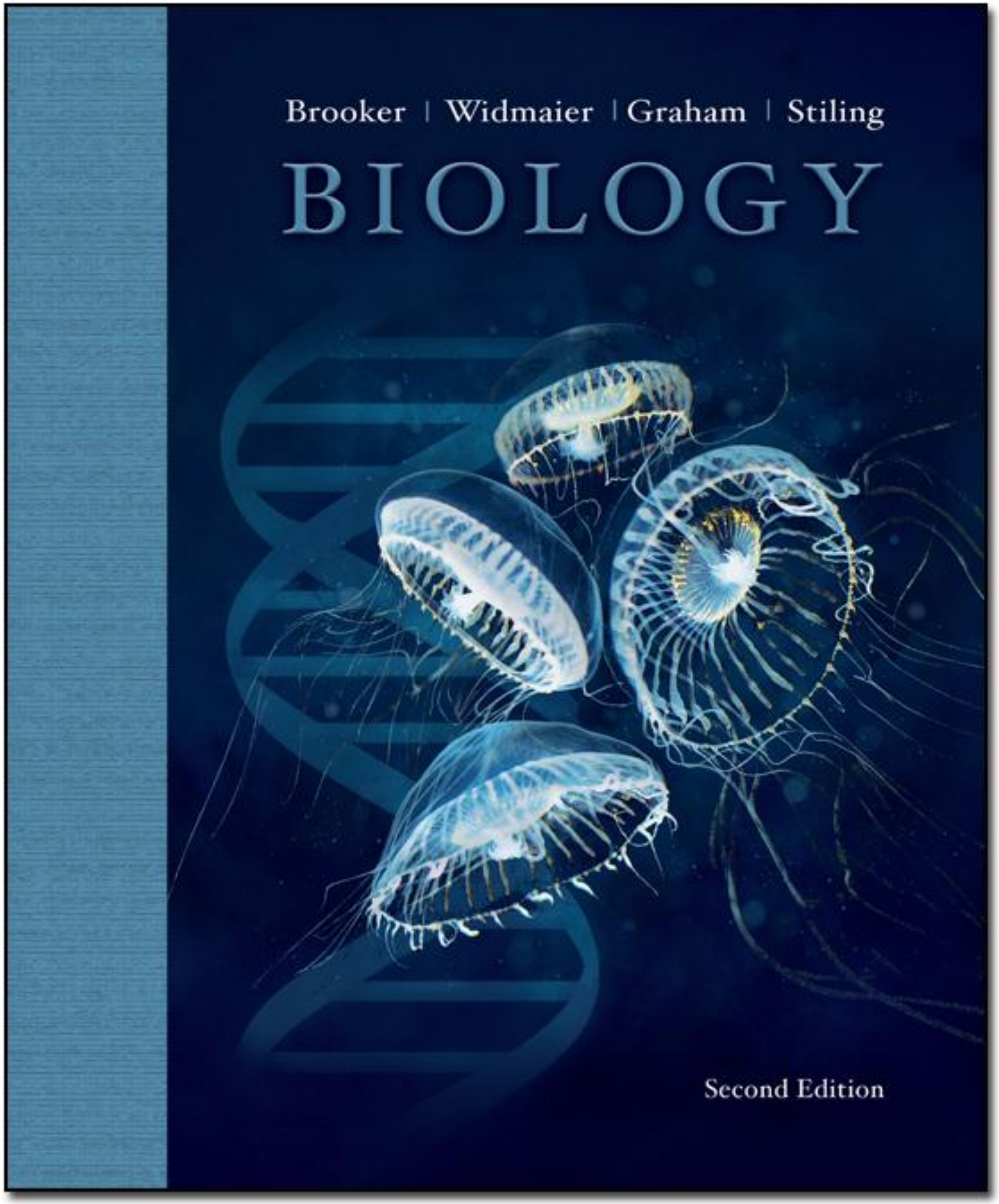
CHAPTER 7 LECTURE SLIDES

Prepared by

Brenda Leady

University of Toledo

To run the animations you must be in **Slideshow View**. Use the buttons on the animation to play, pause, and turn audio/text on or off. Please note: once you have used any of the animation functions (such as Play or Pause), you must first click in the white background before you advance the next slide.



Cellular respiration

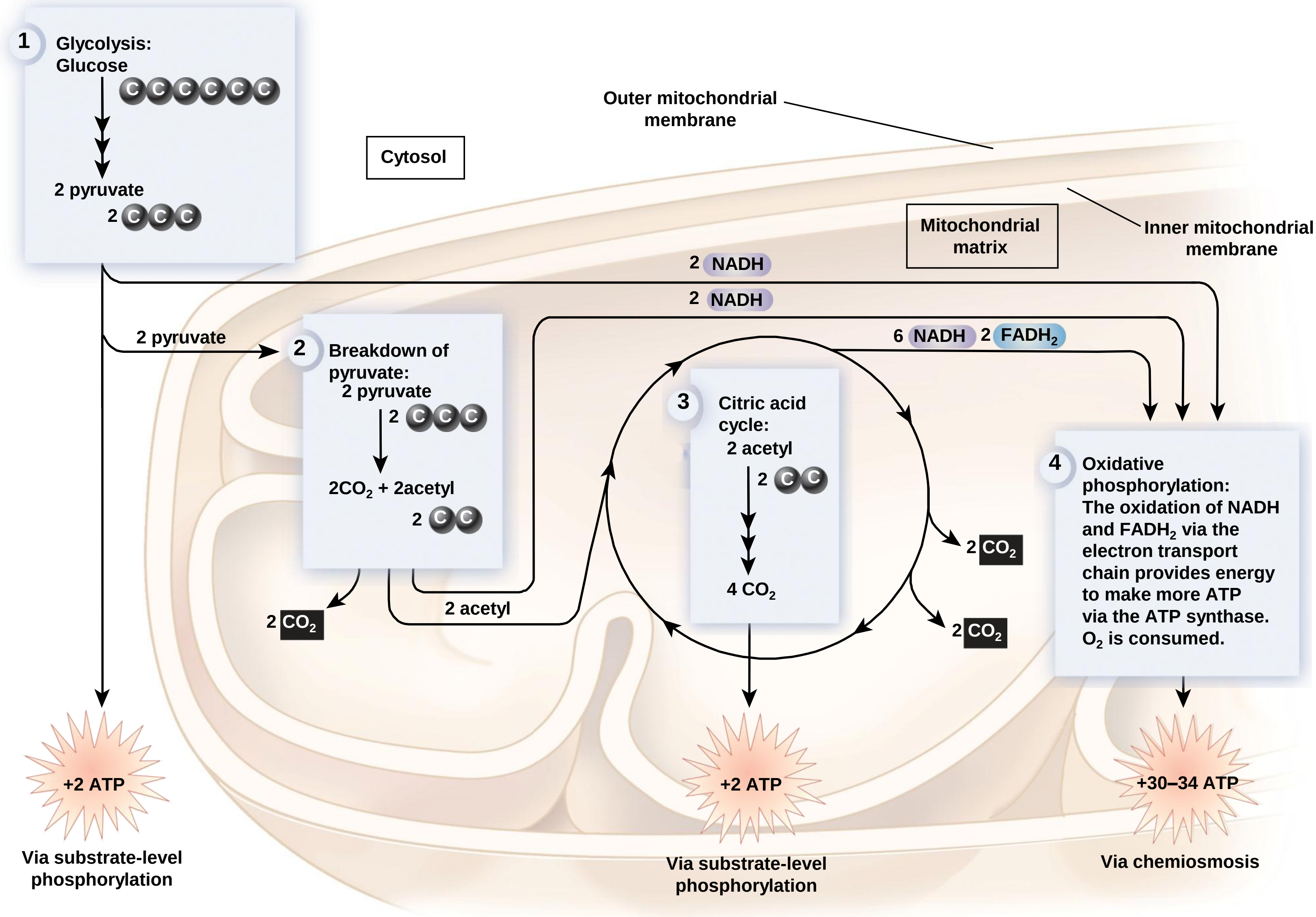
- Process by which living cells obtain energy from organic molecules
- Primary aim to make ATP and NADH
- Aerobic respiration uses oxygen
  - O_2 consumed and CO_2 released
- Focus on glucose but other organic molecules also used

Glucose metabolism

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$$

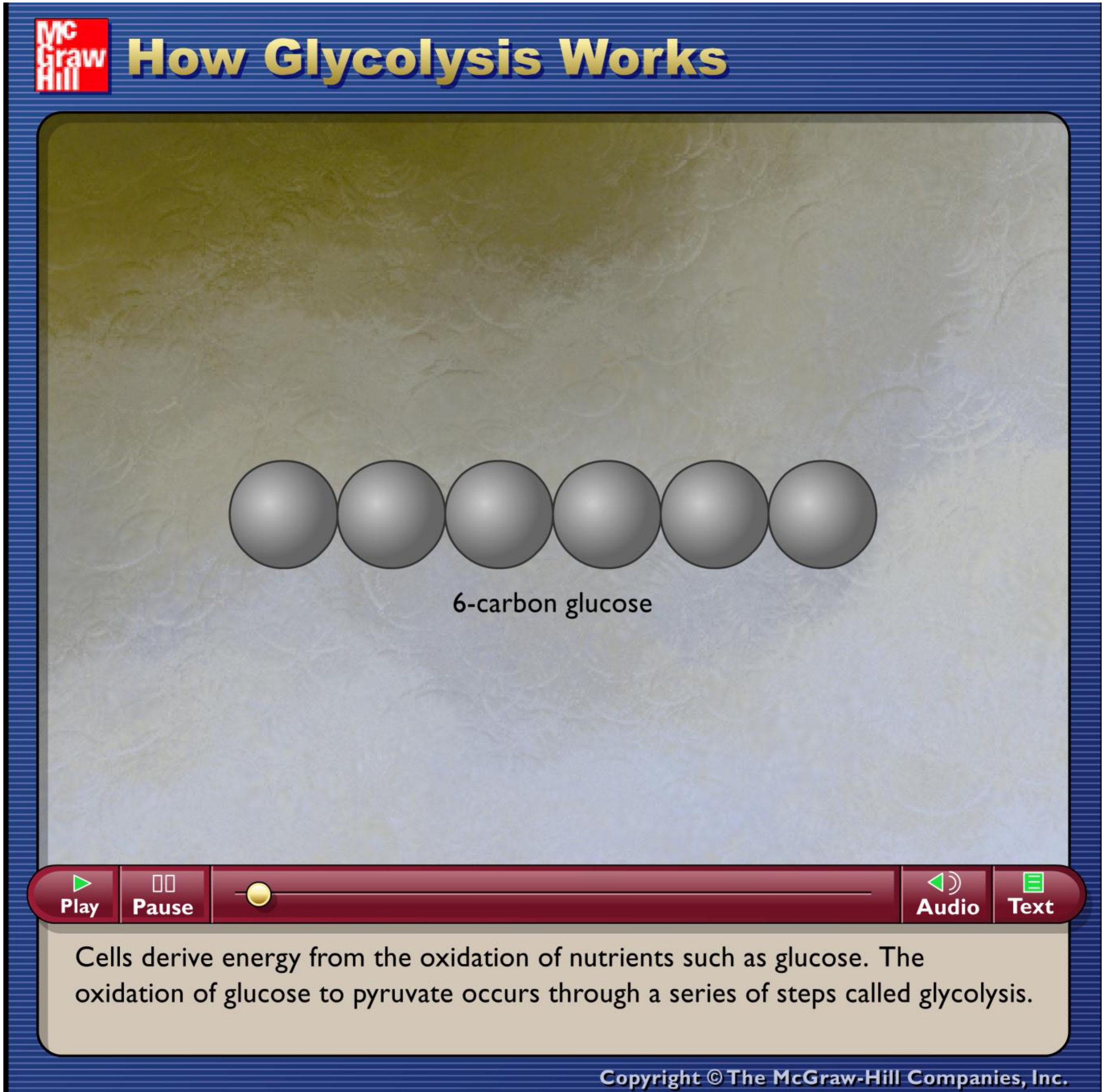
- 4 metabolic pathways

1. Glycolysis
2. Breakdown of pyruvate to an acetyl group
3. Citric acid cycle
4. Oxidative phosphorylation


1 Glycolysis:
Glucose
C C C C C C
2 pyruvate
2 C C C
Cytosol
Outer mitochondrial membrane
Inner mitochondrial membrane
Mitochondrial matrix
2 NADH
2 NADH
6 NADH 2 $FADH_2$
2 pyruvate
2 Breakdown of pyruvate:
2 pyruvate
2 C C C
$2CO_2$ + 2acetyl
2 C C
2 CO_2
2 acetyl
3 Citric acid cycle:
2 acetyl
2 C C
4 CO_2
2 CO_2
2 CO_2
4 Oxidative phosphorylation:
The oxidation of NADH and $FADH_2$ via the electron transport chain provides energy to make more ATP via the ATP synthase.
O_2 is consumed.
+2 ATP
Via substrate-level phosphorylation
+2 ATP
Via substrate-level phosphorylation
+30–34 ATP
Via chemiosmosis

Stage 1: Glycolysis

- Glycolysis can occur with or without oxygen
- Steps in glycolysis nearly identical in all living species
- 10 steps in 3 phases
  1. Energy investment
  2. Cleavage
  3. Energy liberation


How Glycolysis Works
6-carbon glucose
Play
Pause
Audio
Text
Cells derive energy from the oxidation of nutrients such as glucose. The oxidation of glucose to pyruvate occurs through a series of steps called glycolysis.
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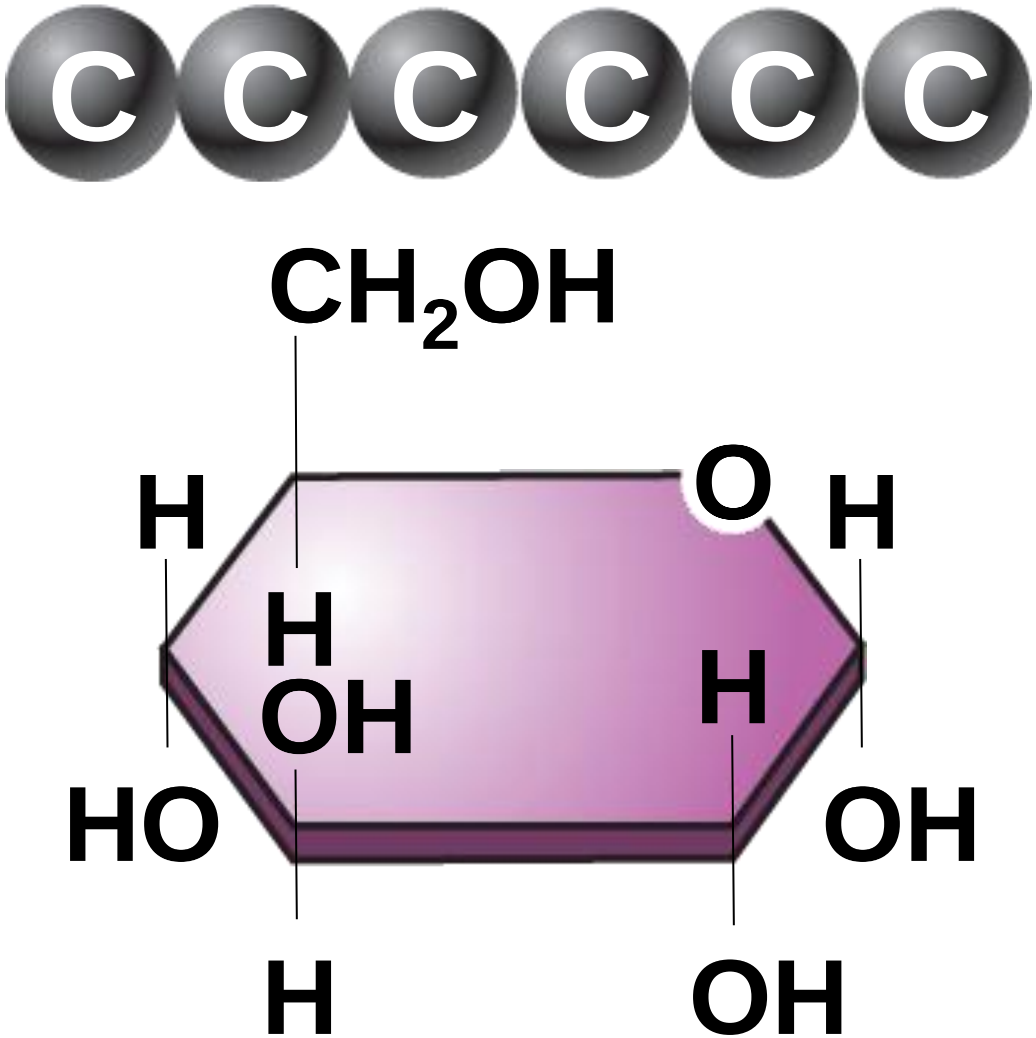
3 phases of glycolysis

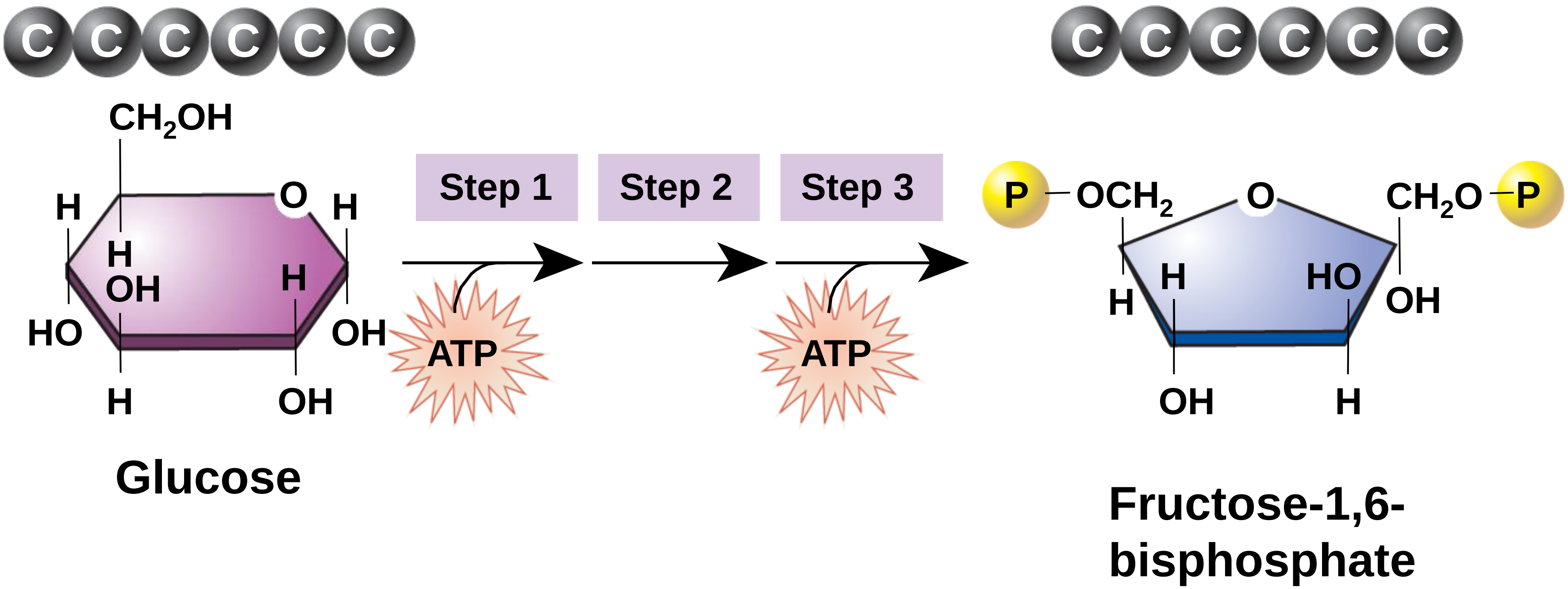
1. Energy investment
   - Steps 1-3
   - 2 ATP hydrolyzed to create fructose-1,6 bisphosphate
2. Cleavage
   - Steps 4-5
   - 6 carbon molecule broken into two 3 carbon molecules of glyceraldehyde-3-phosphate
3. Energy liberation
   - Steps 6-10
   - Two glyceraldehyde-3-phosphate molecules broken down into two pyruvate molecules producing 2 NADH and 4 ATP

