proline Pro P		97.1	5.2	1.95	10.64	
Phenylalanine Phe F		147.2	3.9	2.20	9.31	
Tryptophan Trp W		186.2	1.4	2.46	9.41	

(2) Polar

Serine (Ser, S)

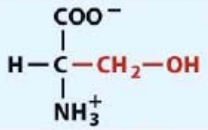
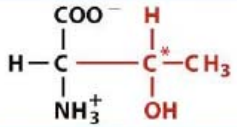
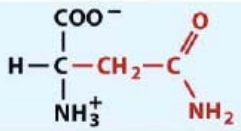
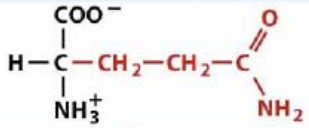
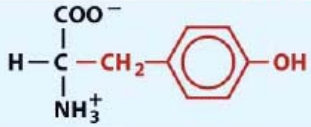
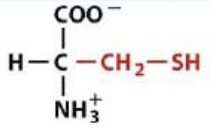
Threonine (Thr, T)

Asparagine (Asn, N)

Glutamine (Gln, Q)

Tyrosine (Tyr, Y)

Cysteine (Cys, C)

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula[a]	Residue Mass (D)[b]	Average Occurrence in Proteins (%)[c]	pK_1 α-COOH[d]	pK_2 α-NH_3^+[d]	pK_R Side Chain[d]
Amino acids with uncharged polar side chains						
Serine Ser S		87.1	6.8	2.19	9.21	
Threonine Thr T		101.1	5.9	2.09	9.10	
Asparagine[e] Asn N		114.1	4.3	2.14	8.72	
Glutamine[e] Gln Q		128.1	4.3	2.17	9.13	
Tyrosine Tyr Y		163.2	3.2	2.20	9.21	10.46 (phenol)
Cysteine Cys C		103.1	1.9	1.92	10.70	8.37 (sulfhydryl)

(3) Charged

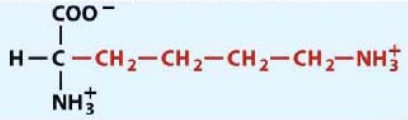
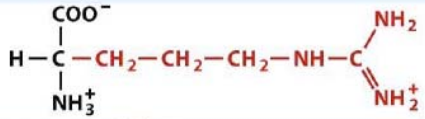
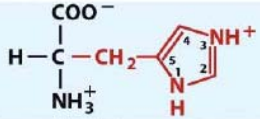
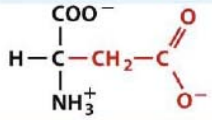
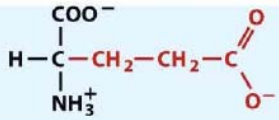
Lysine (Lys, K, +1)

Arginine (Arg, R, +1)

Histidine (His, H, +1)

Aspartic acid (Asp, D, -1)

Glutamic acid (Glu, E, -1)

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula[a]	Residue Mass (D)[b]	Average Occurrence in Proteins (%)[c]	pK_1 α-COOH[d]	pK_2 α-NH_3^+[d]	pK_R Side Chain[d]
Amino acids with charged polar side chains						
Lysine Lys K		128.2	5.9	2.16	9.06	10.54 (ε-NH_3^+)
Arginine Arg R		156.2	5.1	1.82	8.99	12.48 (guanidino)
Histidine[f] His H		137.1	2.3	1.80	9.33	6.04 (imidazole)
Aspartic acid[e] Asp D		115.1	5.3	1.99	9.90	3.90 (β-COOH)
Glutamic acid[e] Glu E		129.1	6.3	2.10	9.47	4.07 (γ-COOH)

Amino acids can form peptide bonds CO-NH linkage

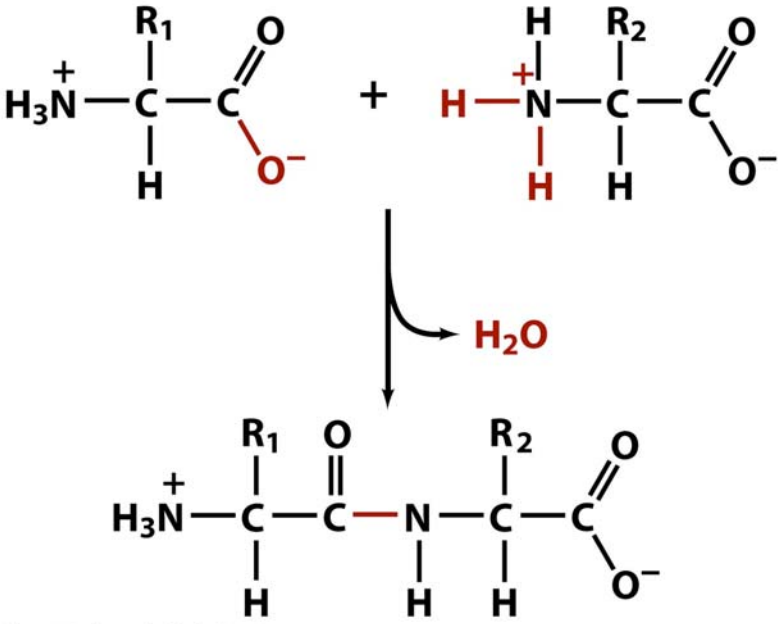


Figure 4-3 Fundamentals of Biochemistry, 2/e
© 2006 John Wiley & Sons

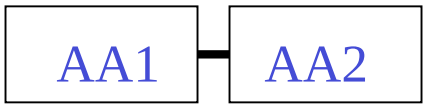
- Amino acid residue
- Dipeptides, tripeptides, oligopeptides
- Polypeptides
- Proteins consist of one or more PP

Peptides are linear polymers that range from 8 to 4000 amino acid residues

Twenty (20) different naturally occurring amino acids

Linear arrays of amino acids can make a huge number of molecules

Consider a peptide with two amino acids



20 x 20 = 400 different molecules

20 x 20 x 20 = 8000 different molecules

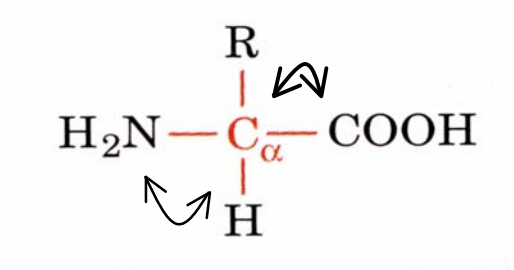
For 100 amino acid protein the # of possibilities are:

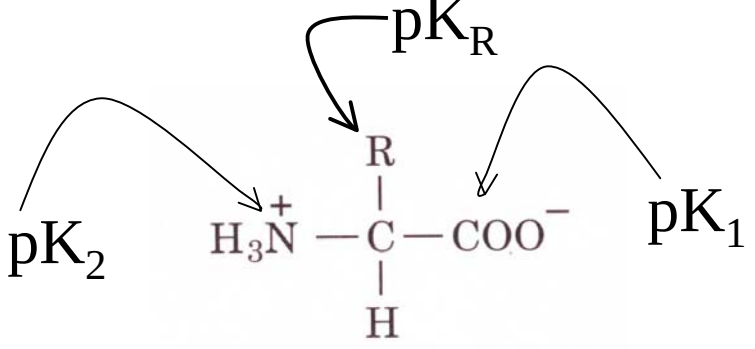
$$20^{100} = 1.27x10^{130}$$

The total number of atoms in the universe is estimated at $9x10^{78}$

Amino Acids:

The building blocks of proteins





α-amino acids because of the α-carboxylic and α-amino groups

pK_1 and pK_2 respectively pK_R is for R group pK's

Remember these values for the pKa's of the termini for ALL AA's

★ $pK_1 \approx 2.2$ while $pK_2 \approx 9.4$

★ In the physiological pH range, both carboxylic and amino groups are completely ionized!! ★

- Hint: draw the structures of an amino acid at several pH values

Acid - Base properties of amino acids

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

Isoelectric point: the pH where a protein carries no net electrical charge

$$pI = \frac{1}{2}\left(pK_i + pK_j\right)$$

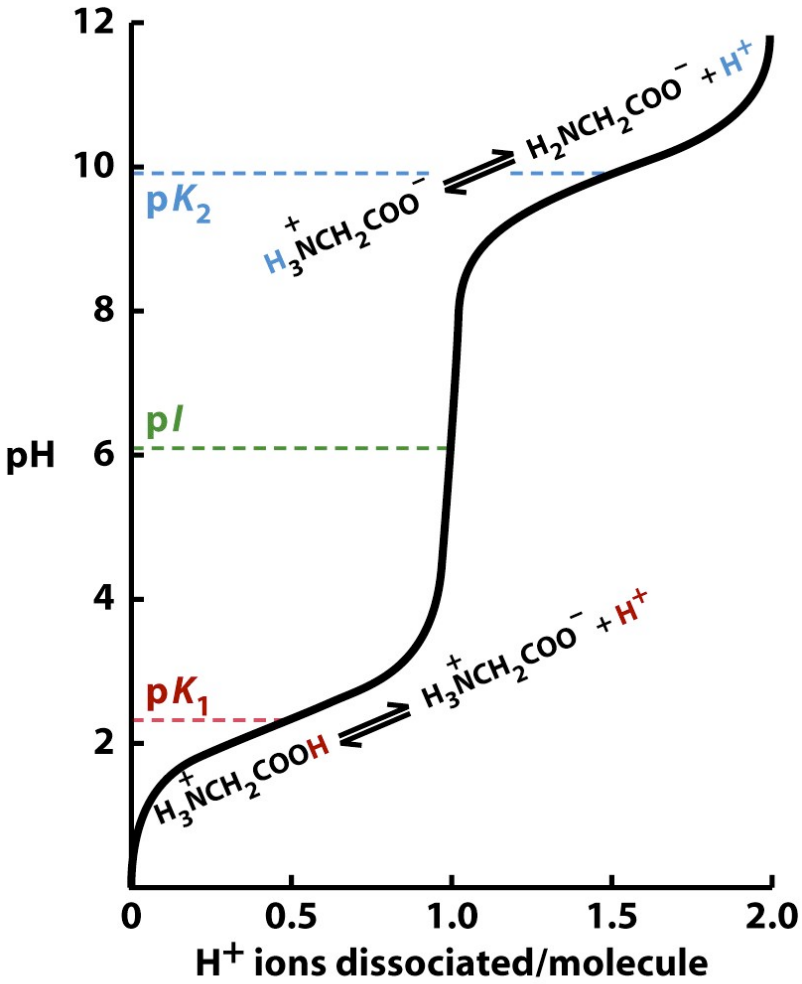


Figure 4-8 Fundamentals of Biochemistry, 2/e

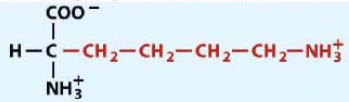
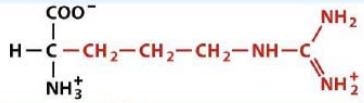
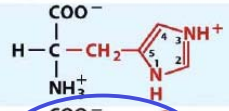
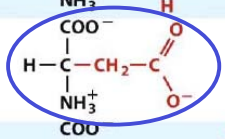
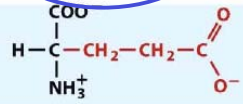
For a monoamino-monocarboxylic residue

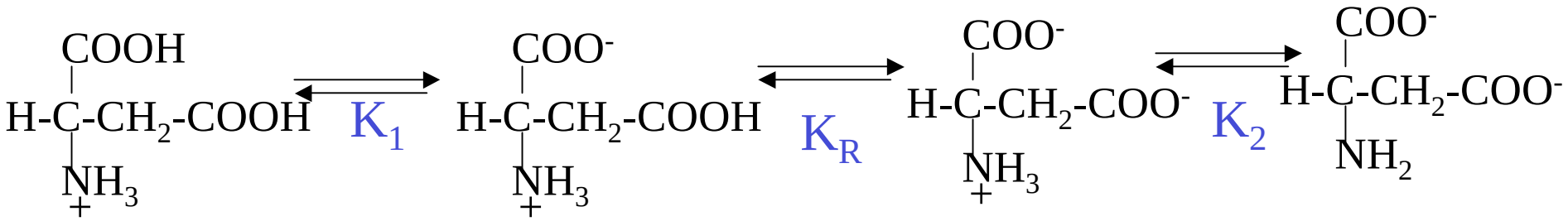
pKi = pK_1 and pKj = pK_2 ;

For D and E, pKi = pK_1 and pKj = pK_R ;

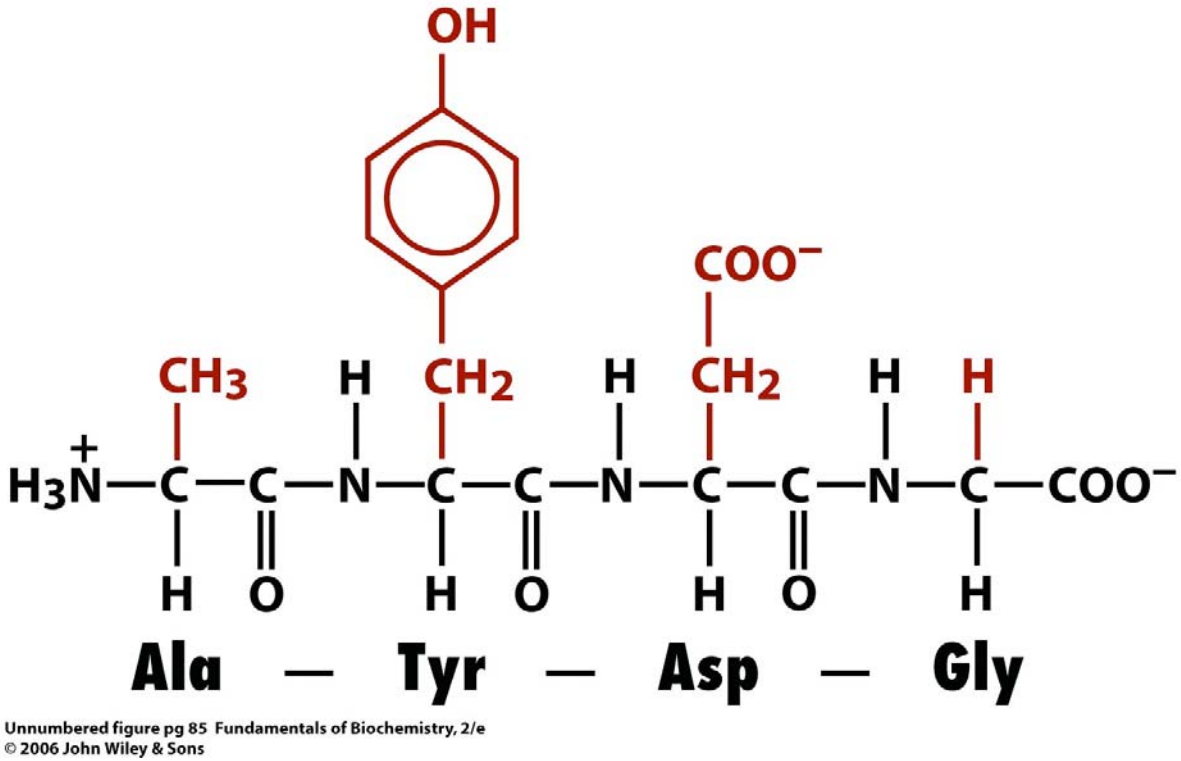
For R, H and K, pKi = K_R and pKj = pK_2

The observed pKa of an amino acid side chain is dependent on its environment in the protein - standard pKa’s can be substantially shifted by the protein environment!!

