بسمه تعالی

کارشناسی ارشد
بیوشیمی و بیولوژی سلول

متابولیسم
(تولید انرژی)

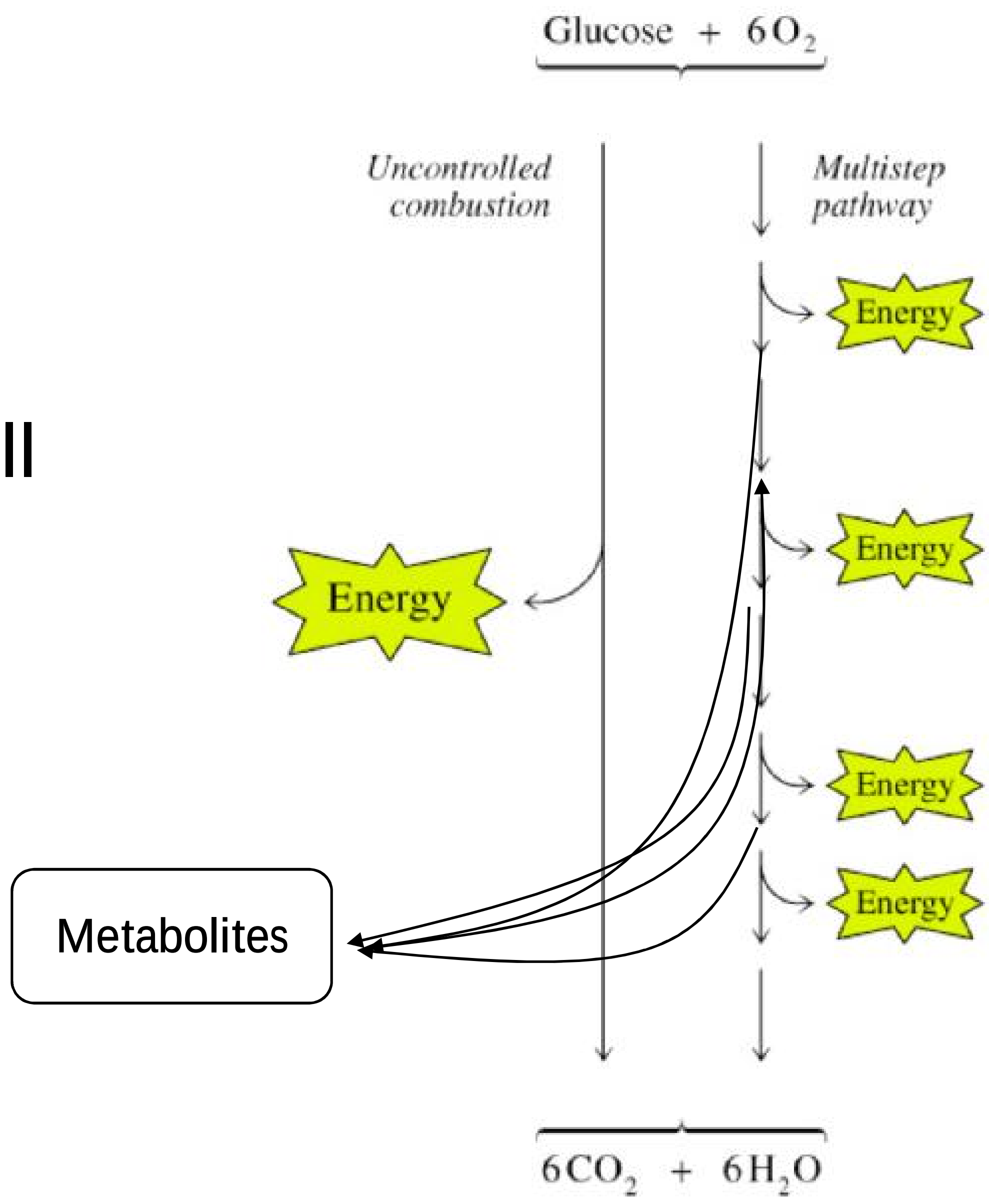
ابراهیم قاسمی

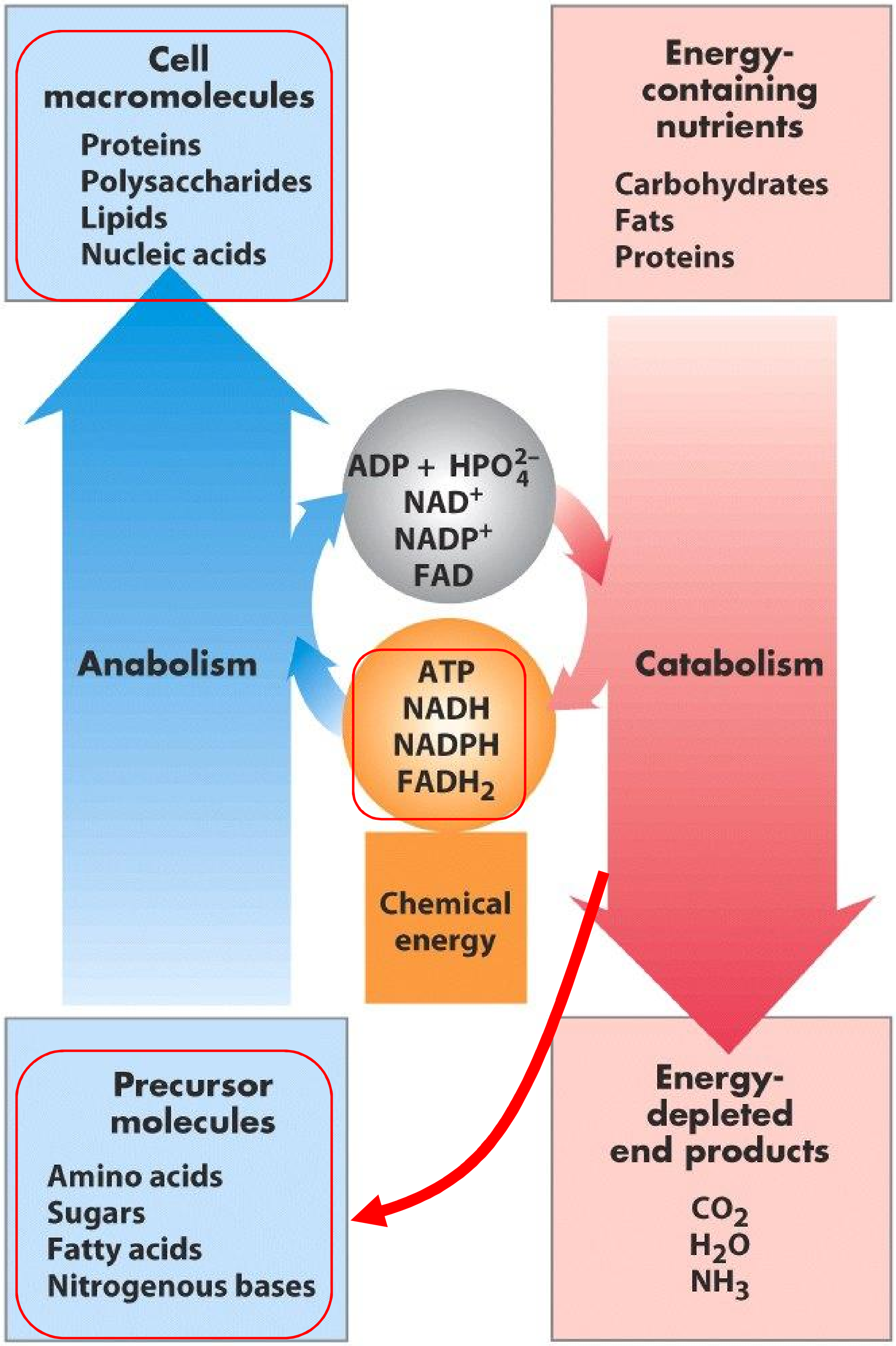
Definition

- Metabolism
- Catabolism (Catabolic reactions)
- Anabolism (Anabolic reactions)
- Metabolites
- Pathway
- Cycle

Metabolism

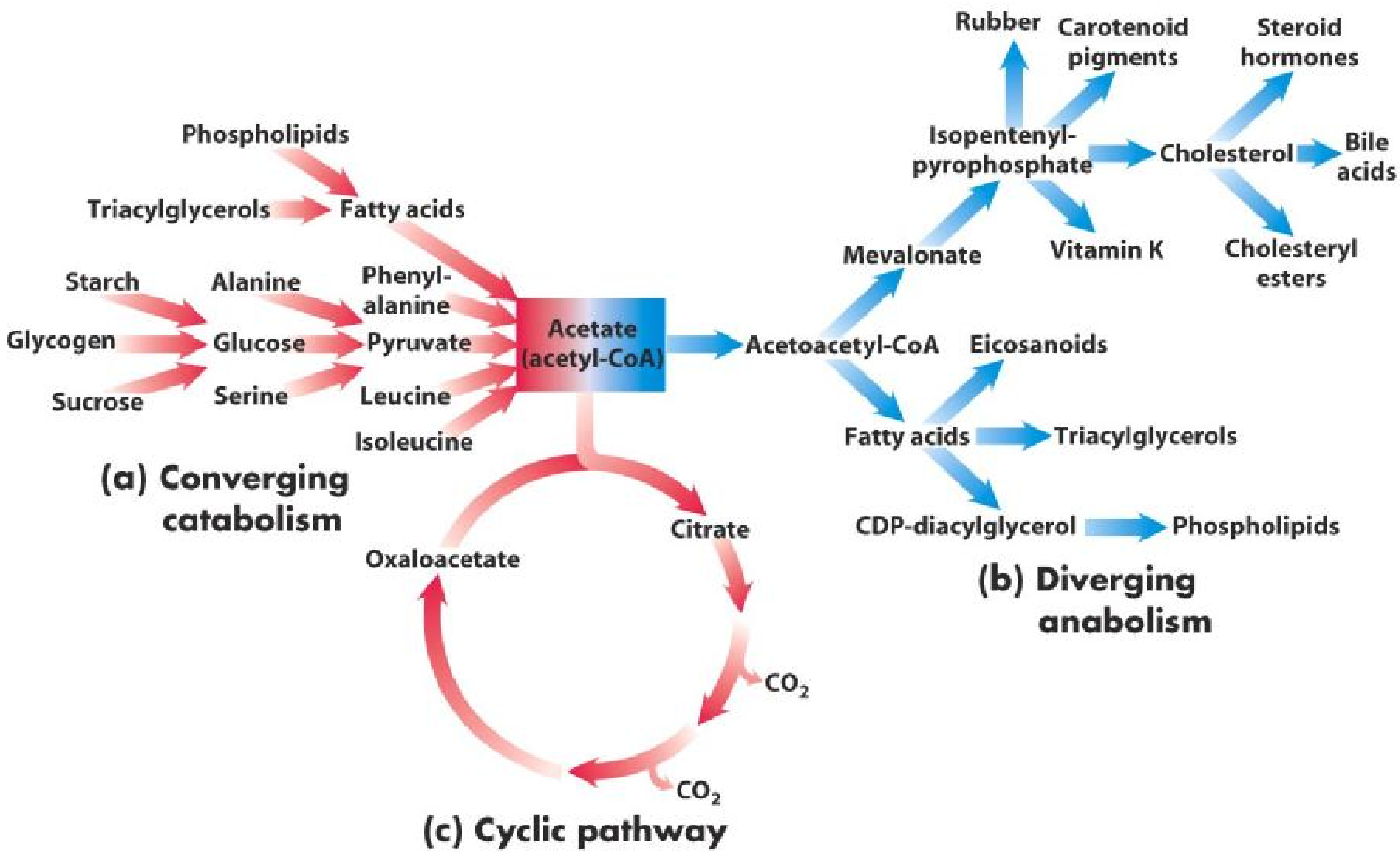
- Sum up all the chemical processes that occur within a cell



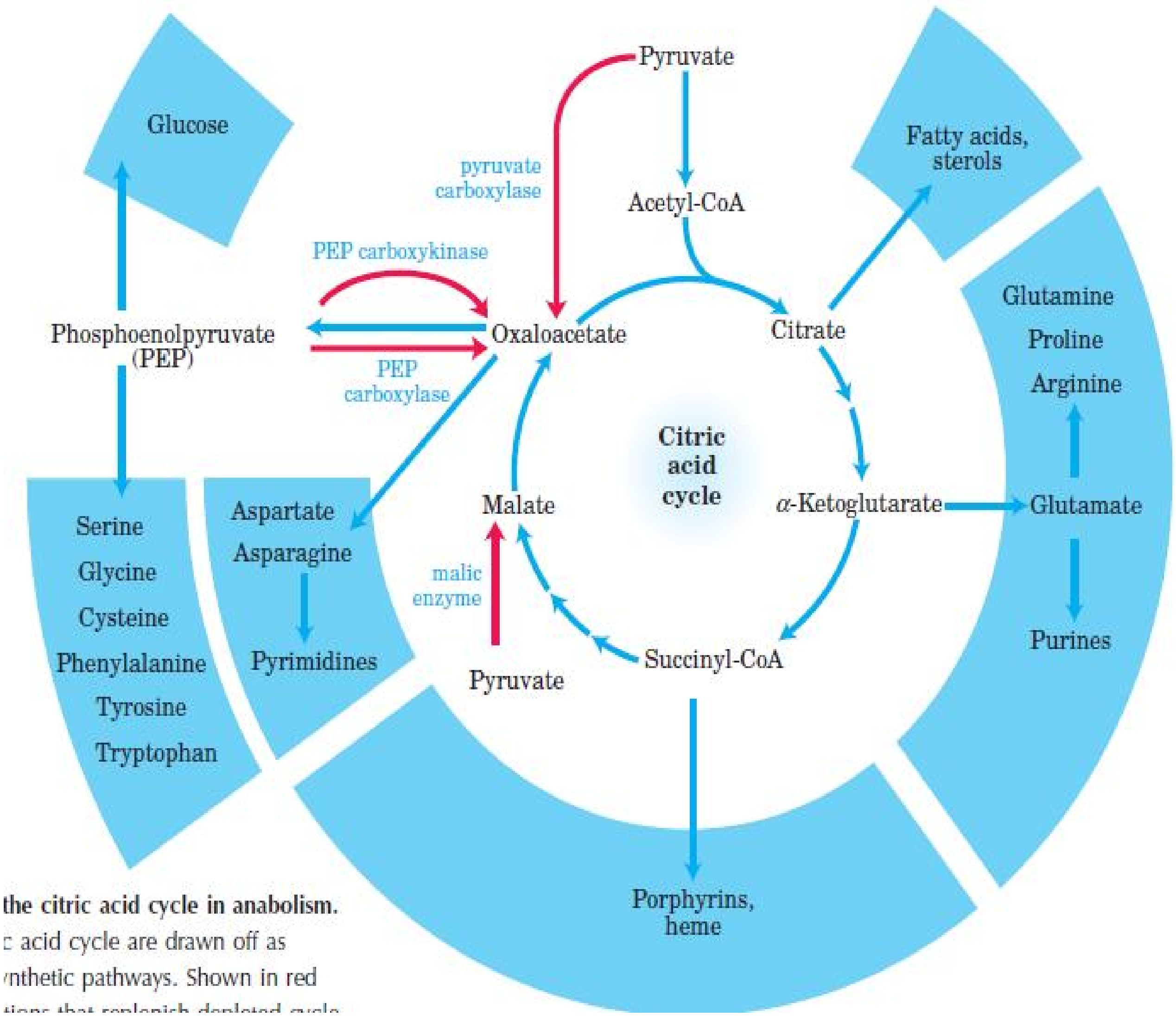


Cell macromolecules
Proteins
Polysaccharides
Lipids
Nucleic acids
Energy-containing nutrients
Carbohydrates
Fats
Proteins
$ADP + HPO_4^{2-}$
NAD^+
$NADP^+$
FAD
Anabolism
Catabolism
ATP
NADH
NADPH
$FADH_2$
Chemical energy
Precursor molecules
Amino acids
Sugars
Fatty acids
Nitrogenous bases
Energy-depleted end products
CO_2
H_2O
NH_3

Catabolism and Anabolism

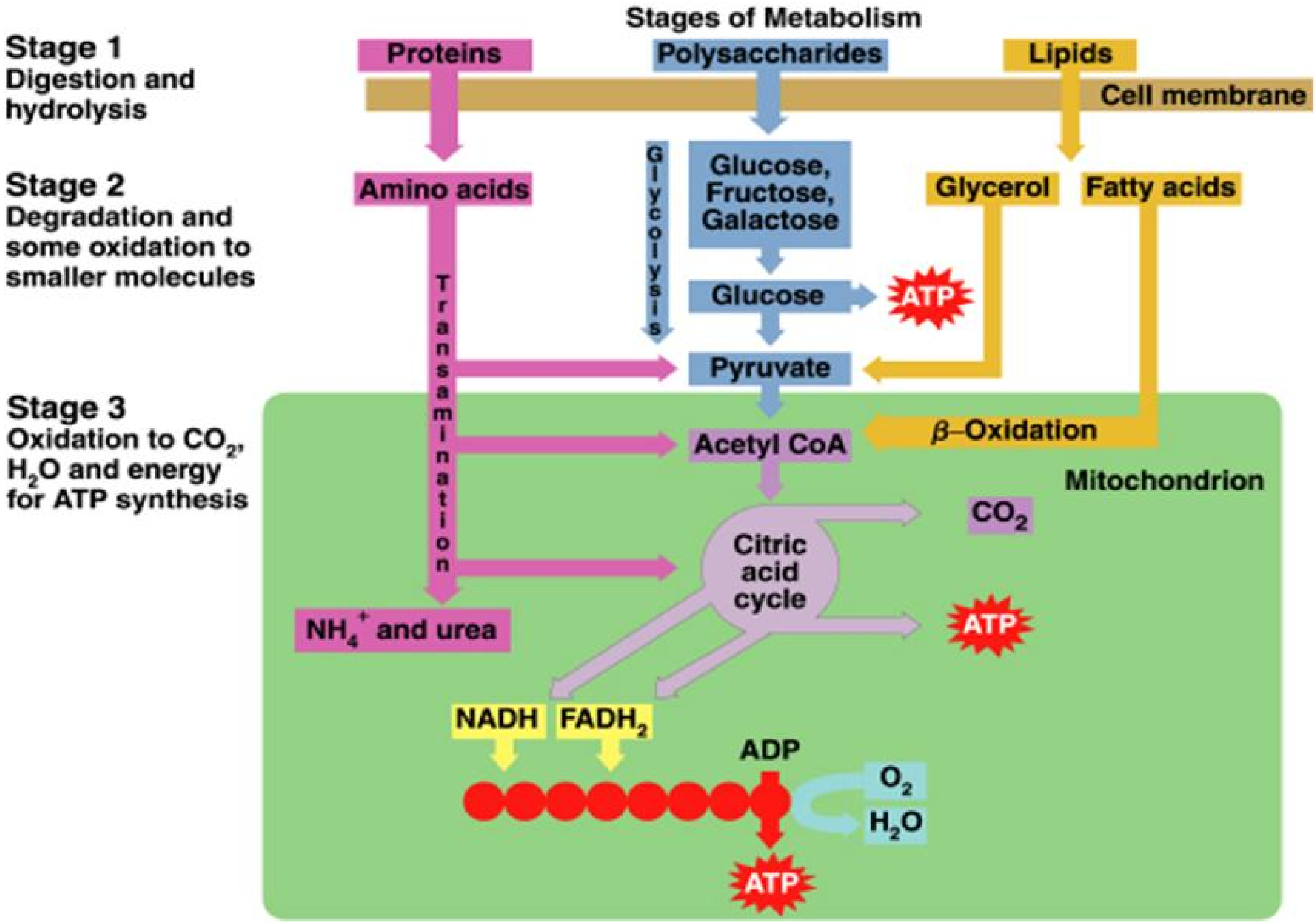


Amphibolic



the citric acid cycle in anabolism.
c acid cycle are drawn off as
ynthetic pathways. Shown in red