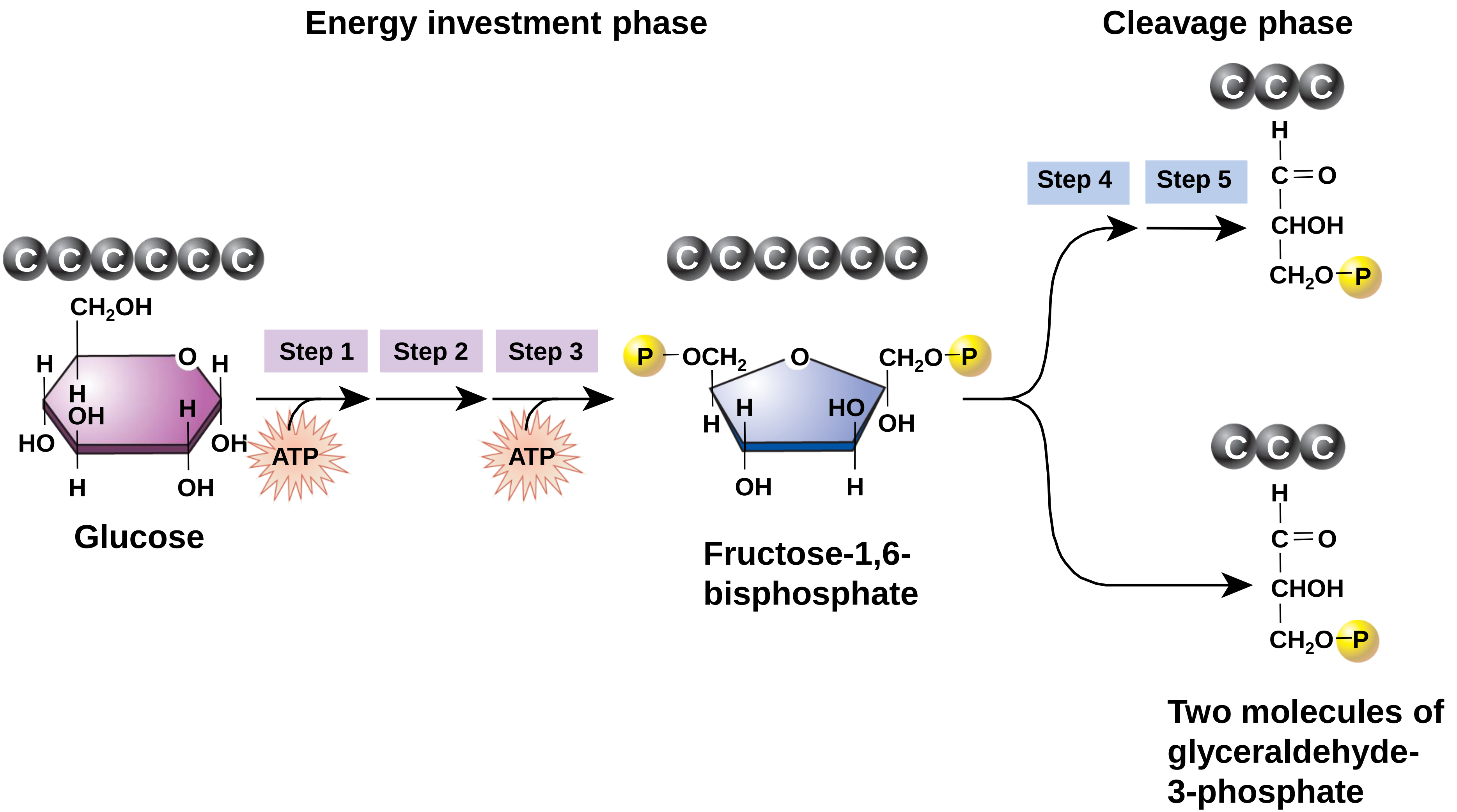
- Net yield in ATP of 2



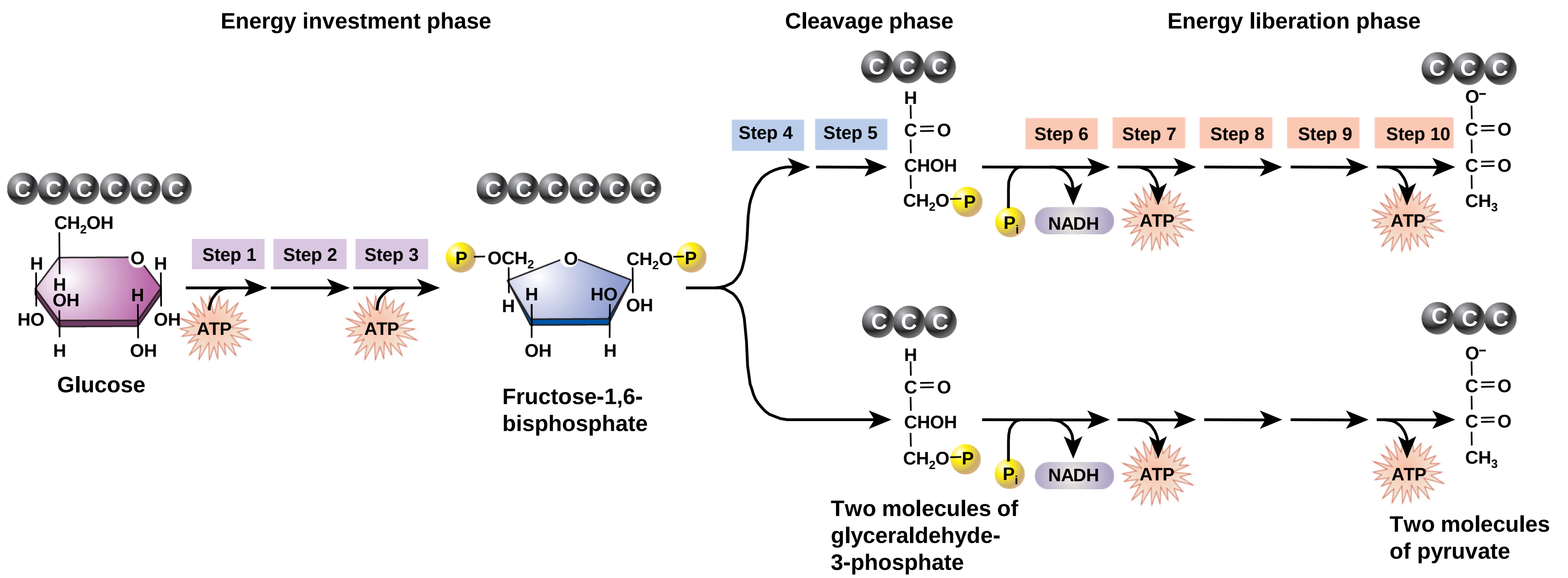
Glucose

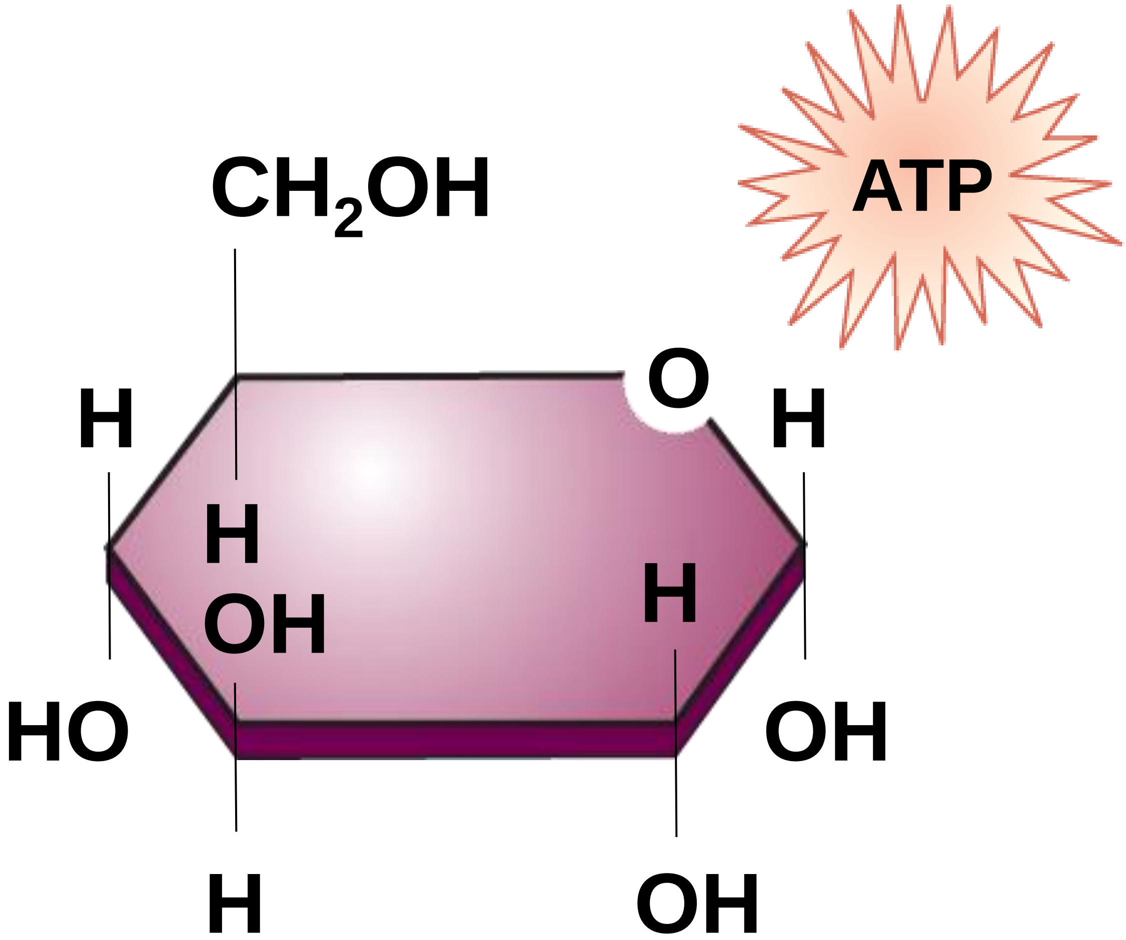
Energy investment phase



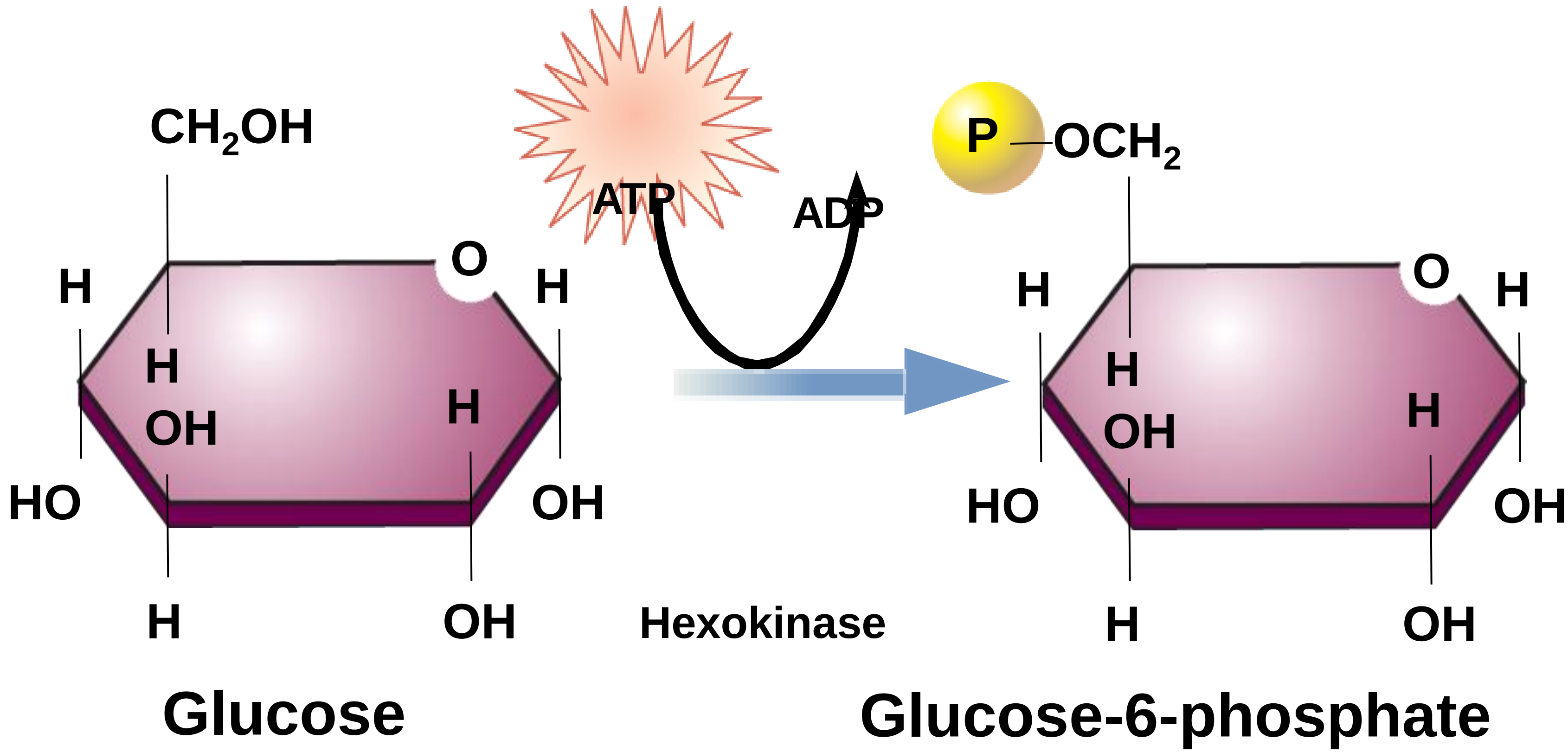


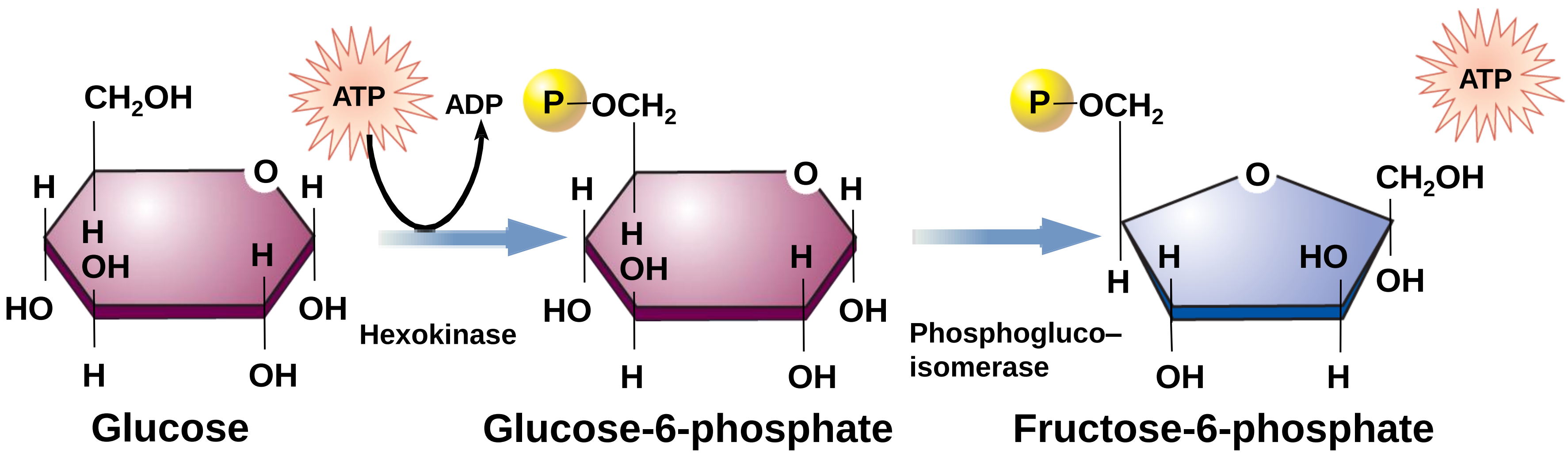
Energy investment phase
Cleavage phase
C C C C C C
CH2OH
H
O
H
H
OH
H
HO
OH
H
OH
Glucose
Step 1
Step 2
Step 3
ATP
ATP
C C C C C C
P
OCH2
O
CH2O
P
H
H
HO
OH
OH
H
Fructose-1,6-bisphosphate
Step 4
Step 5
C C C
H
C=O
CHOH
CH2O
P
C C C
H
C=O
CHOH
CH2O
P
Two molecules of glyceraldehyde-3-phosphate


Energy investment phase
Cleavage phase
Energy liberation phase
C C C C C C
Glucose
Step 1
Step 2
Step 3
ATP
ATP
Fructose-1,6-bisphosphate
Step 4
Step 5
Two molecules of glyceraldehyde-3-phosphate
Step 6
Step 7
Step 8
Step 9
Step 10
NADH
ATP
Two molecules of pyruvate

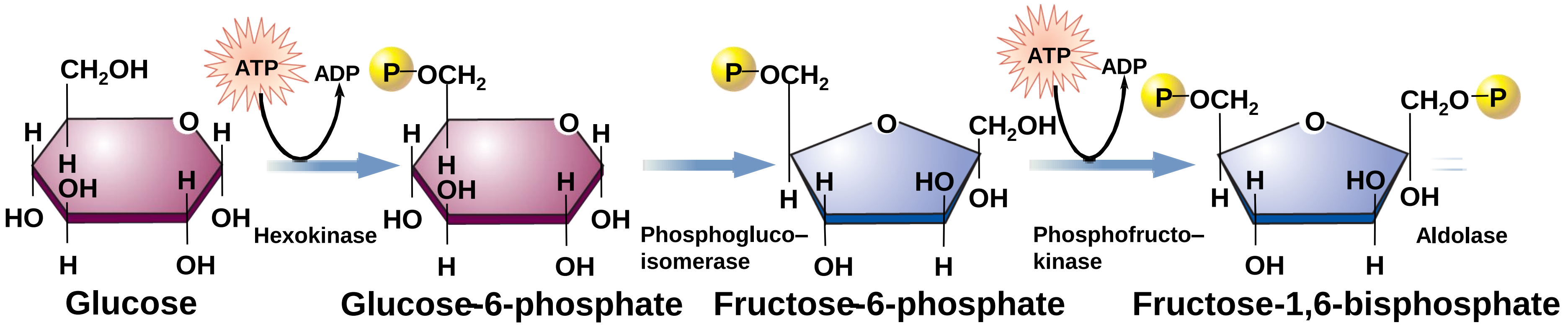


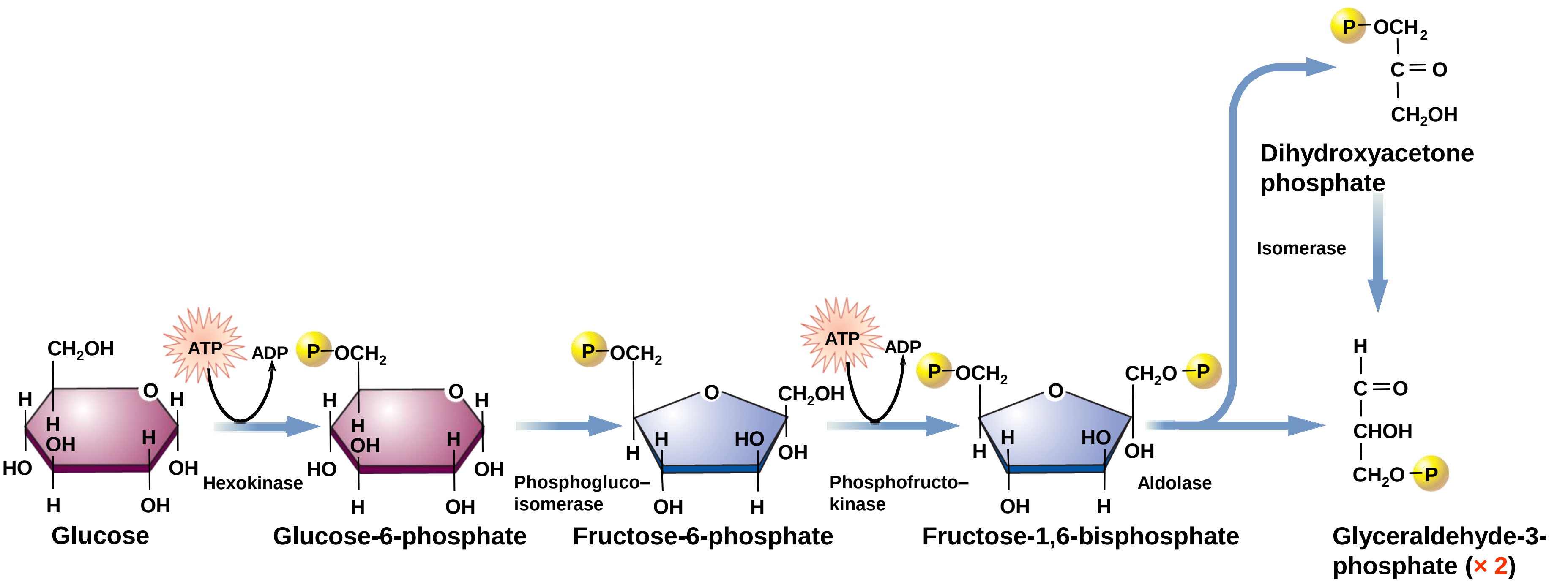
Glucose


CH2OH
O
H
H
H
OH
H
HO
OH
H
OH
ATP
ADP
Hexokinase
P
OCH2
O
H
H
H
OH
H
HO
OH
H
OH
Glucose
Glucose-6-phosphate

