http://www.ukclimbing.com/news/item.php?id=49981

Physiology

- Define: The study of how living organisms function
- Structure & function are important to understand function
- Why study: Curiosity. Better understand how humans function under normal conditions. Thus, modifications of pathological states back to a ‘normal’ state might be possible.

- Many of the physiological process are described by chemical and physical properties

- It is important to integrate these concepts with biology.

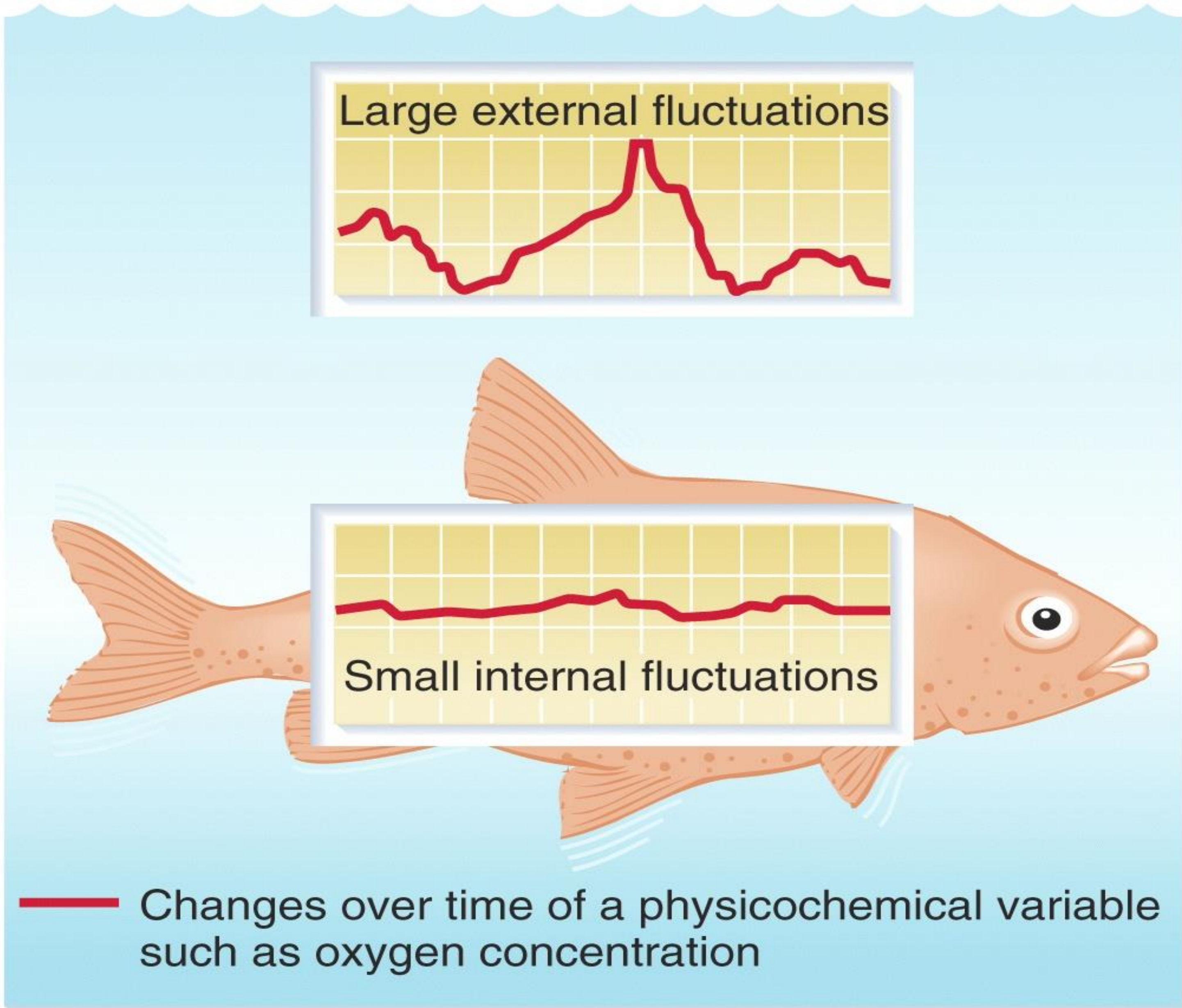
- The physiology of an animal is well suited to the environment in which it has evolved.

This is explained by the process of ADAPTATION- gradual change over many generations.

- Acclimatization is a change of an individual over its lifetime of biochemical or anatomical alterations
- Acclimation is like acclimatization but induced by experimentation.

- Homeostasis- The tendency of an organism to regulate and maintain relative internal stability.

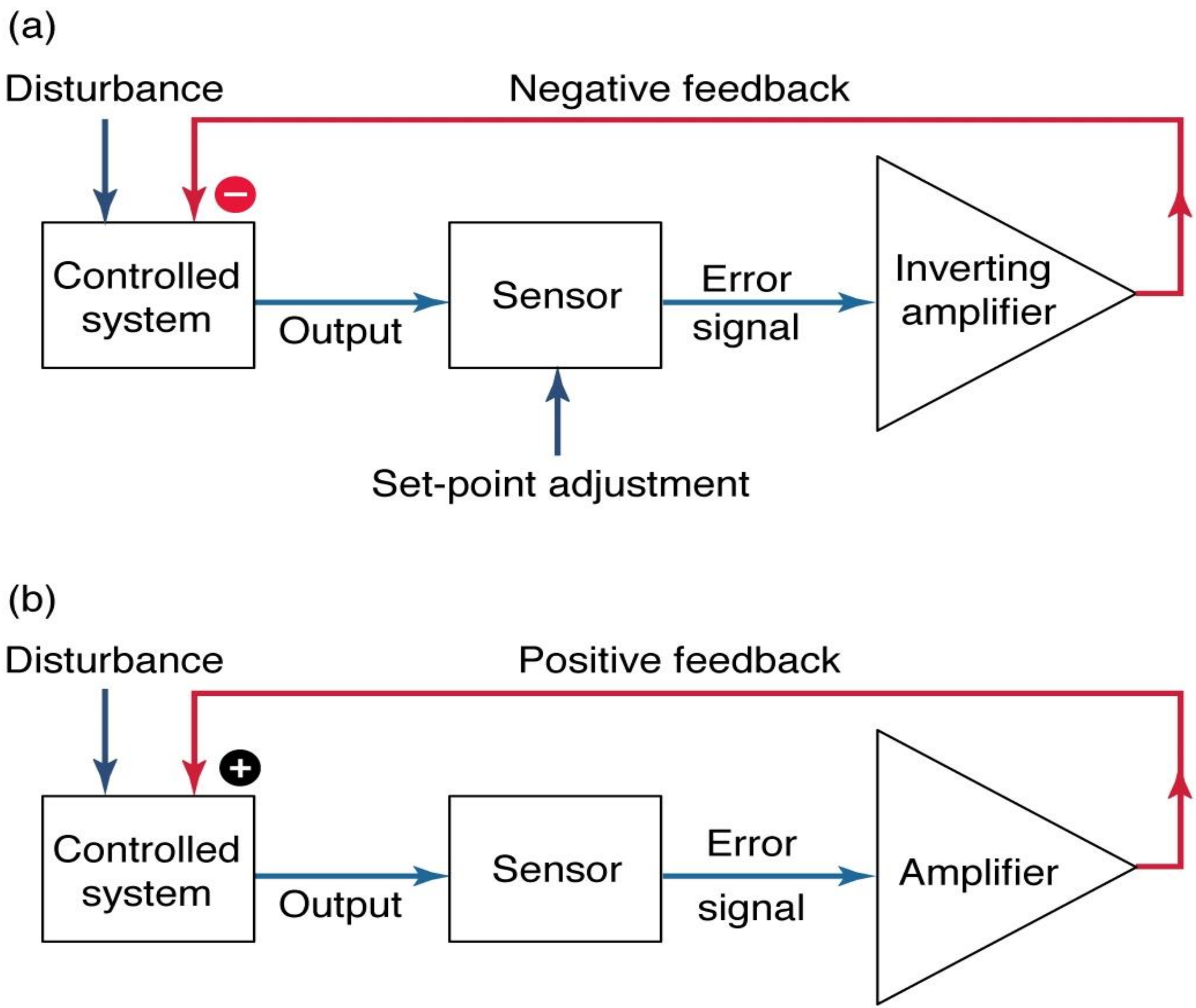
- Cannon coined this term 1929


Large external fluctuations
Small internal fluctuations
Changes over time of a physicochemical variable
such as oxygen concentration

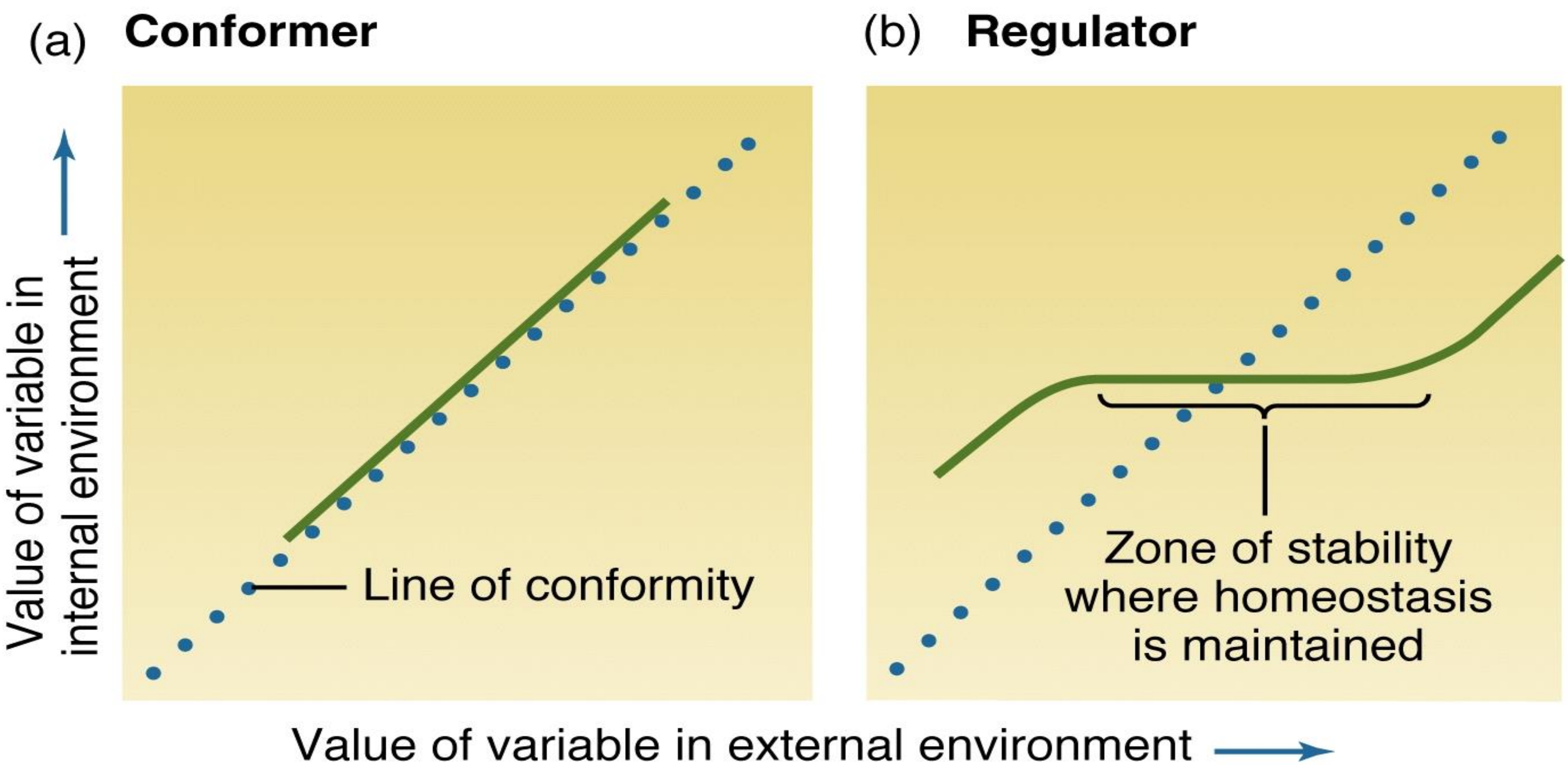
This mostly works by a feed back control.

Such as by a negative feedback.

Examples - Temp, pH, salinity within the body



(a)
Disturbance
Negative feedback
Controlled system
Output
Sensor
Error signal
Inverting amplifier
Set-point adjustment
(b)
Disturbance
Positive feedback
Controlled system
Output
Sensor
Error signal
Amplifier


(a) Conformer
(b) Regulator
Value of variable in internal environment
Line of conformity
Zone of stability where homeostasis is maintained
Value of variable in external environment

Chapter 2

- Read over it for your own benefit
- Know August Krogh principle.

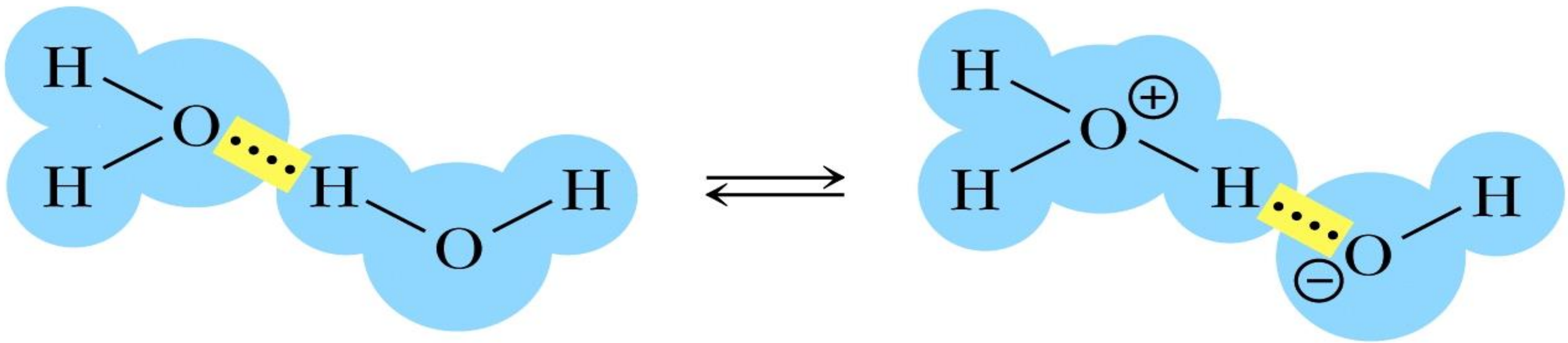
- that there is an animal optimally suited to yield an answer of a physiological problem to be addressed

Chapter 3

- Understanding of molecules and their function for physiological processes.

- Water- it is polar can be used to interact with other ions. It lets Na+Cl- dissolve in body fluids. This is needed for rapid transport of ions.

(a)



- Acid: any substance that can donate a proton.
- Base: any substance that combines with a proton.

(b)

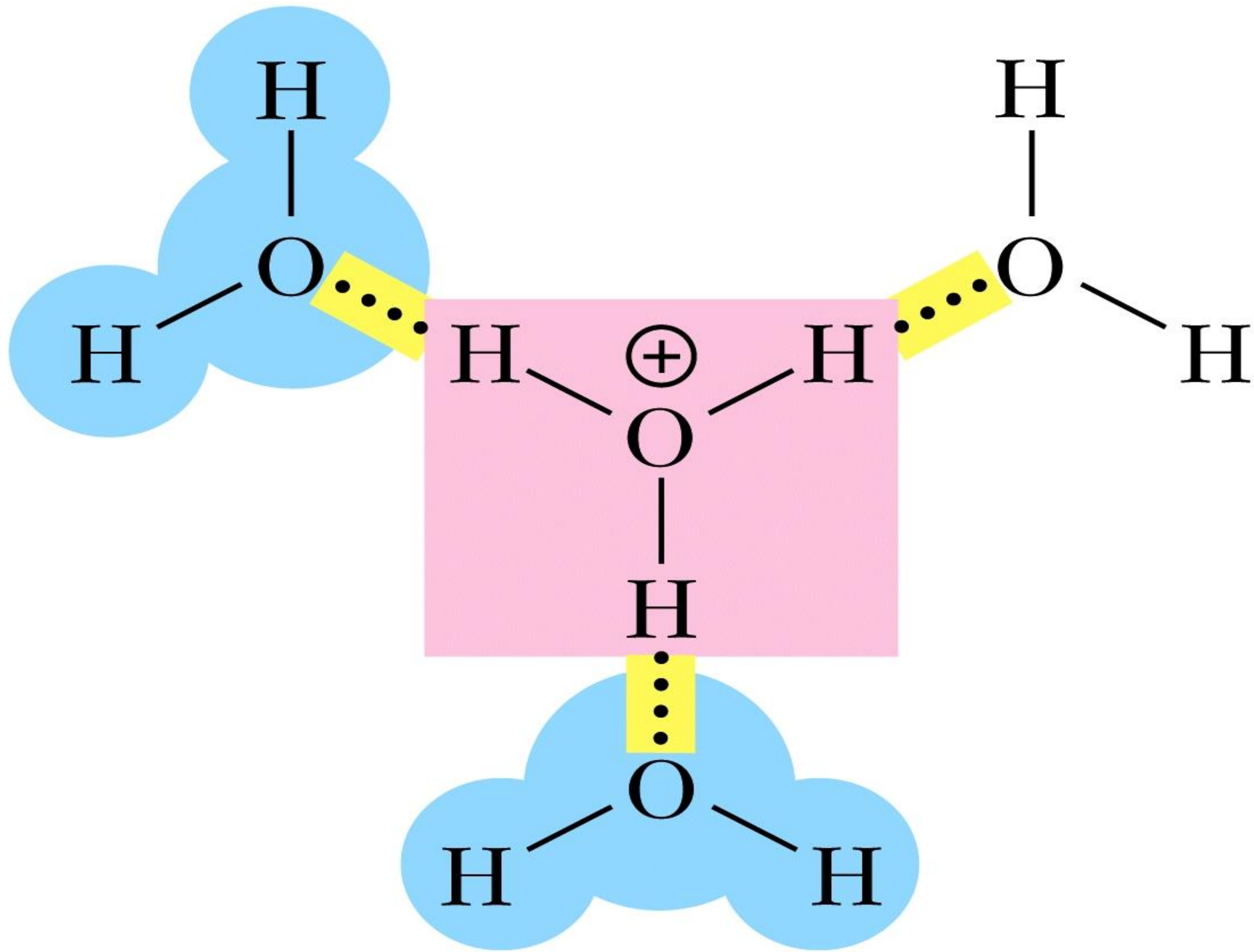
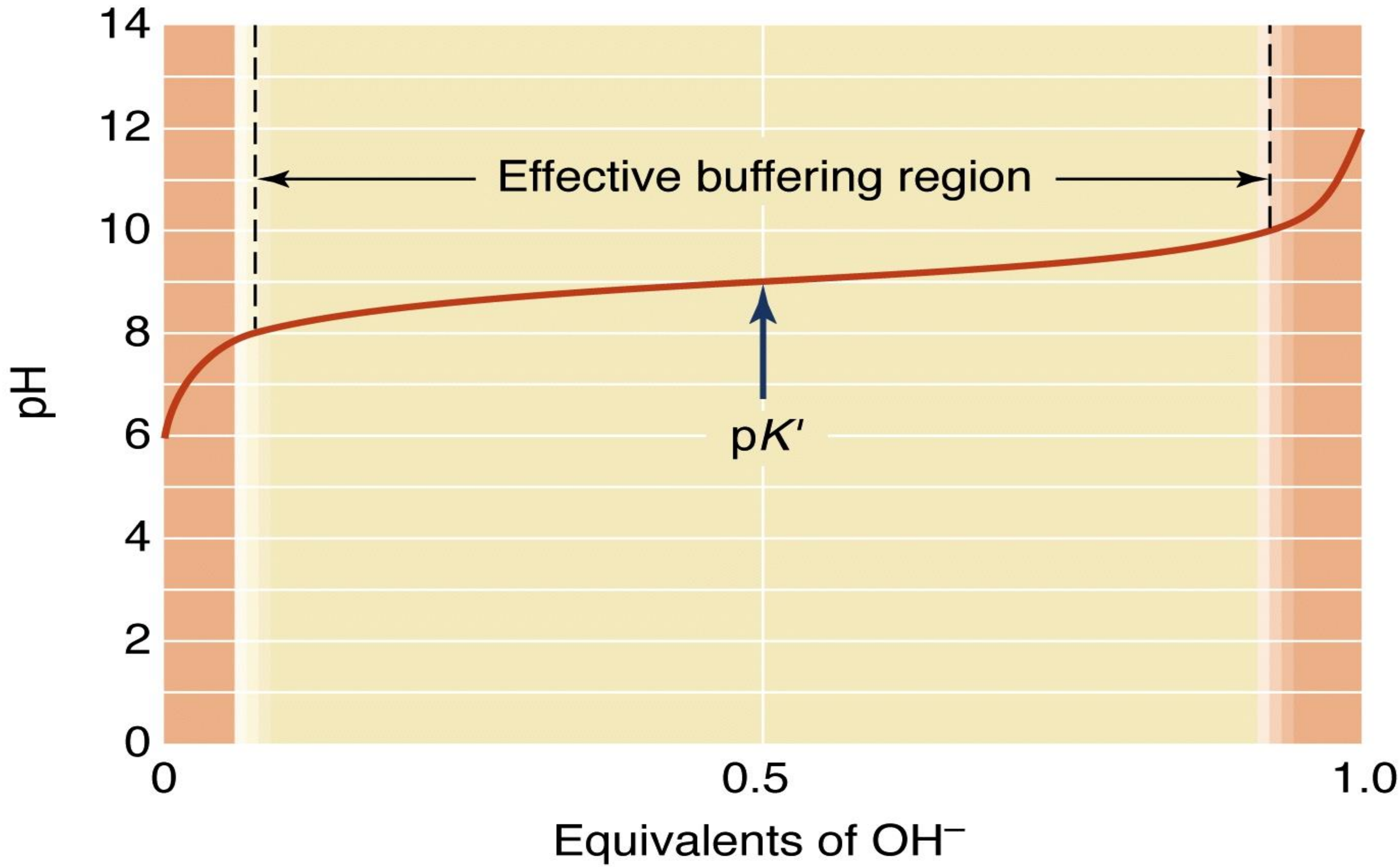


Table 3-2 The pH scale

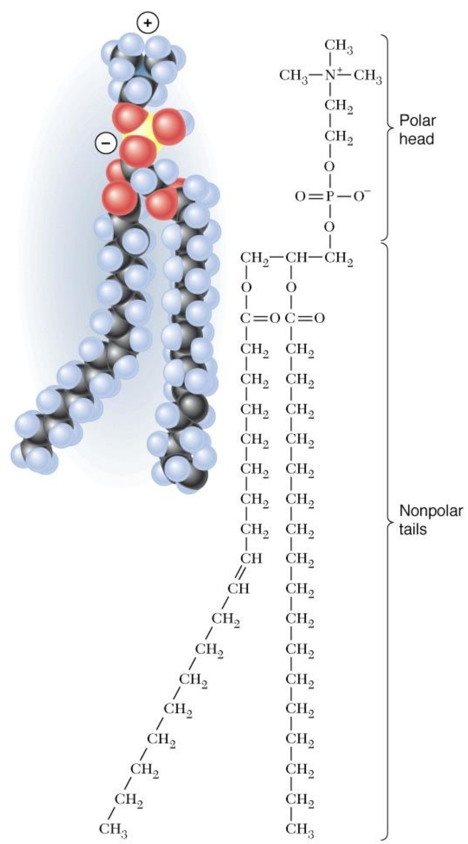
	pH	$[H^+]$ ($mol \cdot L^{-1}$)	$[OH^-]$ ($mol \cdot L^{-1}$)	Examples
	0	10^{0}	10^{-14}	
	1	10^{-1}	10^{-13}	Human gastric fluids
↑ Increasing acidity	2	10^{-2}	10^{-12}	
	3	10^{-3}	10^{-11}	Household vinegar
	4	10^{-4}	10^{-10}	
	5	10^{-5}	10^{-9}	Interior of lysosomes
	6	10^{-6}	10^{-8}	Cytoplasm of muscle
Neutral	**7**	$\mathbf{10^{-7}}$	$\mathbf{10^{-7}}$	**Pure water at 25°C**
	8	10^{-8}	10^{-6}	Seawater
	9	10^{-9}	10^{-5}	
↓ Increasing alkalinity	10	10^{-10}	10^{-4}	Alkaline lakes
	11	10^{-11}	10^{-3}	Household ammonia
	12	10^{-12}	10^{-2}	Saturated lime solution
	13	10^{-13}	10^{-1}	
	14	10^{-14}	10^{0}	



