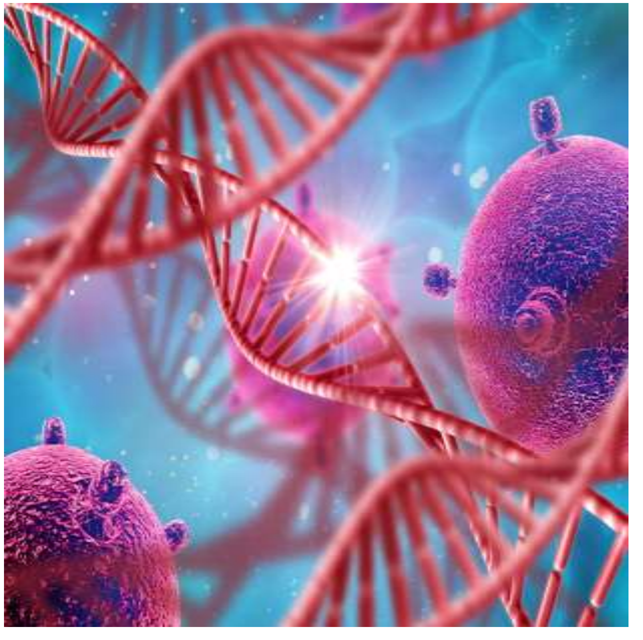
Lecture 17

General Biology & Cytology Course 2301130



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Cellular Respiration

- **Cellular respiration** includes both aerobic and anaerobic respiration but is often used to refer to aerobic respiration

- Although carbohydrates, fats, and proteins are all consumed as fuel, it is helpful to trace cellular respiration with the sugar glucose:

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O + \text{Energy (ATP + heat)}$$

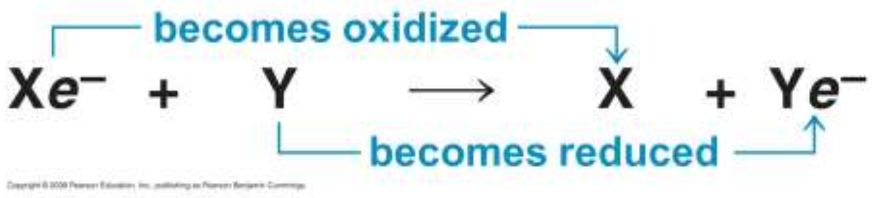
- Redox Reactions (Oxidation and Reduction):

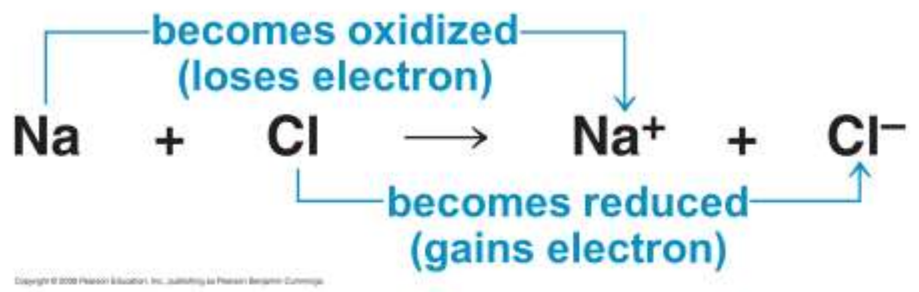
- The transfer of electrons during chemical reactions releases energy stored in organic molecules.

- This released energy is ultimately used to synthesize ATP

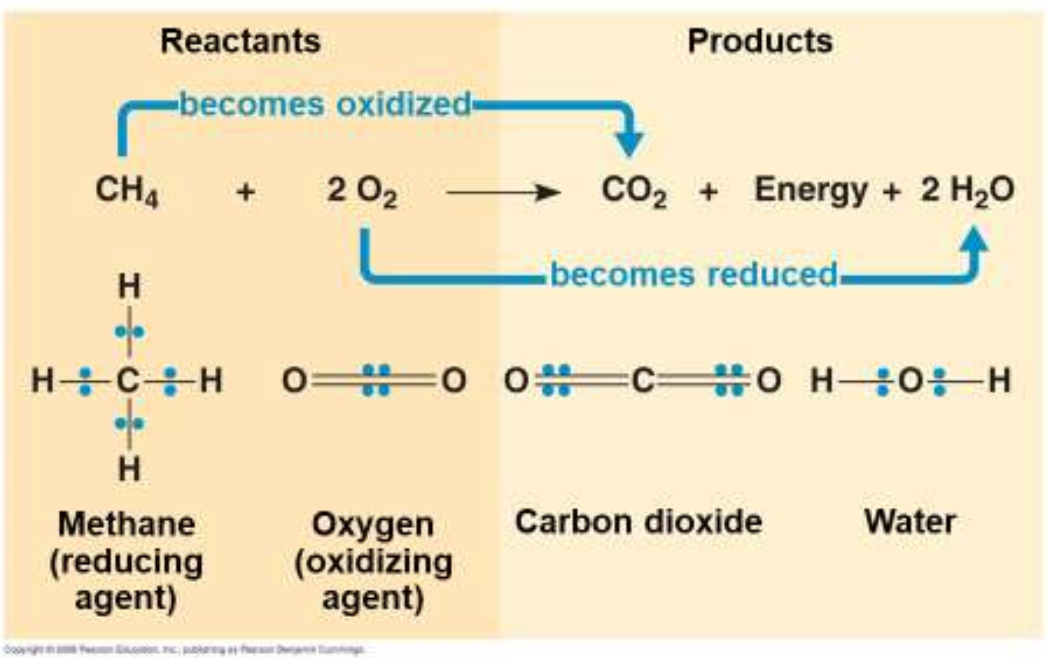
The Principle of Redox

- Chemical reactions that transfer electrons between reactants are called oxidation-reduction reactions, or **redox reactions**
- In **oxidation**, a substance loses electrons, or is oxidized
- In **reduction**, a substance gains electrons, or is reduced (the amount of positive charge is reduced)

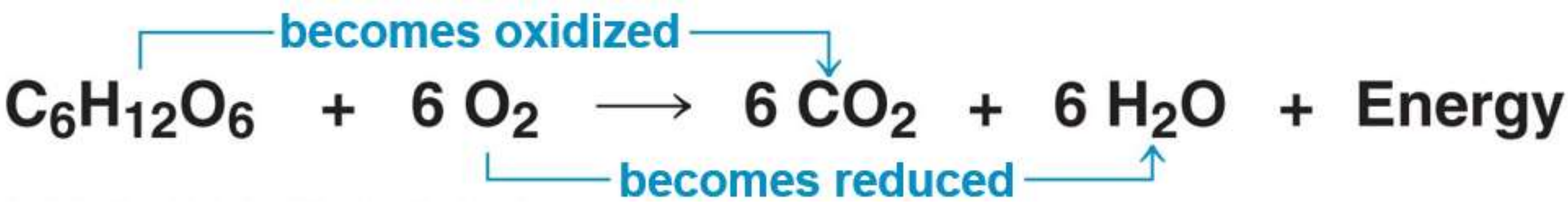




- The electron donor is called the **reducing agent**
- The electron receptor is called the **oxidizing agent**
- Some redox reactions do not transfer electrons but change the electron sharing in covalent bonds
- An example is the reaction between methane and O_2

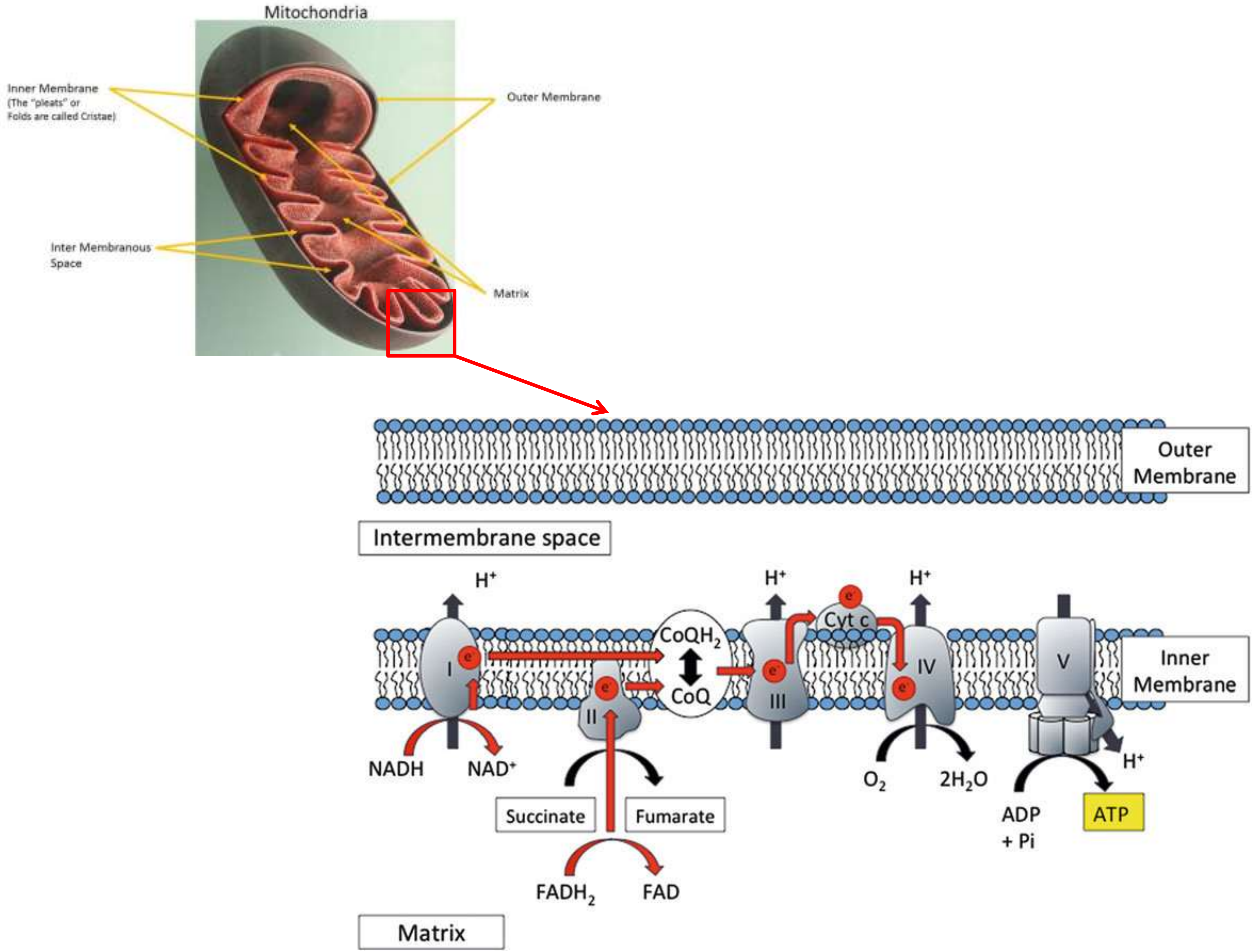


- During cellular respiration, the fuel organic molecules (such as glucose) is oxidized, and O_2 is reduced:

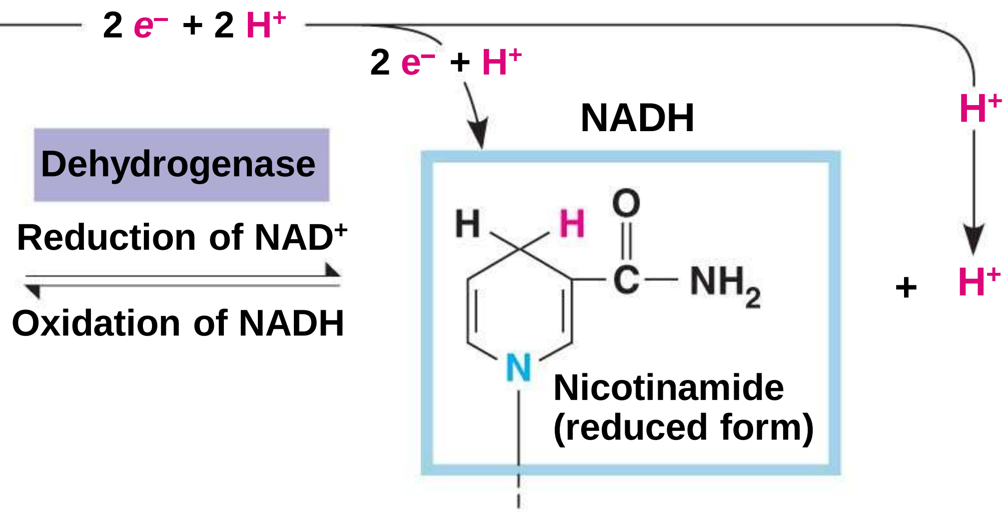


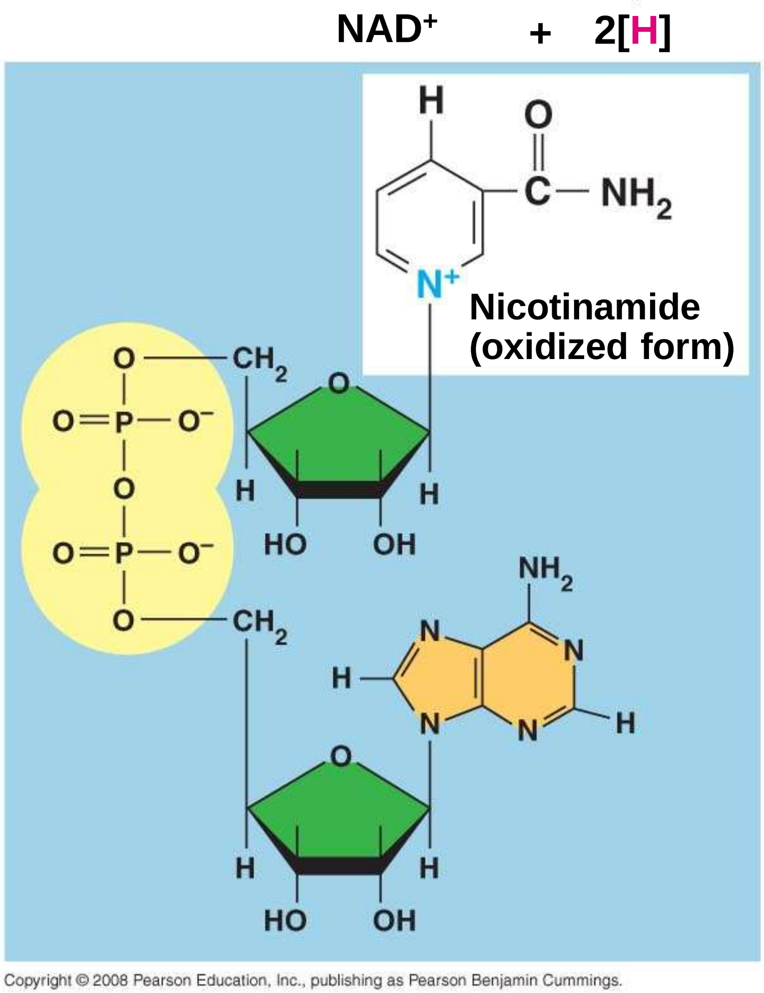
Stepwise Energy Harvest via NAD^+ and the Electron Transport Chain