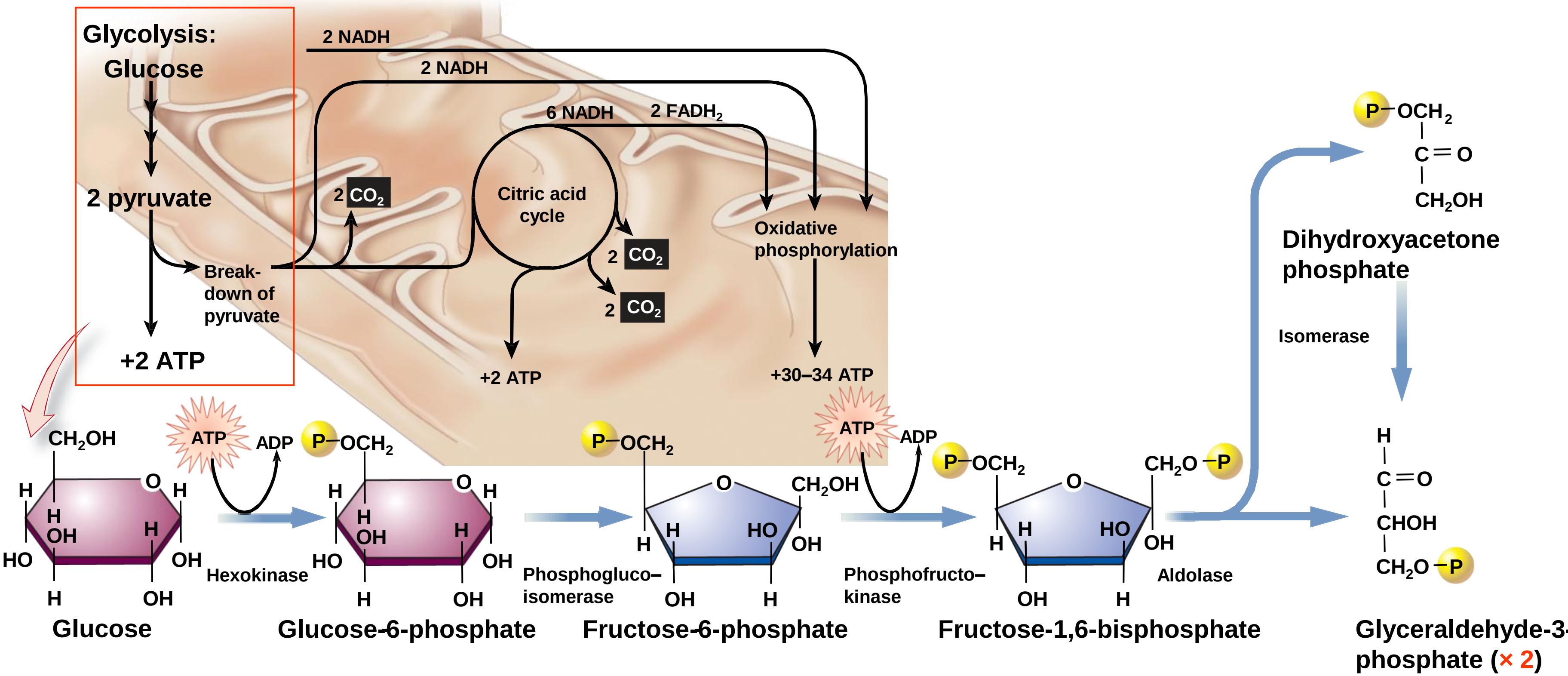


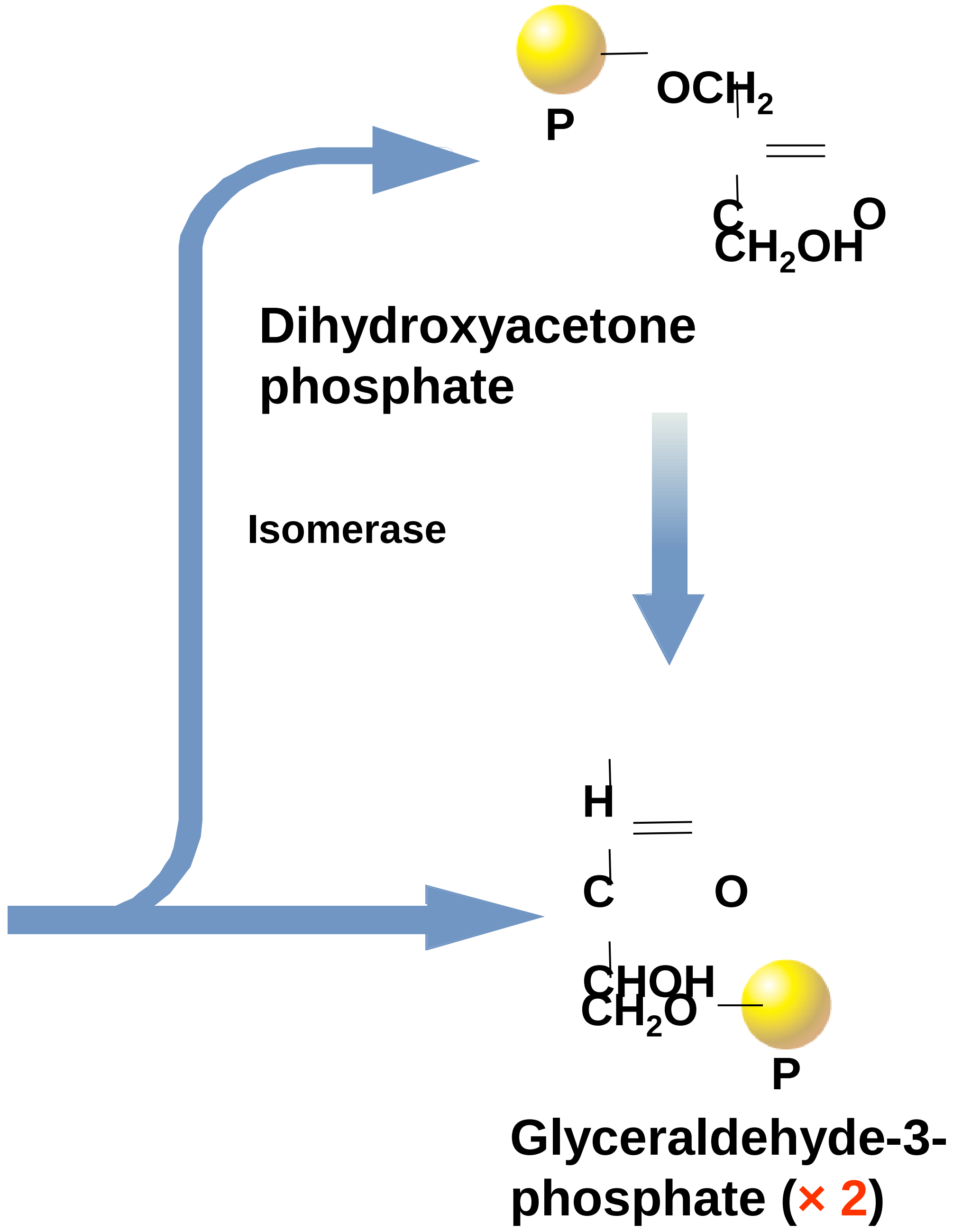
CH2OH
O
H
H
H
OH
H
HO
OH
H
OH
ATP
ADP
Hexokinase
P
OCH2
O
H
H
H
OH
H
HO
OH
H
OH
Phosphogluco–
isomerase
P
OCH2
O
CH2OH
ATP
H
H
HO
OH
OH
H
Glucose
Glucose-6-phosphate
Fructose-6-phosphate

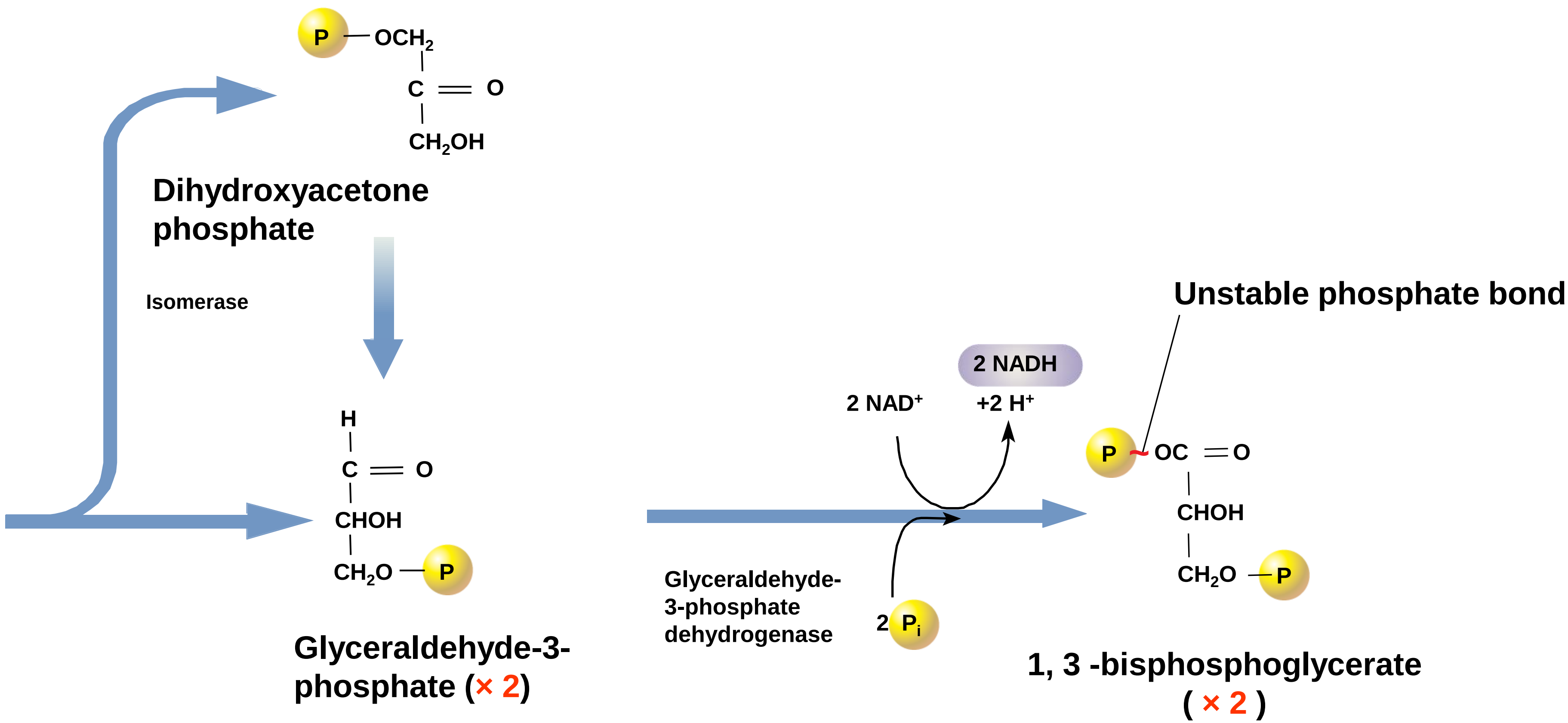

CH2OH
O
H
H
OH
H
HO
OH
H
OH
Glucose
ATP
ADP
Hexokinase
P
OCH2
Glucose-6-phosphate
Phosphogluco–
isomerase
Fructose-6-phosphate
CH2OH
Phosphofructo–
kinase
Fructose-1,6-bisphosphate
CH2O
Aldolase



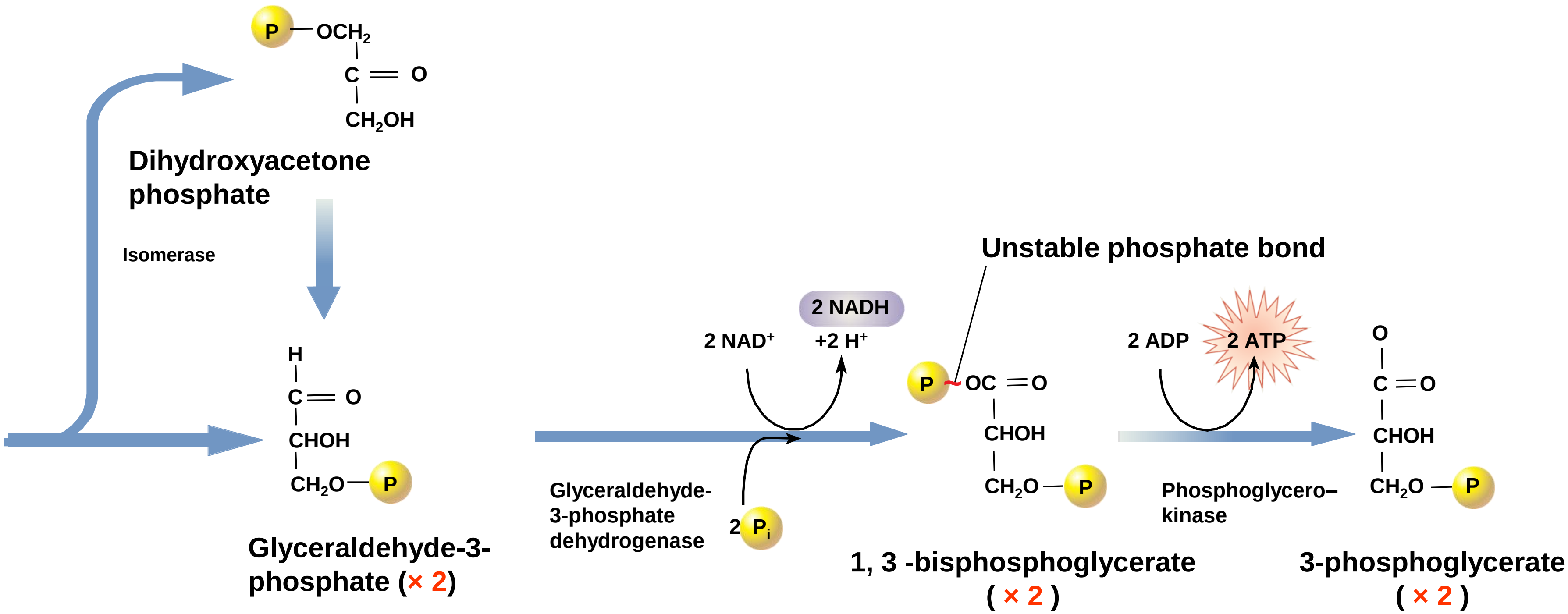
CH2OH
ATP
ADP
P
OCH2
O
H
HO
OH
Hexokinase
Phosphogluco–
isomerase
CH2OH
Phosphofructo–
kinase
CH2O
Aldolase
Isomerase
Dihydroxyacetone
phosphate
C=O
CHOH
Glucose
Glucose-6-phosphate
Fructose-6-phosphate
Fructose-1,6-bisphosphate
Glyceraldehyde-3-
phosphate (× 2)

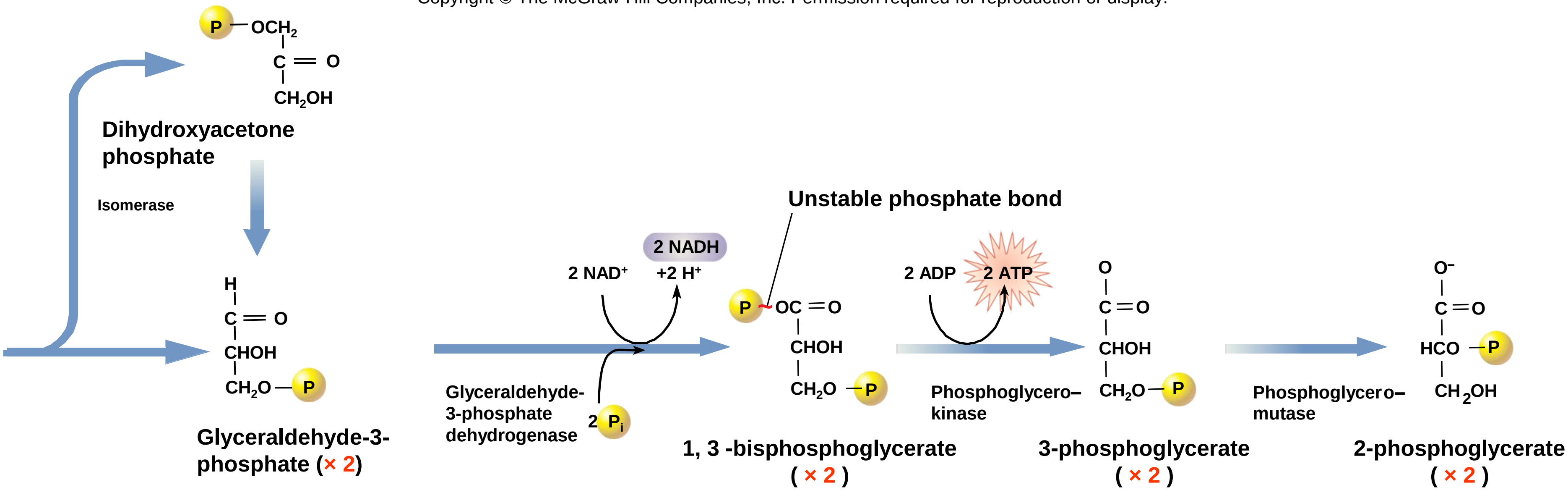

Glycolysis:
Glucose
2 pyruvate
Break-down of pyruvate
+2 ATP
2 NADH
2 NADH
2 CO_2
6 NADH
2 $FADH_2$
Citric acid cycle
2 CO_2
2 CO_2
+2 ATP
Oxidative phosphorylation
+30–34 ATP
CH_2OH
ATP
ADP
P–OCH_2
Hexokinase
Glucose
Glucose-6-phosphate
P–OCH_2
CH_2OH
Phosphogluco–isomerase
Fructose-6-phosphate
ATP
ADP
P–OCH_2
CH_2O–P
Phosphofructo–kinase
Aldolase
Fructose-1,6-bisphosphate
P–OCH_2
C=O
CH_2OH
Dihydroxyacetone phosphate
Isomerase
H
C=O
CHOH
CH_2O–P
Glyceraldehyde-3-phosphate (× 2)