Catabolism



Stages of Metabolism
Stage 1
Digestion and hydrolysis
Stage 2
Degradation and some oxidation to smaller molecules
Stage 3
Oxidation to CO_2, H_2O and energy for ATP synthesis
Proteins
Polysaccharides
Lipids
Cell membrane
Amino acids
Glycolysis
Glucose, Fructose, Galactose
Glycerol
Fatty acids
Glucose
ATP
Transamination
Pyruvate
β–Oxidation
Acetyl CoA
Mitochondrion
CO_2
Citric acid cycle
ATP
NH_4^+ and urea
NADH
$FADH_2$
ADP
O_2
H_2O
ATP

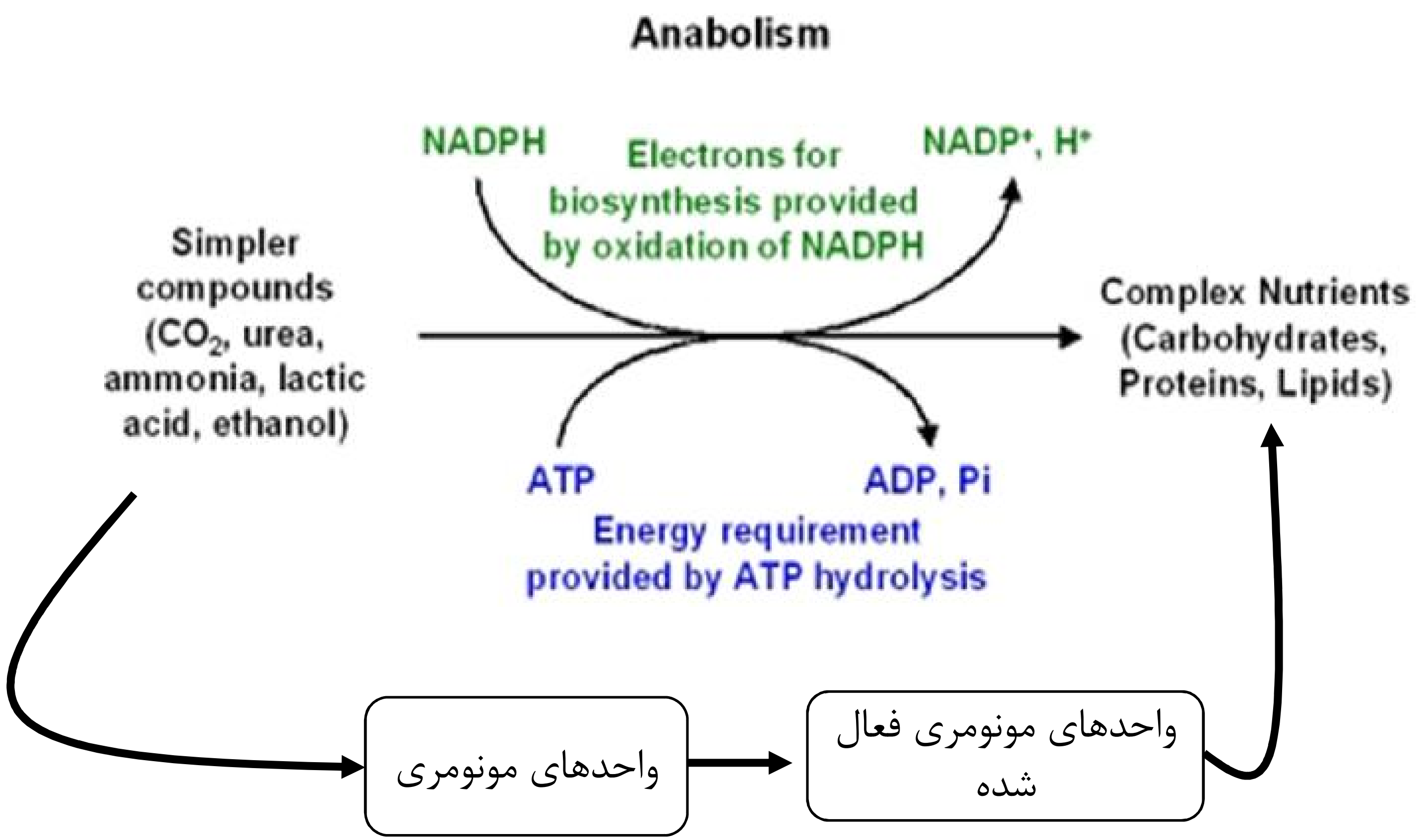
ANABOLISM

- **Anabolic reactions are classified as biosynthetic reactions because they are used to synthesize all the biological molecules needed by the cells of living organisms.**

- **Biosynthetic reactions form the network of pathways that produce the components required by the cell for growth and survival.**

- **These reactions are fueled by the energy stored in high-energy bonds in ATP.**

Anabolism



Anabolism
NADPH
Electrons for biosynthesis provided by oxidation of NADPH
NADP⁺, H⁺
Simpler compounds (CO_2, urea, ammonia, lactic acid, ethanol)
Complex Nutrients (Carbohydrates, Proteins, Lipids)
ATP
ADP, Pi
Energy requirement provided by ATP hydrolysis
واحدهای مونومری
واحدهای مونومری فعال شده

ANABOLISM

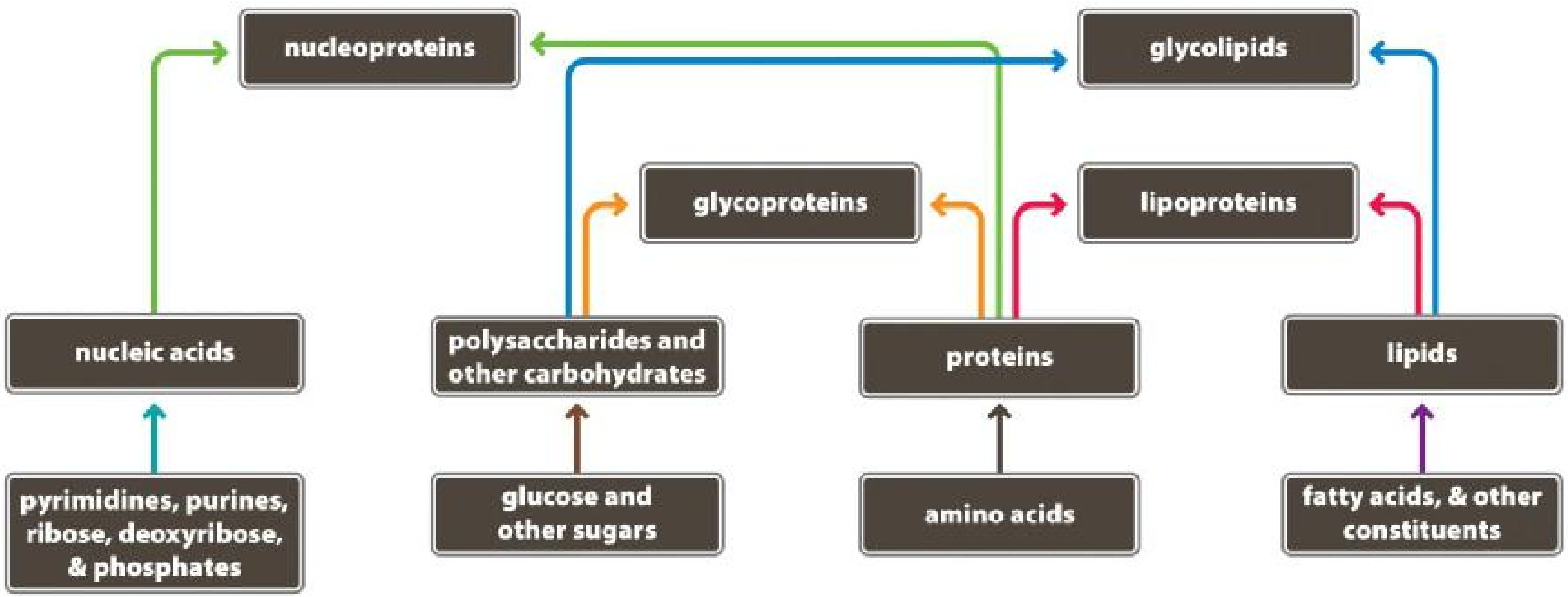


Figure 3.18 Microbiology: A Clinical Approach (© Garland Science)

ATP requirement

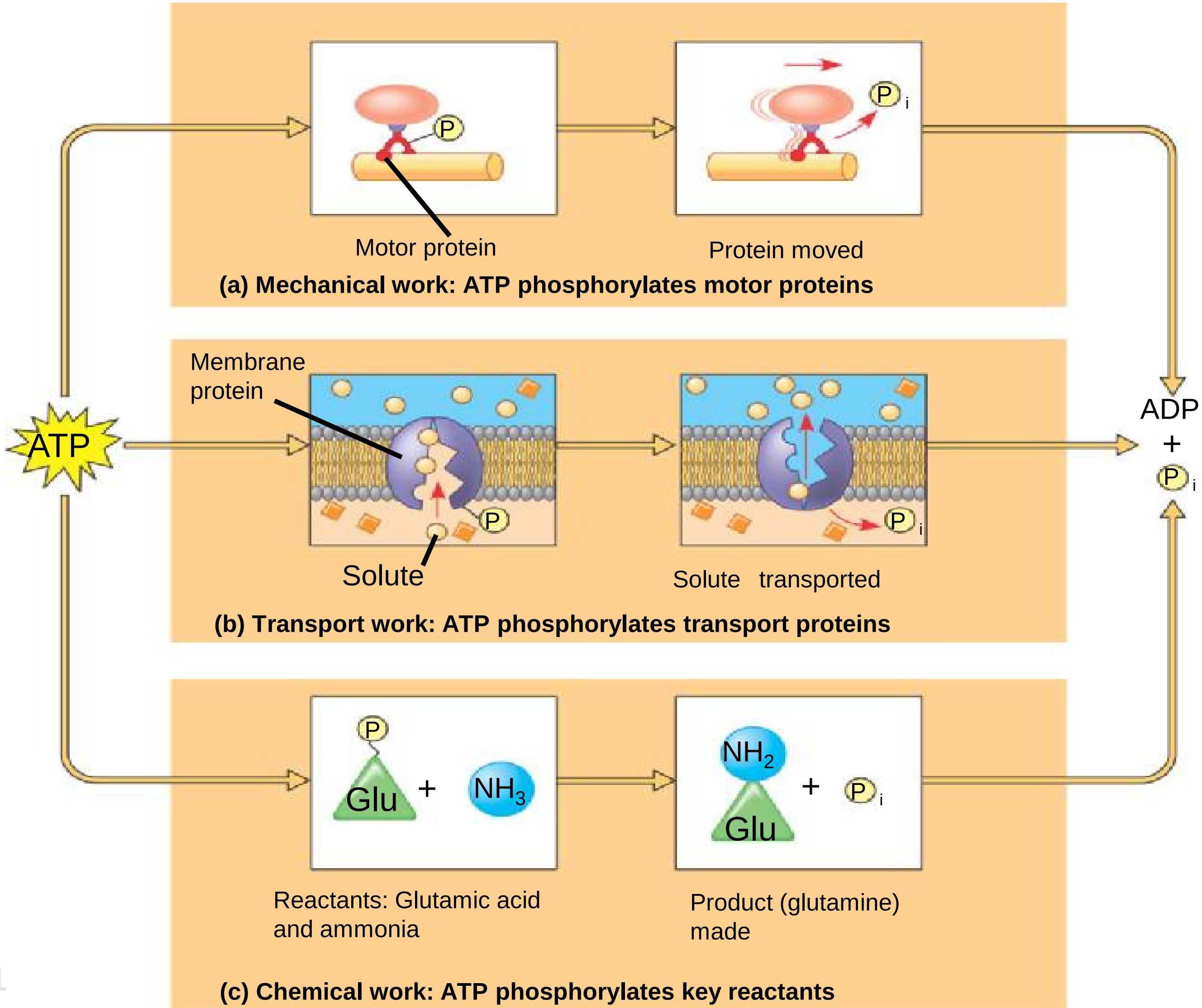


Figure 8.11

ATP need

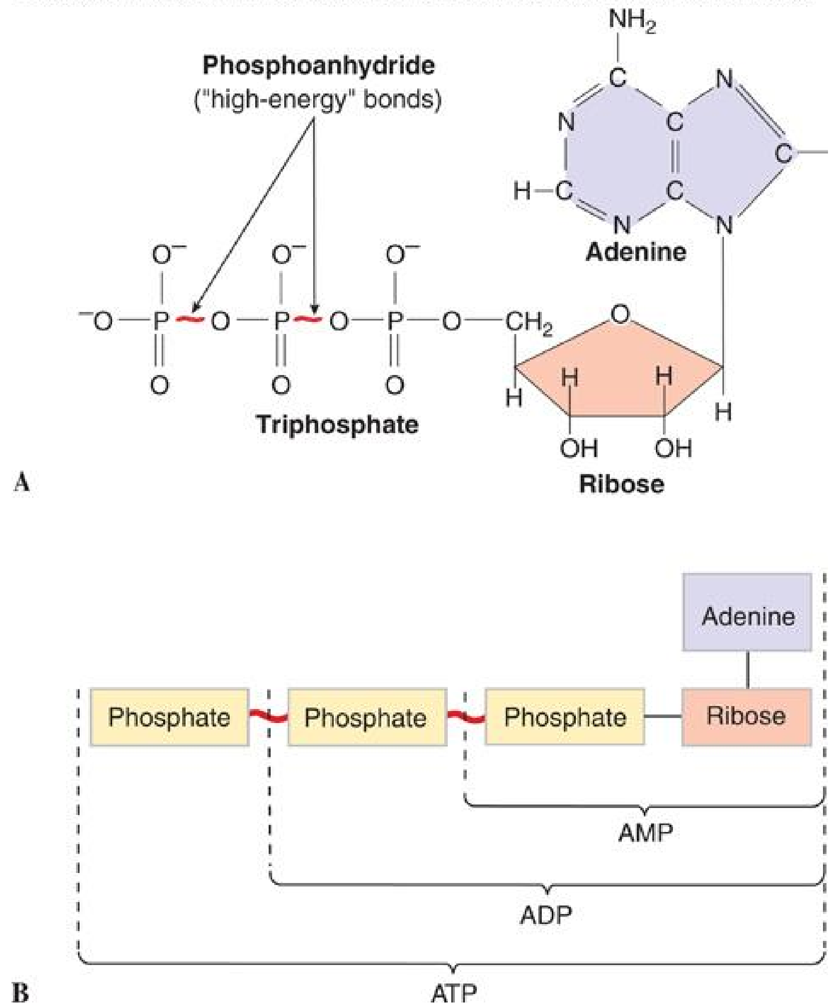
tissue	protein synthesis	Na^+/K^+ ATPase	Ca^{+2} ATPase	other
liver	20%	5-10%	5%	gluconeogenesis (15-40%), substrate recycling (20%), proton leak (20%), urea synthesis (12%)
kidney	6%	40-70%	-	gluconeogenesis (5%)
heart	3%	1-5%	15-30%	actinomyosin ATPase (40-50%), proton leak (15% max)
brain	5%	50-60%	significant	a single cortical action potential was estimated to require 10^8-10^9 ATP, BNID 111183)
skeletal muscle	17%	5-10%	5%	proton leak (50%), nonmitochondrial (14%)

METABOLISM

- **Is used to supply carbon and energy for living functions.**
  - **Growth, …**

ATP

- ATP consists of adenosine (adenine + ribose) and a triphosphate group.
  - The bonds between the phosphate groups are high energy bonds.
  - ATP is very reactive.
  - ATP is not a storehouse of energy – used as soon as it's available.



Organism classification

- Energy sources
  - Phototroph vs. Chemotrophic
- Carbon source
  - Autotroph vs. Heterotroph
- Aerobic vs. Anaerobic vs. Fermentation
  - Electron acceptor
- Anoxygenic vs. oxygenic
  - electron donor

Energy sources

- Phototrophs are the organisms that carry out photon capture to acquire energy

- Chemotrophs: derive their energy from oxidation of a fuel.