- 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



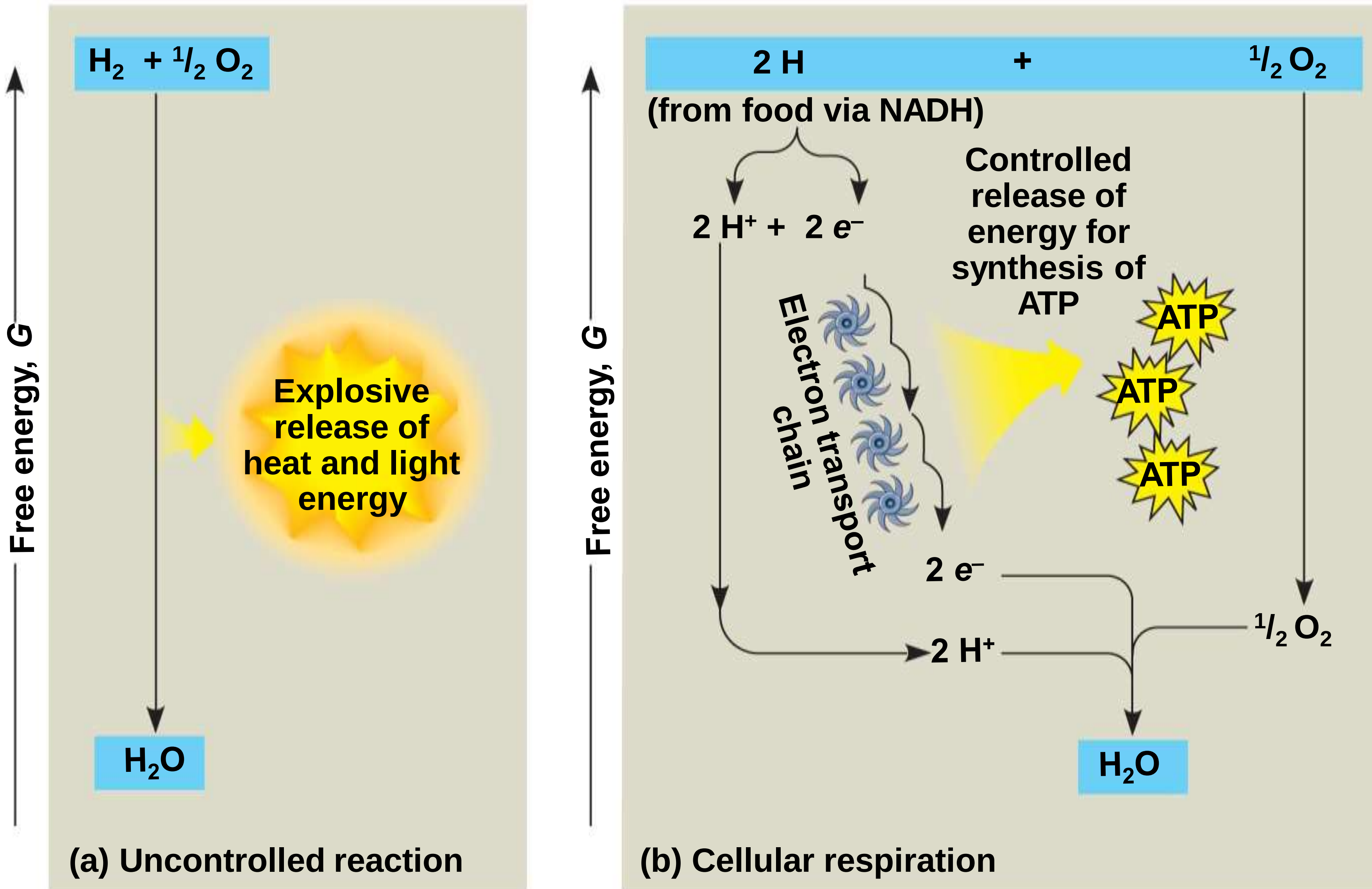
Mitochondria
Inner Membrane
(The "pleats" or
Folds are called Cristae)
Outer Membrane
Inter Membranous
Space
Matrix
Outer Membrane
Intermembrane space
H+
H+
H+
CoQH2
Cyt c
I
e
II
e
CoQ
III
e
IV
e
V
Inner Membrane
NADH
NAD+
Succinate
Fumarate
FADH2
FAD
O2
2H2O
H+
ADP
+ Pi
ATP
Matrix





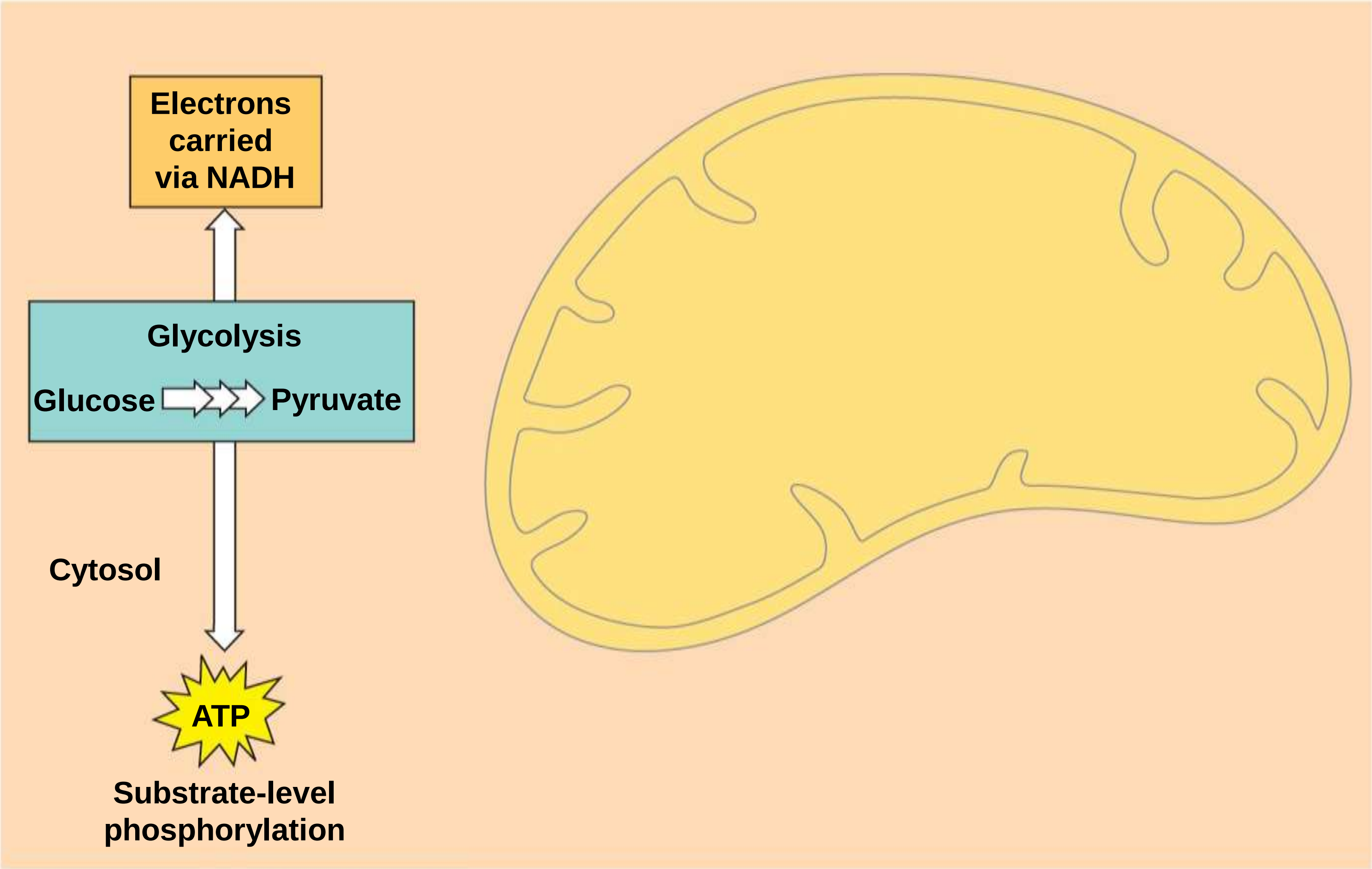
- NADH passes the electrons to the **electron transport chain**
- Unlike an uncontrolled reaction, the electron transport chain passes electrons in a series of steps
- O_2 pulls electrons down the chain in an energy-yielding tumble
- The energy yielded is used to regenerate ATP

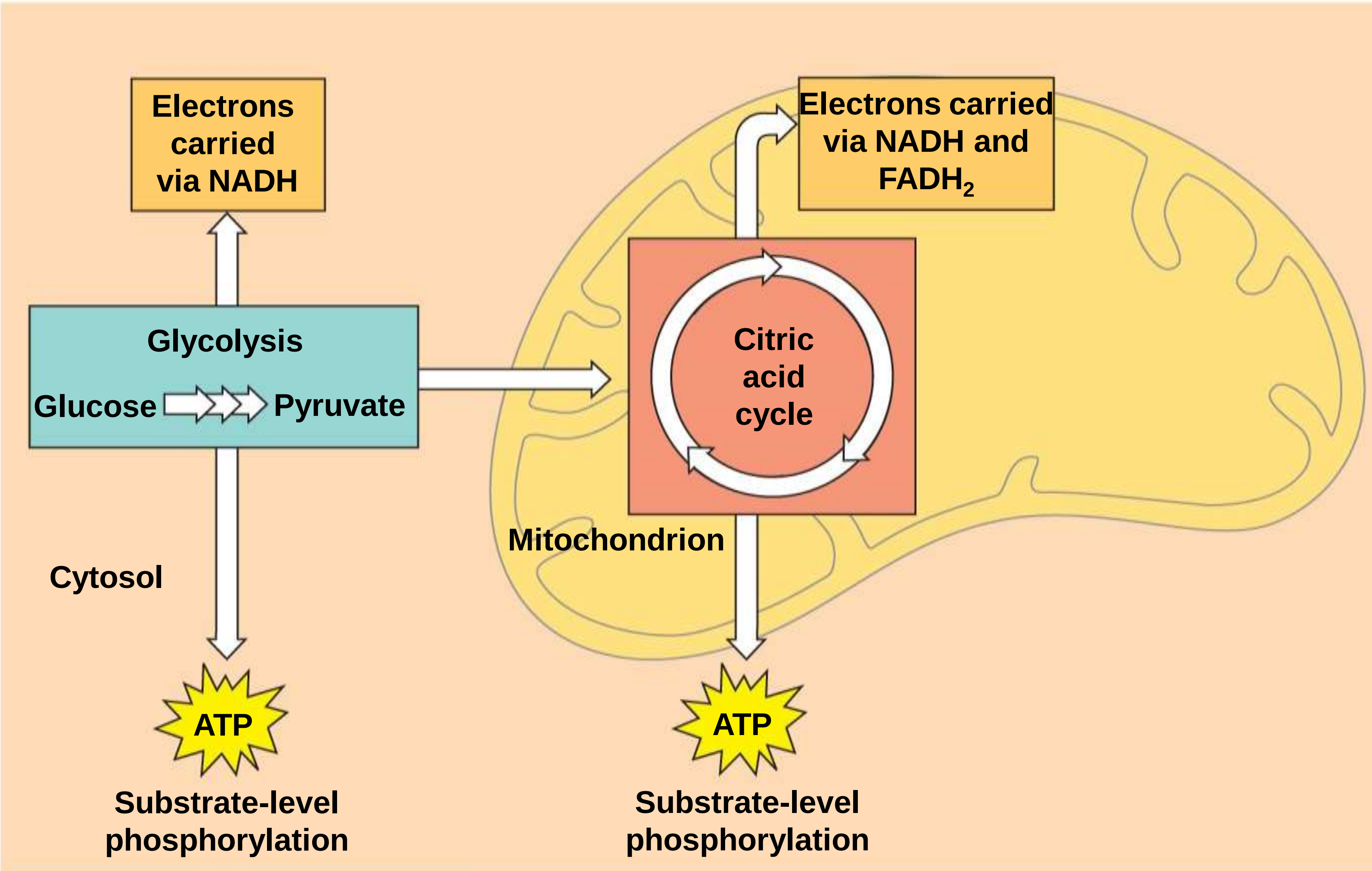
An introduction to electron transport chains

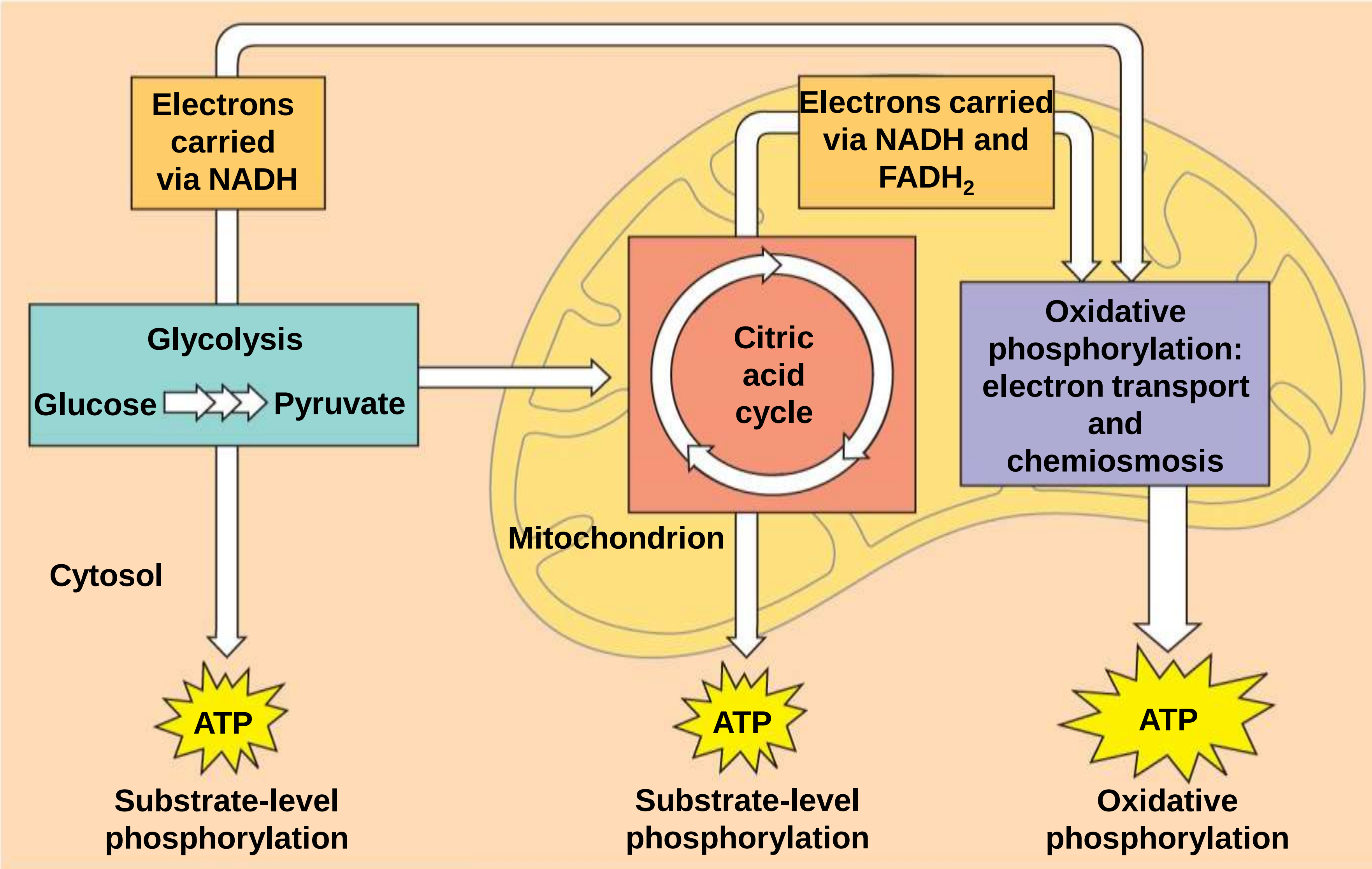


The Stages of Cellular Respiration:

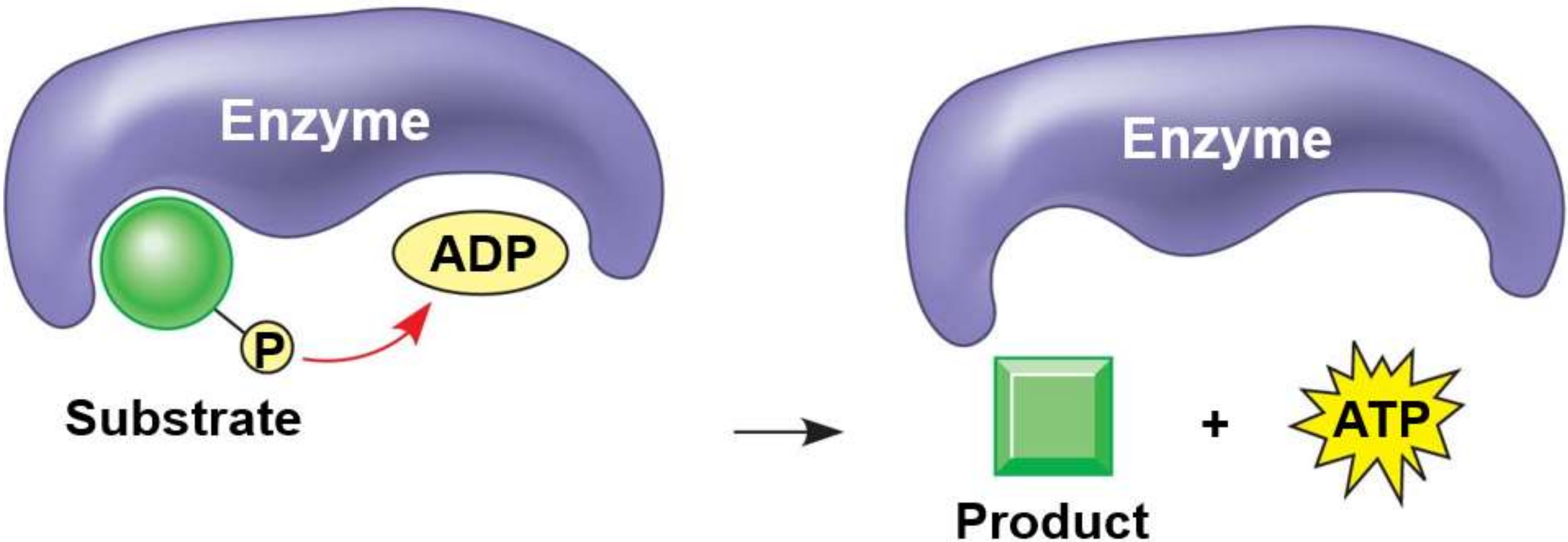
- Cellular respiration has three stages:
  - **Glycolysis** (breaks down glucose into two molecules of pyruvate)
  - The **citric acid cycle** (completes the breakdown of glucose)
  - **Oxidative phosphorylation** (accounts for most of the ATP synthesis)
- The process that generates most of the ATP is called oxidative phosphorylation because it is powered by redox reactions


Electrons carried via NADH
Glycolysis
Glucose
Pyruvate
Cytosol
ATP
Substrate-level phosphorylation


Electrons carried via NADH
Electrons carried via NADH and $FADH_2$
Glycolysis
Glucose
Pyruvate
Citric acid cycle
Mitochondrion
Cytosol
ATP
ATP
Substrate-level phosphorylation
Substrate-level phosphorylation

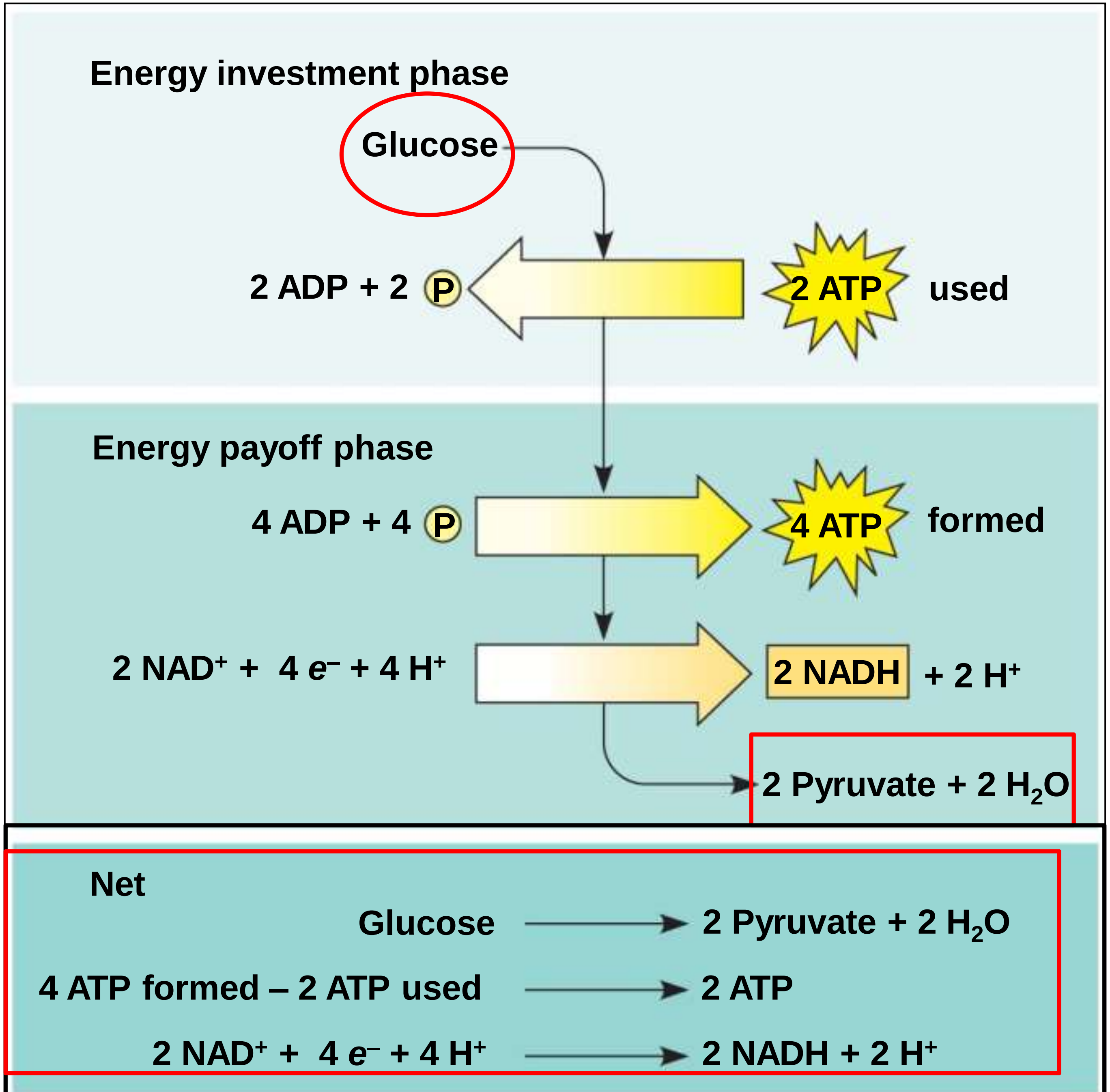

Electrons carried via NADH
Electrons carried via NADH and $FADH_2$
Glycolysis
Glucose
Pyruvate
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
Mitochondrion
Cytosol
ATP
ATP
ATP
Substrate-level phosphorylation
Substrate-level phosphorylation
Oxidative phosphorylation

