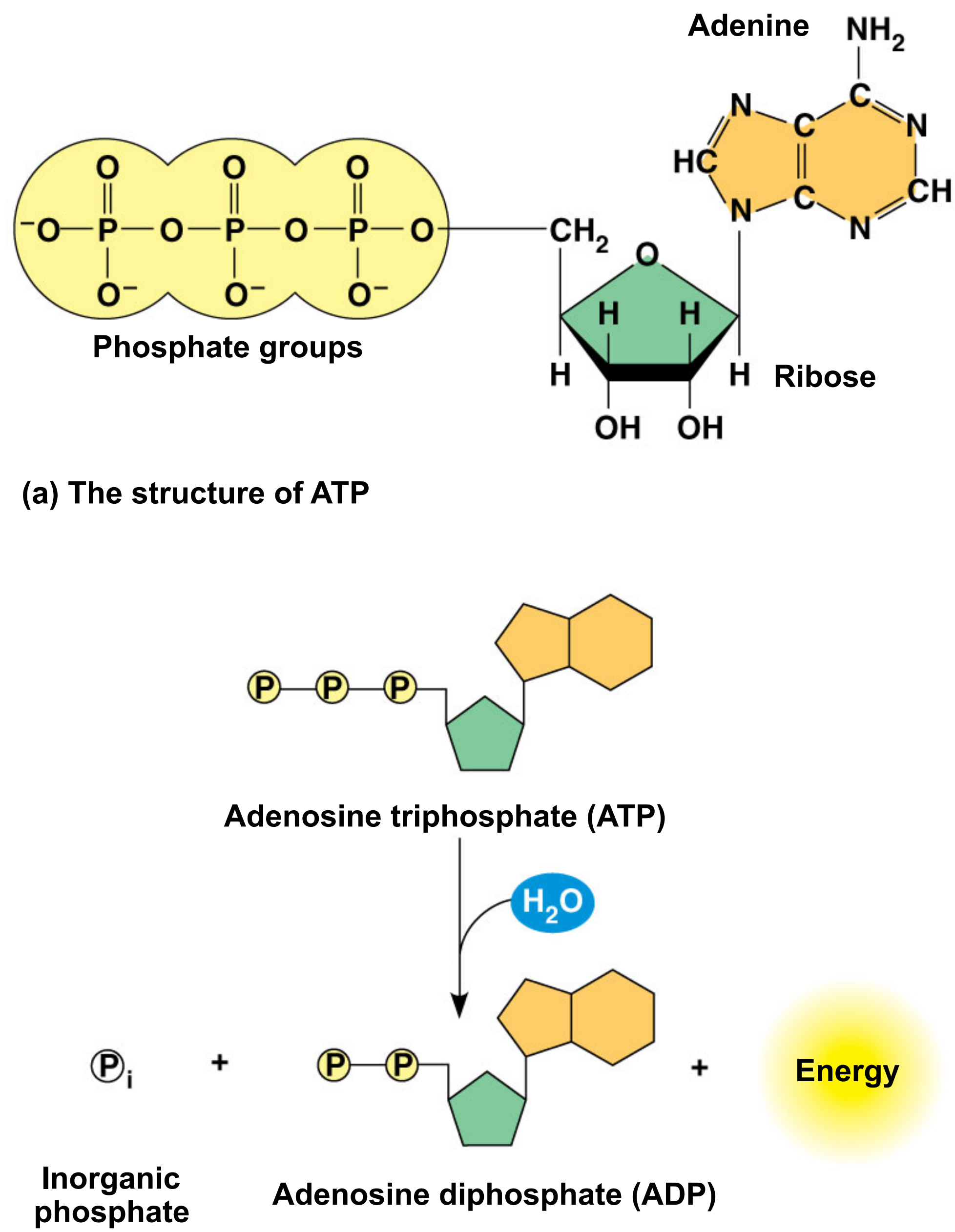
The Structure and Hydrolysis of ATP

- ATP drives endergonic reactions by phosphorylation, transferring a phosphate group to some other molecule, such as a reactant
- The recipient molecule is now called a **phosphorylated intermediate**



(a) The structure of ATP

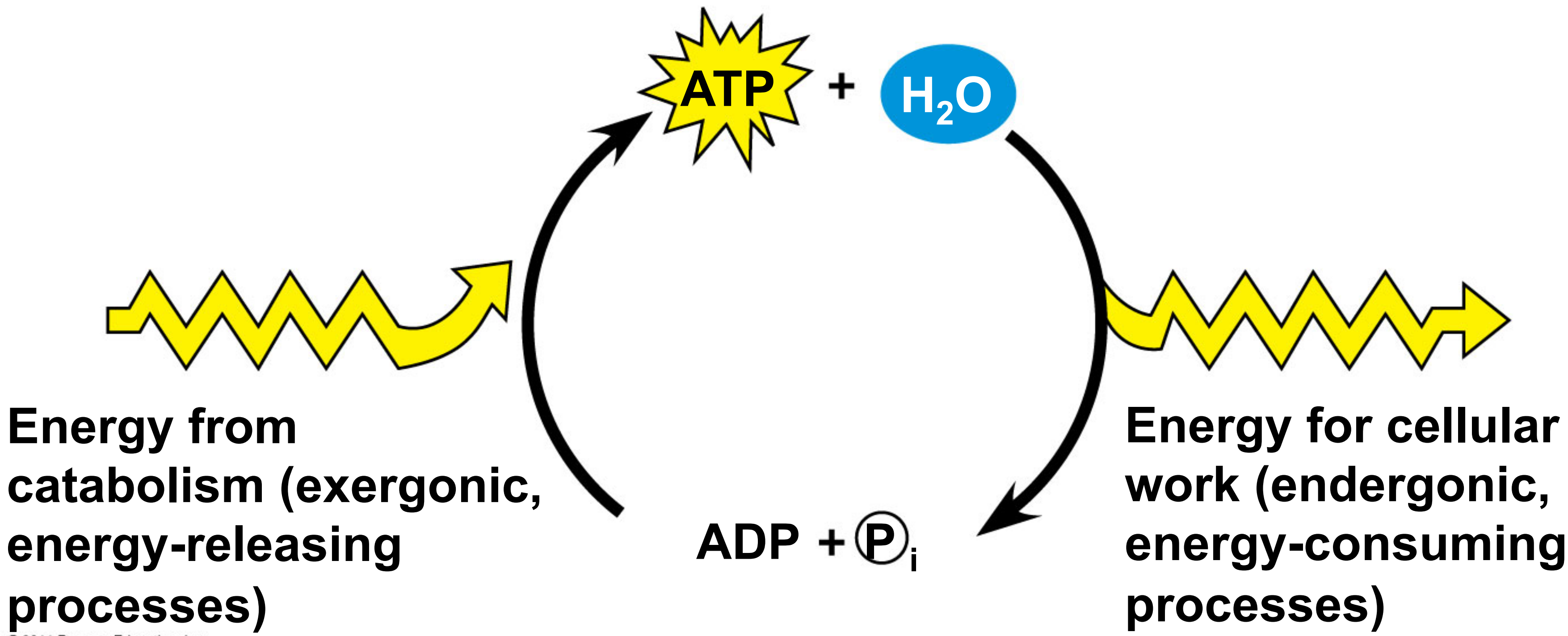
(b) The hydrolysis of ATP

How the Hydrolysis of ATP Performs Work

- The bonds between the phosphate groups of ATP’s tail can be broken by hydrolysis
- Energy is released from ATP when the terminal phosphate bond is broken
- This release of energy comes from the chemical change to a state of lower free energy, not from the phosphate bonds themselves
- The three types of cellular work (mechanical, transport, and chemical) are powered by the hydrolysis of ATP
- In the cell, the energy from the exergonic reaction of ATP hydrolysis can be used to drive an endergonic reaction
- Overall, the coupled reactions are exergonic

The Regeneration of ATP

- ATP is a renewable resource that is regenerated by addition of a phosphate group to adenosine diphosphate (ADP)
- The energy to phosphorylate ADP comes from catabolic reactions in the cell
- The ATP cycle is a revolving door through which energy passes during its transfer from catabolic to anabolic pathways



Enzymes speed up metabolic reactions by lowering energy barriers

- A **catalyst** is a chemical agent that speeds up a reaction without being consumed by the reaction
- An **enzyme** is a catalytic protein
- Hydrolysis of sucrose by the enzyme sucrase is an example of an enzyme-catalyzed reaction

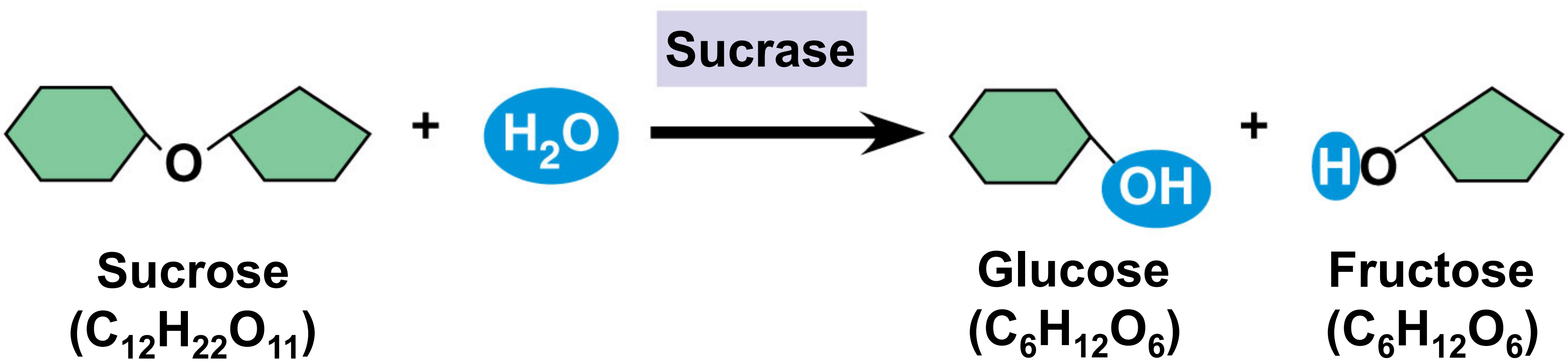
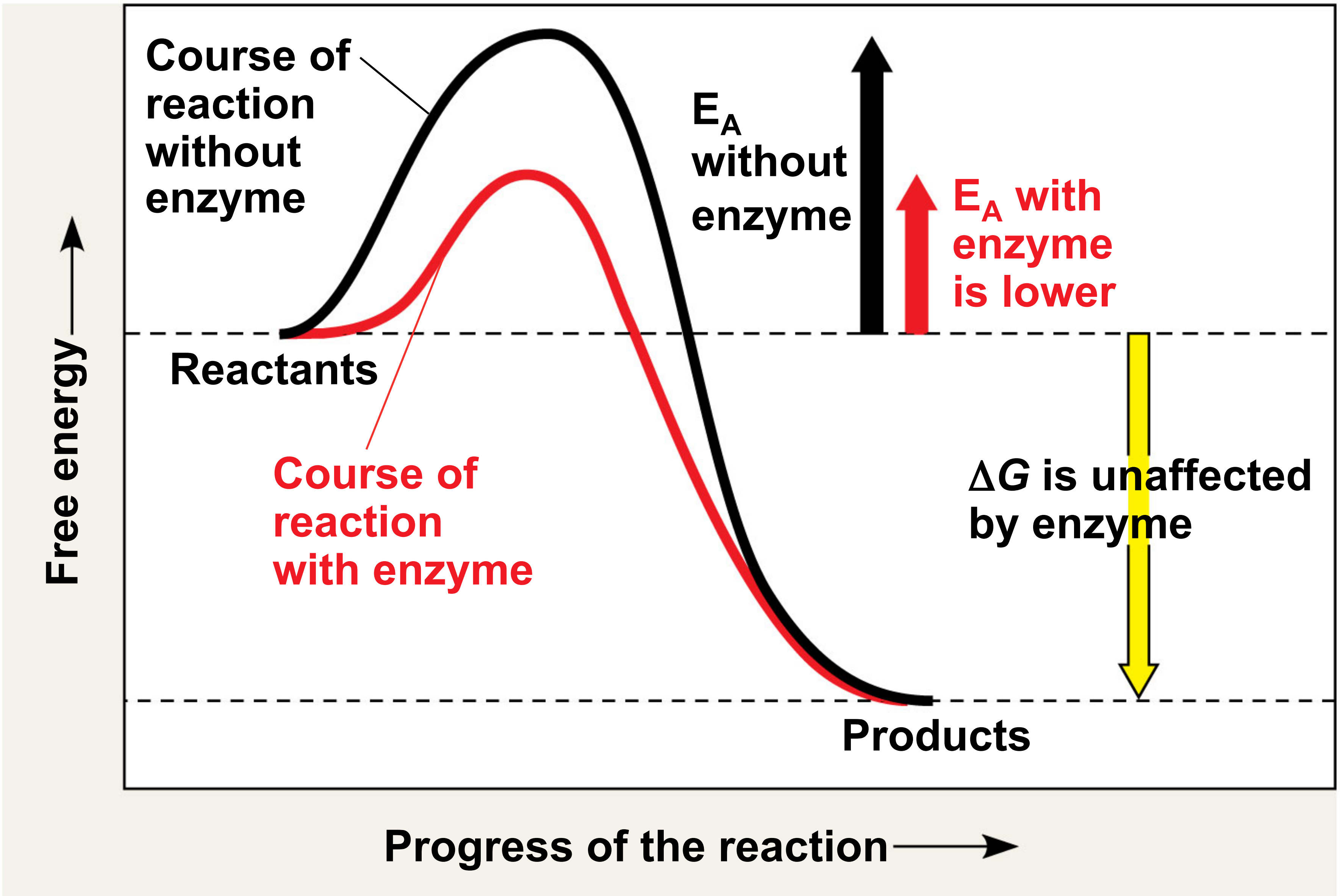