Energy (ATP) production: Phosphorylation

1-Substrate Level Phosphorylation

- Direct transfer of phosphate
- Glycolysis

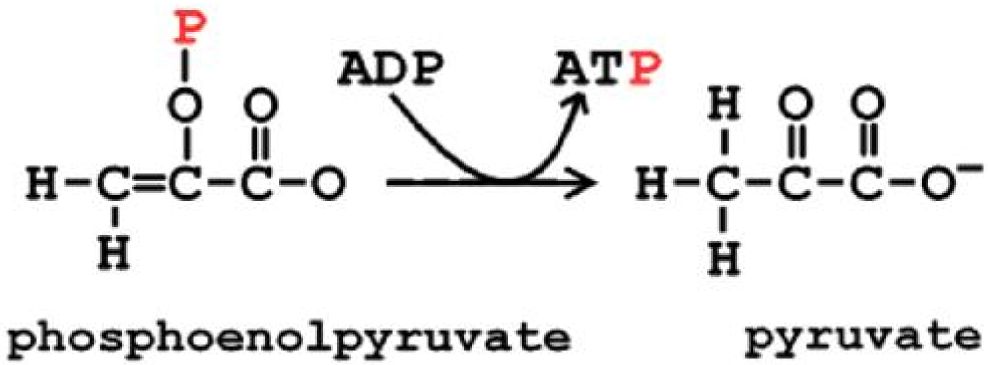
2-Oxidative Phosphorylation

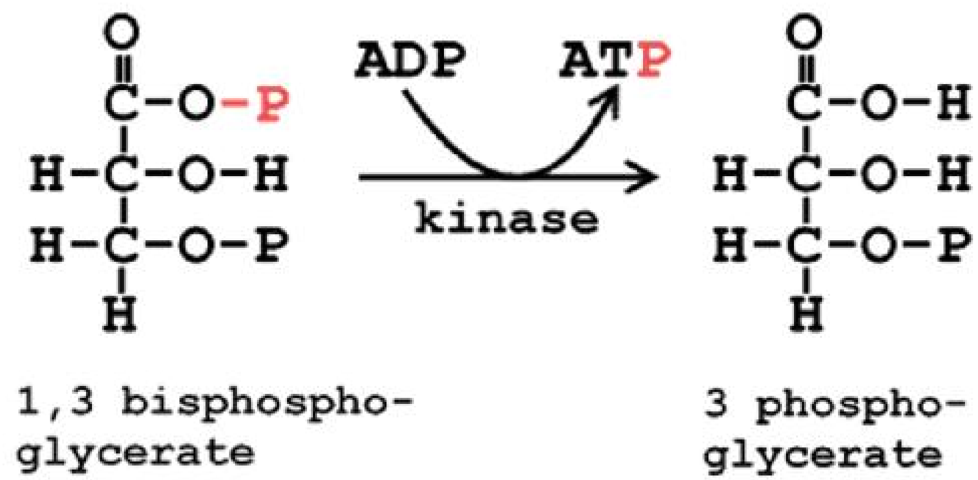
- Electron transfer
- Chemiosmosis

3-Photophosphorylation

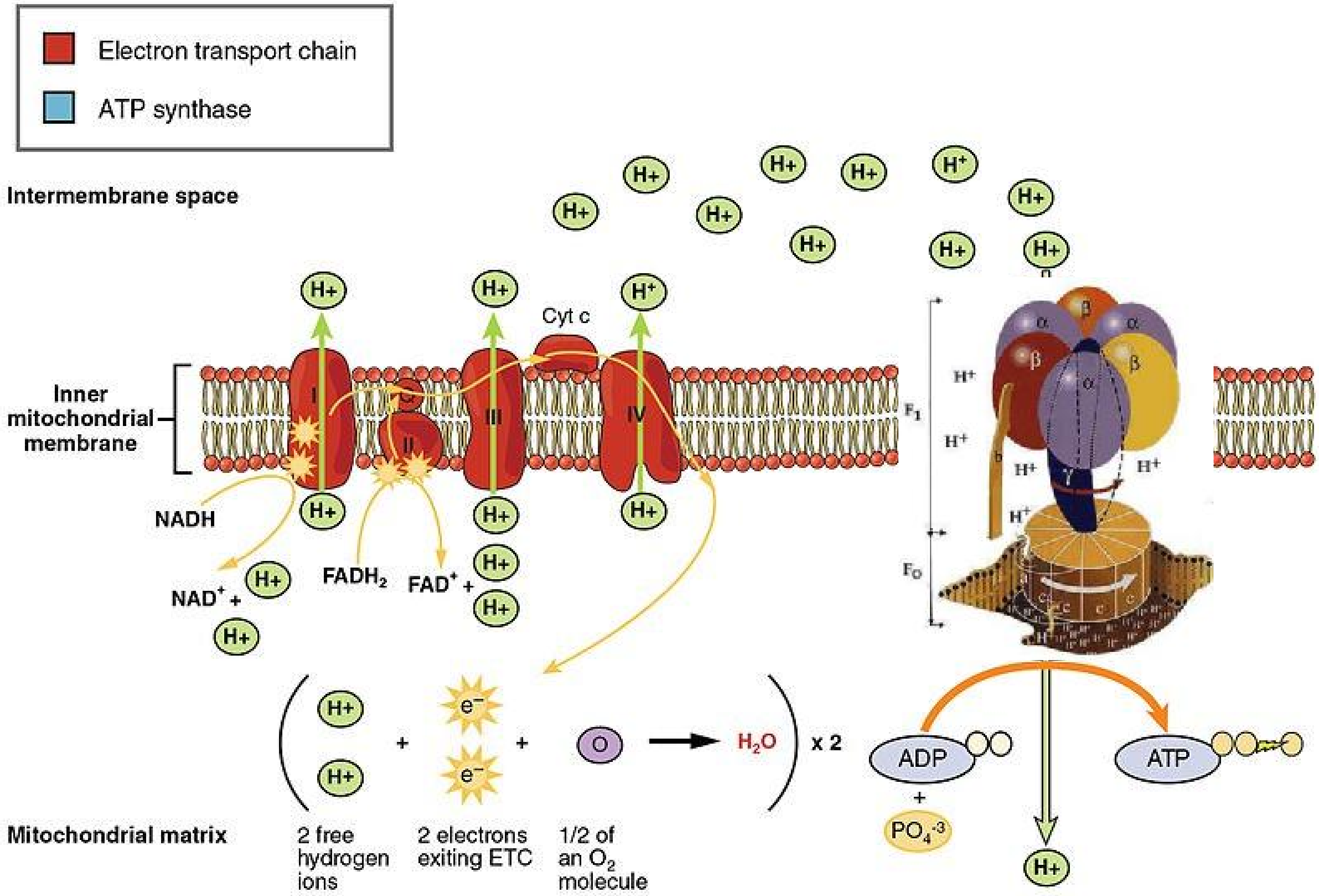
- Light energy to chemical energy

1-Substrate-Level Phosphorylation

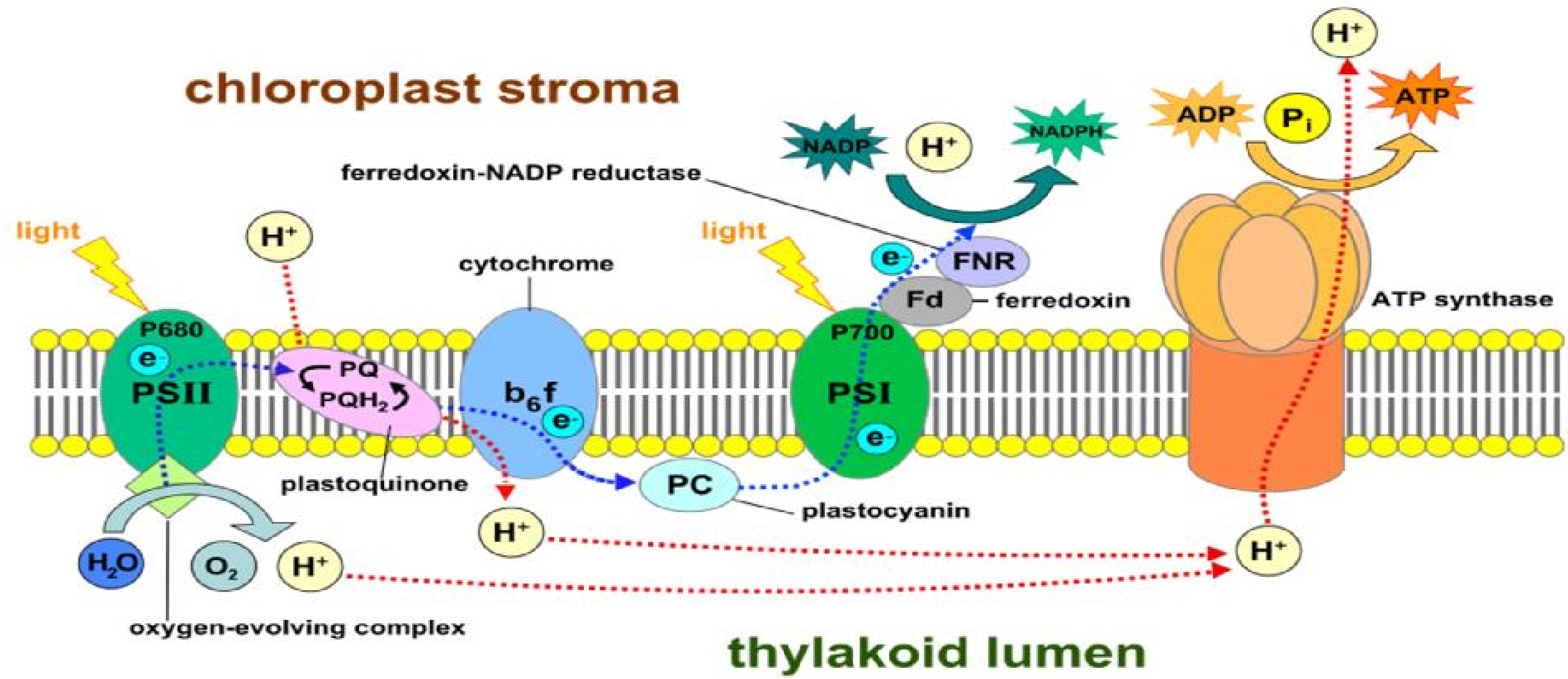


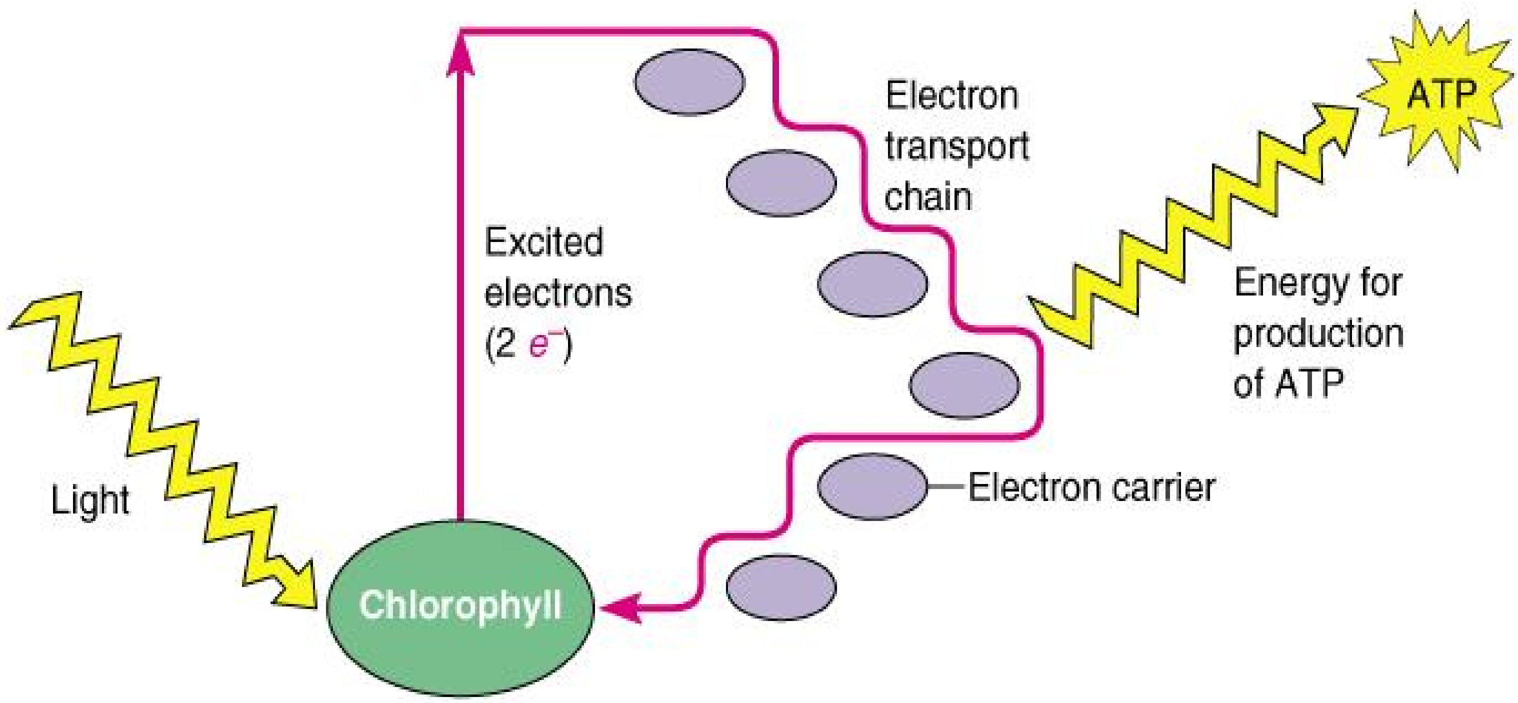


2- Oxidative Phosphorylation

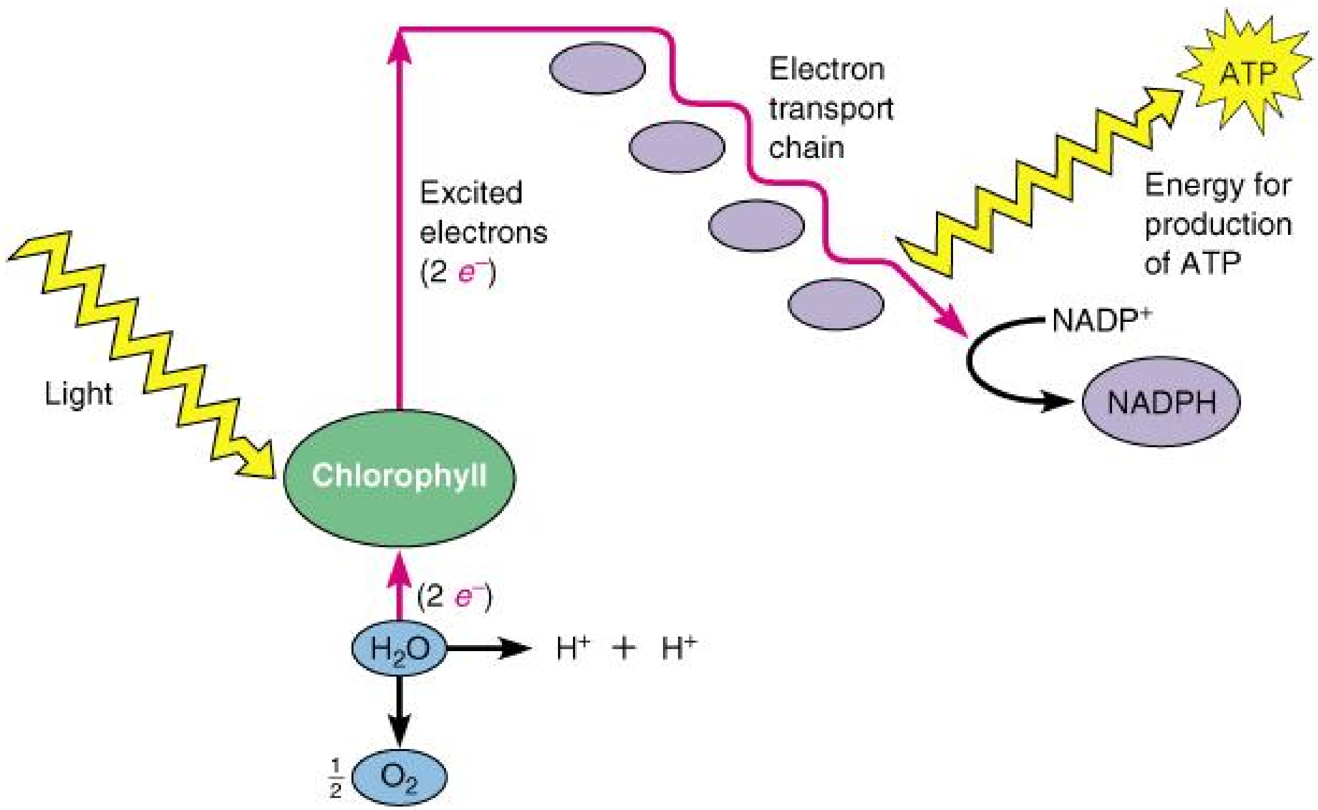


3-Photophosphorylation



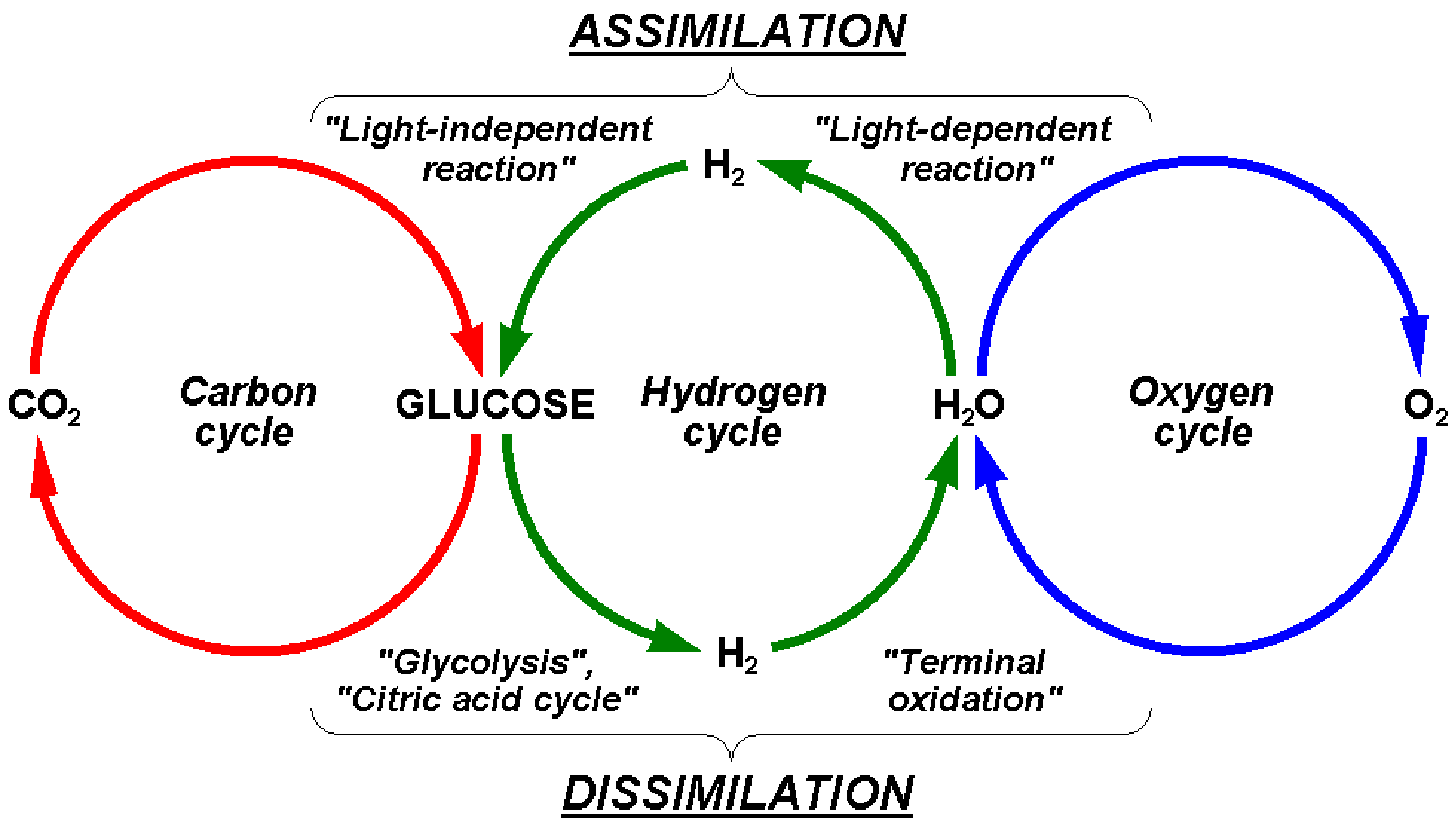


(a) Cyclic photophosphorylation



(b) Noncyclic photophosphorylation

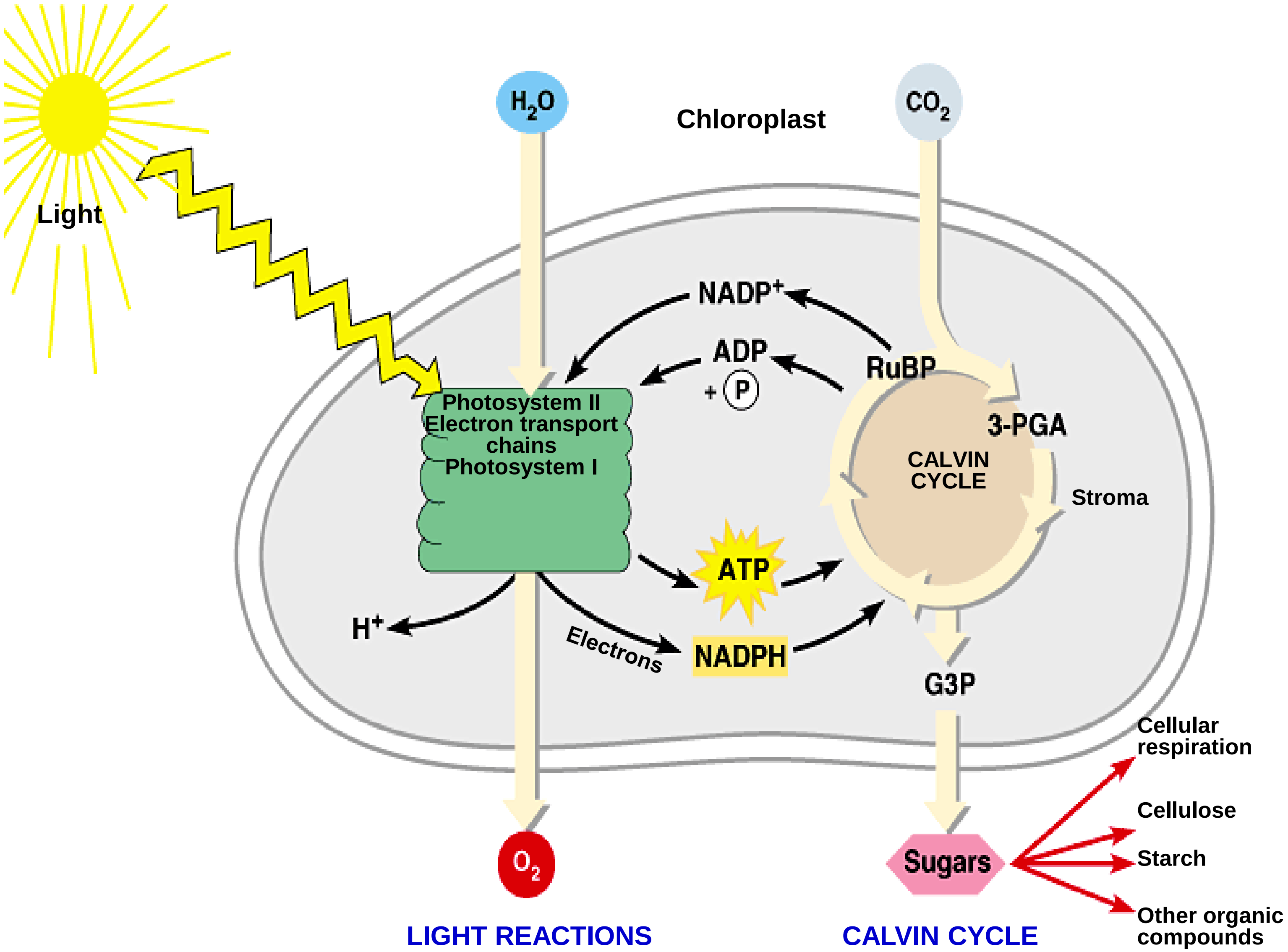
Carbon cycle



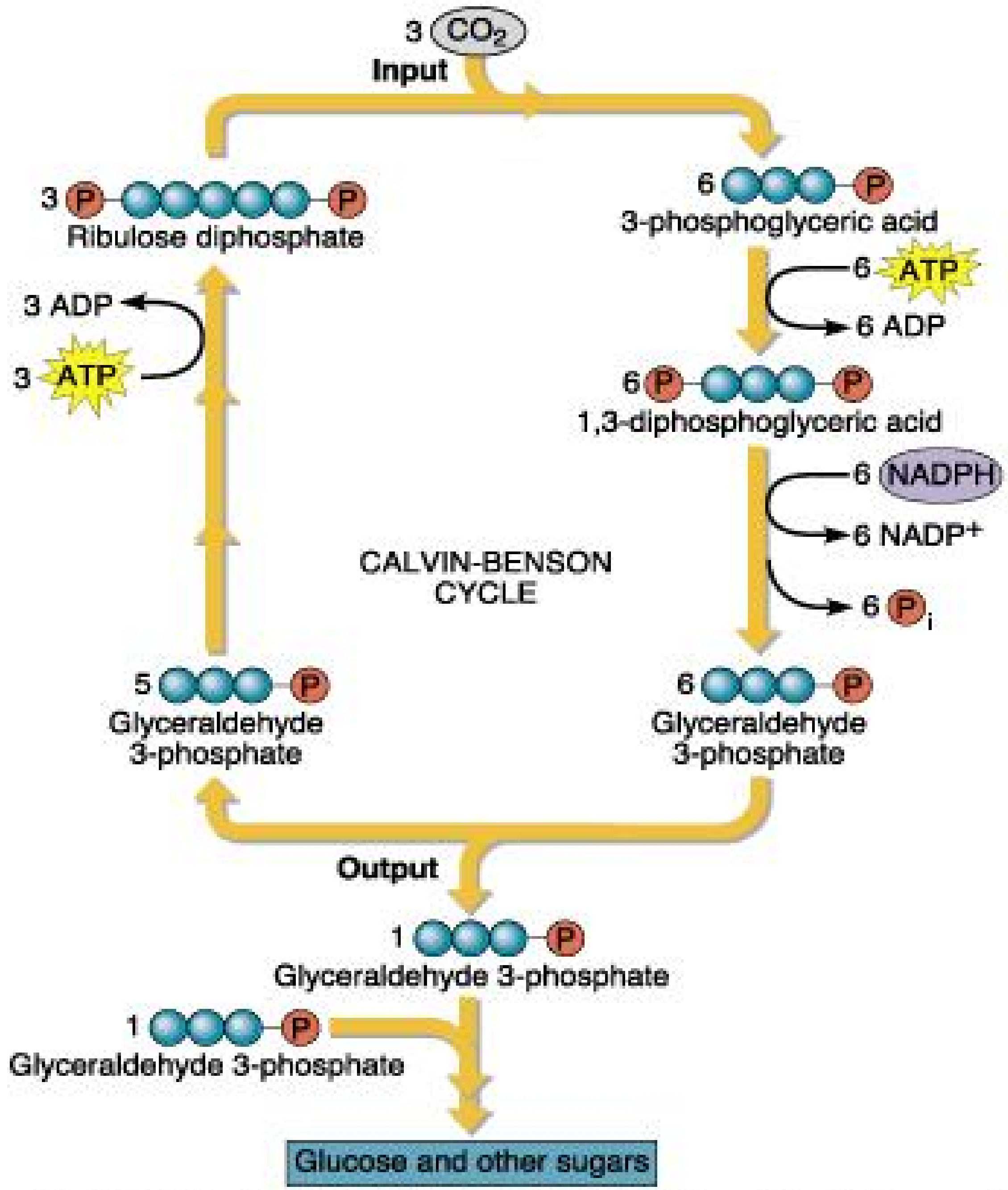
Carbon source

- **There are two processes by which carbon can be obtained:**