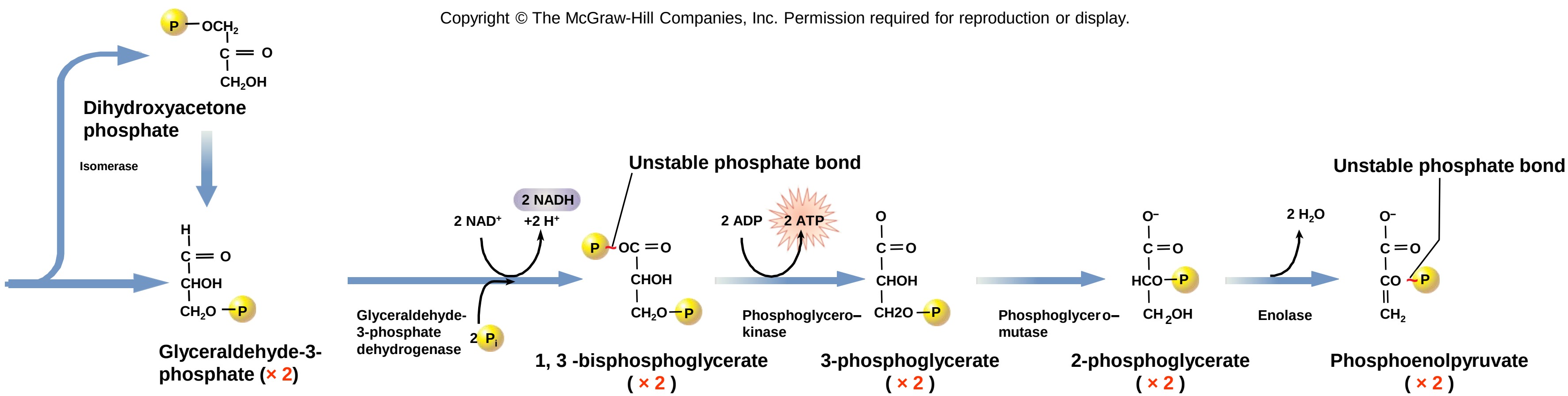

P
OCH2
C O
CH2OH
Dihydroxyacetone phosphate
Isomerase
H
C O
CHOH
CH2O
P
Glyceraldehyde-3-phosphate (× 2)



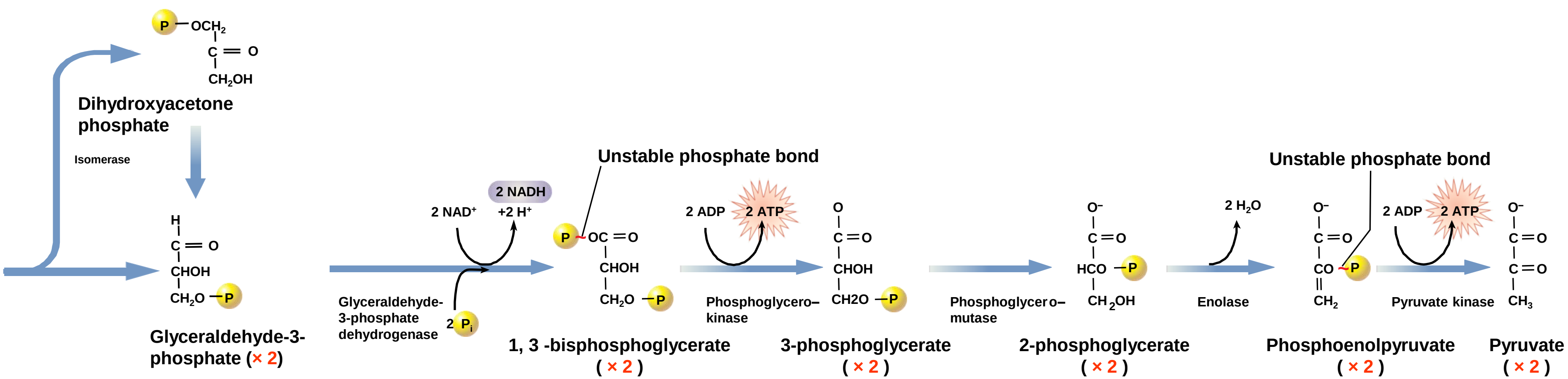
P
OCH2
C
O
CH2OH
Dihydroxyacetone phosphate
Isomerase
H
C
O
CHOH
CH2O
P
Glyceraldehyde-3-phosphate (× 2)
2 NADH
2 NAD+
+2 H+
Glyceraldehyde-3-phosphate dehydrogenase
2 Pi
Unstable phosphate bond
P
OC
O
CHOH
CH2O
P
1, 3 -bisphosphoglycerate (× 2)


P
OCH2
C = O
CH2OH
Dihydroxyacetone phosphate
Isomerase
H
C = O
CHOH
CH2O
P
Glyceraldehyde-3-phosphate (× 2)
2 NAD+
2 NADH
+2 H+
Glyceraldehyde-3-phosphate dehydrogenase
2 Pi
Unstable phosphate bond
P
OC = O
CHOH
CH2O
P
1, 3 -bisphosphoglycerate (× 2)
2 ADP
2 ATP
Phosphoglycero–kinase
O
C = O
CHOH
CH2O
P
3-phosphoglycerate (× 2)


P OCH2
C = O
CH2OH
Dihydroxyacetone phosphate
Isomerase
H
C = O
CHOH
CH2O P
Glyceraldehyde-3-phosphate (× 2)
2 NAD+
2 NADH
+2 H+
Glyceraldehyde-3-phosphate dehydrogenase
2 Pi
Unstable phosphate bond
P ~ OC = O
CHOH
CH2O P
1, 3 -bisphosphoglycerate (× 2)
2 ADP
2 ATP
Phosphoglycero– kinase
O
C = O
CHOH
CH2O P
3-phosphoglycerate (× 2)
Phosphoglycero– mutase
O–
C = O
HCO P
CH2OH
2-phosphoglycerate (× 2)



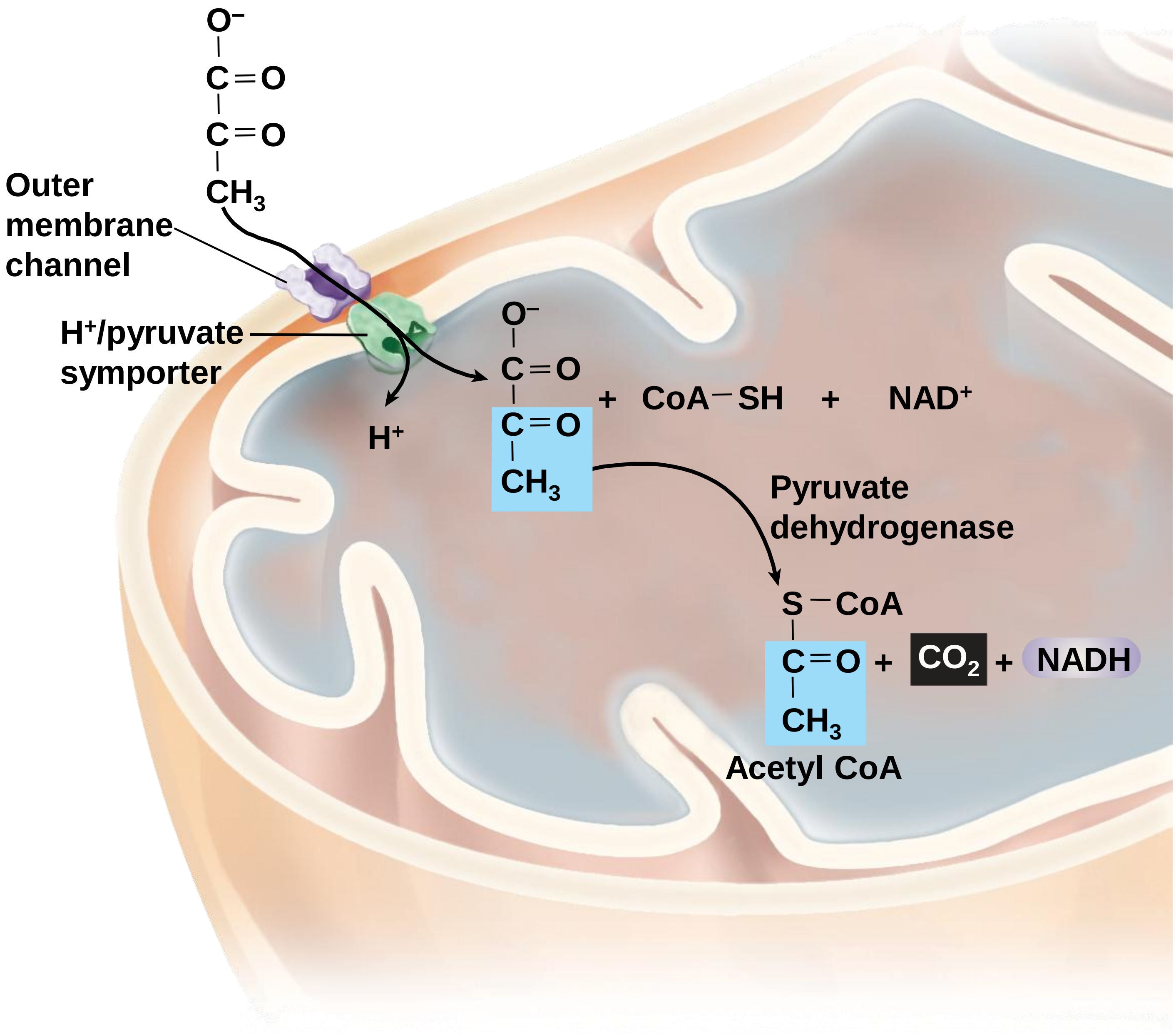
Dihydroxyacetone phosphate
Isomerase
Glyceraldehyde-3-phosphate (× 2)
2 NAD+
2 NADH
+2 H+
Glyceraldehyde-3-phosphate dehydrogenase
2 Pi
Unstable phosphate bond
1, 3 -bisphosphoglycerate (× 2)
2 ADP
2 ATP
Phosphoglycero–kinase
3-phosphoglycerate (× 2)
Phosphoglycero–mutase
2-phosphoglycerate (× 2)
2 H2O
Enolase
Unstable phosphate bond
Phosphoenolpyruvate (× 2)



Dihydroxyacetone phosphate
Isomerase
Glyceraldehyde-3-phosphate (× 2)
2 NADH
2 NAD+
+2 H+
Glyceraldehyde-3-phosphate dehydrogenase
Unstable phosphate bond
1, 3 -bisphosphoglycerate (× 2)
2 ADP
2 ATP
Phosphoglycero–kinase
3-phosphoglycerate (× 2)
Phosphoglycero–mutase
2-phosphoglycerate (× 2)
Enolase
Unstable phosphate bond
Phosphoenolpyruvate (× 2)
Pyruvate kinase
Pyruvate (× 2)

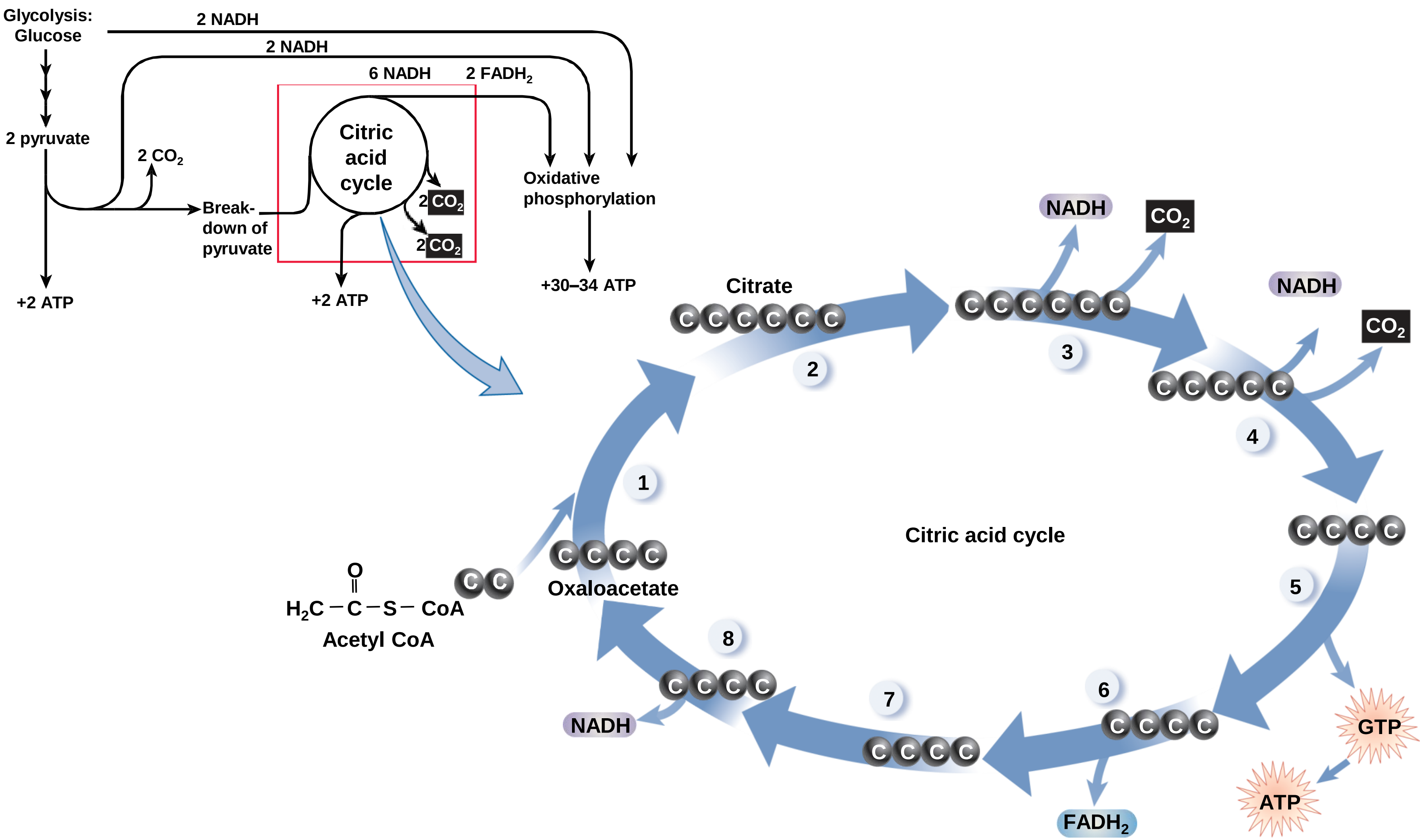
Stage 2: Breakdown of pyruvate to an acetyl group

- In eukaryotes, pyruvate in transported to the mitochondrial matrix
- Broken down by pyruvate dehydrogenase
- Molecule of CO_2 removed from each pyruvate
- Remaining acetyl group attached to CoA to make acetyl CoA
- 1 NADH is made for each pyruvate


O−
C=O
C=O
CH3
Outer membrane channel
H+/pyruvate symporter
H+
O−
C=O
C=O
CH3
+ CoA−SH + NAD+
Pyruvate dehydrogenase
S−CoA
C=O + CO2 + NADH
CH3
Acetyl CoA

Stage 3: Citric acid cycle

- Metabolic cycle
  - Particular molecules enter while other leave, involving a series of organic molecules regenerated with each cycle
- Acetyl is removed from Acetyl CoA and attached to oxaloacetate to form citrate or citric acid
- Series of steps releases 2CO_2, 1ATP, 3NADH, and 1 $FADH_2$
- Oxaloacetate is regenerated to start the cycle again


Glycolysis:
Glucose
2 NADH
2 NADH
6 NADH
2 $FADH_2$
2 pyruvate
2 CO_2
Citric
acid
cycle
2 CO_2
2 CO_2
Break-
down of
pyruvate
Oxidative
phosphorylation
+2 ATP
+2 ATP
+30–34 ATP
Citrate
NADH
CO_2
NADH
CO_2
1
2
3
4
5
6
7
8
Citric acid cycle
Oxaloacetate
O
$H_2C - C - S - CoA$
Acetyl CoA
NADH
$FADH_2$
GTP
ATP

