

7

Cellular Respiration and Fermentation



Life Is Work

- Living cells require energy from outside sources
- Some animals, such as the giraffe, obtain energy by eating plants, and some animals feed on other organisms that eat plants

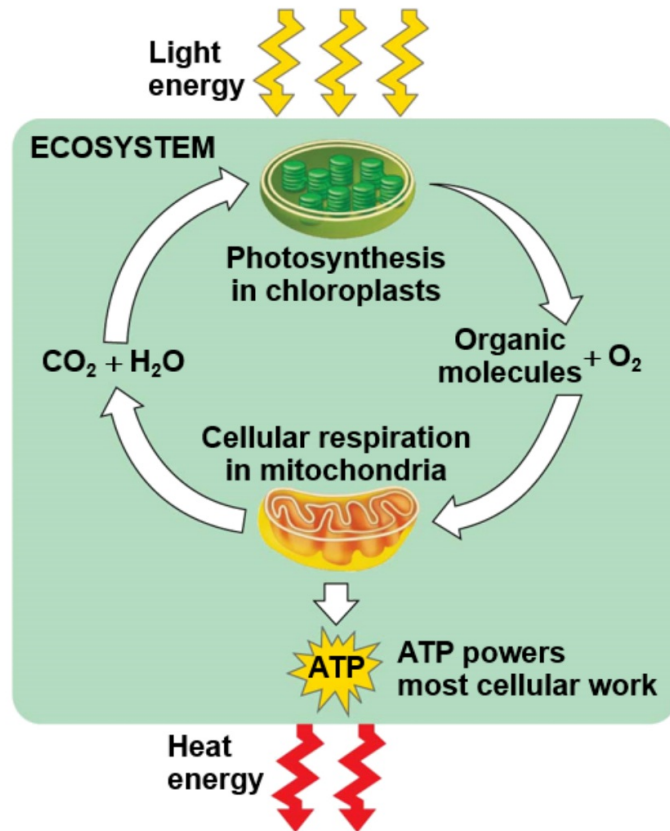
- Energy flows into an ecosystem as sunlight and leaves as heat
- Photosynthesis generates O_2 and organic molecules, which are used as fuel for cellular respiration
- Cells use chemical energy stored in organic molecules to regenerate ATP, which powers work

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Animation: Carbon Cycle



Figure 7.2



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Concept 7.1: Catabolic pathways yield energy by oxidizing organic fuels

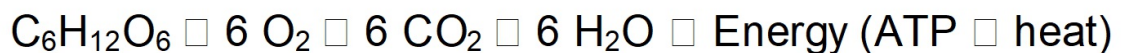
- Catabolic pathways involving electron transfer are central processes to cellular respiration

Catabolic Pathways and Production of ATP

- The breakdown of organic molecules is exergonic
- **Fermentation** is a partial degradation of sugars that occurs without O_2
- **Aerobic respiration** consumes organic molecules and O_2 and yields ATP
- Anaerobic respiration is similar to aerobic respiration but consumes compounds other than O_2

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- **Cellular respiration** includes both aerobic and anaerobic processes 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



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Redox Reactions: Oxidation and Reduction

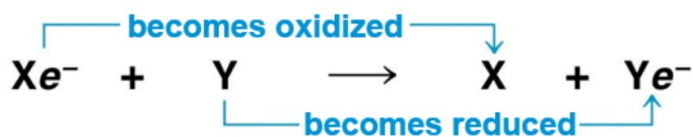
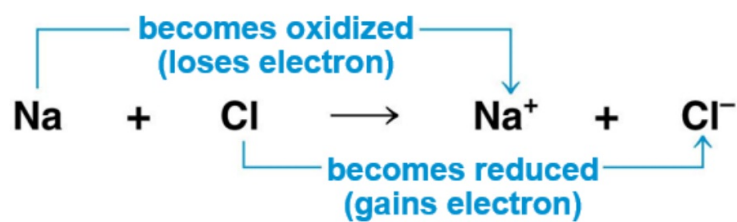
- The transfer of electrons during chemical reactions releases energy stored in organic molecules
- This released energy is ultimately used to synthesize ATP