Figure 8.13


Course of reaction without enzyme
E_A without enzyme
E_A with enzyme is lower
Reactants
Course of reaction with enzyme
ΔG is unaffected by enzyme
Products
Free energy
Progress of the reaction

Oxidation of Organic Fuel Molecules During Cellular Respiration

- During cellular respiration, the fuel (such as glucose) is oxidized, and O_2 is reduced

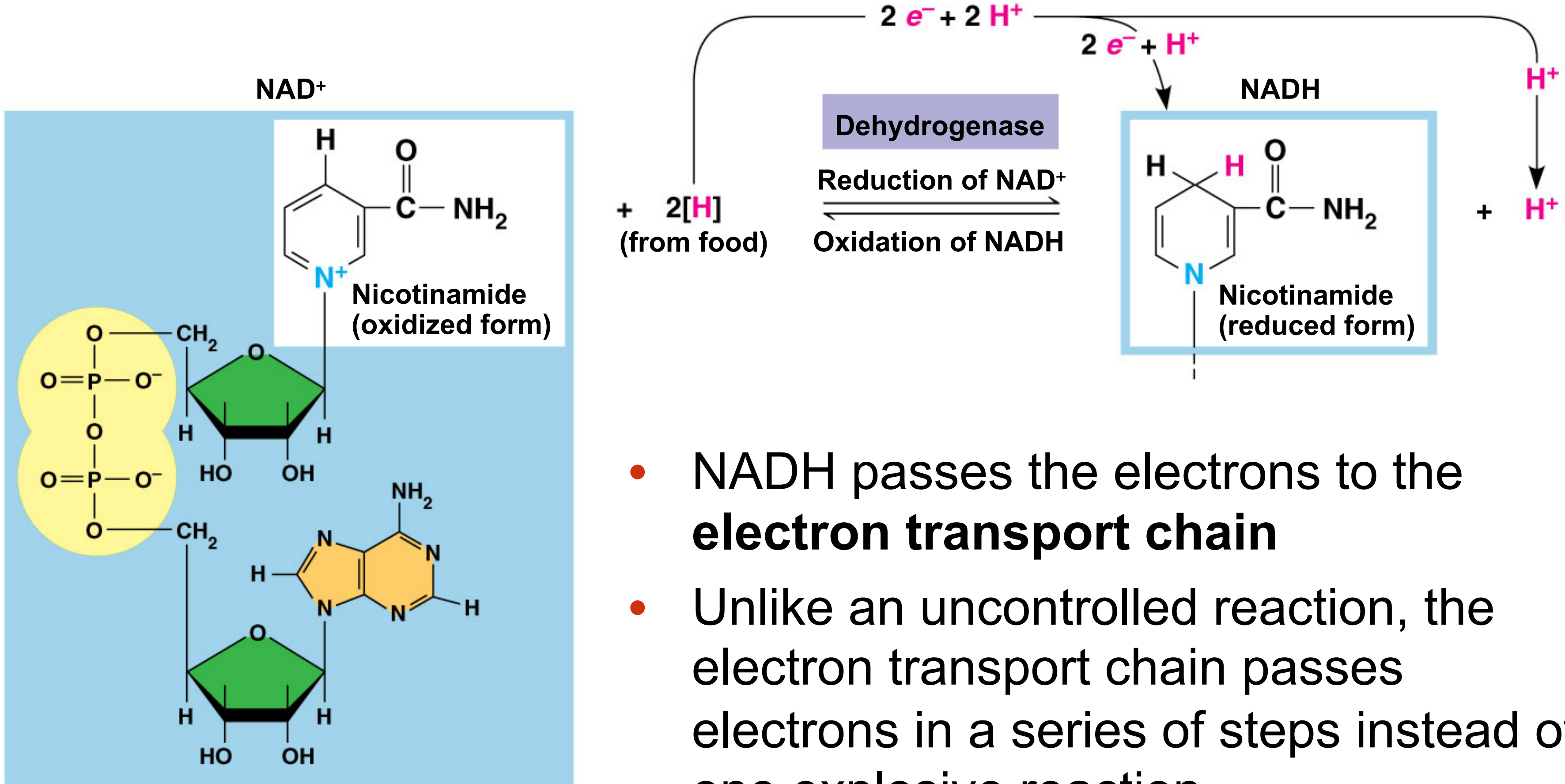
becomes oxidized ($C_6H_{12}O_6 \rightarrow 6\ CO_2$)

$$C_6H_{12}O_6 + 6\ O_2 \longrightarrow 6\ CO_2 + 6\ H_2O + \text{Energy}$$

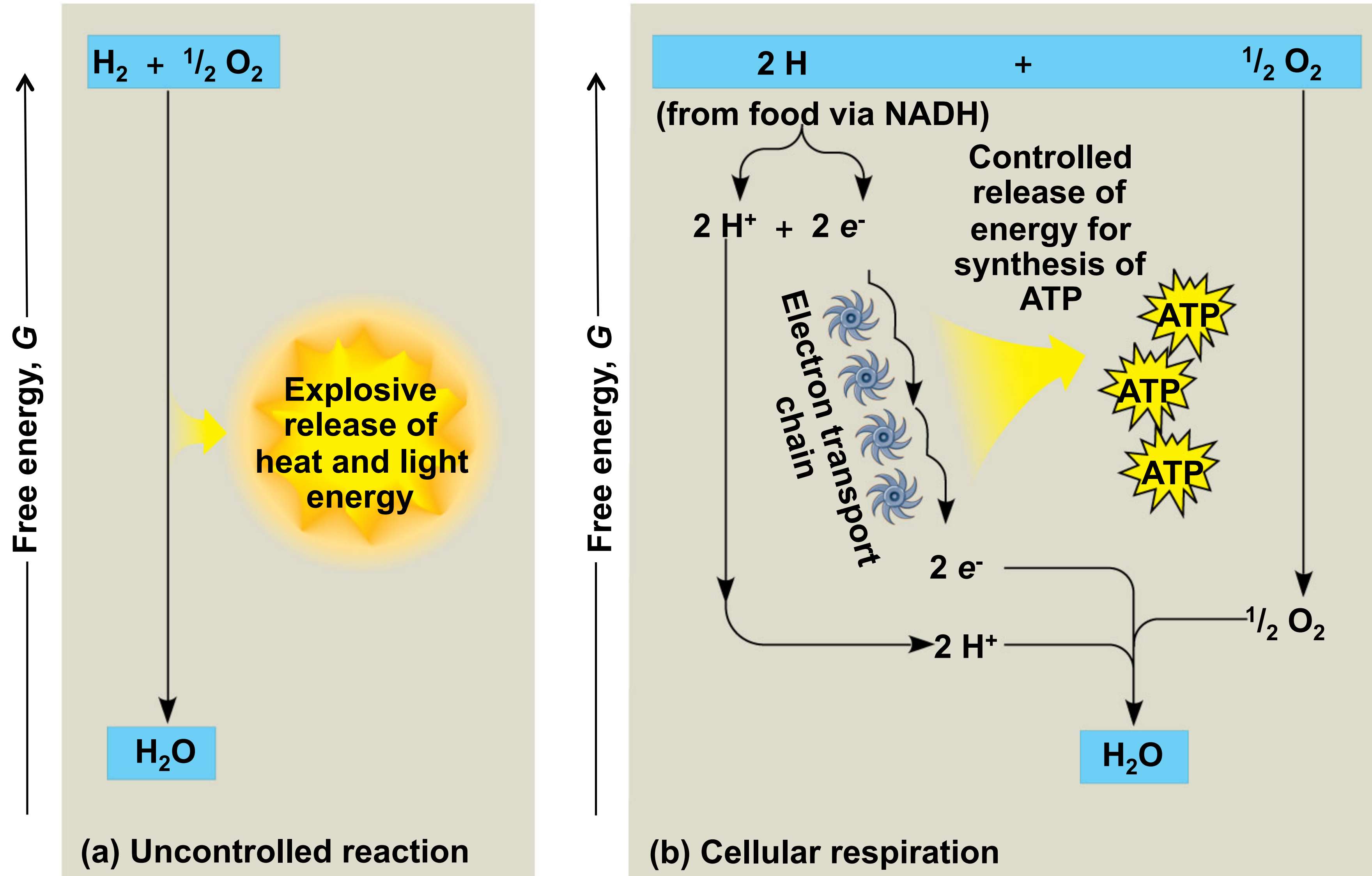
becomes reduced ($6\ O_2 \rightarrow 6\ H_2O$)

Stepwise Energy Harvest via NAD$^+$ and the Electron Transport Chain

- In cellular respiration, glucose and other organic molecules are broken down in a series of steps
- Electrons from organic compounds are usually first transferred to **NAD$^+$**, a coenzyme
- As an electron acceptor, NAD$^+$ functions as an oxidizing agent during cellular respiration
- Each NADH (the reduced form of NAD$^+$) represents stored energy that is tapped to synthesize ATP



- NADH passes the electrons to the **electron transport chain**
- Unlike an uncontrolled reaction, the electron transport chain passes electrons in a series of steps instead of one explosive reaction
- O_2 pulls electrons down the chain in an energy-yielding tumble
- The energy yielded is used to regenerate ATP

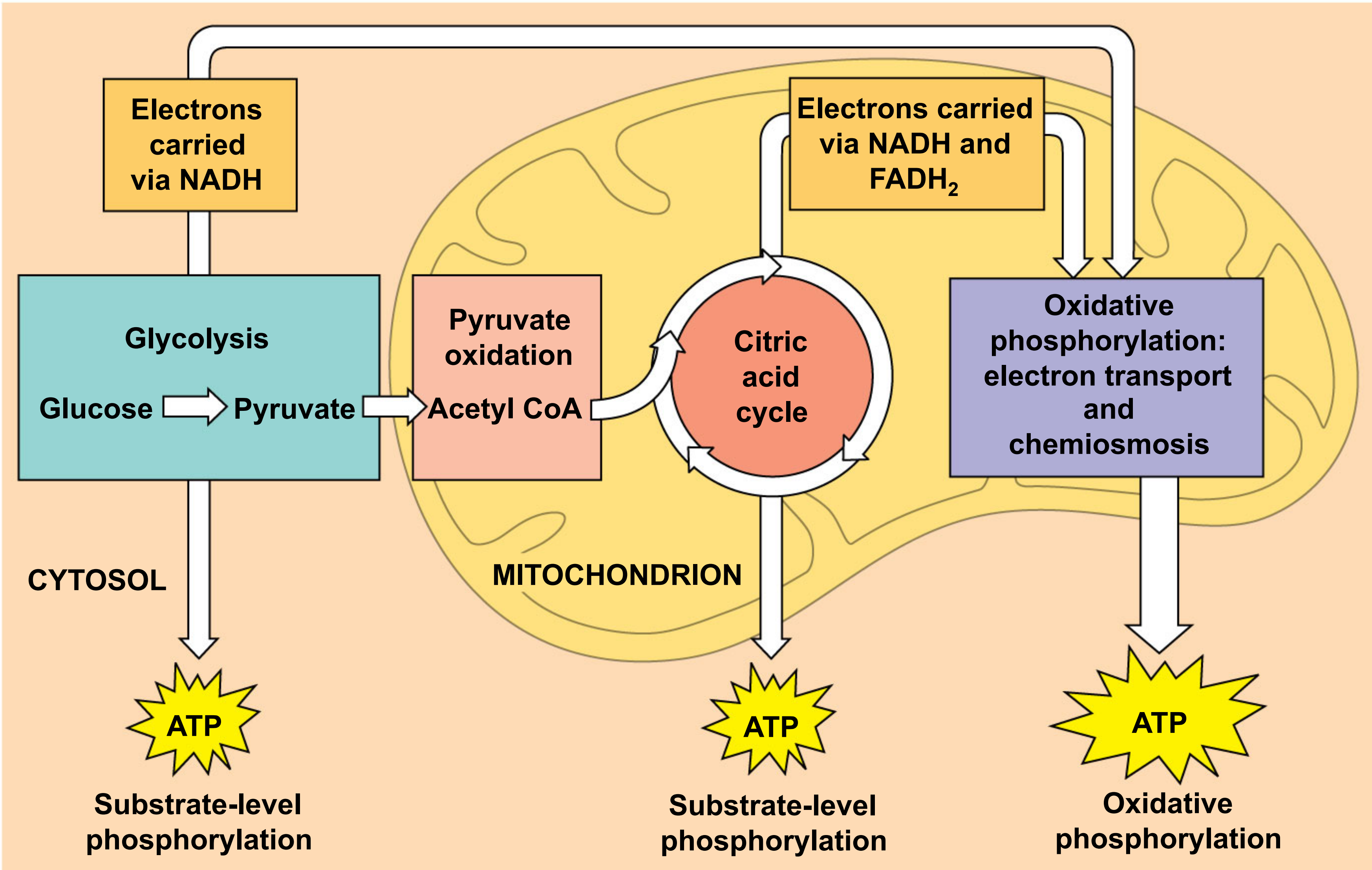


Free energy, G
H_2 + $^1/_2$ O_2
Explosive release of heat and light energy
H_2O
(a) Uncontrolled reaction
Free energy, G
2 H + $^1/_2$ O_2
(from food via NADH)
$2 H^+$ + $2 e^-$
Controlled release of energy for synthesis of ATP
ATP
ATP
ATP
Electron transport chain
$2 e^-$
$^1/_2$ O_2
$2 H^+$
H_2O
(b) Cellular respiration