14
12
10
8
6
4
2
0
pH
Effective buffering region
pK′
0
0.5
1.0
Equivalents of OH⁻

FATS:

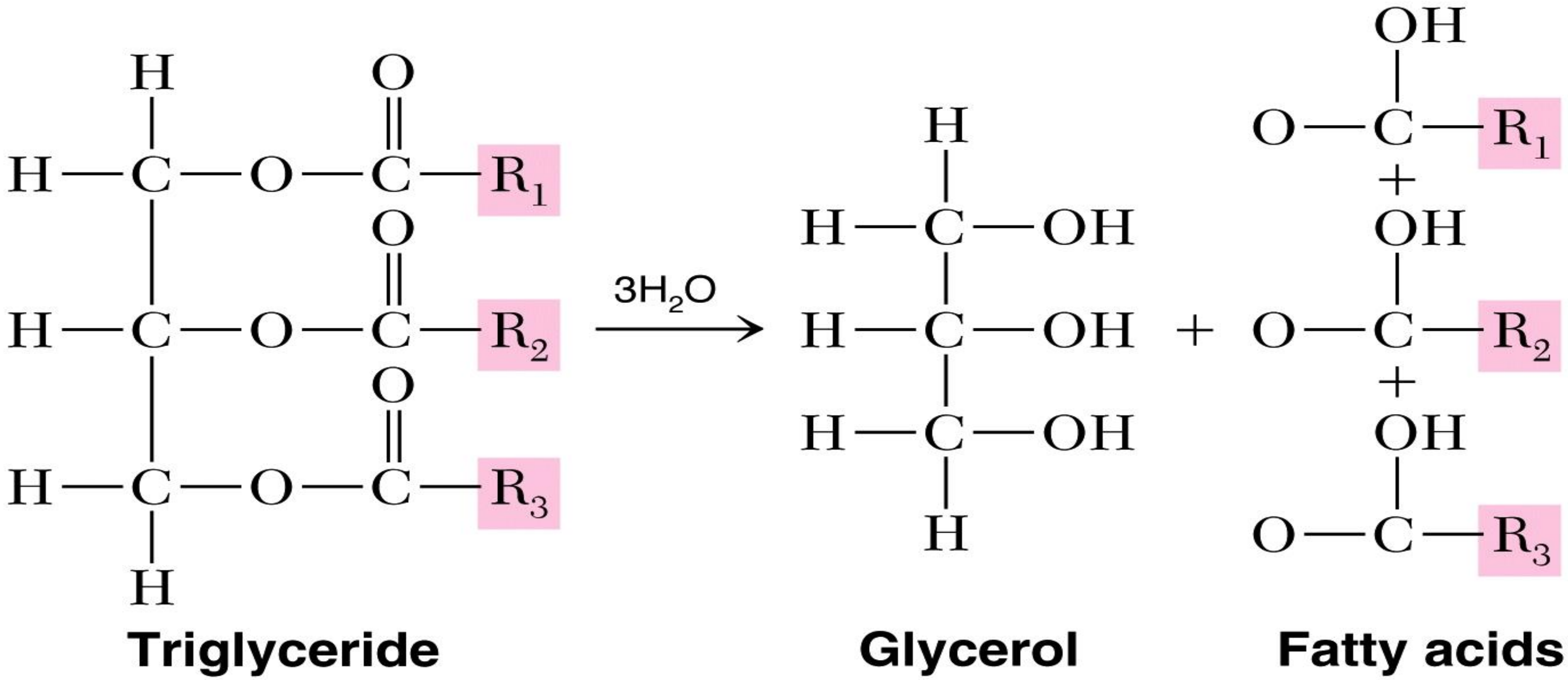
1. Lipids
2. Phospholipids for membranes
3. Waxes- water proof the surface of insects



Biological Molecules

LIPIDS

Fats - triglyceride



2. Phospholipids for membranes

Saturated- each carbon has a single bond and is staurated with ‘H’

Unsaturated- some carbons have a double bond and thus are not saturated with ‘H’.

	Unsat	Sat
1. Melting Pt.:	Decreased	increased
2. Metab:	-	easily converted to sterols (ie, Cholesterol).

Need for cholesterol for steroid based hormone production.

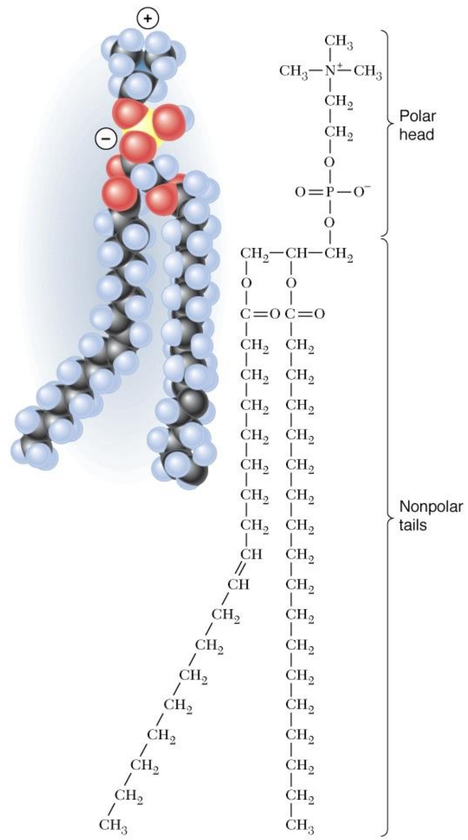
Fats are good as a energy store. 1. Little water needed. 2. Stored in adipose tissue. 3. High "H & C" with little "O" so one gets a good energy yield. (1 gram of fat=2 grams of carbohydrates)

Table 3-3 **The energy content of the three major categories of foodstuffs**

Substrate	Energy content ($kcal \cdot g^{-1}$)
Carbohydrates	4.0
Proteins	4.5
Fats	9.5

FATS:

1. Lipids
2. Phospholipids for membranes
3. Waxes- water proof the surface of insects



Carbohydrates

I. Monosaccharides

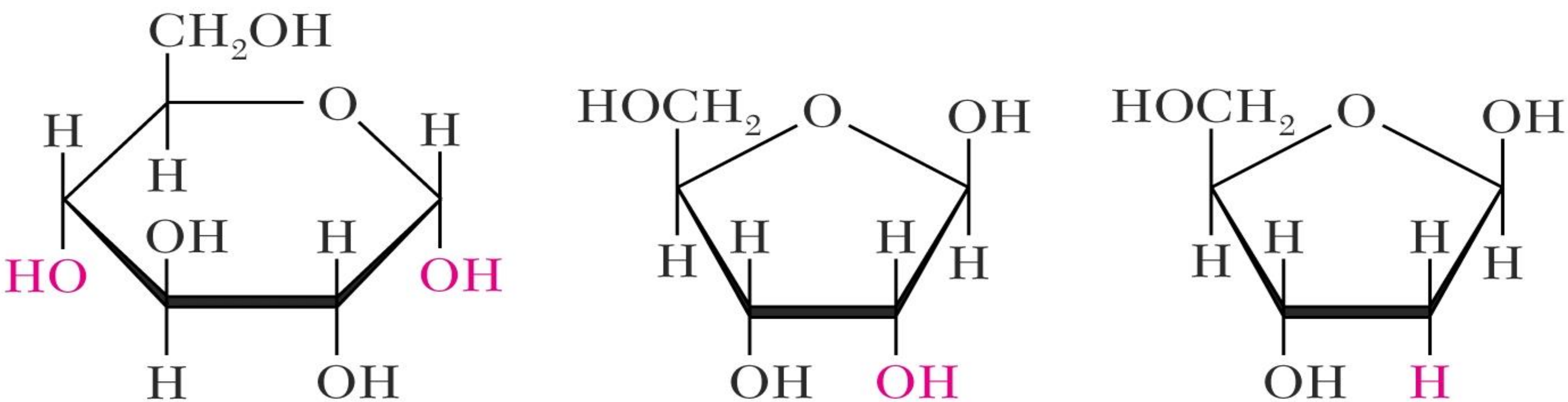
II. Disaccharides

I. Monosaccharides

-Six carbon-- hexoses

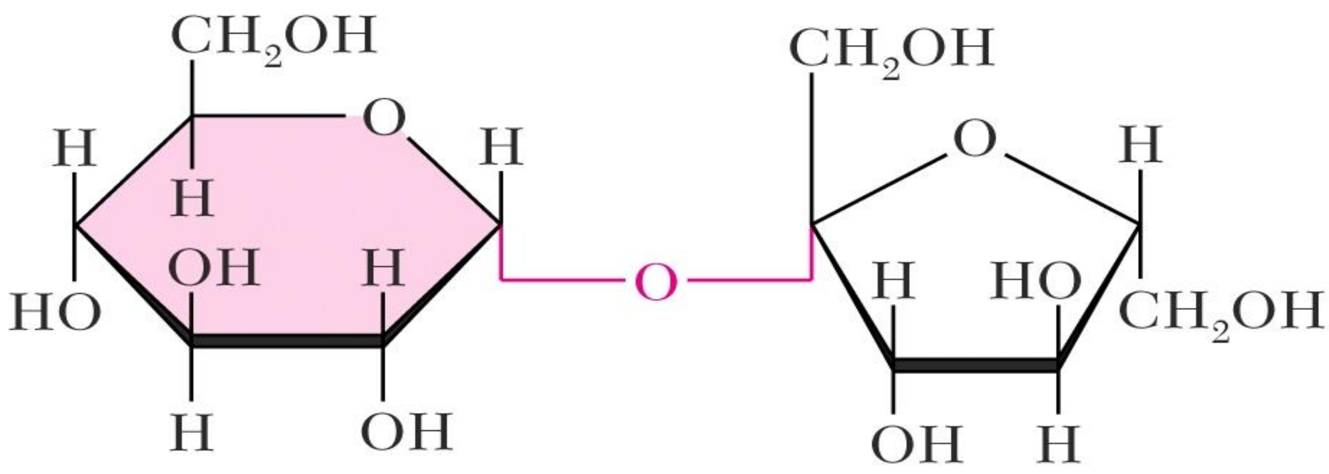
-five carbon-- pentoses

(a) Monosaccharide sugars

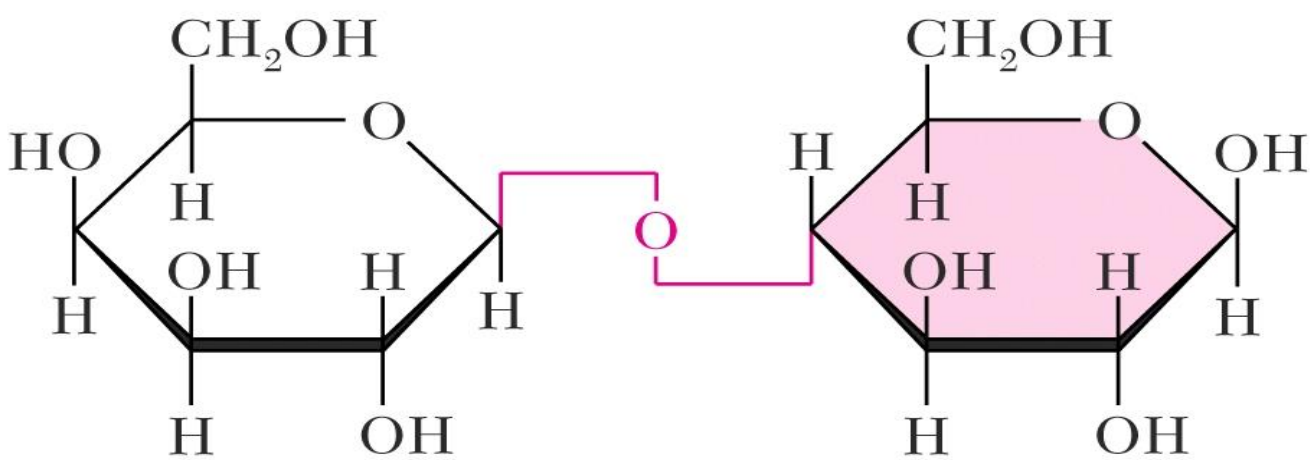


Glucose Ribose 2-Deoxyribose

(b) Disaccharide sugars



Sucrose (α form)



Lactose (β form)

The disaccharides are units of monosaccharides

A. Polymers – Plants—starch

-- Animals– glycogen

Little water needed for storage. So good energy for plants and animals.

B. Cellulose

C. Chitin (exoskeleton in insects/crustaceans)

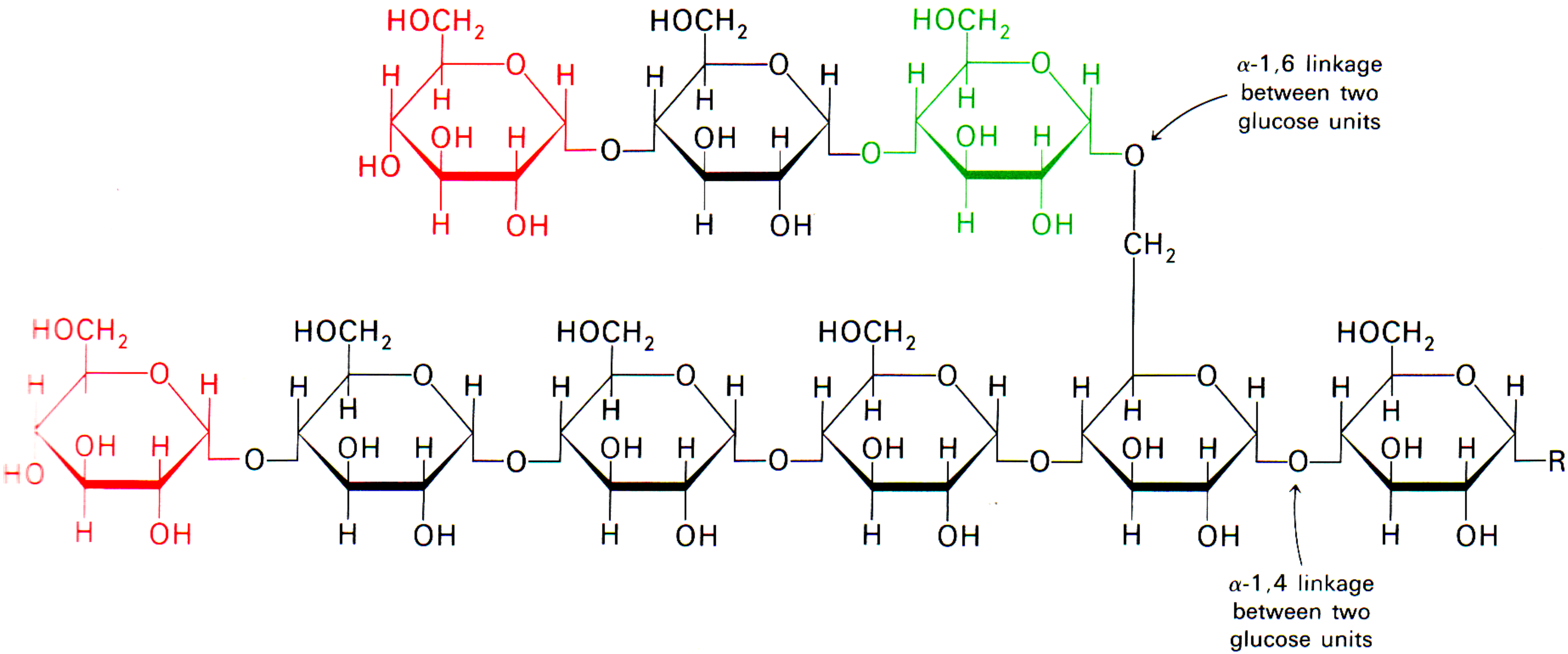
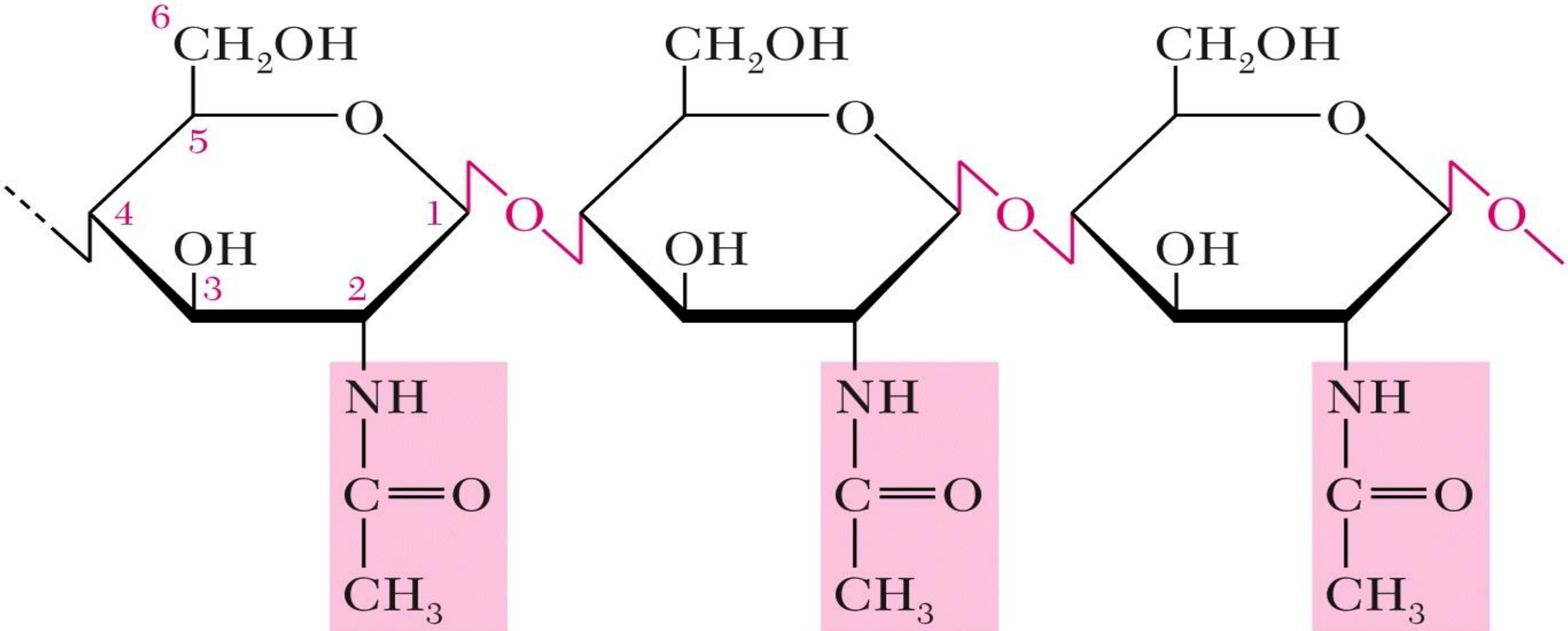

α-1,6 linkage between two glucose units
α-1,4 linkage between two glucose units

Table 16-1
Glycogen storage diseases

Type	*Defective enzyme*	*Organ affected*	*Glycogen in the affected organ*	*Clinical features*
I VON GIERKE'S DISEASE	Glucose 6-phosphatase	Liver and kidney	Increased amount; normal structure.	Massive enlargement of the liver. Failure to thrive. Severe hypoglycemia, ketosis, hyperuricemia, hyperlipemia.
II POMPE'S DISEASE	α-1,4-Glucosidase (lysosomal)	All organs	Massive increase in amount; normal structure.	Cardiorespiratory failure causes death, usually before age 2.
III CORI'S DISEASE	Amylo-1,6-glucosidase (debranching enzyme)	Muscle and liver	Increased amount; short outer branches.	Like Type I, but milder course.
IV ANDERSEN'S DISEASE	Branching enzyme (α-1,4 $\longrightarrow$ α-1,6)	Liver and spleen	Normal amount; very long outer branches.	Progressive cirrhosis of the liver. Liver failure causes death usually before age 2.
V McARDLE'S DISEASE	Phosphorylase	Muscle	Moderately increased amount; normal structure.	Limited ability to perform strenuous exercise because of painful muscle cramps. Otherwise patient is normal and well developed.
VI HERS' DISEASE	Phosphorylase	Liver	Increased amount.	Like Type I, but milder course.
VII	Phosphofructokinase	Muscle	Increased amount; normal structure.	Like Type V.
VIII	Phosphorylase kinase	Liver	Increased amount; normal structure.	Mild liver enlargement. Mild hypoglycemia.

Note: Types I through VII are inherited as autosomal recessives. Type VIII is sex-linked.


6
CH2OH
O
5
4
1
OH
3
2
O
NH
C=O
CH3
CH2OH
O
OH
O
NH
C=O
CH3
CH2OH
O
OH
O
NH
C=O
CH3

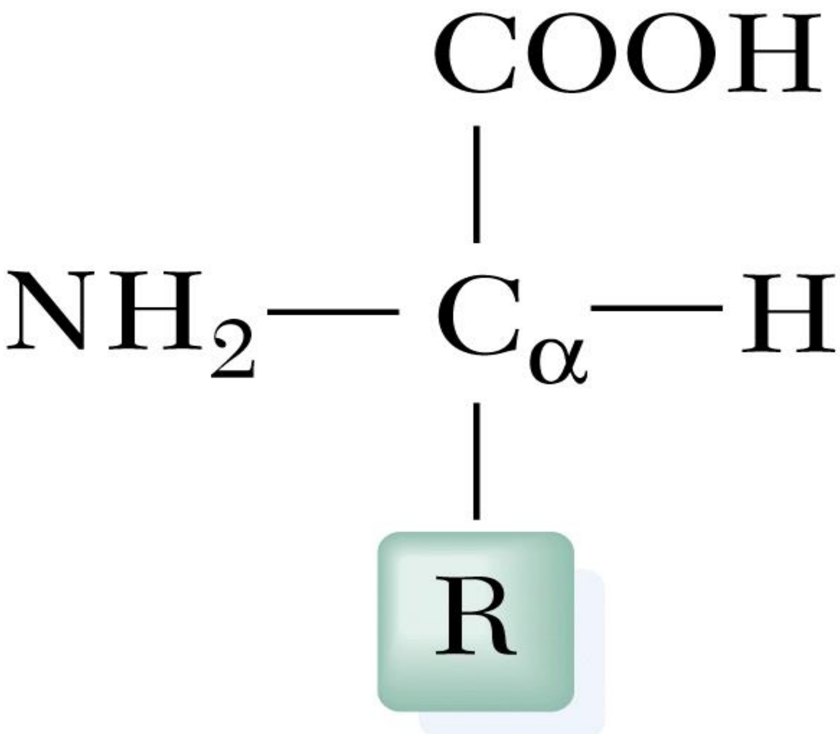
Chitin

Proteins

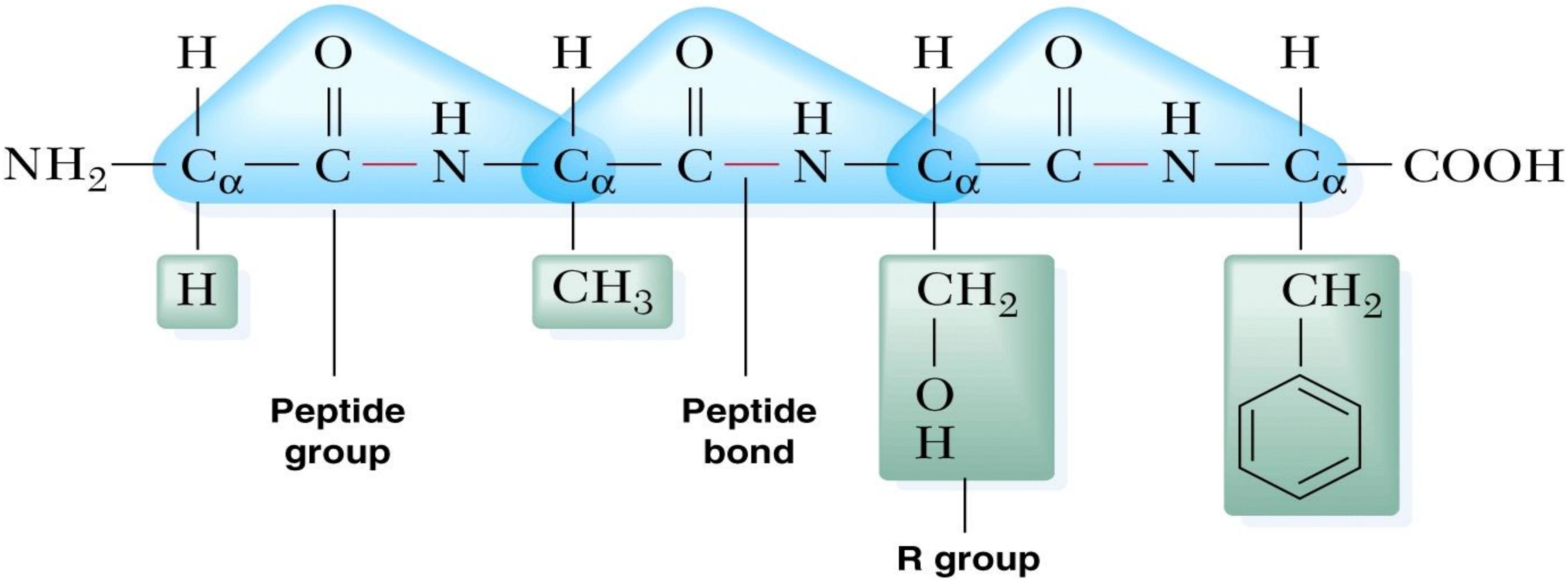
- A lot in cells. ½ of the dry mass.
- Various structures.