  - **Autotrophy – carbon is obtained from inorganic substances (e.g. plants using CO_2 to make sugar)**
  - **Heterotrophy – carbon is obtained from other organic molecules**

Autotroph



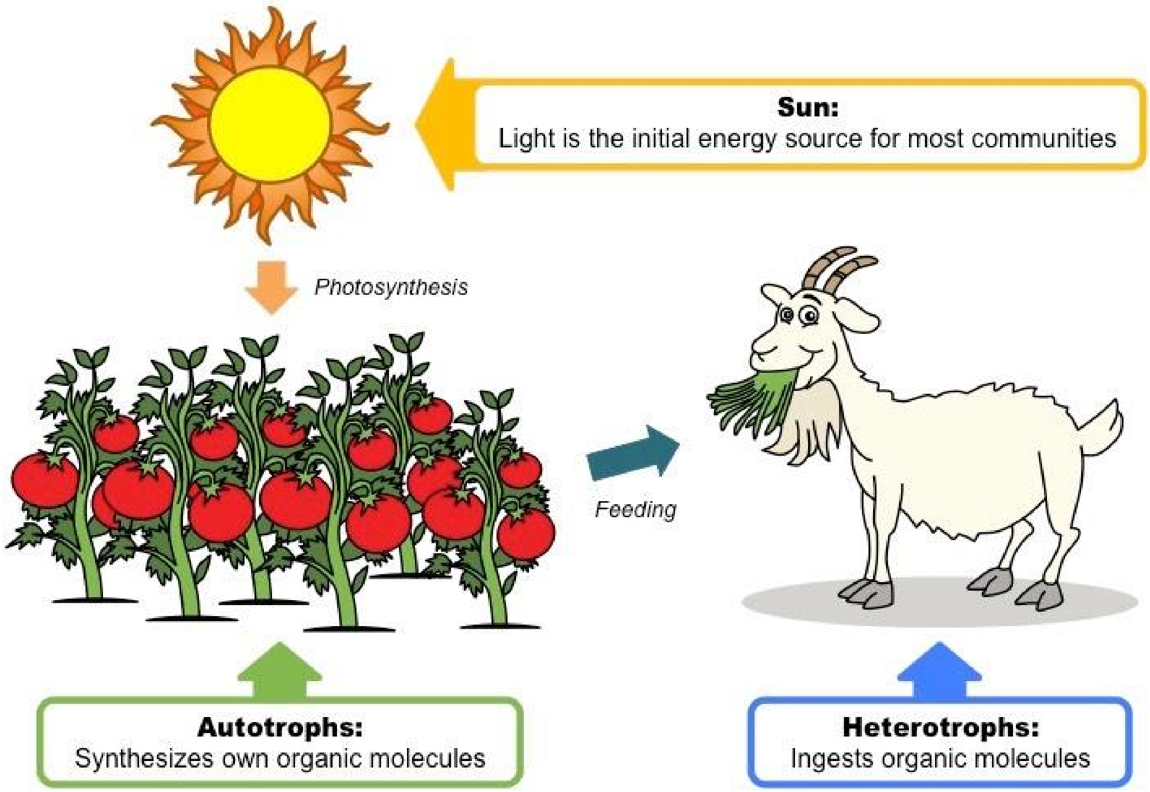
Light
H_2O
Chloroplast
CO_2
$NADP^+$
ADP
+ P
RuBP
3-PGA
Photosystem II
Electron transport chains
Photosystem I
CALVIN CYCLE
Stroma
ATP
H^+
Electrons
NADPH
G3P
Cellular respiration
Cellulose
Starch
Other organic compounds
O_2
Sugars
LIGHT REACTIONS
CALVIN CYCLE

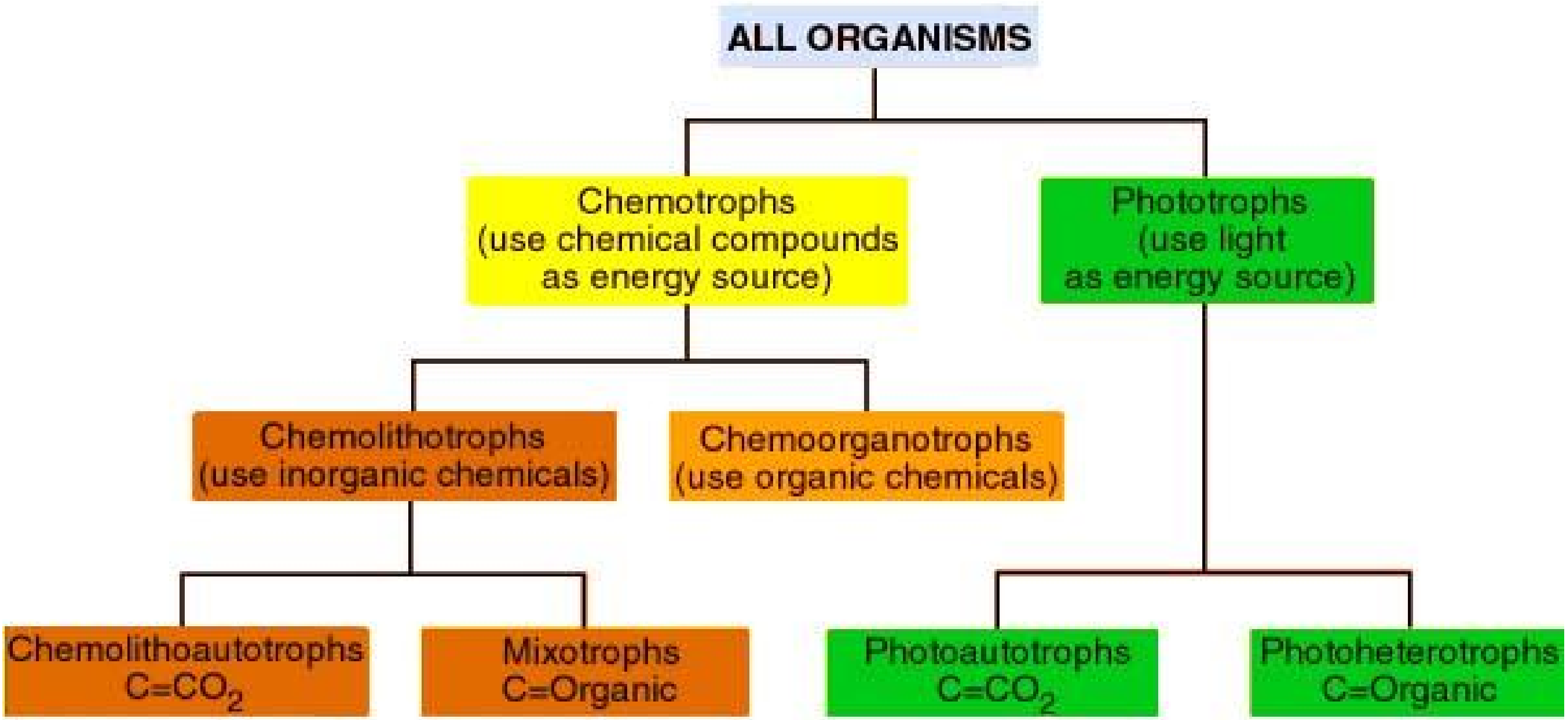


3 CO_2
Input
3 P P
Ribulose diphosphate
6 P
3-phosphoglyceric acid
6 ATP
6 ADP
3 ADP
3 ATP
6 P P
1,3-diphosphoglyceric acid
6 NADPH
6 $NADP^+$
6 P_i
CALVIN-BENSON
CYCLE
5 P
Glyceraldehyde
3-phosphate
6 P
Glyceraldehyde
3-phosphate
Output
1 P
Glyceraldehyde 3-phosphate
1 P
Glyceraldehyde 3-phosphate
Glucose and other sugars