The Stages of Cellular Respiration: *A Preview*

- Harvesting of energy from glucose has three stages
  - **Glycolysis** (breaks down glucose into two molecules of pyruvate)
  - The **citric acid cycle** (completes the breakdown of glucose)
  - **Oxidative phosphorylation** (accounts for most of the ATP synthesis)

Figure 9.6-3



Electrons carried via NADH
Electrons carried via NADH and $FADH_2$
Glycolysis
Glucose
Pyruvate
Pyruvate oxidation
Acetyl CoA
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
CYTOSOL
MITOCHONDRION
ATP
ATP
ATP
Substrate-level phosphorylation
Substrate-level phosphorylation
Oxidative phosphorylation

Oxidative Phosphorylation

- The process that generates most of the ATP is called oxidative phosphorylation because it is powered by redox reactions
- Oxidative phosphorylation accounts for almost 90% of the ATP generated by cellular respiration
- A smaller amount of ATP is formed in glycolysis and the citric acid cycle by **substrate-level phosphorylation**
- For each molecule of glucose degraded to CO_2 and water by respiration, the cell makes up to 32 molecules of ATP

Glycolysis harvests chemical energy by oxidizing glucose to pyruvate

- Glycolysis ("splitting of sugar") breaks down glucose into two molecules of pyruvate
- Glycolysis occurs in the cytoplasm and has two major phases
  - Energy investment phase
  - Energy payoff phase
- Glycolysis occurs whether or not O_2 is present

Figure 9.8

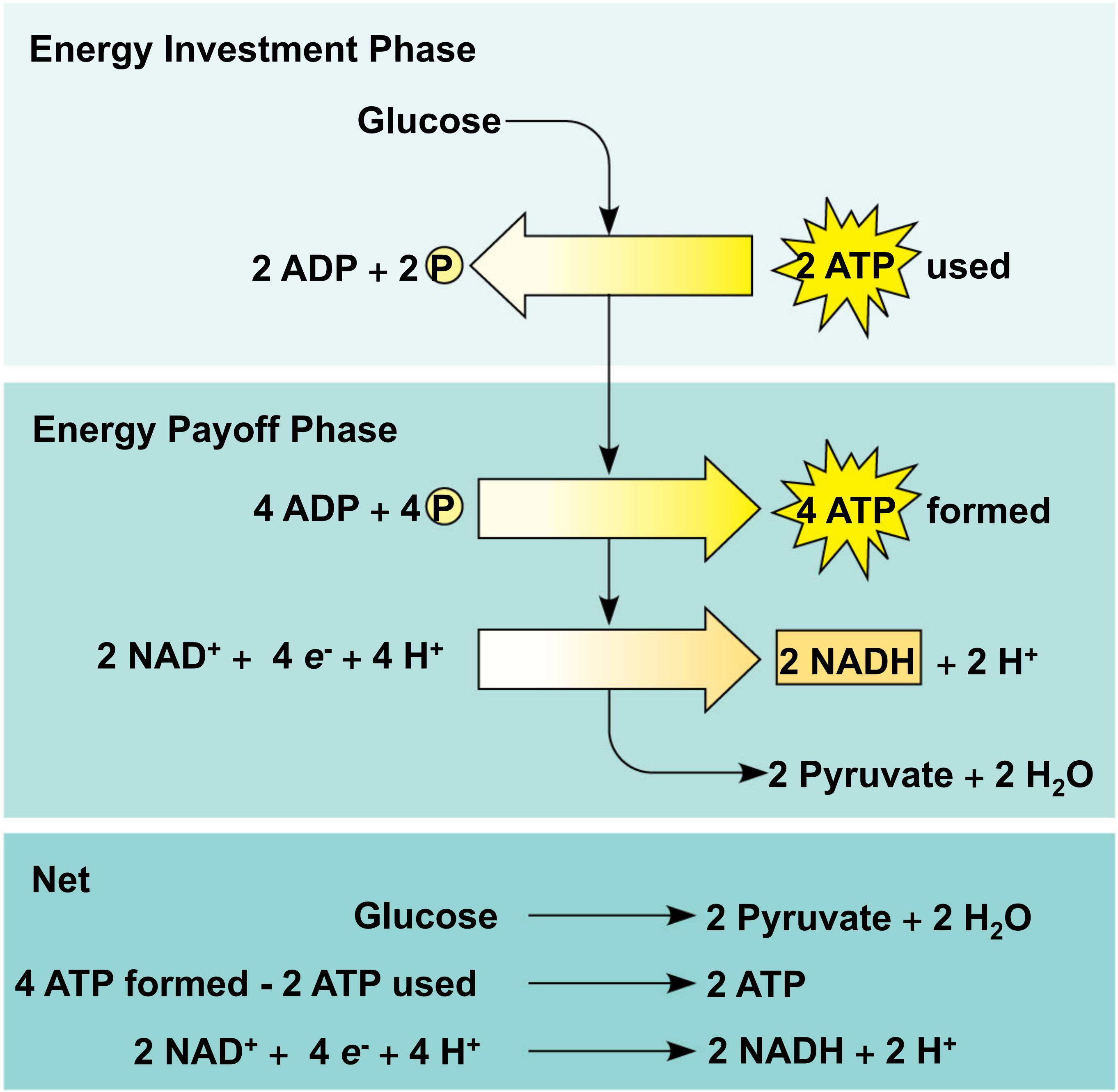
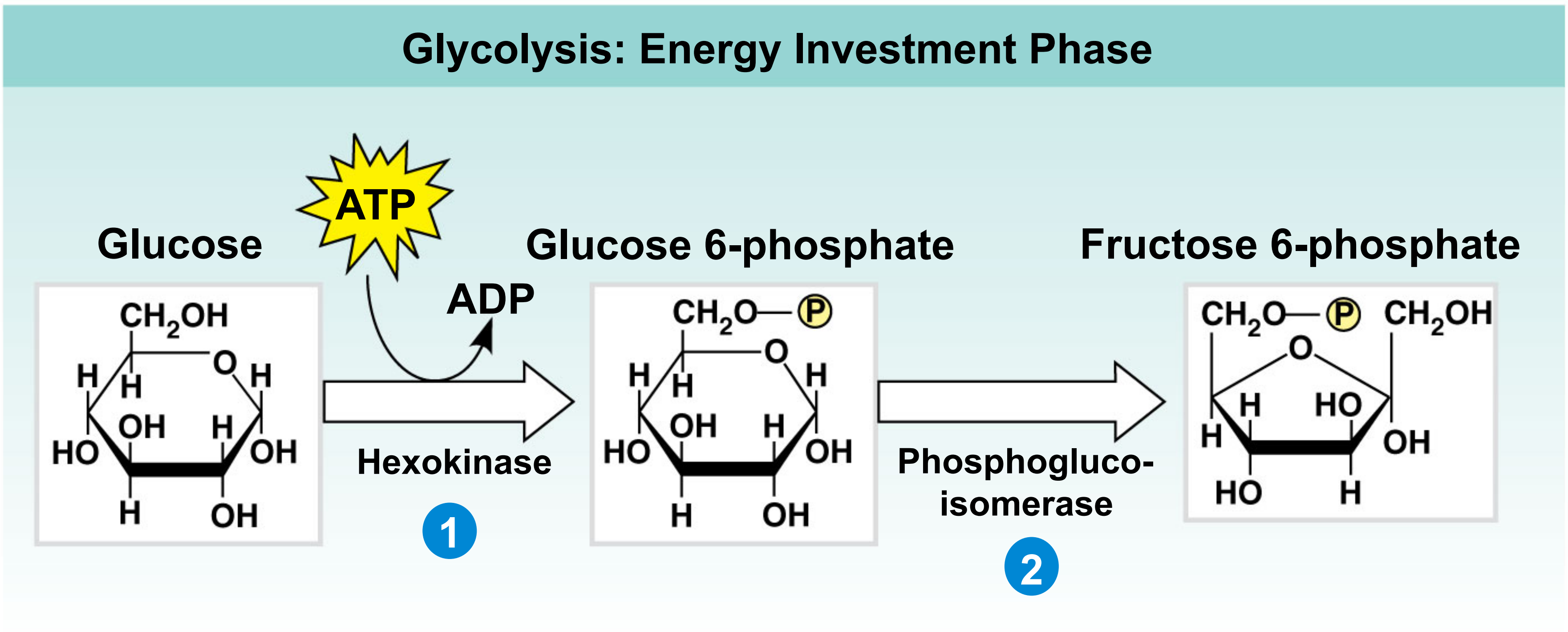
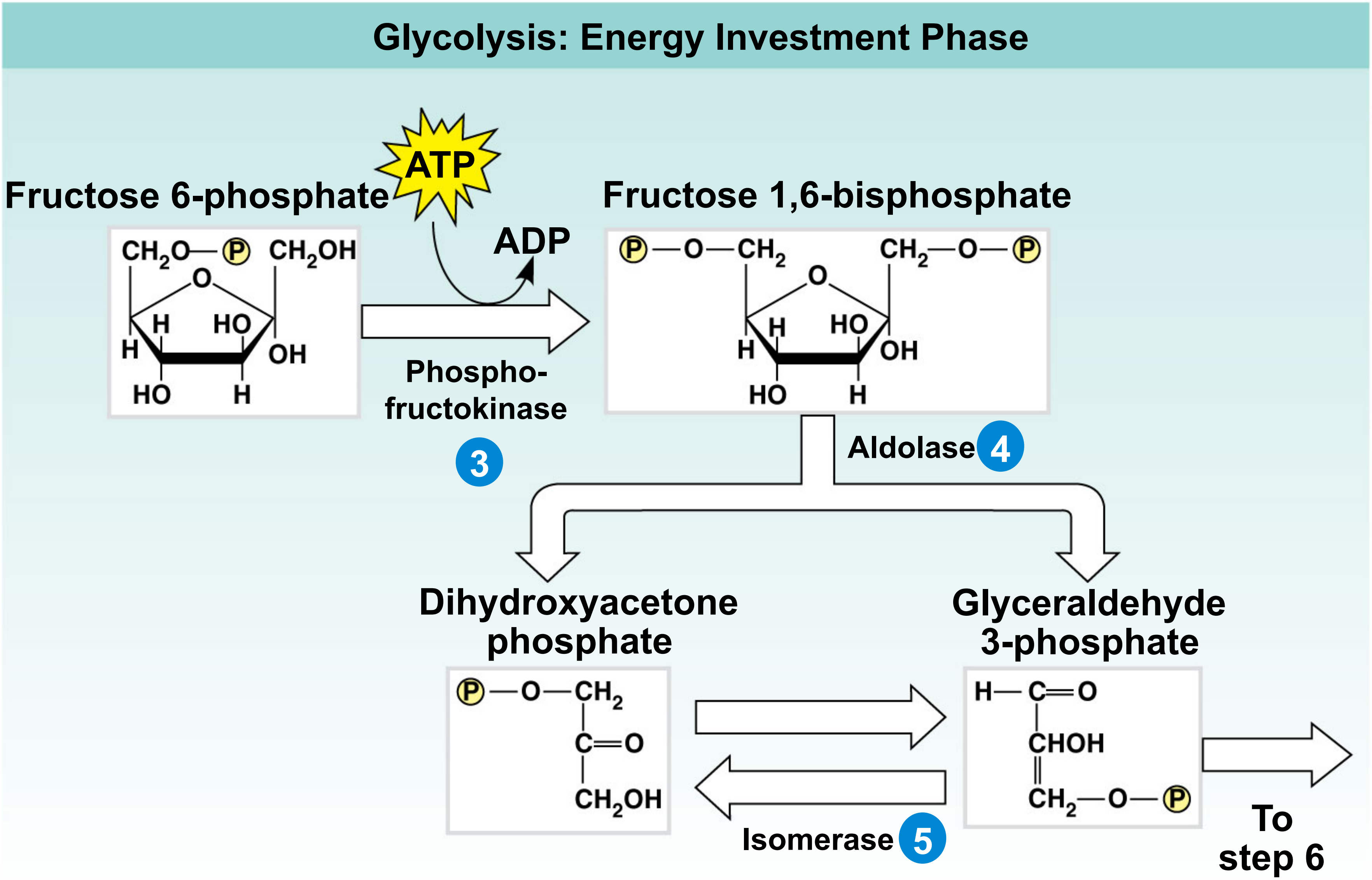

Energy Investment Phase
Glucose
2 ADP + 2 P
2 ATP used
Energy Payoff Phase
4 ADP + 4 P
4 ATP formed
2 NAD+ + 4 e- + 4 H+
2 NADH + 2 H+
2 Pyruvate + 2 H2O
Net
Glucose → 2 Pyruvate + 2 H2O
4 ATP formed - 2 ATP used → 2 ATP
2 NAD+ + 4 e- + 4 H+ → 2 NADH + 2 H+