-Primary, secondary, tertiary, and quaternary

(a) General structure of alpha-amino acids

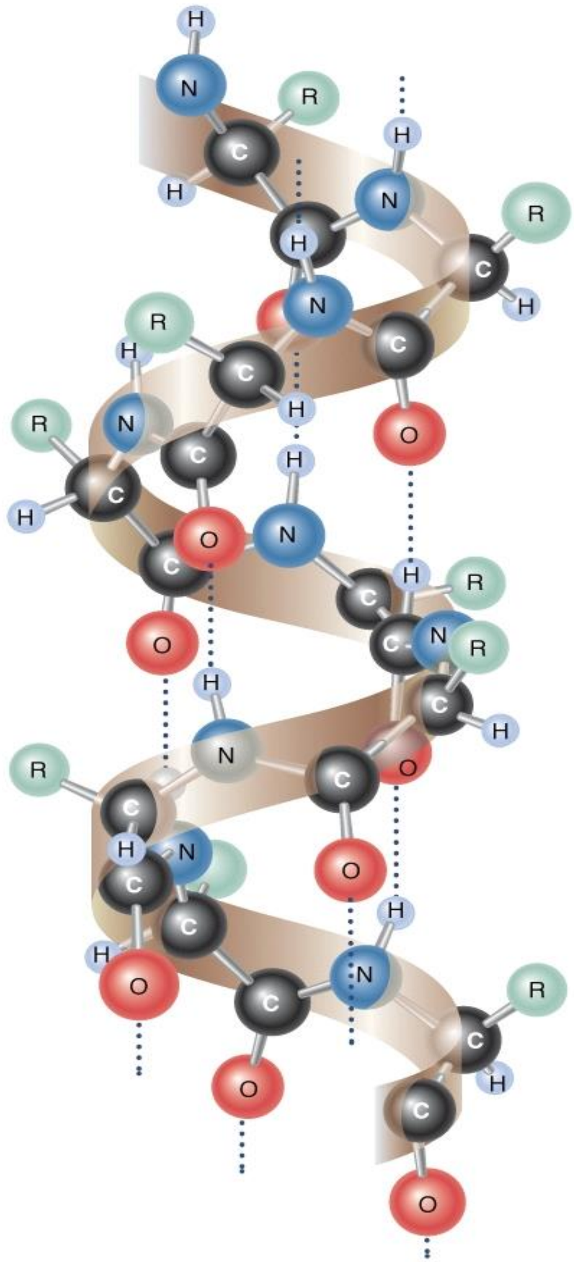


(b) Structure of a tetrapeptide



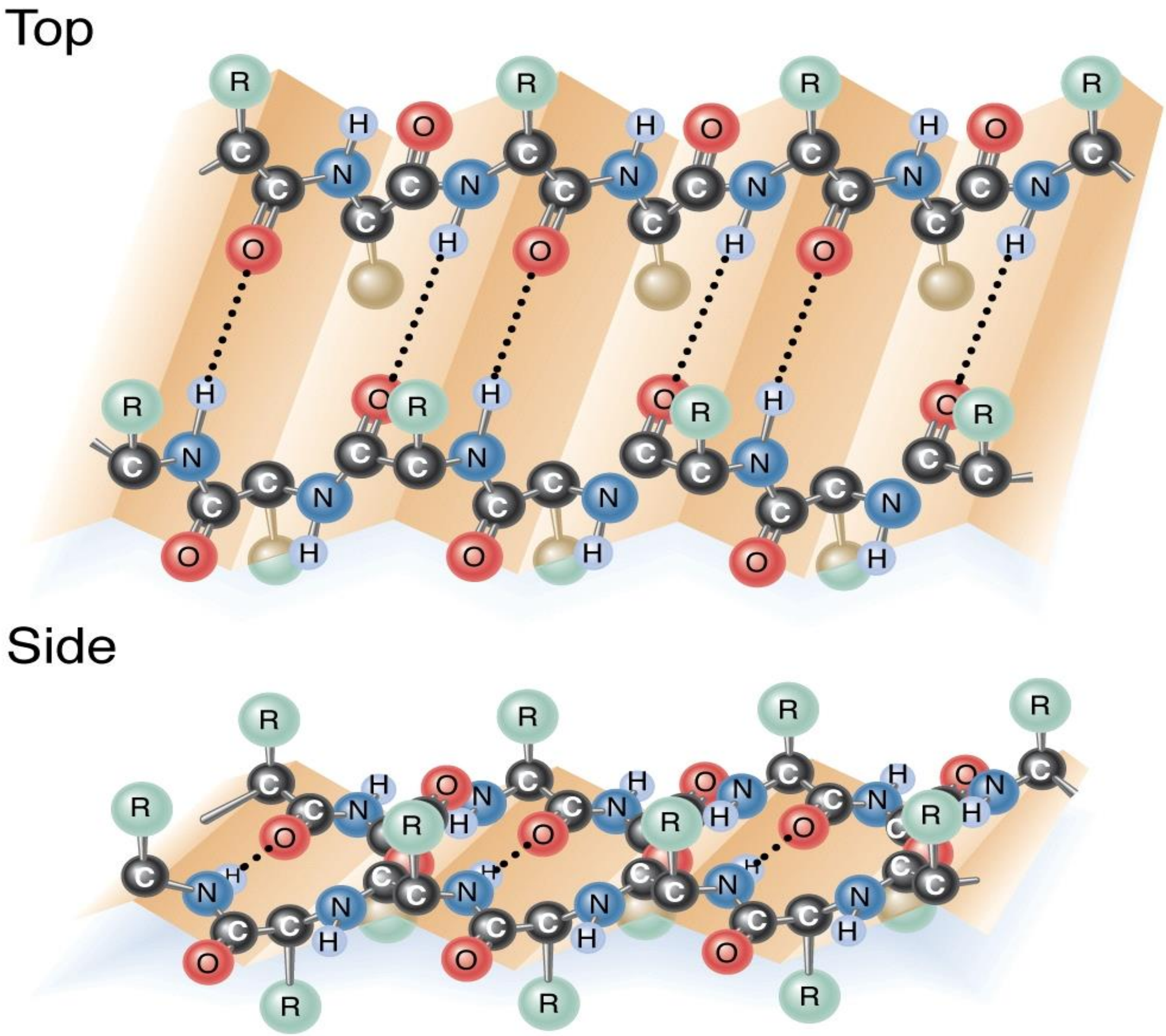
Secondary

Alpha helix



Secondary

Beta- sheet

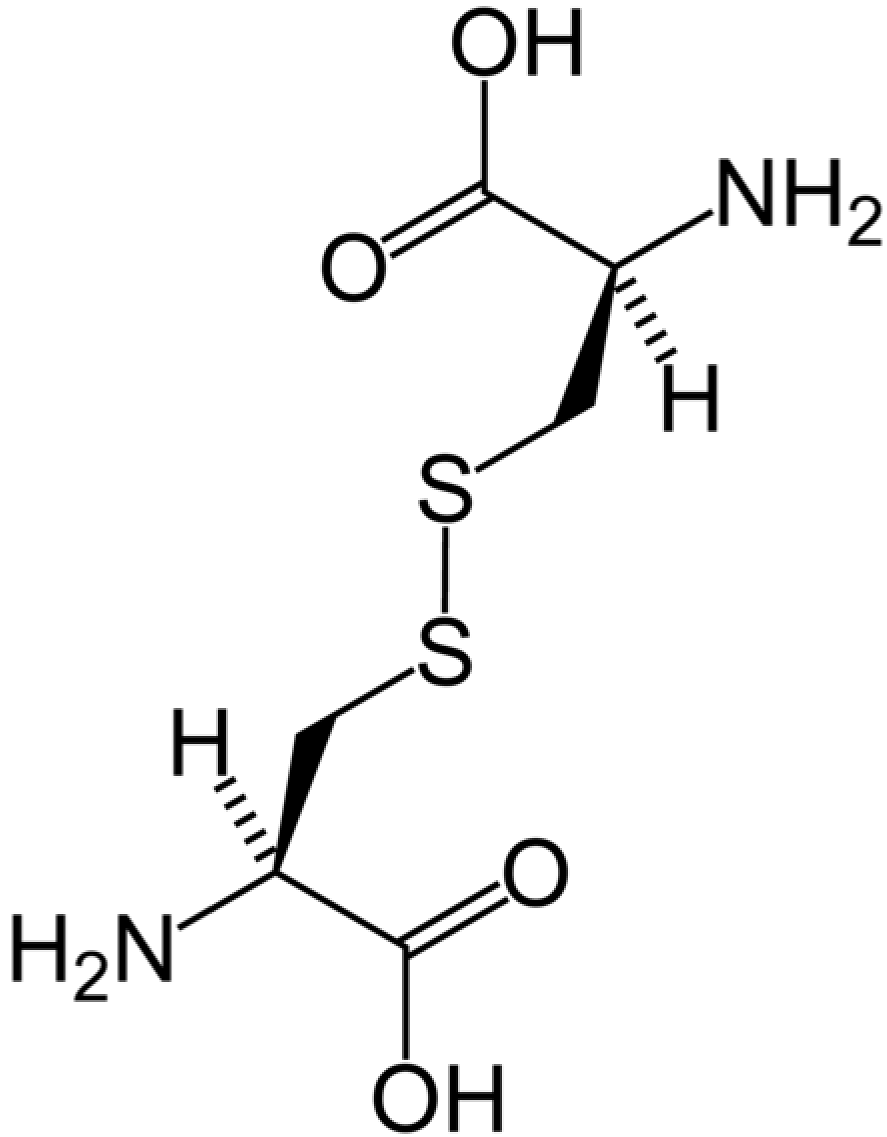


Secondary types

- alpha helix: alpha-Keratins for hair and wool

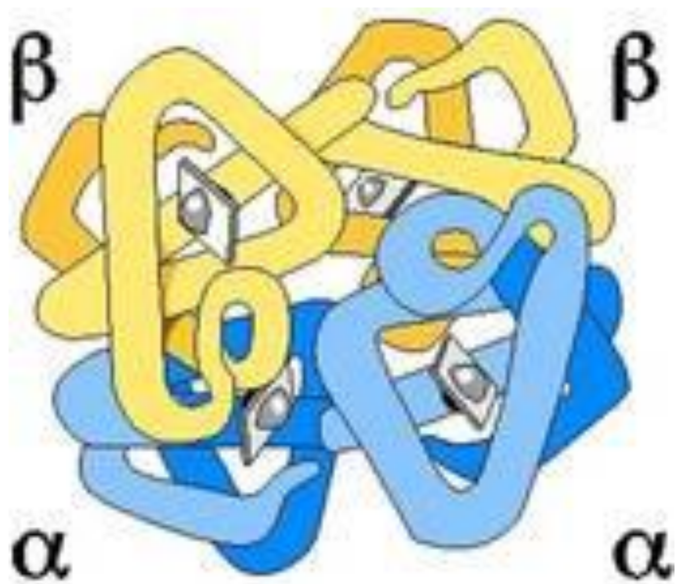
- Beta sheets: (Harder) beta- Keratins for reptile scales and turtle shells

Tertiary



Quaternary- a couple of subunits coming together like Heme units.

ie., Hemoglobin



Molecular chaperones

- Fold other proteins. Maintain their structure.
- To protect proteins from degradation and preserve the overall integrity of intracellular protein pool.
- Example HSP or stress proteins.

DNA & RNA

- DNA isolated in 1869 by Friedrich Miescher. White blood cells and fish sperm.
- DNA- genes
- RNA translating the coded DNA message.

- DNA with mRNA--- Transcription
- mRNA to protein --- Translation

A-T and C-G in DNA

But A-U in RNA

Energy in Living cells

- Chemical Rxs taking place (types of tissues)
- Where within the cells? (organelles)

Animals are like chemical machines.

Different forms of Energy- ie., thermal and mechanical.

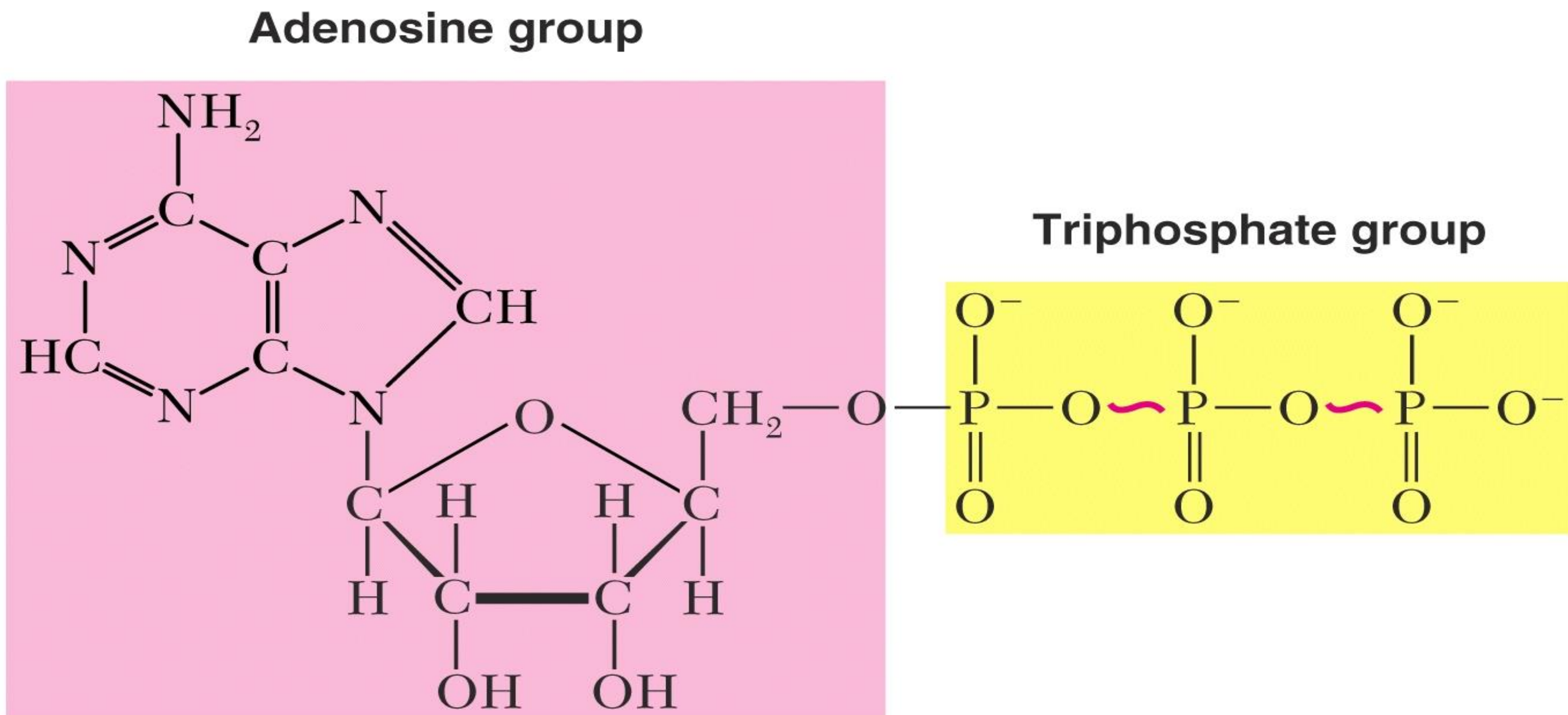
- A measure of a systems energy that it can provide.

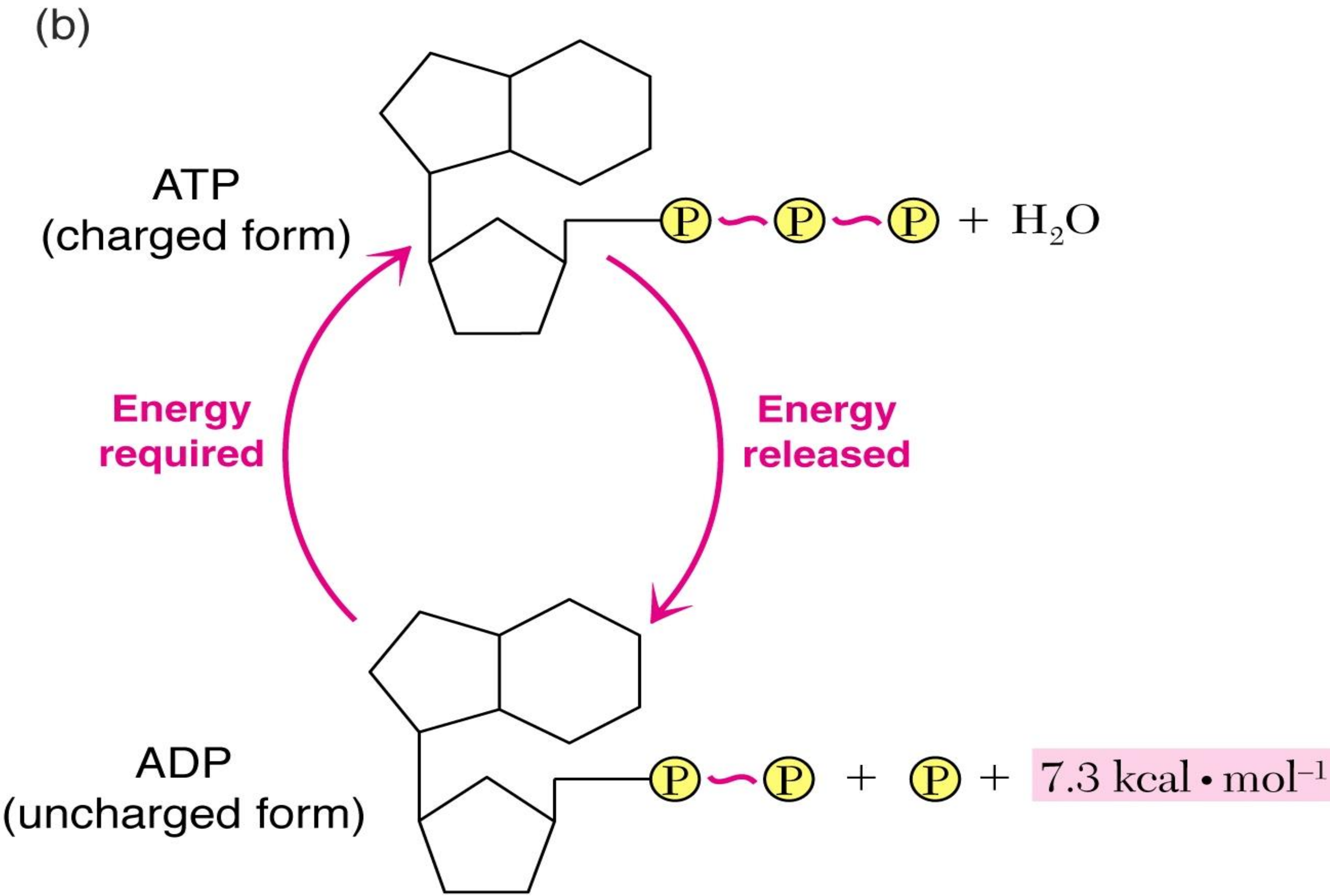
$\Delta G = \Delta H - T\Delta S$ Is Gibbs free Energy

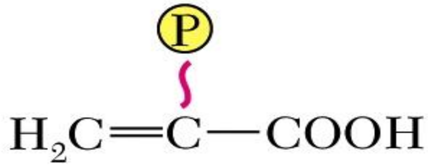
ΔH is heat; ΔS is Entropy

If ΔG is neg then the Rx is spontaneous. Also hold for biochemical Rxs.

(a)

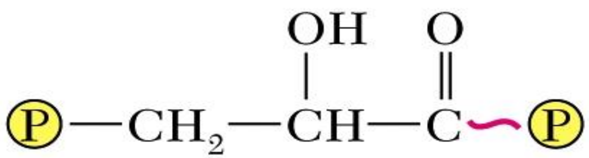



(b)
ATP
(charged form)
P ~ P ~ P + H_2O
Energy
required
Energy
released
ADP
(uncharged form)
P ~ P + P + 7.3 kcal • mol^{-1}