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula[a]	Residue Mass (D)[b]	Average Occurrence in Proteins (%)[c]	pK_1 α-COOH[d]	pK_2 α-NH_3^+[d]	pK_R Side Chain[d]
Amino acids with charged polar side chains						
Lysine Lys K		128.2	5.9	2.16	9.06	10.54 (ε-NH_3^+)
Arginine Arg R		156.2	5.1	1.82	8.99	12.48 (guanidino)
Histidine[f] His H		137.1	2.3	1.80	9.33	6.04 (imidazole)
Aspartic acid[e] Asp D		115.1	5.3	1.99	9.90	3.90 (β-COOH)
Glutamic acid[e] Glu E		129.1	6.3	2.10	9.47	4.07 (γ-COOH)



Nomenclature



Unnumbered figure pg 85 Fundamentals of Biochemistry, 2/e

The tetrapeptide Ala-Tyr-Asp-Gly or AYDG

Chapter 5 - part 2 (protein purification)

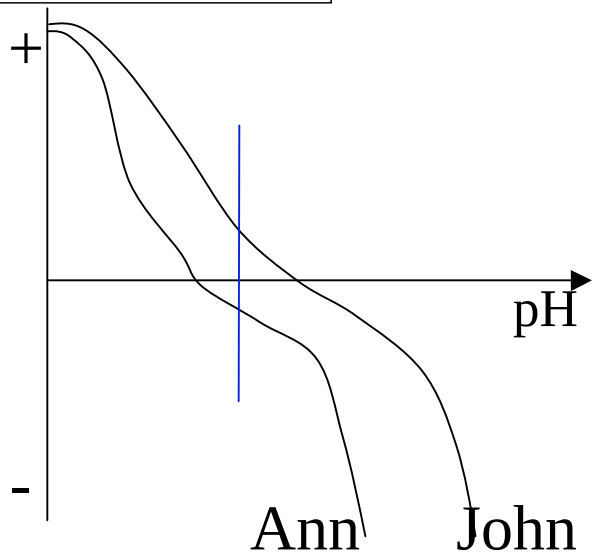
Characteristic	Procedure
Charge	1. Ion exchange, 2. Electrophoresis, 3. Isoelectric focusing
Polarity	1. Adsorption chromatography 2. Paper chromatography 3. Reverse phase chromatography 4. Hydrophobic interaction
Size	1. Dialysis and ultrafiltration, 2. Gel electrophoresis, 3. Gel filtration, 4. Ultracentrifugation
Specificity	1. Affinity chromatography 2. Immunopurification
Solubility	1.Salt precipitation 2. Detergent solubilization

*The most frequently used anion exchanger is: **DEAE**

Matrix-CH_2-CH_2-$NH(CH_2CH_3)_2^+$ A^-

*The most frequently used cation exchanger is: **CM**

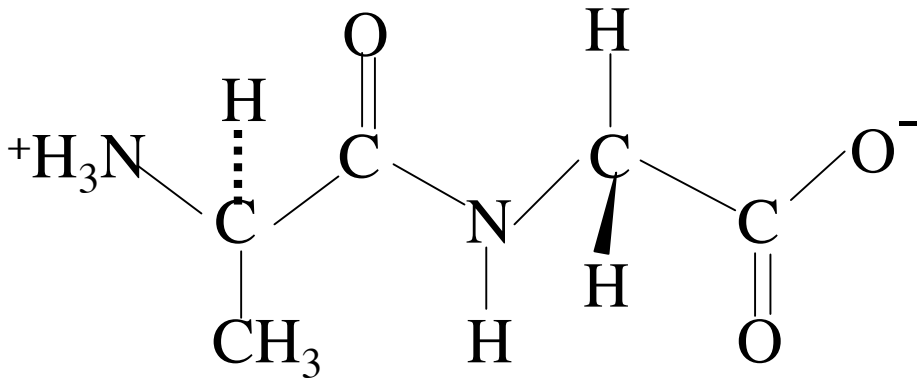
Matrix-CH_2-COO^- A^+



Chapter 6

•You must understand well peptide bond and definitions.

Companion Book #2
In the dipeptide below, indicate which bonds are described by ϕ and ψ.



•Secondary structural element definition and tertiary structure.

Chapter 7

Hb Structure & function relationship

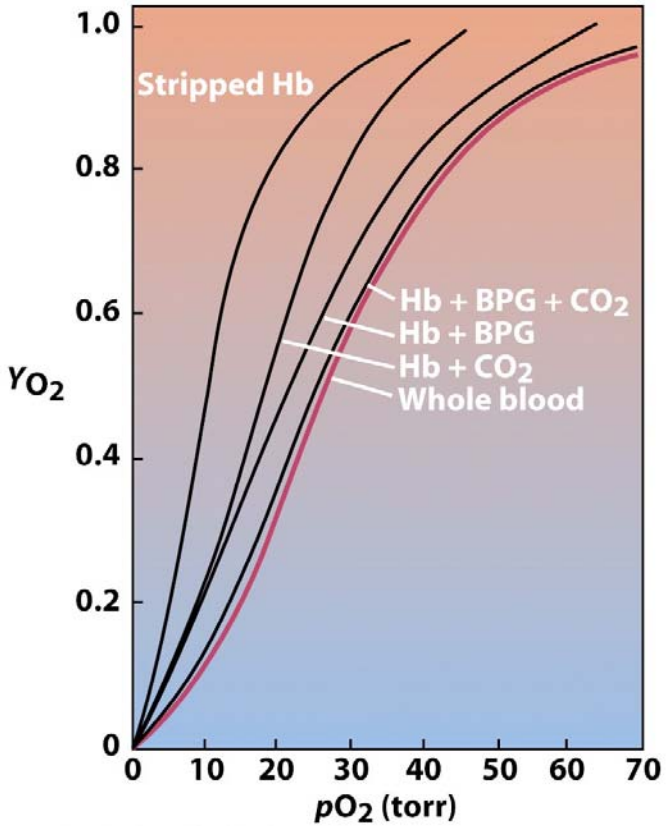
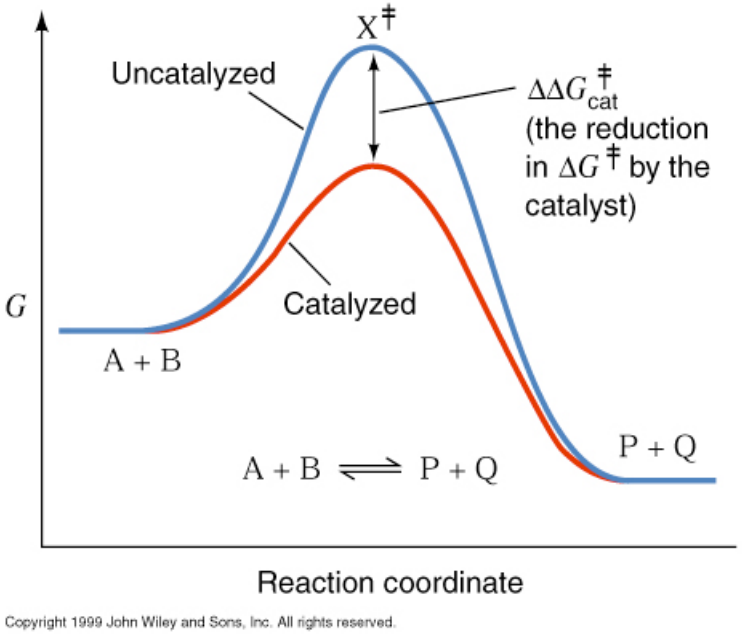


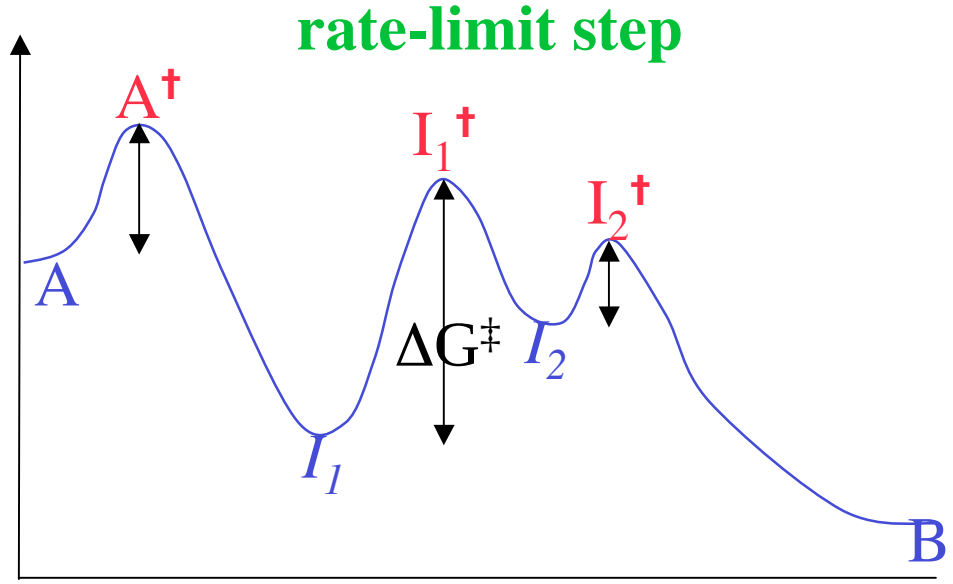
Figure 7-14 Fundamentals of Biochemistry, 2/e

Chapter 11

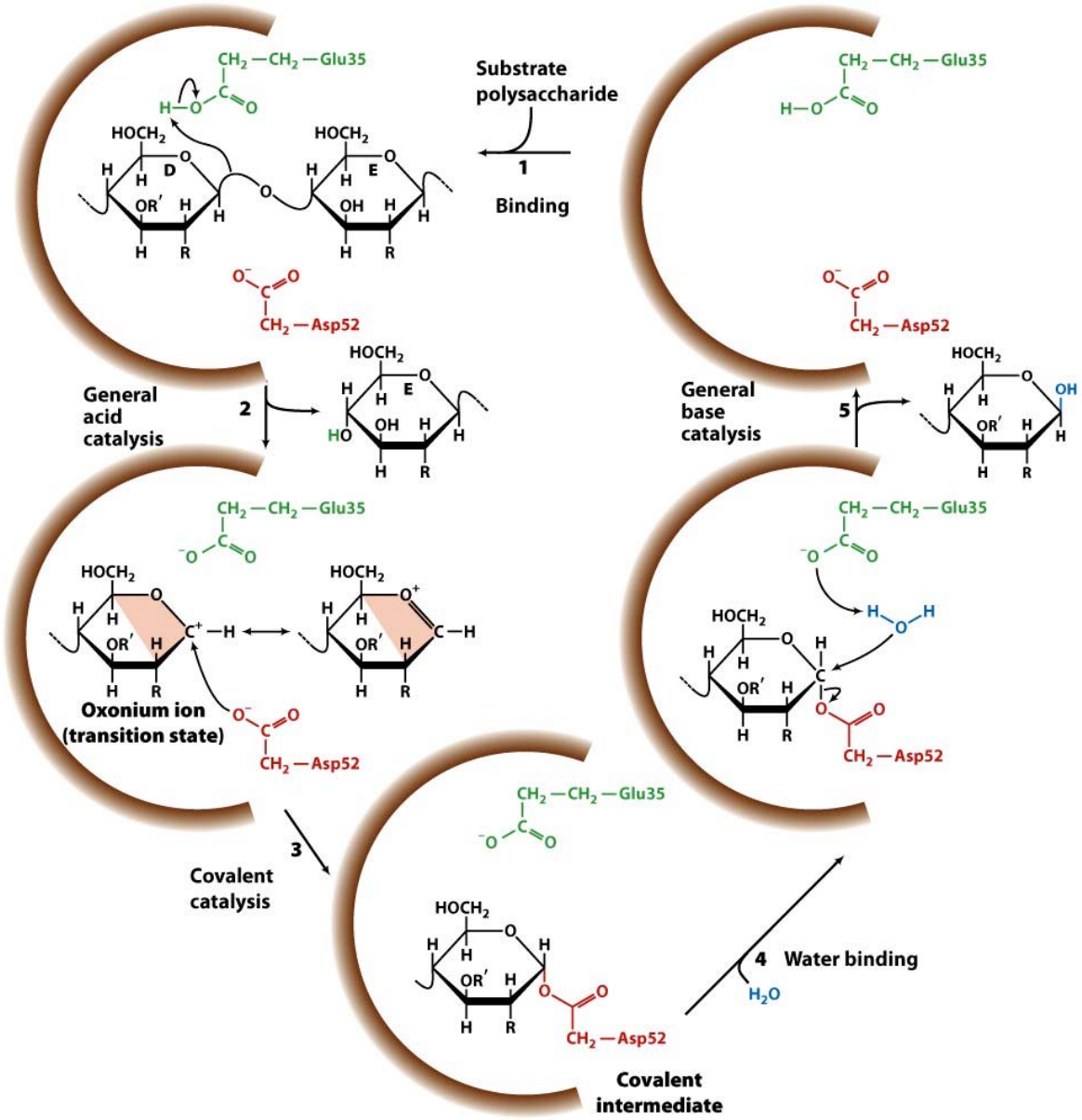
What do enzymes do to increase rates of enzymatically catalyzed reactions?

