Overview: Life Is Work

- Living cells require energy from outside sources
- Some animals obtain energy by eating plants, and some animals feed on other organisms that eat plants
• Energy flows into an ecosystem as sunlight and leaves as heat

• Photosynthesis generates $O_2$ and organic molecules, which are used in cellular respiration

• Cells use chemical energy stored in organic molecules to regenerate ATP, which powers work
Fig. 9-2

ECOSYSTEM

Photosynthesis in chloroplasts

CO₂ + H₂O

Cellular respiration in mitochondria

Organic molecules + O₂

ATP powers most cellular work

ATP

Heat energy

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Concept 9.1: Catabolic pathways yield energy by oxidizing organic fuels

• Several processes are central to cellular respiration and related pathways
Catabolic Pathways and Production of ATP

- The breakdown of organic molecules is exergonic

- **Fermentation** is a partial degradation of sugars that occurs without O₂

- **Aerobic respiration** consumes organic molecules and O₂ and yields ATP

- Anaerobic respiration is similar to aerobic respiration but consumes compounds other than O₂
• **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 follow cellular respiration with the sugar glucose:

$$C_6H_{12}O_6 + 6 \text{ O}_2 \rightarrow 6 \text{ CO}_2 + 6 \text{ H}_2\text{O} + \text{Energy (ATP + heat)}$$
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).
Fig. 9-UN1

Na $+ \quad \text{becomes oxidized} \quad (\text{loses electron}) \quad \text{Cl} \quad \text{becomes reduced} \quad (\text{gains electron}) \quad \rightarrow \quad \text{Na}^{+} \quad + \quad \text{Cl}^{-}$
$Xe^- + Y \rightarrow X + Y e^-$

becomes oxidized

becomes reduced
• The electron donor is called the reducing agent
• The electron receptor is called the oxidizing agent
Oxidation of Organic Fuel Molecules During Cellular Respiration

- During cellular respiration, the fuel (such as glucose) is oxidized, and O$_2$ is reduced:
\[
\text{becomes oxidized}
\]

\[
\text{becomes reduced}
\]

\[
C_6H_{12}O_6 + 6 \, O_2 \rightarrow 6 \, CO_2 + 6 \, H_2O + \text{Energy}
\]
\[
\text{Dehydrogenase} \quad \begin{array}{c}
\text{H} - \text{C} - \text{OH} + \text{NAD}^+ \\
\rightarrow \text{C} = \text{O} + \text{NADH} + \text{H}^+
\end{array}
\]
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 used 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

- O₂ pulls electrons down the chain in an energy-yielding tumble

- The energy yielded is used to regenerate ATP
Fig. 9-5

(a) Uncontrolled reaction

\[ \text{H}_2 + \frac{1}{2} \text{O}_2 \rightarrow \text{H}_2\text{O} \]

Explosive release of heat and light energy

(b) Cellular respiration

\[ 2 \text{H} + \frac{1}{2} \text{O}_2 \rightarrow \text{H}_2\text{O} \]

(2 H from food via NADH)

Controlled release of energy for synthesis of ATP

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The Hindenburg was filled with hydrogen not helium.
The Stages of Cellular Respiration: A Preview

• Cellular respiration has three stages:
  – **Glycolysis** (breaks down glucose into two molecules of pyruvate)
  – The **citric acid cycle** (completes the breakdown of glucose) – aka Krebs cycle
  – **Oxidative phosphorylation** (accounts for most of the ATP synthesis)
Fig. 9-6-1

Electrons carried via NADH

Glycolysis
Glucose → Pyruvate

Cytosol

ATP

Substrate-level phosphorylation
Fig. 9-6-2

Mitochondrion

Substrate-level phosphorylation

ATP

Cytosol

Glucose → Pyruvate

Glycolysis

Electrons carried via NADH

Electrons carried via NADH and FADH$_2$

Citric acid cycle

Mitochondrion

ATP

Substrate-level phosphorylation
Fig. 9-6-3

Substrate-level phosphorylation

- Glucose → Pyruvate
- ATP
- Cytosol

Mitochondrion

Citric acid cycle

- Electrons carried via NADH
- Electrons carried via NADH and FADH₂
- ATP

Oxidative phosphorylation

- Electron transport and chemiosmosis
- ATP

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• 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 Krebs cycle by substrate-level phosphorylation
Fig. 9-7

Enzyme

Substrate

ADP

P

→

Product

ATP
Concept 9.2: 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
Energy investment phase