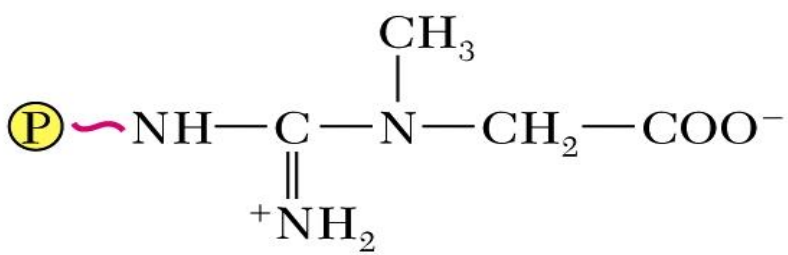
Phosphoenolpyruvate

$\Delta G° = -14.8\ \text{kcal} \cdot \text{mol}^{-1}$



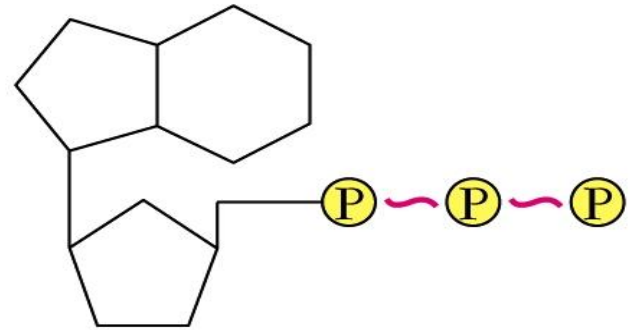
1,3-Diphosphoglycerate

$\Delta G° = -11.8\ \text{kcal} \cdot \text{mol}^{-1}$



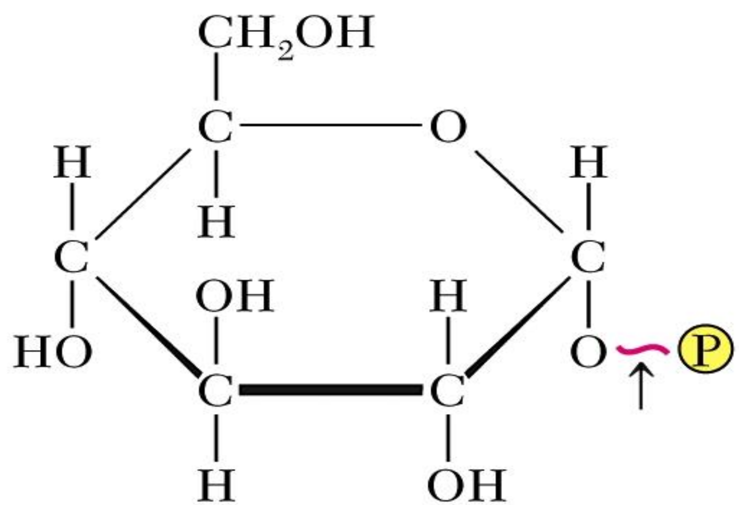
Phosphocreatine

$\Delta G° = -10.3\ \text{kcal} \cdot \text{mol}^{-1}$



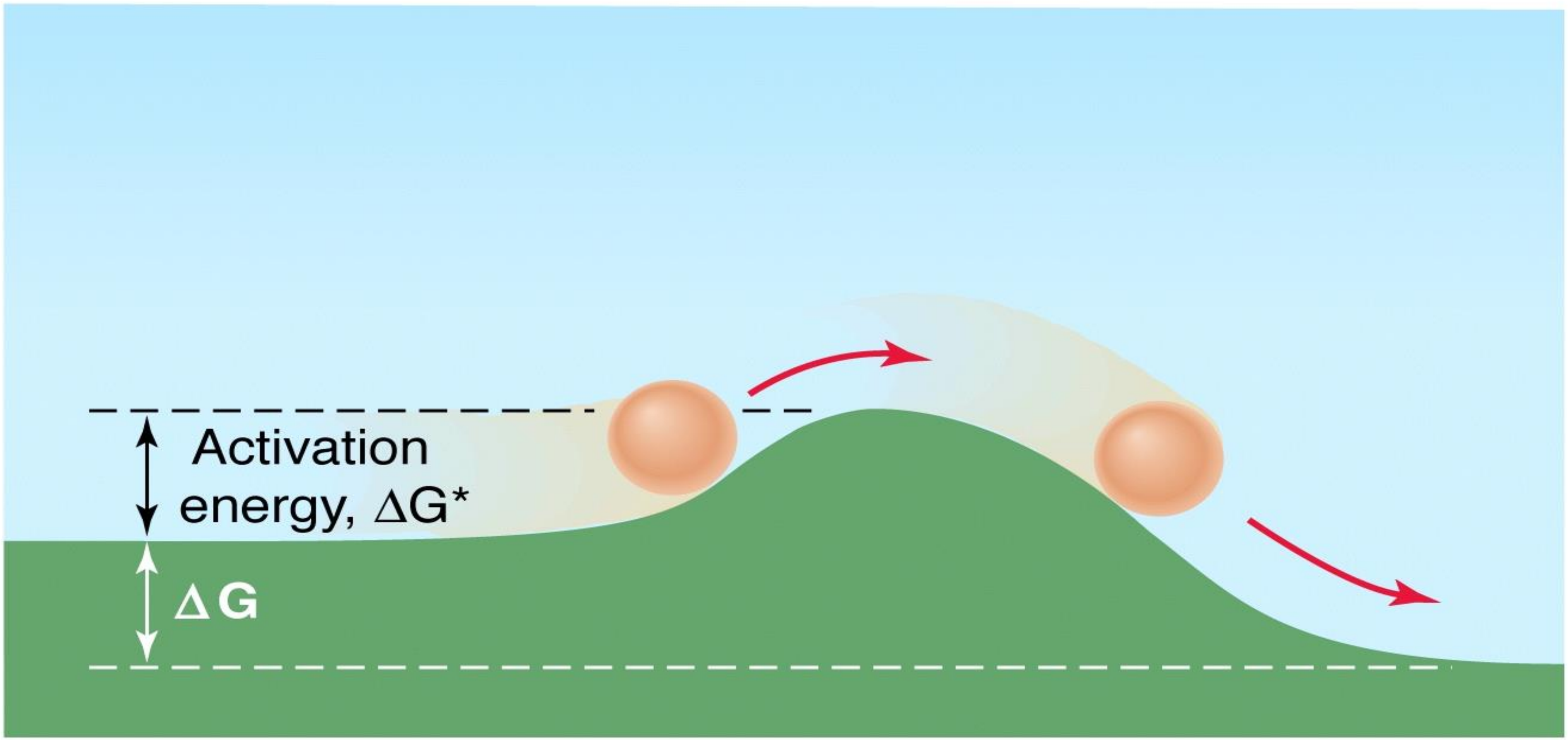
ATP

$\Delta G° = -7.3\ \text{kcal} \cdot \text{mol}^{-1}$

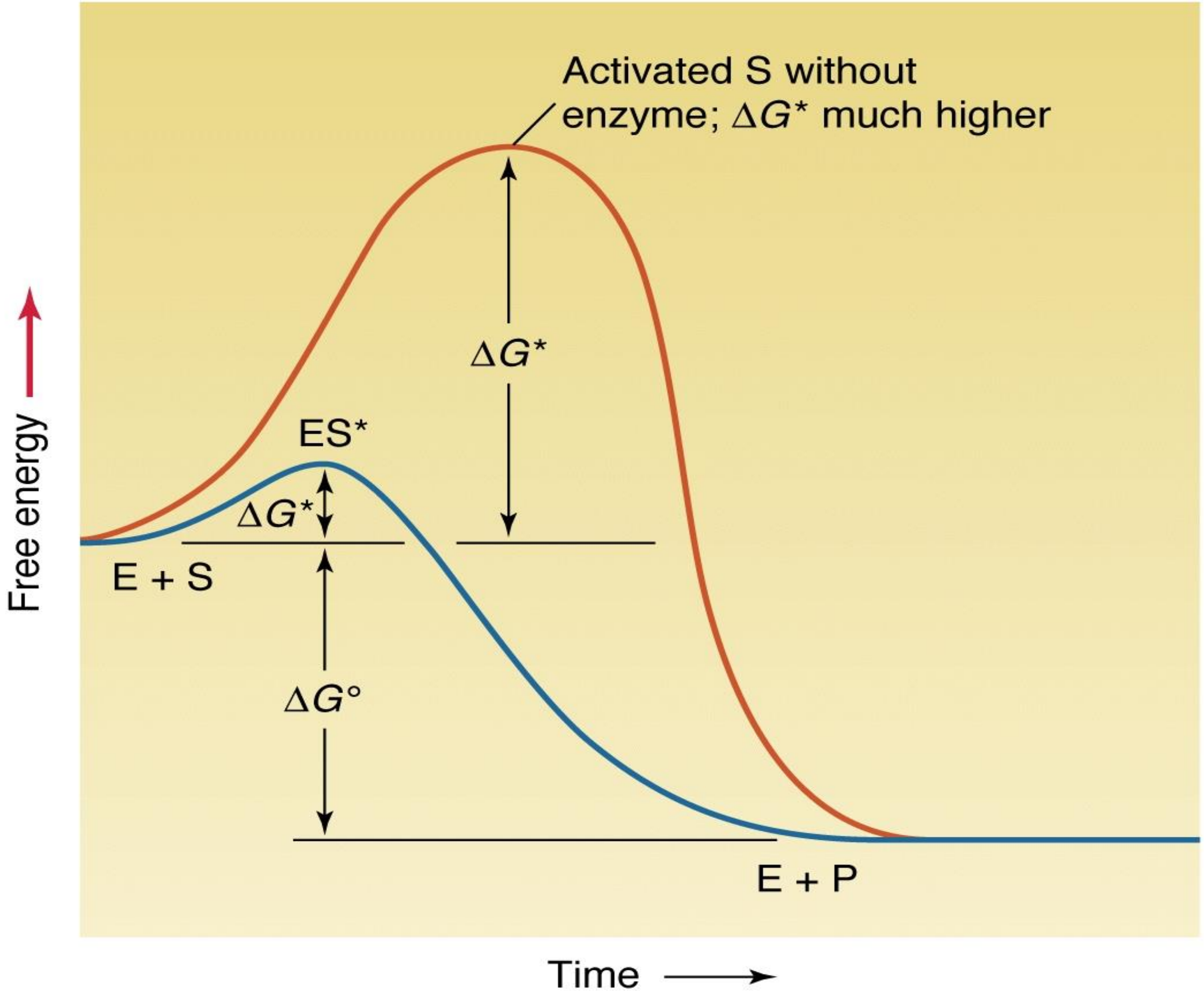


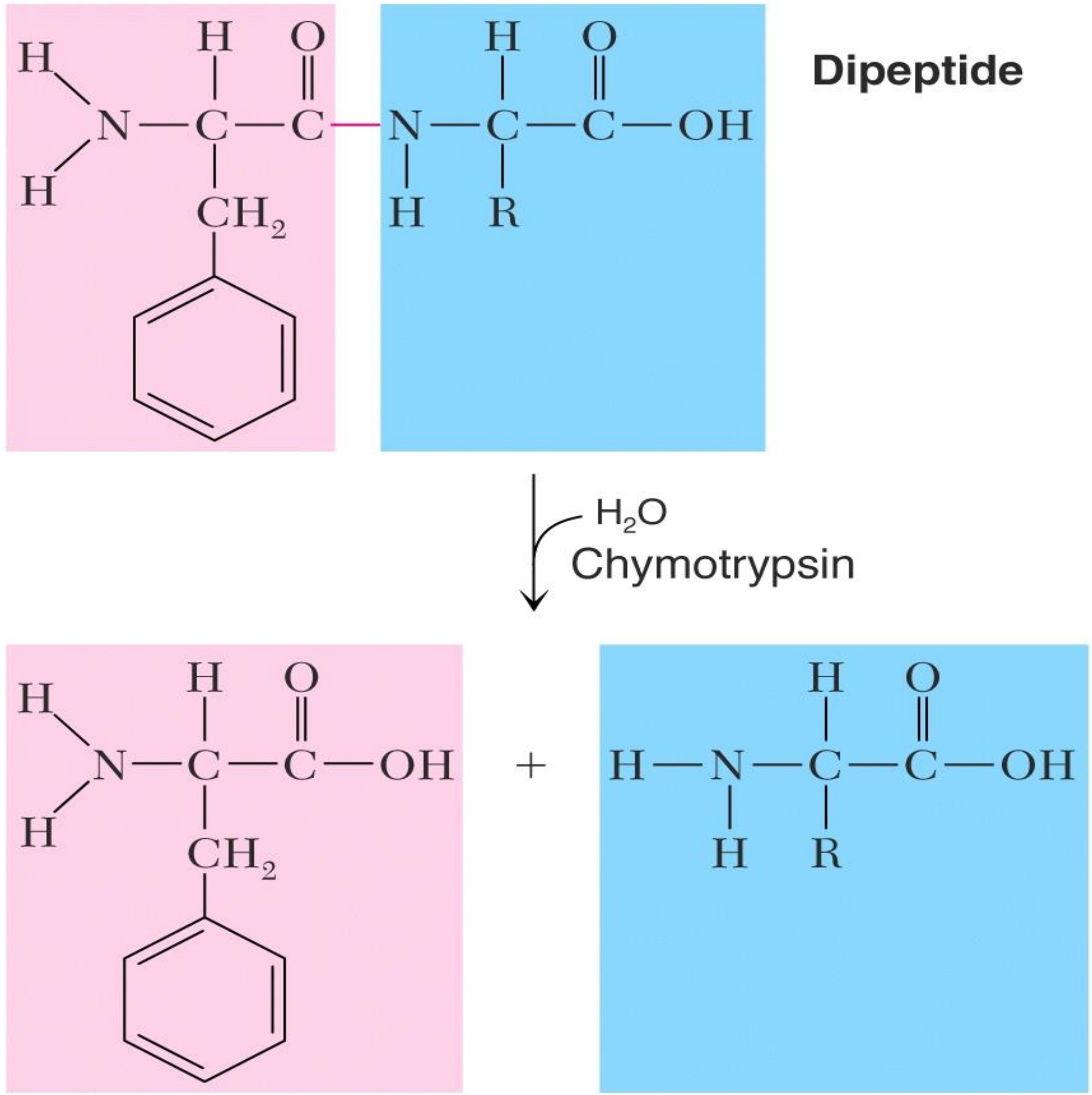
Glucose 1-phosphate

$\Delta G° = -5.0\ \text{kcal} \cdot \text{mol}^{-1}$



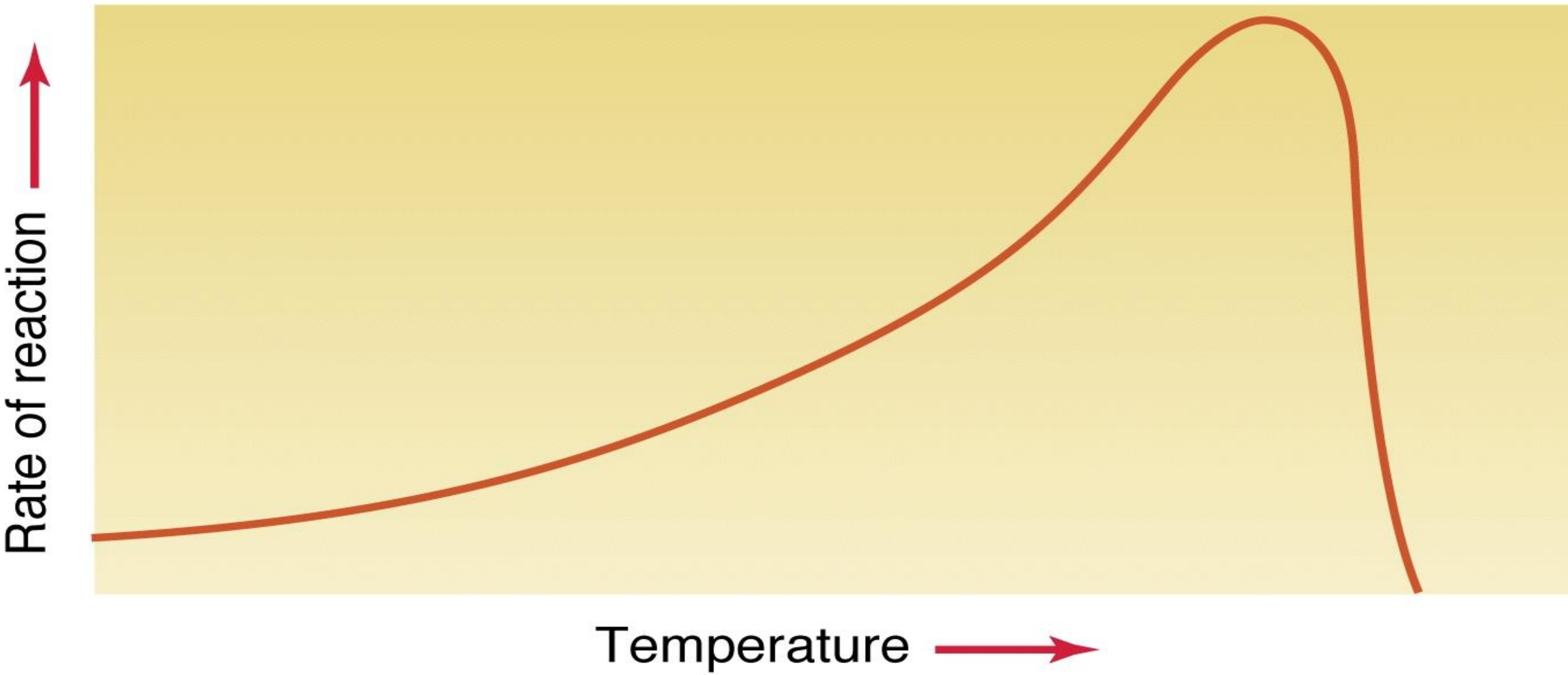
Activation
energy, ΔG*
ΔG


Activated S without
enzyme; ΔG* much higher
ΔG*
ES*
ΔG*
E + S
ΔG°
E + P
Free energy
Time



Dipeptide
H
O
H
N
C
C
N
C
C
OH
H
CH2
H
R
H2O
Chymotrypsin
+

(a) Enzyme activity versus temperature



(b) Enzyme activity versus pH

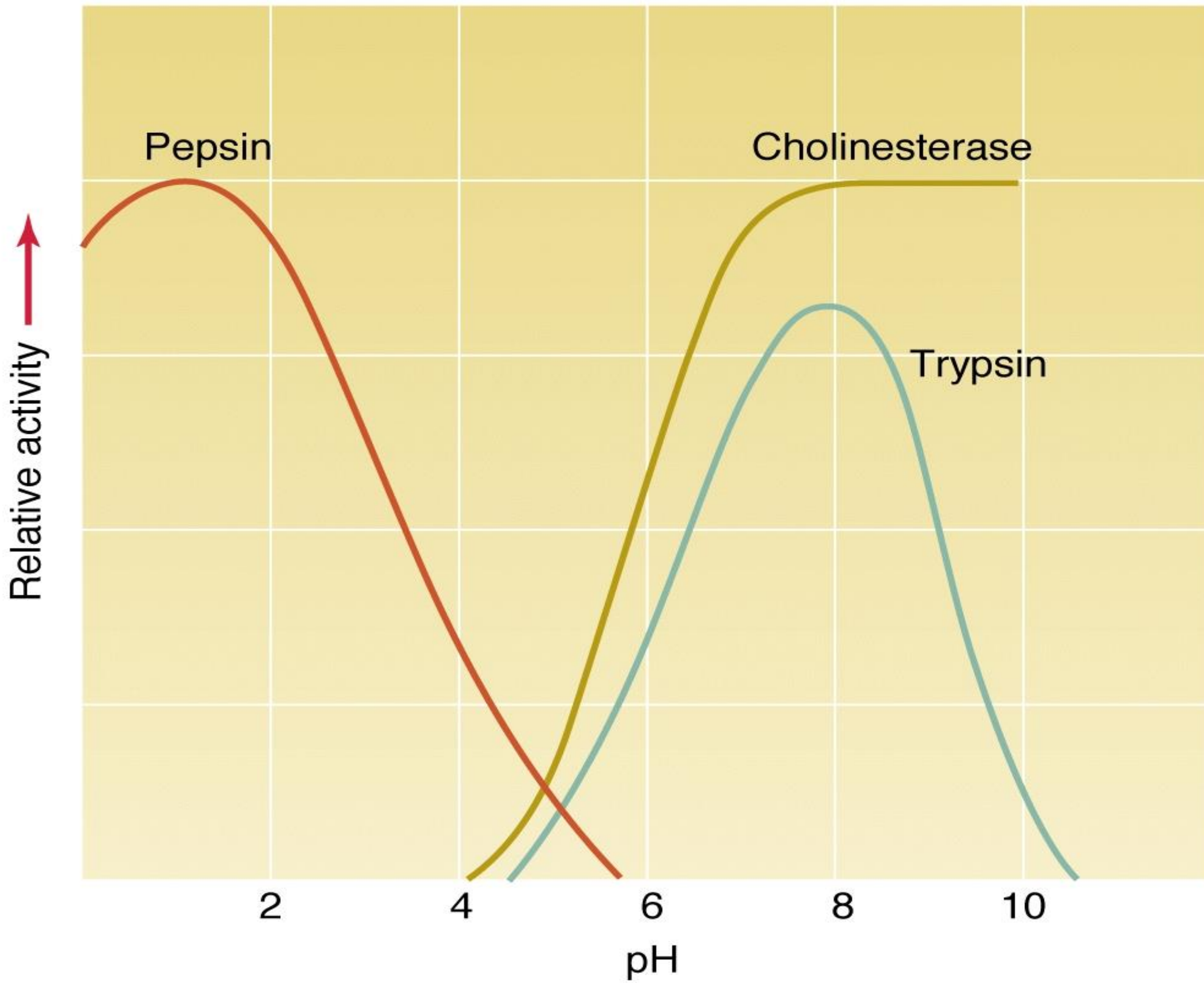


Table 3-6 Metal ions functioning as cofactors

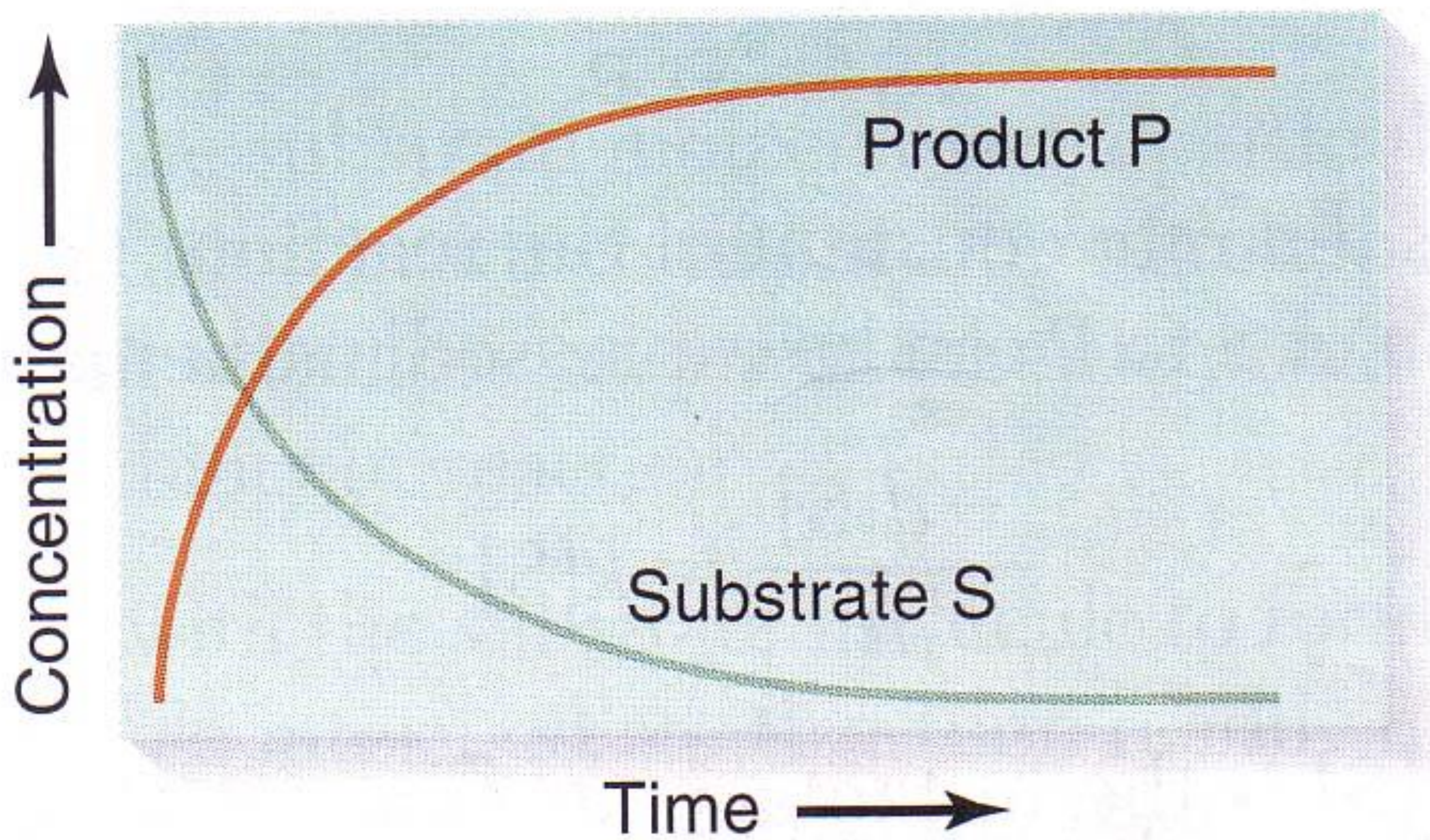
Metal ion	Some enzymes requiring this cofactor
Ca^{2+}	Phosphodiesterase
	Protein kinase C
Cu^{2+} (Cu^{+})	Cytochrome oxidase
	Tyrosinase
Fe^{2+} or Fe^{3+}	Catalase
	Cytochromes
	Ferredoxin
	Peroxidase
K^{+}	Pyruvate phosphokinase (also requires Mg^{2+})
Mg^{2+}	Phosphohydrolases
	Phosphotransferases
Mn^{2+}	Arginase
	Phosphotransferases
Na^{+}	Plasma membrane ATPase (also requires K^{+} and Mg^{2+})
Zn^{2+}	Alcohol dehydrogenase
	Carbonic anhydrase
	Carboxypeptidase

Source: Adapted from Nelson and Cox, 2000.