Figure 9.9a



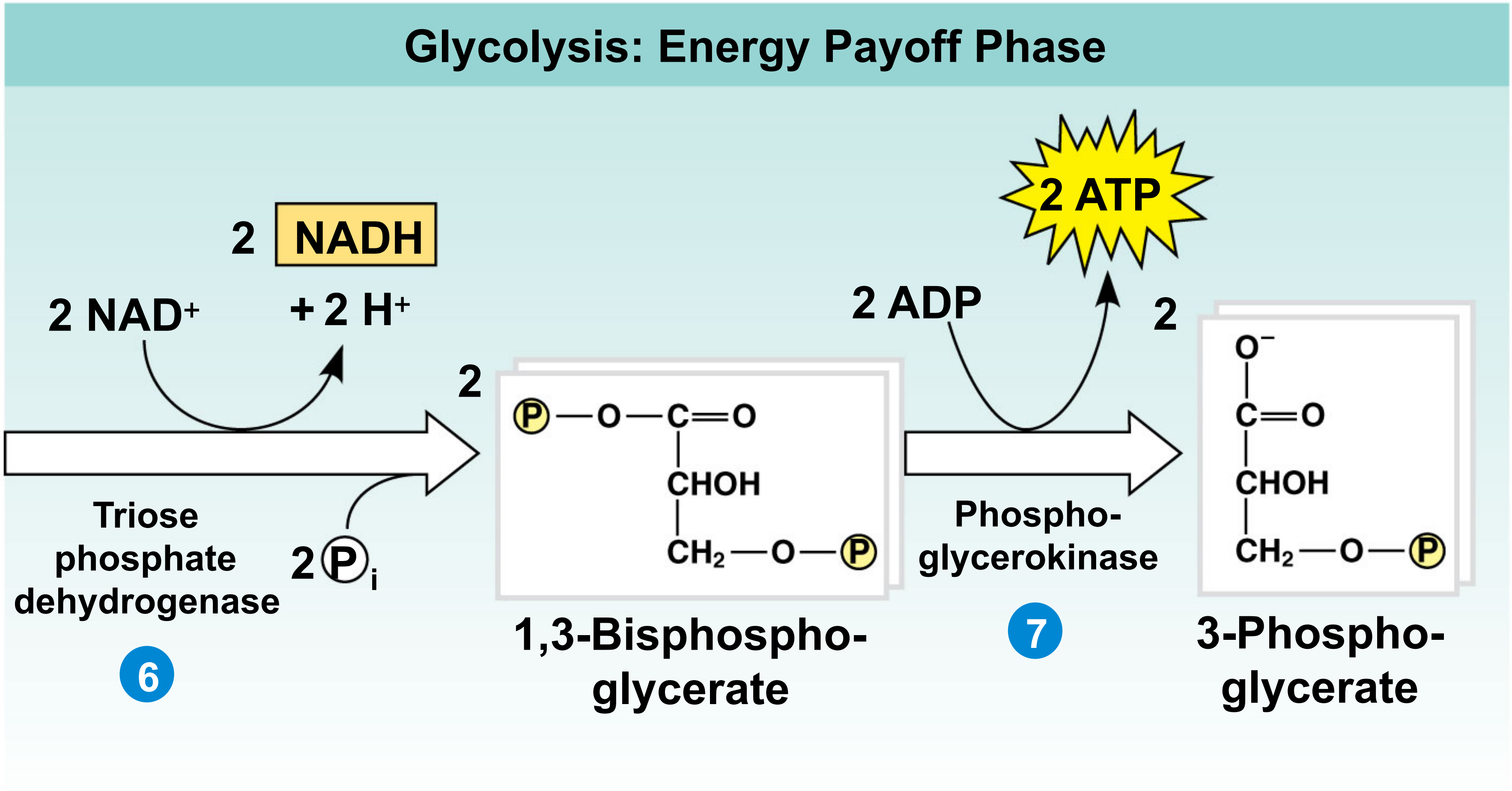
Glycolysis: Energy Investment Phase
ATP
Glucose
ADP
Glucose 6-phosphate
Fructose 6-phosphate
CH2OH
O
H
HO
OH
CH2O—P
Hexokinase
1
Phosphogluco-
isomerase
2

Figure 9.9b



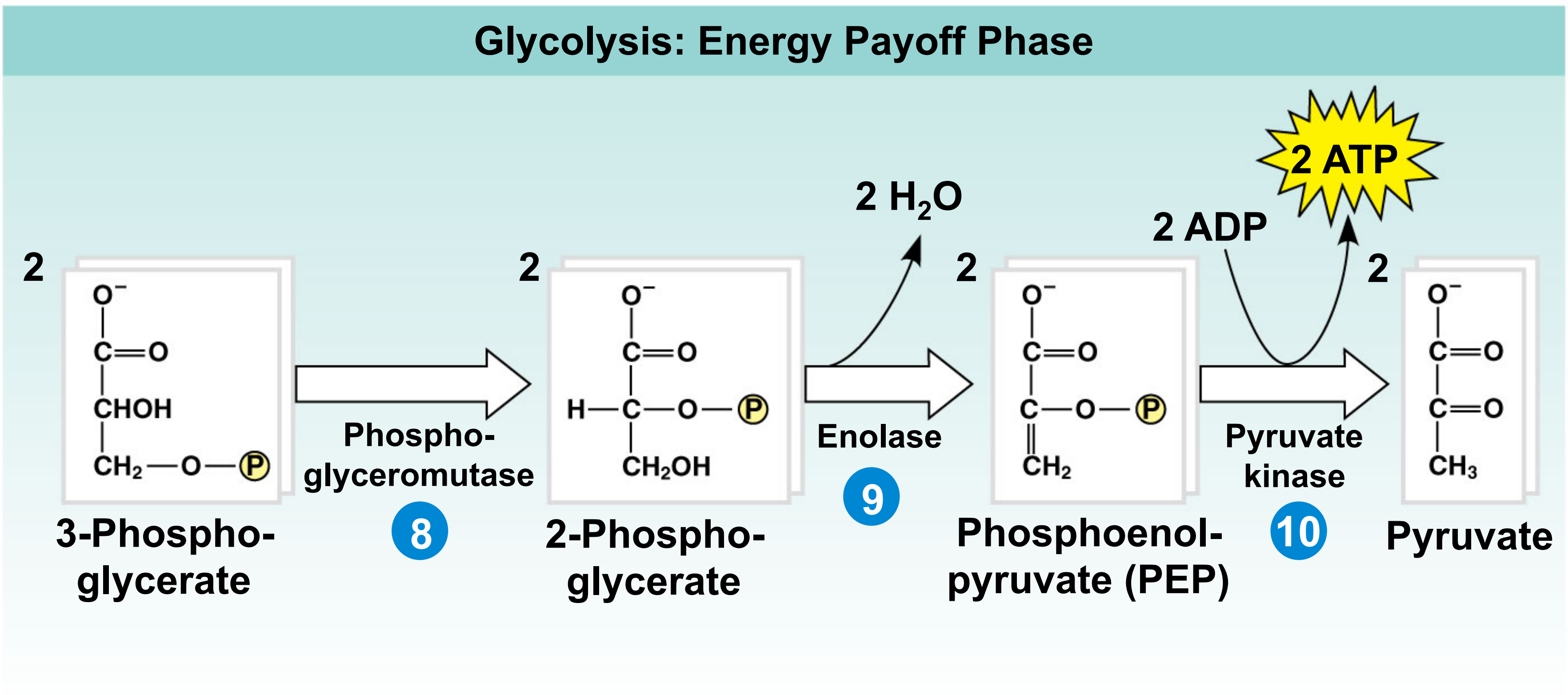
Glycolysis: Energy Investment Phase
Fructose 6-phosphate
ATP
ADP
Fructose 1,6-bisphosphate
CH2O—P CH2OH
O
H HO
H OH
HO H
Phospho-
fructokinase
3
P—O—CH2 CH2—O—P
Aldolase 4
Dihydroxyacetone
phosphate
Glyceraldehyde
3-phosphate
P—O—CH2
C=O
CH2OH
H—C=O
CHOH
CH2—O—P
Isomerase 5
To
step 6

Figure 9.9c

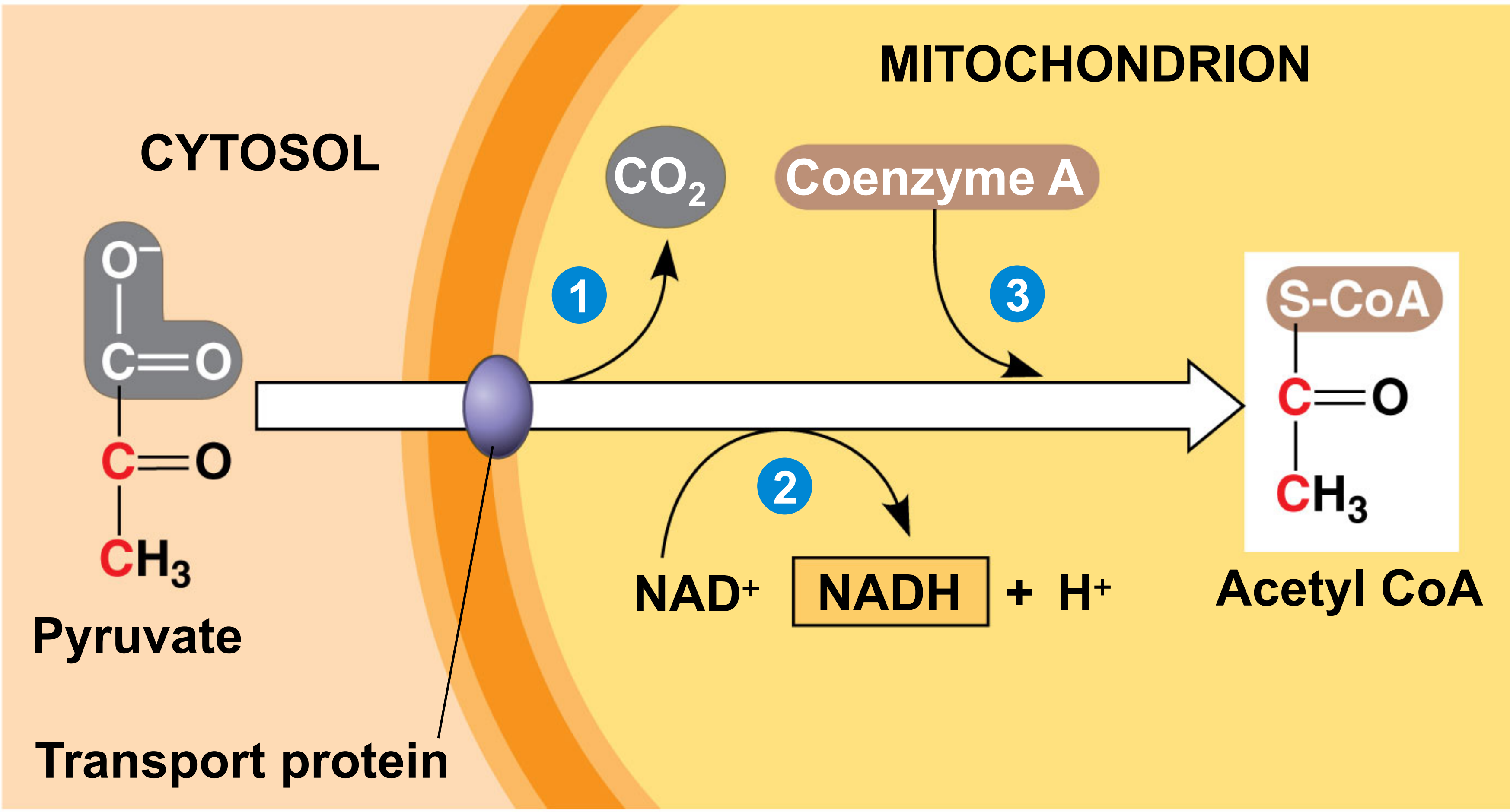


Glycolysis: Energy Payoff Phase
2 NADH
2 NAD+
+ 2 H+
2
Triose phosphate dehydrogenase
6
2 Pi
P—O—C=O
CHOH
CH2—O—P
1,3-Bisphosphoglycerate
2 ADP
2 ATP
Phosphoglycerokinase
7
2
O−
C=O
CHOH
CH2—O—P
3-Phosphoglycerate