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The Principle of Redox

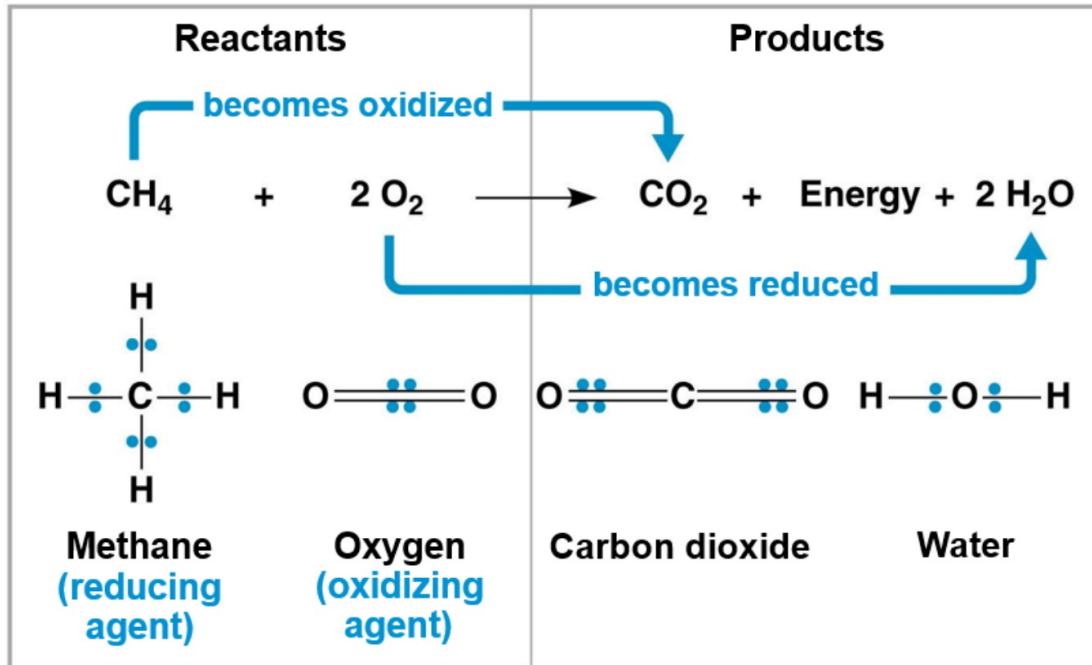
- Chemical reactions that transfer electrons between reactants are called oxidation-reduction reactions, or **redox reactions**
- In **oxidation**, a substance loses electrons, or is oxidized
- In **reduction**, a substance gains electrons, or is reduced (the amount of positive charge is reduced)

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- The electron donor is called the **reducing agent**
- The electron acceptor 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 O₂

Figure 7.3

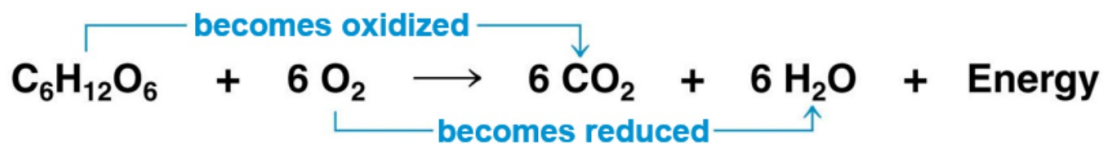


- Redox reactions that move electrons closer to electronegative atoms, like oxygen, release chemical energy that can be put to work

Oxidation of Organic Fuel Molecules During Cellular Respiration

- During cellular respiration, fuel (such as glucose) is oxidized, and O₂ is reduced
- Organic molecules with an abundance of hydrogen, like carbohydrates and fats, are excellent fuels
- As hydrogen (with its electron) is transferred to oxygen, energy is released that can be used in ATP synthesis