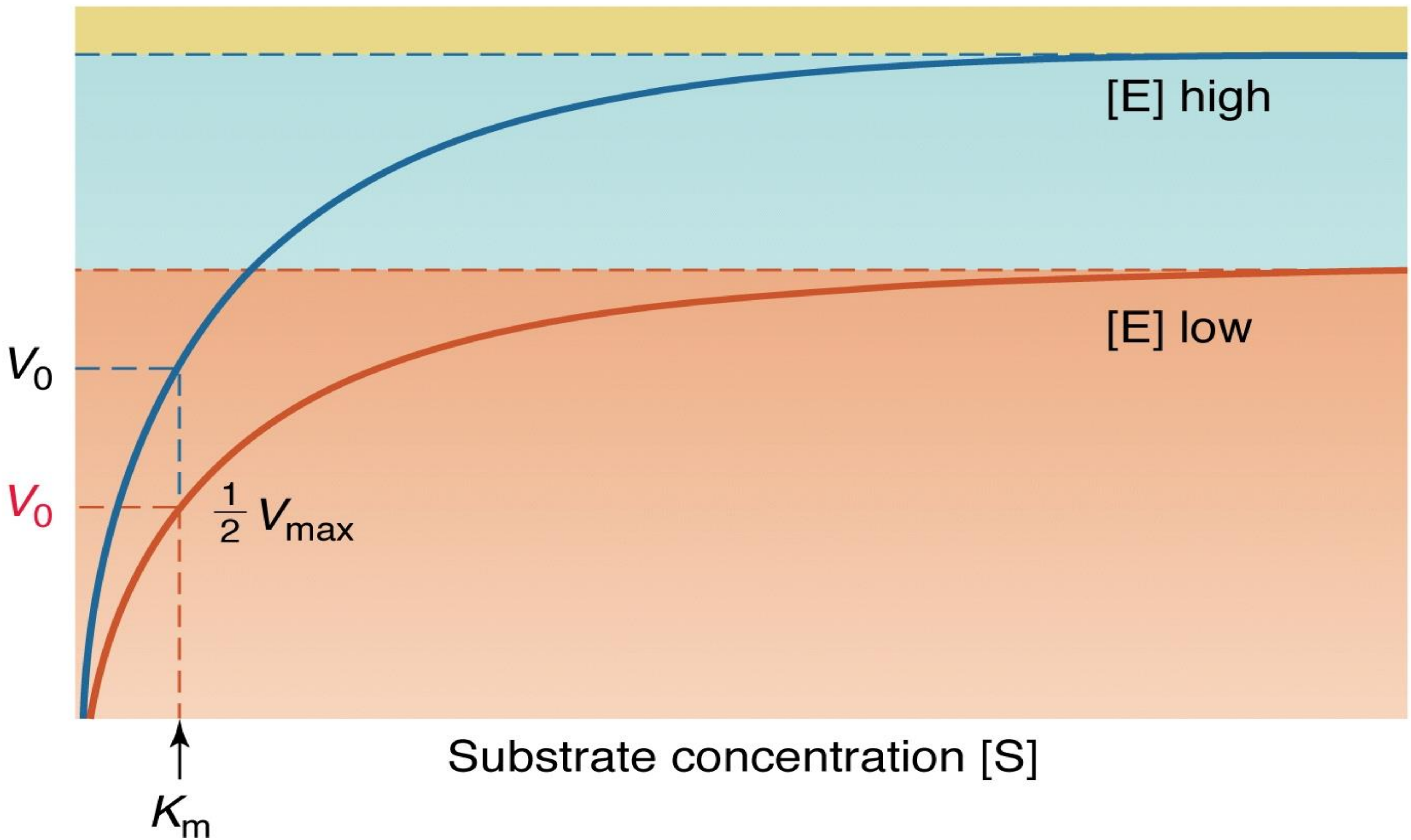
- Rx $A+B \rightleftharpoons C+D$

  Reactants to Products

Substrate goes to a Product $S \xrightarrow[k]{} P$



Product P
Substrate S
Concentration
Time



[E] high
[E] low
V_0
V_0
$\frac{1}{2} V_{max}$
Substrate concentration [S]
K_m

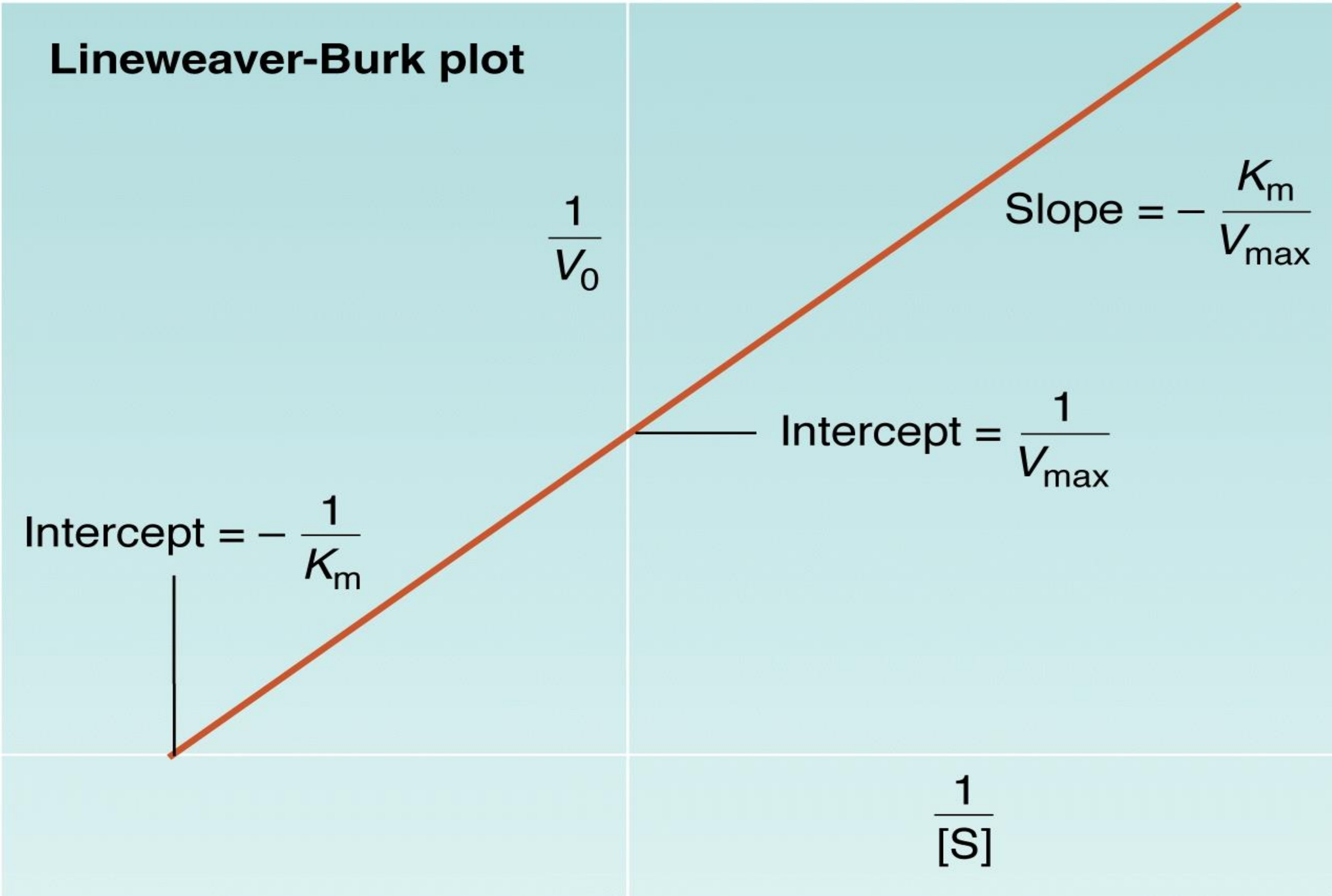
- Then the Michaelis-Menton equation for a single enzyme Vo of initial rate varies but can be used for determining other factors.

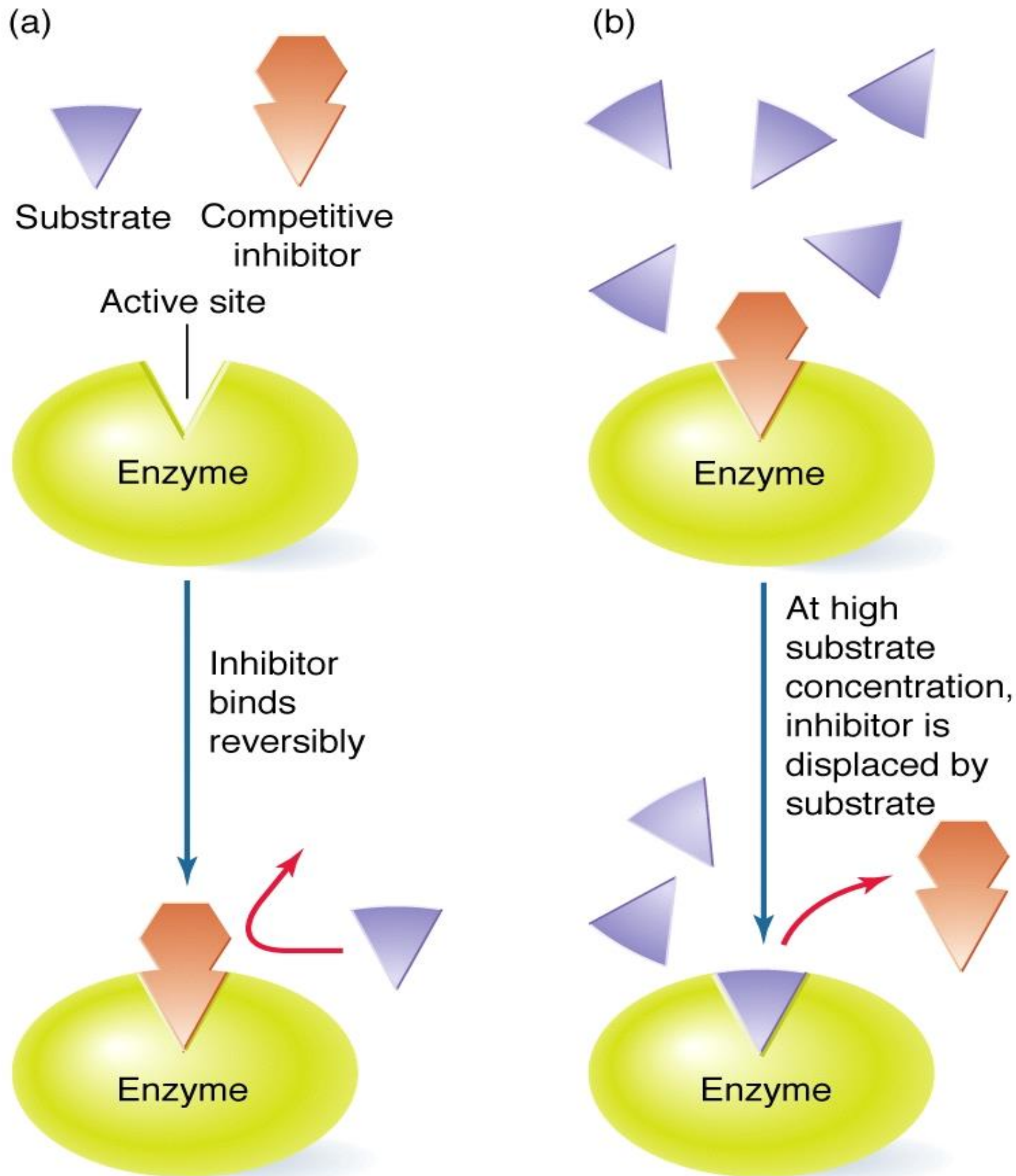
Key is when Vo = ½ Vmax

Then; $\frac{V_{max}}{2} = \frac{V_{max}[S]}{K_m + [S]}$ will be Km=[S]

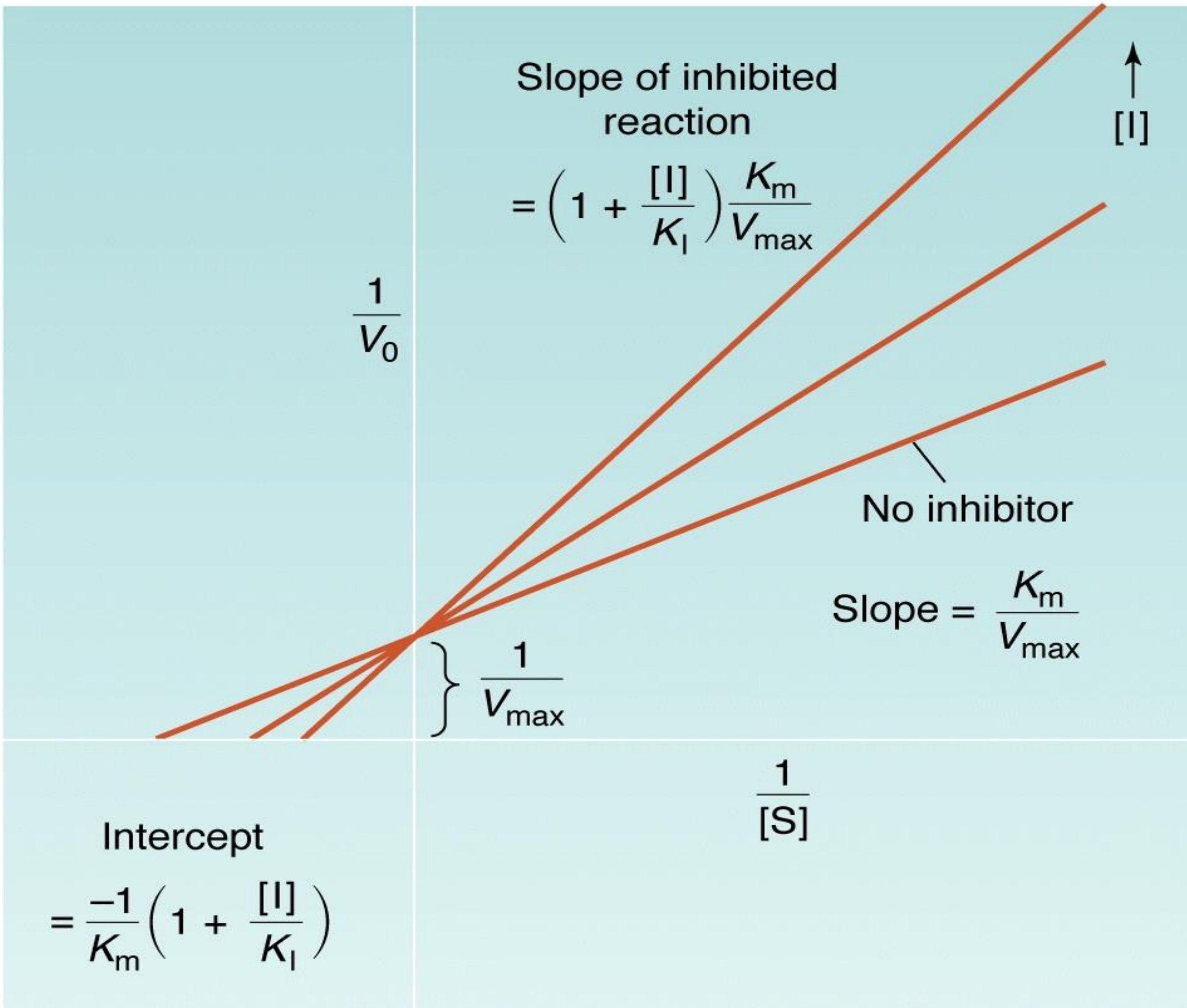
So Km can be determined by a plot. In this kind of plot many values are needed for the curve. A linear plot is easier and more accurate.

$$\frac{1}{Vo} = \frac{Km}{Vm[S]} + \frac{1}{Vmax}$$

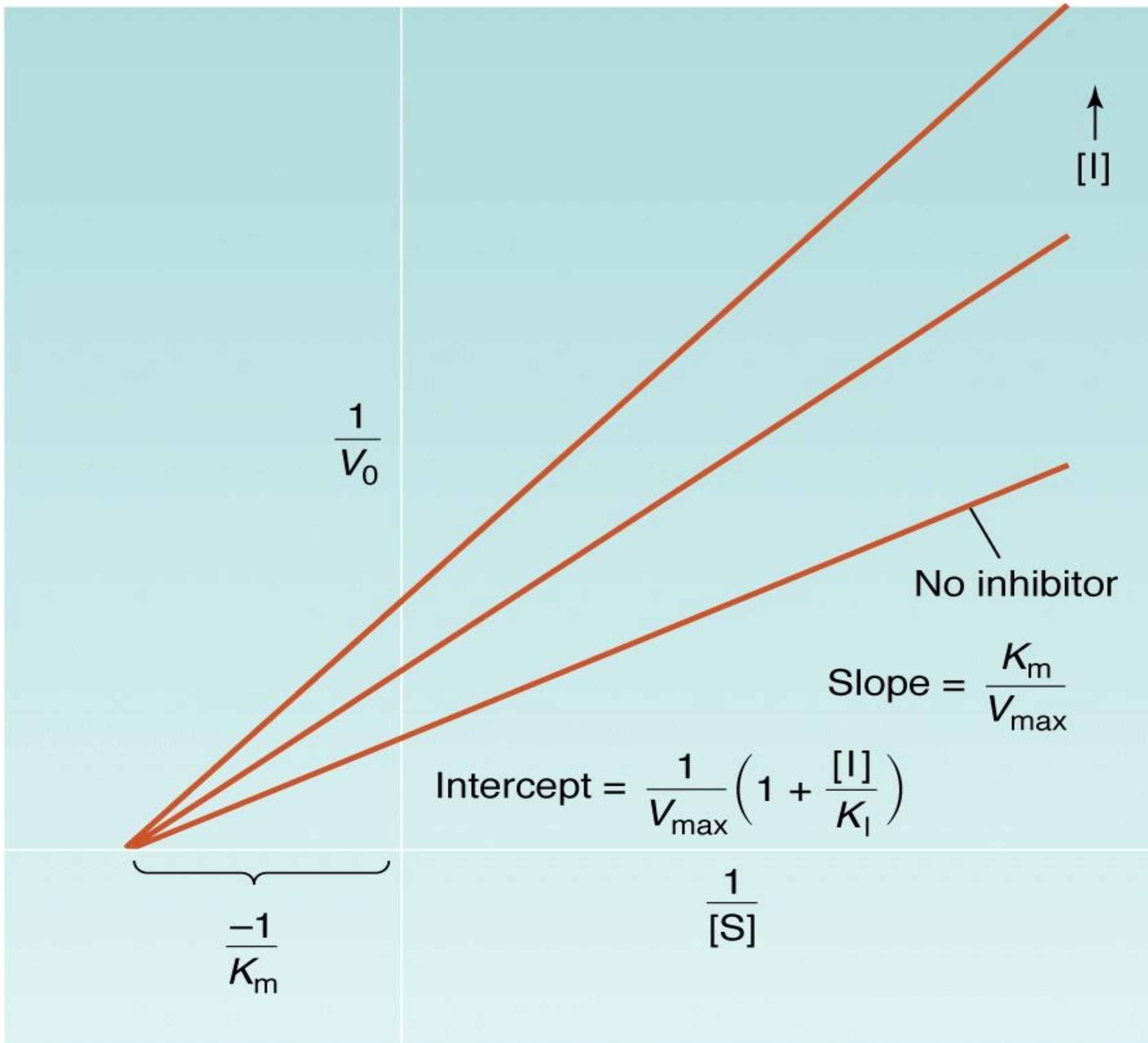

Lineweaver-Burk plot
$\frac{1}{V_0}$
Slope = $-\frac{K_m}{V_{max}}$
Intercept = $\frac{1}{V_{max}}$
Intercept = $-\frac{1}{K_m}$
$\frac{1}{[S]}$

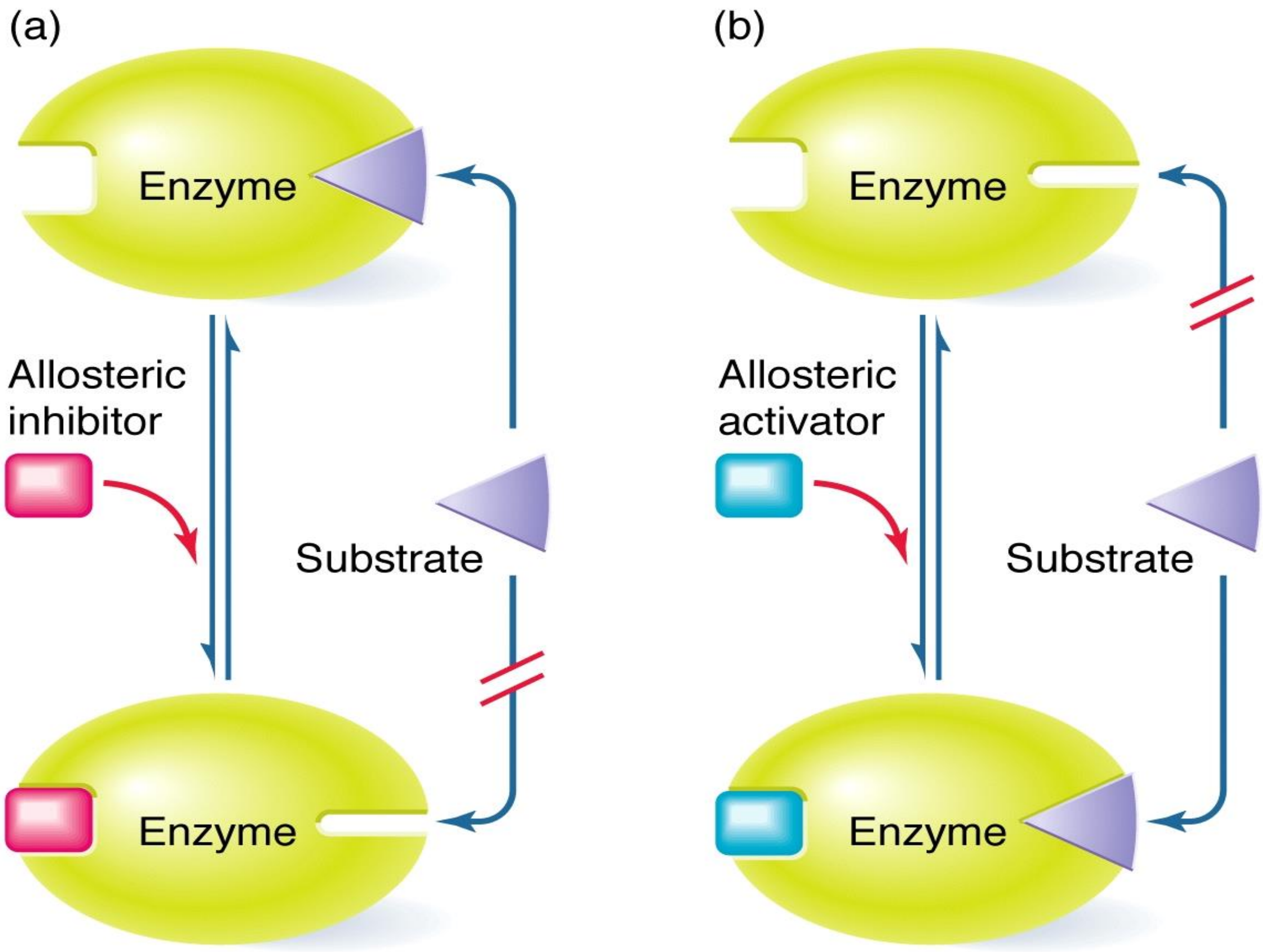

(a)
Substrate
Competitive inhibitor
Active site
Enzyme
Inhibitor binds reversibly
Enzyme
(b)
Enzyme
At high substrate concentration, inhibitor is displaced by substrate
Enzyme

(a) Competitive inhibition



(b) Noncompetitive inhibition




(a)
Enzyme
Allosteric
inhibitor
Substrate
Enzyme
(b)
Enzyme
Allosteric
activator
Substrate
Enzyme

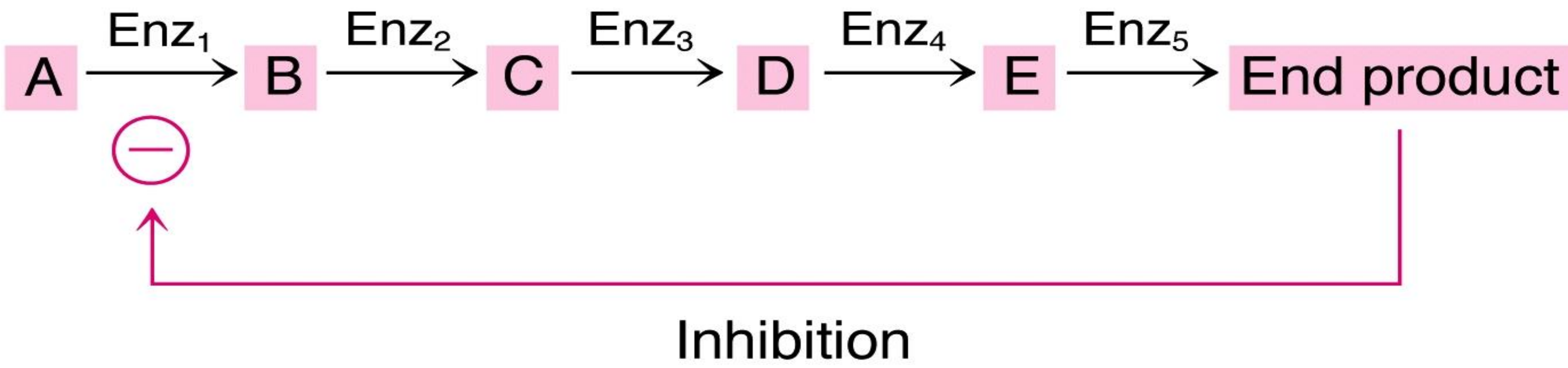
Metabolic Rx in the body must be regulated.