Figure 9.9d

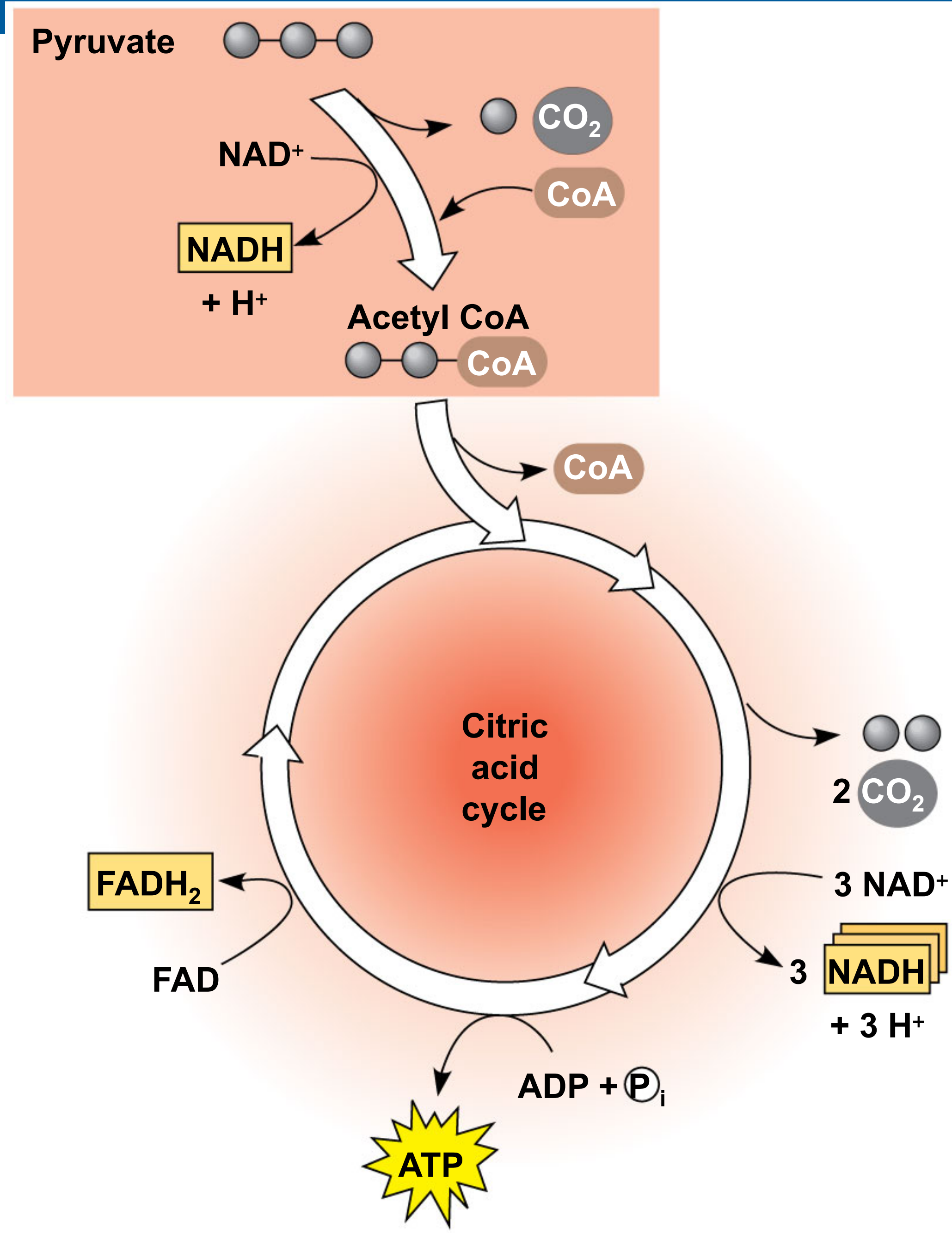

Glycolysis: Energy Payoff Phase
2
O⁻
C=O
CHOH
CH2—O—P
3-Phospho-
glycerate
Phospho-
glyceromutase
8
2
O⁻
C=O
H—C—O—P
CH2OH
2-Phospho-
glycerate
2 H2O
Enolase
9
2
O⁻
C=O
C—O—P
CH2
Phosphoenol-
pyruvate (PEP)
2 ADP
2 ATP
Pyruvate
kinase
10
2
O⁻
C=O
C=O
CH3
Pyruvate

After pyruvate is oxidized, the citric acid cycle completes the energy-yielding oxidation of organic molecules

- In the presence of O_2, pyruvate enters the mitochondrion (in eukaryotic cells) where the oxidation of glucose is completed
- 

The Citric Acid Cycle

- The citric acid cycle, also called the Krebs cycle, completes the break down of pyrvate to CO_2
- The cycle oxidizes organic fuel derived from pyruvate, generating 1 ATP, 3 NADH, and 1 $FADH_2$ per turn



- The citric acid cycle has eight steps, each catalyzed by a specific enzyme
- The acetyl group of acetyl CoA joins the cycle by combining with oxaloacetate, forming citrate
- The next seven steps decompose the citrate back to oxaloacetate, making the process a cycle
- The NADH and $FADH_2$ produced by the cycle relay electrons extracted from food to the electron transport chain

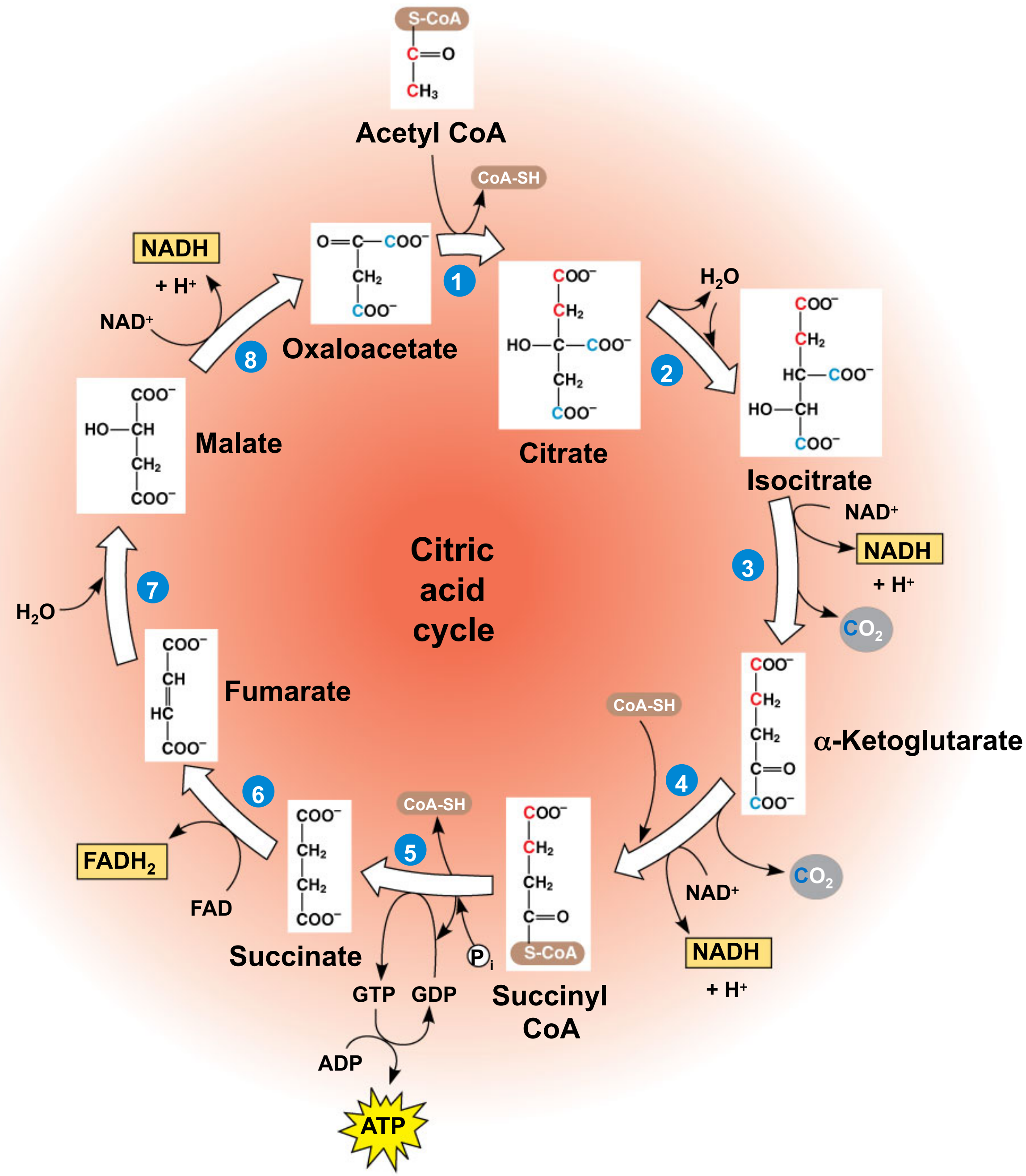
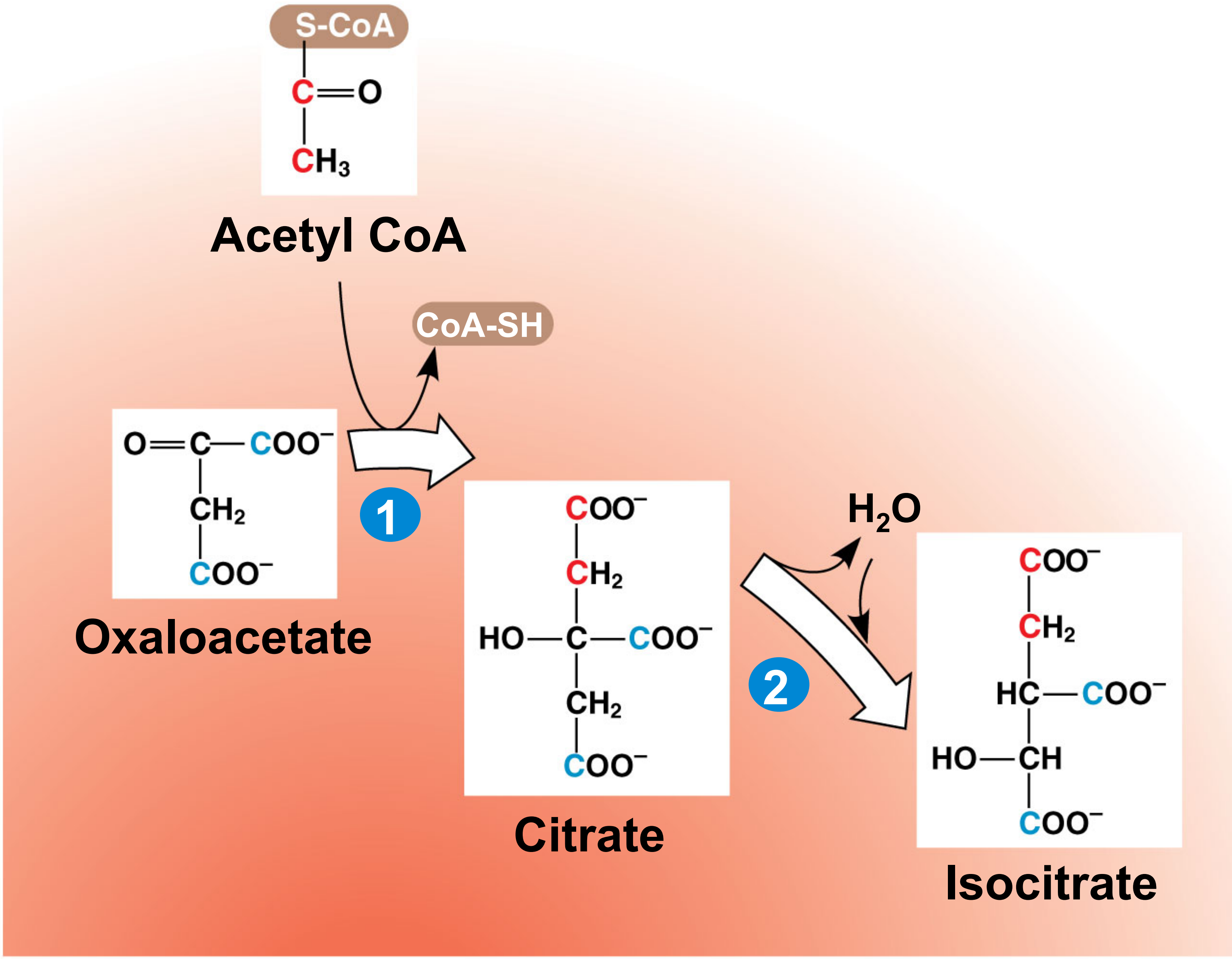


Figure 9.12a



S-CoA
C=O
CH3
Acetyl CoA
CoA-SH
O=C—COO⁻
CH2
COO⁻
Oxaloacetate
1
COO⁻
CH2
HO—C—COO⁻
CH2
COO⁻
Citrate
2
H2O
COO⁻
CH2
HC—COO⁻
HO—CH
COO⁻
Isocitrate