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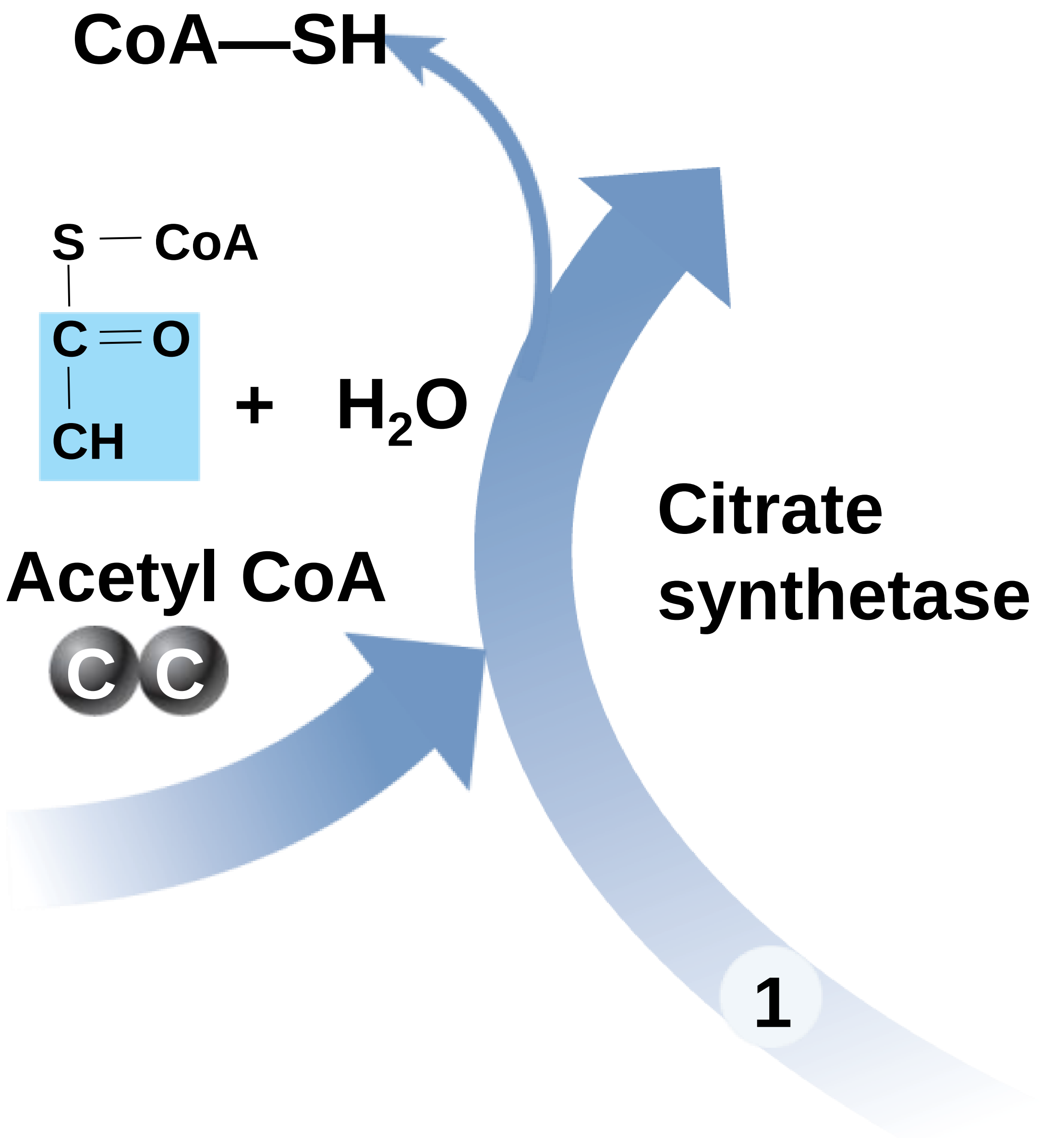
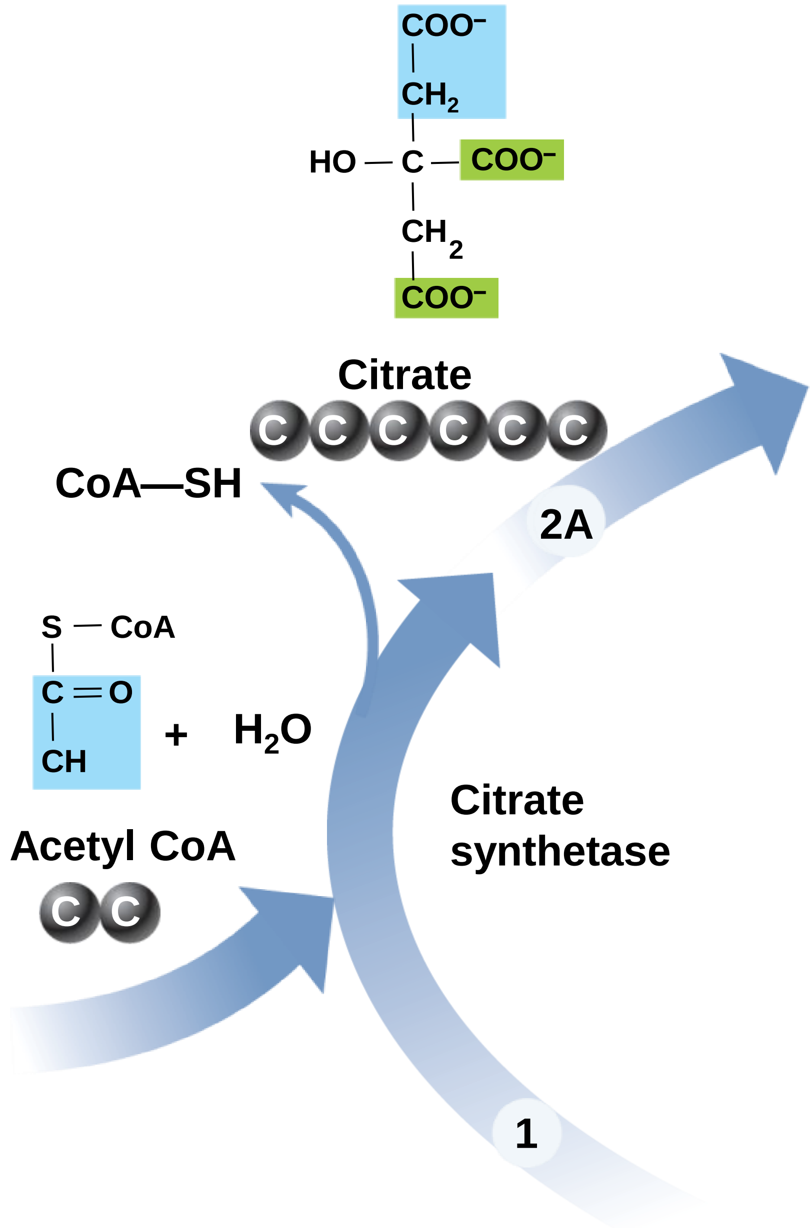
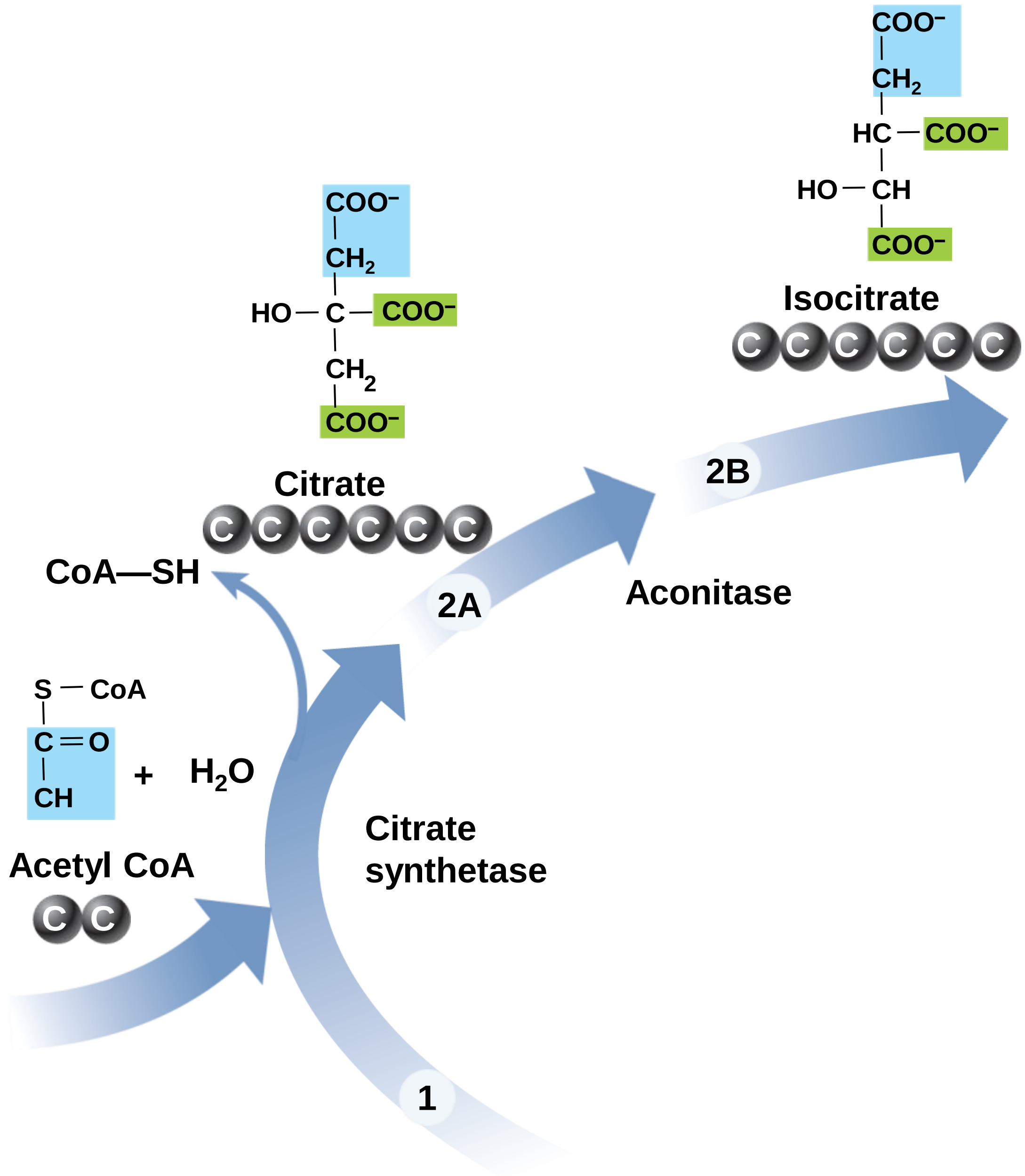
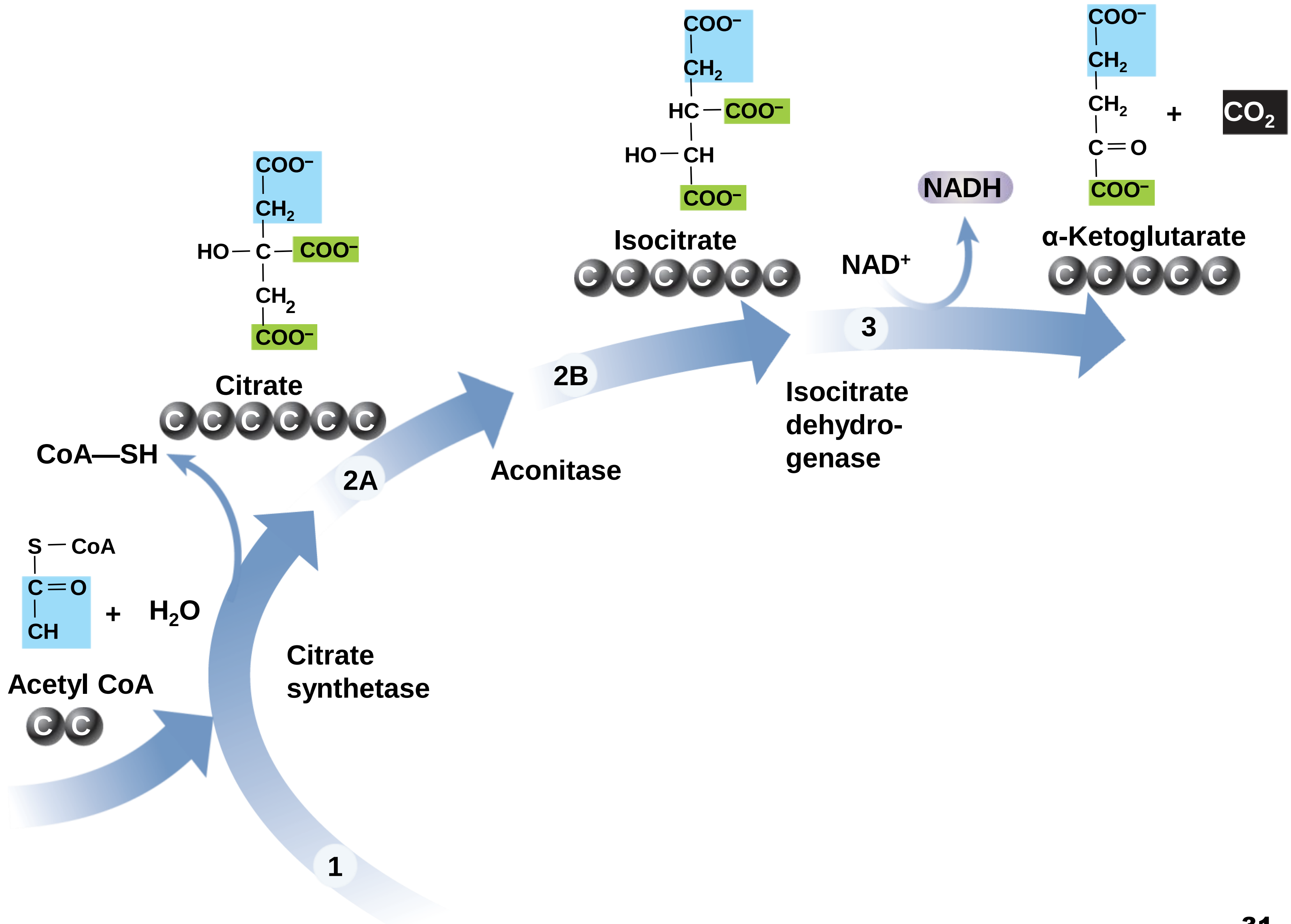
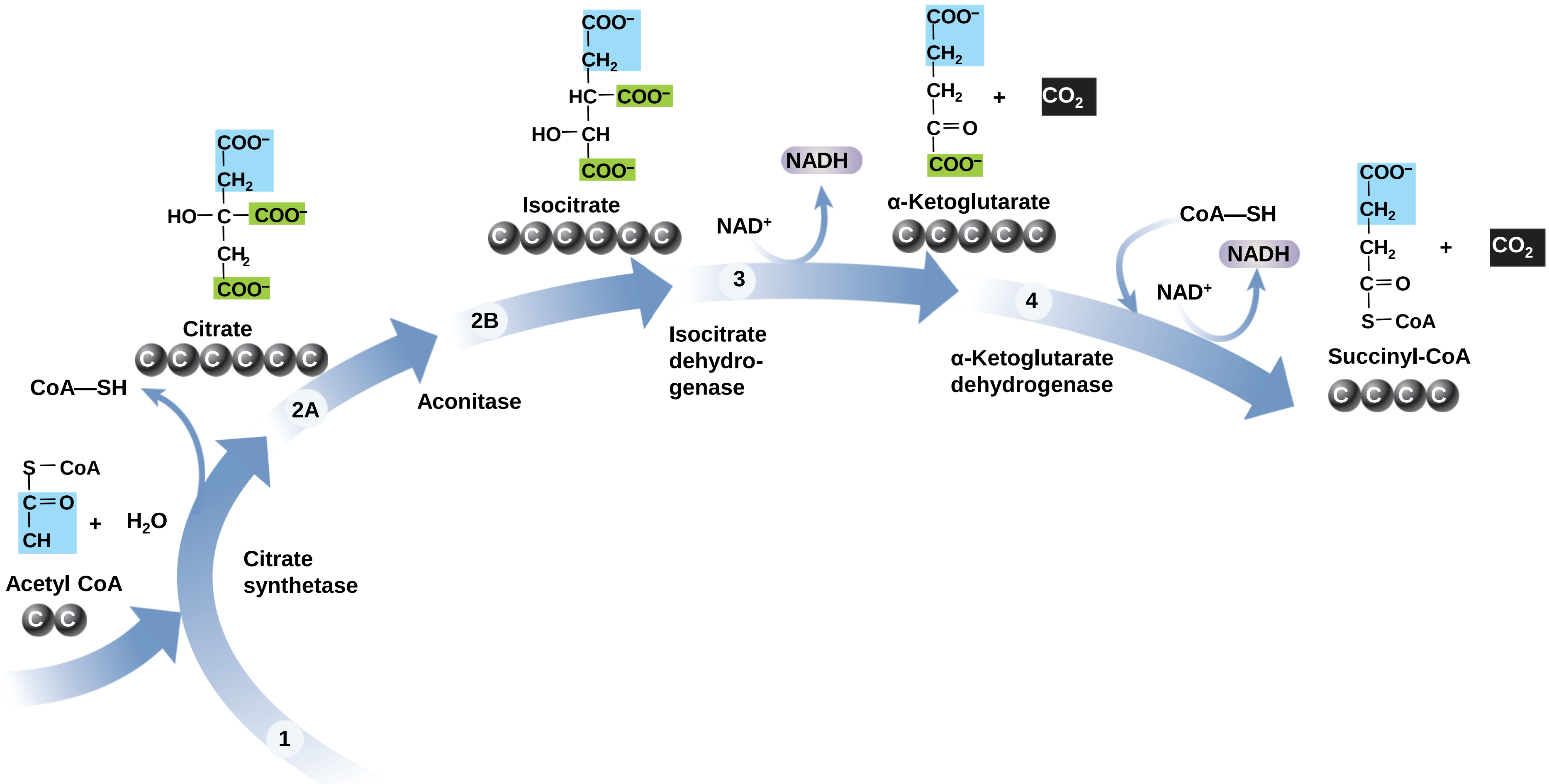



COO⁻
CH2
HO — C — COO⁻
CH2
COO⁻
Citrate
C C C C C C
CoA—SH
2A
S — CoA
C = O
CH
+ H2O
Acetyl CoA
C C
Citrate synthetase
1

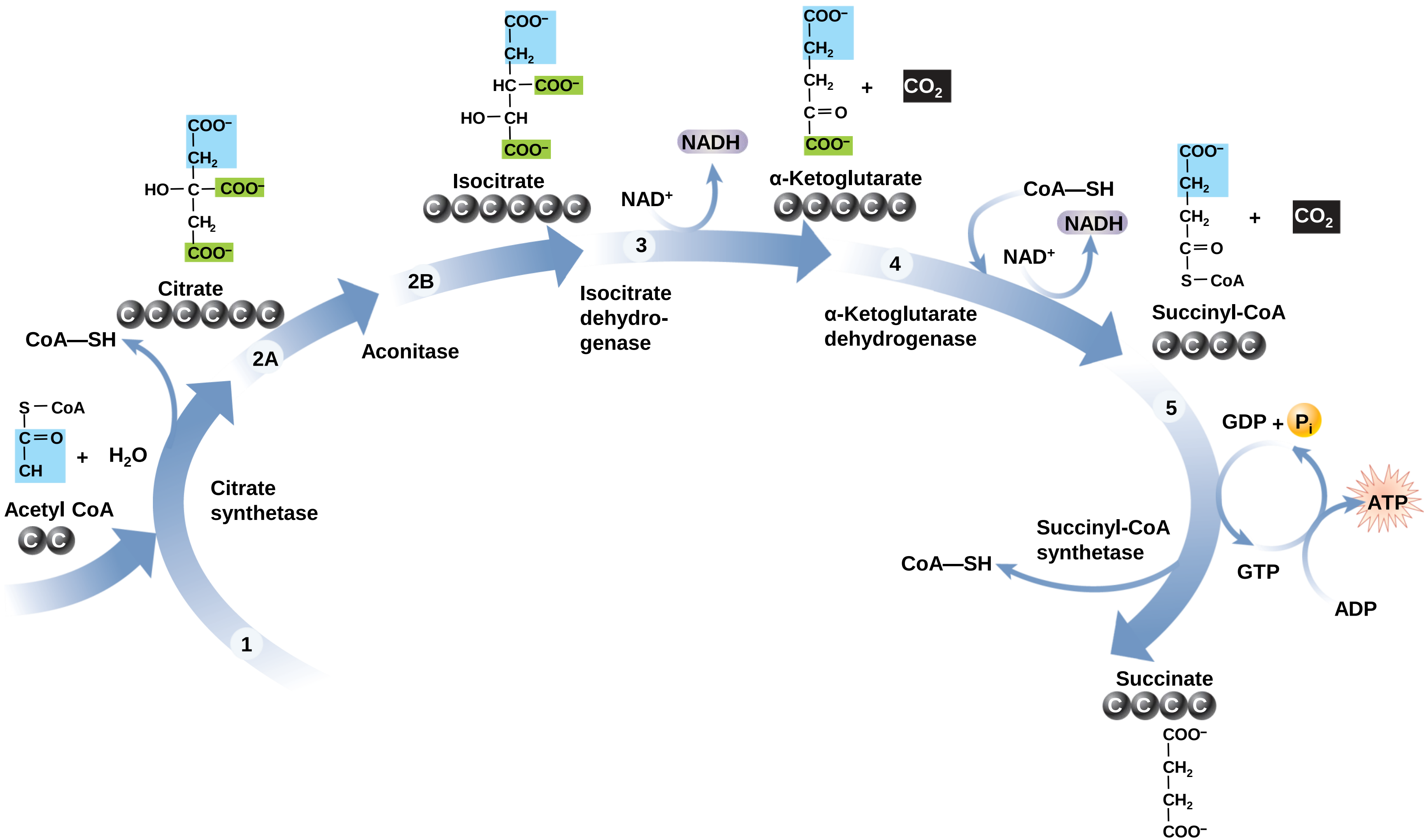

COO⁻
CH2
HC — COO⁻
HO — CH
COO⁻
Isocitrate
C C C C C C
COO⁻
CH2
HO — C — COO⁻
CH2
COO⁻
Citrate
C C C C C C
2B
2A
Aconitase
CoA—SH
S — CoA
C = O
CH
+
H2O
Acetyl CoA
C C
Citrate
synthetase
1