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

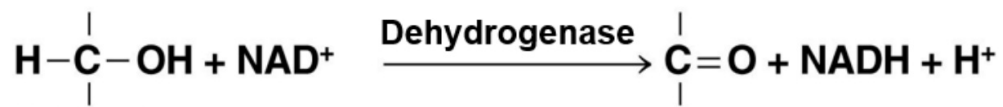
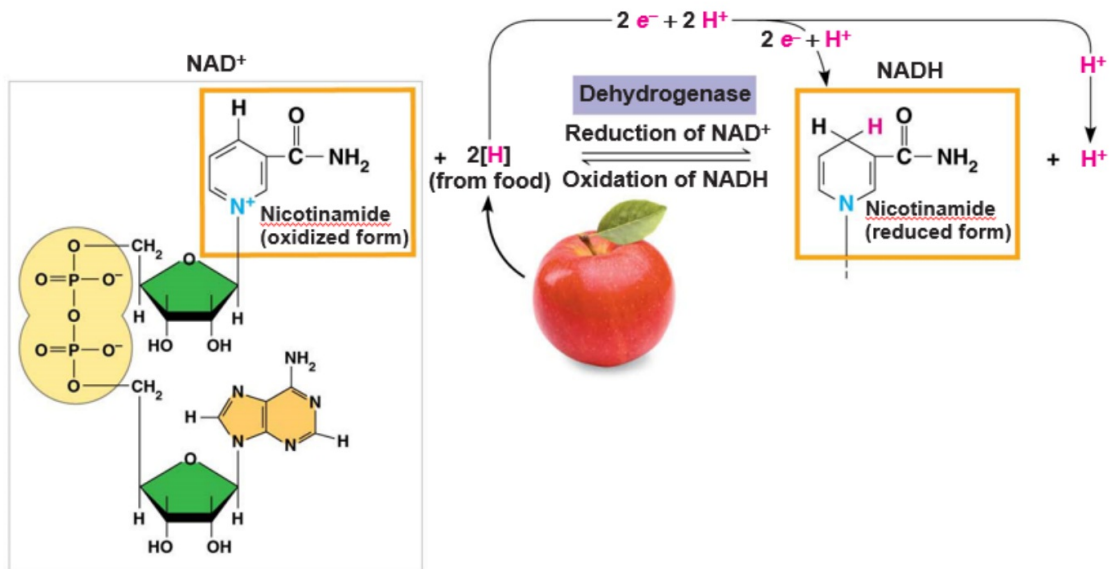
- In cellular respiration, glucose and other organic molecules are broken down in a series of steps
- Electrons from organic compounds are usually first transferred to **NAD^+** , a coenzyme
- As an electron acceptor, NAD^+ functions as an oxidizing agent during cellular respiration
- Each NADH (the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

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- Enzymes called dehydrogenases facilitate the transfer of two electrons and one hydrogen ion to NAD^+
- One hydrogen ion is released in this process

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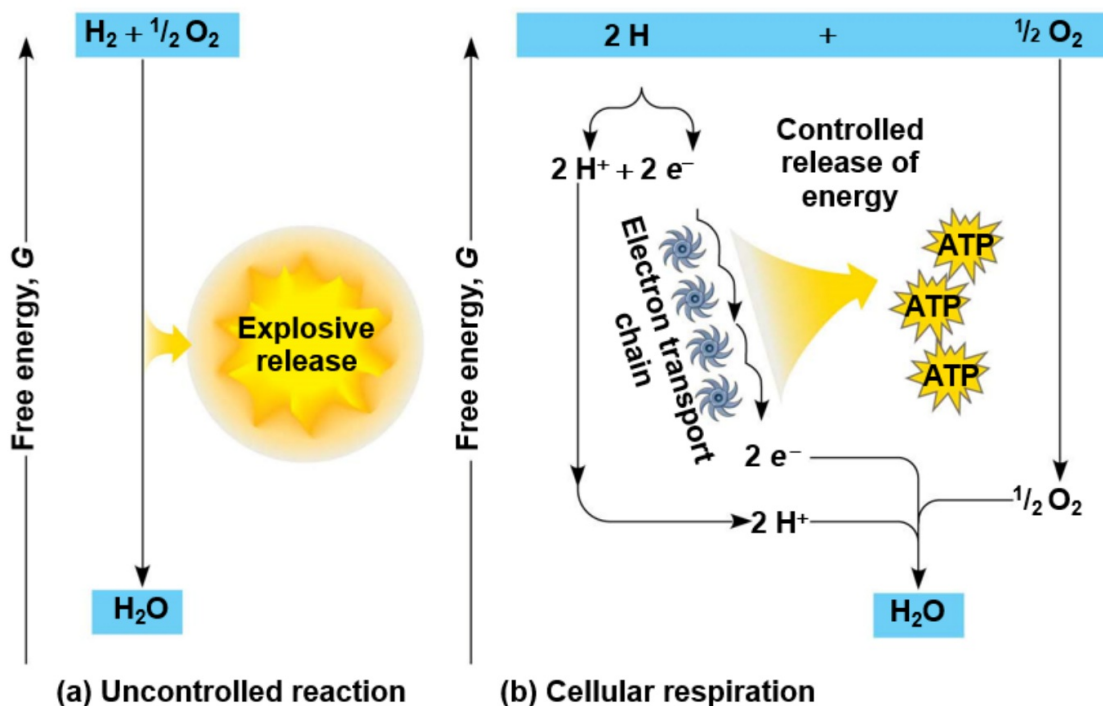
Figure 7.4