- 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**

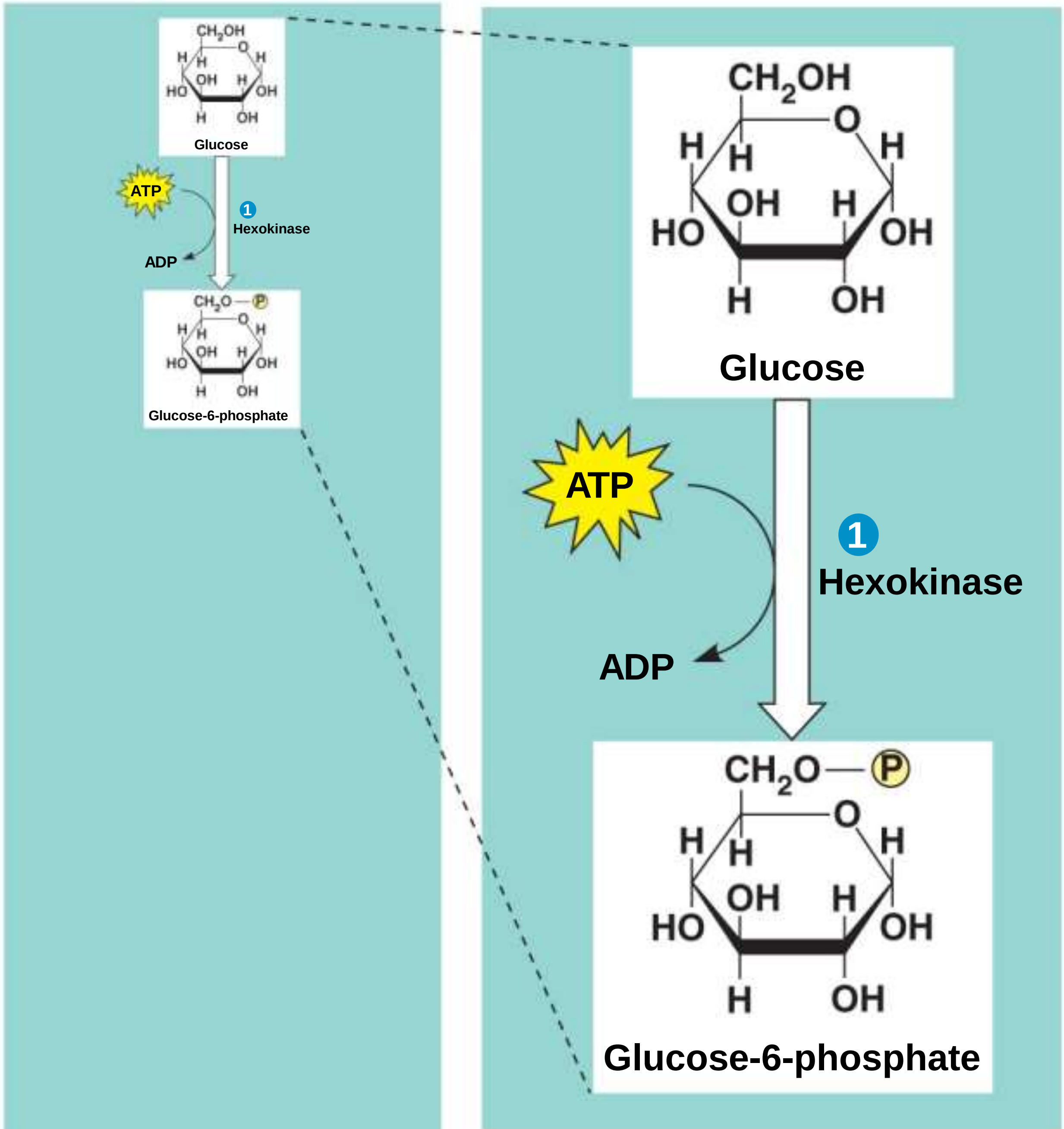


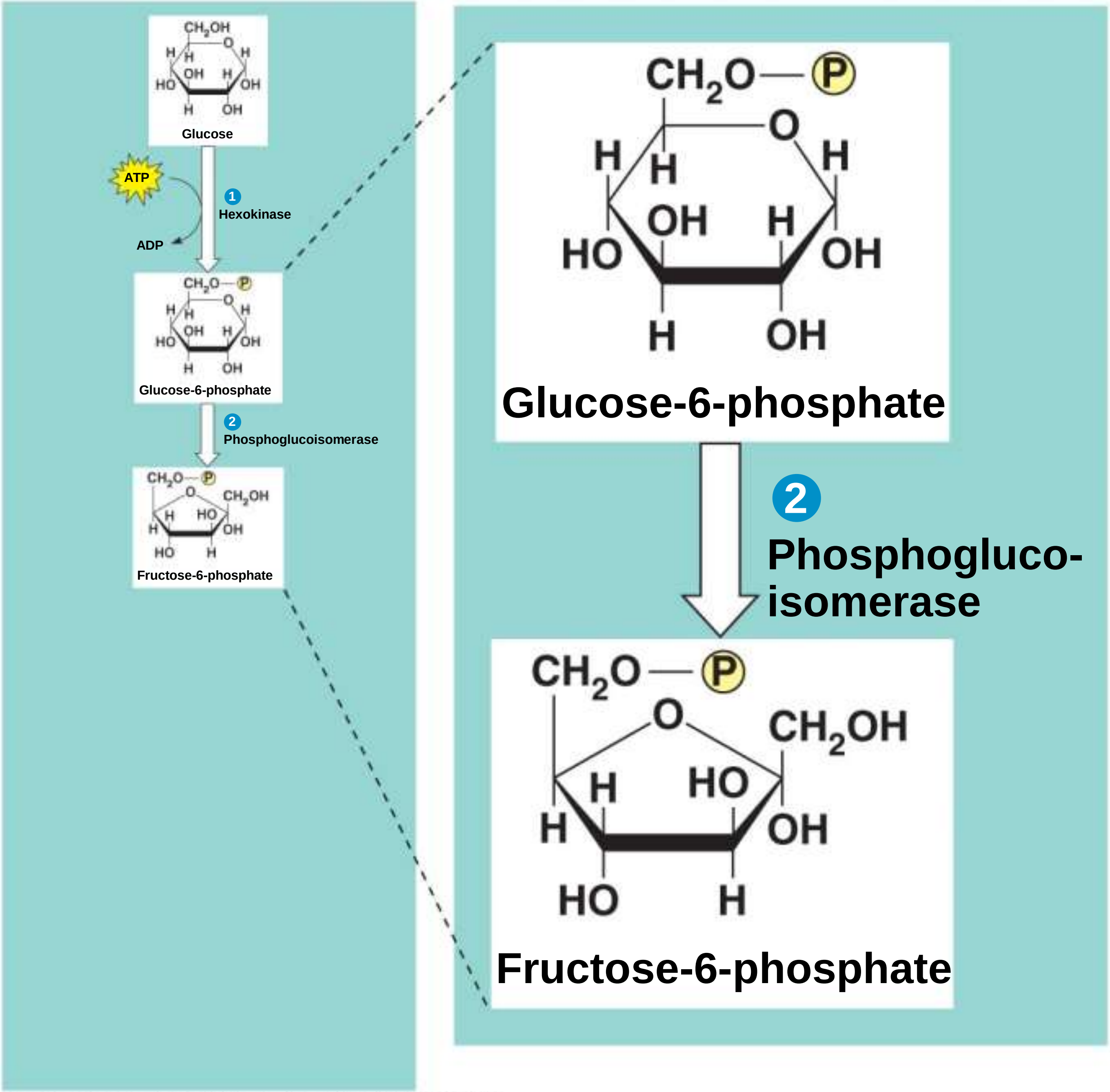
Glycolysis

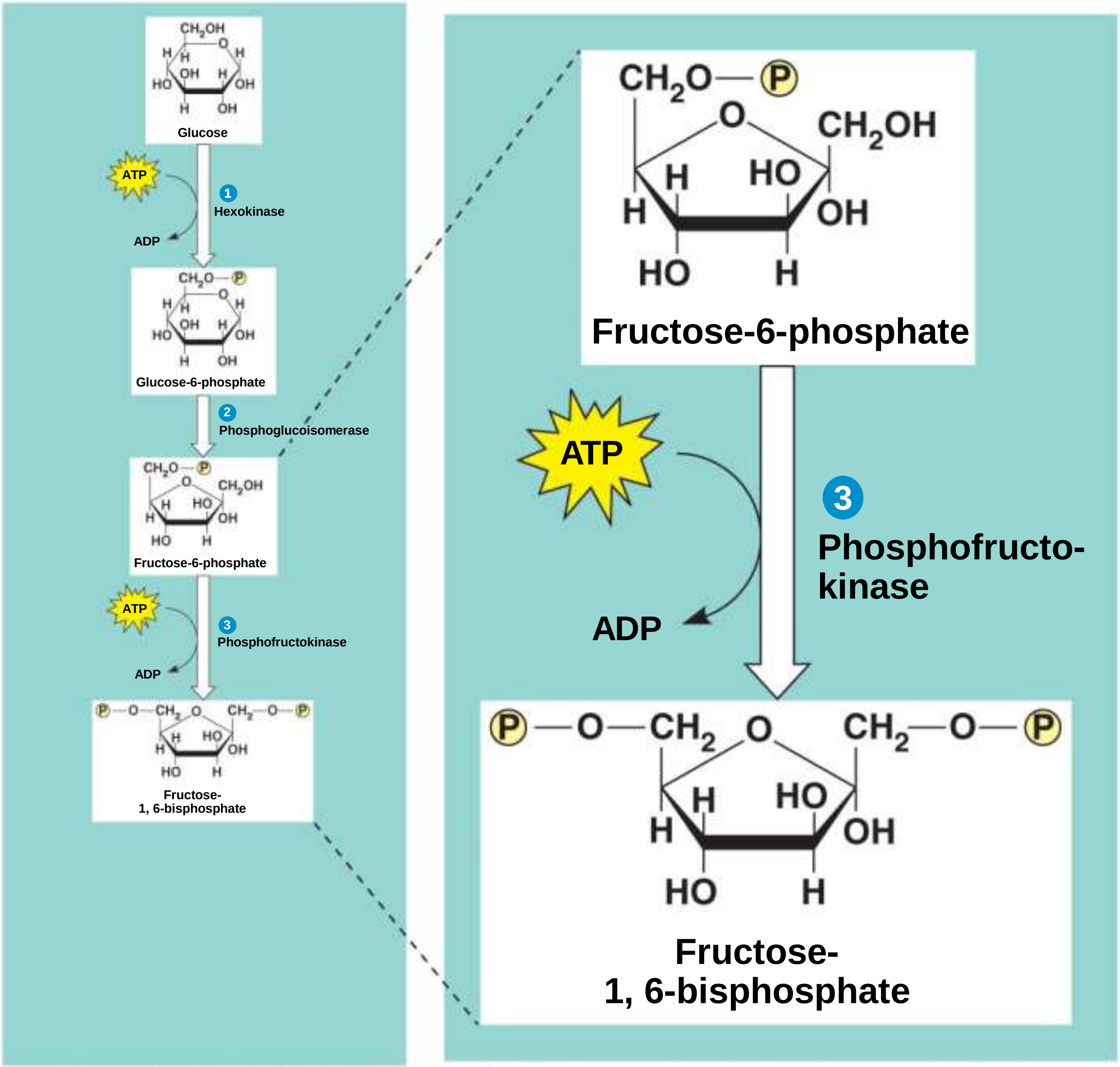
- Glycolysis ("splitting of sugar") breaks down glucose into two molecules of pyruvate
- Glycolysis occurs in the cytoplasm and has two major phases:
  - Energy investment phase
  - Energy payoff phase

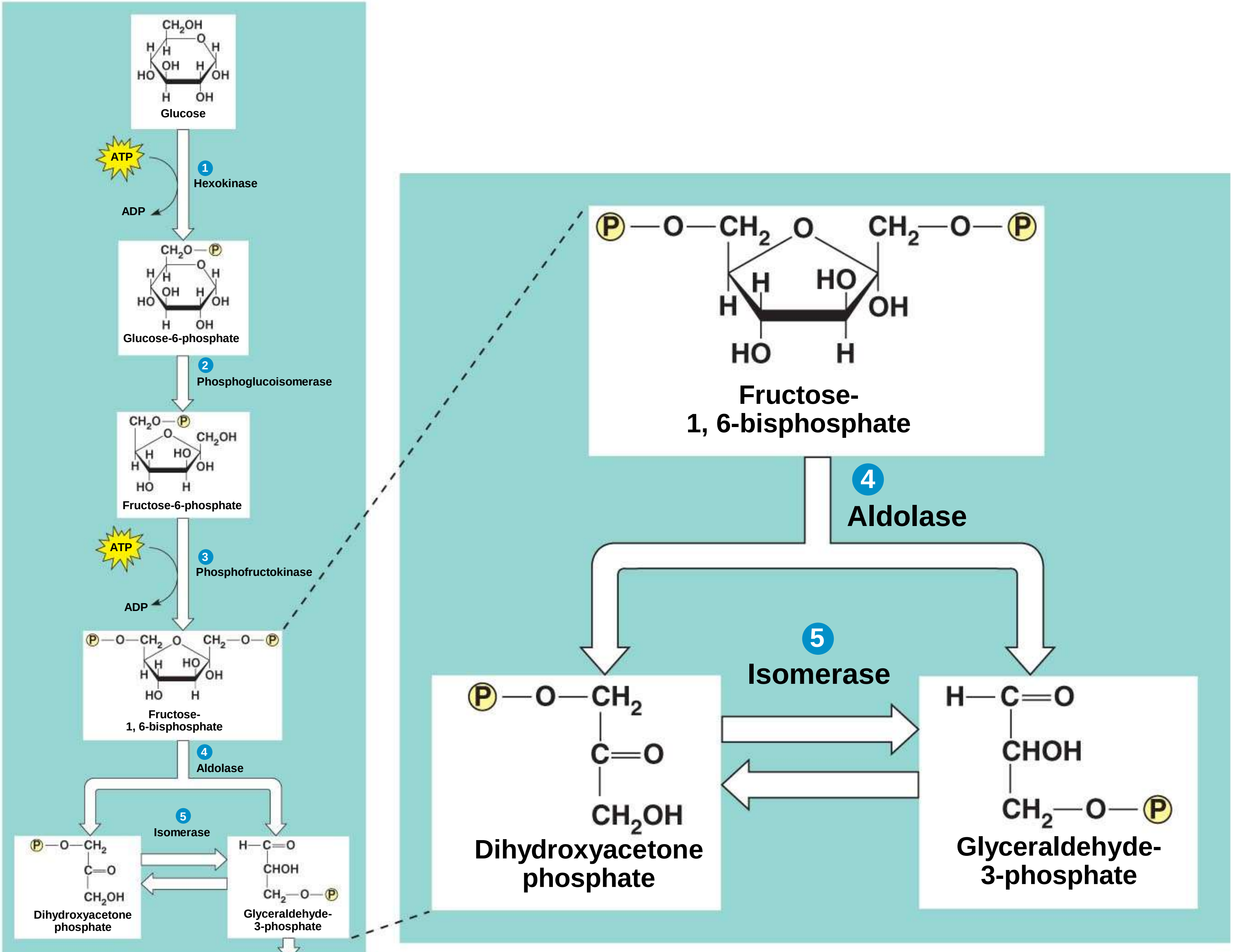


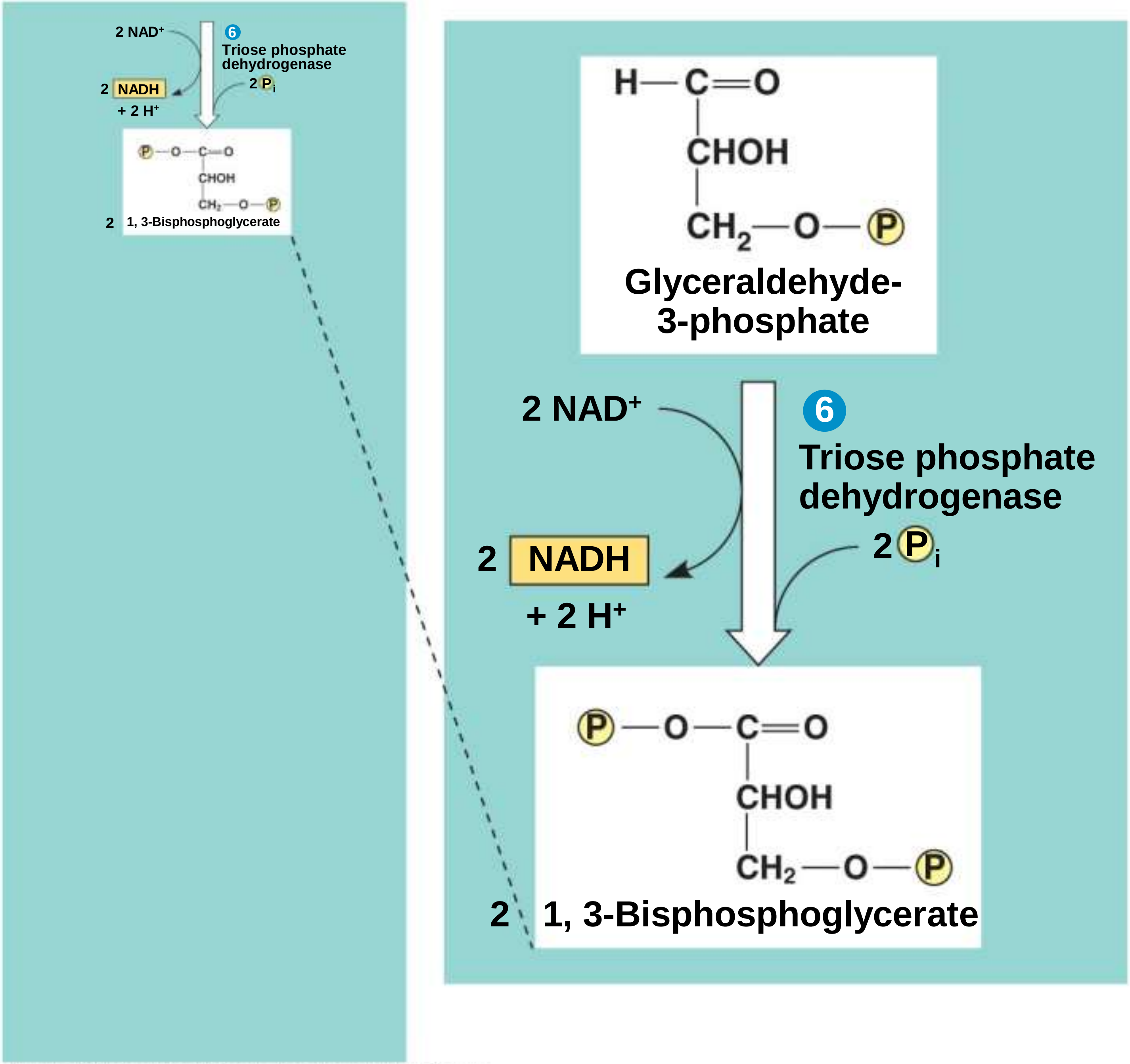
Energy investment phase
Glucose
2 ADP + 2 P
2 ATP
used
Energy payoff phase
4 ADP + 4 P
4 ATP
formed
2 NAD+ + 4 e− + 4 H+
2 NADH
+ 2 H+
2 Pyruvate + 2 H2O
Net
Glucose
2 Pyruvate + 2 H2O
4 ATP formed – 2 ATP used
2 ATP
2 NAD+ + 4 e− + 4 H+
2 NADH + 2 H+