Figure 9.12b

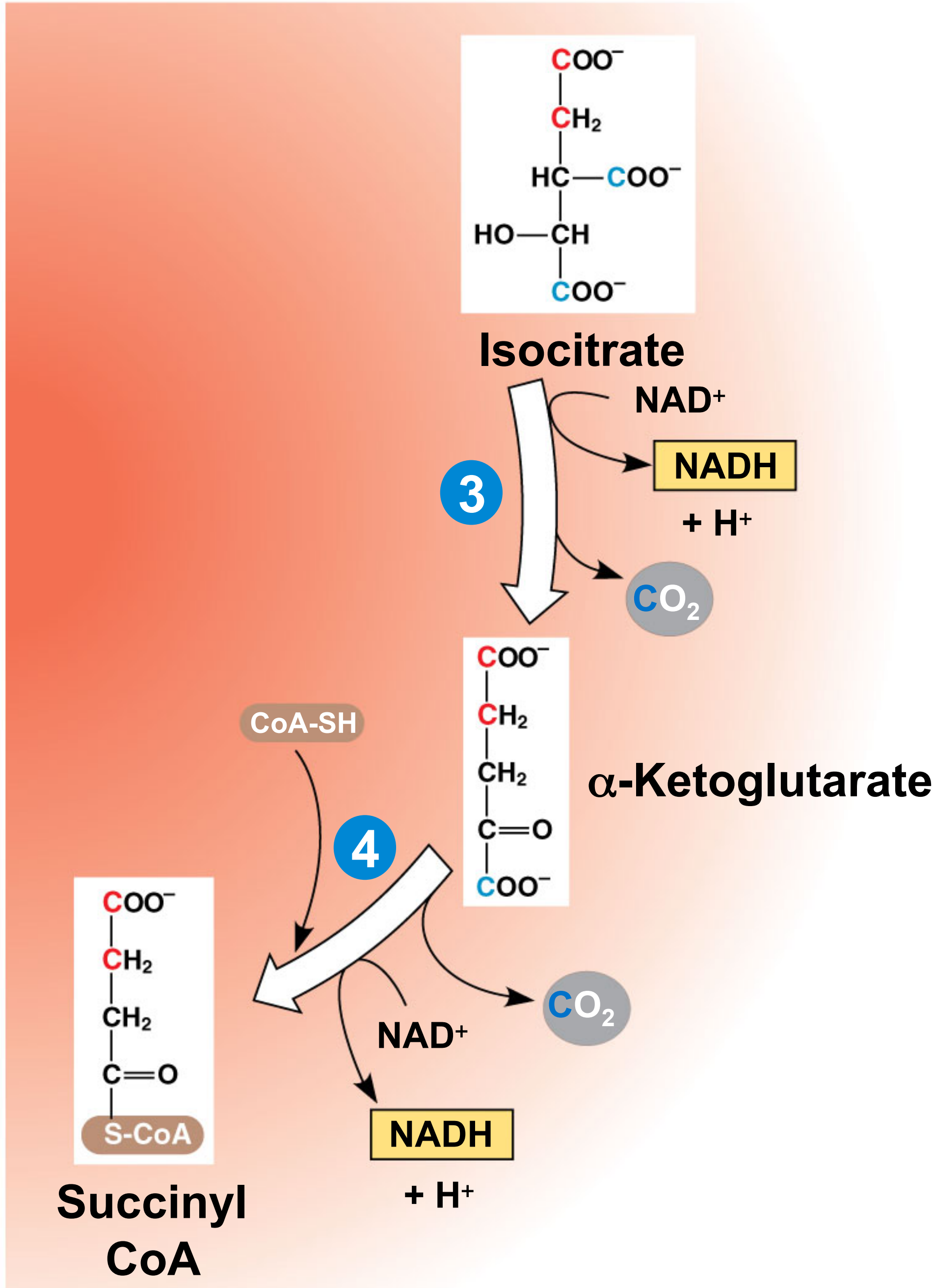
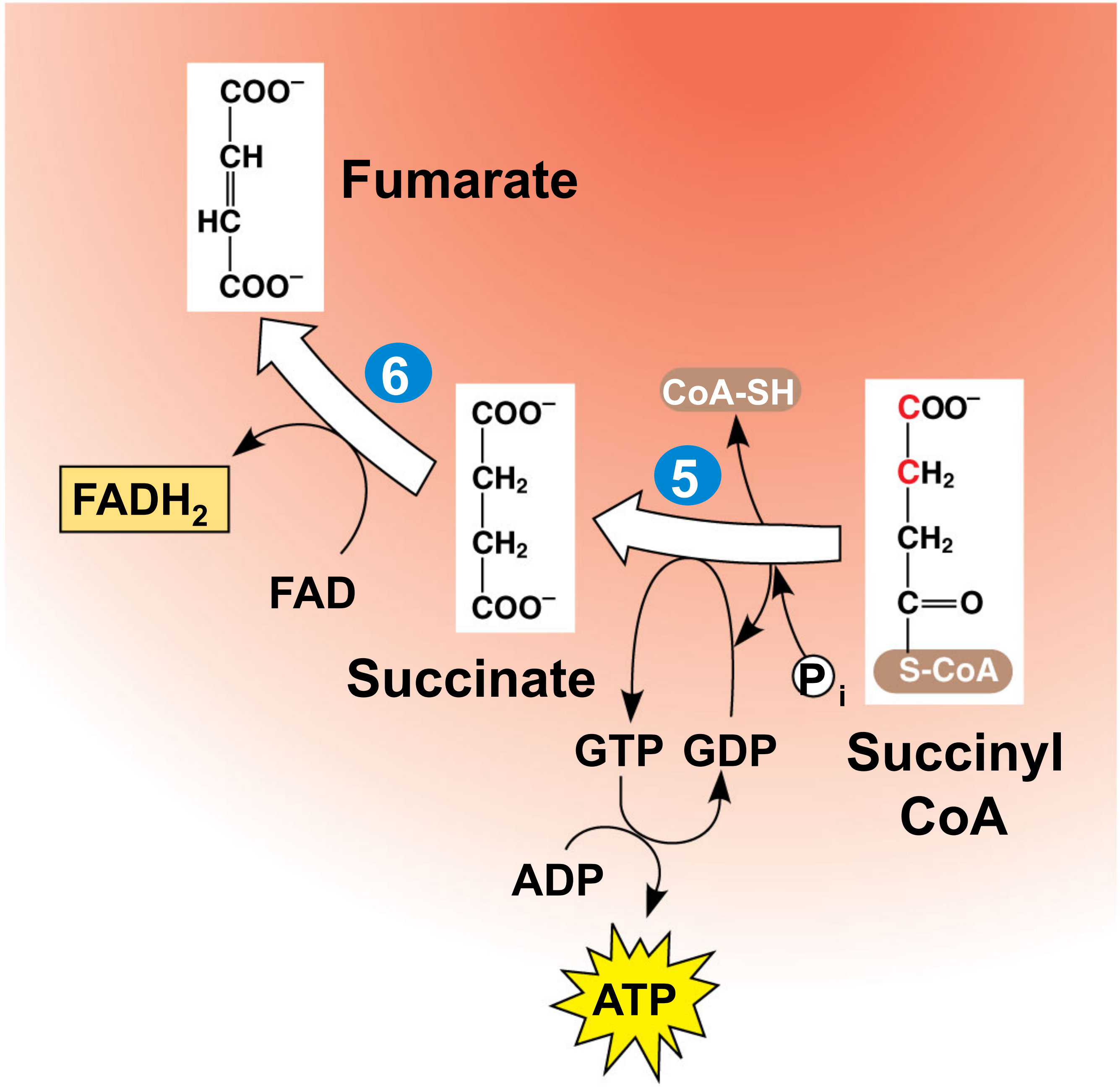
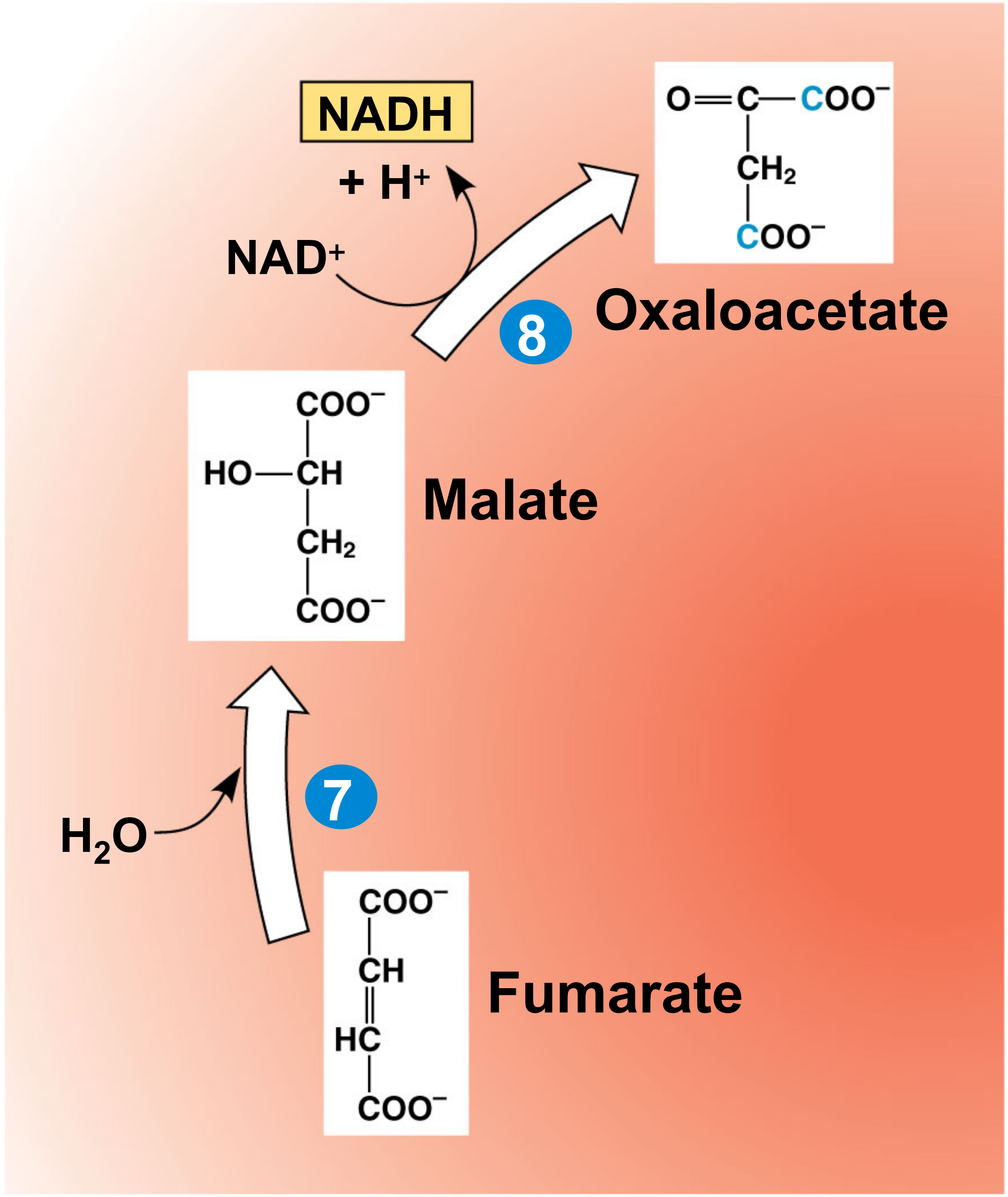

COO⁻
CH₂
HC—COO⁻
HO—CH
COO⁻
Isocitrate
NAD+
NADH
+ H+
3
CO2
COO⁻
CH₂
CH₂
C═O
COO⁻
α-Ketoglutarate
CoA-SH
4
CO2
NAD+
NADH
+ H+
COO⁻
CH₂
CH₂
C═O
S-CoA
Succinyl CoA

Figure 9.12c



COO⁻
CH
HC
COO⁻
Fumarate
6
FADH2
FAD
COO⁻
CH2
CH2
COO⁻
Succinate
CoA-SH
5
COO⁻
CH2
CH2
C=O
S-CoA
P i
GTP GDP
Succinyl CoA
ADP
ATP

Figure 9.12d

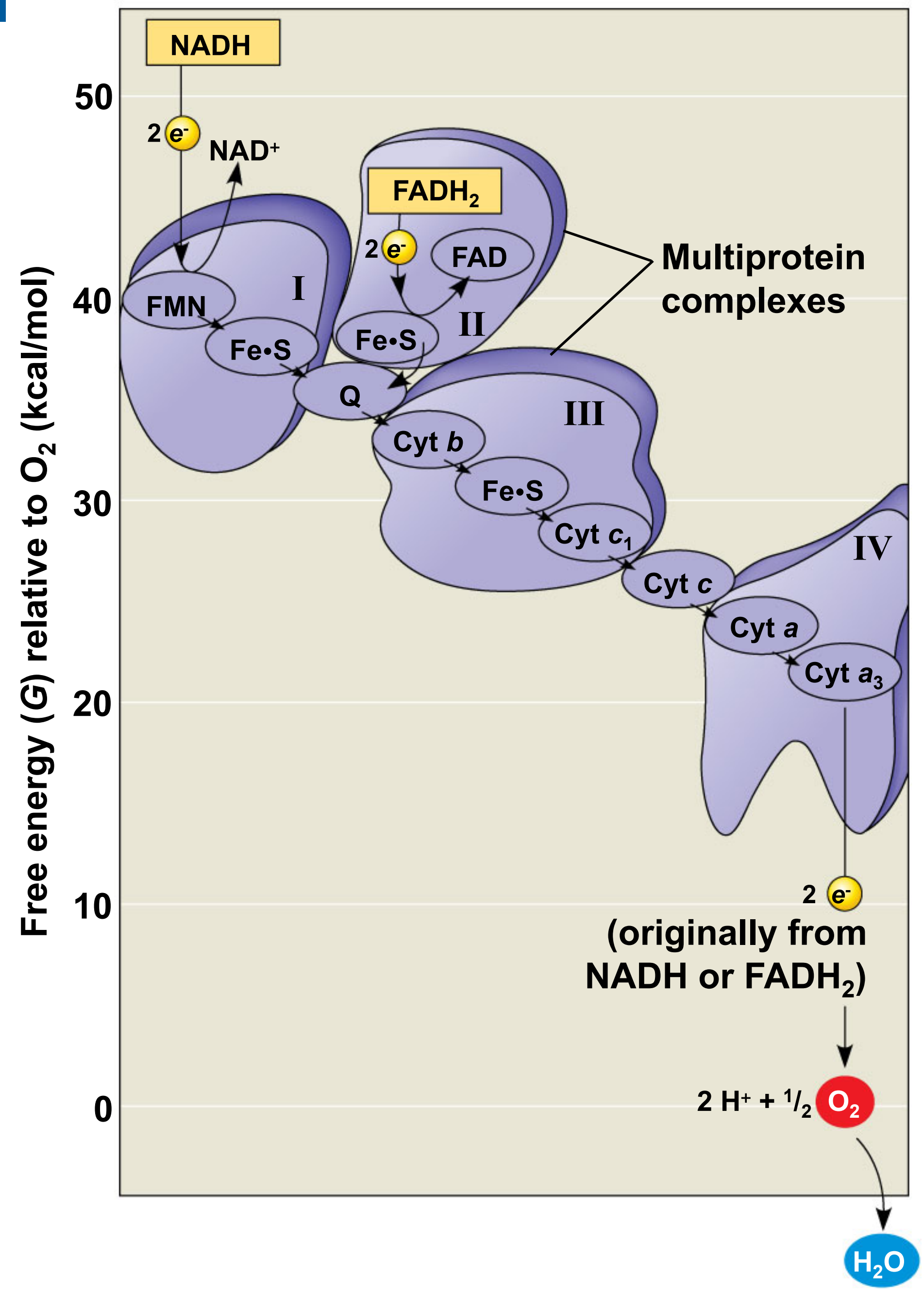

NADH
+ H+
NAD+
O=C—COO−
CH2
COO−
Oxaloacetate
8
COO−
HO—CH
CH2
COO−
Malate
7
H2O
COO−
CH
HC
COO−
Fumarate

During oxidative phosphorylation, chemiosmosis couples electron transport to ATP synthesis