Glucose → 2 ADP + 2 P

2 ATP used

Energy payoff phase

4 ADP + 4 P → 2 NAD^+ + 4 e^- + 4 H^+

2 NADH + 2 H^+

2 Pyruvate + 2 H_2O

Net

Glucose → 2 Pyruvate + 2 H_2O

4 ATP formed – 2 ATP used → 2 ATP

2 NAD^+ + 4 e^- + 4 H^+ → 2 NADH + 2 H^+
Fig. 9-9-2

1. Hexokinase

2. Phosphoglucoisomerase

Glucose → Glucose-6-phosphate → Fructose-6-phosphate
Fig. 9-9-3

1. Hexokinase
   - ATP → Glucose-6-phosphate → ADP

2. Phosphoglucoisomerase
   - Glucose-6-phosphate → Fructose-6-phosphate

3. Phosphofructokinase
   - ATP → Fructose-6-phosphate → ADP
   - ADP → Fructose-1, 6-bisphosphate
Fig. 9-9-5

2 NAD⁺ + 2 H⁺  \rightarrow  \text{Triose phosphate dehydrogenase} \rightarrow 2 \text{Pi}

2 NADH + 2 H⁺  \rightarrow  \text{Triose phosphate dehydrogenase} \rightarrow 2 \text{Pi}

\[ \text{Glyceraldehyde-3-phosphate} \]

\[ \text{1, 3-Bisphosphoglycerate} \]

\[ \text{1, 3-Bisphosphoglycerate} \]
2 NAD$^+$

NADH$^2^+$

Triose phosphate dehydrogenase + 2 H$^+$

2 P$i$

2 ADP

1, 3-Bisphosphoglycerate

Phosphoglycerokinase

2 ATP

2 3-Phosphoglycerate

Phosphoglycerokinase

2 ADP

2 ATP

1, 3-Bisphosphoglycerate

3-Phosphoglycerate

Phosphoglycerate kinase

2 ATP

2 ADP

3-Phosphoglycerate

2 1, 3-Bisphosphoglycerate
3-Phosphoglycerate

Triose phosphate dehydrogenase

2 NAD⁺ → 2 NADH + 2 H⁺

2 P_i

2 ADP

Phosphoglycerokinase

1, 3-Bisphosphoglycerate

2 ATP → 3-Phosphoglycerate

Phosphoglyceromutase

2-Phosphoglycerate

Phosphoglyceromutase

2-Phosphoglycerate
Triose phosphate dehydrogenase

2 NAD⁺ → 2 NADH + 2 H⁺

Fig. 9-9-9

Pyruvate kinase

2 Pyruvate → 2 ADP + 2 ATP

Phosphoenolpyruvate kinase

2 Phosphoenolpyruvate → 2 ADP + 2 ATP

Enolase

2 H₂O → 2 2-Phosphoglycerate

Phosphoglyceromutase

2 2-Phosphoglycerate → 2 3-Phosphoglycerate

Phosphoglycerokinase

2 3-Phosphoglycerate → 2 1, 3-Bisphosphoglycerate + 2 H⁺
Concept 9.3: The citric acid cycle completes the energy-yielding oxidation of organic molecules

- In the presence of $O_2$, pyruvate enters the mitochondrion

- Before the Krebs cycle can begin, pyruvate must be converted to **acetyl CoA** *(decarboxylation)*, which links the cycle to glycolysis
Fig. 9-10

CYTOSOL

Pyruvate

Transport protein

MITOCHONDRION

NAD⁺ → NADH + H⁺

1. Pyruvate
2. CO₂
3. Transport protein
4. Acetyl CoA

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• 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
Fig. 9-11

Pyruvate → NAD+ → CO2 → NADH + H+ → Acetyl CoA → CoA

Citric acid cycle:
- FADH2 → FAD
- 3 NAD+ → 2 CO2
- 3 NADH + 3 H+ → ADP + P_i → ATP
• 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
Fig. 9-12-1

Acetyl CoA → Oxaloacetate → Citrate → Citric acid cycle
Fig. 9-12-3

Acetyl CoA

Oxaloacetate

CoA—SH

CoA—SH

Citrate

H2O

Citric acid cycle

Isocitrate

NAD+

NADH + H+

α-Keto-glutarate

CO2
Fig. 9-12-4

Acetyl CoA

Oxaloacetate

Citrate

Isocitrate

α-Keto-glutarate

Succinyl CoA

Citric acid cycle

NAD+

NADH + H+

CO₂

1. Oxaloacetate

2. Citrate

3. Isocitrate

4. Succinyl CoA
Fig. 9-12-5

Acetyl CoA → Oxaloacetate → Citrate → Isocitrate → α-Ketoglutarate → Succinyl CoA → Succinate

1. Oxaloacetate + CoA—SH → Citrate
2. Citrate + H2O → Isocitrate + NAD+ → NADH + H+ + CO2
3. Isocitrate → α-Ketoglutarate + CO2 + NAD+
4. α-Ketoglutarate + CoA—SH → Succinyl CoA + NAD+
5. Succinate + GTP → ADP + Pi + Succinate + ATP

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Fig. 9-12-7

Acetyl CoA

Oxaloacetate

Citrate

H₂O

Isocitrate

NAD⁺

NADH + H⁺

α-Ketoglutarate

CoA—SH

Citric acid cycle

Malate

Fumarate

Succinate

Succinyl CoA

FAD

FADH₂

GTP

GDP

ATP

ADP

PP

GDP

GTP

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Fig. 9-12-8

Acetyl CoA → CoA—SH

1. Oxaloacetate

2. Citrate

3. Isocitrate

4. α-Ketoglutarate

5. Succinyl CoA

6. Succinate

7. Fumarate

8. Malate

NADH + H+ → NAD+

FADH₂ → FAD

H₂O → CO₂

Citric acid cycle

GTP → GDP → ADP → ATP
Concept 9.4: 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$_2$O
Fig. 9-13