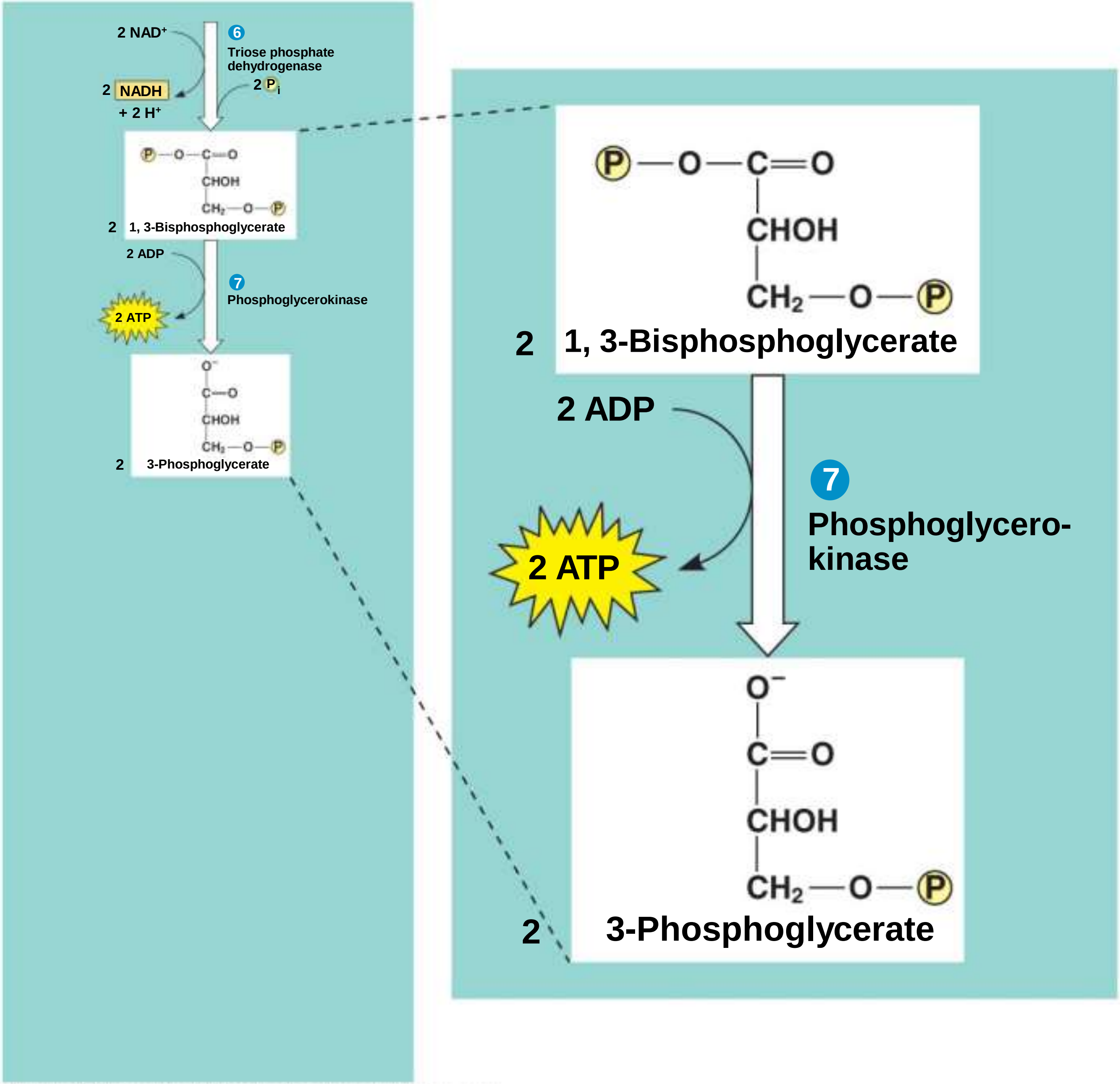

Glucose
ATP
1
Hexokinase
ADP
Glucose-6-phosphate
CH2OH
CH2O—P
HO
OH
H
O

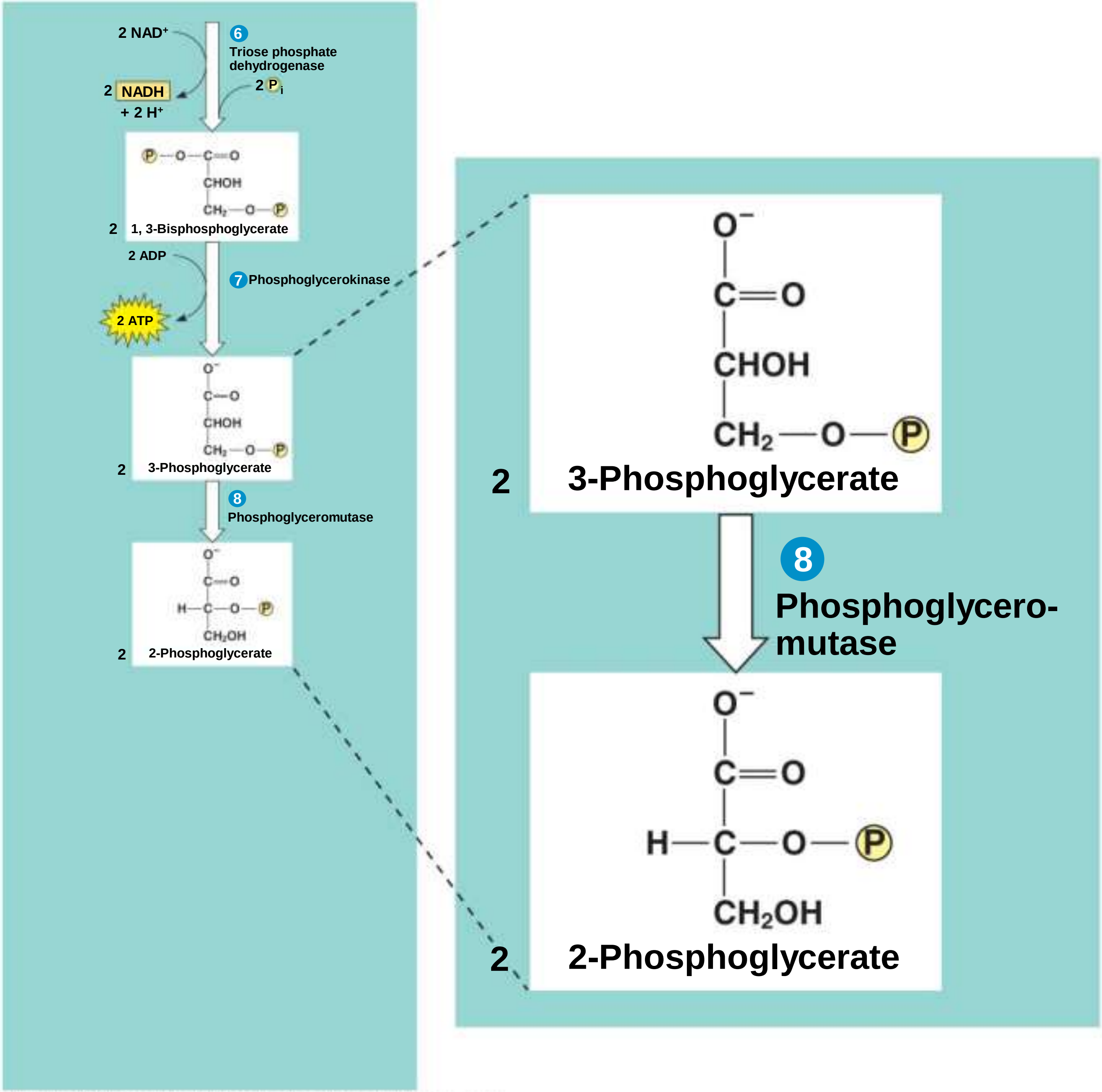

Glucose
ATP
ADP
1 Hexokinase
Glucose-6-phosphate
2 Phosphoglucoisomerase
Fructose-6-phosphate
Glucose-6-phosphate
2 Phosphogluco-isomerase
Fructose-6-phosphate


Glucose
ATP
1
Hexokinase
ADP
Glucose-6-phosphate
2
Phosphoglucoisomerase
Fructose-6-phosphate
ATP
3
Phosphofructokinase
ADP
Fructose-
1, 6-bisphosphate
Fructose-6-phosphate
ATP
ADP
3
Phosphofructo-
kinase
Fructose-
1, 6-bisphosphate

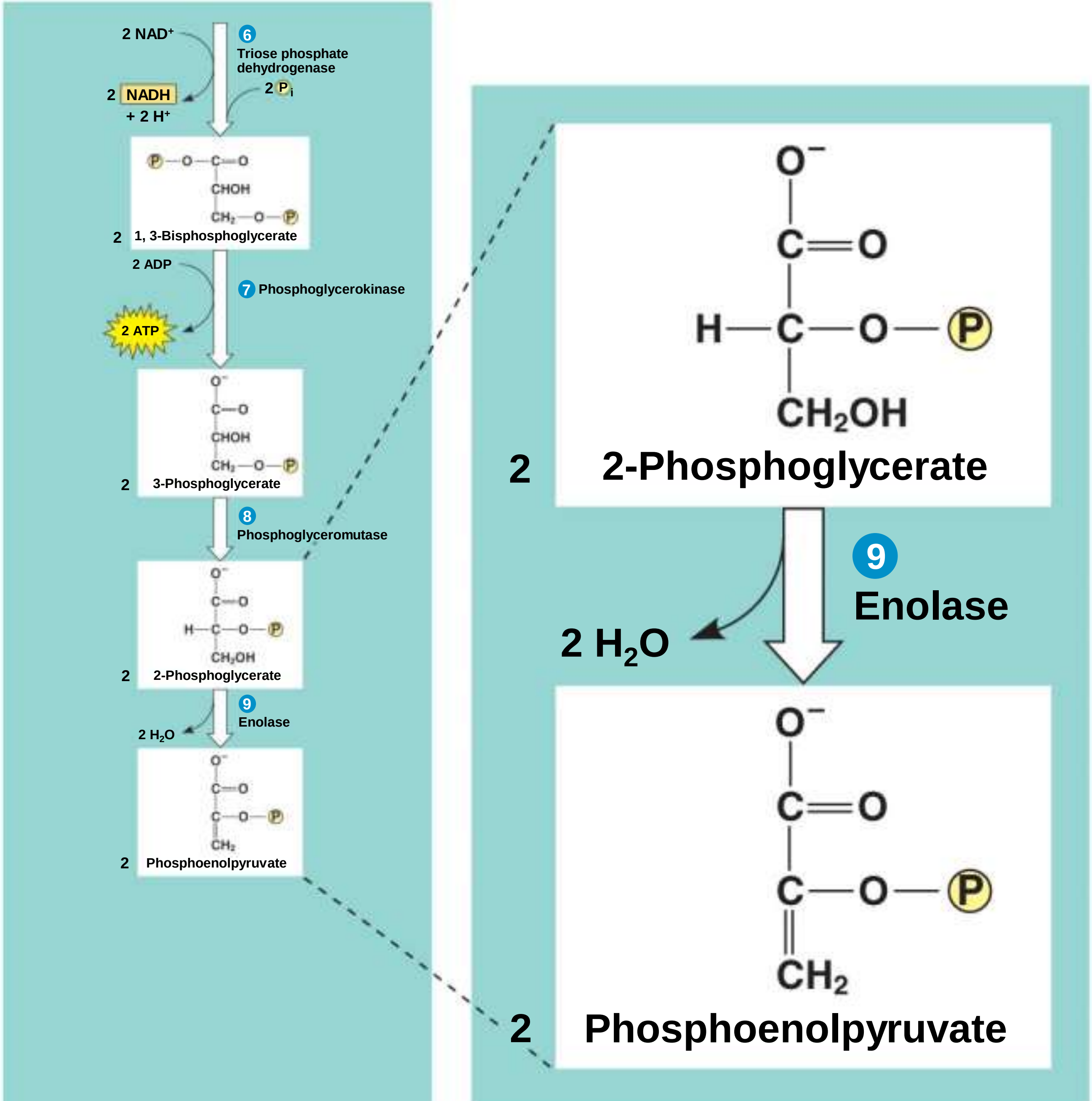

Glucose
ATP
ADP
1
Hexokinase
Glucose-6-phosphate
2
Phosphoglucoisomerase
Fructose-6-phosphate
ATP
ADP
3
Phosphofructokinase
Fructose-
1, 6-bisphosphate
4
Aldolase
5
Isomerase
Dihydroxyacetone
phosphate
Glyceraldehyde-
3-phosphate
Fructose-
1, 6-bisphosphate
4
Aldolase
5
Isomerase
Dihydroxyacetone
phosphate
Glyceraldehyde-
3-phosphate

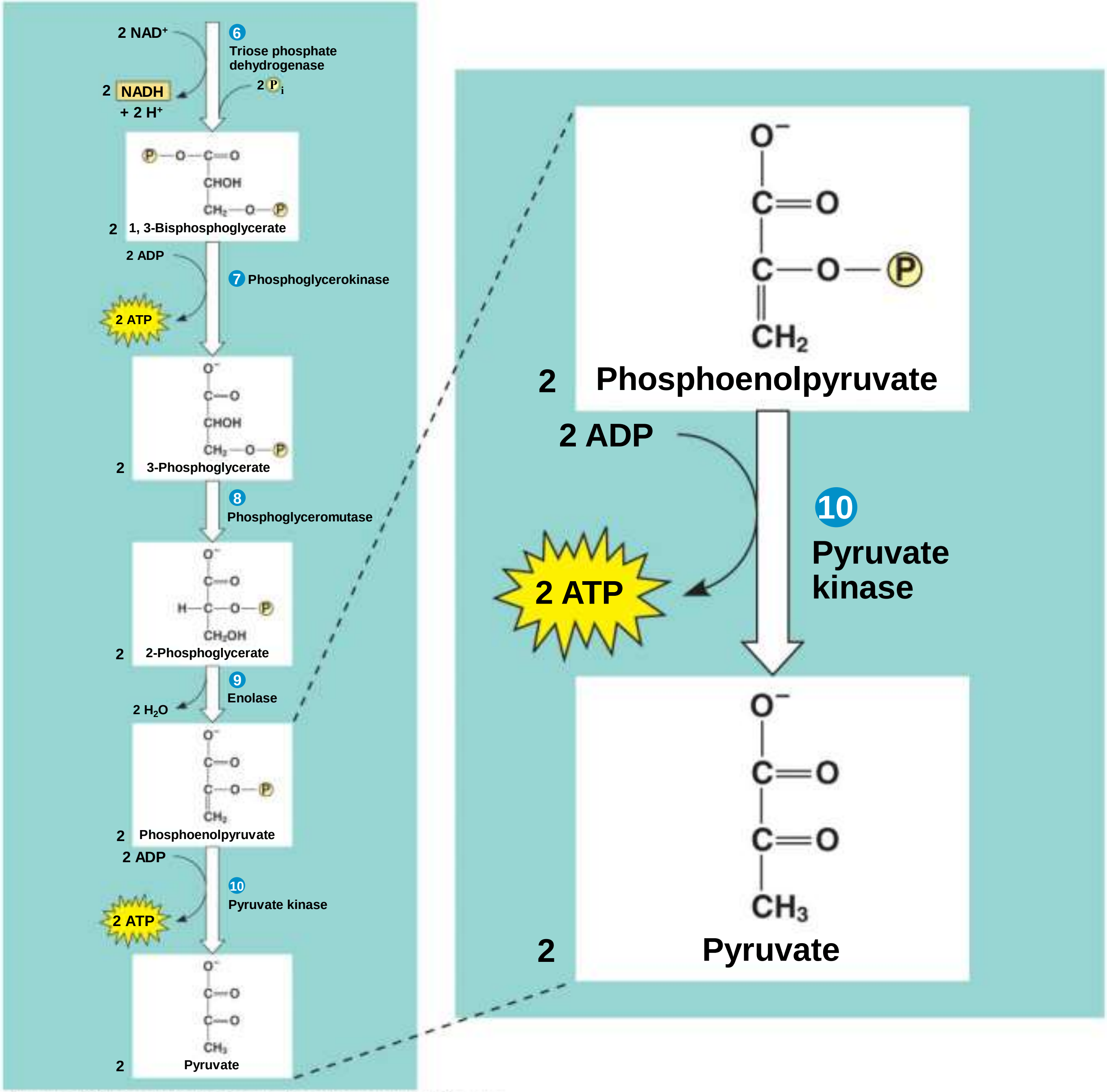

2 NAD+
6
Triose phosphate dehydrogenase
2 NADH
+ 2 H+
2 Pi
2 1, 3-Bisphosphoglycerate
Glyceraldehyde-3-phosphate
2 NAD+
6
Triose phosphate dehydrogenase
2 Pi
2 NADH
+ 2 H+
2 1, 3-Bisphosphoglycerate