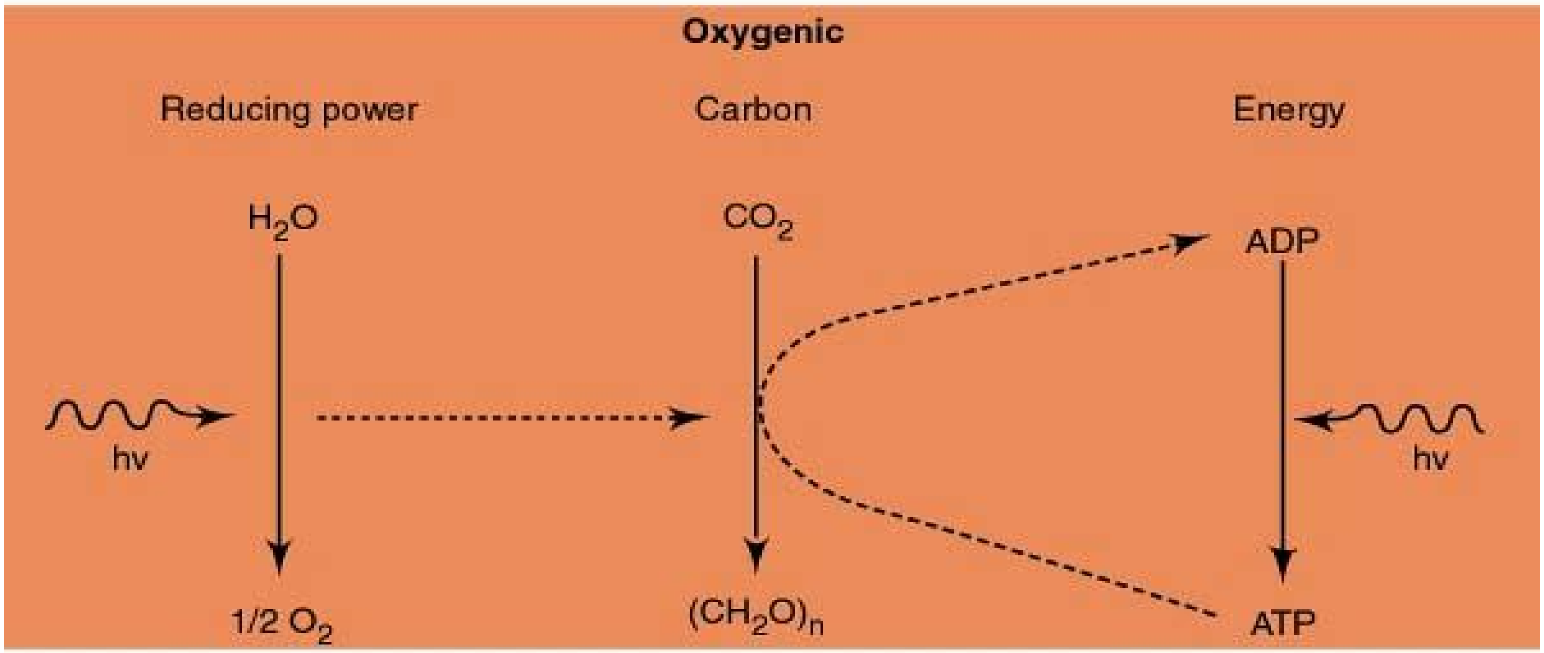
Autotroph and Heterotroph

- Autotroph (Photosynthesis) vs. Heterotroph

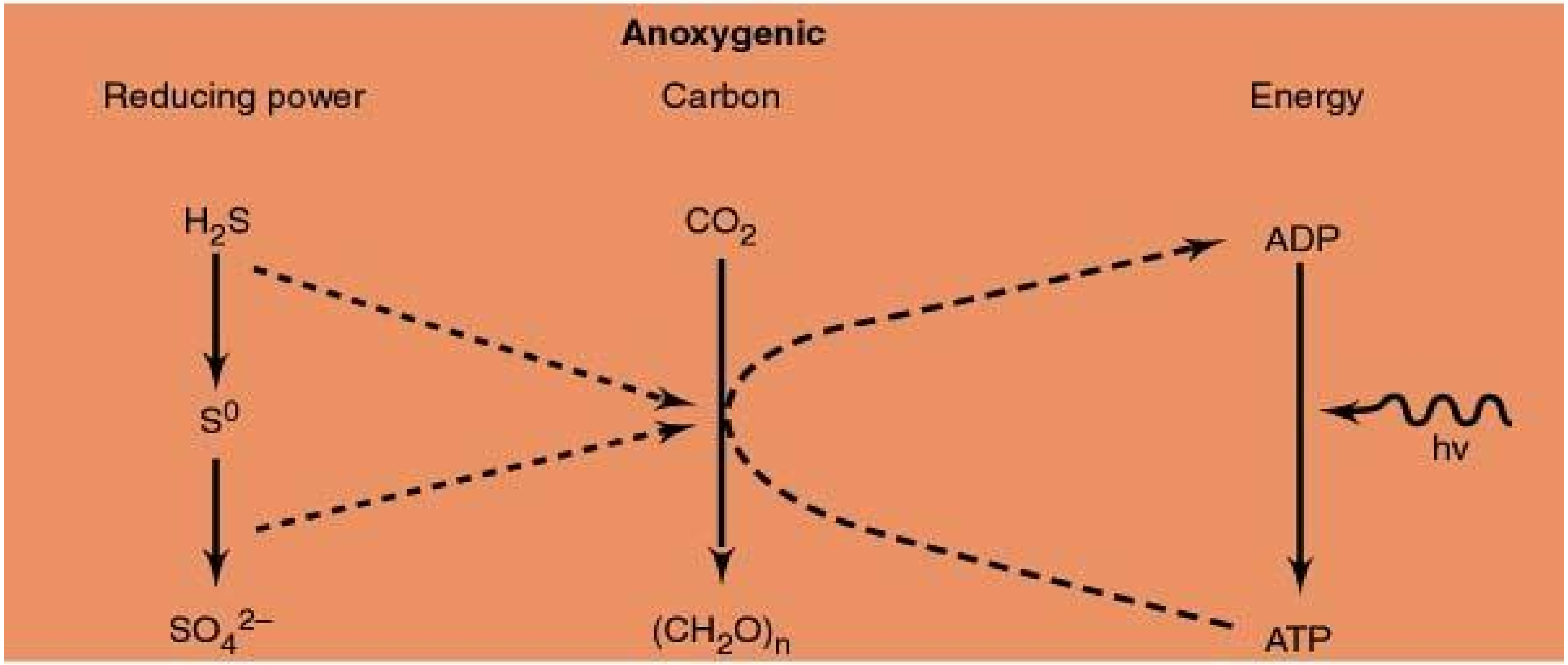



ALL ORGANISMS
Chemotrophs
(use chemical compounds
as energy source)
Phototrophs
(use light
as energy source)
Chemolithotrophs
(use inorganic chemicals)
Chemoorganotrophs
(use organic chemicals)
Chemolithoautotrophs
$C=CO_2$
Mixotrophs
C=Organic
Photoautotrophs
$C=CO_2$
Photoheterotrophs
C=Organic

Anoxygenic versus oxygenic phototrophs



Anoxygenic versus oxygenic phototrophs

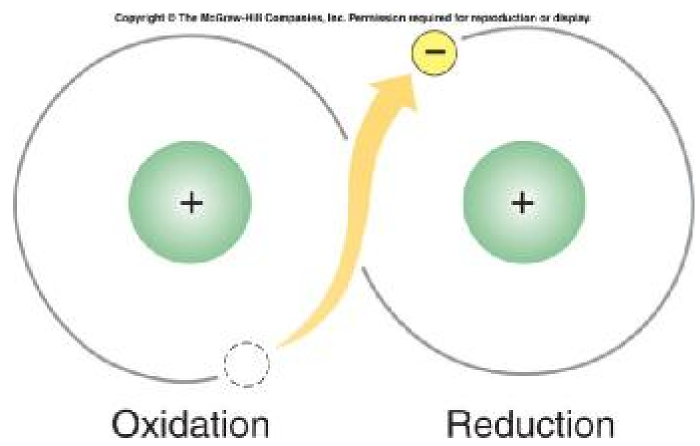


Cellular Respiration (heterotroph)

- The oxidation of food molecules to obtain energy from nutrients into adenosine triphosphate (ATP)

- Oxidation (Nutrients) and reduction reactions always occur together.

- Energy is transferred from one atom to another via redox reactions.



Oxidation of nutrients

- **Aerobes: Use molecular oxygen as the final electron acceptor**
  - **Almost 20 times more energy is released than if another acceptor is used (anaerobes).**

- **Anaerobes: Use other molecules as final electron acceptor**
  - **Inorganic acceptor except O_2: Anaerobic respiration**
  - **Endogenous organic molecules: Fermentation**

- **In some occasions: Fermentation is regarded as Anaerobic respiration**

Electron acceptor

Table 5.4 Comparison of Aerobic Respiration, Anaerobic Respiration, and Fermentation

	Aerobic Respiration	Anaerobic Respiration	Fermentation
Oxygen required	Yes	No	No
Type of phosphorylation	Substrate-level and oxidative	Substrate-level and oxidative	Substrate-level
Final electron (hydrogen) acceptor	Oxygen	NO_3^-, SO_4^{2-}, CO_3^{2-}, or exogenous organic molecules	Endogenous organic molecules
Potential molecules of ATP produced	36–38	2–36	2

Nutrients

- Glucose
- Fatty acids
- Amino acids

Aerobic respiration

- **Glycolysis, β-oxidation, Trans-amination**

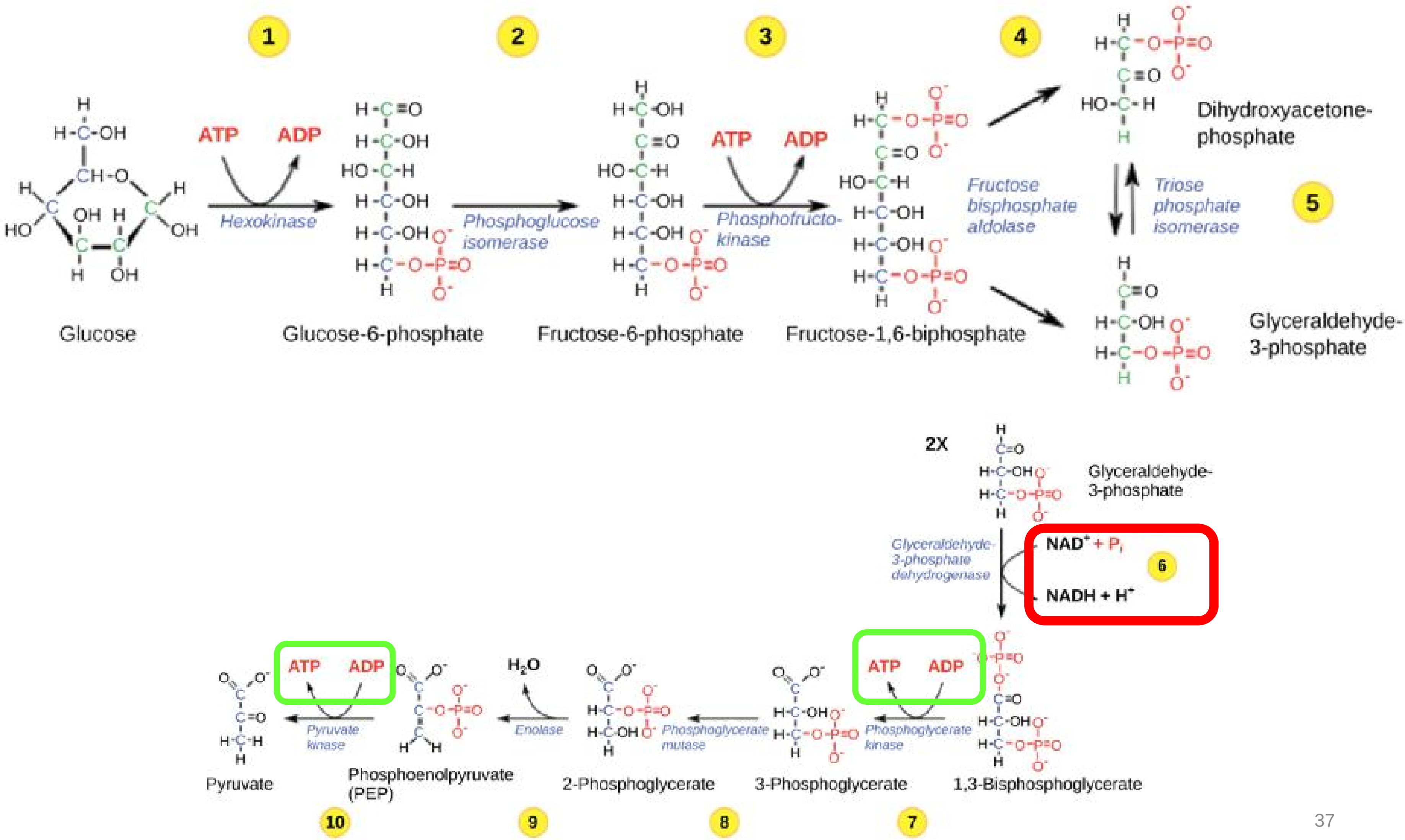
- **Krebs cycle**

- **Electron transport chain**

Glycolysis

- All living organisms use glycolysis.
  - Begins after stores of phosphagens (ATP, creatine phosphate, arginine phosphate – cephalopods) are depleted
  - begins rapidly after initiation of activity or exposure to hypoxia/anoxia
  - Glucose ® 2 moles ATP per mole glucose
  - Glycogen ® 3 moles ATP per mole glucose

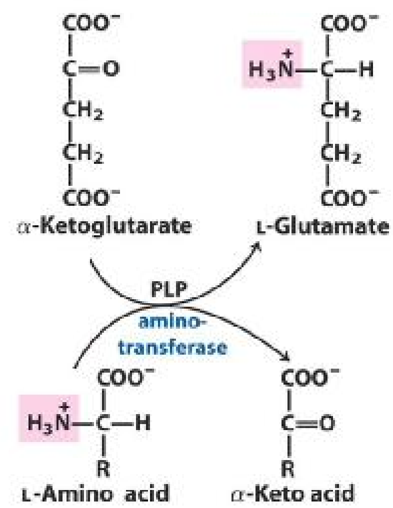
Glycolysis

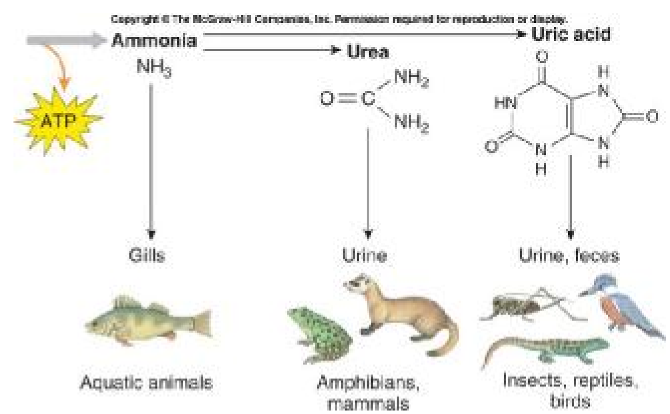

1
2
3
4
5
ATP
ADP
Hexokinase
Phosphoglucose isomerase
Phosphofructo-kinase
Fructose bisphosphate aldolase
Triose phosphate isomerase
Glucose
Glucose-6-phosphate
Fructose-6-phosphate
Fructose-1,6-biphosphate
Dihydroxyacetone-phosphate
Glyceraldehyde-3-phosphate
2X
Glyceraldehyde-3-phosphate dehydrogenase
NAD+ + Pi
NADH + H+
6
Pyruvate
Phosphoenolpyruvate (PEP)
2-Phosphoglycerate
3-Phosphoglycerate
1,3-Bisphosphoglycerate
Pyruvate kinase
Enolase
Phosphoglycerate mutase
Phosphoglycerate kinase
H2O
10
9
8
7

Amino acids transamination

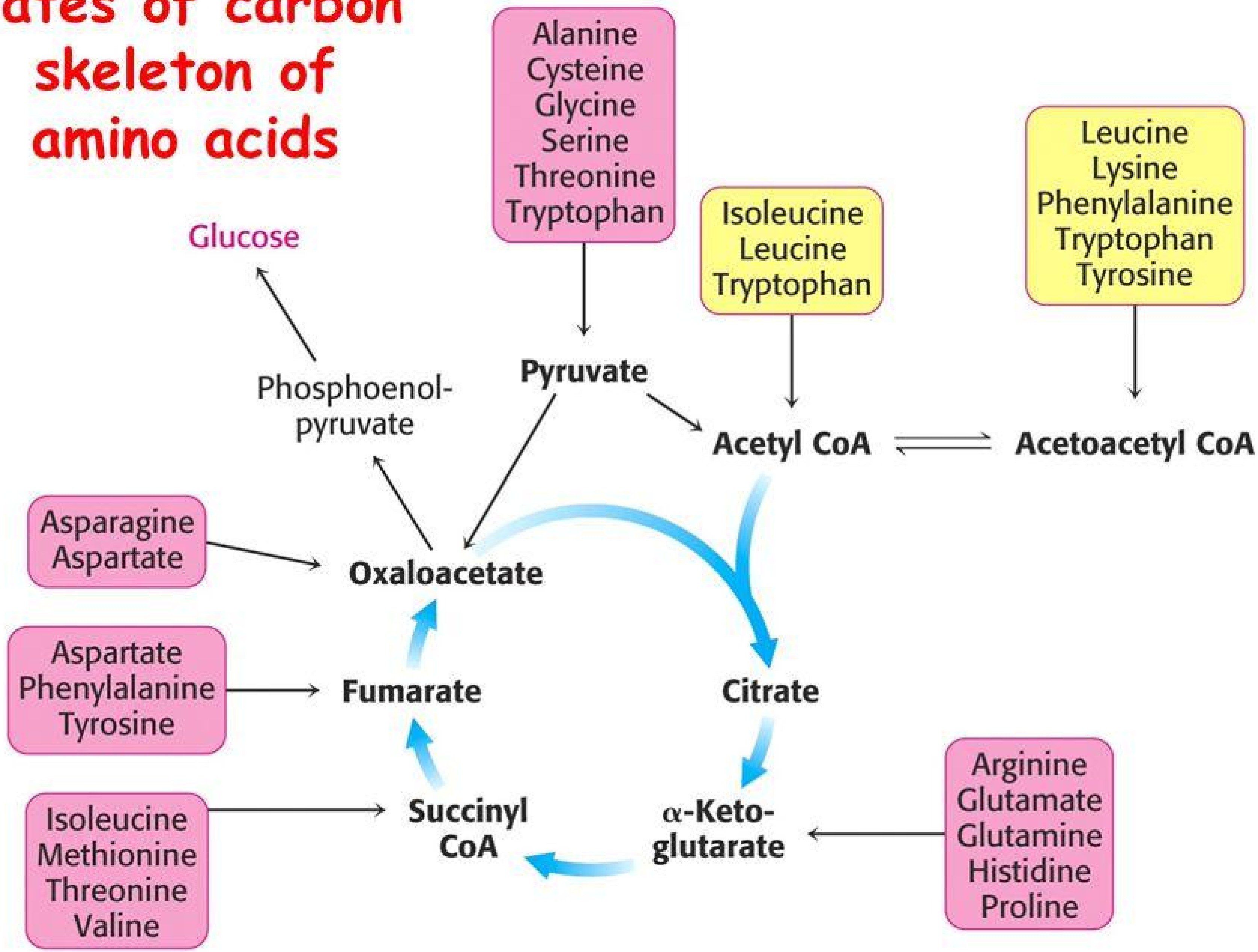
- Excess proteins can serve as fuel like carbohydrates and fats.
- Nitrogen is removed producing carbon skeletons and ammonia.
- Carbon skeletons oxidized
- Ammonia is highly toxic, but soluble.