•Answer: They decrease the energy of the transition state (i.e. the activation free energy for the reaction, ($\Delta G^{\ddagger}$)) by preferentially stabilizing the transition state.



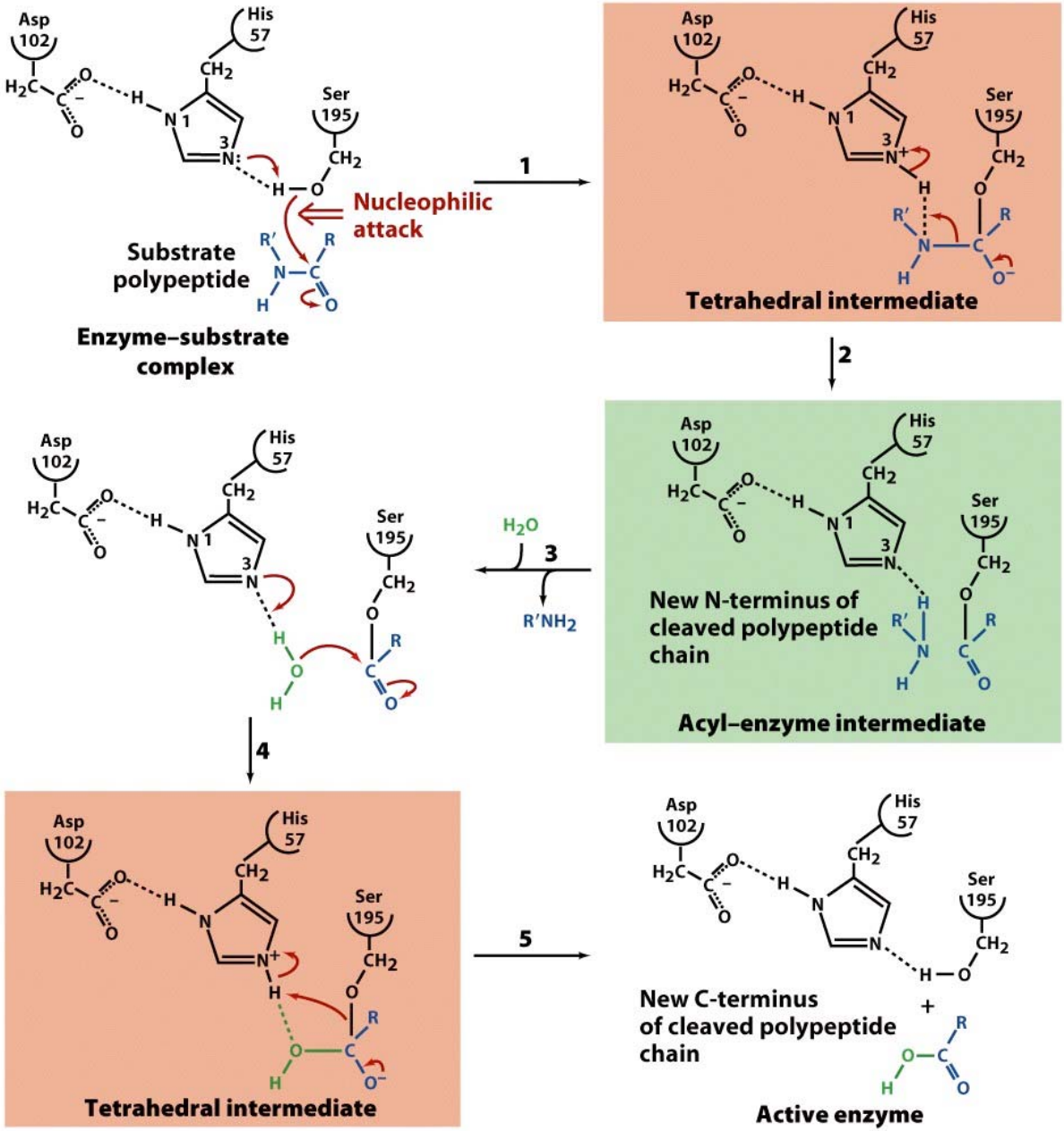


$A \longrightarrow I_1 \longrightarrow I_2 \longrightarrow B$



Glu35: acid catalyst
Asp52: covalent catalyst

The reaction is facilitated by the distortion of residue D to the planar half-chair conformation

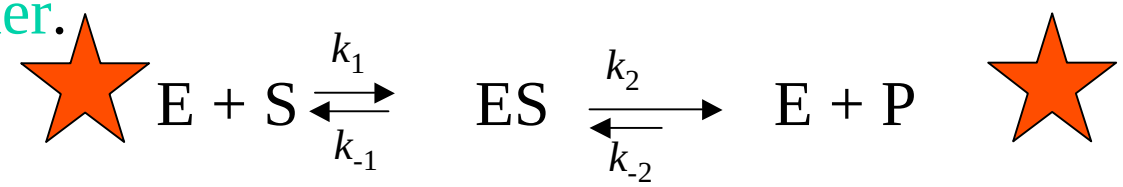


Enzyme Kinetics, Inhibition, and Regulation

Chapter 12

Enzyme Kinetics

- When the concentration of reactant (substrate, S) is much higher than the concentration of enzyme, E, the rate of the enzyme is independent of substrate concentration and the kinetics are zero order.



- Where E=enzyme, S=substrate, ES=enzyme/substrate complex, P=product, k_1 is the forward rate constant, k_{-1} is the reverse rate constant, k_2 is the forward rate constant from ES to E + P, and k_{-2} from E + P to ES

Michaelis-Menten Kinetics

- Some simplifying assumptions are required in order to evaluate enzyme kinetics in a meaningful way

1. Assumption of equilibrium: $k_{-1} >> k_2$ so that the first step of the reaction (i.e. the formation of the ES)

$$K_S = \frac{k_{-1}}{k_1} = \frac{[E][S]}{[ES]}$$, where K_S is the dissociation const. for 1st step

ES is known as the Michaelis complex

2. Assumption of steady state: ES maintains a steady state since [S]>>[E] so the concentration of [ES] is constant

$$\frac{d[ES]}{dt} = 0$$

Michaelis-Menten Equation

- The Michaelis constant is defined as:

$$K_M = \frac{k_{-1} + k_2}{k_1}$$

- The maximal velocity of an enzymatic reaction is:

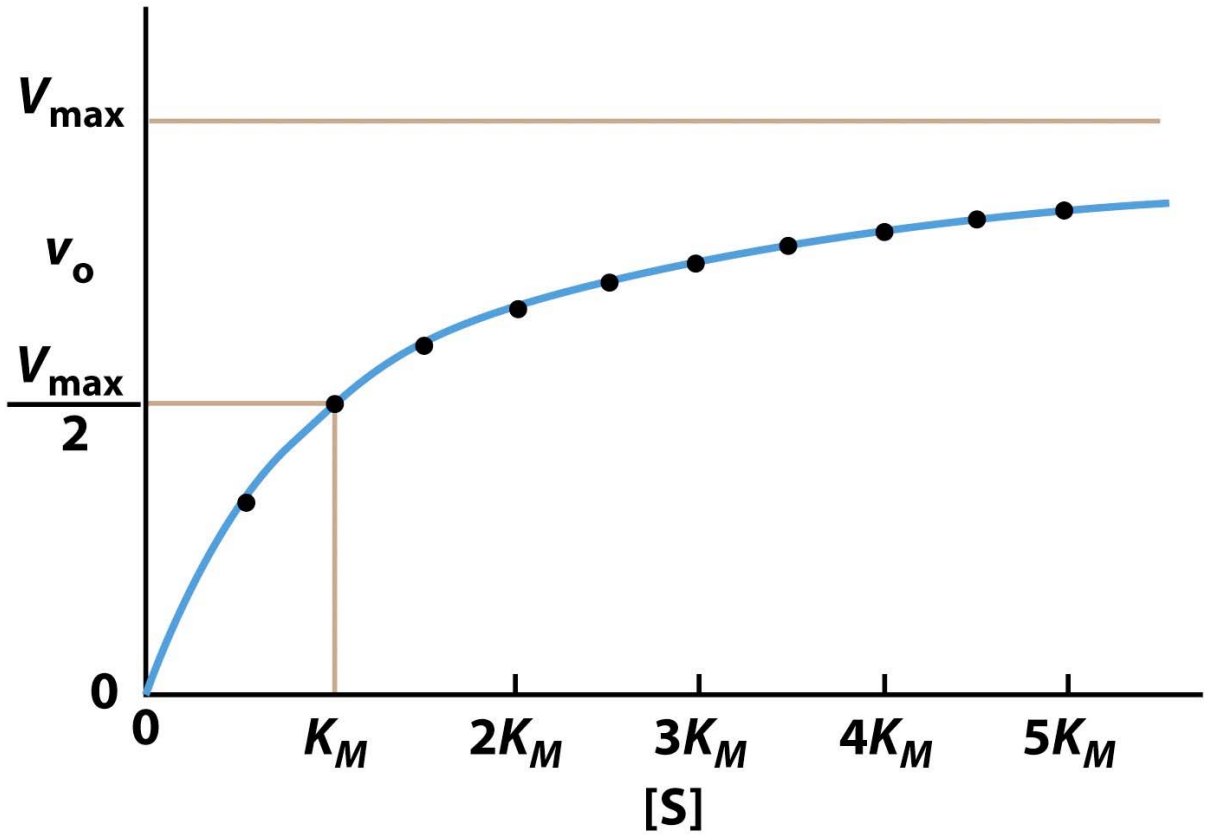
$$V_{max} = k_2 [E]_T$$

- The initial velocity (Michaelis-Menten Equation) is:

$$v_0 = \frac{V_{max}[S]}{K_M + [S]}$$

Plot of Michaelis-Menten Kinetics

- Here is another VERY useful expression (you can see it on the figure and below)
- K_M is the substrate concentration at which the velocity of the reaction is half maximal



Catalytic Turnover and Efficiency

- The catalytic constant, k_{cat}, is defined as:

$$k_{cat} = \frac{V_{max}}{[E]_T}$$

- This is also known as the turnover number because is it the number of catalytic reactions per active site per unit time
- The catalytic efficiency is defined as k_{cat}/K_M

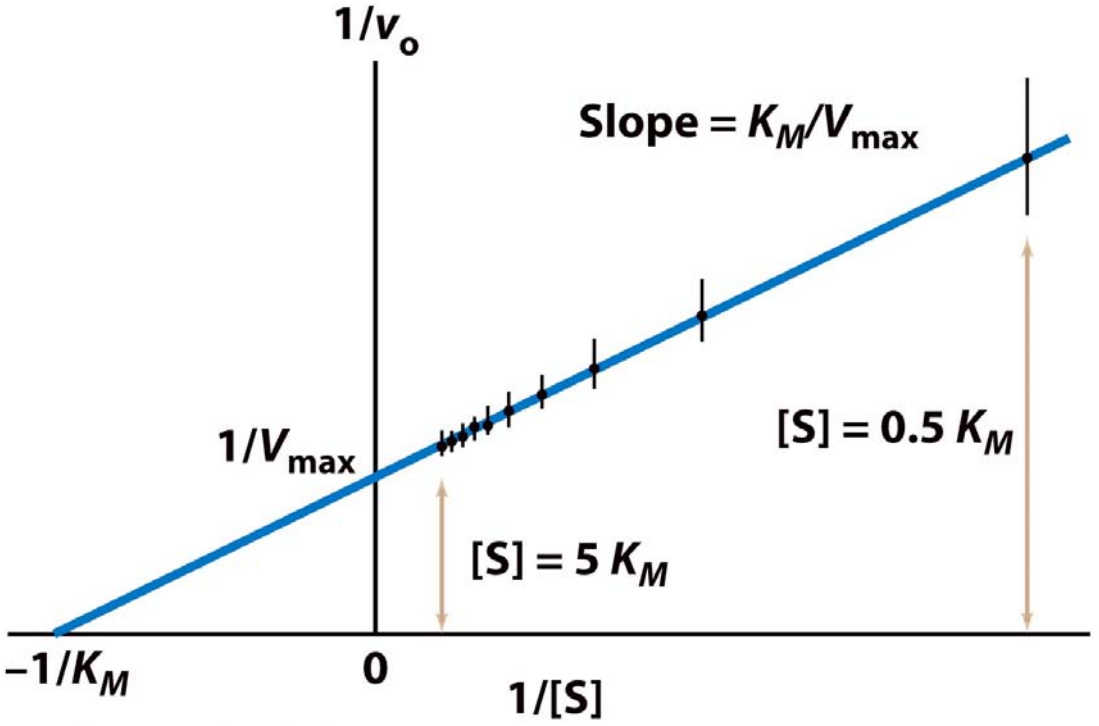
Table 12-1 The Values of K_M, k_{cat}, and k_{cat}/K_M for Some Enzymes and Substrates

Enzyme	Substrate	K_M (M)	k_{cat} (s^{-1})	k_{cat}/K_M ($M^{-1} \cdot s^{-1}$)
Acetylcholinesterase	Acetylcholine	9.5×10^{-5}	1.4×10^{4}	1.5×10^{8}
Carbonic anhydrase	CO_2	1.2×10^{-2}	1.0×10^{6}	8.3×10^{7}
	HCO_3^-	2.6×10^{-2}	4.0×10^{5}	1.5×10^{7}
Catalase	H_2O_2	2.5×10^{-2}	1.0×10^{7}	4.0×10^{8}
Chymotrypsin	*N*-Acetylglycine ethyl ester	4.4×10^{-1}	5.1×10^{-2}	1.2×10^{-1}
	N-Acetylvaline ethyl ester	8.8×10^{-2}	1.7×10^{-1}	1.9
	N-Acetyltyrosine ethyl ester	6.6×10^{-4}	1.9×10^{2}	2.9×10^{5}
Fumarase	Fumarate	5.0×10^{-6}	8.0×10^{2}	1.6×10^{8}
	Malate	2.5×10^{-5}	9.0×10^{2}	3.6×10^{7}
Urease	Urea	2.5×10^{-2}	1.0×10^{4}	4.0×10^{5}