2 NAD+
6
Triose phosphate dehydrogenase
2 NADH + 2 H+
2 Pi
1, 3-Bisphosphoglycerate
2 ADP
7
Phosphoglycerokinase
2 ATP
3-Phosphoglycerate
2 1, 3-Bisphosphoglycerate
2 ADP
2 ATP
7
Phosphoglycero-kinase
2 3-Phosphoglycerate



2 NAD+
6 Triose phosphate dehydrogenase
2 NADH + 2 H+
2 Pi
2 1, 3-Bisphosphoglycerate
2 ADP
7 Phosphoglycerokinase
2 ATP
2 3-Phosphoglycerate
8 Phosphoglyceromutase
2 2-Phosphoglycerate
2 3-Phosphoglycerate
8 Phosphoglycero-mutase
2 2-Phosphoglycerate


2 NAD+
6
Triose phosphate dehydrogenase
2 NADH
+ 2 H+
2 Pi
1, 3-Bisphosphoglycerate
2 ADP
7 Phosphoglycerokinase
2 ATP
3-Phosphoglycerate
8
Phosphoglyceromutase
2-Phosphoglycerate
9
Enolase
2 H2O
Phosphoenolpyruvate
CH2OH
2 2-Phosphoglycerate
9
Enolase
2 H2O
CH2
2 Phosphoenolpyruvate

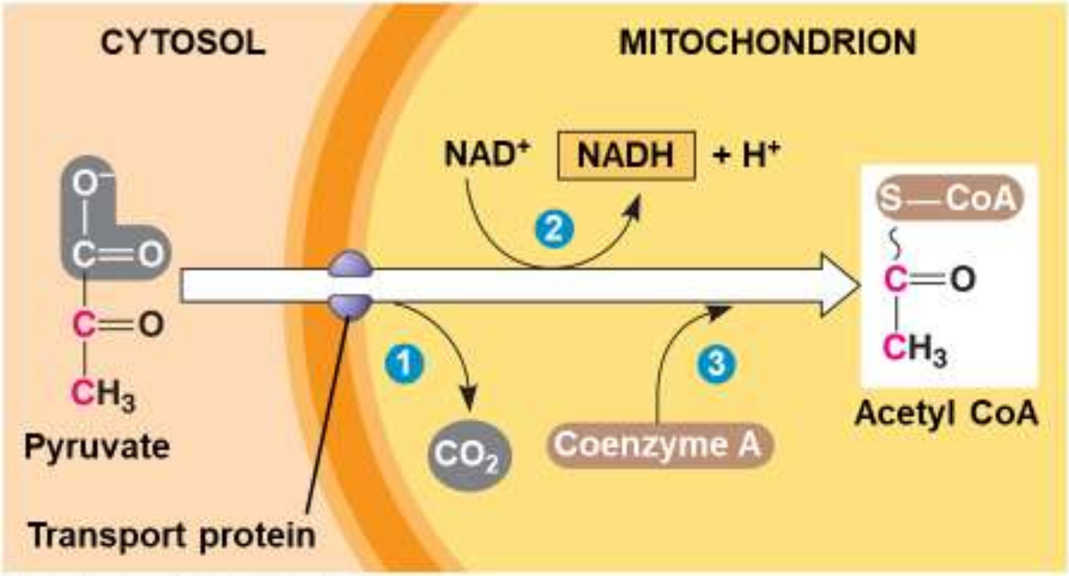


2 NAD+
6 Triose phosphate dehydrogenase
2 NADH + 2 H+
2 P i
2 1, 3-Bisphosphoglycerate
2 ADP
7 Phosphoglycerokinase
2 ATP
2 3-Phosphoglycerate
8 Phosphoglyceromutase
2 2-Phosphoglycerate
9 Enolase
2 H2O
2 Phosphoenolpyruvate
2 ADP
10 Pyruvate kinase
2 ATP
2 Pyruvate
2 Phosphoenolpyruvate
2 ADP
10 Pyruvate kinase
2 ATP
2 Pyruvate

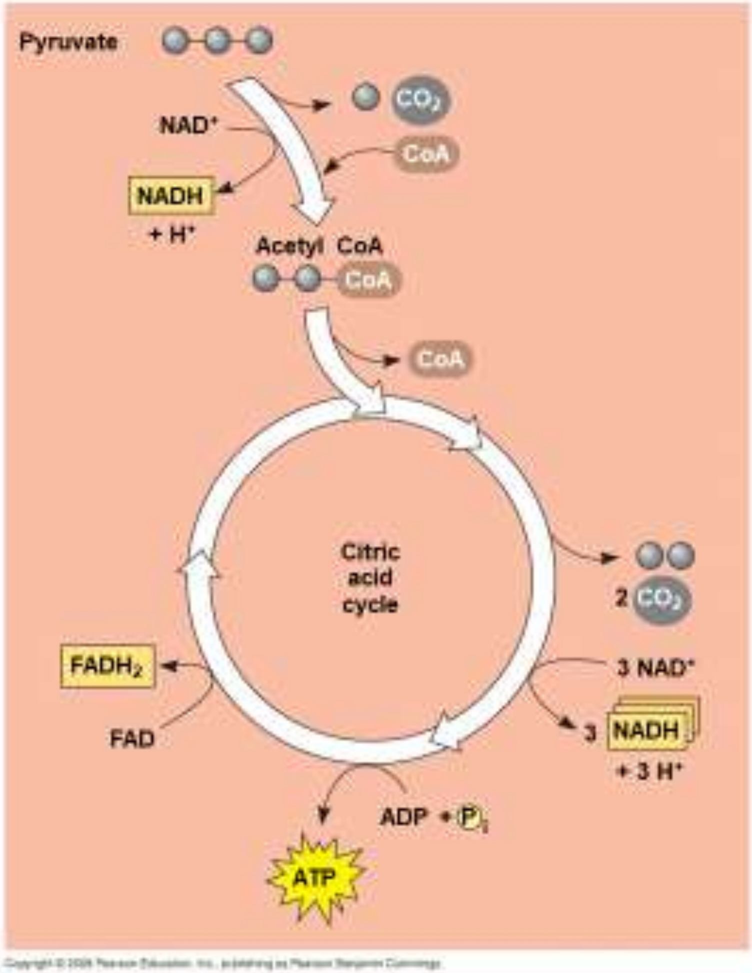
The citric acid cycle completes the energy-yielding oxidation of organic molecules

- In the presence of O_2, pyruvate enters the mitochondrion
- Before the citric acid cycle can begin, pyruvate must be converted to **acetyl CoA**, which links the cycle to glycolysis

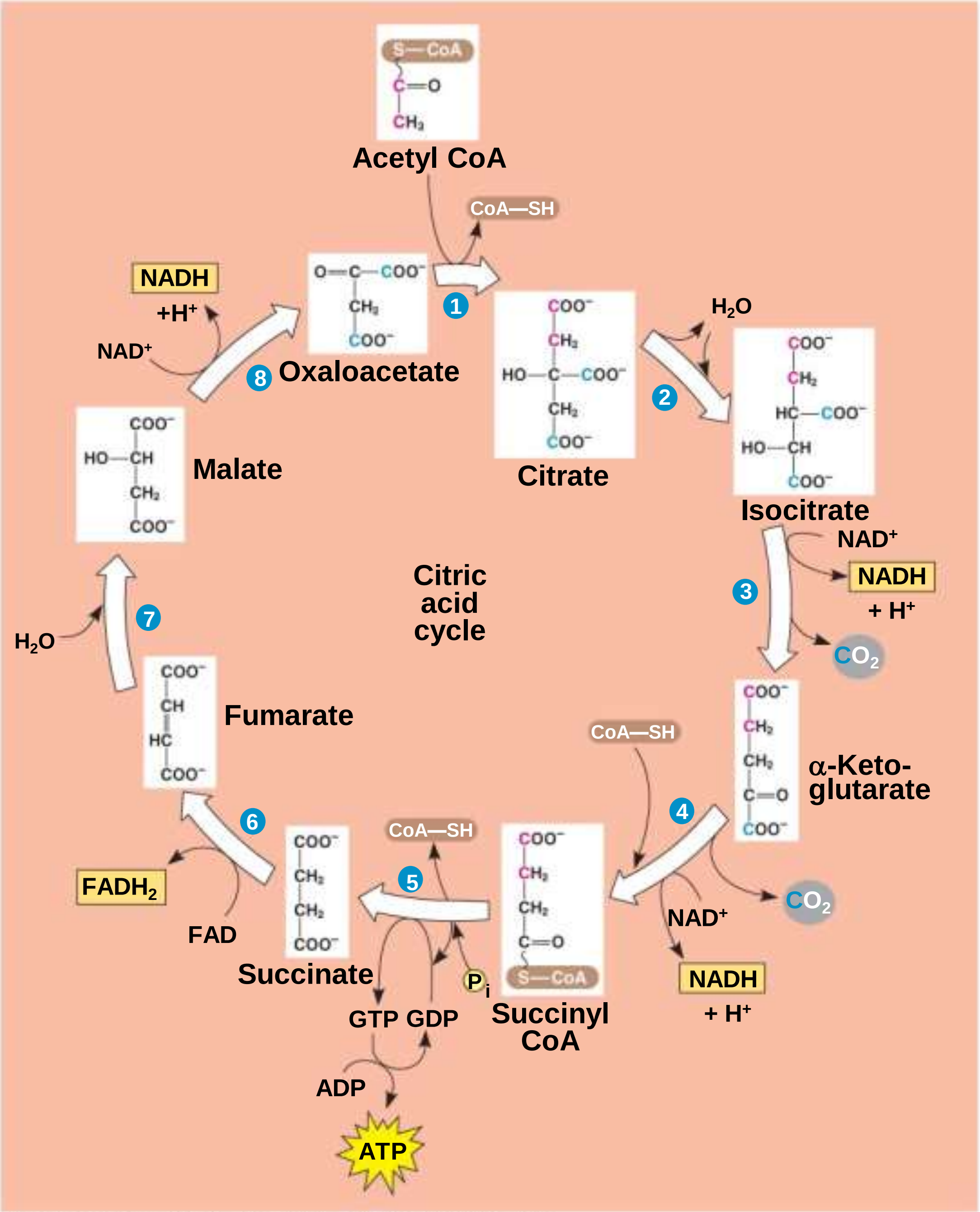
Conversion of pyruvate to acetyl CoA, the junction between glycolysis and the citric acid cycle



- The citric acid cycle, also called the **Krebs cycle**, takes place within the mitochondrial matrix
- 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



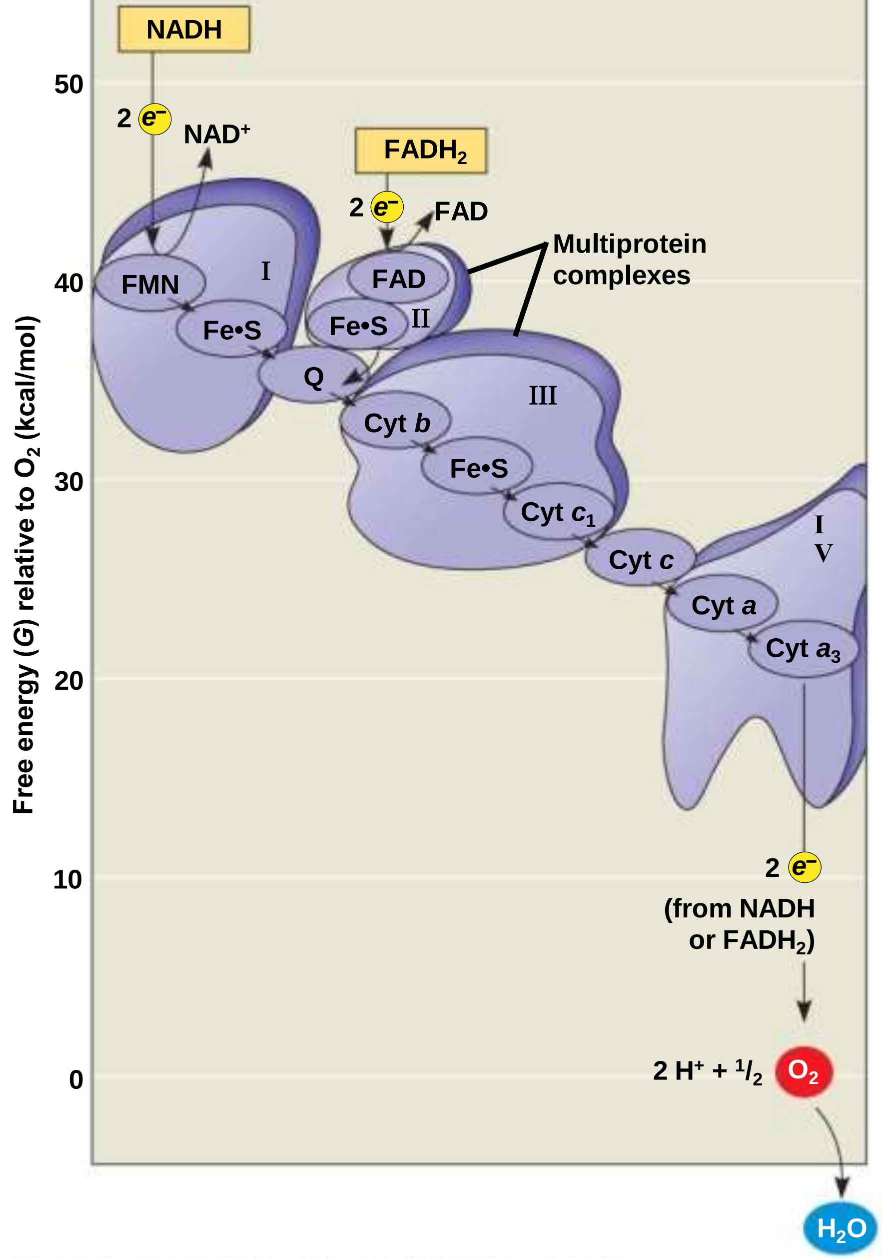
S—CoA
C=O
CH3
Acetyl CoA
CoA—SH
1
O=C—COO⁻
CH2
COO⁻
Oxaloacetate
NADH
+H+
NAD+
8
COO⁻
CH2
HO—C—COO⁻
CH2
COO⁻
Citrate
H2O
2
COO⁻
CH2
HC—COO⁻
HO—CH
COO⁻
Isocitrate
NAD+
NADH
+ H+
3
CO2
COO⁻
HO—CH
CH2
COO⁻
Malate
Citric
acid
cycle
7
H2O
COO⁻
CH
HC
COO⁻
Fumarate
COO⁻
CH2
CH2
C=O
COO⁻
α-Keto-
glutarate
CoA—SH
4
CO2
NAD+
NADH
+ H+
6
FADH2
FAD
COO⁻
CH2
CH2
COO⁻
Succinate
CoA—SH
5
COO⁻
CH2
CH2
C=O
S—CoA
Succinyl
CoA
Pi
GTP GDP
ADP
ATP