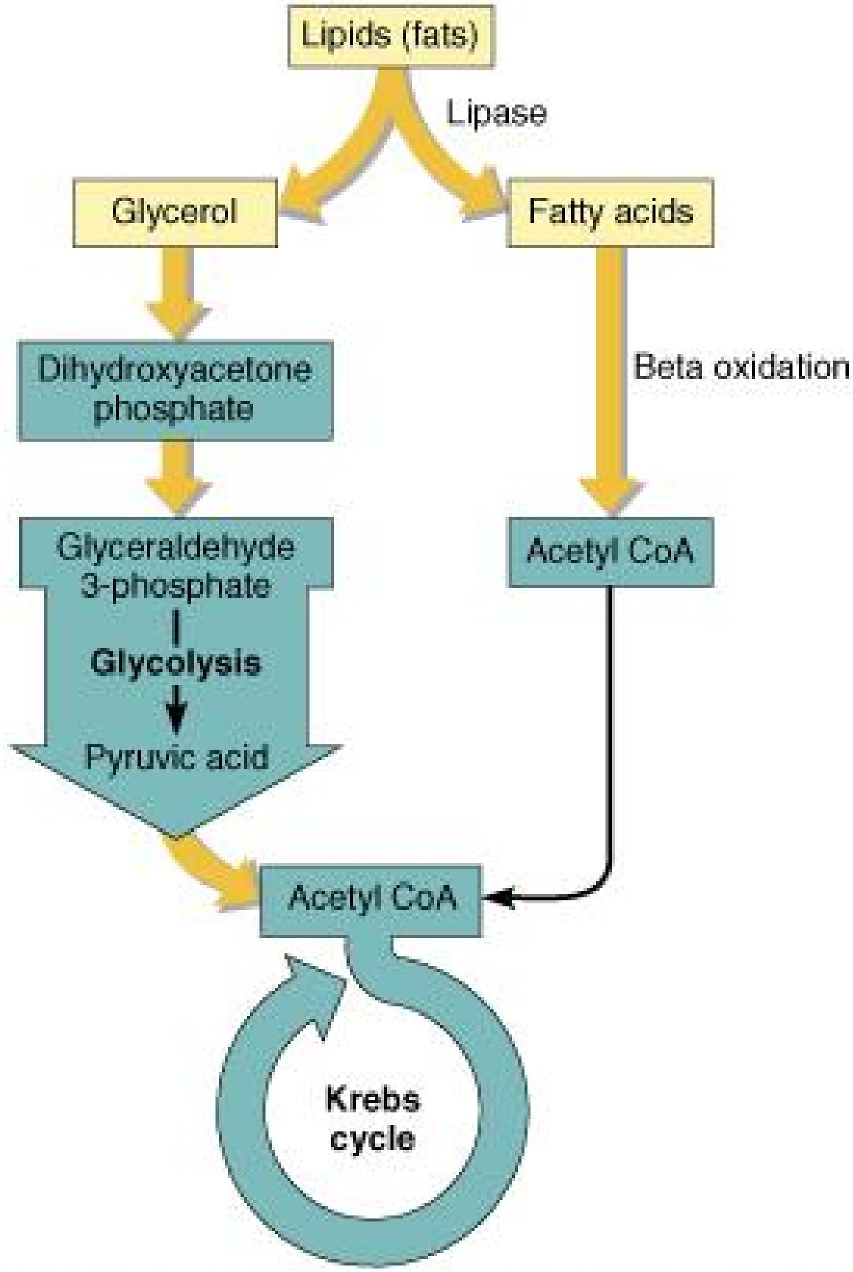
α-ketoglutarate and glutamate play central roles in amino acid catabolism





Fates of carbon skeleton of amino acids




Lipids (fats)
Lipase
Glycerol
Fatty acids
Dihydroxyacetone phosphate
Beta oxidation
Glyceraldehyde 3-phosphate
Glycolysis
Pyruvic acid
Acetyl CoA
Acetyl CoA
Krebs cycle

The β-Oxidation Pathway

Each pass removes one acetyl moiety in the form of acetyl-CoA.

Formation of each acetyl-CoA requires removal of 4 H atoms {2 e^- pairs and 4 H^+})

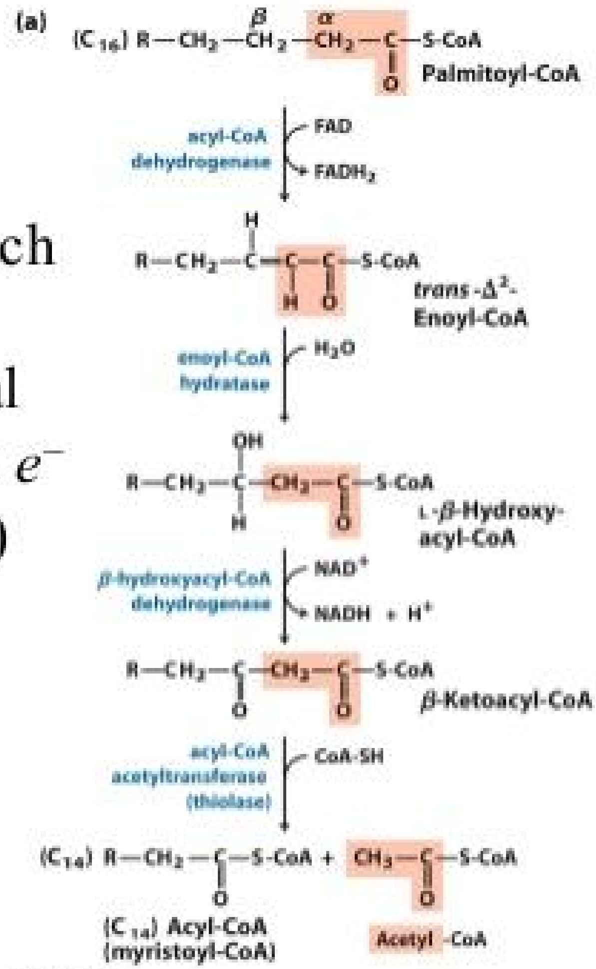
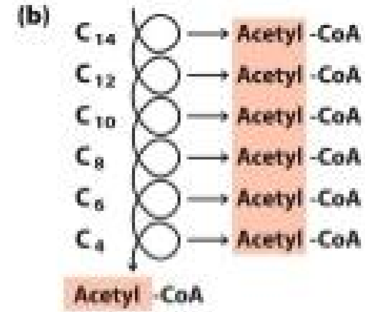


Figure 17-8
Lehninger Principles of Biochemistry, Sixth Edition



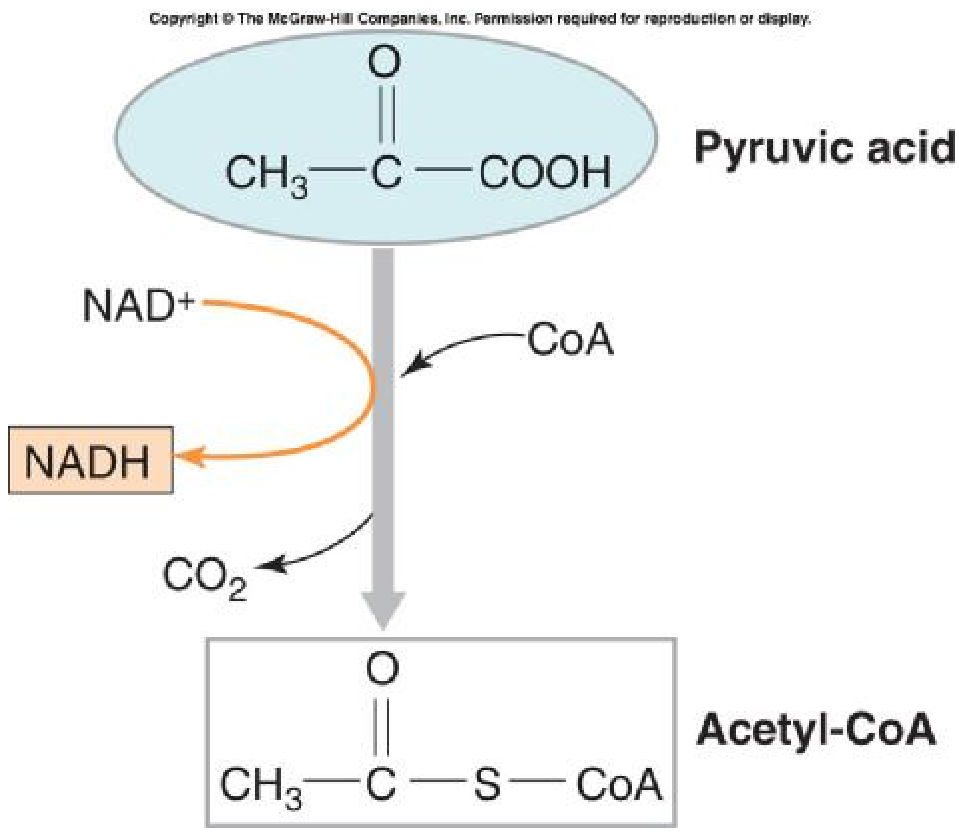
Palmitate (C16) undergoes seven passes through the oxidative sequence

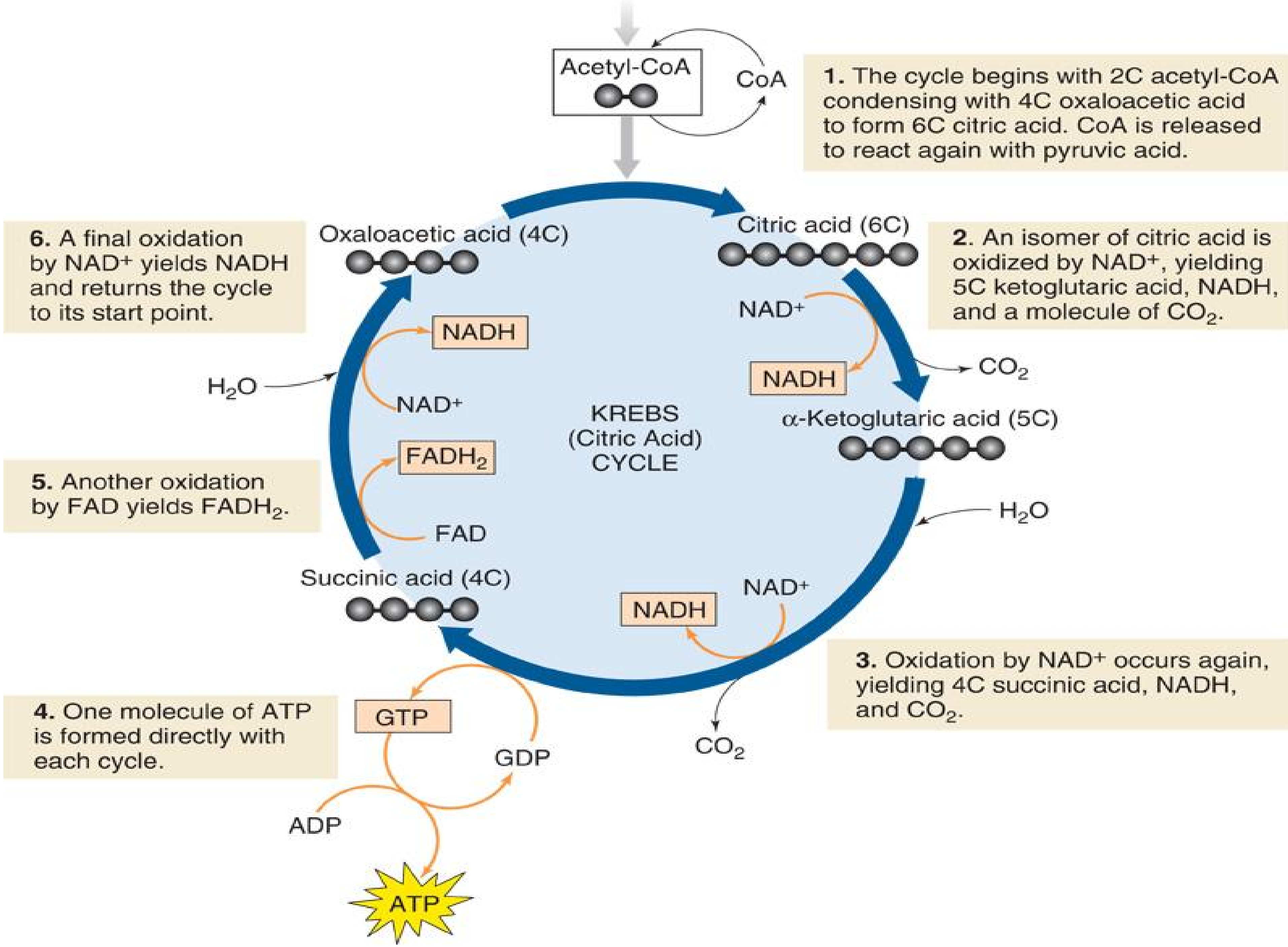
Aerobic Metabolism

- Pathways are available to use carbohydrates, fats, and proteins.
- When oxygen is available, a second oxidative stage of cellular respiration takes place.
- All substrates eventually feed into the *Krebs Cycle* (occurs in mitochondrial matrix), which feeds electrons (in the form of NADH or $FADH_2$ = *reducing equivalents*) into the electron transport system of the inner mitochondrial membrane.
- The ETS generates ATP.

Producing Acetyl-CoA

- The 3-carbon pyruvate loses a carbon producing an acetyl group.




Acetyl-CoA
CoA
1. The cycle begins with 2C acetyl-CoA condensing with 4C oxaloacetic acid to form 6C citric acid. CoA is released to react again with pyruvic acid.
Oxaloacetic acid (4C)
Citric acid (6C)
2. An isomer of citric acid is oxidized by NAD^+, yielding 5C ketoglutaric acid, NADH, and a molecule of CO_2.
6. A final oxidation by NAD^+ yields NADH and returns the cycle to its start point.
NAD^+
NADH
NADH
CO_2
H_2O
NAD^+
KREBS (Citric Acid) CYCLE
α-Ketoglutaric acid (5C)
$FADH_2$
5. Another oxidation by FAD yields $FADH_2$.
H_2O
FAD
Succinic acid (4C)
NAD^+
NADH
3. Oxidation by NAD^+ occurs again, yielding 4C succinic acid, NADH, and CO_2.
4. One molecule of ATP is formed directly with each cycle.
GTP
GDP
CO_2
ADP
ATP