Free energy (G) relative to O\textsubscript{2} (kcal/mol)

- NADH
- FADH\textsubscript{2}
- Multiprotein complexes

(from NADH or FADH\textsubscript{2})

2 H\textsuperscript{+} + 1/2 O\textsubscript{2} → H\textsubscript{2}O
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.
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.
INTERMEMBRANE SPACE

Rotor

H^+

Stator

Internal rod

Catalytic knob

ADP + P_i

ATP

MITOCHONDRIAL MATRIX
• 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
Protein complex of electron carriers

Electron transport chain

Chemiosmosis

Oxidative phosphorylation

1 Electron transport chain

2 Chemiosmosis

https://www.youtube.com/watch?v=q-fKQuZ8dco

https://www.youtube.com/watch?v=rdF3mnyS1p0
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 36-38 ATP (theoretical yield under ideal conditions, actual amounts significantly less, maybe only 29-30)
Fig. 9-17

Maximum per glucose: About 36 or 38 ATP

Oxidative phosphorylation: electron transport and chemiosmosis

Citric acid cycle

Glycolysis

Glucose → Pyruvate

2 NADH or 2 FADH$_2$

2 NADH

6 NADH → 2 FADH$_2$

Electron shuttles span membrane

Mitochondrion

Cytoplasm

+ 2 ATP

+ 2 ATP

+ about 32 or 34 ATP

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Summary Aerobic Respiration

- Energy produced from complete oxidation of one glucose using aerobic respiration.

<table>
<thead>
<tr>
<th>Pathway</th>
<th>ATP produced</th>
<th>NADH produced</th>
<th>FADH$_2$ produced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycolysis</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Intermediate step</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Krebs cycle</td>
<td>2</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>
Summary Aerobic Respiration

- ATP produced from complete oxidation of one glucose using aerobic respiration. (theoretical yield)

<table>
<thead>
<tr>
<th>Pathway</th>
<th>By substrate-level phosphorylation</th>
<th>By oxidative phosphorylation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>From NADH</td>
</tr>
<tr>
<td>Glycolysis</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Intermediate step</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Krebs cycle</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Total ATP</td>
<td>4</td>
<td>30</td>
</tr>
</tbody>
</table>

36-38 ATPs are produced in eukaryotes
Concept 9.5: 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 are alcohol fermentation and lactic acid fermentation
• In **alcohol fermentation**, pyruvate is converted to ethanol in two steps, with the first releasing $\text{CO}_2$

• Alcohol fermentation by yeast is used in brewing, winemaking, and baking
Fig. 9-18a

2 ADP + 2 $\text{P}_i$ → 2 ATP

Glucose → Glycolysis

2 NAD$^+$ → 2 NADH + 2 H$^+$

2 Pyruvate → 2 CO$_2$

H C H OH → 2 Ethanol

H C C O → 2 Acetaldehyde

(a) Alcohol fermentation
• In lactic acid fermentation, pyruvate is reduced to NADH, forming lactate as an end product, with no release of CO₂

• 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 O₂ is scarce
Fig. 9-18b

Glucose $\rightarrow$ Glycolysis

- $2 \text{ADP} + 2 \text{P}_i \rightarrow 2 \text{ATP}$
- $2 \text{NAD}^+ \rightarrow 2 \text{NADH} + 2 \text{H}^+$
- $2 \text{Pyruvate}$
- $2 \text{Lactate}$

(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
The Evolutionary Significance of Glycolysis

• Glycolysis occurs in nearly all organisms

• Glycolysis probably evolved in ancient prokaryotes before there was oxygen in the atmosphere
Concept 9.6: Glycolysis and the citric acid cycle connect to many other metabolic pathways

- Glycolysis and the citric acid cycle are major intersections to various catabolic and anabolic pathways
The Versatility of Catabolism

• 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 or protein
Biosynthesis (Anabolic Pathways)

• 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.
Since phosphofructokinase can be inhibited by end product, what kind of enzyme is this?
Origin of Mitochondria (and Chloroplasts)  
Endosymbiotic Theory

- explains the origin of mitochondria and chloroplasts
- one ancient prokaryotic cell engulfed by another
- they lived symbiotically
- over the eons, endosymbionts specialized for energy production
- led to evolution of eukaryotic cells
Origin of Mitochondria (and Chloroplasts)

- **Endosymbiotic Theory**

Cyanophora paradoxa – a eukaryote that has a prokaryotic-like cyanelle for photosynthesis
You should now be able to:

1. Explain in general terms how redox reactions are involved in energy exchanges

2. Name the three stages of cellular respiration; for each, state the region of the eukaryotic cell where it occurs and the products that result

3. In general terms, explain the role of the electron transport chain in cellular respiration
4. Explain where and how the respiratory electron transport chain creates a proton gradient

5. Distinguish between fermentation and anaerobic respiration

6. Distinguish between obligate and facultative anaerobes