Not all or none Rxs for process like ATP (energy)

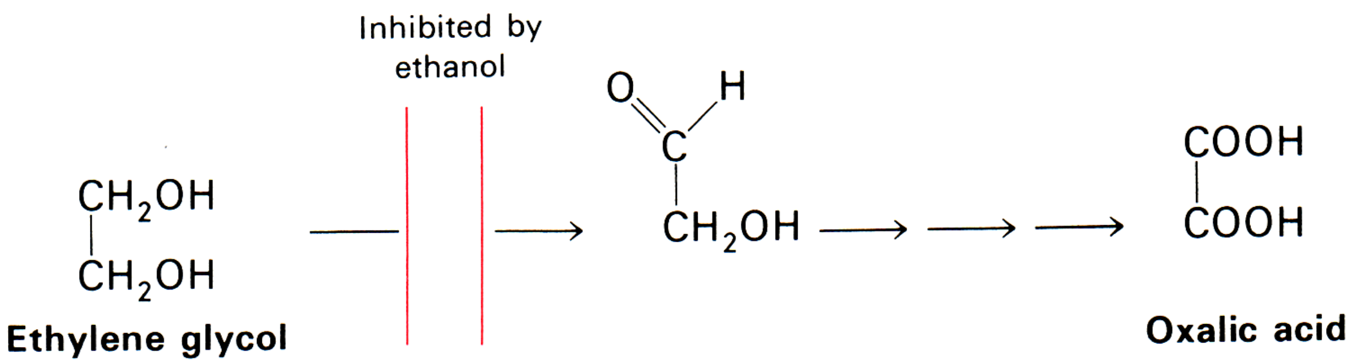
Many Rx regulated by enzymes. They are proteins; they are made and broken down.

These are amino acids so Temp, pH, and salts will have an effect on their function.

Also the cell does not want to much excess protein around so make Enzymes as needed.

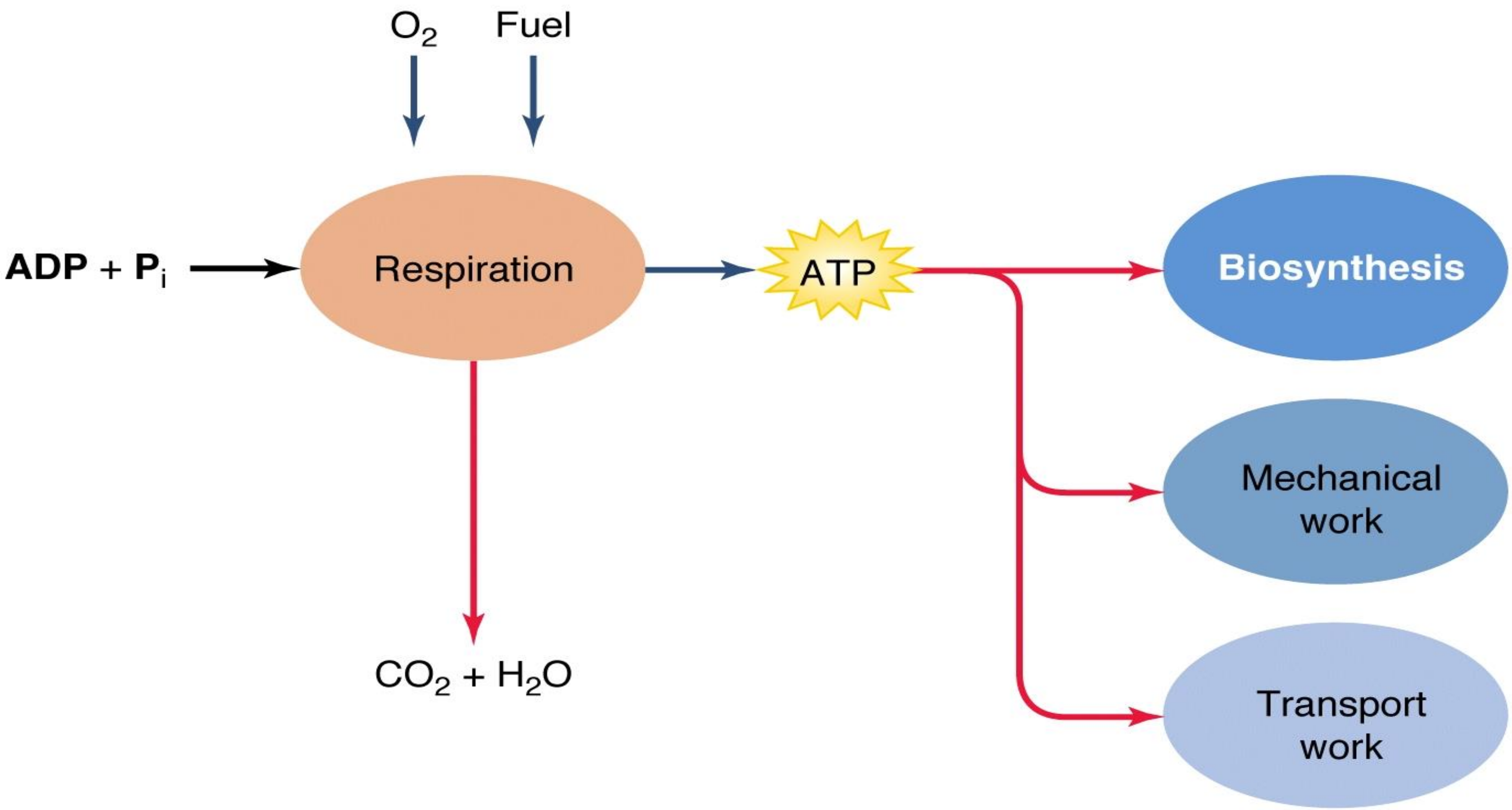

A
Enz1
B
Enz2
C
Enz3
D
Enz4
E
Enz5
End product
Inhibition

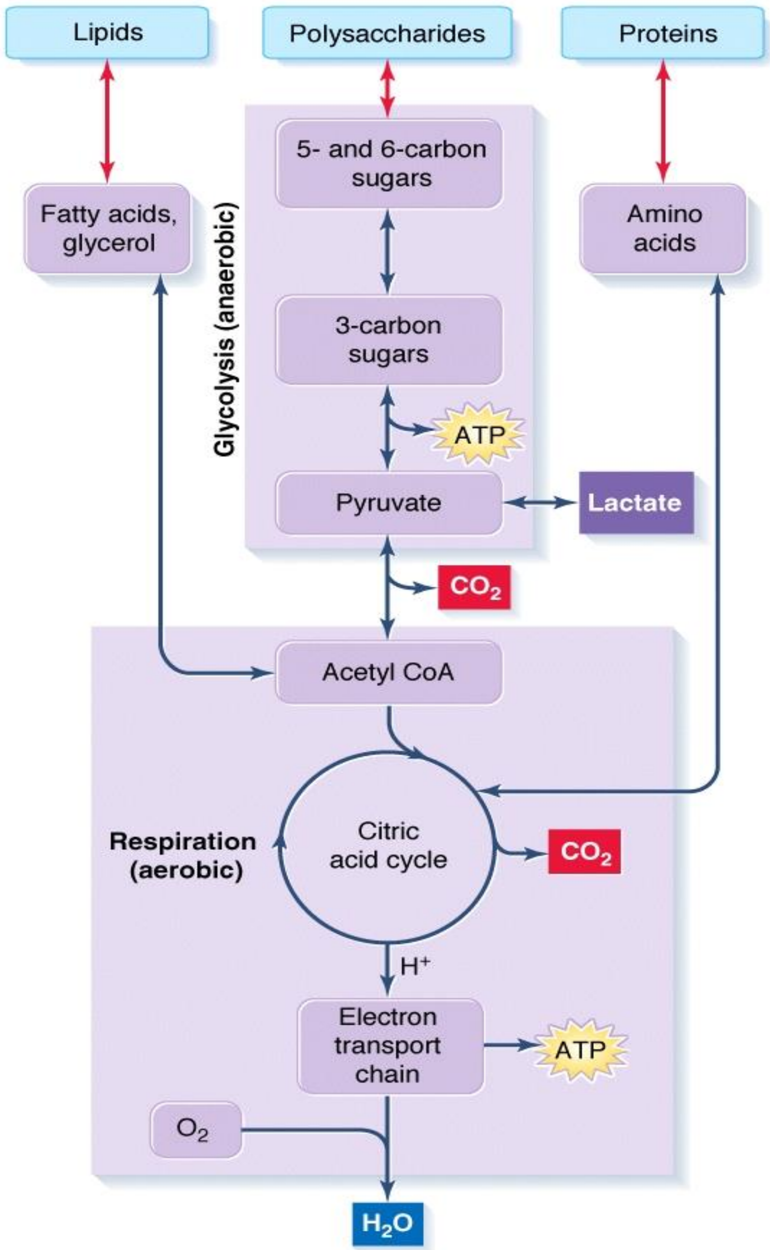
Ex: The neurotransmitter/hormone: Norepinephrine can inhibit tyrosine hydroxylase which is an enzyme that makes Norepi.



Formation of oxalic acid from ethylene glycol is inhibited by ethanol.

Energy within the cells used to drive the tissue- to organ- to system.



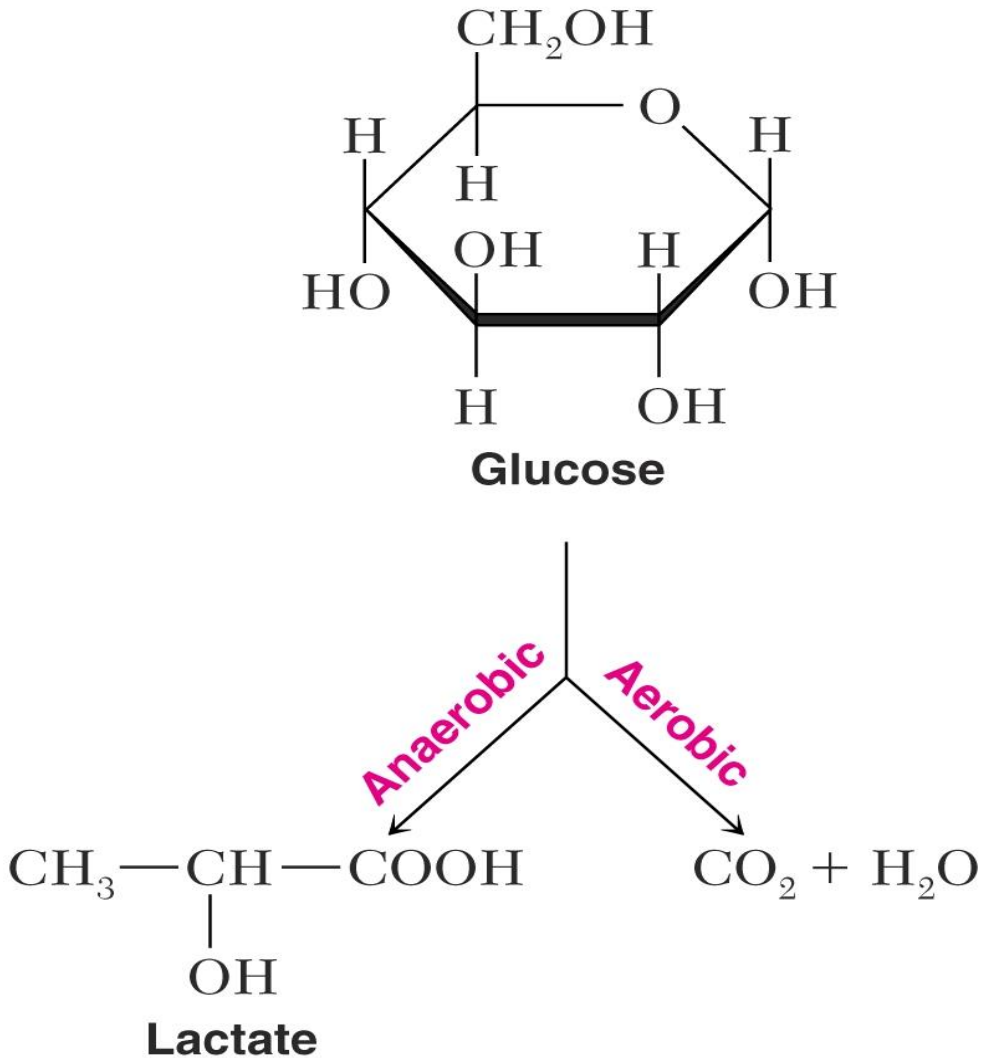


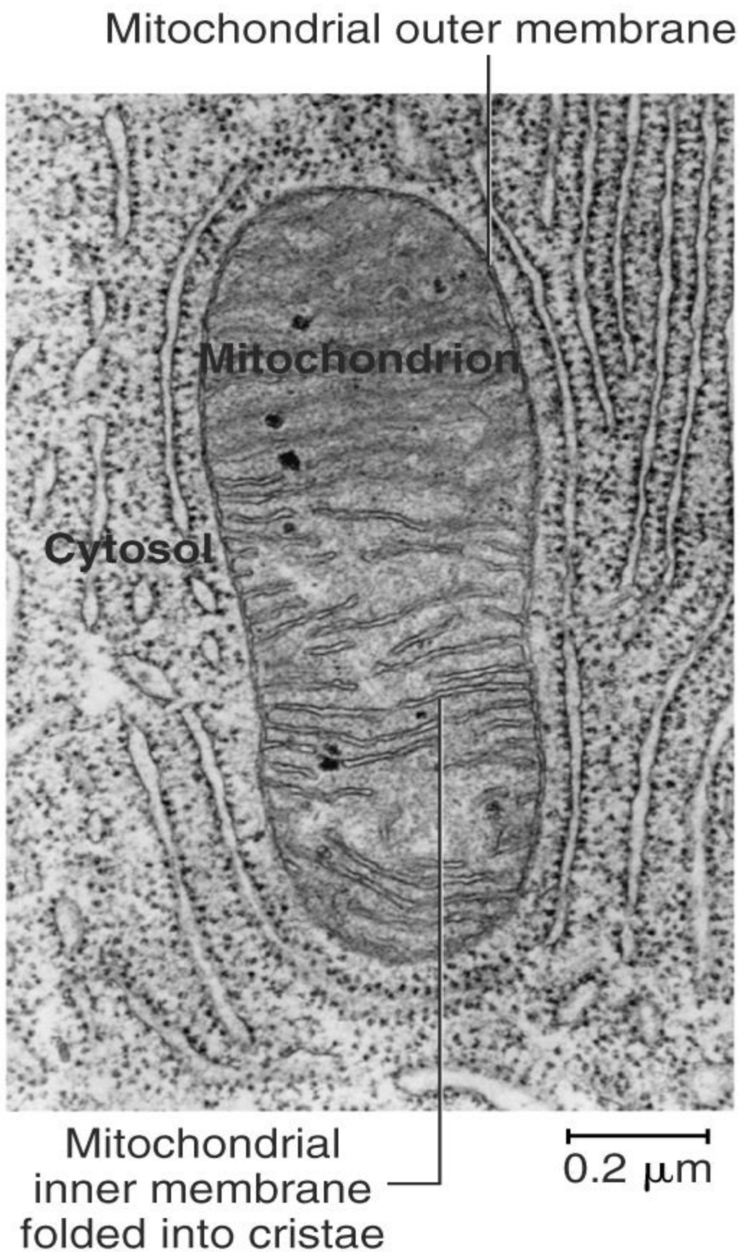
2 ATP

36 ATP (?)

Total 38 ATP (?)

$C_6H_{12}O_6 + 6\ O_2 = 6\ CO_2 + 6\ H_2O$ with O_2 metabolism





Inner membrane ETC and most ATP is produced

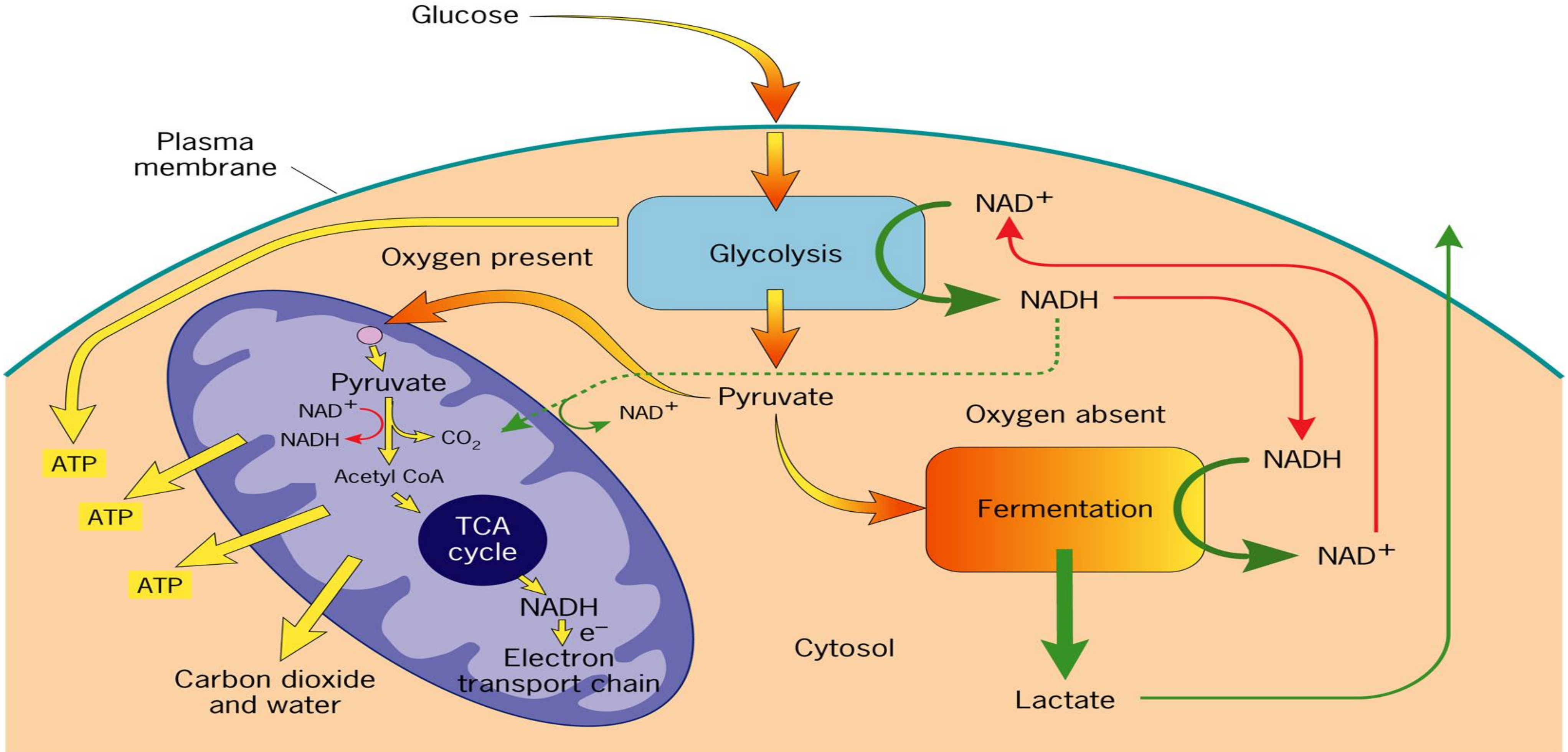
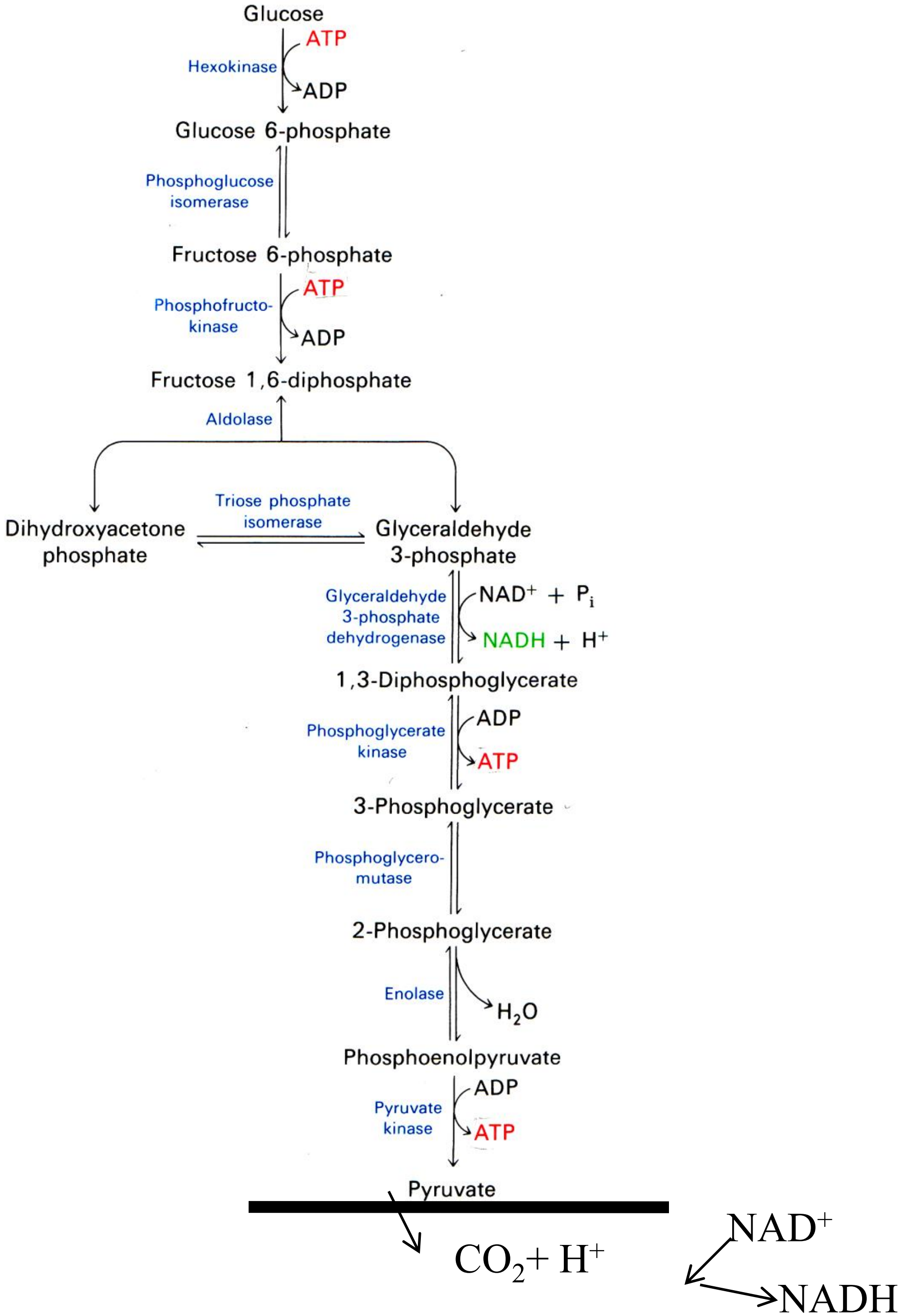
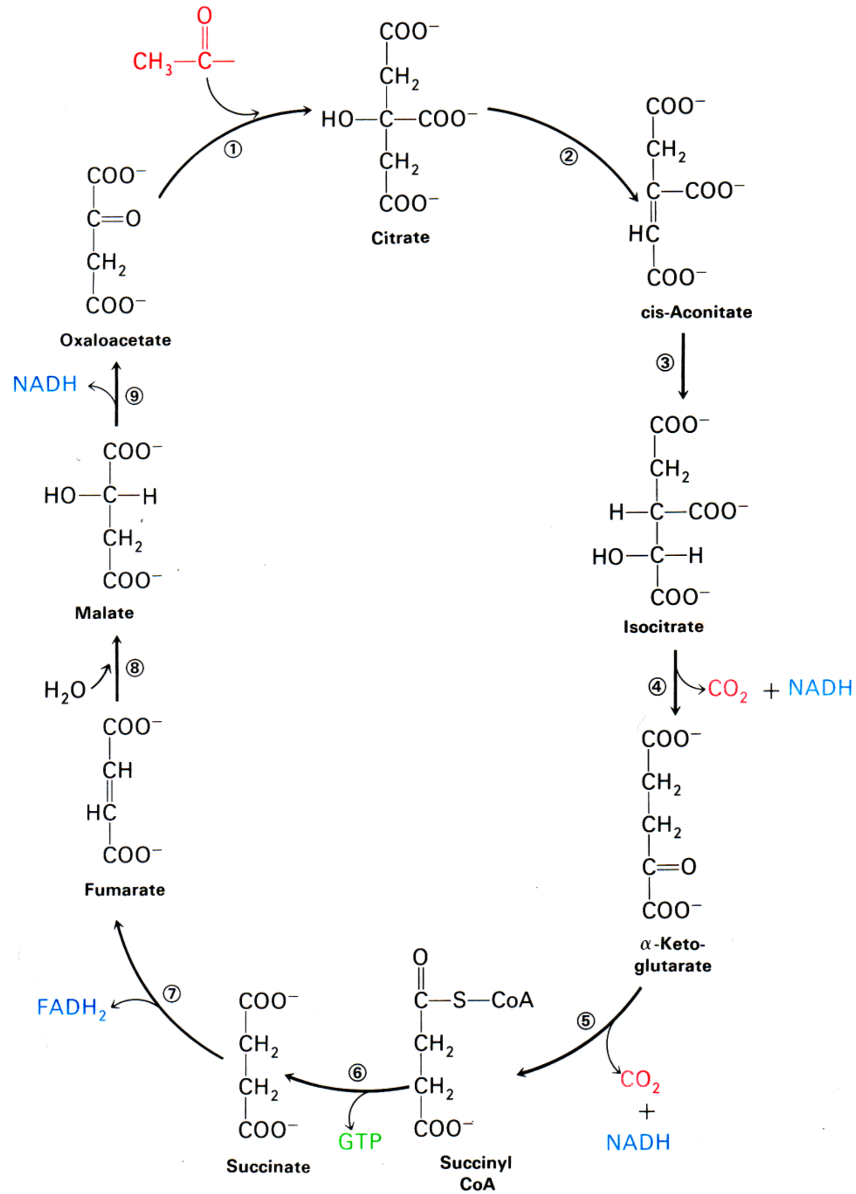
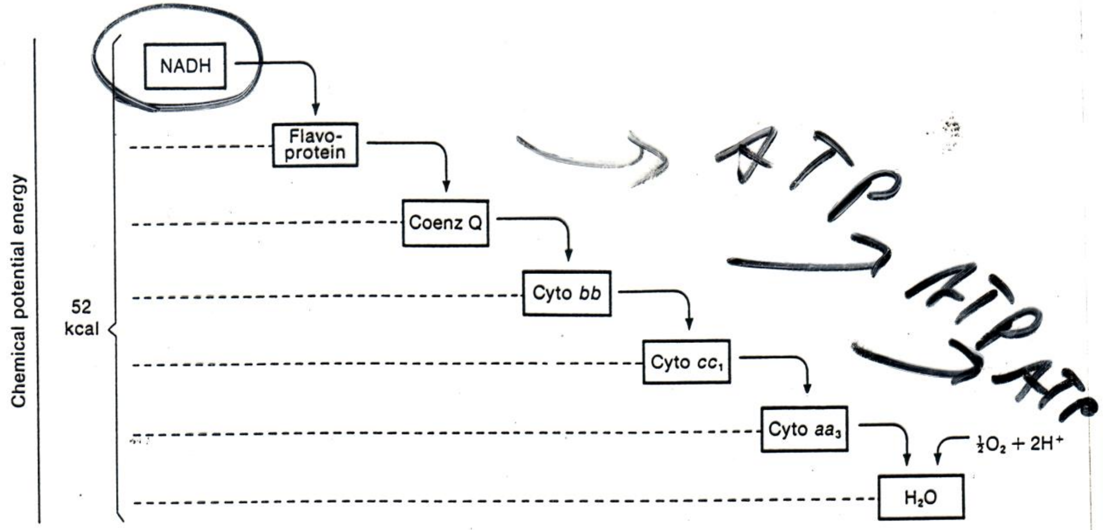