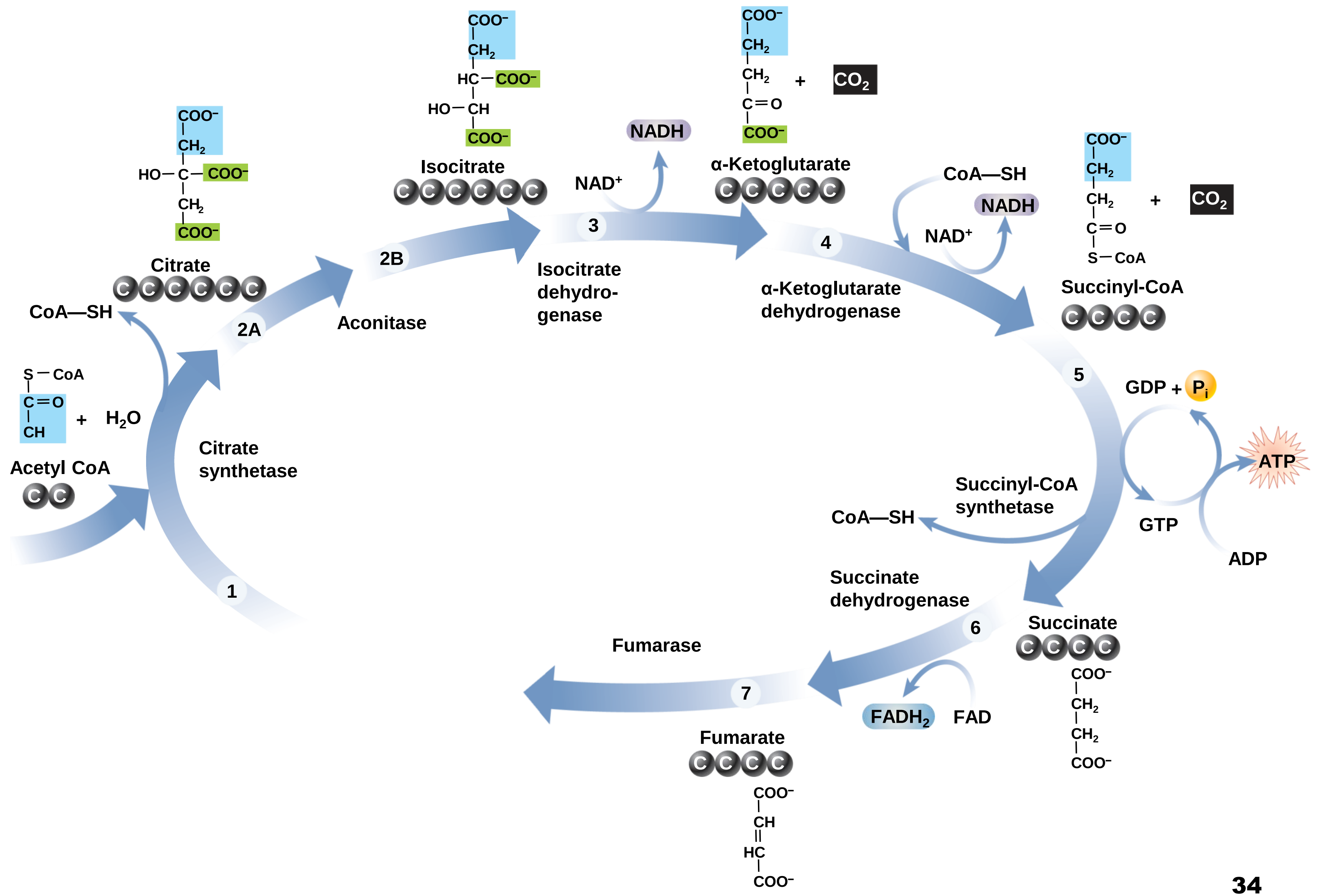
COO⁻
CH2
HC — COO⁻
HO — CH
COO⁻
Isocitrate
C C C C C C
COO⁻
CH2
CH2
C = O
COO⁻
+ CO2
NADH
α-Ketoglutarate
C C C C C
COO⁻
CH2
HO — C — COO⁻
CH2
COO⁻
Citrate
C C C C C C
NAD+
3
2B
Isocitrate dehydro-genase
CoA—SH
2A
Aconitase
S — CoA
C = O
CH
+ H2O
Acetyl CoA
C C
Citrate synthetase
1

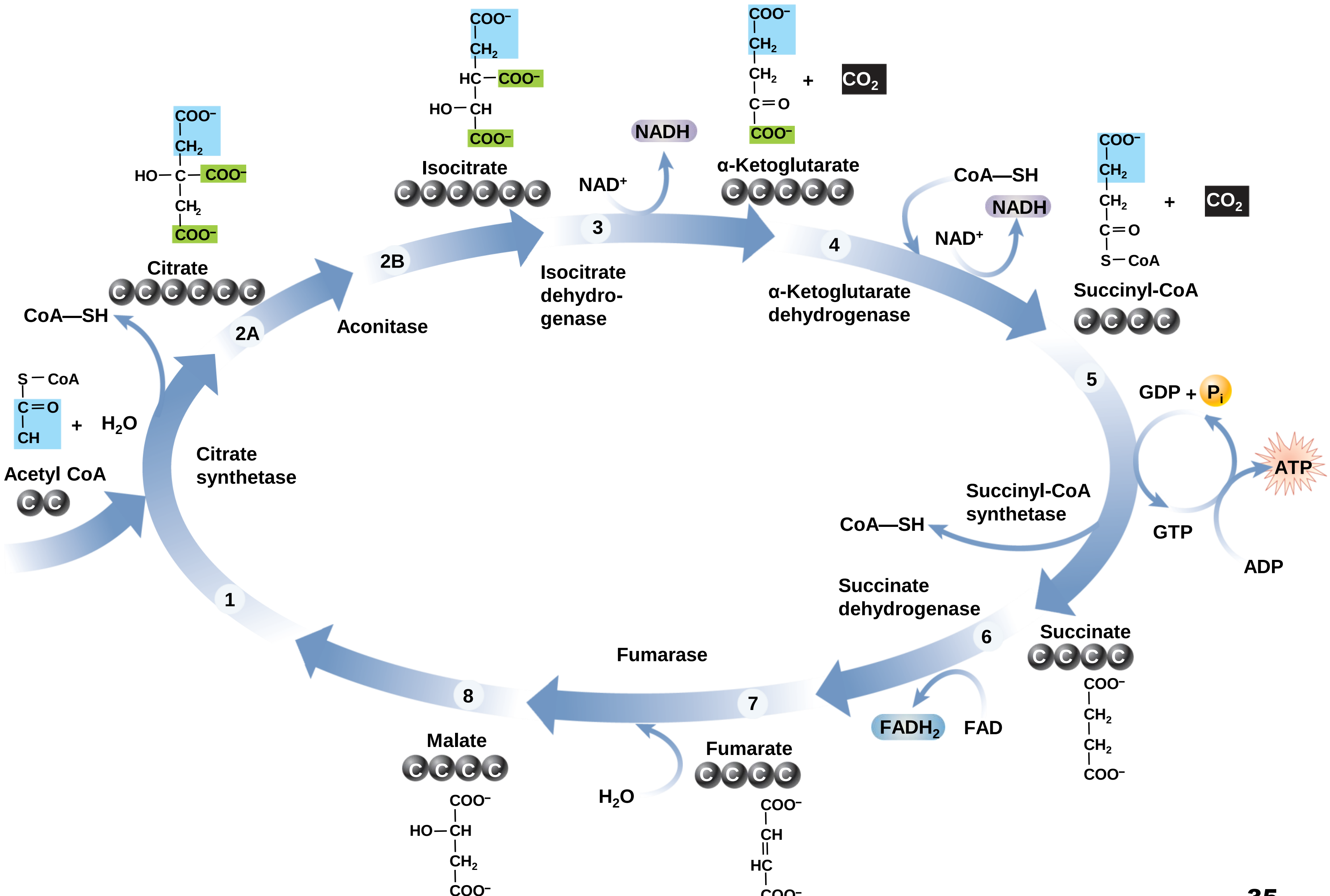


Acetyl CoA
S — CoA
C = O
CH
+ H2O
Citrate synthetase
1
CoA—SH
Citrate
COO−
CH2
HO — C — COO−
CH2
COO−
2A
Aconitase
2B
Isocitrate
COO−
CH2
HC — COO−
HO — CH
COO−
3
NAD+
NADH
Isocitrate dehydro-genase
α-Ketoglutarate
COO−
CH2
CH2
C = O
COO−
+ CO2
4
CoA—SH
NAD+
NADH
α-Ketoglutarate dehydrogenase
Succinyl-CoA
COO−
CH2
CH2
C = O
S — CoA
+ CO2

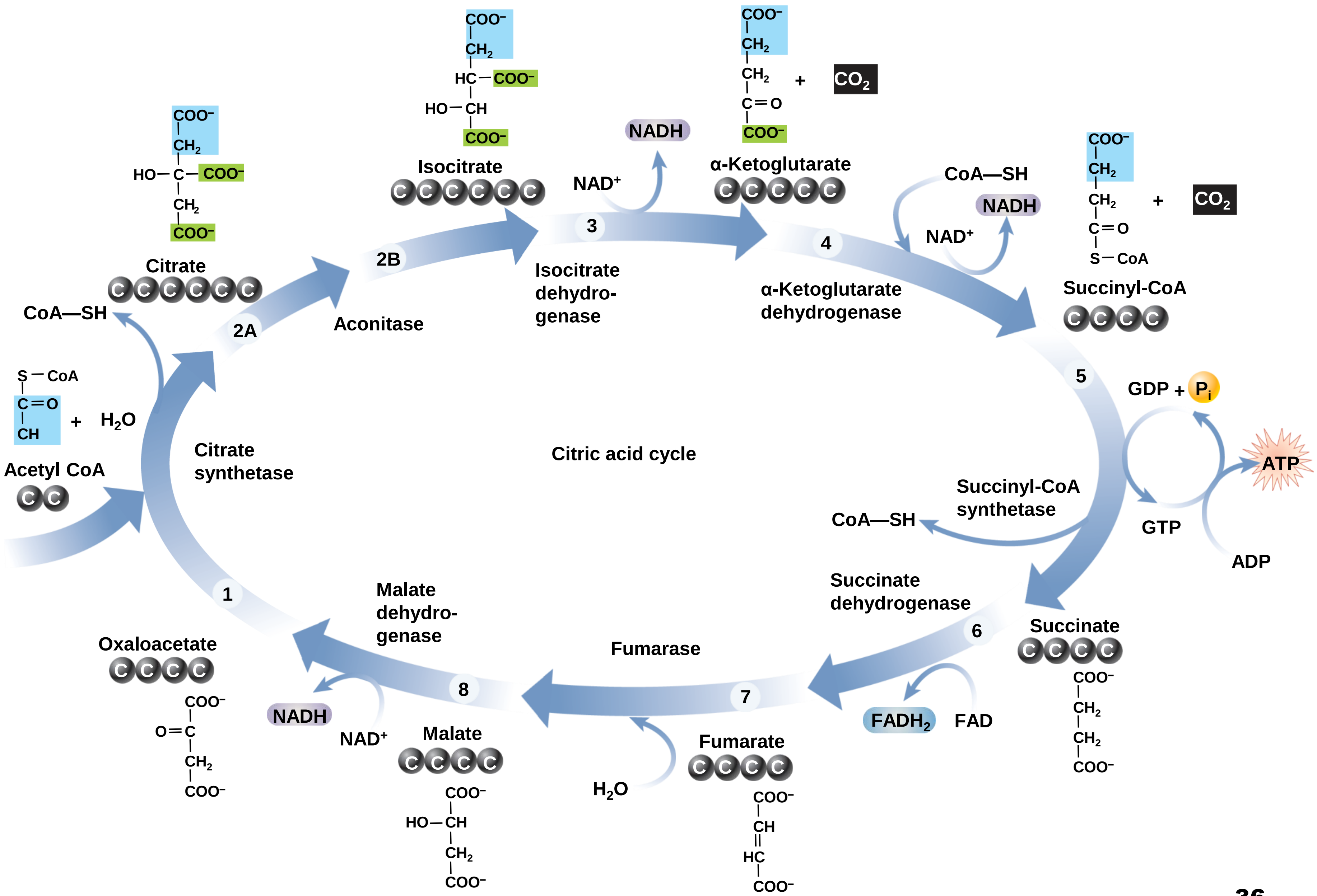


Citrate
Isocitrate
NADH
α-Ketoglutarate
CO2
CoA—SH
NADH
NAD+
Succinyl-CoA
CO2
2B
3
4
NAD+
CoA—SH
Aconitase
Isocitrate dehydro-genase
α-Ketoglutarate dehydrogenase
2A
Acetyl CoA
H2O
Citrate synthetase
5
GDP + Pi
ATP
Succinyl-CoA synthetase
CoA—SH
GTP
ADP
1
Succinate


Acetyl CoA
H_2O
CoA—SH
Citrate synthetase
1
Citrate
2A
Aconitase
2B
Isocitrate
NAD^+
NADH
3
Isocitrate dehydro-genase
α-Ketoglutarate
CO_2
4
α-Ketoglutarate dehydrogenase
CoA—SH
NAD^+
NADH
Succinyl-CoA
CO_2
5
GDP + P_i
GTP
ATP
ADP
Succinyl-CoA synthetase
CoA—SH
Succinate
Succinate dehydrogenase
6
FAD
$FADH_2$
Fumarase
7
Fumarate



Acetyl CoA
H2O
CoA—SH
Citrate
Citrate synthetase
1
2A
Aconitase
2B
Isocitrate
3
NAD+
NADH
Isocitrate dehydro-genase
α-Ketoglutarate
CO2
4
CoA—SH
NAD+
NADH
α-Ketoglutarate dehydrogenase
Succinyl-CoA
CO2
5
GDP + Pi
ATP
GTP
ADP
Succinyl-CoA synthetase
CoA—SH
Succinate
Succinate dehydrogenase
6
FADH2
FAD
Fumarate
7
Fumarase
H2O
8
Malate



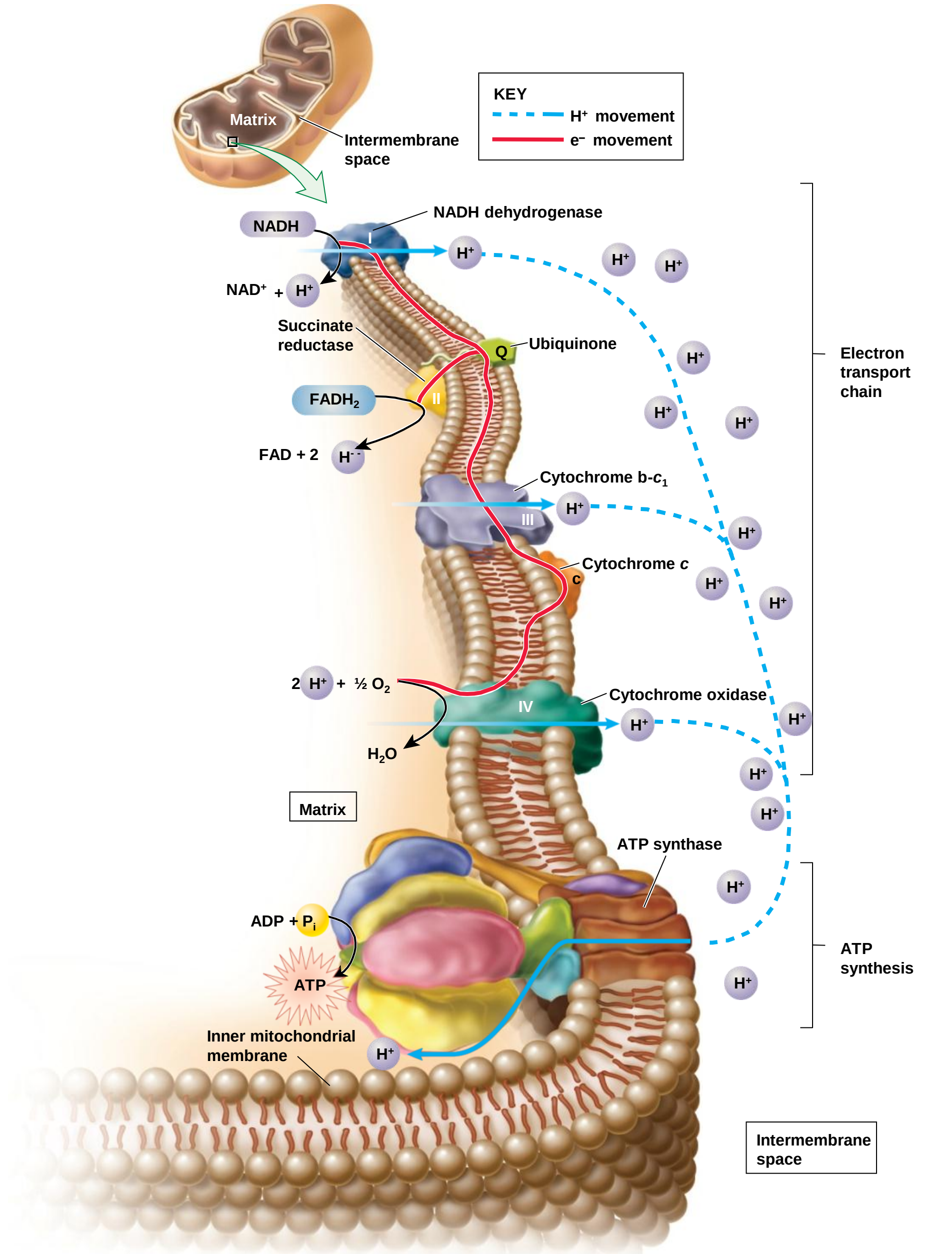
Citric acid cycle
Acetyl CoA
S — CoA
C=O
CH
+ H_2O
CoA—SH
Citrate synthetase
1
Citrate
2A
Aconitase
2B
Isocitrate
3
NAD+
NADH
Isocitrate dehydrogenase
α-Ketoglutarate
+ CO_2
4
CoA—SH
NAD+
NADH
α-Ketoglutarate dehydrogenase
Succinyl-CoA
+ CO_2
5
GDP + P_i
ATP
GTP
ADP
CoA—SH
Succinyl-CoA synthetase
Succinate
Succinate dehydrogenase
6
FAD
$FADH_2$
Fumarate
7
Fumarase
H_2O
Malate
8
NAD+
NADH
Malate dehydrogenase
Oxaloacetate

Stage 4: Oxidative phosphorylation

- High energy electrons removed from NADH and $FADH_2$ to make ATP
- Typically requires oxygen
- Oxidative process involves electron transport chain
- Phosphorylation occurs by ATP synthase

Oxidation: ETC

- Electron transport chains (ETC)
  - Group of protein complexes and small organic molecules embedded in the inner mitochondrial membrane
- Can accept and donate electrons in a linear manner in a series of redox reactions
- Movement of electrons generates H^+ electrochemical gradient/ proton-motive force
  - Excess of positive charges outside of matrix



Matrix
Intermembrane space
KEY
H+ movement
e− movement
NADH dehydrogenase
NADH
NAD+ + H+
I
H+
Succinate reductase
Ubiquinone
Q
II
FADH2
FAD + 2 H
Electron transport chain
Cytochrome b-c1
III
Cytochrome c
c
2 H+ + ½ O2
Cytochrome oxidase
IV
H2O
Matrix
ATP synthase
ADP + Pi
ATP
ATP synthesis
Inner mitochondrial membrane
Intermembrane space