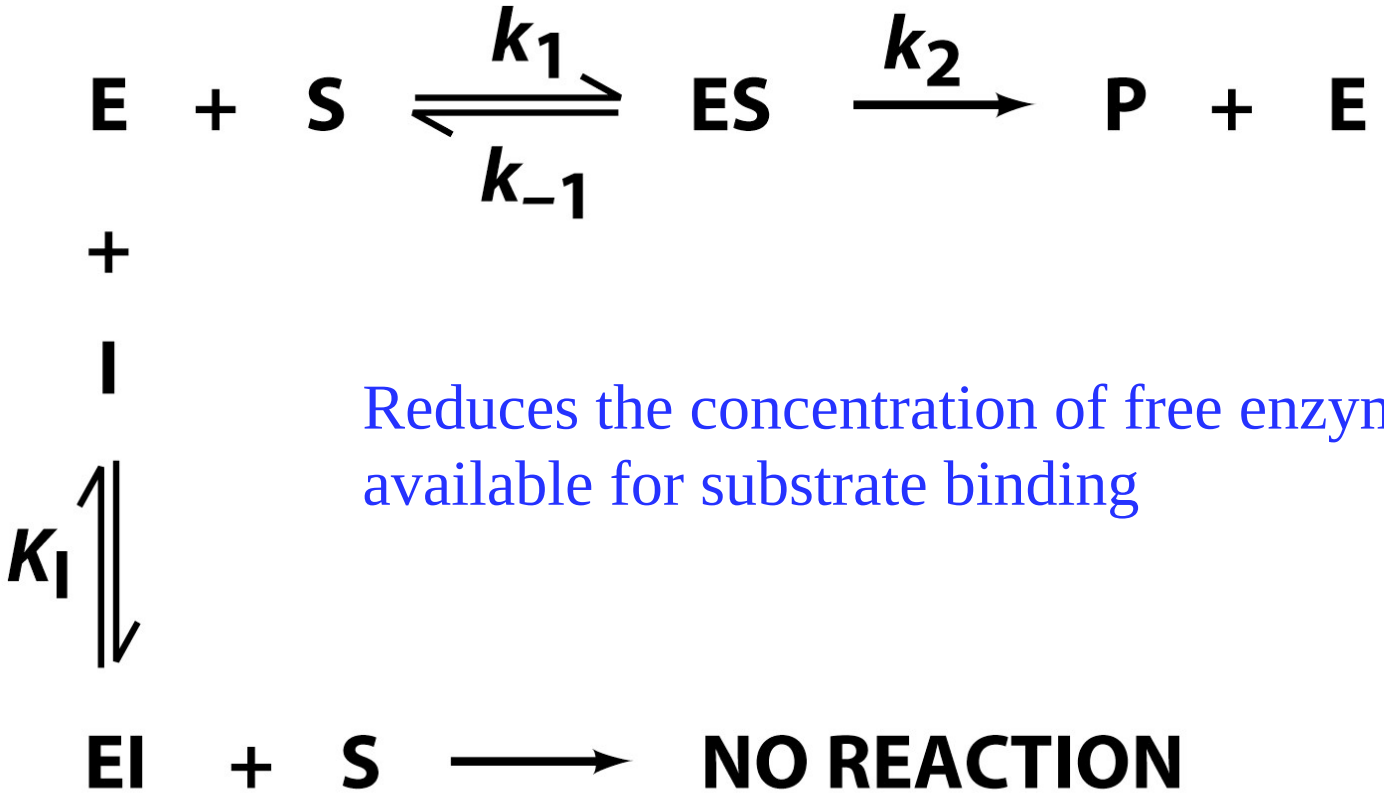
Analysis of Kinetic Data

- Lineweaver-Burk or double-reciprocal plot
- y=mx+b

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

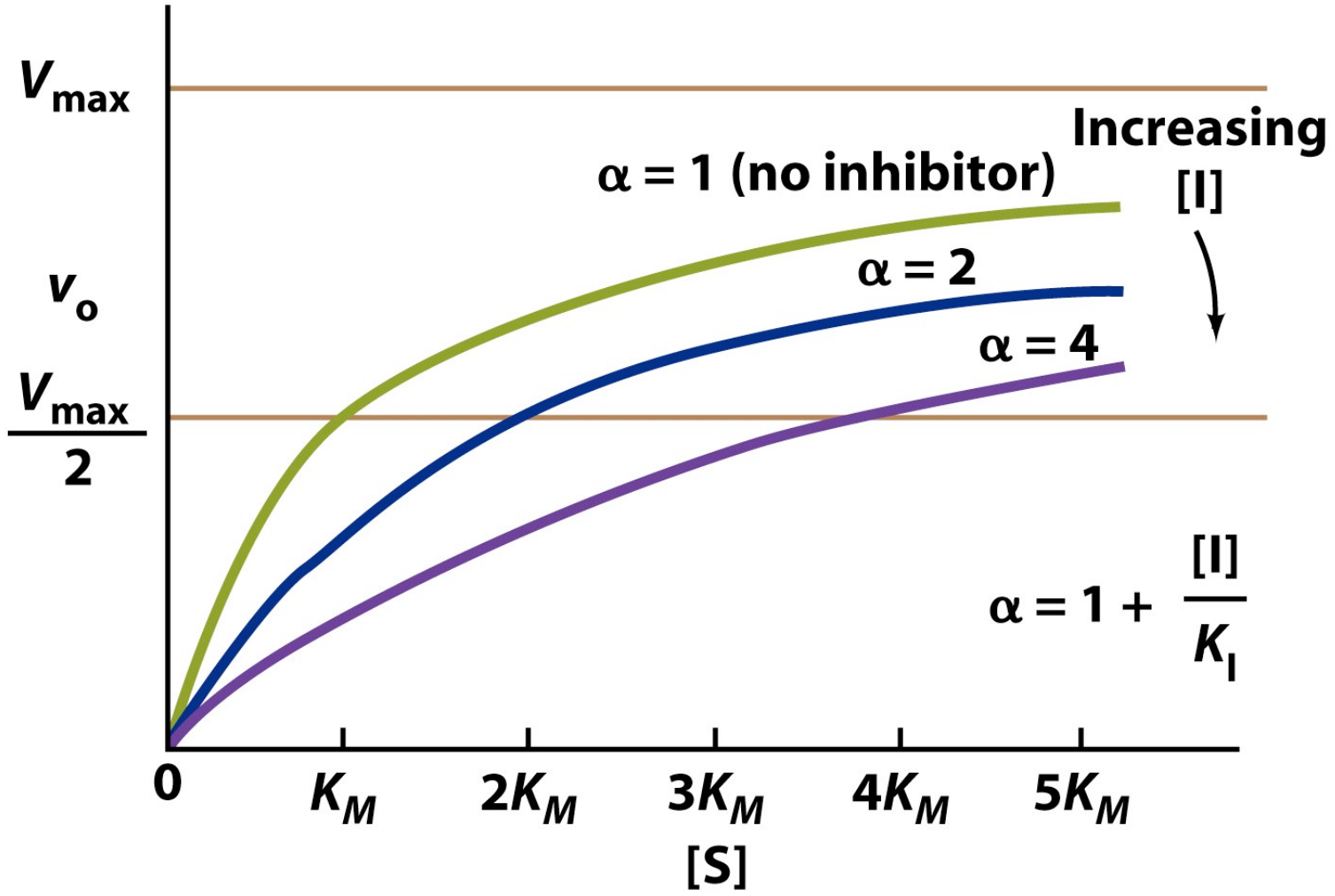


Competitive inhibition

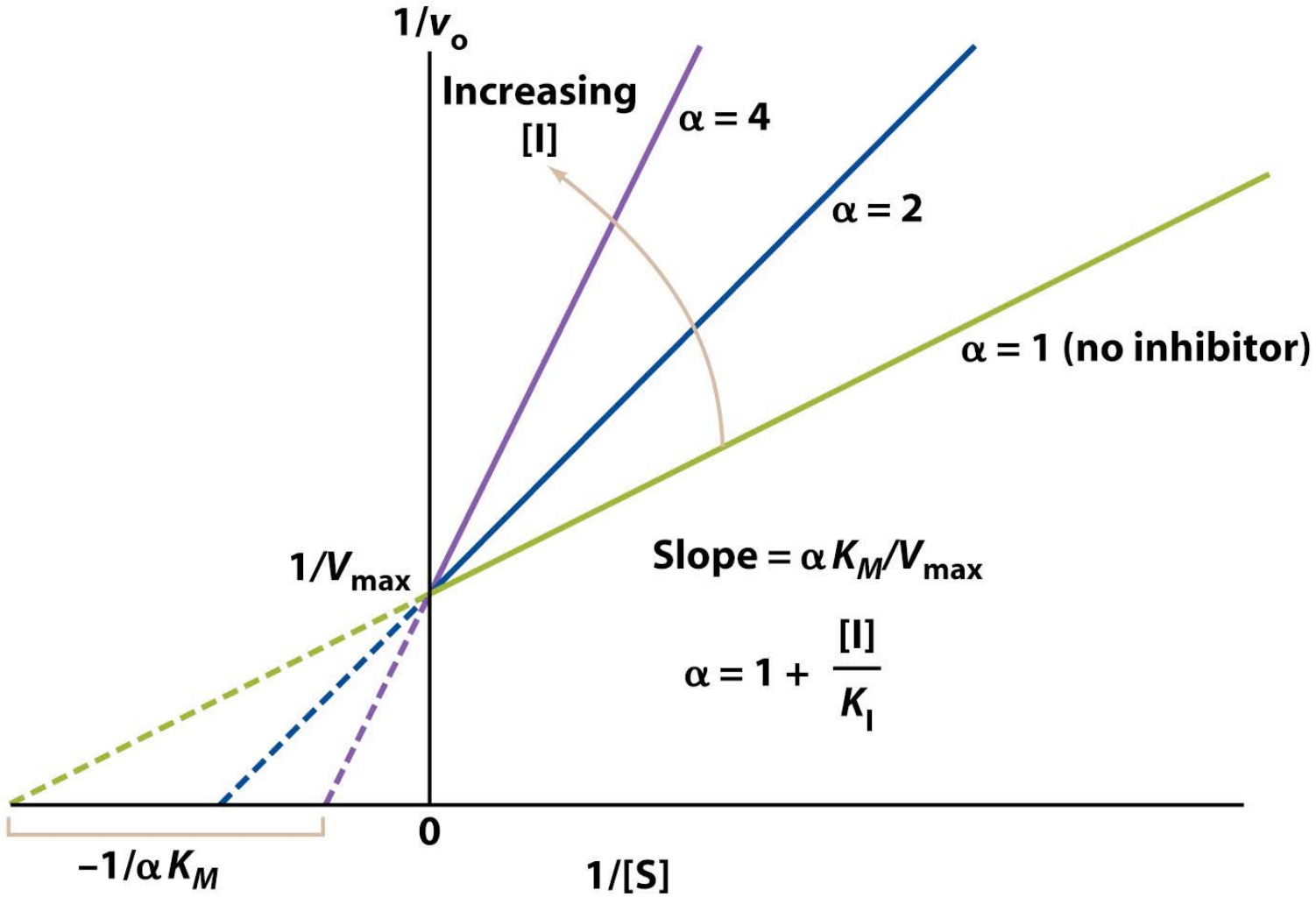


Reduces the concentration of free enzyme available for substrate binding

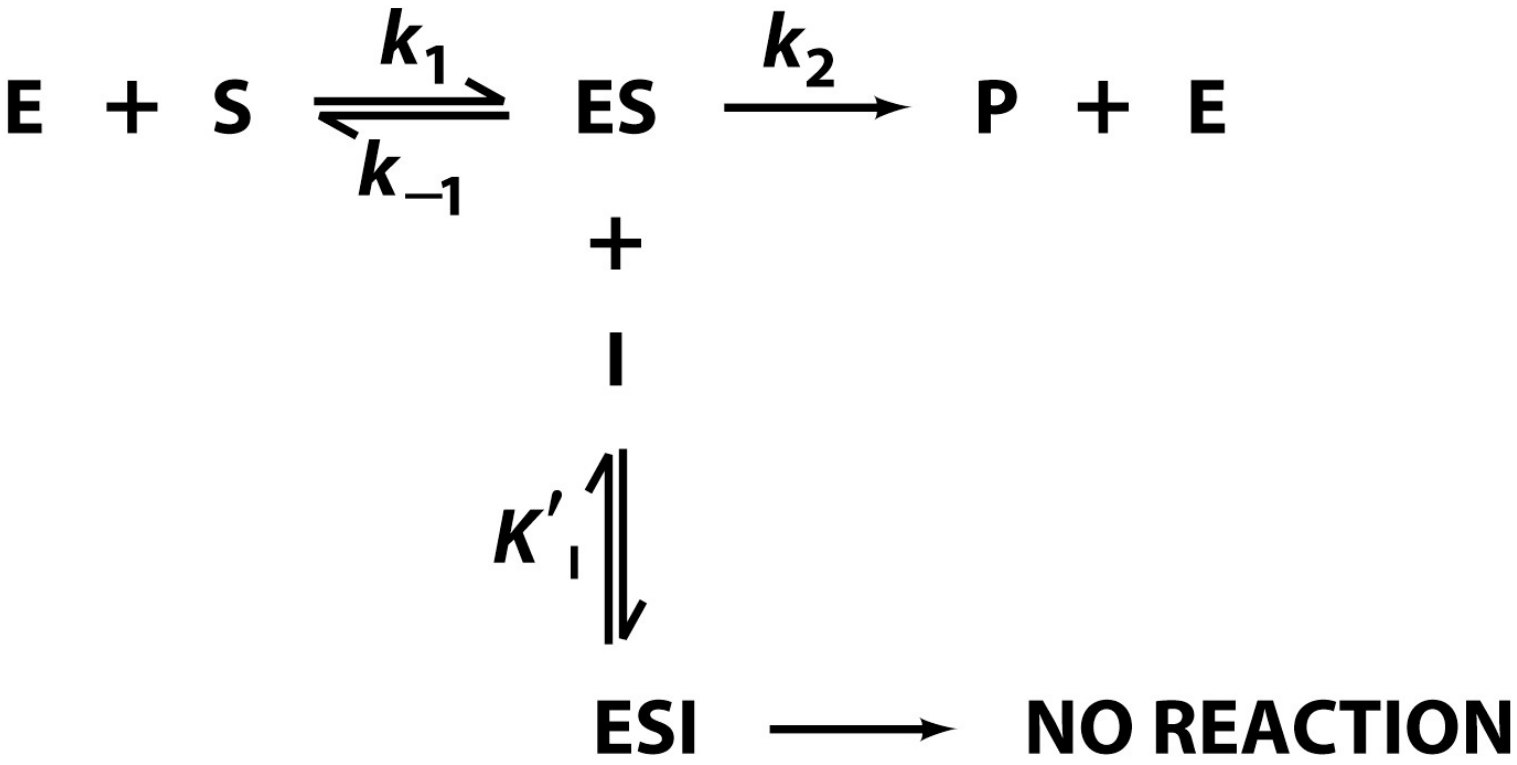
Plot of v_0 vs. [S] for a Michaelis-Menten rxn. with diff. [I]