Glucose
Plasma membrane
Glycolysis
NAD+
NADH
Oxygen present
Pyruvate
NAD+
NADH
CO2
Acetyl CoA
TCA cycle
NADH
e−
Electron transport chain
ATP
ATP
ATP
Carbon dioxide and water
NAD+
Pyruvate
Oxygen absent
NADH
Fermentation
NAD+
Cytosol
Lactate

Figure 5.5


Glucose
ATP
Hexokinase
ADP
Glucose 6-phosphate
Phosphoglucose isomerase
Fructose 6-phosphate
ATP
Phosphofructo-kinase
ADP
Fructose 1,6-diphosphate
Aldolase
Dihydroxyacetone phosphate
Triose phosphate isomerase
Glyceraldehyde 3-phosphate
Glyceraldehyde 3-phosphate dehydrogenase
$NAD^+ + P_i$
$NADH + H^+$
1,3-Diphosphoglycerate
Phosphoglycerate kinase
ADP
ATP
3-Phosphoglycerate
Phosphoglycero-mutase
2-Phosphoglycerate
Enolase
H_2O
Phosphoenolpyruvate
ADP
Pyruvate kinase
ATP
Pyruvate
$CO_2 + H^+$
NAD^+
NADH


Citrate
cis-Aconitate
Isocitrate
CO_2 + NADH
α-Keto-glutarate
CO_2
+
NADH
Succinyl CoA
GTP
Succinate
$FADH_2$
Fumarate
H_2O
Malate
NADH
Oxaloacetate



3-37 Electron pressure produced by a cascading of electrons during electron transport in the respiratory chain.

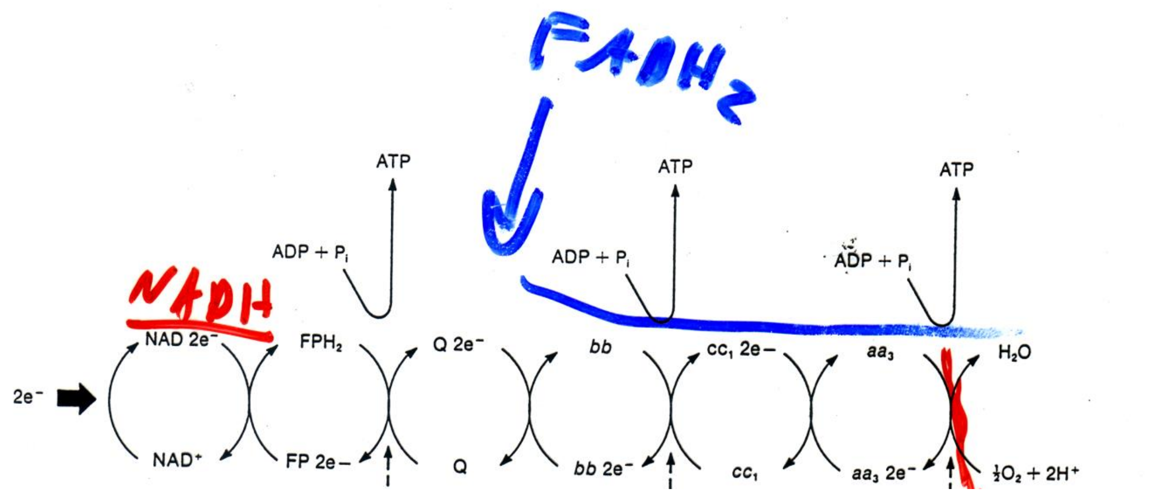


Table 14-4
ATP yield from the complete oxidation of glucose

Reaction sequence	*ATP yield per glucose*	
Glycolysis: glucose into pyruvate (in the cytosol)		
Phosphorylation of glucose	−1	
Phosphorylation of fructose 6-phosphate	−1	
Dephosphorylation of 2 molecules of 1,3-DPG	+2	
Dephosphorylation of 2 molecules of phosphoenolpyruvate	+2	
2 NADH are formed in the oxidation of 2 molecules of glyceraldehyde 3-phosphate		
Conversion of pyruvate into acetyl CoA (inside mitochondria)		
2 NADH are formed		
Citric acid cycle (inside mitochondria)		
2 molecules of guanosine triphosphate are formed from 2 molecules of succinyl CoA	+2	
6 NADH are formed in the oxidation of 2 molecules each of isocitrate, α-ketoglutarate, and malate		
2 $FADH_2$ are formed in the oxidation of 2 molecules of succinate		
Oxidative phosphorylation (inside mitochondria)		
2 NADH formed in glycolysis; each yields 2 ATP (assuming transport of NADH by the glycerol phosphate shuttle)	+4	6
2 NADH formed in the oxidative decarboxylation of pyruvate; each yields 3 ATP	+6	
2 $FADH_2$ formed in the citric acid cycle; each yields 2 ATP	+4	
6 NADH formed in the citric acid cycle; each yields 3 ATP	+18	
NET YIELD PER GLUCOSE	+36	38

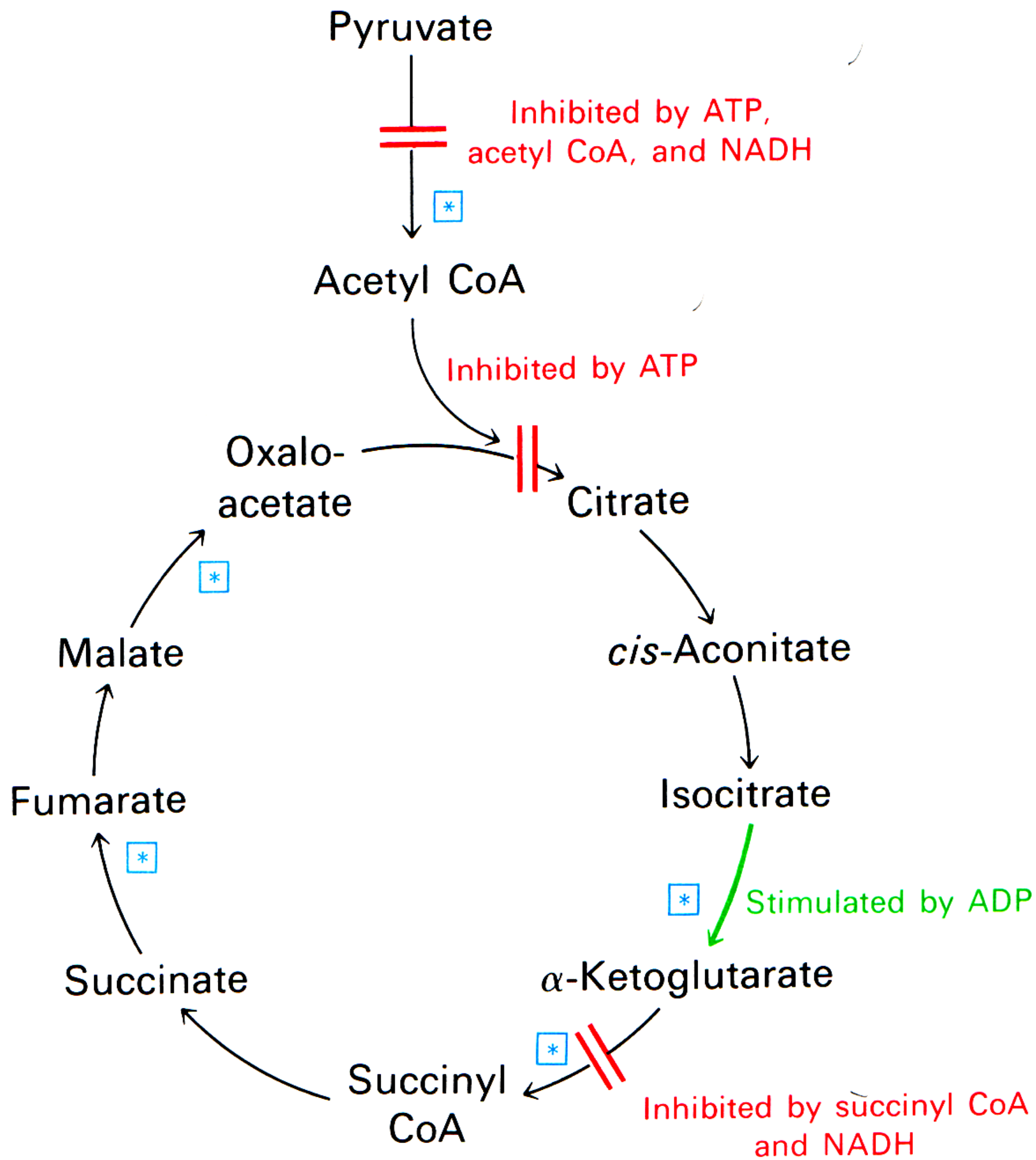
TCA and ETC:

Molecule	ATP worth	Total
4 NADH	3	12
1 $FADH_2$	2	2
1GTP	1	1
		15

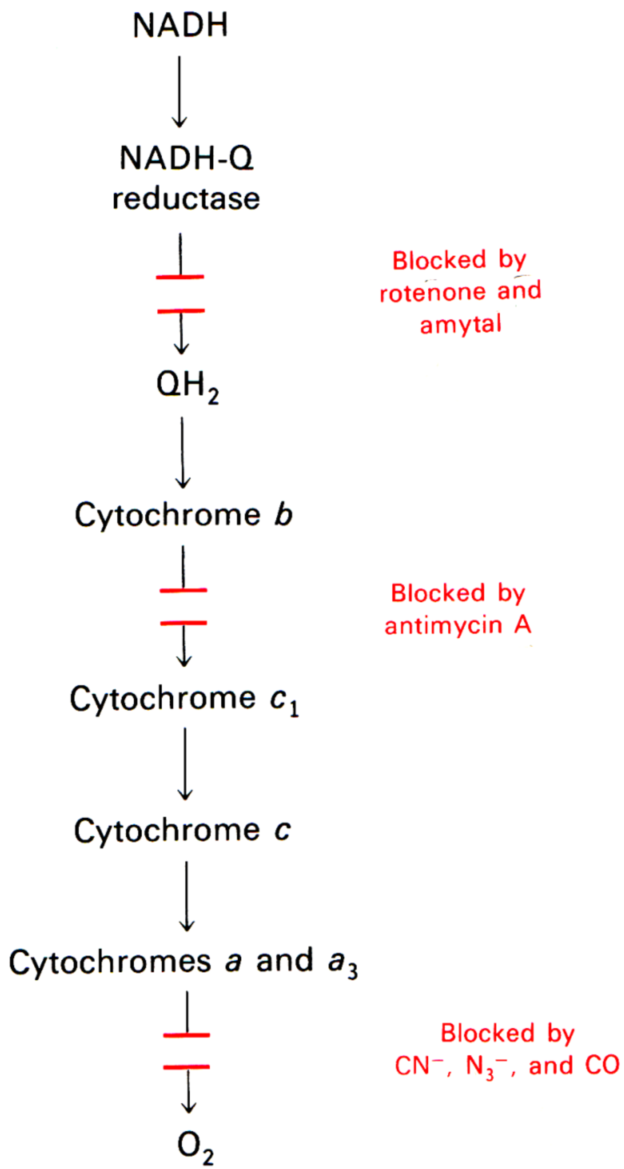
X2 TCA cycles =30 ATP

Glycolysis:

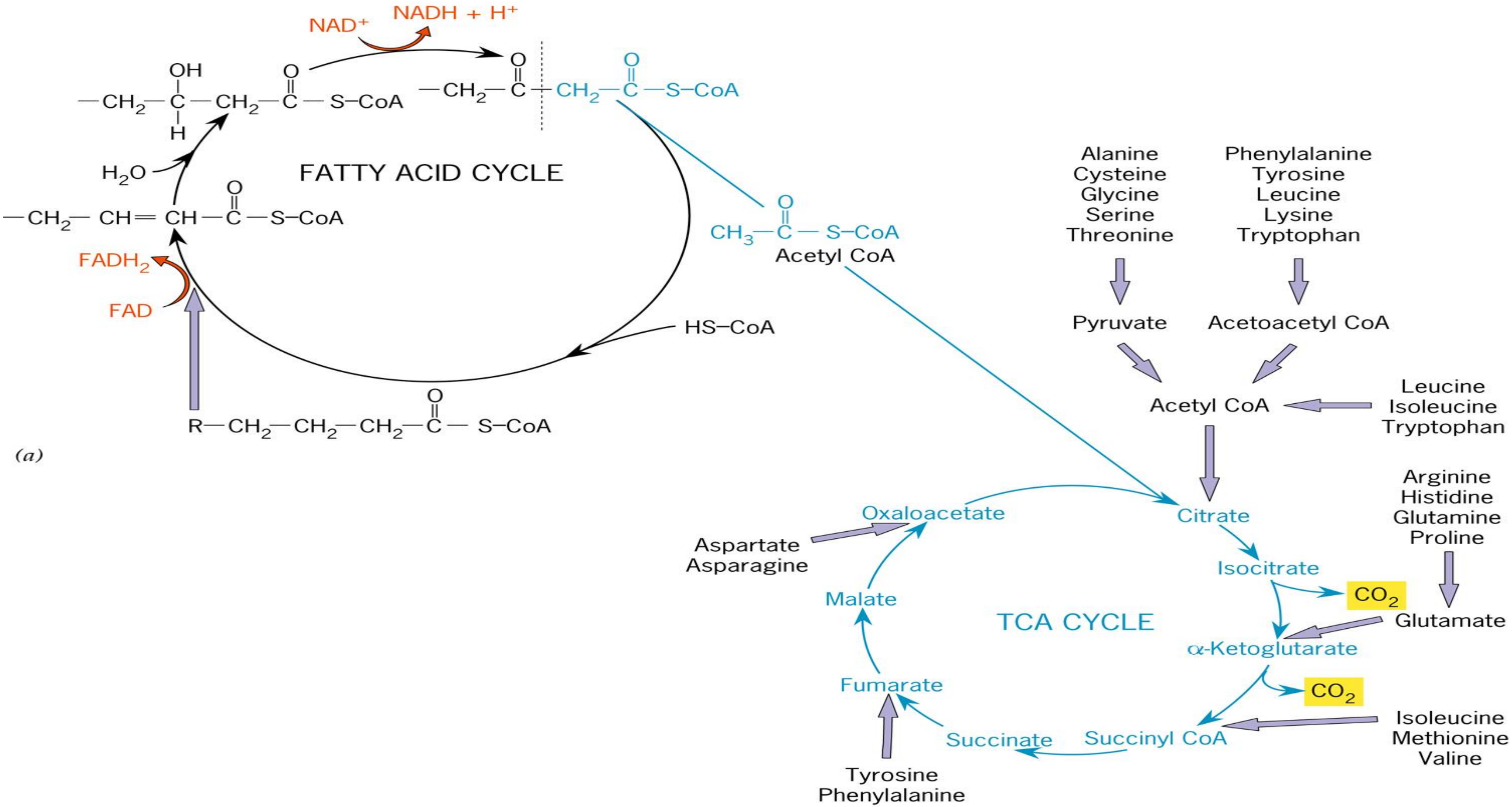
Gly Net ATP	2
	32 Total
2 NADH in Gly (3 ATP/each)	6
	38 Total
But use 2 ATP for the transport into Mit	-2 (1 ATP for each NADH)
	36 ATP Grand total



Pyruvate
Inhibited by ATP,
acetyl CoA, and NADH
*
Acetyl CoA
Inhibited by ATP
Oxalo-
acetate
Citrate
cis-Aconitate
Isocitrate
Stimulated by ADP
*
α-Ketoglutarate
*
Inhibited by succinyl CoA
and NADH
Succinyl
CoA
Succinate
*
Fumarate
Malate
*

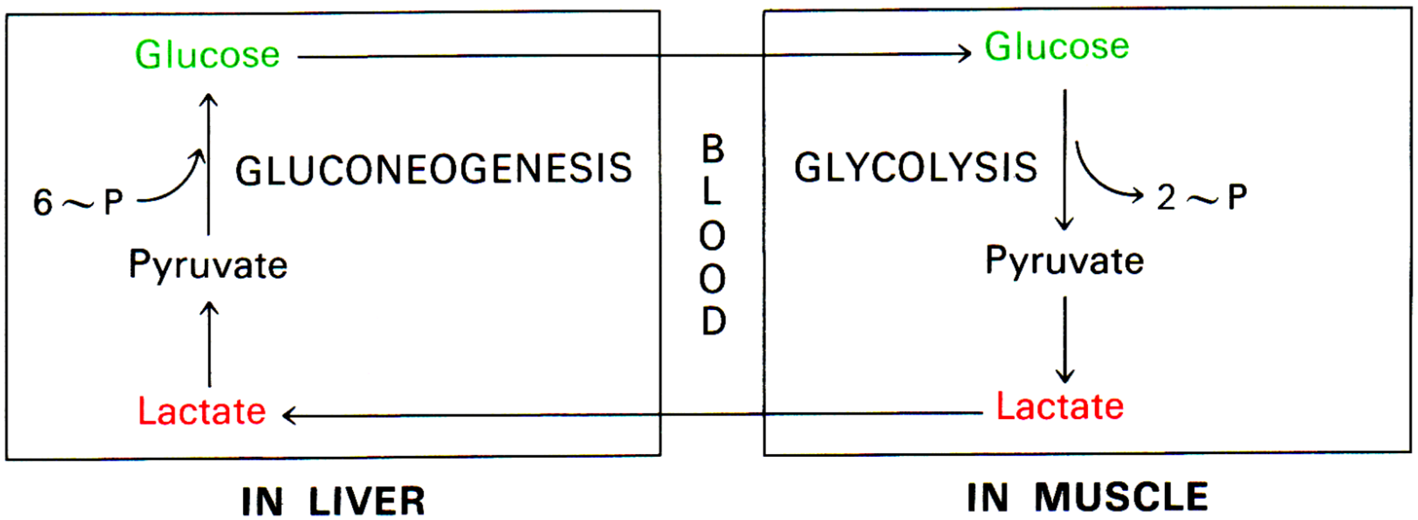


Endosymbiotic theory
Lynn Margulis


NAD+
NADH + H+
OH
O
—CH2—C—CH2—C—S–CoA
H
O
O
—CH2—C—CH2—C—S–CoA
H2O
FATTY ACID CYCLE
O
—CH2—CH=CH—C—S–CoA
FADH2
FAD
O
CH3—C—S–CoA
Acetyl CoA
HS–CoA
O
R—CH2—CH2—CH2—C—S–CoA
Alanine
Cysteine
Glycine
Serine
Threonine
Phenylalanine
Tyrosine
Leucine
Lysine
Tryptophan
Pyruvate
Acetoacetyl CoA
Acetyl CoA
Leucine
Isoleucine
Tryptophan
Arginine
Histidine
Glutamine
Proline
Oxaloacetate
Citrate
Aspartate
Asparagine
Isocitrate
CO2
Malate
TCA CYCLE
Glutamate
α-Ketoglutarate
CO2
Fumarate
Succinate
Succinyl CoA
Isoleucine
Methionine
Valine
Tyrosine
Phenylalanine

(a)

(b)


Glucose
GLUCONEOGENESIS
6 ~ P
Pyruvate
Lactate
B
L
O
O
D
Glucose
GLYCOLYSIS
2 ~ P
Pyruvate
Lactate
IN LIVER
IN MUSCLE