Phosphorylation: ATP synthase

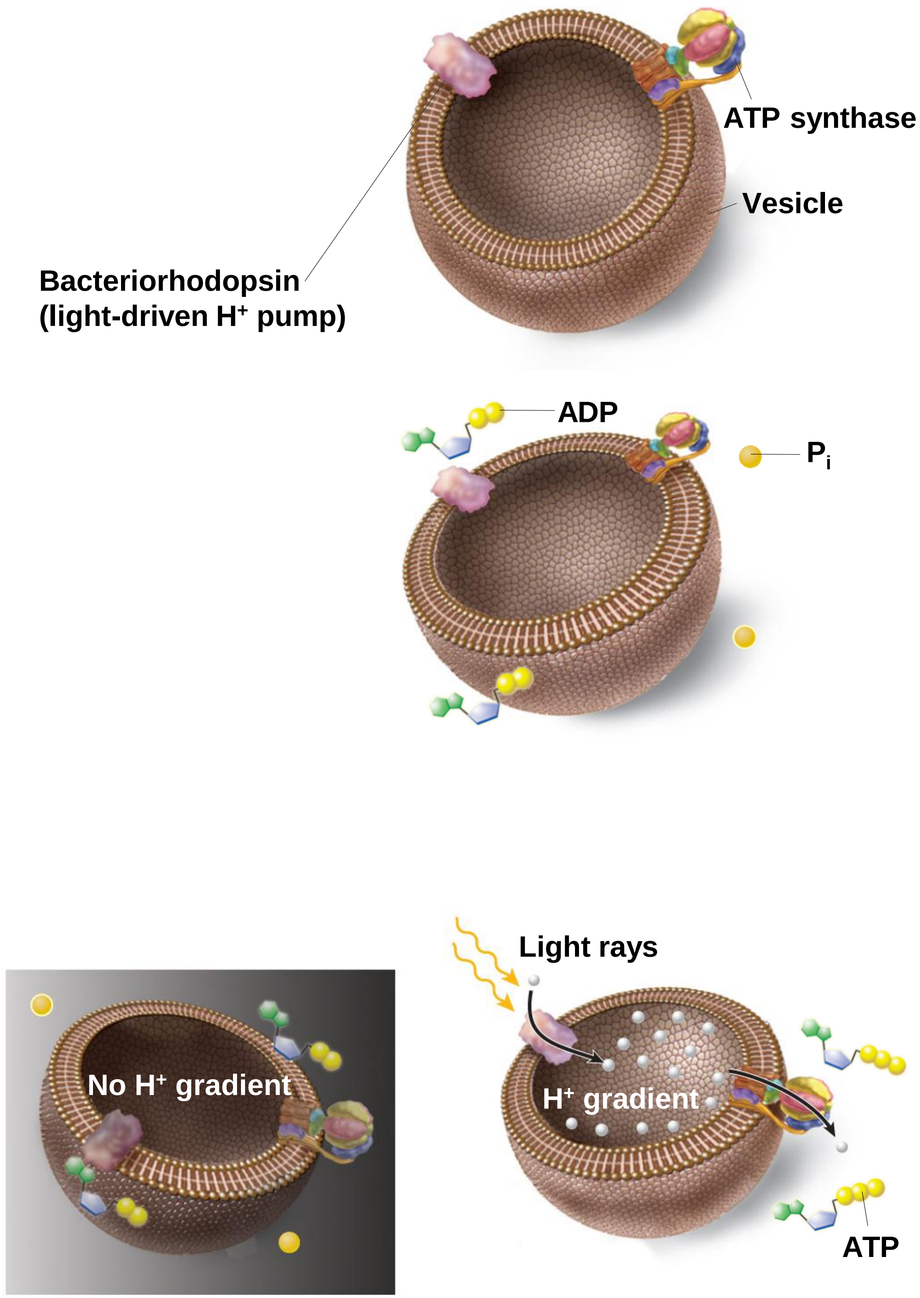
- Lipid bilayer of inner mitochondrial membrane relatively impermeable to H^+
- Can only pass through ATP synthase
- Harnesses free energy release to synthesize ATP from ADP
- Chemiosmosis- chemical synthesis of ATP as a result of pushing H^+ across a membrane

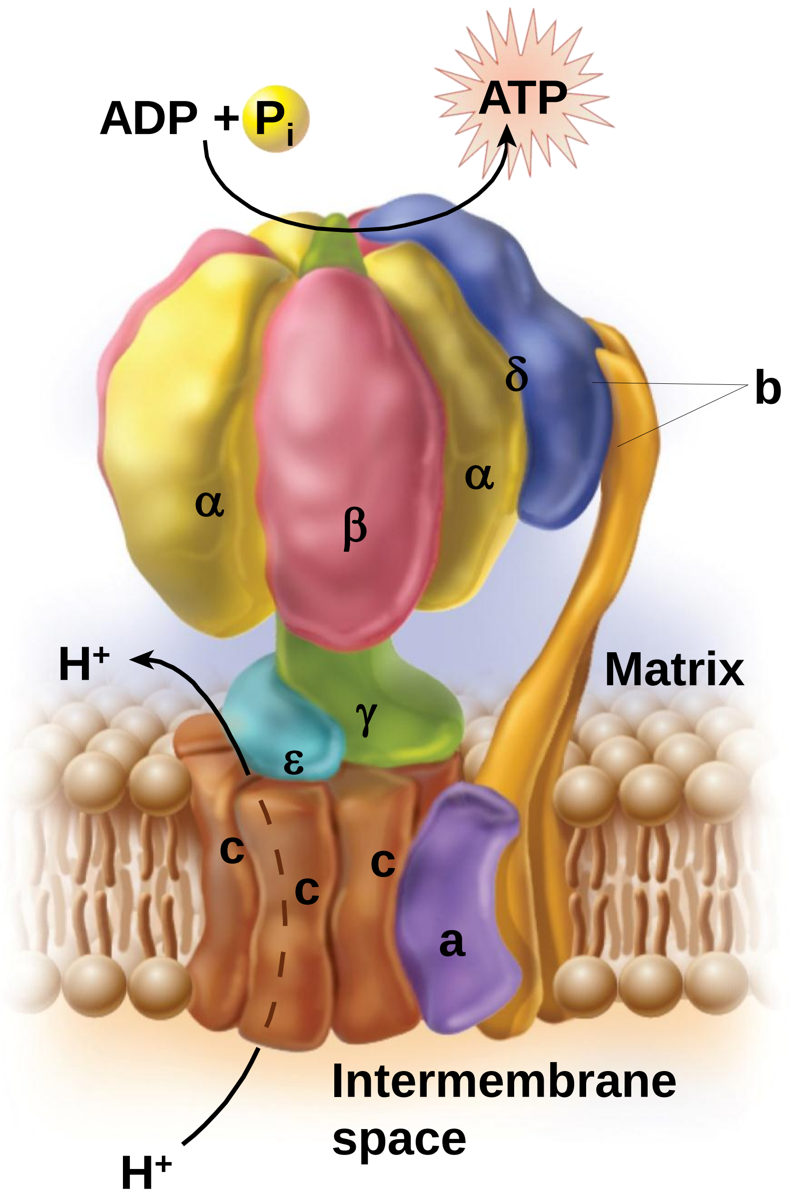
NADH oxidation and ATP synthesis

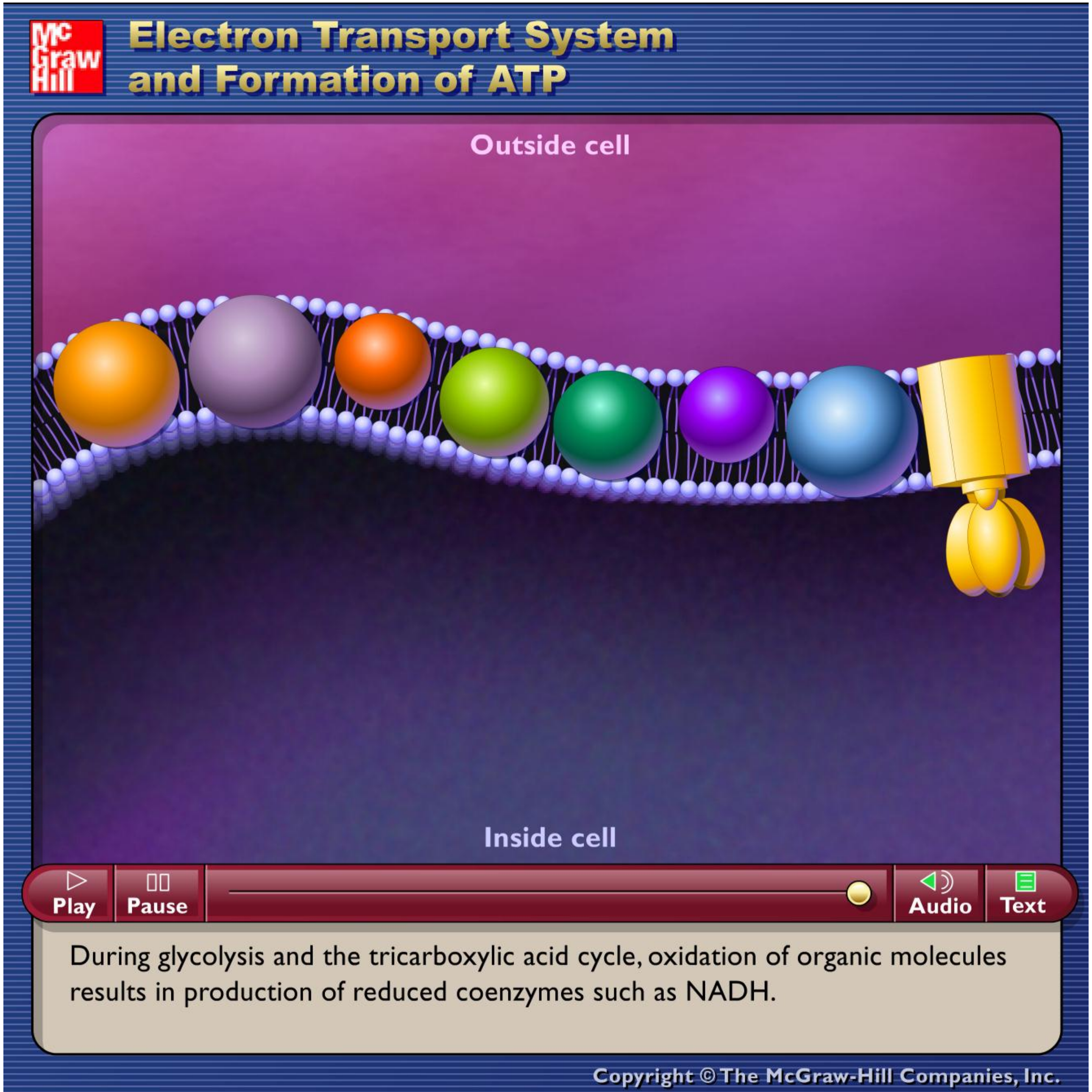
- Oxidation of NADH results in electrochemical gradient used to synthesize ATP
- 30-34 ATP molecules per glucose molecule broken down into CO_2 and H_2O
- Rarely achieve maximal amount
  - NADH used in anabolic pathways
  - H^+ gradient used for other purposes

ATP synthase

- Enzyme harnesses free energy as H^+ flow through membrane embedded region
- Energy conversion- H^+ electrochemical gradient or proton motive force converted to chemical bond energy in ATP
- Racker and Stoeckenius confirmed ATP uses an H^+ electrochemical gradient
- Rotary machine that makes ATP as it spins


ATP synthase
Vesicle
Bacteriorhodopsin
(light-driven H+ pump)
ADP
Pi
Light rays
No H+ gradient
H+ gradient
ATP


ADP + Pi
ATP
δ
b
α
α
β
H+
Matrix
γ
ε
c
c
c
a
Intermembrane space
H+


Electron Transport System
and Formation of ATP
Outside cell
Inside cell
Play
Pause
Audio
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During glycolysis and the tricarboxylic acid cycle, oxidation of organic molecules results in production of reduced coenzymes such as NADH.
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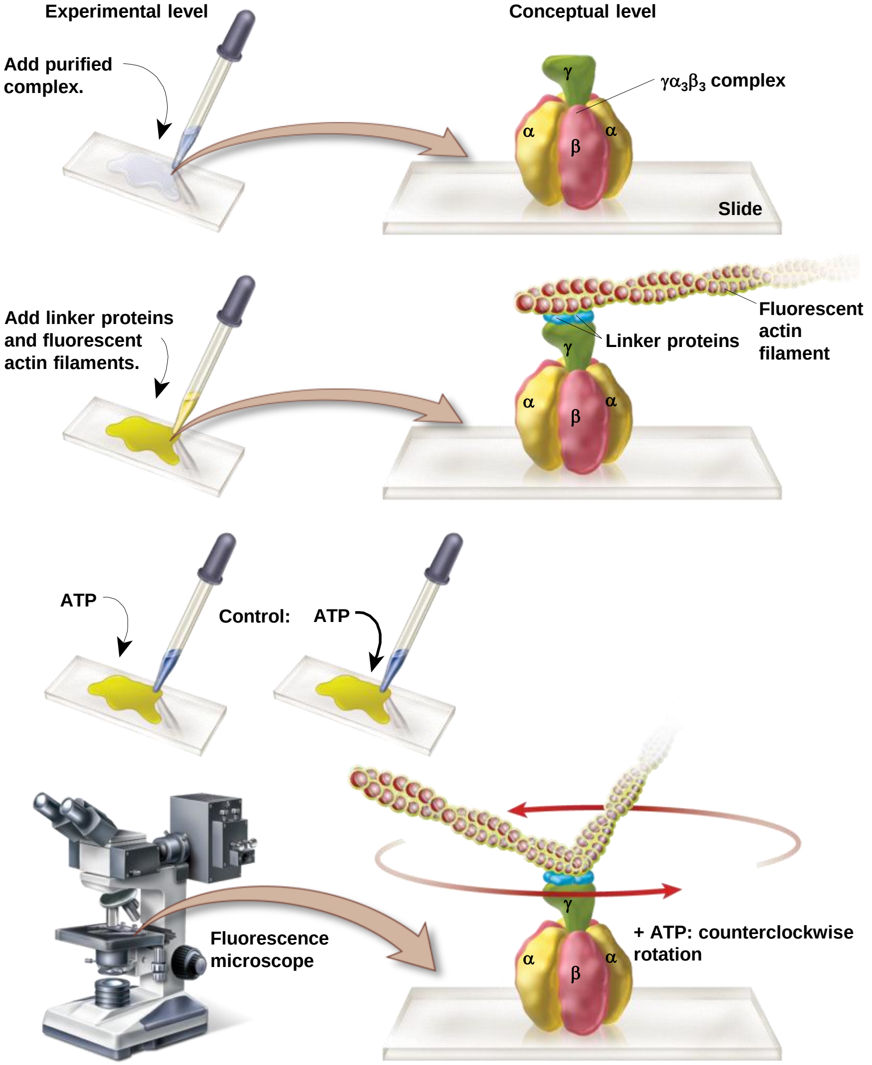
Yoshida and Kinosita deomonstrate that the γ subunit of the ATP synthase spins

- Masasuke Yoshida, Kazuhiko Kinosita, and colleagues set out to experimentally visualize the rotary nature of the ATP synthase
- Released membrane embedded portion and adhered it to a slide
- Visualize γ subunit using fluorescence
- Added ATP to make reaction run backward
- Rotated counterclockwise to hydrolyze ATP
  - Rotate clockwise to synthesize ATP

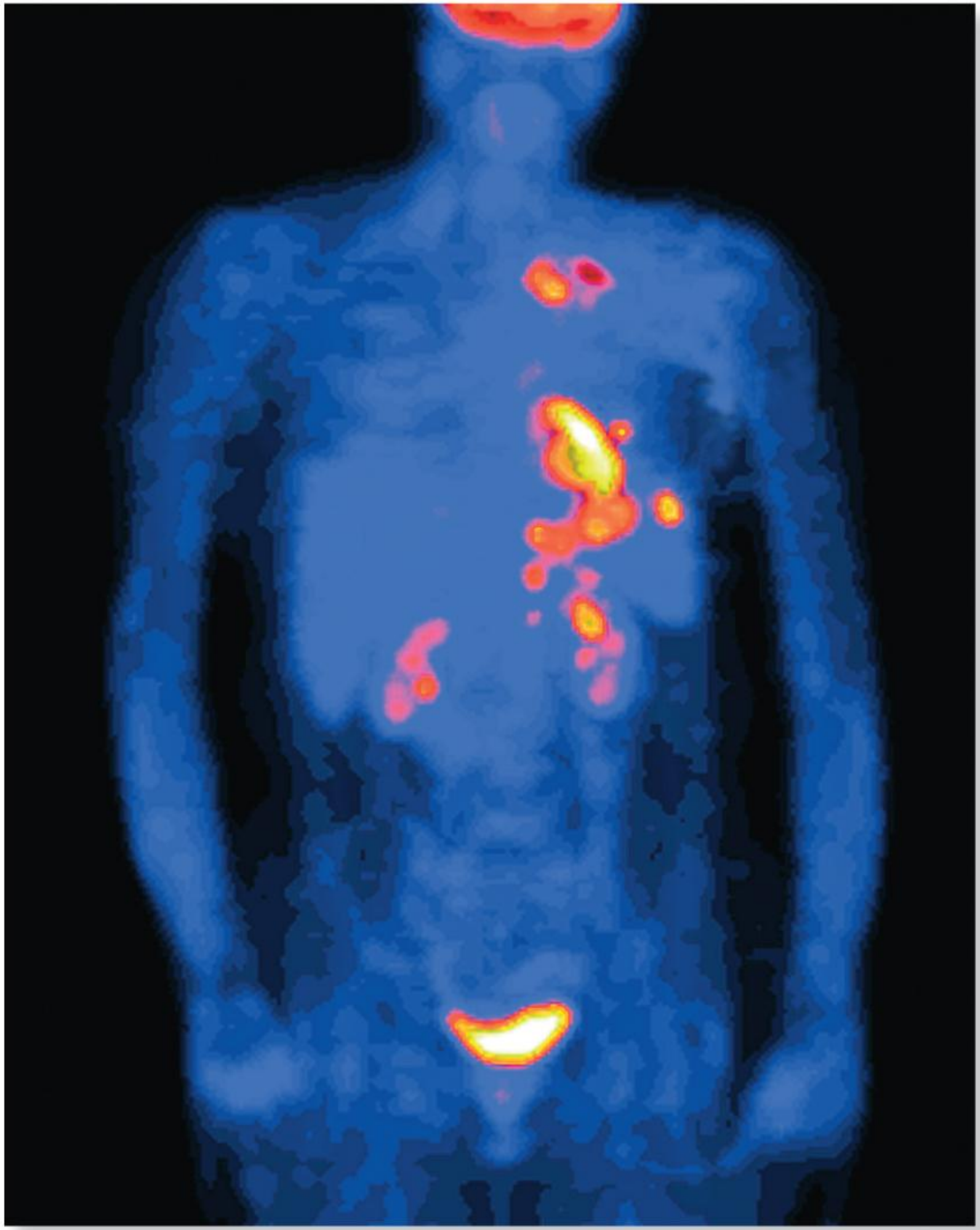
FEATURE INVESTIGATION



ATP	Rotation
No ATP added	No rotation observed.
ATP added	Rotation was observed as shown below. This is a time-lapse view of the rotation in action.