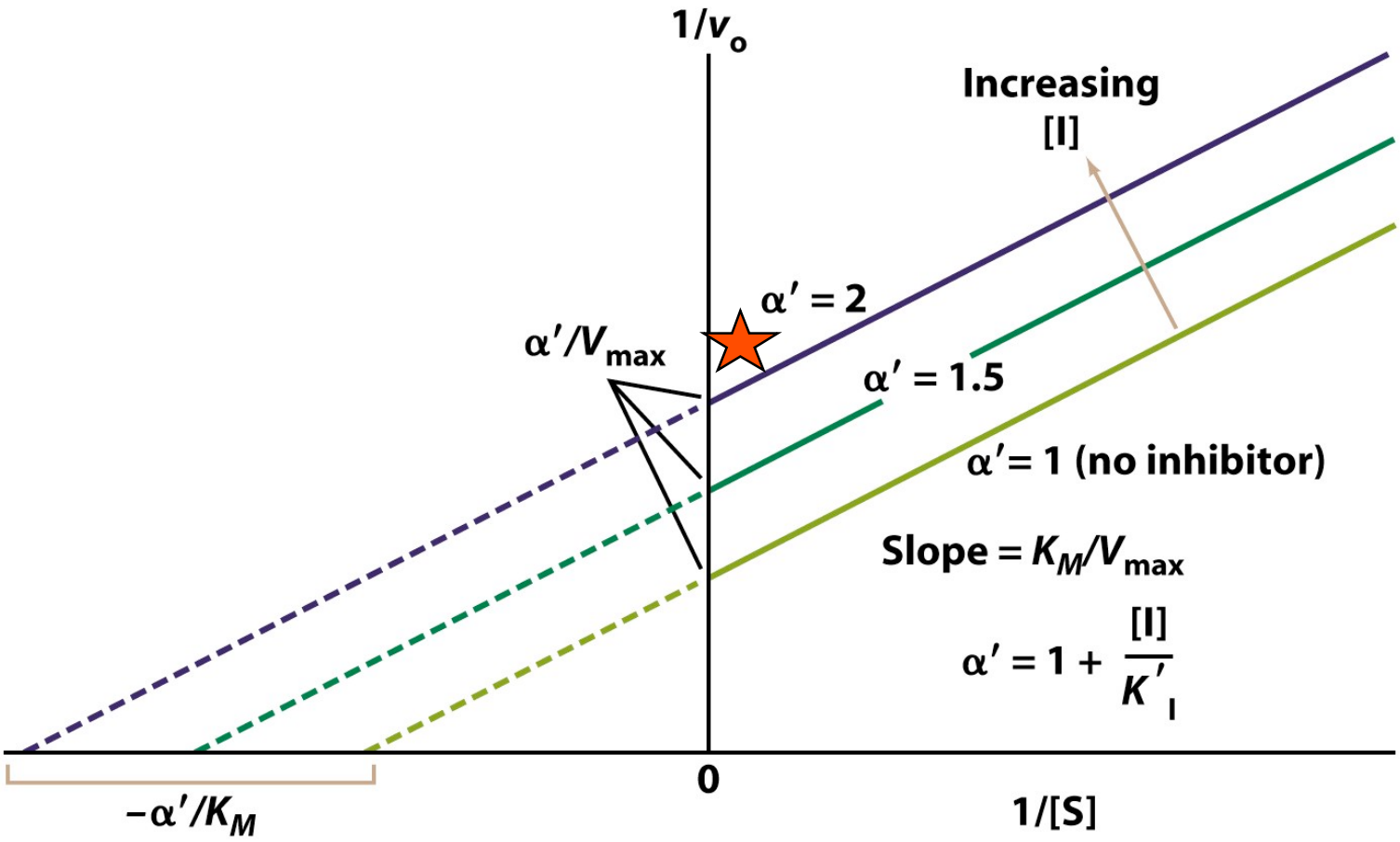
Lineweaver-Burke plot of competitively inhibited M-M reaction



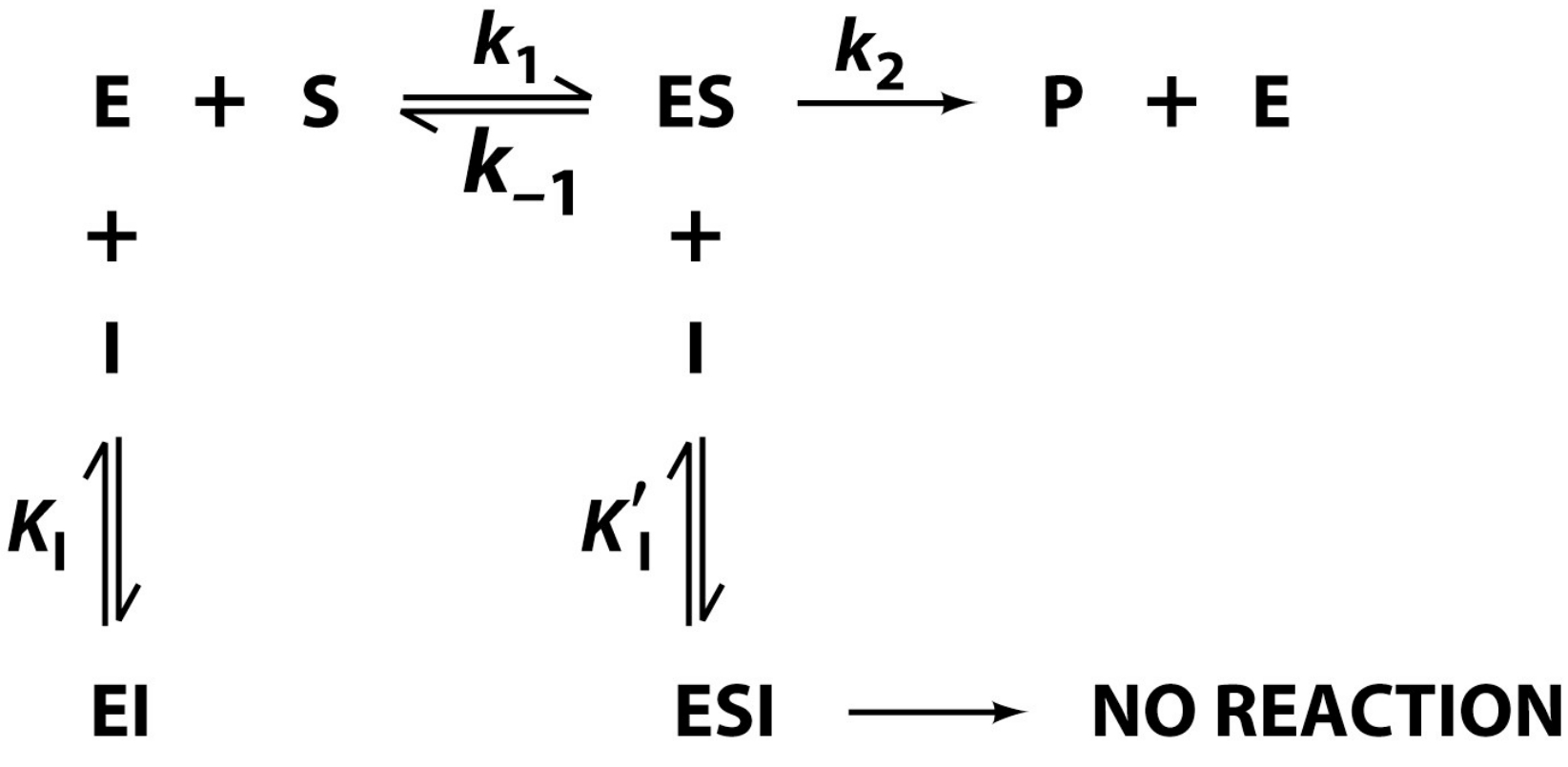
Uncompetitive inhibition



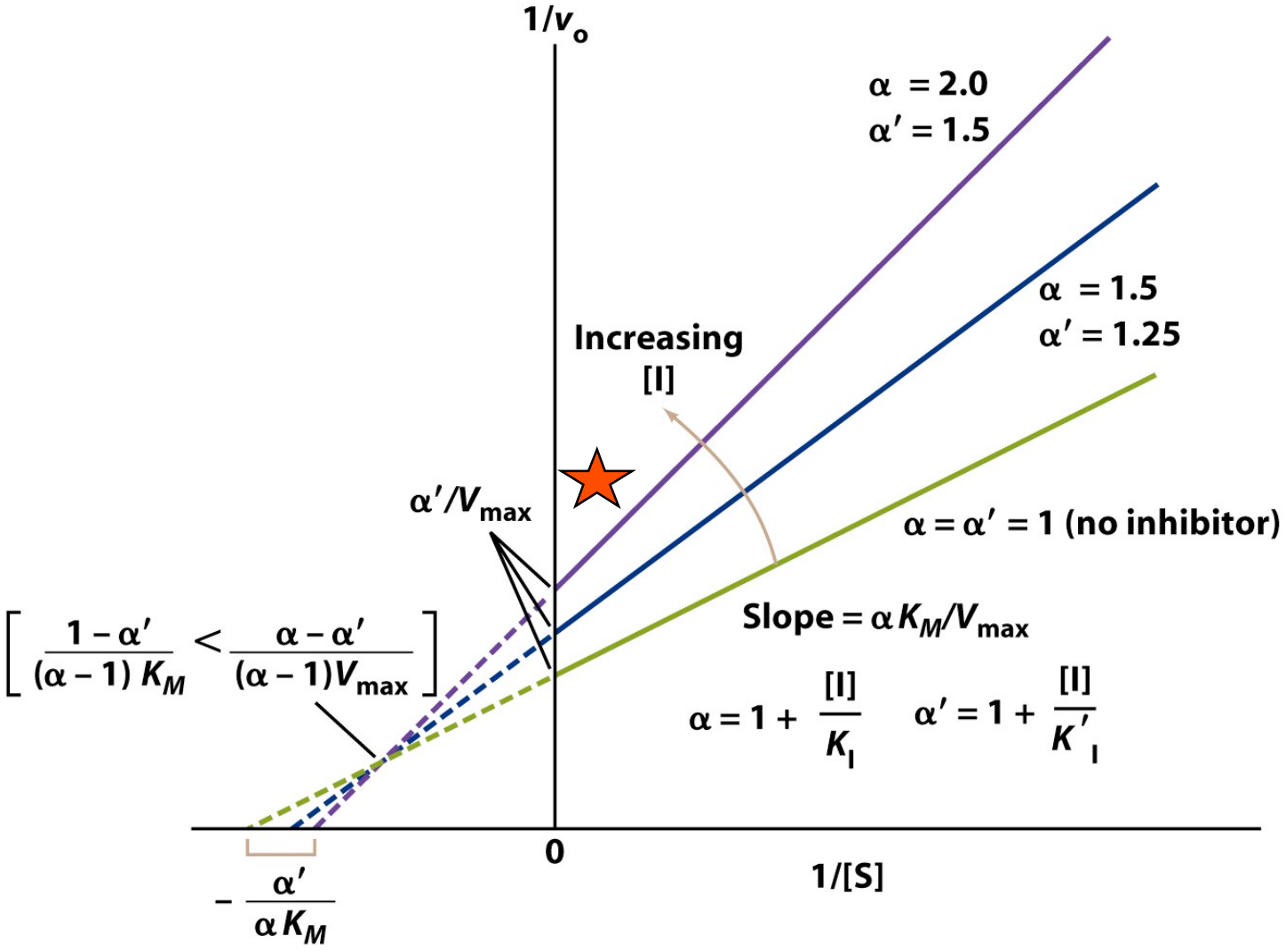
Lineweaver-Burke plot with uncompetitive inhibition



Mixed inhibition



Lineweaver-Burke plot with mixed inhibition



Effects of inhibitors on Michaelis-Menten reactions

Table 12-2

Type of inhibition	Michaelis-Menton equation ★	Lineweaver-Burke equation ★	Effect of inhibition
None	$v_0 = \frac{V_{max}[S]}{K_M + [S]}$	$\frac{1}{v_0} = \frac{K_M}{V_{max}}\frac{1}{[S]} + \frac{1}{V_{max}}$	None
Competitive	$v_0 = \frac{V_{max}[S]}{\alpha K_M + [S]}$	$\frac{1}{v_0} = \frac{\alpha K_M}{V_{max}}\frac{1}{[S]} + \frac{1}{V_{max}}$	Increases K_M
Uncompetitive	$v_0 = \frac{V_{max}[S]}{K_M + \alpha'[S]}$	$\frac{1}{v_0} = \frac{K_M}{V_{max}}\frac{1}{[S]} + \frac{\alpha'}{V_{max}}$	Decreases K_M and V_{max}
Mixed (non-Competitive)	$v_0 = \frac{V_{max}[S]}{\alpha K_M + \alpha'[S]}$	$\frac{1}{v_0} = \frac{\alpha K_M}{V_{max}}\frac{1}{[S]} + \frac{\alpha'}{V_{max}}$	Decreases V_{max}; ↑ or ↓ K_M