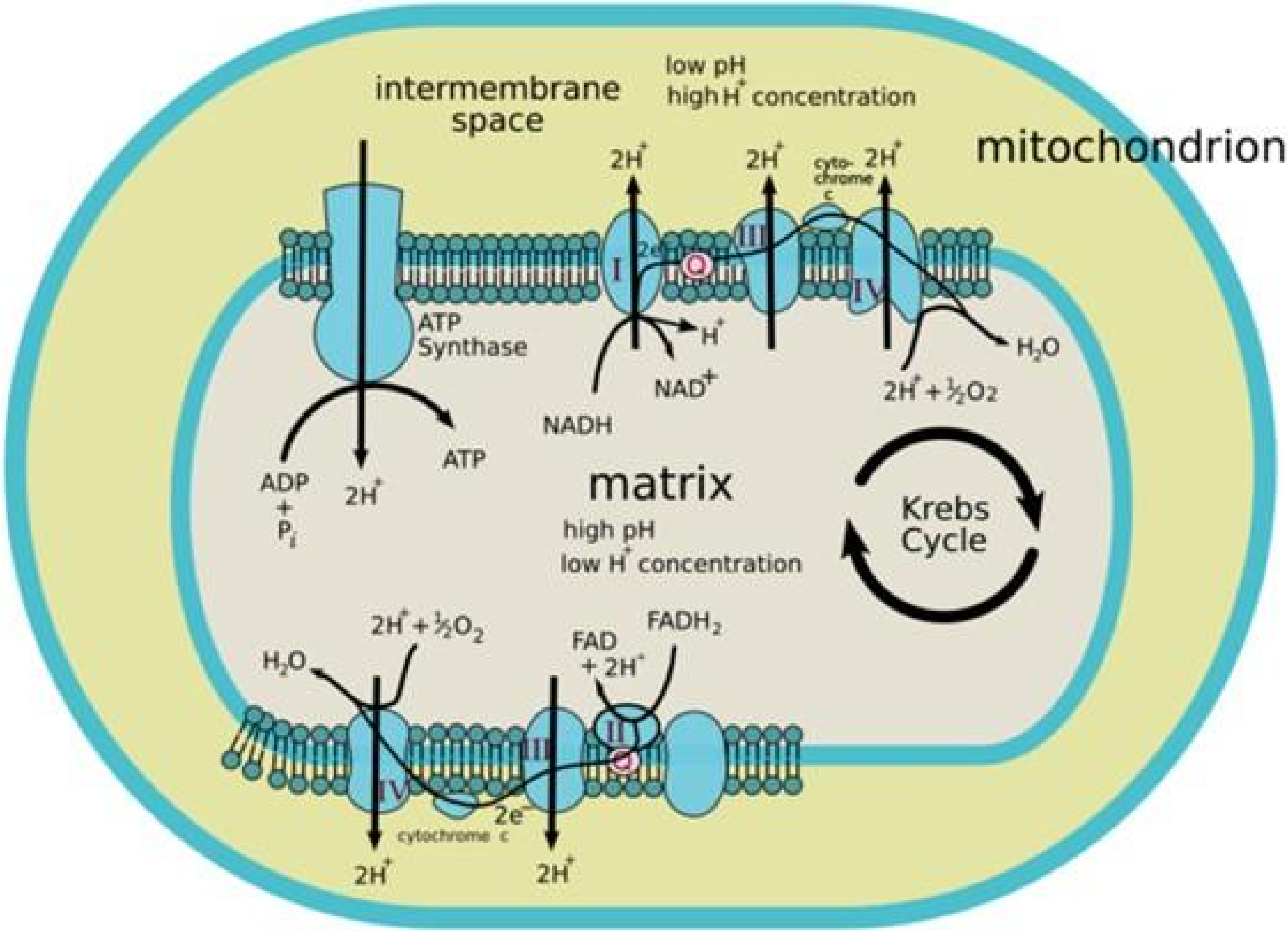
Krebs Cycle

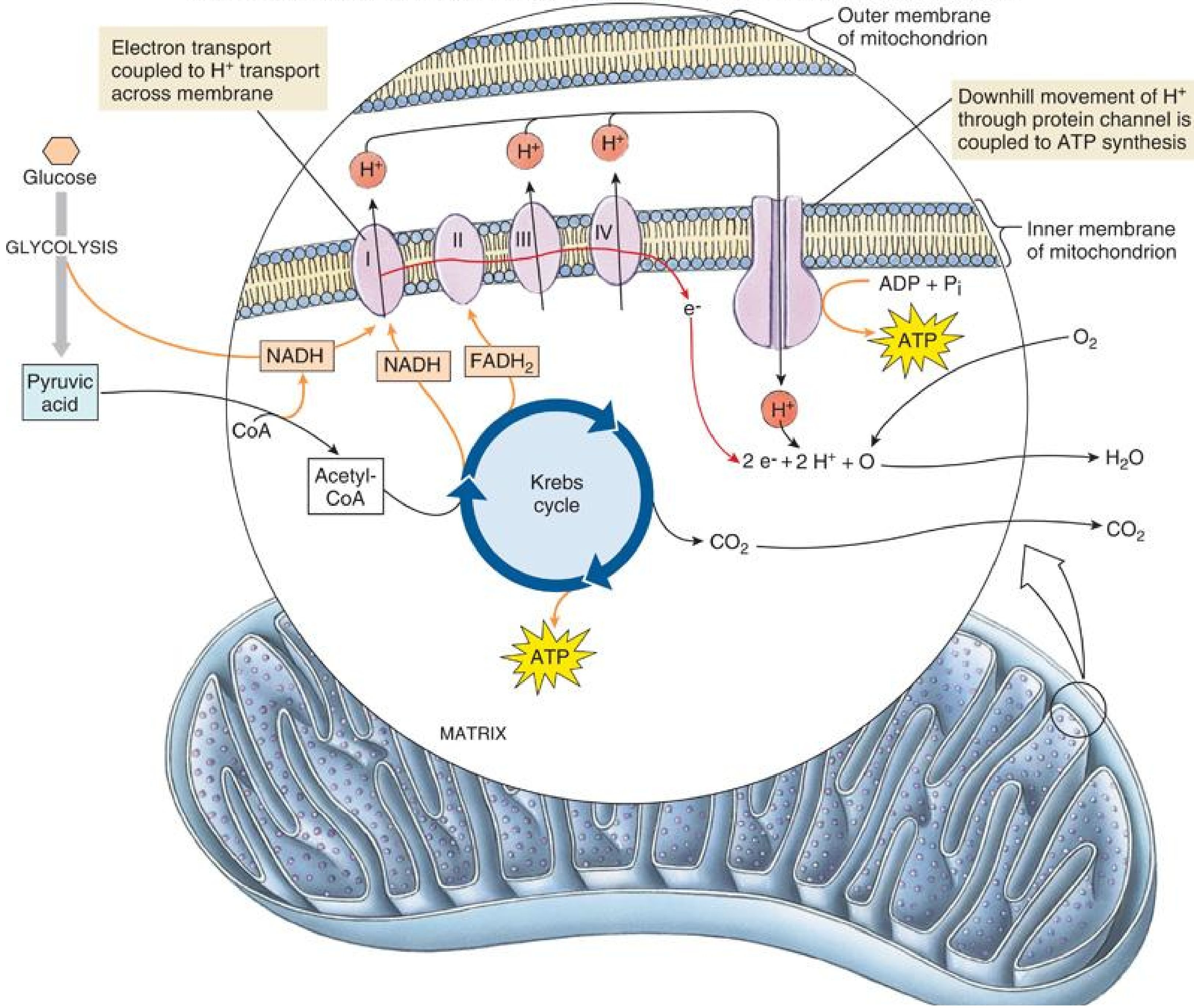
- End Products of aerobic metabolism:
  - Carbos and fats = CO_2 and water
  - Proteins/amino acids = CO_2 + water + HCO_3^- + NH_4^+
- CO_2 removed at lungs or gills
- Ammonia incorporated into nitrogenous waste products and excreted

ELECTRON TRANSPORT CHAIN

- **Electrons are transferred to a final electron acceptor.**
  - **In aerobic respiration, the final acceptor is oxygen.**
  - **In anaerobic respiration, the final acceptor is an inorganic oxygen-containing molecule.**
  - **As electrons are transferred along the electron transport chain, protons are pumped out of the cell.**
  - **This causes the proton concentration outside the cell to be higher than inside the cell, causing a concentration gradient to form.**

Mitochondrial Electron Transport Chain

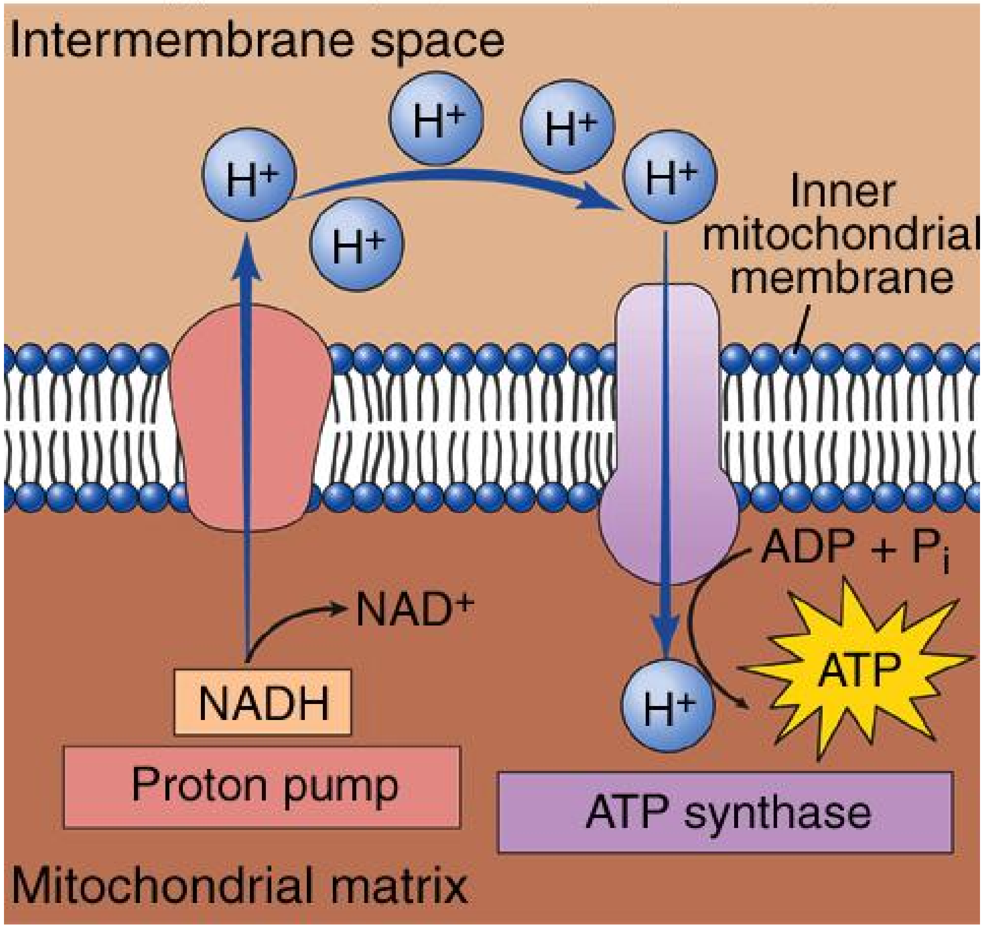




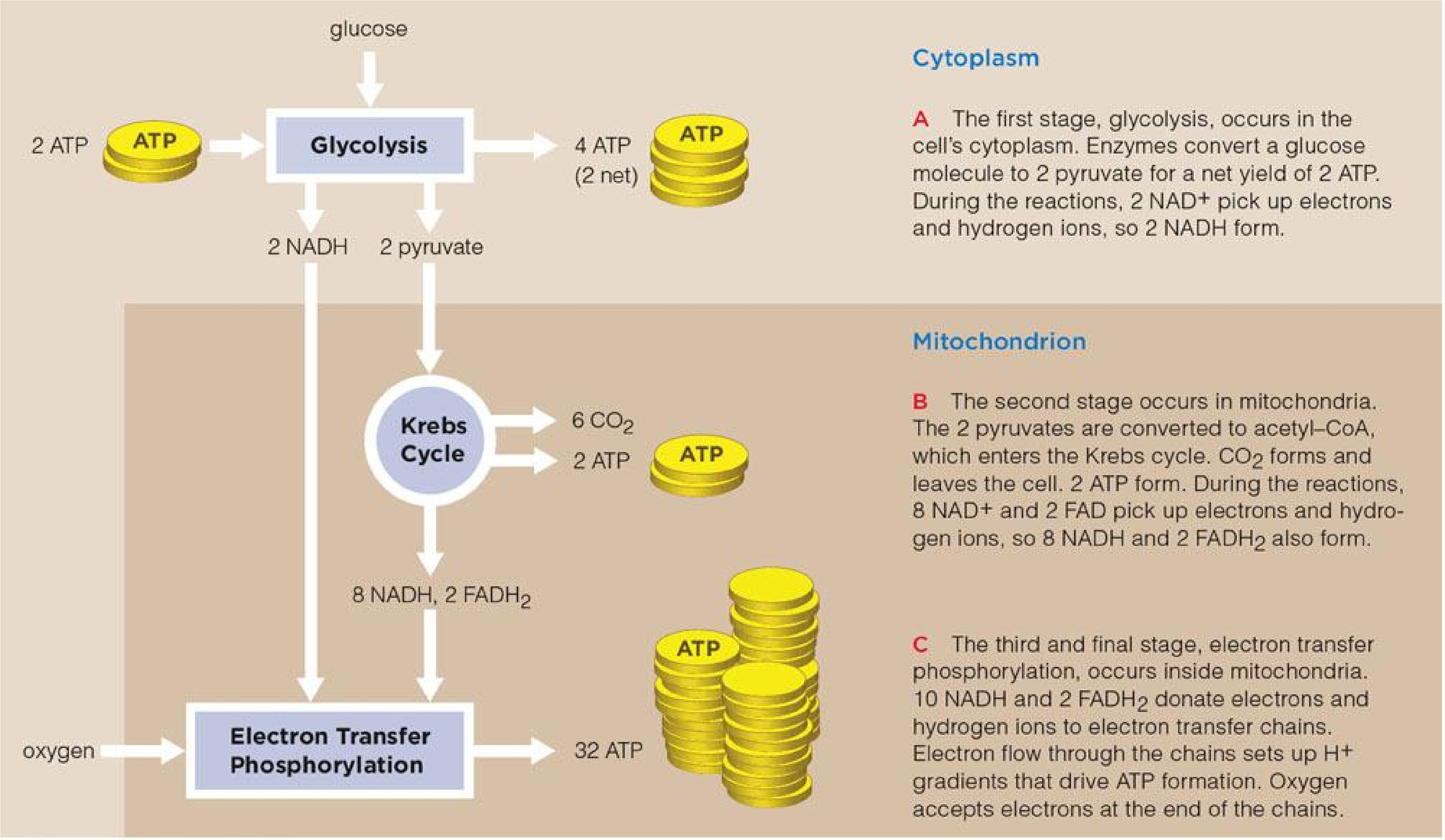
Outer membrane of mitochondrion
Electron transport coupled to H+ transport across membrane
Downhill movement of H+ through protein channel is coupled to ATP synthesis
H+
H+
H+
H+
Glucose
GLYCOLYSIS
I
II
III
IV
Inner membrane of mitochondrion
ADP + Pi
e-
ATP
NADH
NADH
FADH2
O2
Pyruvic acid
H+
CoA
2 e- + 2 H+ + O
H2O
Acetyl-CoA
Krebs cycle
CO2
CO2
ATP
MATRIX

Producing ATP- Chemiosmosis

- A strong gradient with many protons outside the matrix and few inside is set up.



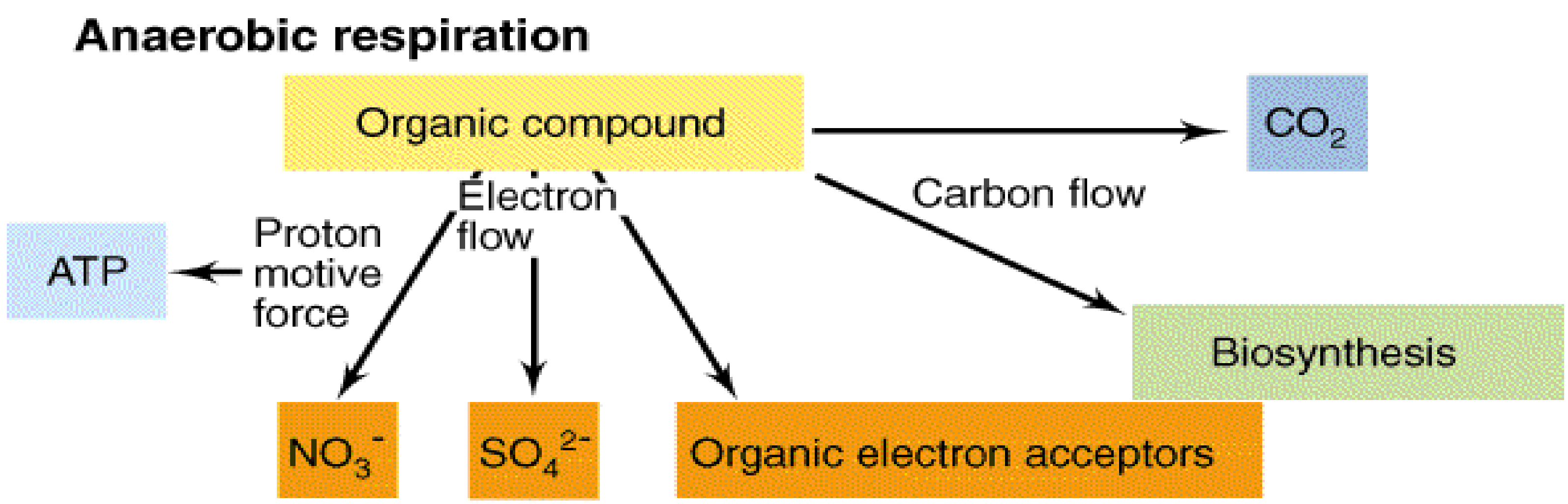
Overview of Aerobic Respiration



aerobic respiration

- O_2/H_2O coupling is the most oxidizing, more energy in aerobic respiration.
- Therefore, anaerobic is less energy efficient.