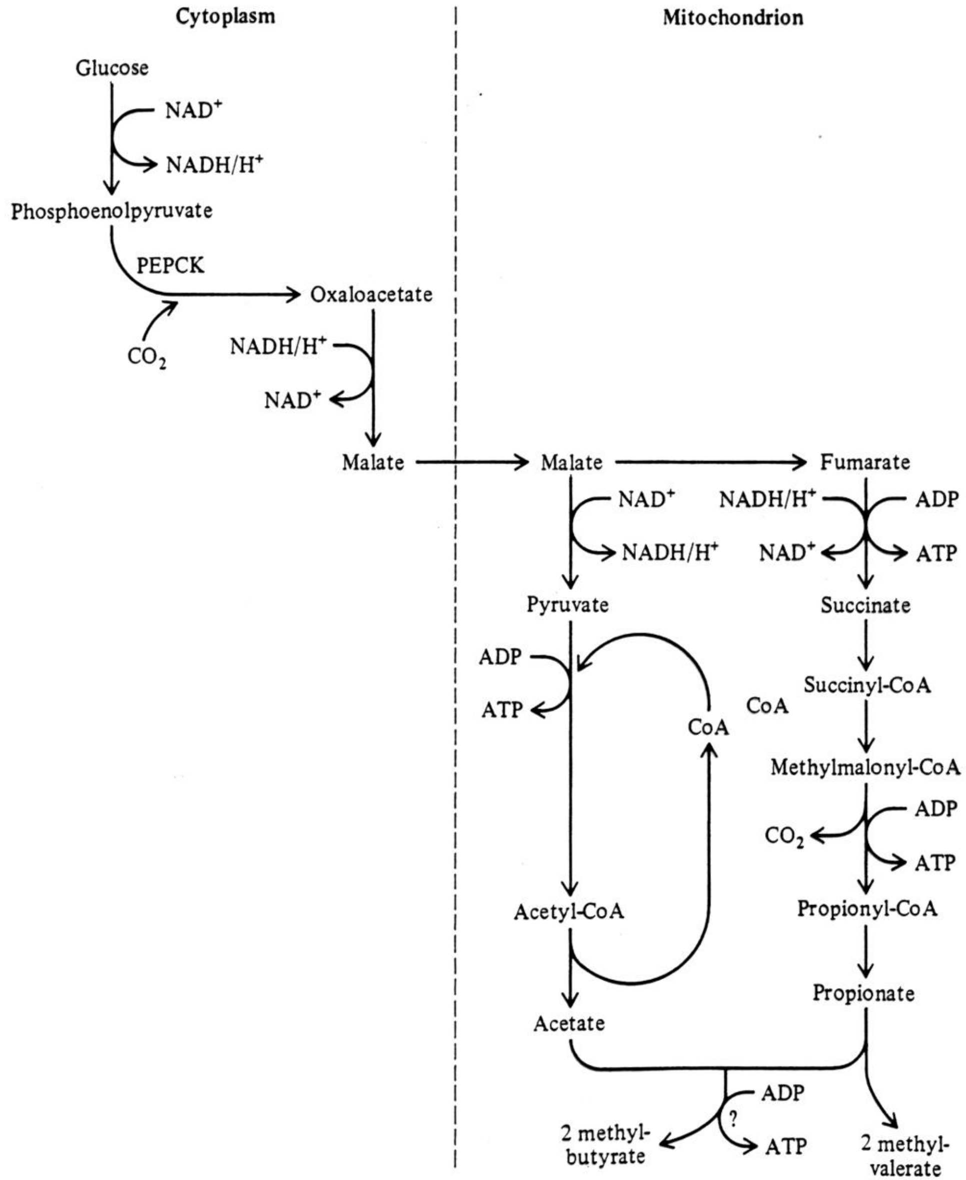


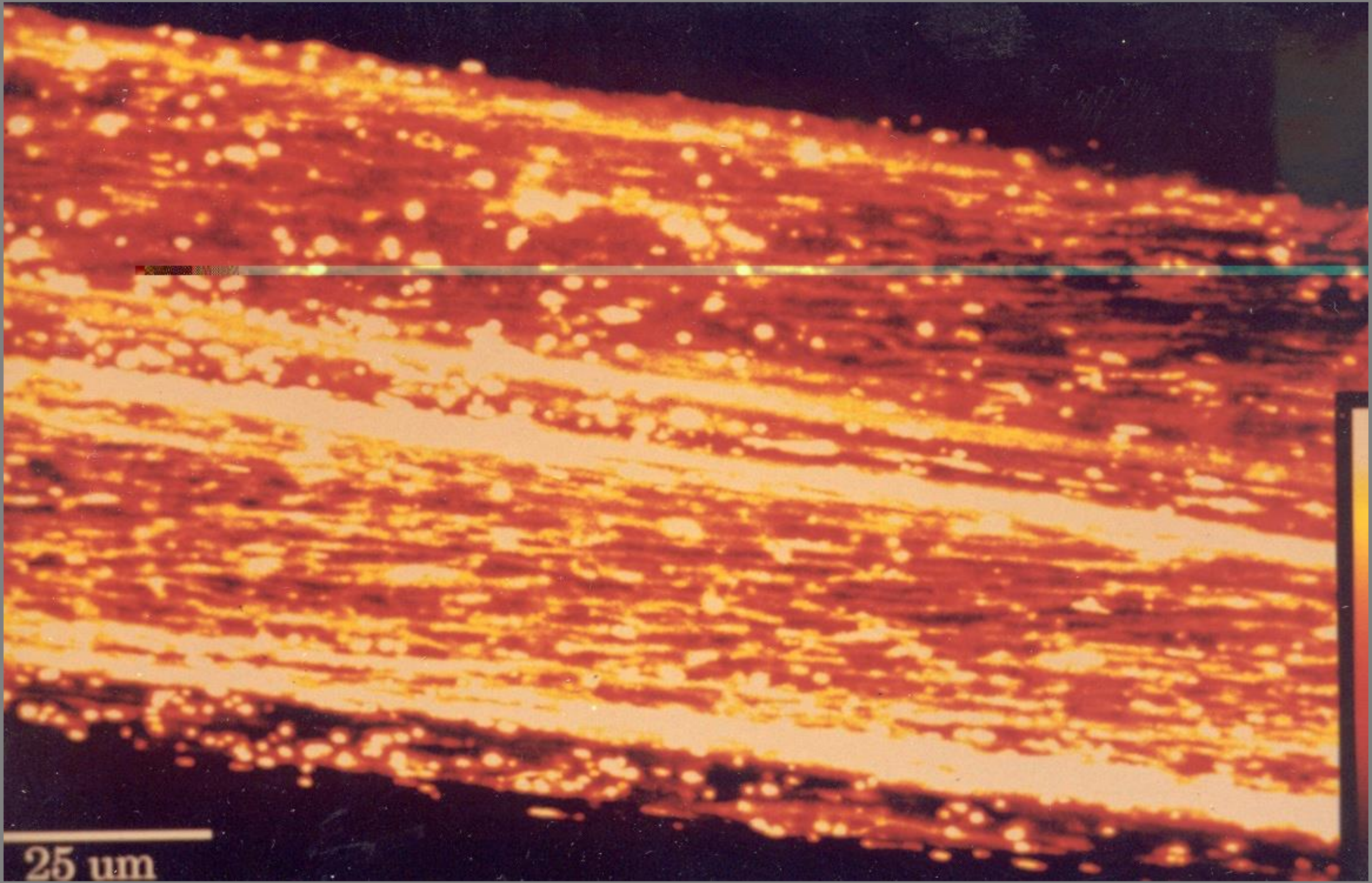
FIGURE 3–18 Linkage of glycolysis with citric acid cycle pathways is an anaerobic metabolic pathway that provides additional ATP formation. These pathways are found, for example, in many platyhelminth worms.

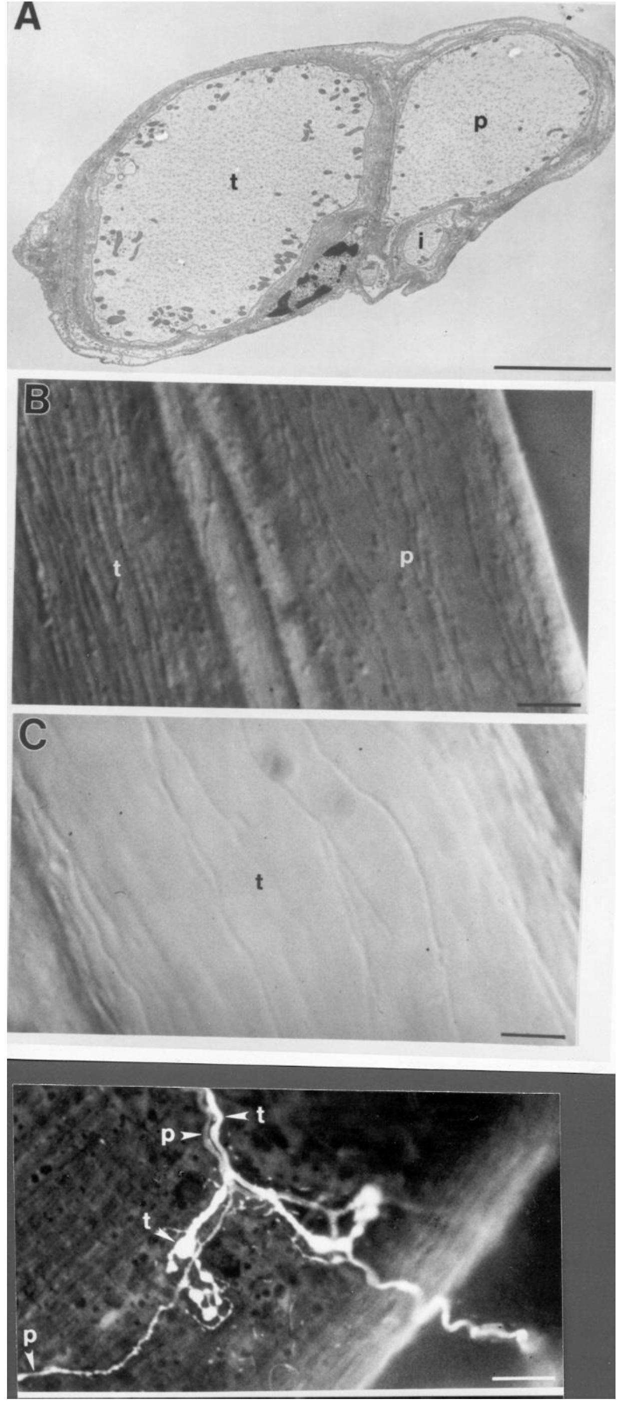
Anaerobic- Bacteria, some yeasts, some invertebrates can live in low O_2.

Ex. Clostridium botulinum can not grow in O_2.

Aerobic- require a supply of O_2. Some tissues like muscle can function anaerobically and build up an "O_2 debt" but pay back occurs.

With O_2 the cells are 20 times more efficient to produce ATP.


25 um


A
t
p
i
B
t
p
C
t
t
p
t
p

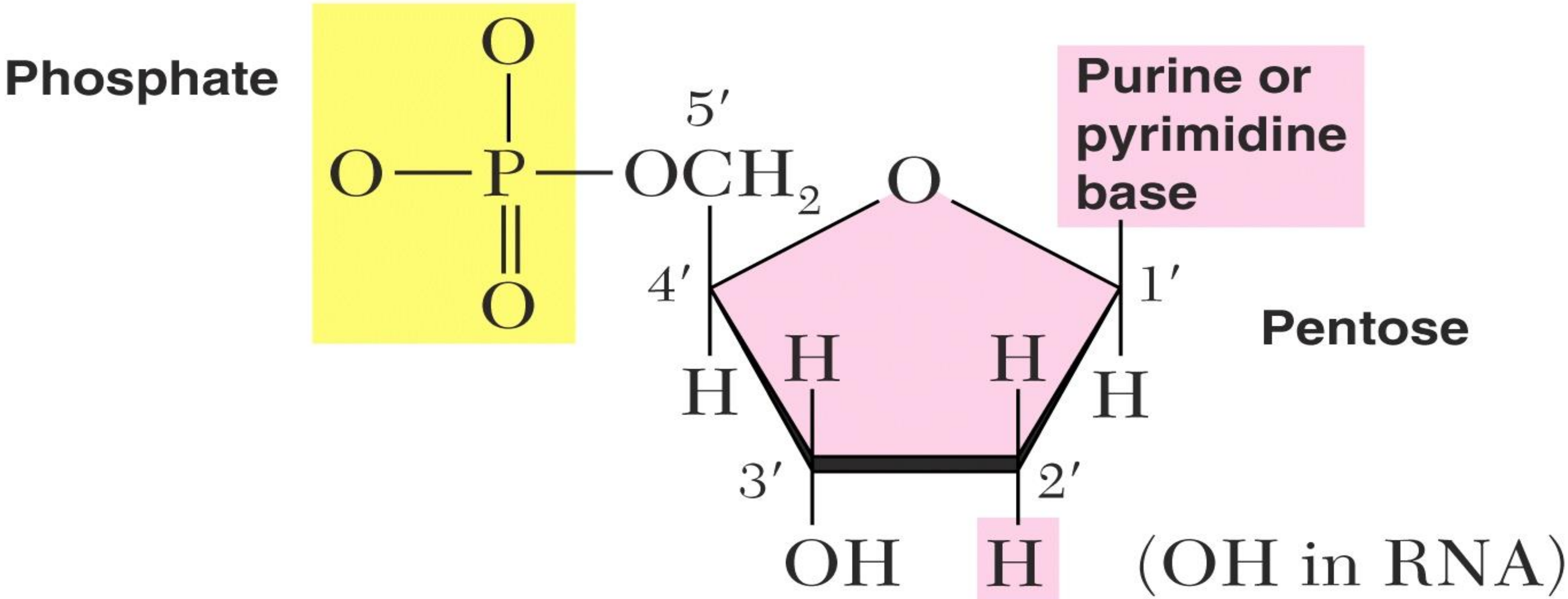
Homework problems

Competitive

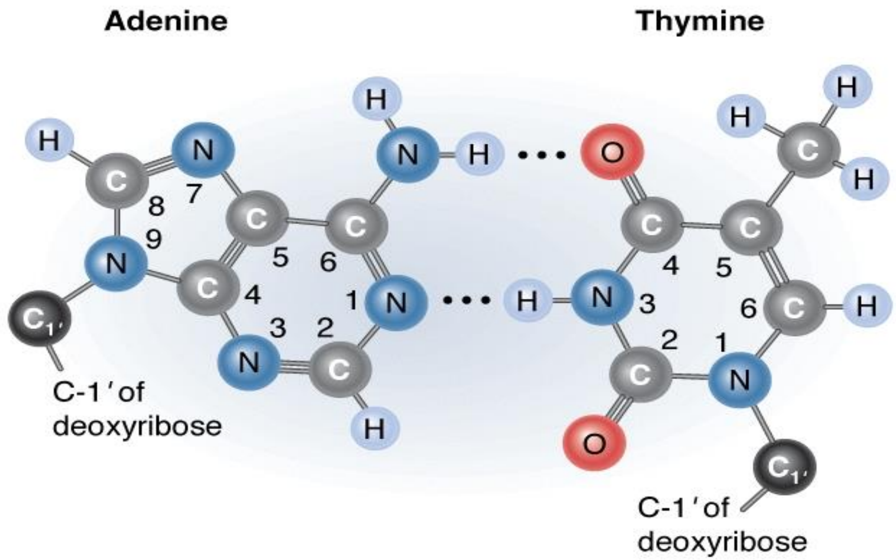
1. Binds at active site
2. Increase [S] removes inhibition
3. Increase [I] more block till saturated
   (alter rate and Increase Km, without a change on Vmax)
4. Slope changes

Non- Competitive

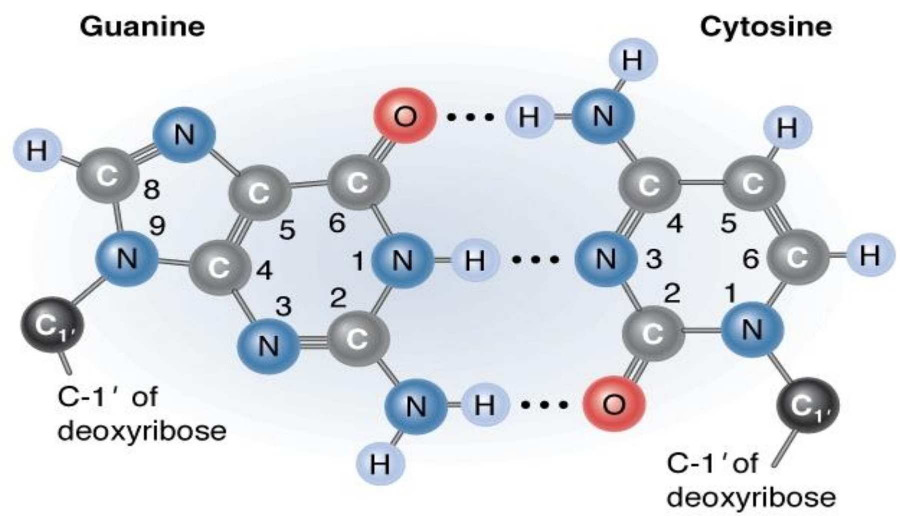
1. Dose not binds at active site
2. Increase [S] no effect
3. Increase [I] more block till saturated
   (no change on Km, but decrease Vmax)
4. Slope changes

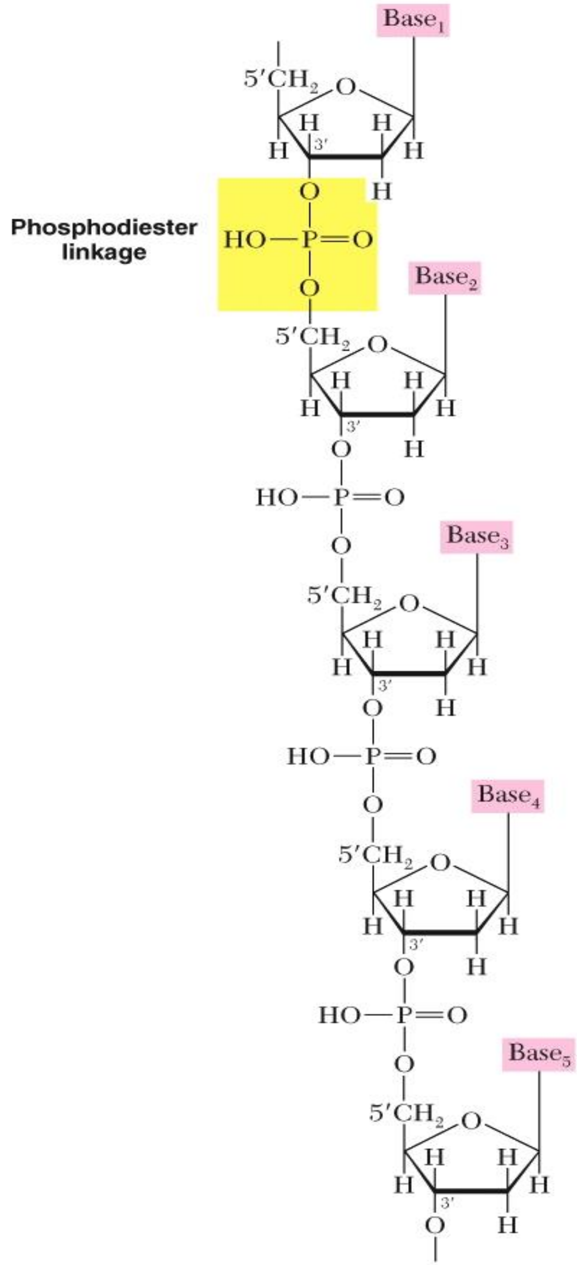

Phosphate
O
O
P
O
OCH2
5′
O
Purine or
pyrimidine
base
4′
1′
Pentose
H
H
H
H
3′
2′
OH
H
(OH in RNA)

ADENINE- THYMINE BASE PAIR

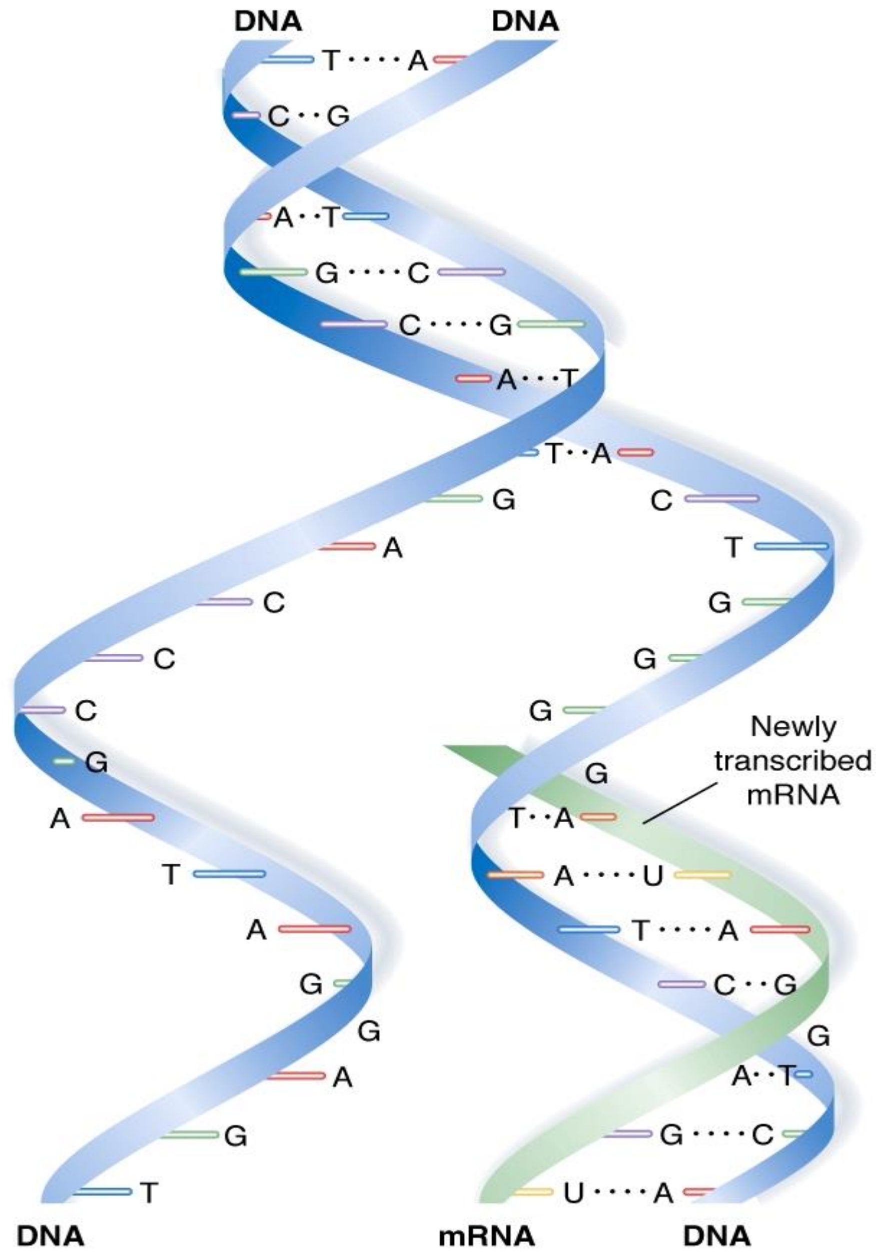


GUANINE - CYTOSINE BASE PAIR

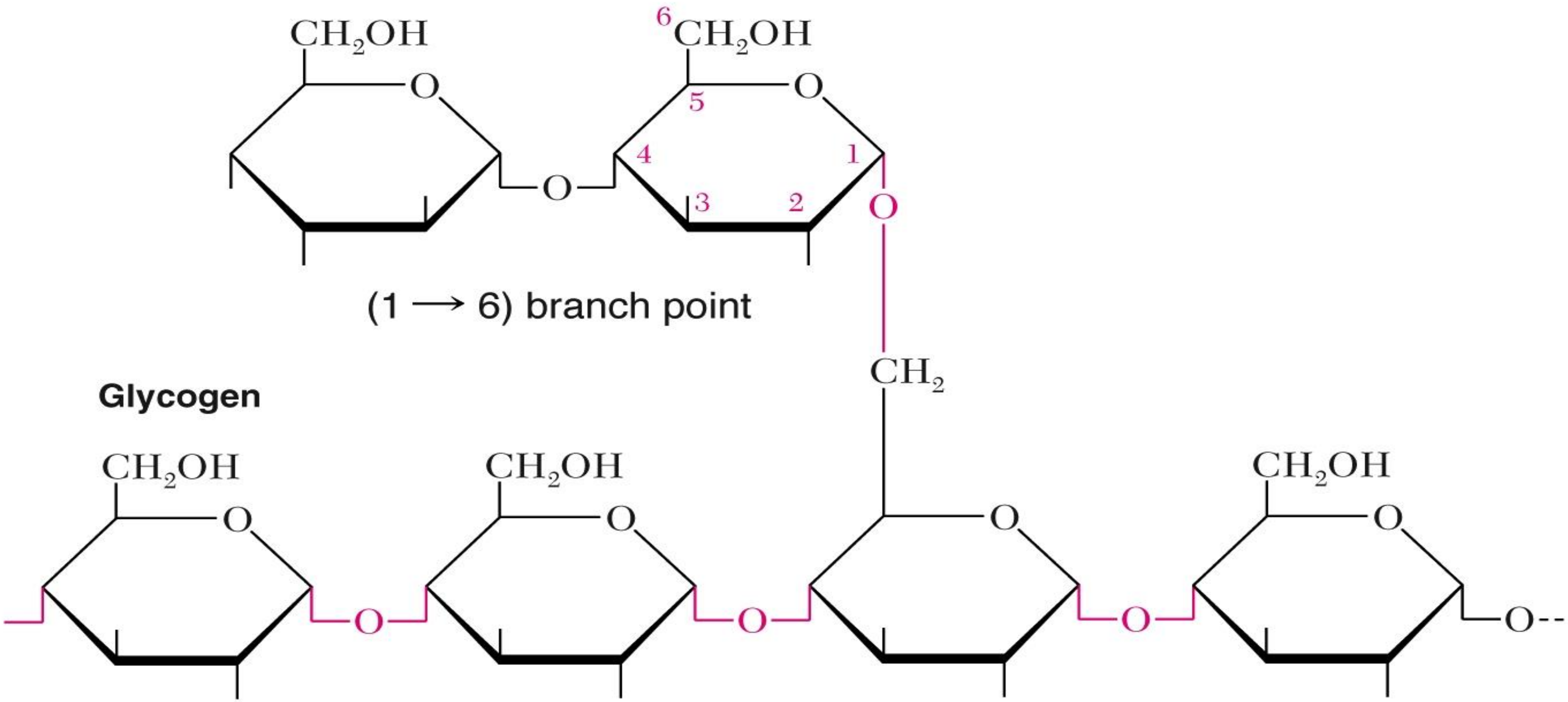




Phosphodiester linkage
Base1
Base2
Base3
Base4
Base5
5′CH2
HO—P=O
3′


DNA
DNA
T····A
C··G
A··T
G····C
C····G
A···T
T··A
G
C
A
T
C
G
C
G
C
G
G
G
A
T··A
T
A····U
A
T····A
G
C··G
G
G
A
A··T
G
G····C
T
U····A
Newly
transcribed
mRNA
DNA
mRNA
DNA

Glycogen



(1 ⟶ 4) chain