★ $\alpha = 1 + \frac{[I]}{K_I}; \alpha' = 1 + \frac{[I]}{K_I'}$ ★

Metabolism

Chapter 14

High-Energy Compounds

ATP and Phosphoryl Group Transfeer

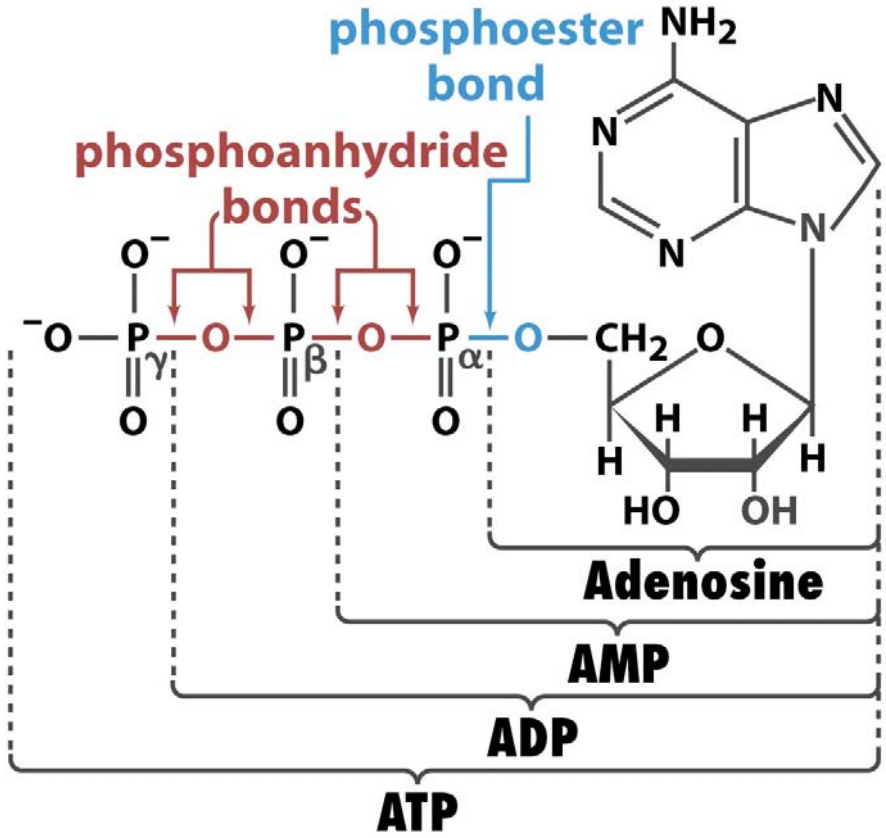
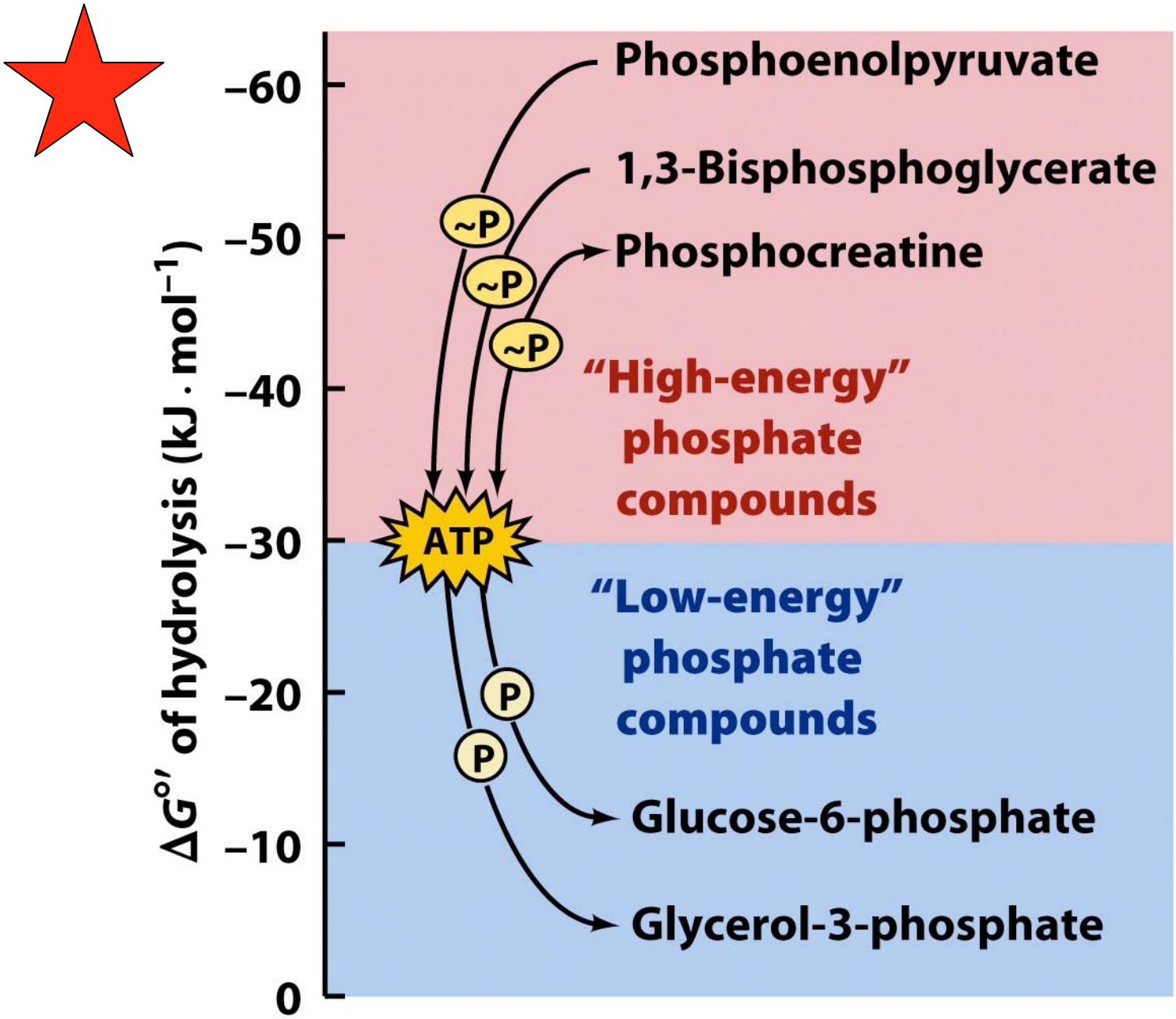


Figure 13-3 Fundamentals of Biochemistry, 2/e

Adenosine diphosphate, one phosphoester bond and one phosphoanhydride bond

Adenosine monophosphate one phosphoester bond.

Which bonds are exergonic?



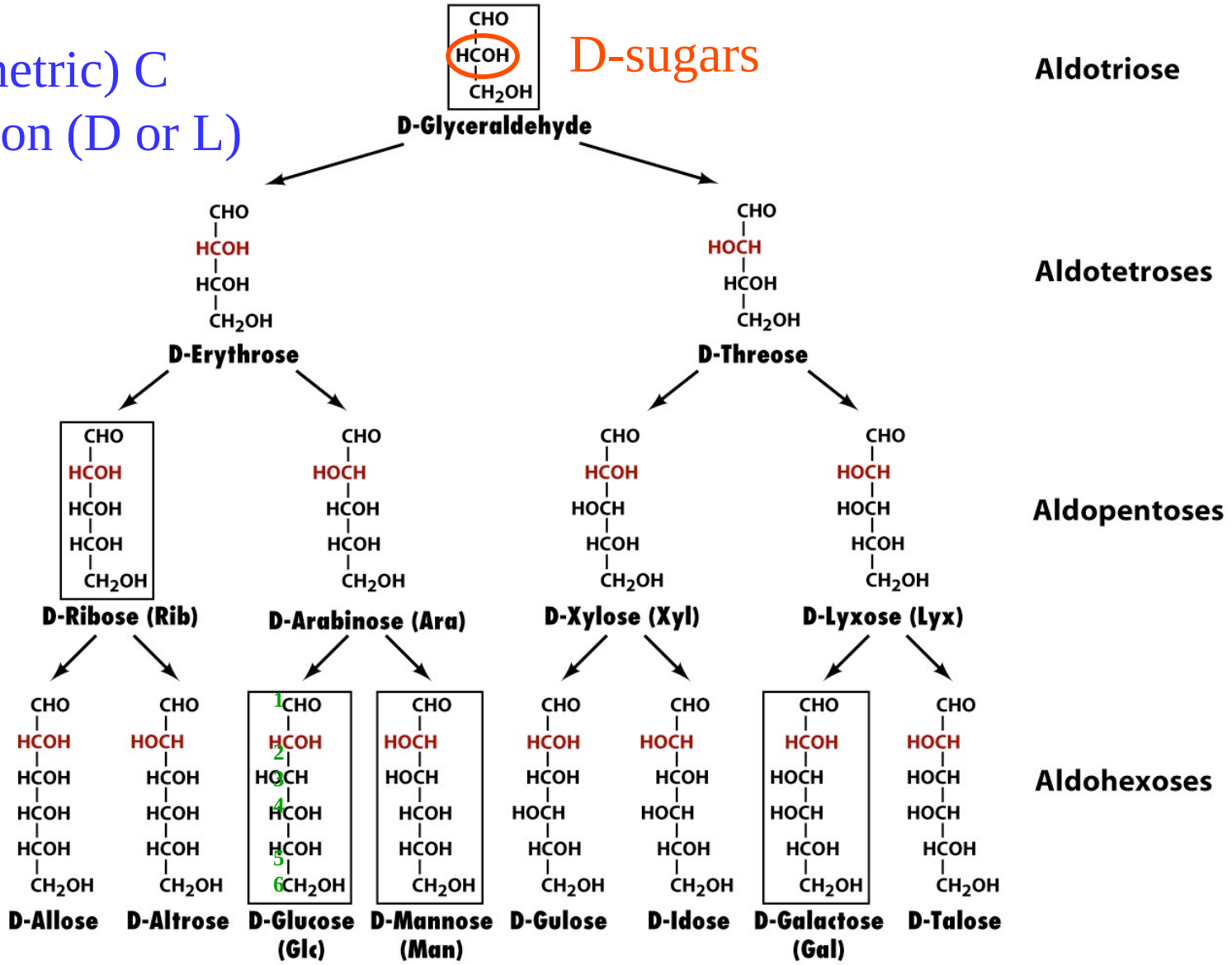
Carbohydrates
(Chapter 8)

Carbohydrates

- Monosaccharides are aldehyde or ketone derivatives of straight-chain polyhydroxyl alcohols continuing at least three carbon atoms
- Aldoses: The carbonyl group is an aldehyde
- Ketoses: The carbonyl group is a ketone
- Trioses: three carbon atoms
- Tetroses: four carbon atoms
- Pentoses: five carbon atoms
- Hexoses: six carbon atoms
- Epimers: sugar molecules differing in stereochemical configuration at one carbon atom
- D-sugars are those that have the same stereochemical configuration at the asymmetric center farthest from their carbonyl group as does D-glyceraldehyde

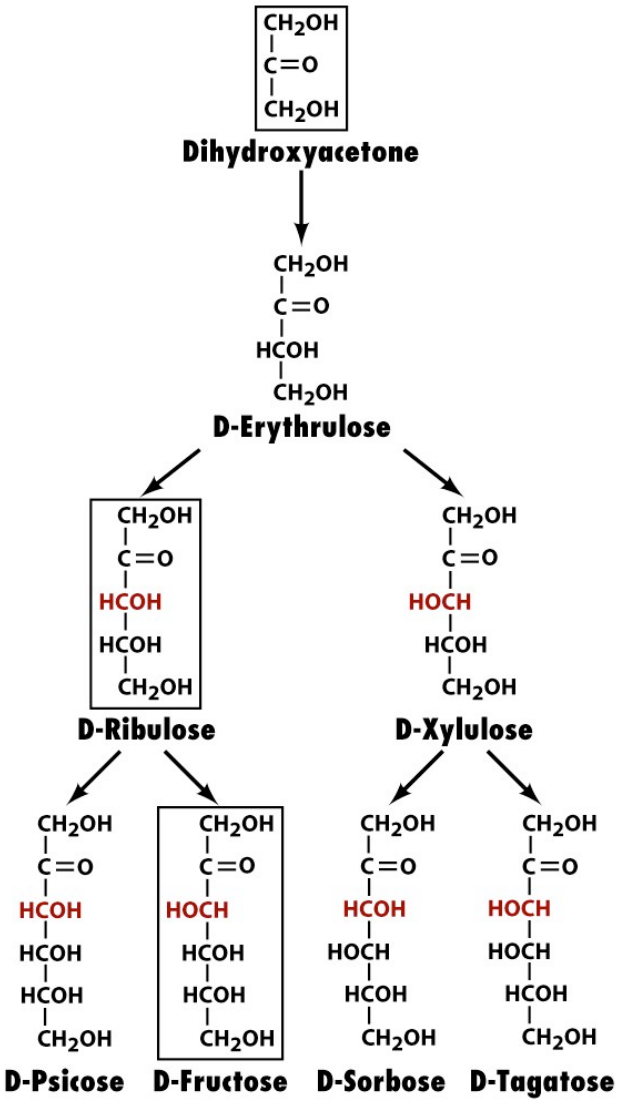
Monosaccharides (D-aldoses)