- Following glycolysis and the citric acid cycle, NADH and $FADH_2$ account for most of the energy extracted from food
- These two electron carriers donate electrons to the electron transport chain, which powers ATP synthesis via oxidative phosphorylation
- Electrons are transferred from NADH or $FADH_2$ to the electron transport chain
- Electrons are passed through a number of proteins including **cytochromes** (each with an iron atom) to O_2
- The electron transport chain generates no ATP directly
- It breaks the large free-energy drop from food to O_2 into smaller steps that release energy in manageable amounts

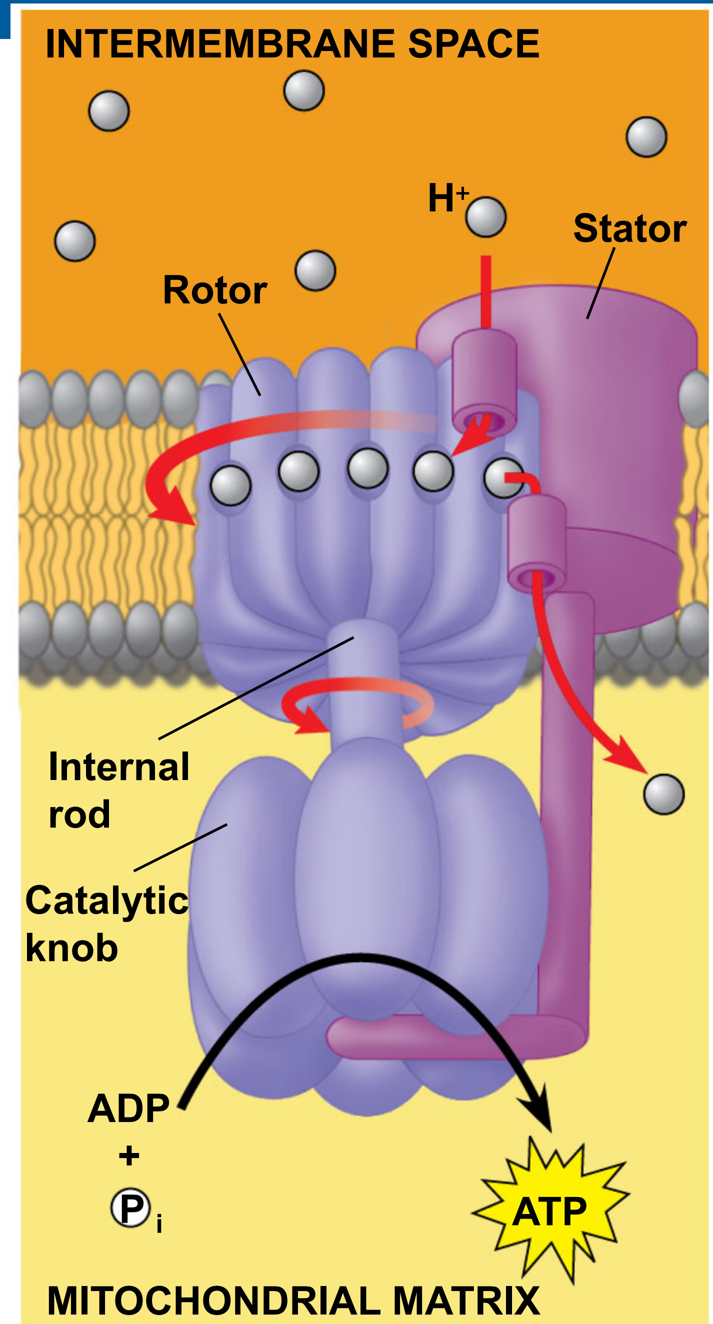
The Pathway of Electron Transport

- The electron transport chain is in the inner membrane (cristae) of the mitochondrion
- Most of the chain's components are proteins, which exist in multiprotein complexes
- The carriers alternate reduced and oxidized states as they accept and donate electrons
- Electrons drop in free energy as they go down the chain and are finally passed to O_2, forming H_2O

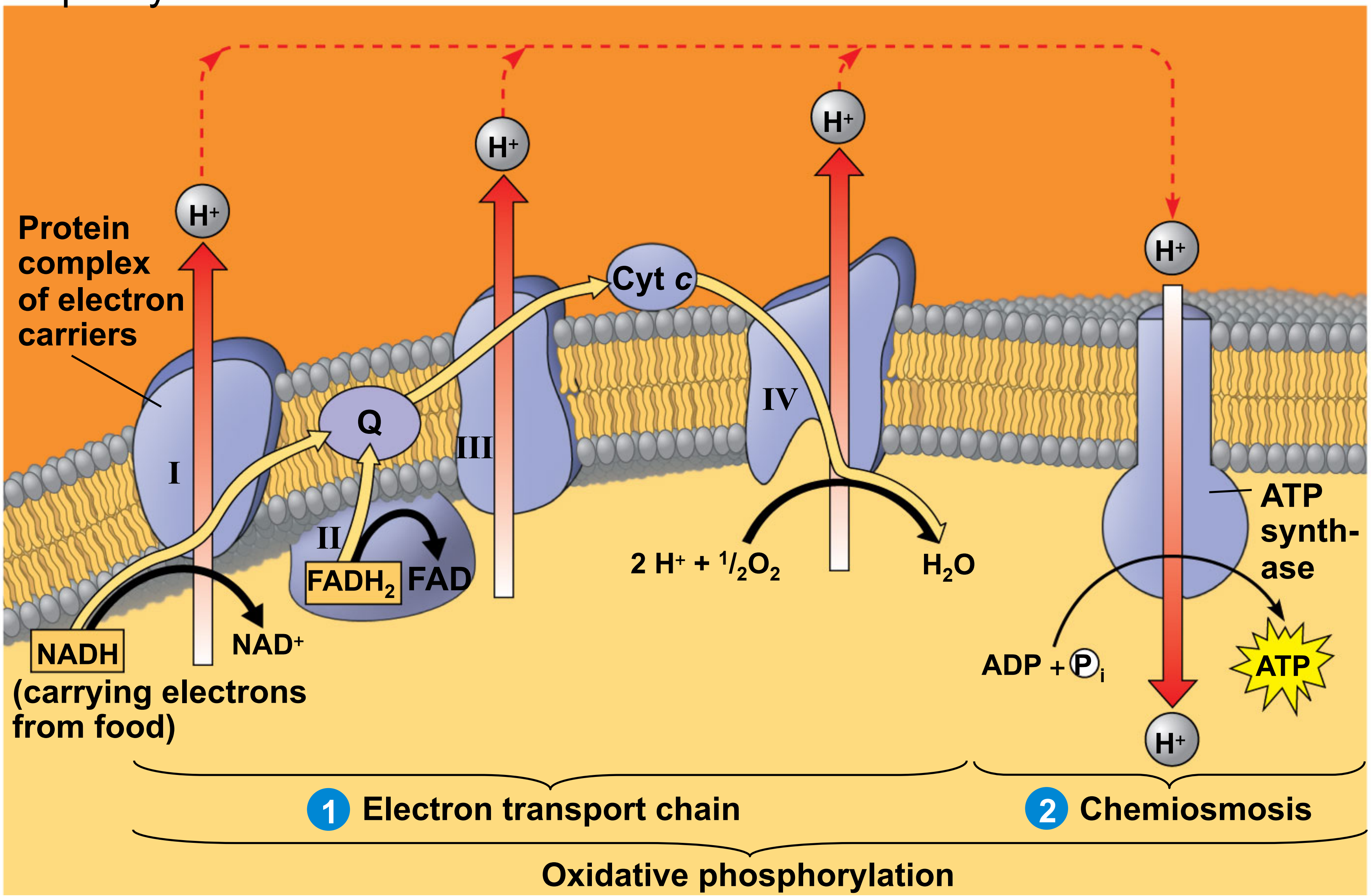


Energy-Coupling Mechanism

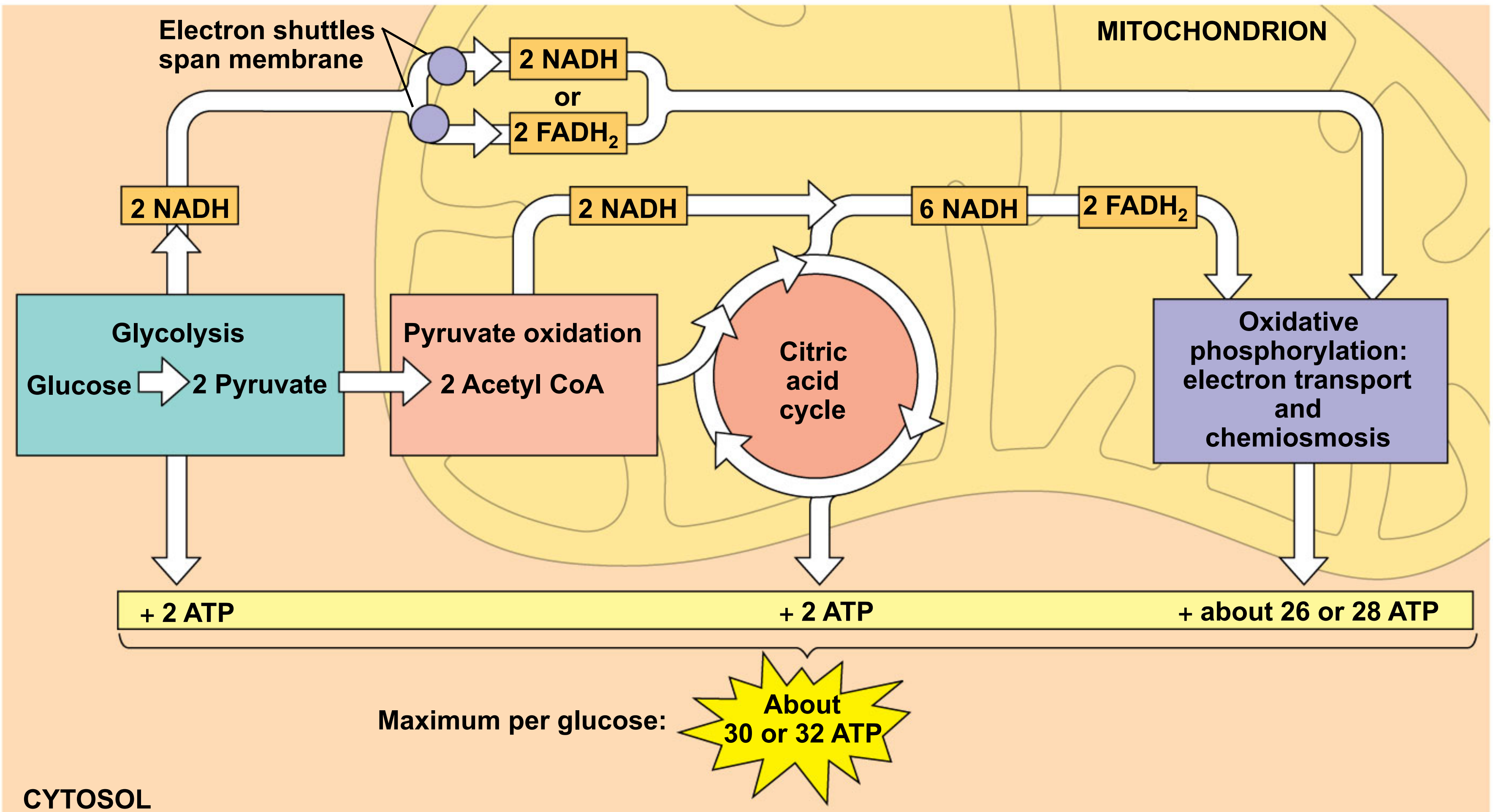
- Electron transfer in the electron transport chain causes proteins to pump H^+ from the mitochondrial matrix to the intermembrane space
- H^+ then moves back across the membrane, passing through the proton, **ATP synthase**
- ATP synthase uses the exergonic flow of H^+ to drive phosphorylation of ATP
- This is an example of **chemiosmosis**, the use of energy in a H^+ gradient to drive cellular work



- The energy stored in a H^+ gradient across a membrane couples the redox reactions of the electron transport chain to ATP synthesis
- The H^+ gradient is referred to as a **proton-motive force**, emphasizing its capacity to do work



- During cellular respiration, most energy flows in this sequence:
  glucose → NADH → electron transport chain → proton-motive force → ATP
- About 34% of the energy in a glucose molecule is transferred to ATP during cellular respiration, making about 32 ATP
- There are several reasons why the number of ATP is not known exactly