- NADH passes the electrons to the **electron transport chain**
- Electrons are passed to increasingly electronegative carrier molecules down the chain through a series of redox reactions
- Electron transfer to oxygen occurs in a series of energy-releasing steps instead of one explosive reaction
- The energy yielded is used to regenerate ATP

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Figure 7.5



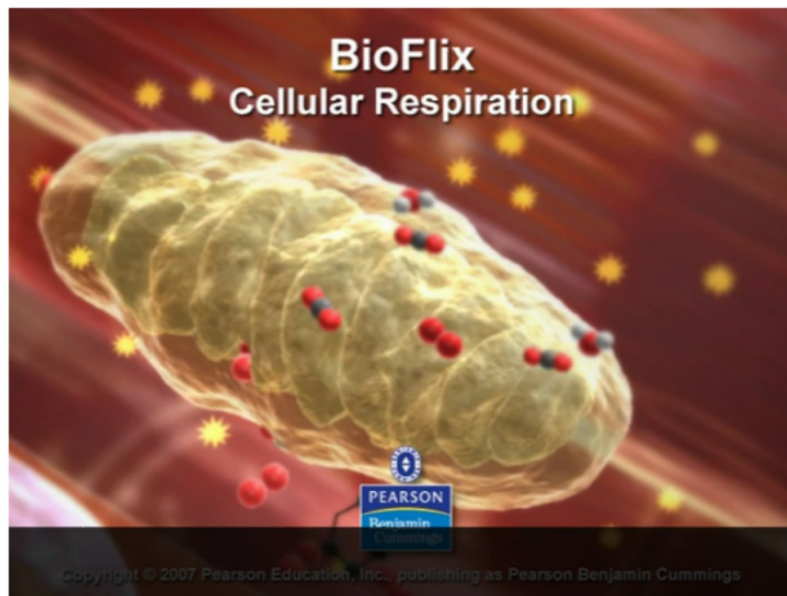
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The Stages of Cellular Respiration: *A Preview*