Cancer cells usually favor glycolysis

- Many disease associated with alterations in carbohydrate metabolism
- Warburg effect- cancer cells preferentially use glycolysis while decreasing oxidative phosphorylation
- Used to diagnose cancers in PET scans
- Glycolytic enzymes overexpressed in 80% of all types of cancers
- Caused by genetic and environmental factors- mutations and low oxygen



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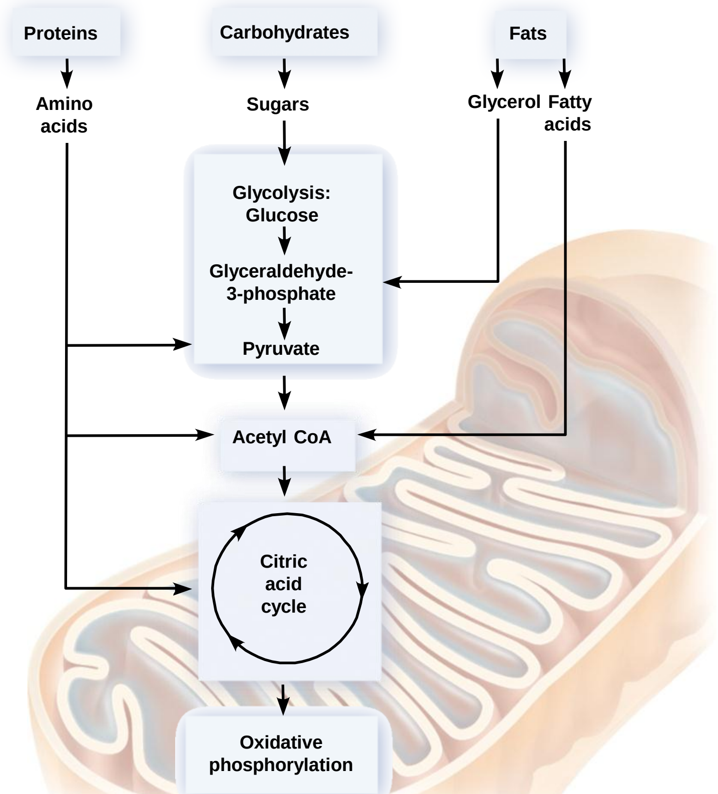
Other organic molecules

- Focus on glucose but other carbohydrates, proteins and fats also used for energy
- Enter into glycolysis or citric acid cycle at different points
- Utilizing the same pathways for breakdown increases efficiency
- Metabolism can also be used to make other molecules (anabolism)

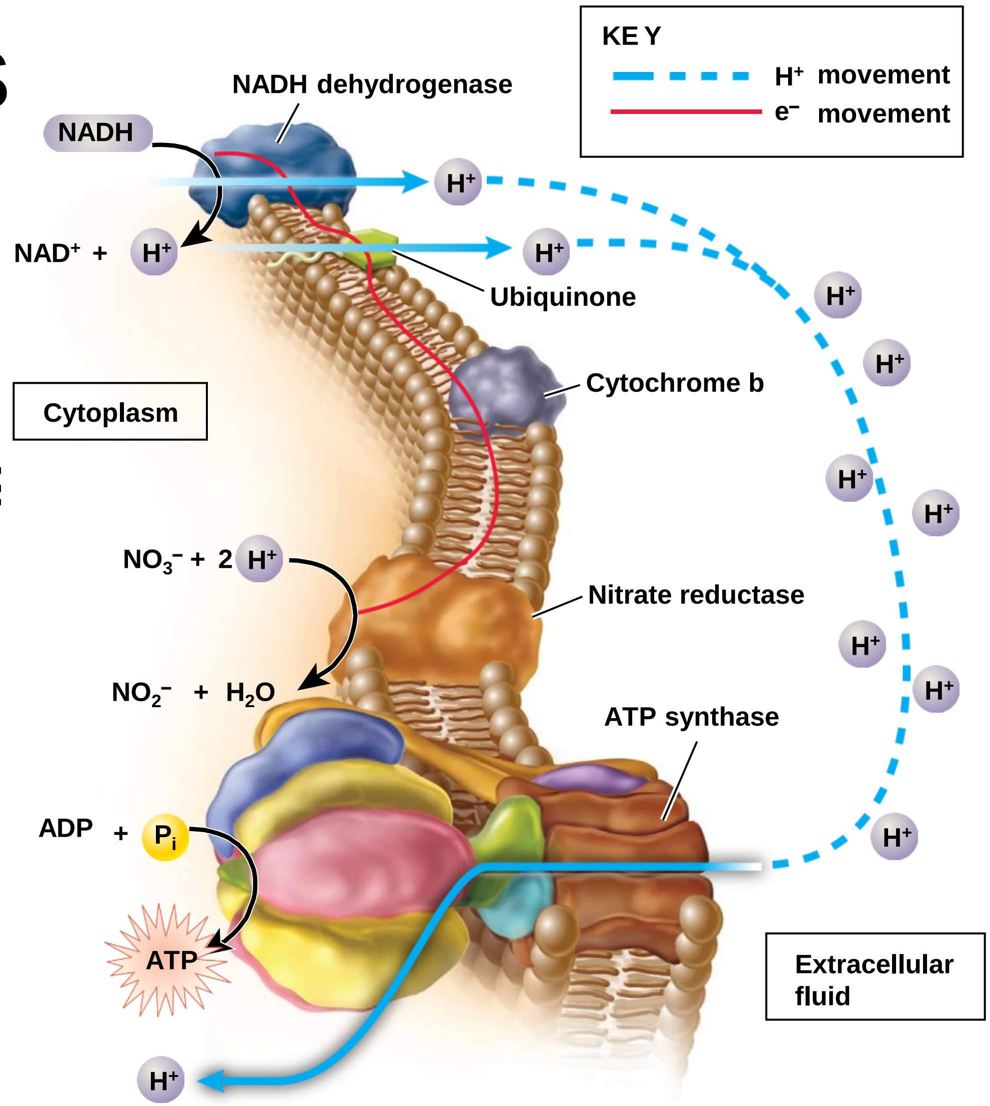

Proteins
Carbohydrates
Fats
Amino acids
Sugars
Glycerol
Fatty acids
Glycolysis:
Glucose
Glyceraldehyde-3-phosphate
Pyruvate
Acetyl CoA
Citric acid cycle
Oxidative phosphorylation

Anaerobic metabolism

- For environments that lack oxygen or during oxygen deficits
- 2 strategies
  - Use substance other than O_2 as final electron acceptor in electron transport chain
  - Produce ATP only via substrate-level phosphorylation

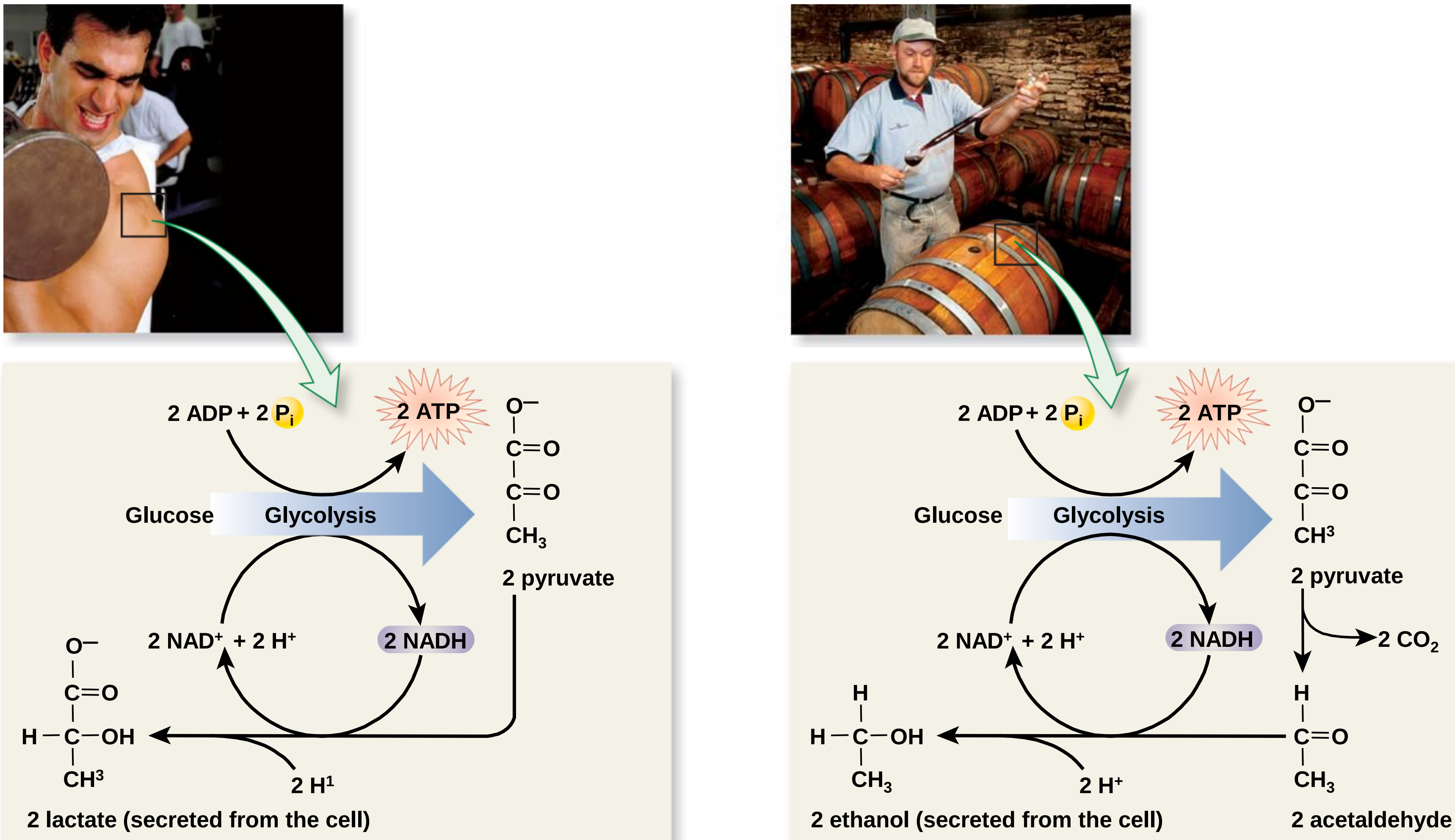
Other acceptors

- E. coli uses nitrate (NO_3^-) under anaerobic conditions
- Makes ATP via chemiosmosis even under aerobic conditions



Fermentation

- Many organisms can only use O_2 as final electron acceptor
- Make ATP via glycolysis only
- Need to regenerate NAD^+ to keep glycolysis running
- Muscle cells produce lactate
- Yeast make ethanol
- Produces far less ATP



(a) Production of lactic acid

(b) Production of ethanol

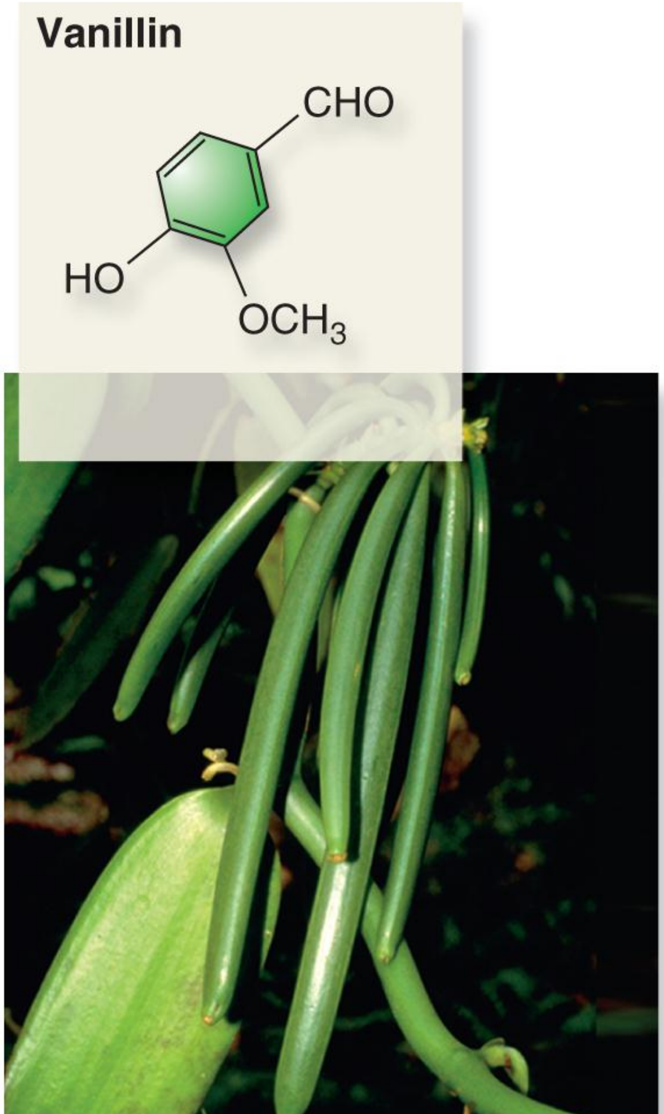
(weights): © Bill Aron/Photo Edit; (wine barrels): © Jeff Greenberg/The Image Works

Secondary Metabolism

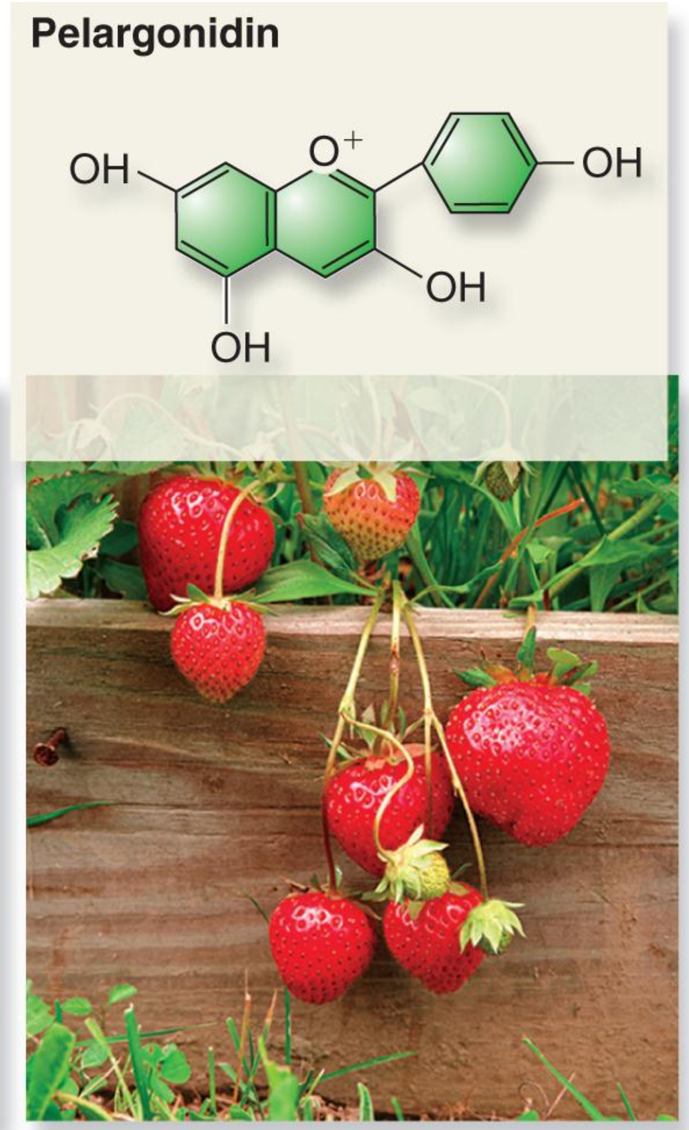
- Primary metabolism- essential for cell structure and function
- Secondary metabolism- synthesis of secondary metabolites that are not necessary for cell structure and growth
- Secondary metabolites unique to a species or group
- Roles in defense, attraction, protection, competition

4 categories

- Phenolics
  - Antioxidants with intense flavors and smells
- Alkaloids
  - Bitter-tasting molecules for defense
- Terpenoids
  - Intense smells and colors
- Polyketides
  - Chemical weapons

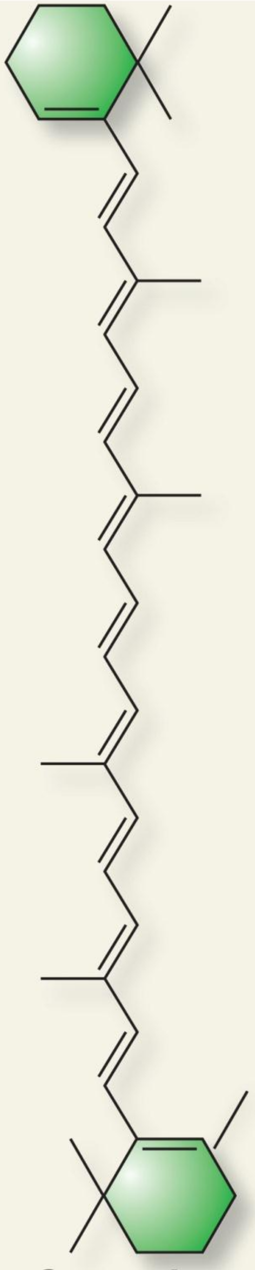


(a) Flavonoids in vanilla provide flavor

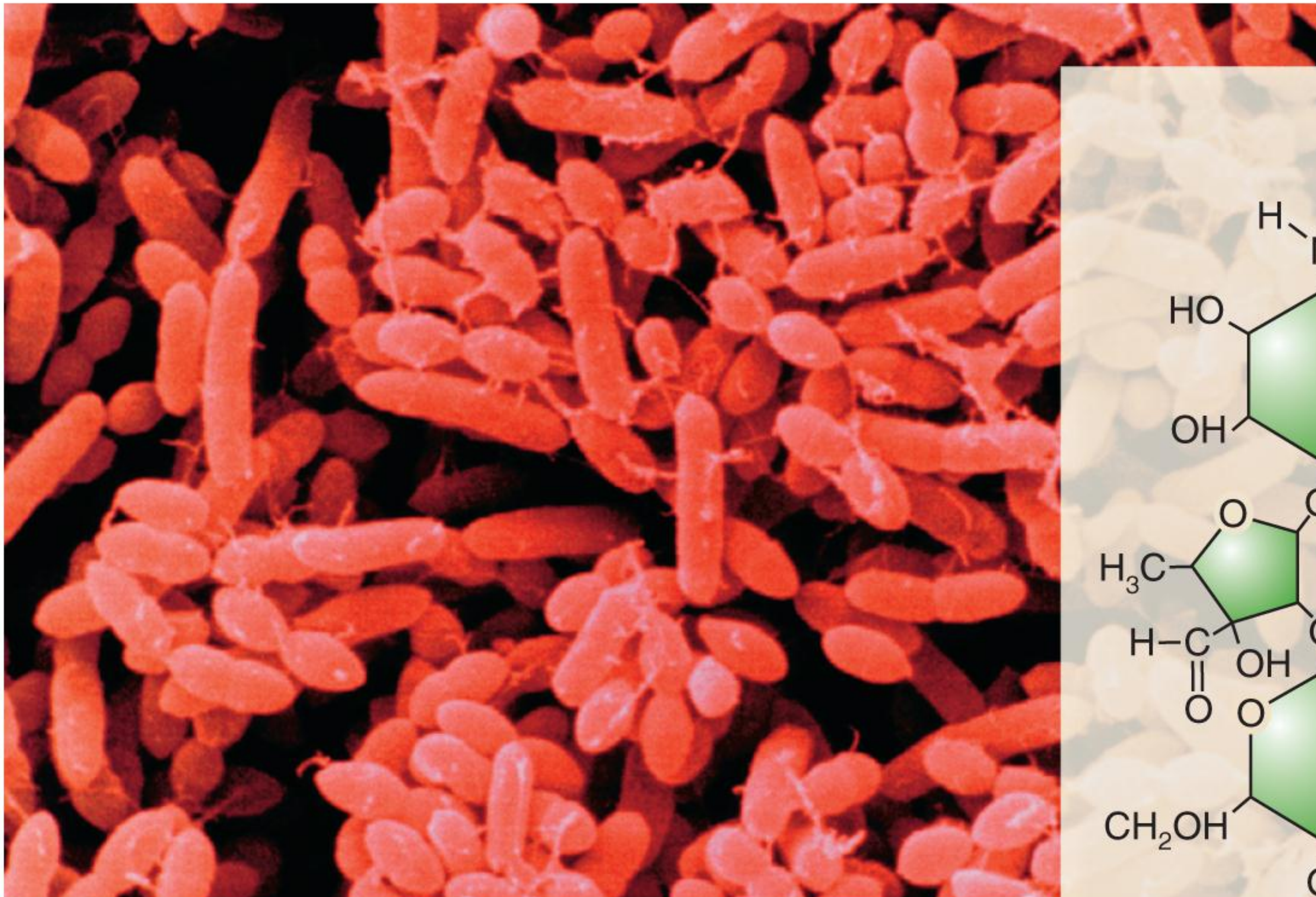


(b) Anthocyanins such as pelargonidin give red color

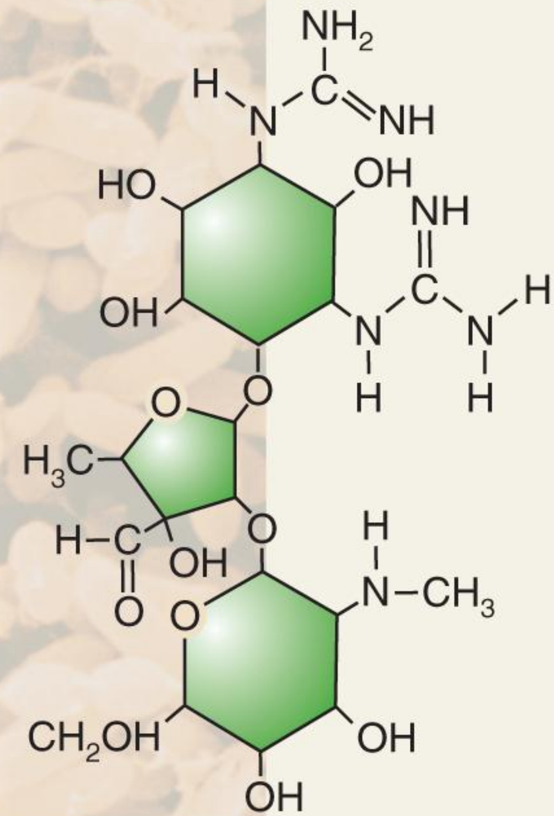
Deadly nightshade



β-carotene



***Streptomyces griseus*, a soil bacterium**



Streptomycin