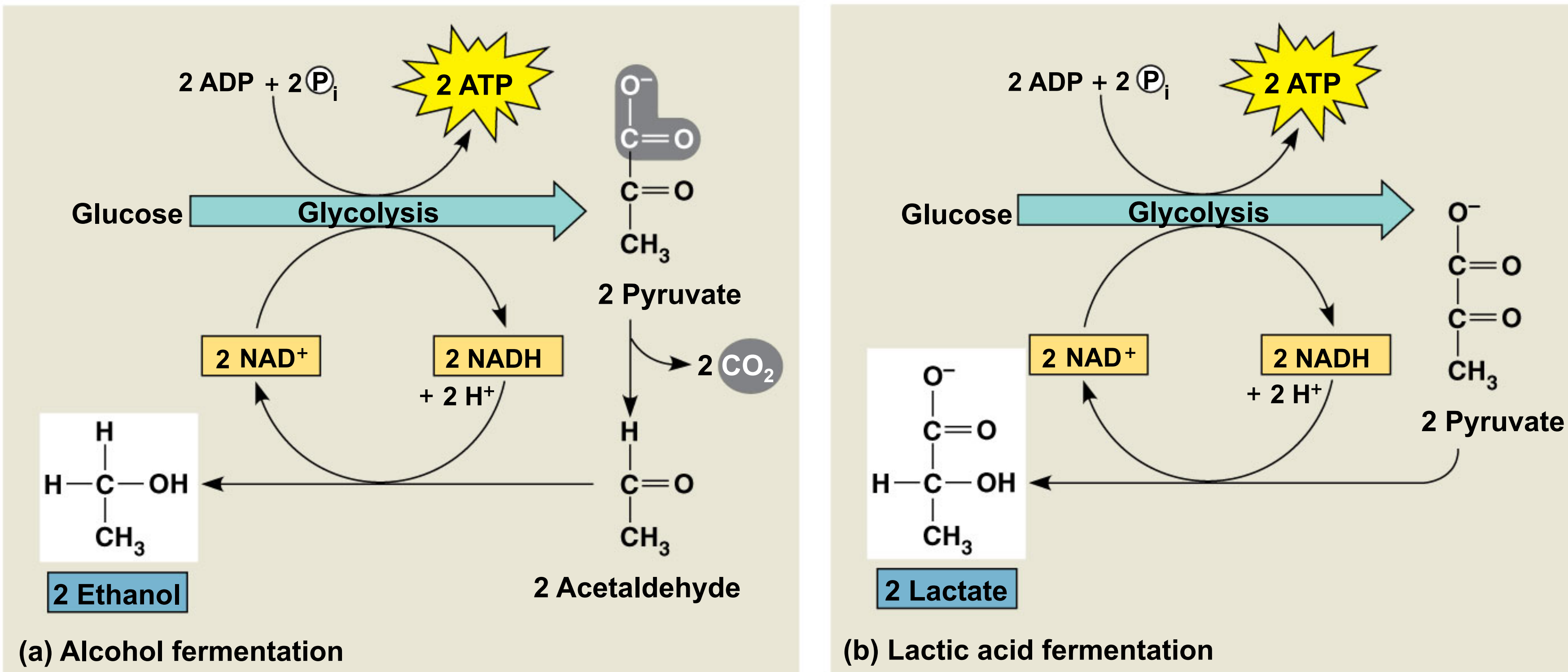
Fermentation and anaerobic respiration enable cells to produce ATP without the use of oxygen

- Most cellular respiration requires O_2 to produce ATP
- Without O_2, the electron transport chain will cease to operate
- In that case, glycolysis couples with fermentation or anaerobic respiration to produce ATP
- Anaerobic respiration uses an electron transport chain with a final electron acceptor other than O_2, for example sulfate
- Fermentation uses substrate-level phosphorylation instead of an electron transport chain to generate ATP

Types of Fermentation

- Fermentation consists of glycolysis plus reactions that regenerate NAD^+, which can be reused by glycolysis
- Two common types are **alcohol fermentation** and **lactic acid fermentation**
- In alcohol fermentation, pyruvate is converted to ethanol in two steps, with the first releasing CO_2
- Alcohol fermentation by yeast is used in brewing, winemaking, and baking
- In lactic acid fermentation, pyruvate is reduced to NADH, forming lactate as an end product, with no release of CO_2
- Lactic acid fermentation by some fungi and bacteria is used to make cheese and yogurt
- Human muscle cells use lactic acid fermentation to generate ATP when O_2 is scarce

Figure 9.17

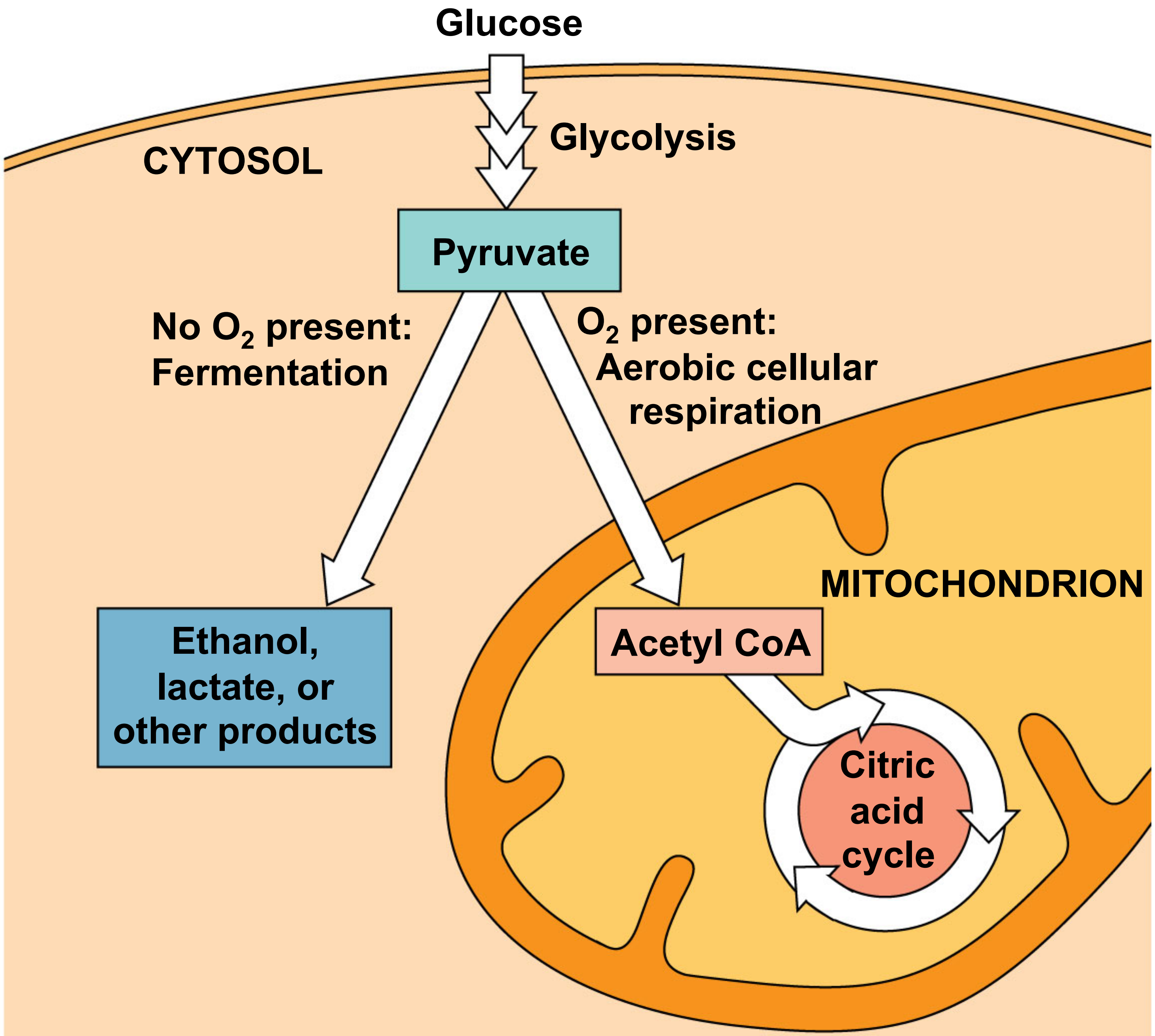


2 ADP + 2 Ⓟi
2 ATP
Glucose
Glycolysis
O⁻
C=O
C=O
CH3
2 Pyruvate
2 NAD+
2 NADH
+ 2 H+
2 CO2
H
C=O
CH3
2 Acetaldehyde
H
H—C—OH
CH3
2 Ethanol
(a) Alcohol fermentation
2 ADP + 2 Ⓟi
2 ATP
Glucose
Glycolysis
O⁻
C=O
C=O
CH3
2 Pyruvate
2 NAD+
2 NADH
+ 2 H+
O⁻
C=O
H—C—OH
CH3
2 Lactate
(b) Lactic acid fermentation

Comparing Fermentation with Anaerobic and Aerobic Respiration

- All use glycolysis (net ATP =2) to oxidize glucose and harvest chemical energy of food
- In all three, NAD^+ is the oxidizing agent that accepts electrons during glycolysis
- The processes have different final electron acceptors: an organic molecule (such as pyruvate or acetaldehyde) in fermentation and O_2 in cellular respiration
- Cellular respiration produces 32 ATP per glucose molecule; fermentation produces 2 ATP per glucose molecule
- **Obligate anaerobes** carry out fermentation or anaerobic respiration and cannot survive in the presence of O_2
- Yeast and many bacteria are **facultative anaerobes**, meaning that they can survive using either fermentation or cellular respiration
- In a facultative anaerobe, pyruvate is a fork in the metabolic road that leads to two alternative catabolic routes

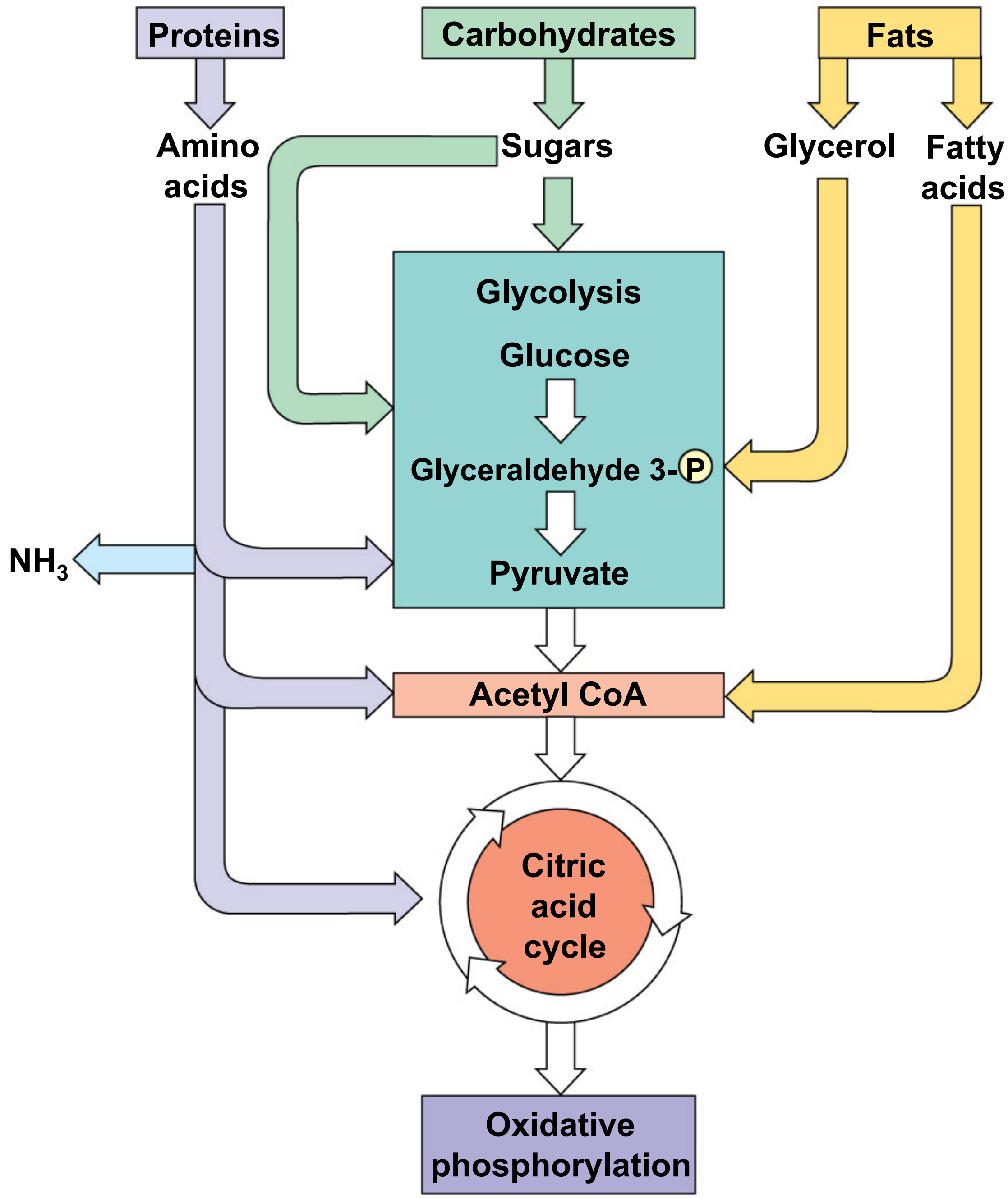
Figure 9.18



Glucose
Glycolysis
CYTOSOL
Pyruvate
No O_2 present:
Fermentation
O_2 present:
Aerobic cellular
respiration
MITOCHONDRION
Ethanol,
lactate, or
other products
Acetyl CoA
Citric
acid
cycle

Glycolysis and the citric acid cycle connect to many other metabolic pathways

- Gycolysis and the citric acid cycle are major intersections to various catabolic and anabolic pathways
- Catabolic pathways funnel electrons from many kinds of organic molecules into cellular respiration
- Glycolysis accepts a wide range of carbohydrates
- Proteins must be digested to amino acids; amino groups can feed glycolysis or the citric acid cycle
- Fats are digested to glycerol (used in glycolysis) and fatty acids (used in generating acetyl CoA)
- Fatty acids are broken down by **beta oxidation** and yield acetyl CoA
- An oxidized gram of fat produces more than twice as much ATP as an oxidized gram of carbohydrate



- The body uses small molecules to build other substances
- These small molecules may come directly from food, from glycolysis, or from the citric acid cycle

Regulation of Cellular Respiration via Feedback Mechanisms

- Feedback inhibition is the most common mechanism for control
- If ATP concentration begins to drop, respiration speeds up; when there is plenty of ATP, respiration slows down
- Control of catabolism is based mainly on regulating the activity of enzymes at strategic points in the catabolic pathway