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

The Pathway of Electron Transport

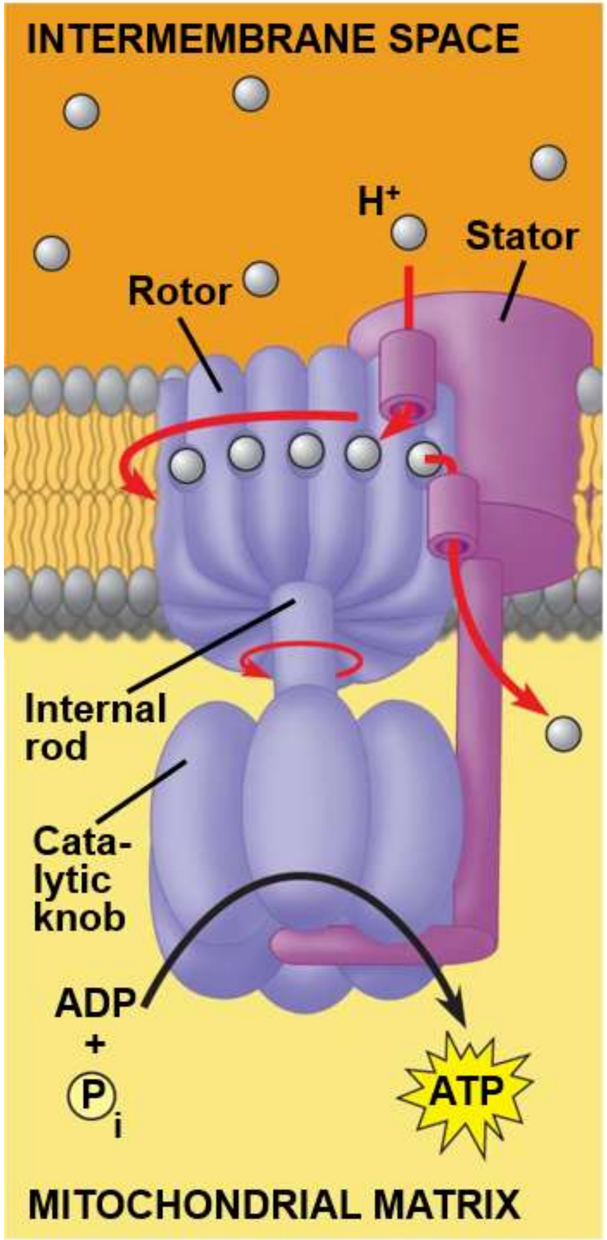
- The electron transport chain is in the **cristae** of the mitochondrion
- Most of the chain's components are proteins, which exist in multiprotein complexes
- The carriers alternate reduced and oxidized states as they accept and donate electrons
- Electrons drop in free energy as they go down the chain and are finally passed to O_2, forming H_2O.
- 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
- The chain's function is to break the large free-energy drop from food to O_2 into smaller steps that release energy in manageable amounts



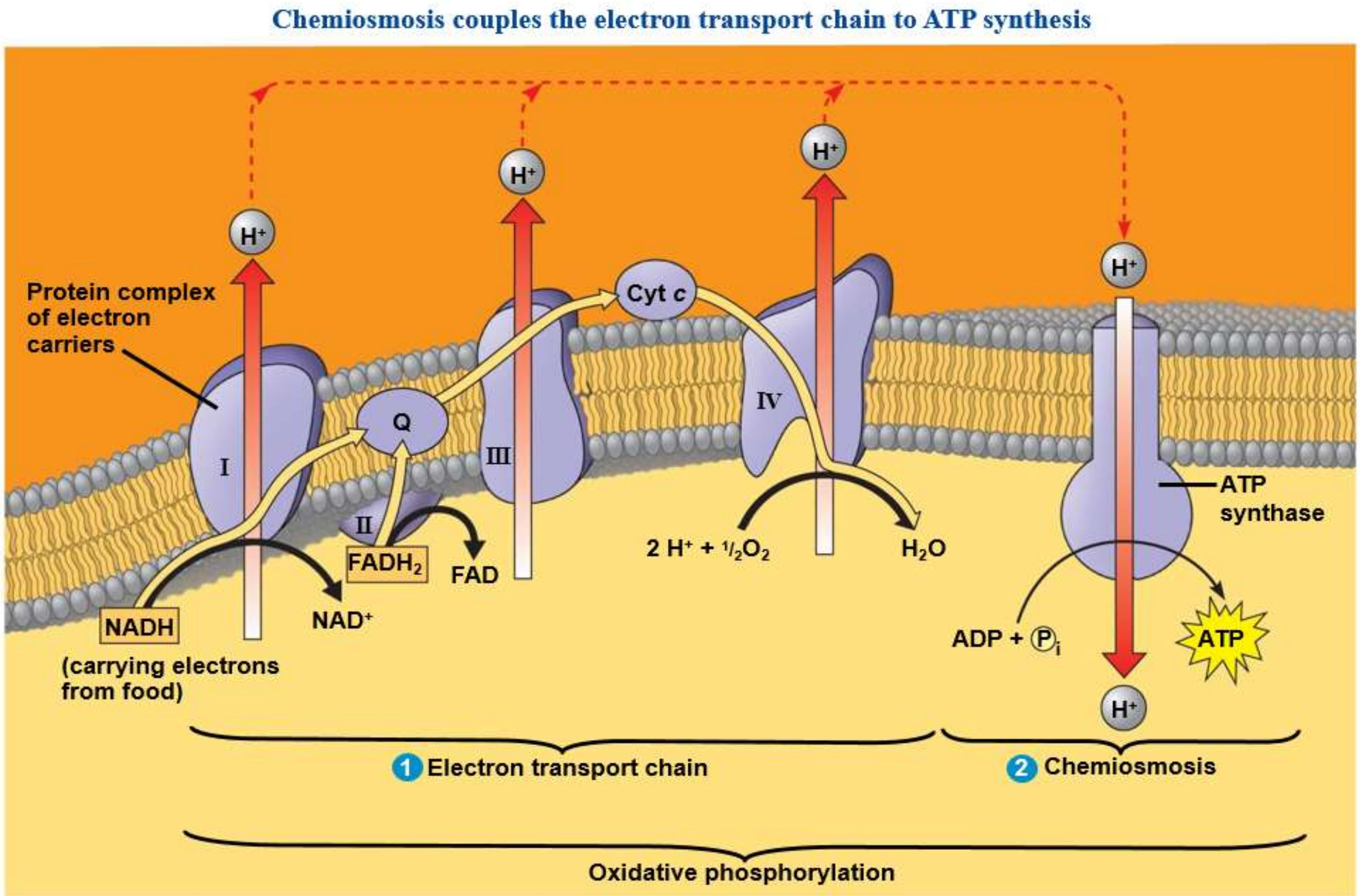
NADH
2 e⁻
NAD+
FADH2
2 e⁻
FAD
Multiprotein complexes
FMN
I
Fe•S
FAD
Fe•S
II
Q
III
Cyt b
Fe•S
Cyt c1
Cyt c
IV
Cyt a
Cyt a3
2 e⁻
(from NADH or FADH2)
2 H+ + 1/2 O2
H2O
Free energy (G) relative to O2 (kcal/mol)
50
40
30
20
10
0

Chemiosmosis: The 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 channels in **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



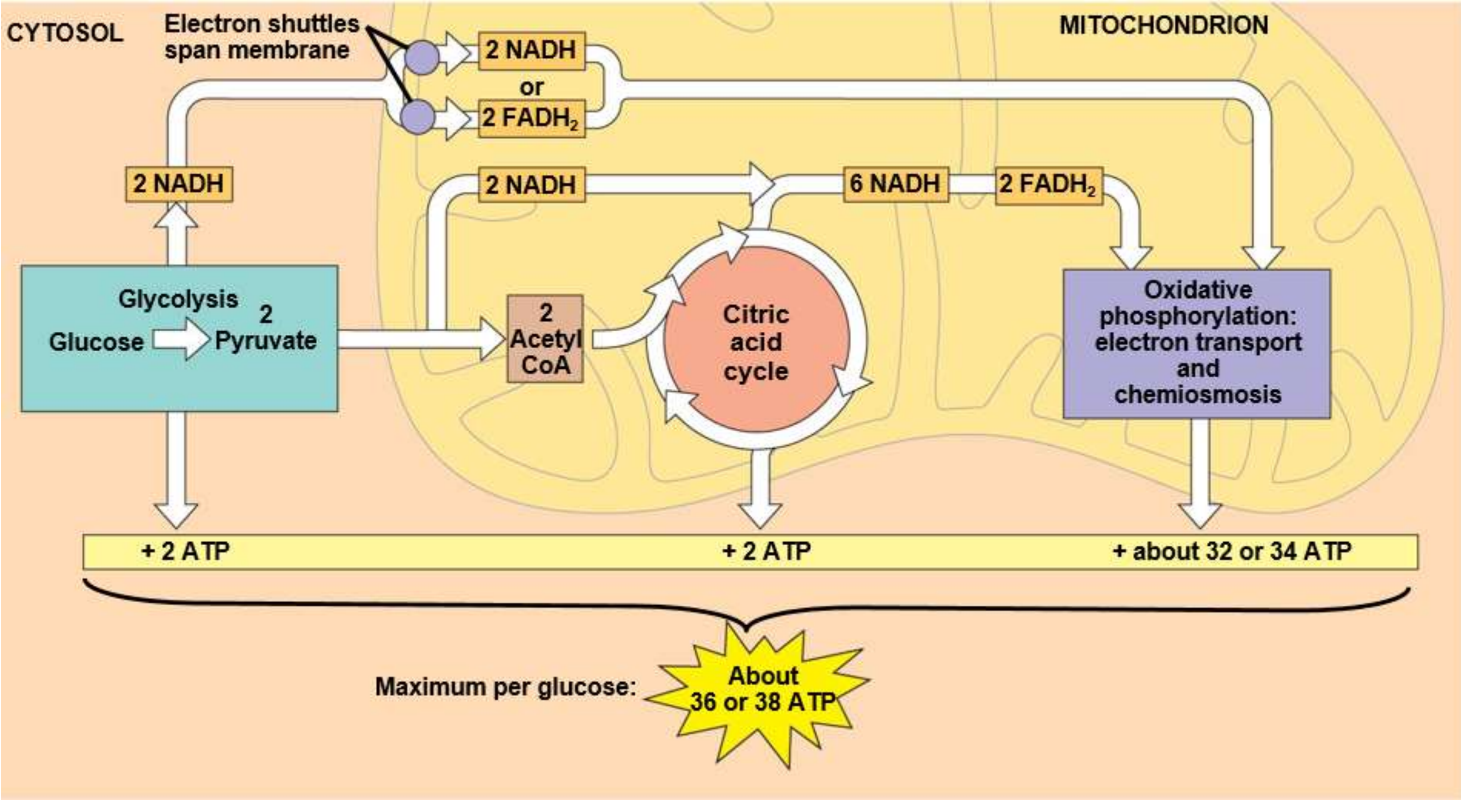
- The energy stored in a H^+ gradient across a membrane couples the redox reactions of the electron transport chain to ATP synthesis
- The H^+ gradient is referred to as a **proton-motive force**, emphasizing its capacity to do work.



- **An Accounting of ATP Production by Cellular Respiration**:
- ✓ During cellular respiration, most energy flows in this sequence:

  glucose → NADH → electron transport chain → proton-motive force → ATP

- ✓ About 40% of the energy in a glucose molecule is transferred to ATP during cellular respiration, making about 38 ATP



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

- Most cellular respiration requires O_2 to produce ATP
- Glycolysis can produce ATP with or without O_2 (in aerobic or anaerobic conditions)
- In the absence of O_2, glycolysis couples with fermentation or anaerobic respiration to produce ATP
- Anaerobic respiration uses an electron transport chain with an electron acceptor other than O_2, for example sulfate
- Fermentation uses 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:**

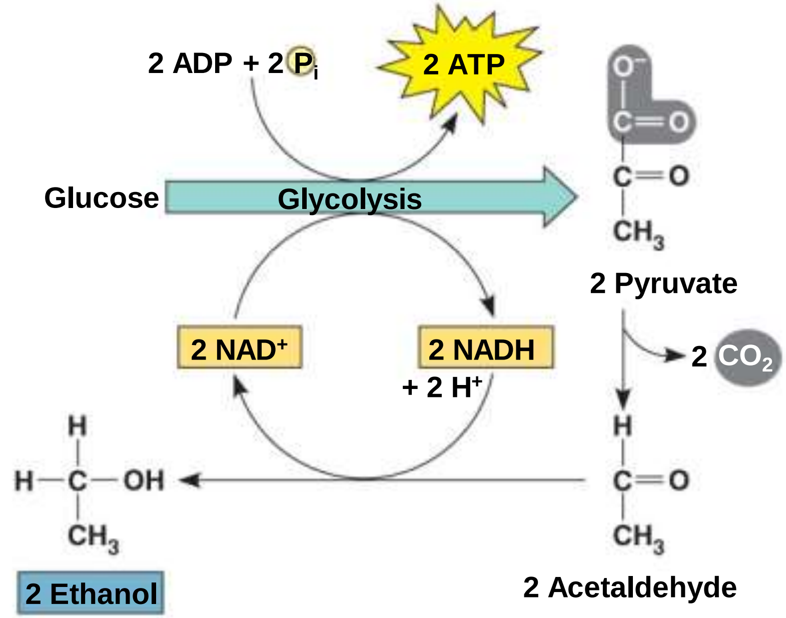
1. In **alcohol fermentation**, pyruvate is converted to ethanol in two steps, with the first releasing CO_2

✓ Alcohol fermentation by yeast is used in brewing, winemaking, and baking.