- Chiral (asymmetric) C
- Fisher projection (D or L)
- Stereoisomers
- Epimer



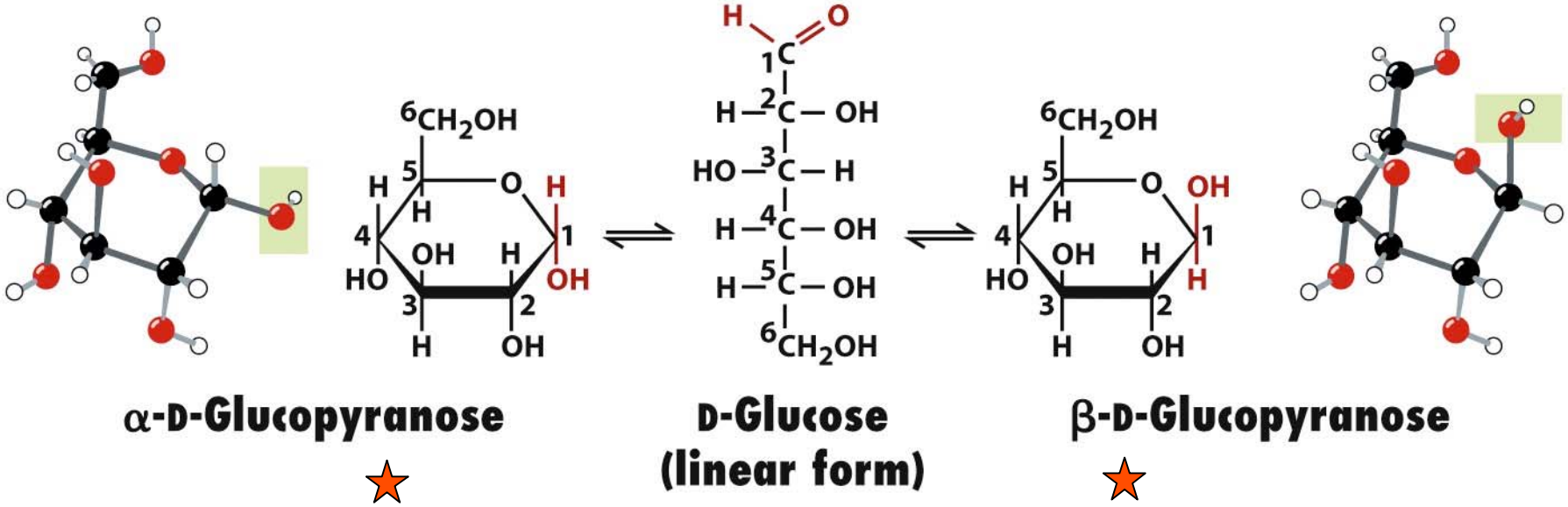
D-ketoses

- Chiral (asymmetric) C
- Fisher projection (D or L)
- Stereoisomers
- Epimer



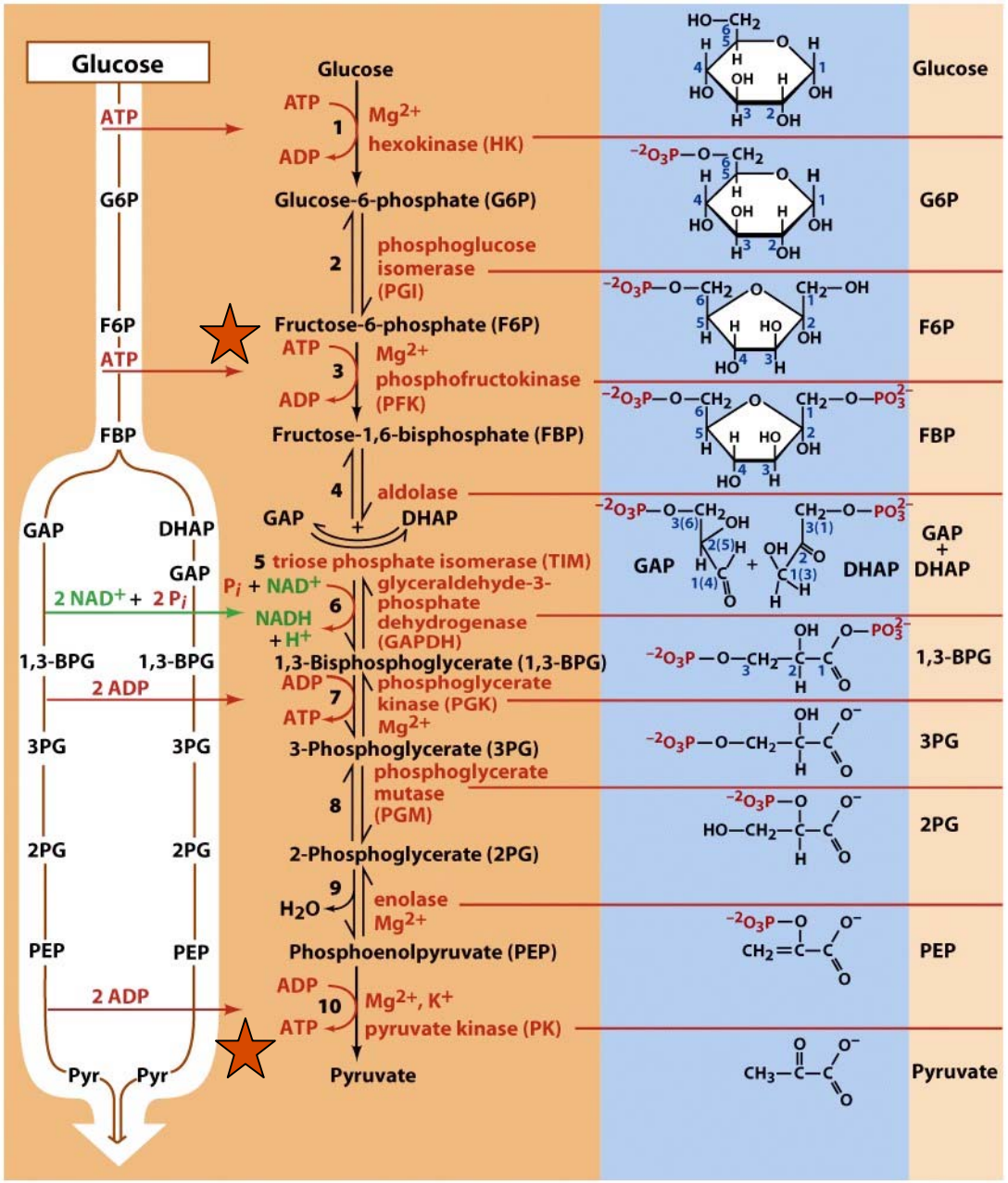
α- and β-anomers

anomeric carbon: carbonyl C



- On going from linear to cyclic, two forms are possible
- anomers: α (down – opposite side of ring from CH_2OH)or β (up – same side of ring from CH_2OH): They differ only by their **configuration** about the anomeric C
- anomers freely interconvert in aqueous solution: at equilibrium, β anomer (63.6%) + α anomer (36.4%)

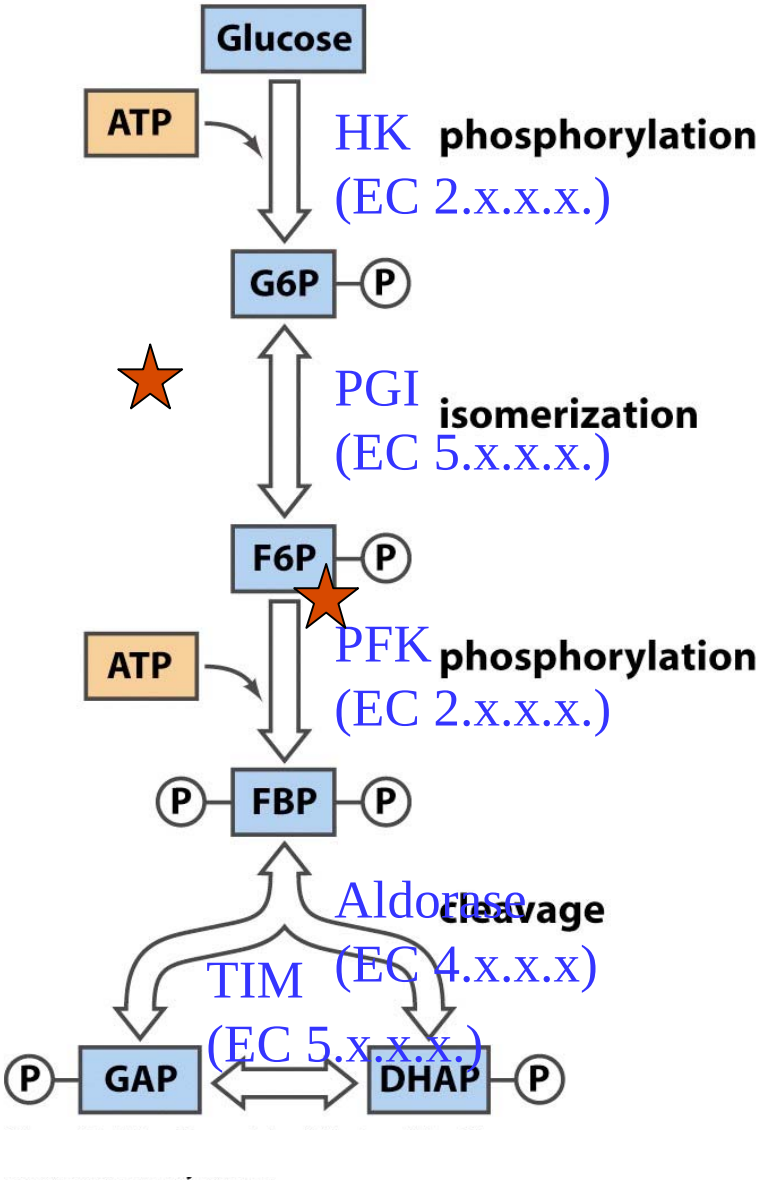
Glucose Catabolism (Chapter 15)

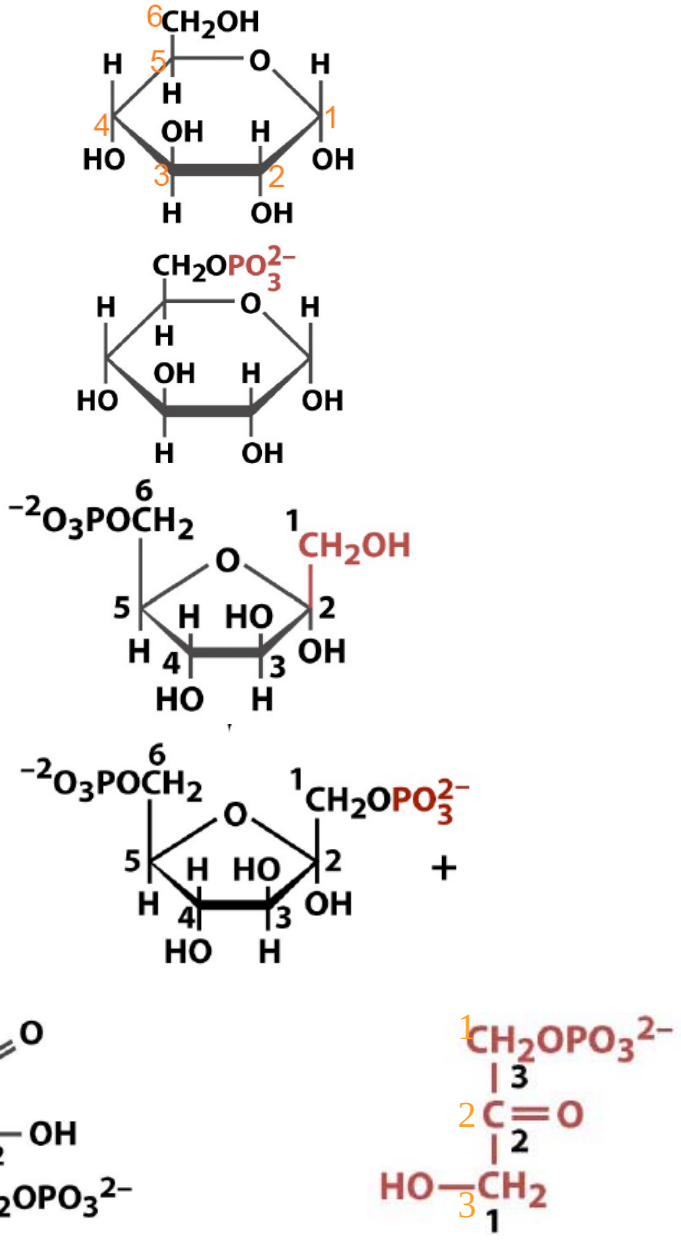


- **Stage I**: Energy investment (rxns. 1-5), glucose phosphorylated and cleaved to yield 2 G3P and consumes 2 ATP
- **State II**: Energy recovery (rxns. 6-10), G3P converted to pyruvate with generation of 4 ATP
- Net profit of 2 ATP per glucose