Alternative energy generating patterns

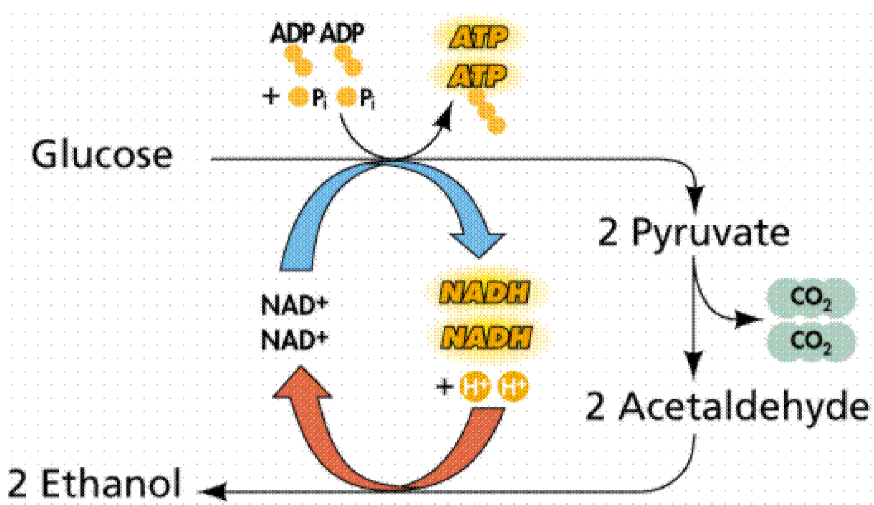


Anaerobic Respiration

- Final electron acceptor : never be O2
- Use of another compound than O_2 as final electron acceptor in the ETC
- Examples
  - Nitrate reducer : final electroon acceptor is sodium nitrate (NaNO3)
    - Nitrate ion NO_3- *[Pseudomonas, E coli, Bacillus]*
    - NO2-
    - N2O
    - N2
  - Sulfate reducer: final electron acceptor is sodium sulfate (Na2 SO4)
    - Sulfate ion SO_4= to H_2S
    - *Methanogens*
  - Methane reducer: final electron acceptor is CO2
    - Carbonate ion CO_3= to CH_4
    - *Methanogens*

FERMENTATION

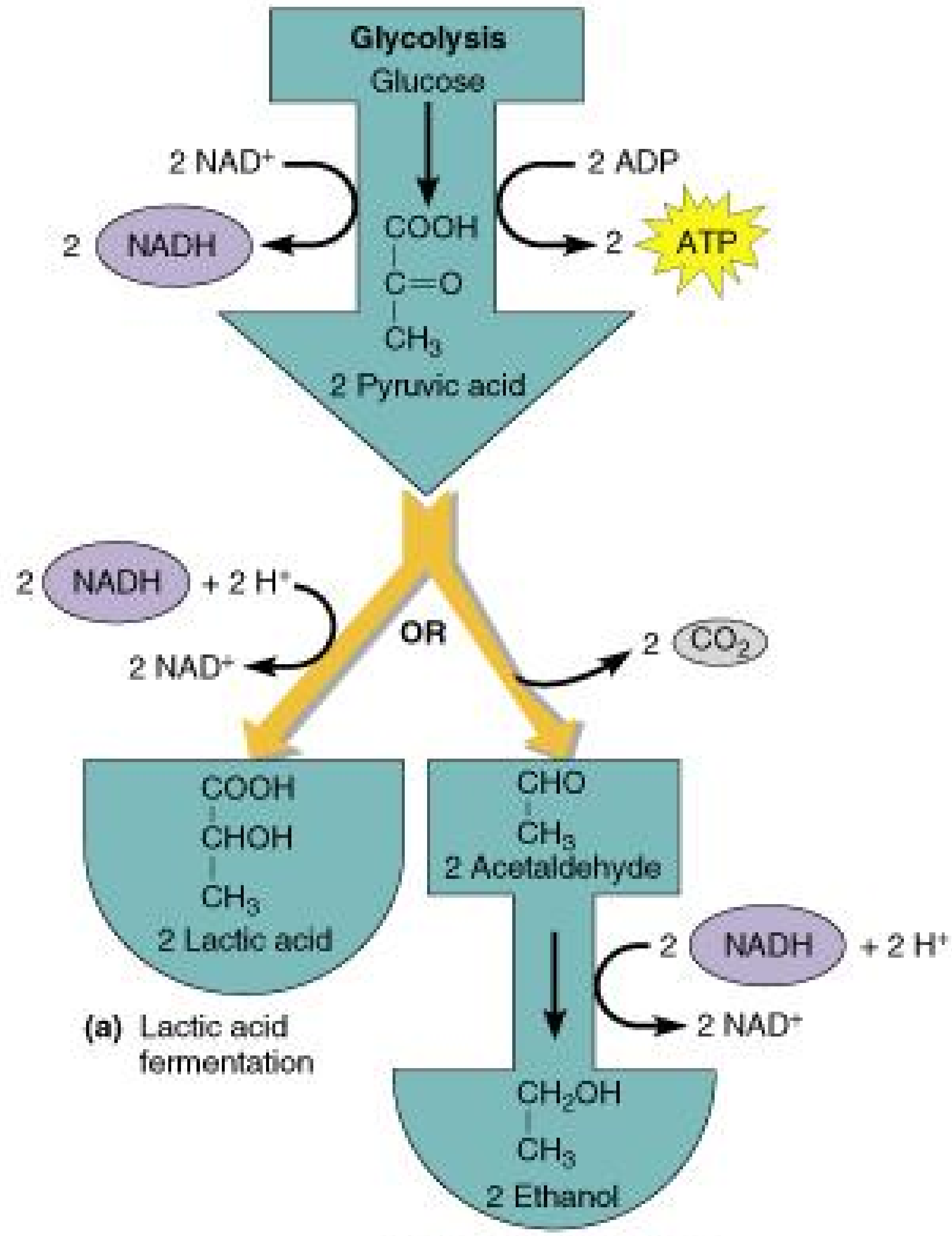
- Fermentation is the enzymatic breakdown of carbohydrates in which the final electron acceptor is an organic molecule.
- During glycolysis, all the NAD+ becomes saturated with electrons (NADH). When this happens, glycolysis will stop.



Fermentation Summary

- Anaerobic
- Cytoplasm
- Partial Oxidation
- Small amounts of ATP generated via substrate level phosphorylation
- Organic intermediaries as final electron acceptors
- End products
  - Acid: Lactic Acid, Acetic Acid, Butyric Acid, Acetone
  - Alcohol: Ethanol, Isopropyl
  - Gas : CO_2, H_2
  - Contaminants

Fermentation

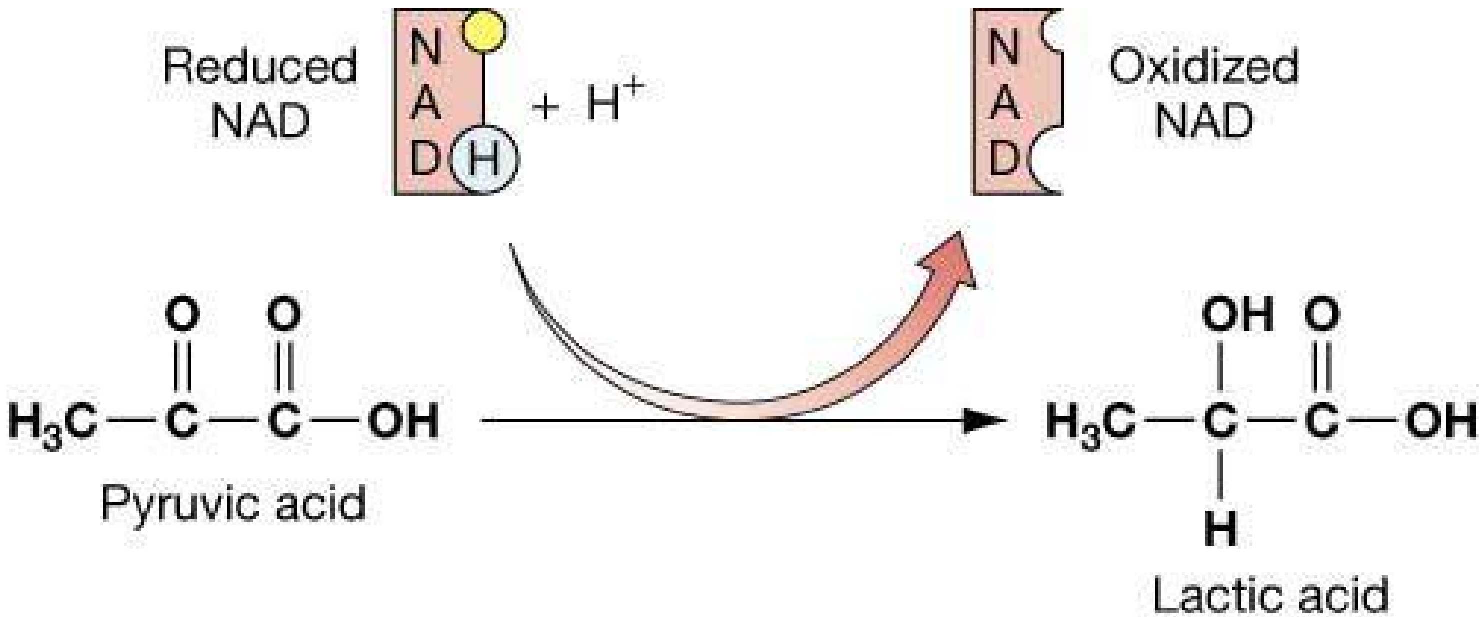


(a) Lactic acid fermentation

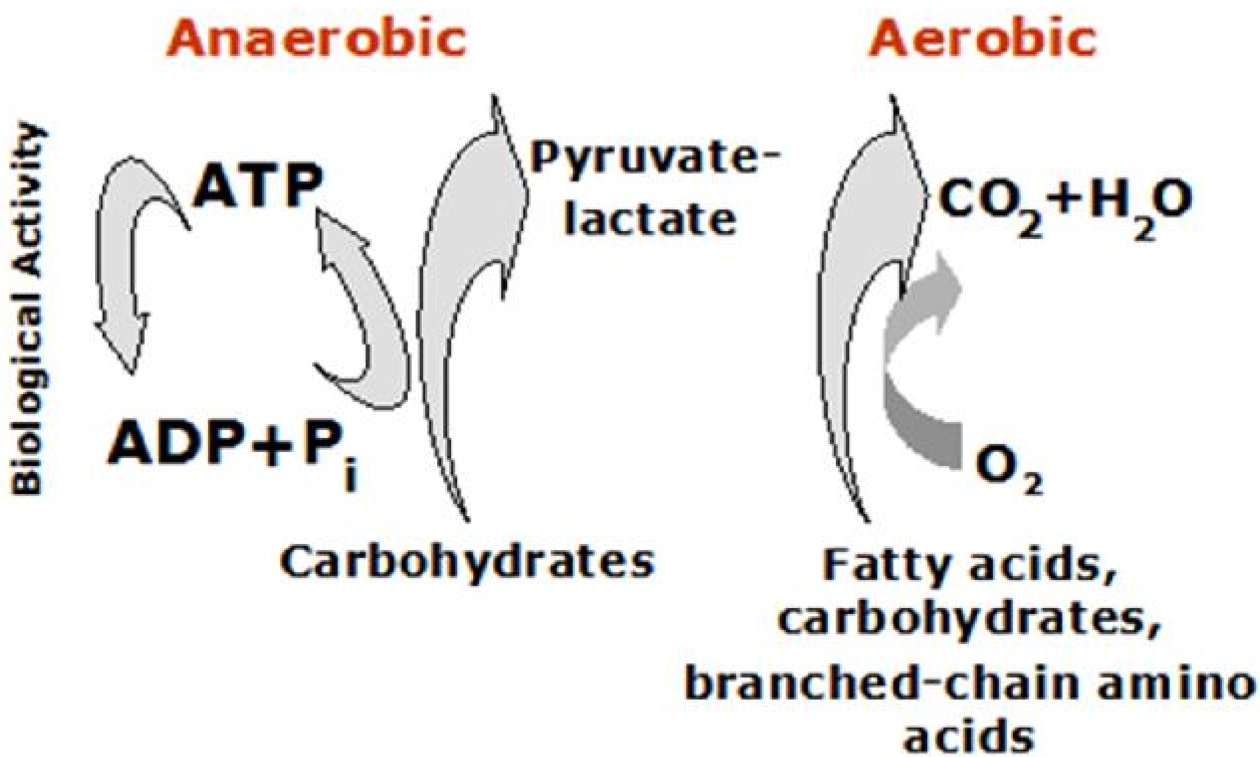
(b) Alcohol fermentation

Lactic acid fermentation

- Pyruvate is used as the electron acceptor resetting the NAD+ for use in glycolysis.



Energy Sources in Working Muscle



… Fermentation

3- Mixed acid fermentation

P.A -----> lactic acid
acetic acid
$H_2 + CO_2$
succinic acid
ethyl alcohol

eg. E.coli and some enterbacter

4- Butylene-glycol F.

P.A -----> 2,3, butylene glycol

eg. Pseudomonas

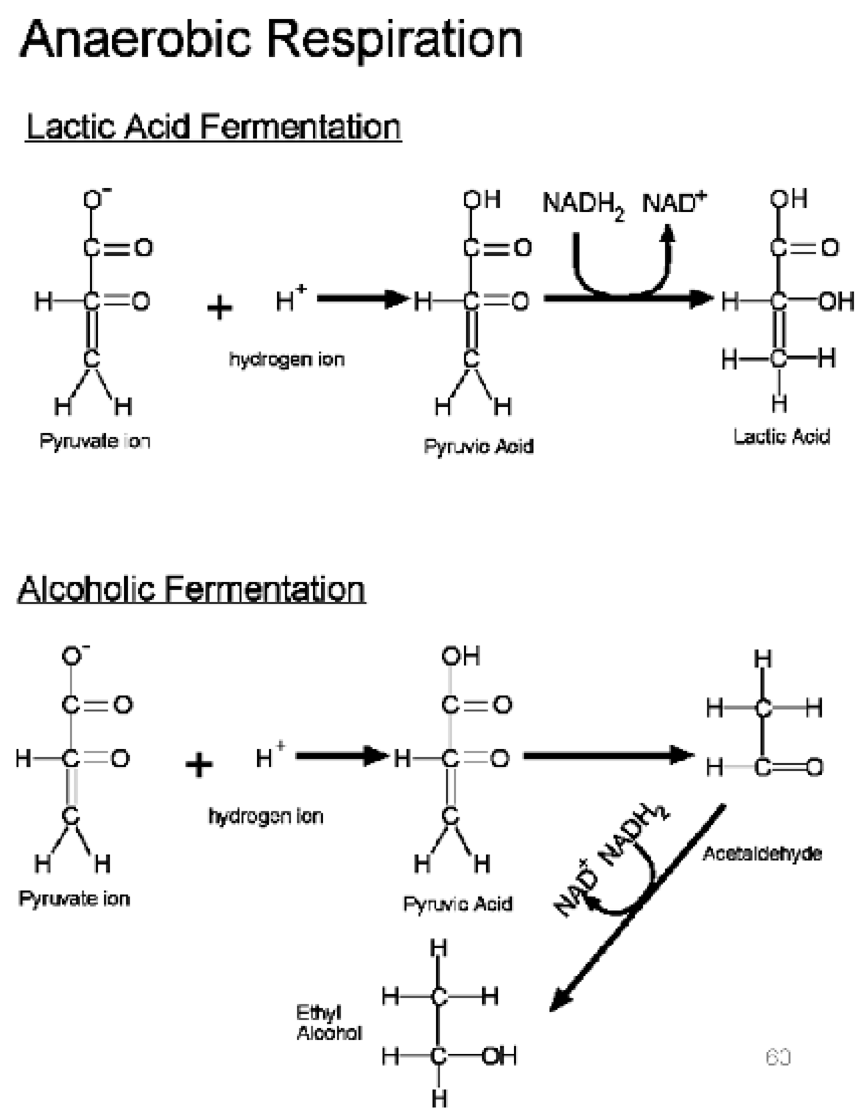
5- Propionic acid F.

P.A -----> 2 propionic acid

eg. Propionibacterium

Anaerobic Processes

- Lactic Acid
  - *Lactobacillus*
- Mixed Acid
  - *Enterobacteriaceae*
- Butanediol
  - *Klebsiella*
  - *Enterobacter*
- Butyric Acid
  - *Clostridia*
- Butanol-Acetone
  - *Clostridia*
- Propionic Acid
  - *Corynebacteria*



Different microorganisms use different fermentation pathways

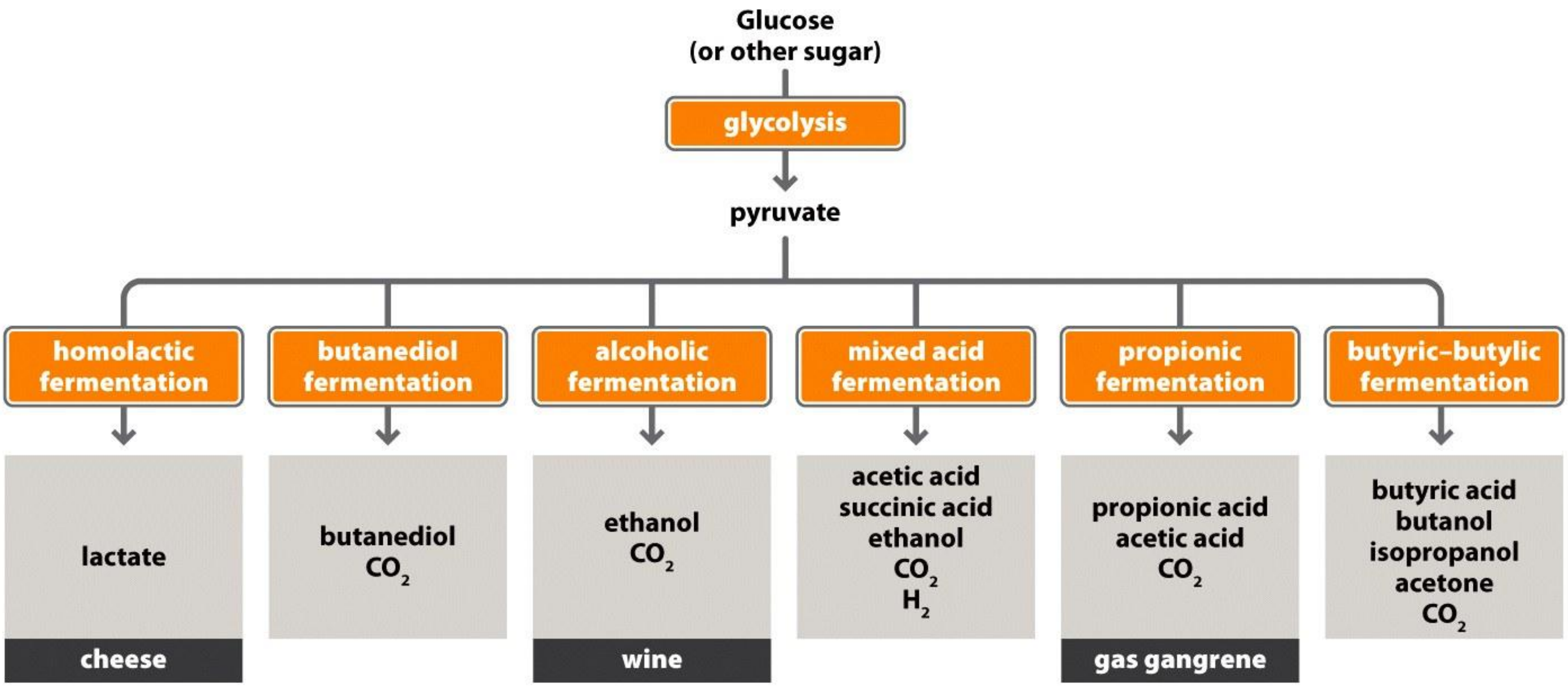


Figure 3.15 Microbiology: A Clinical Approach (© Garland Science)