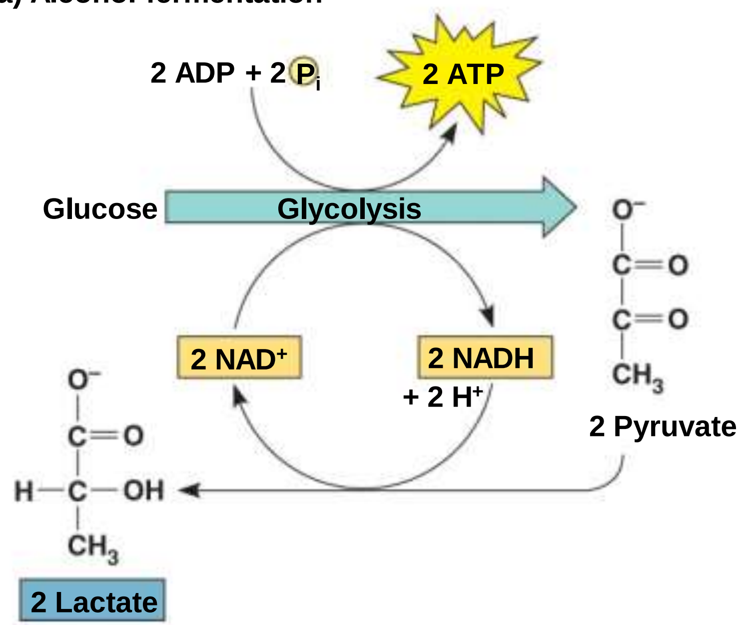
2. In **lactic acid fermentation**, pyruvate is reduced to NADH, forming lactate as an end product, with no release of CO_2

✓ 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



(a) Alcohol fermentation



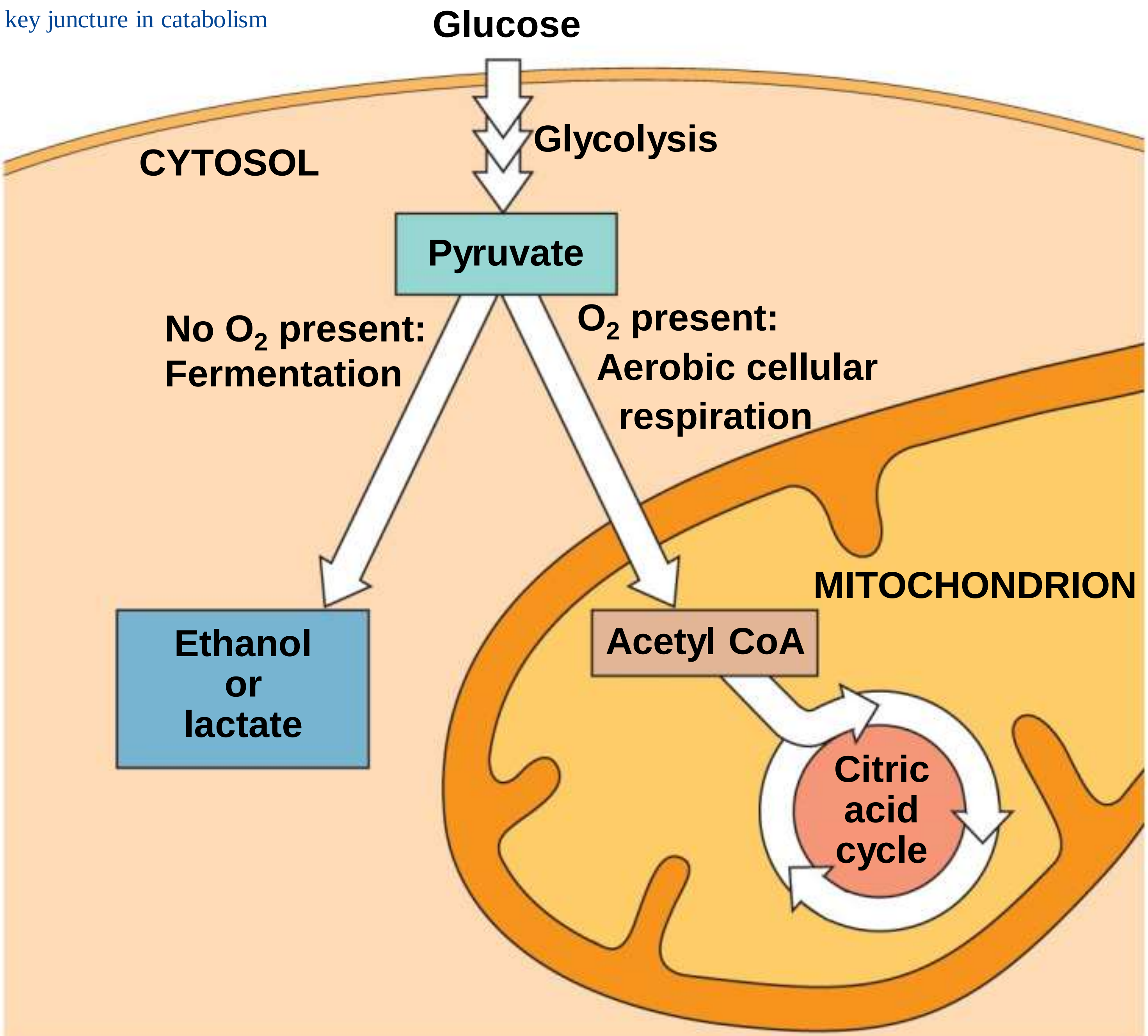
(b) Lactic acid fermentation

Fermentation and Aerobic Respiration Compared

- Both processes use glycolysis to oxidize glucose and other organic fuels to pyruvate
- 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 38 ATP per glucose molecule; fermentation produces 2 ATP per glucose molecule

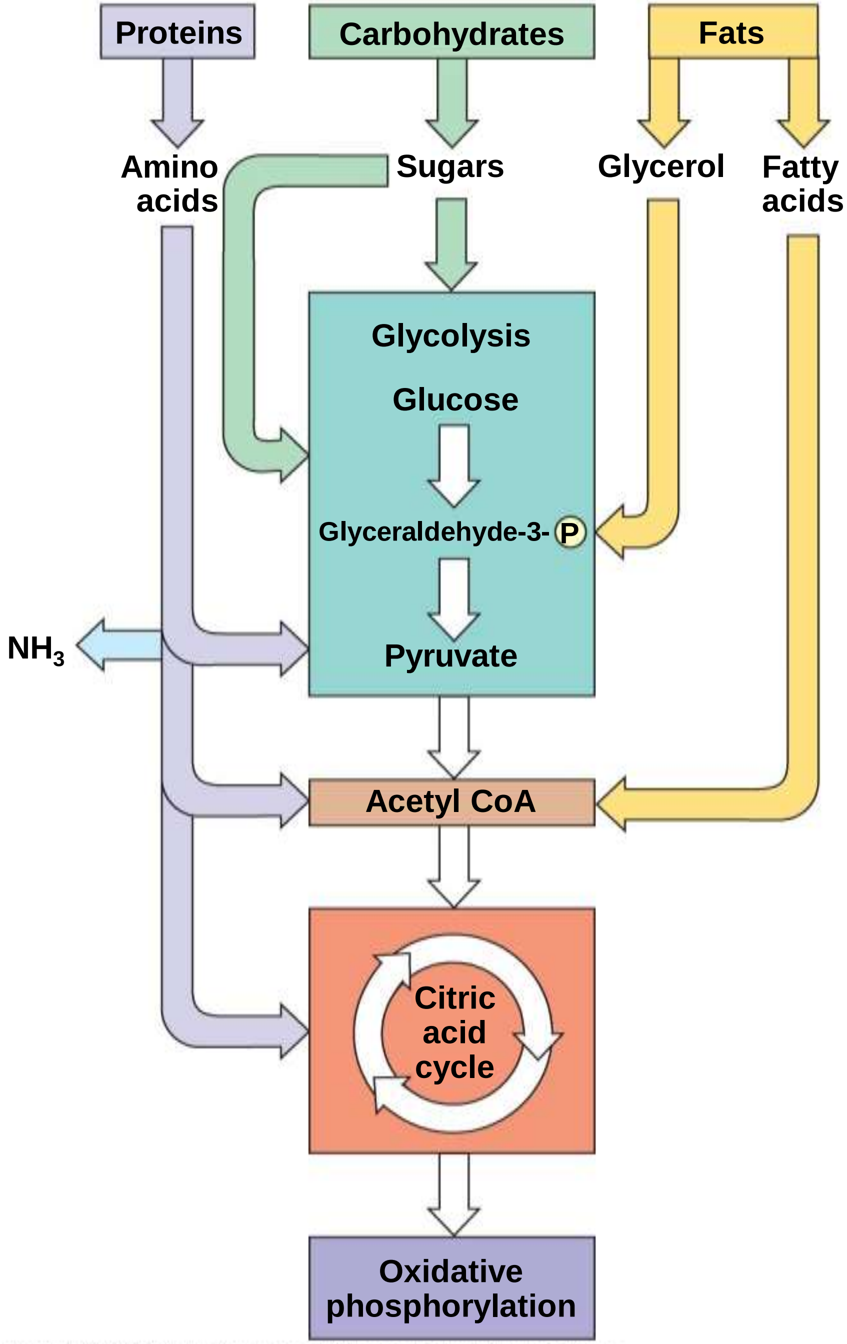
- **Obligate anaerobes** carry out fermentation or anaerobic respiration and cannot survive in the presence of O_2
- Yeast and many bacteria are **facultative anaerobes**, meaning that they can survive using either fermentation or cellular respiration
- In a facultative anaerobe, pyruvate is a fork in the metabolic road that leads to two alternative catabolic routes

Pyruvate as a key juncture in catabolism



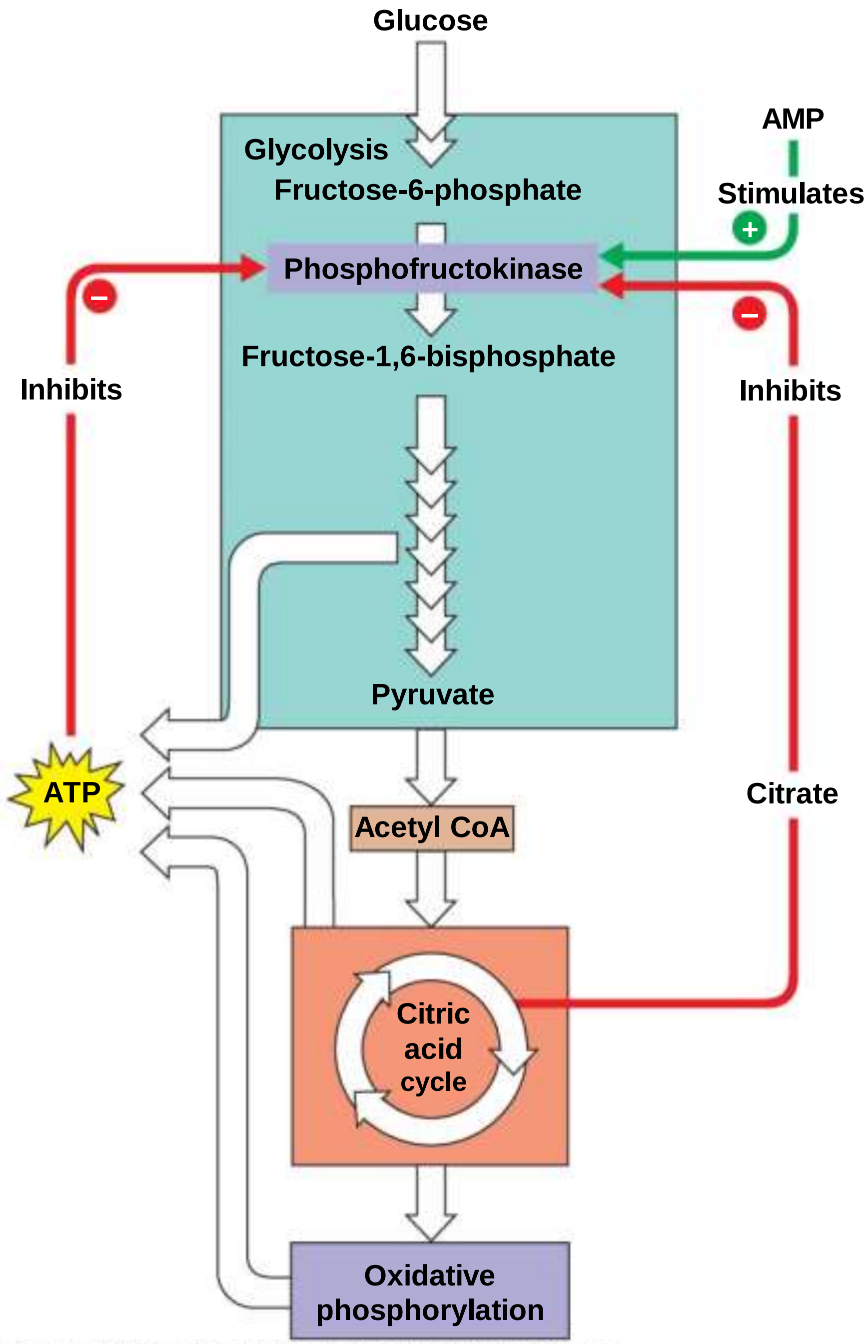
- Gycolysis and the citric acid cycle are major intersections to various catabolic and anabolic pathways.

- ✓ 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


Proteins
Carbohydrates
Fats
Amino acids
Sugars
Glycerol
Fatty acids
Glycolysis
Glucose
Glyceraldehyde-3- P
Pyruvate
NH3
Acetyl CoA
Citric acid cycle
Oxidative phosphorylation

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


Glucose
Glycolysis
Fructose-6-phosphate
AMP
Stimulates
+
Phosphofructokinase
–
–
Inhibits
Fructose-1,6-bisphosphate
Inhibits
Pyruvate
ATP
Citrate
Acetyl CoA
Citric acid cycle
Oxidative phosphorylation