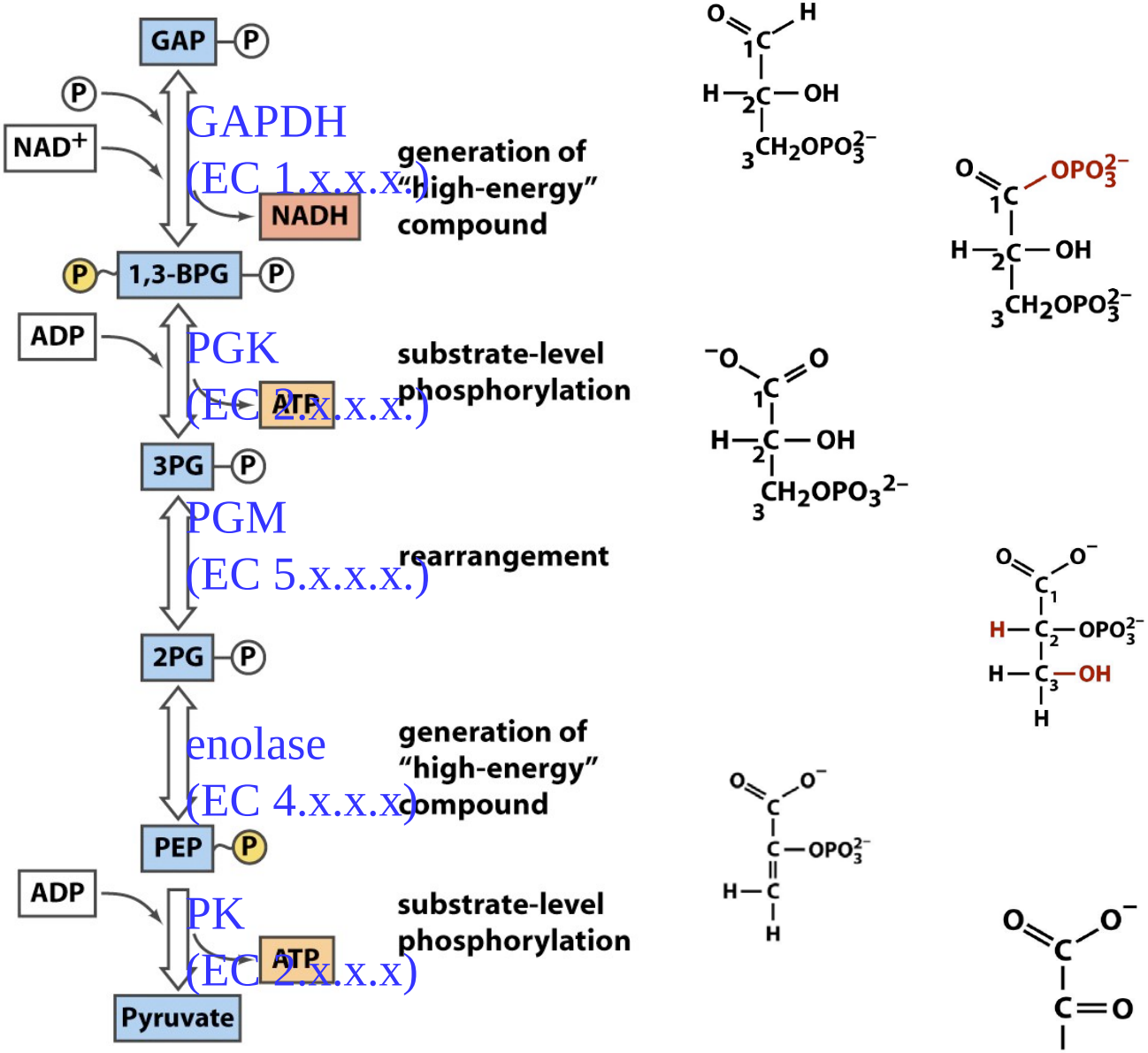
Glucose + $2NAD^+$ + 2ADP +2P*i* → 2NADH + ★ 2pyruvate + 2ATP + $2H_2O$ + $2H^+$

Summary of Stage I of glycolysis pathway





Summary of Stage II of glycolysis pathway

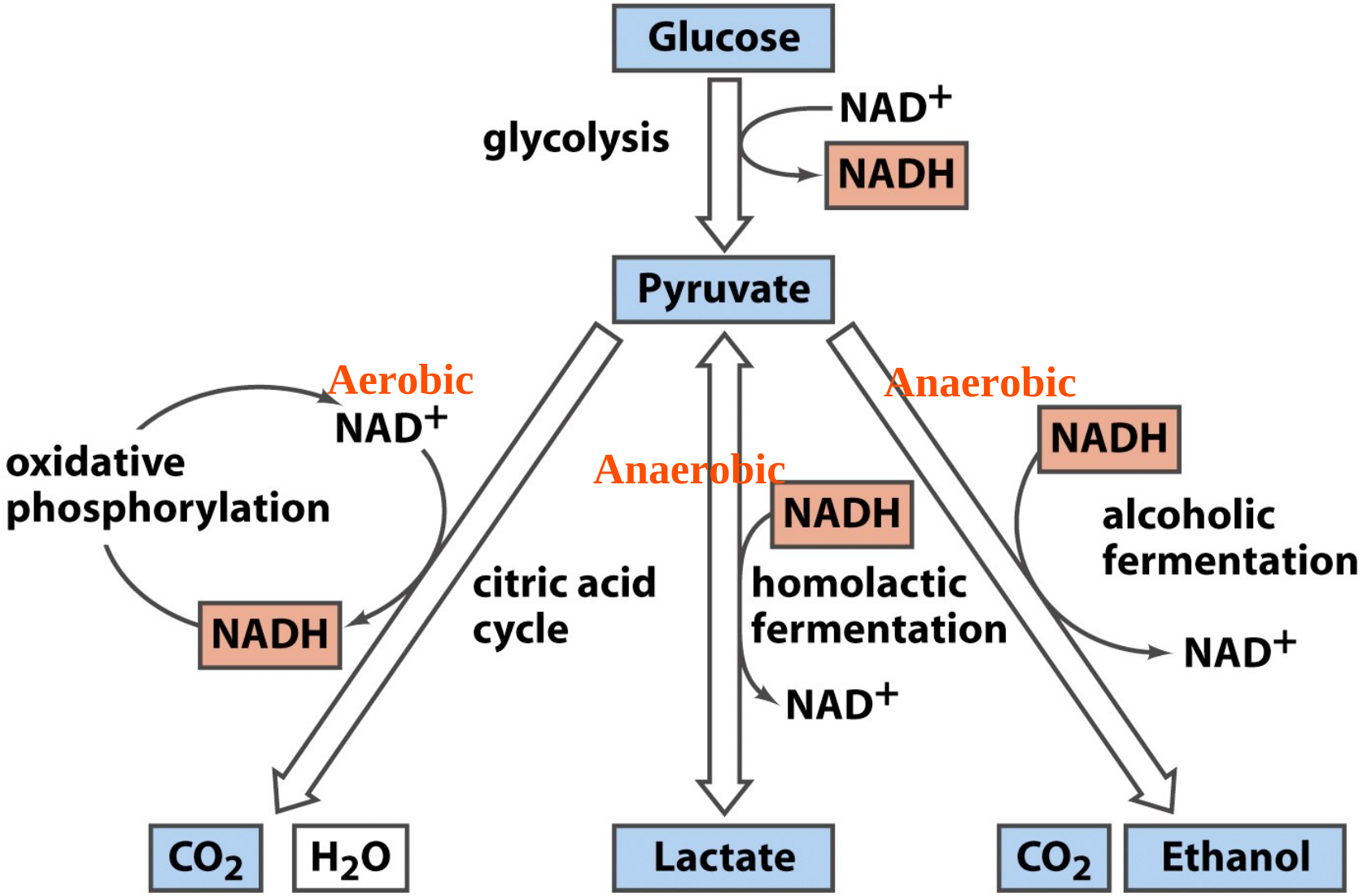


Products of glycolysis

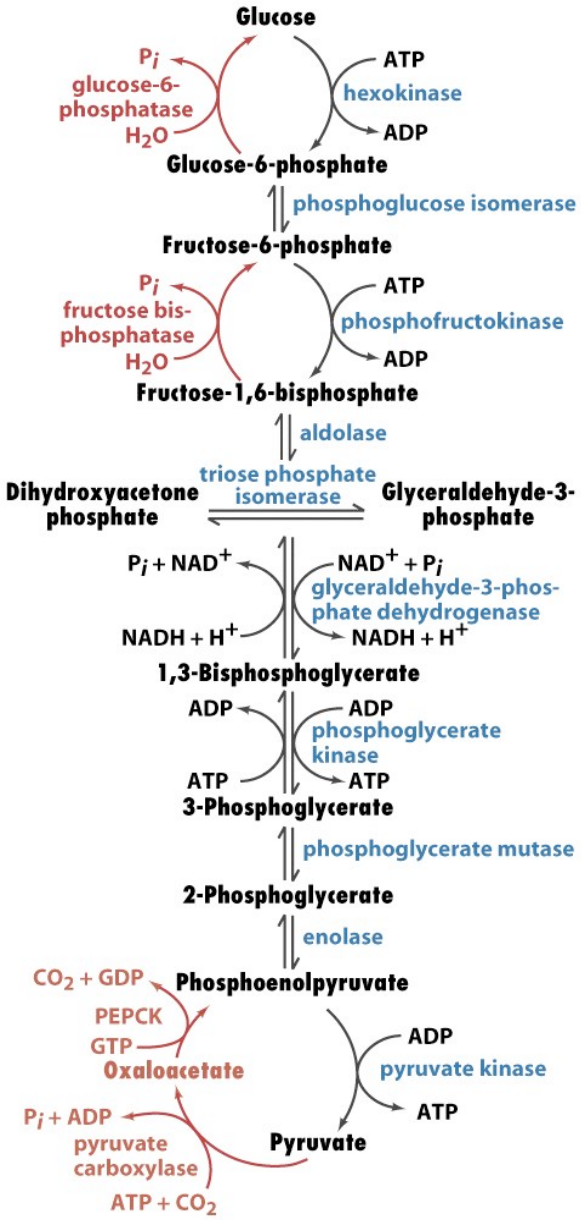
- ATP: The initial investment of 2ATP's per glucose in Stage I of glycolysis is paid back by the generation of 4ATP's in State II of the pathway for a net generation of 2ATP's
- NADH: Two NAD+'s are reduced to 2NADH's. The oxidation of NADH to NAD+ is accomplished via electron transport of other processes resulting in the synthesis of ATP
- Pyruvate: Under aerobic conditions pyruvate is oxidized to CO_2 via the citric acid cycle. In anaerobic metabolism, pyruvate is metabolized to regenerate NAD+.
- Overall reaction of glycolysis

$Glucose + 2NAD^+ + 2ADP + 2P_i \rightarrow 2NADH + 2pyruvate + 2ATP + 2H_2O + 2H^+$

Metabolic fate of pyruvate



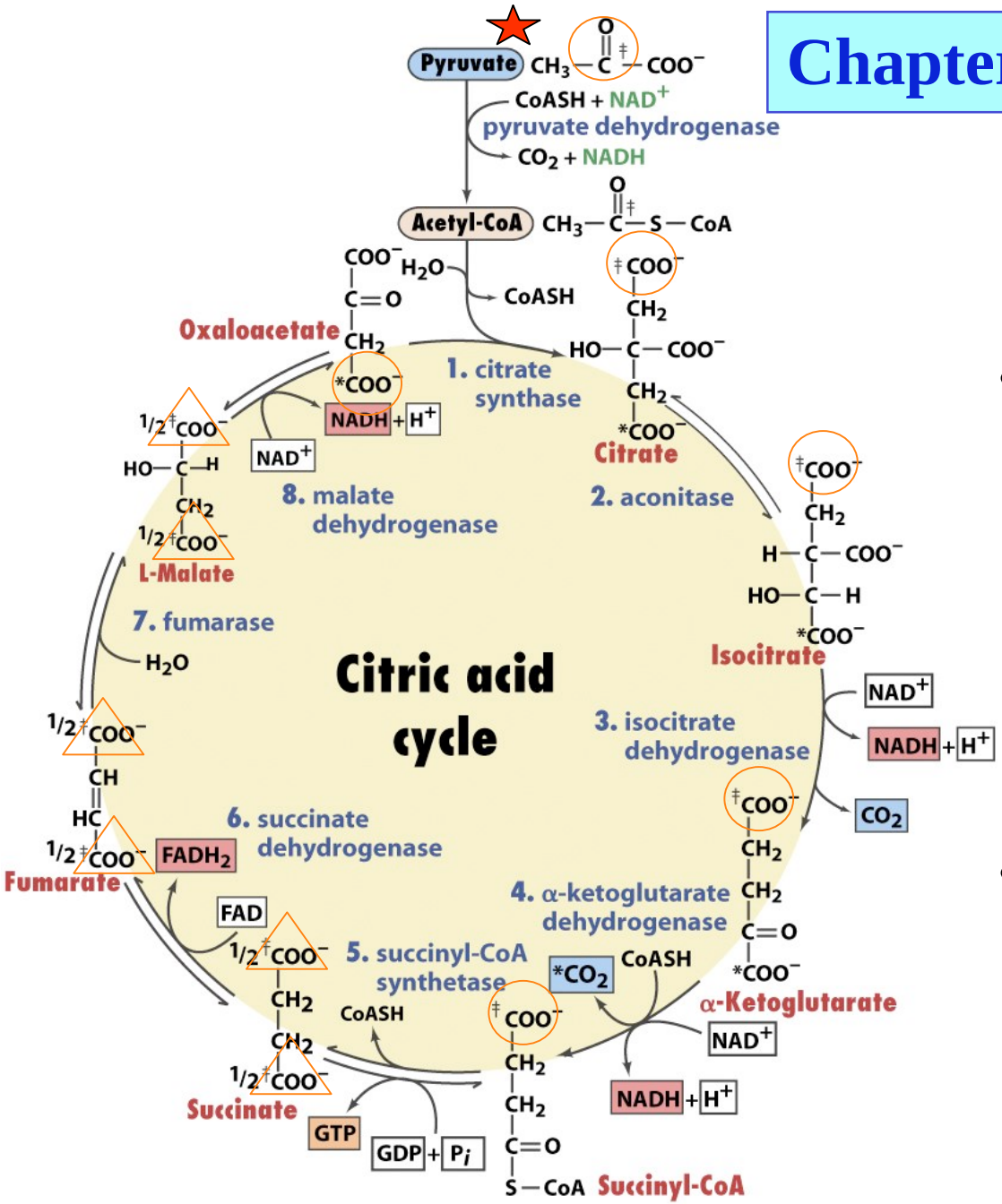
Chapter 16 - Gluconeogenesis



Glycolysis and Gluconeogenesis pathways.

They differ and are regulated in three places (colored in red). Recall that these are the three irreversible steps in glycolysis.

Chapter 17 - Citric Acid Cycle



You MUST know this entire figure, including molecules, enzymes, and cofactors.

- In eukaryotes, all of the enzymes in the TCA are located in the mitochondria, so all substrates including NAD+ and GDP must be generated or transported there
- The carbon atoms of the $2CO_2$ molecules generated in one turn of the cycle do not come from the acetyl group of acetyl-CoA but from oxaloacetate