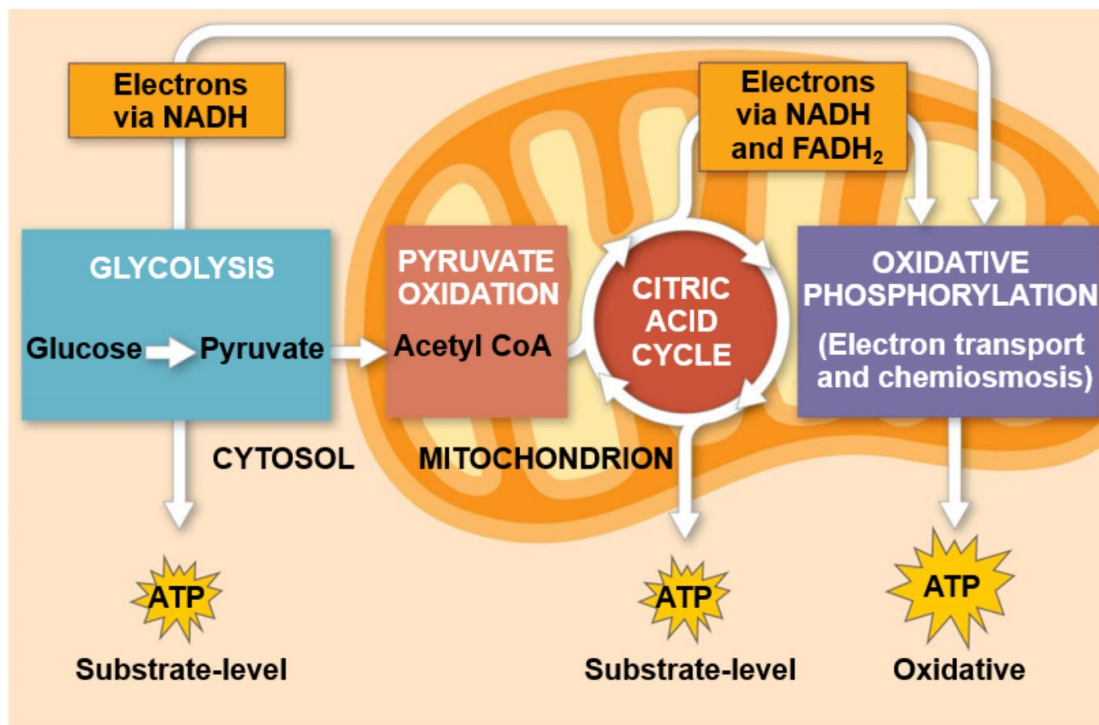
- Harvesting of energy from glucose has three stages
 - **Glycolysis** breaks down glucose into two molecules of pyruvate in the cytosol
 - Pyruvate oxidation and the **citric acid cycle** completes the breakdown of glucose in the mitochondrial matrix
 - **Oxidative phosphorylation** accounts for most of the ATP synthesis and occurs in the inner membrane of the mitochondria

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Animation: Cellular Respiration



1. **GLYCOLYSIS** (color-coded blue throughout the chapter)
2. **PYRUVATE OXIDATION and the CITRIC ACID CYCLE** (color-coded orange)
3. **OXIDATIVE PHOSPHORYLATION: Electron transport and chemiosmosis** (color-coded purple)



- Oxidative phosphorylation accounts for almost 90% of the ATP generated by cellular respiration
- This process involves the transfer of inorganic phosphates to ADP

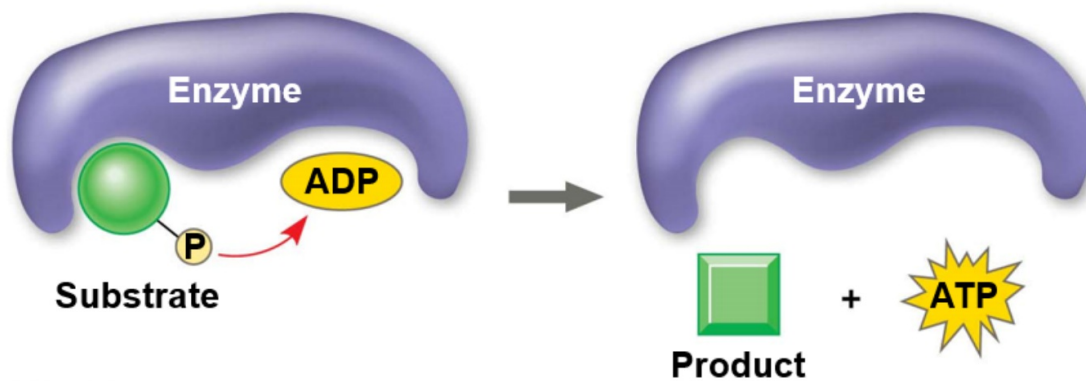
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- A smaller amount of ATP is formed in glycolysis and the citric acid cycle by **substrate-level phosphorylation**
- In this process, an enzyme transfers a phosphate group directly from a substrate molecule to ADP

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- For each molecule of glucose degraded to CO_2 and water by respiration, the cell makes up to 32 molecules of ATP

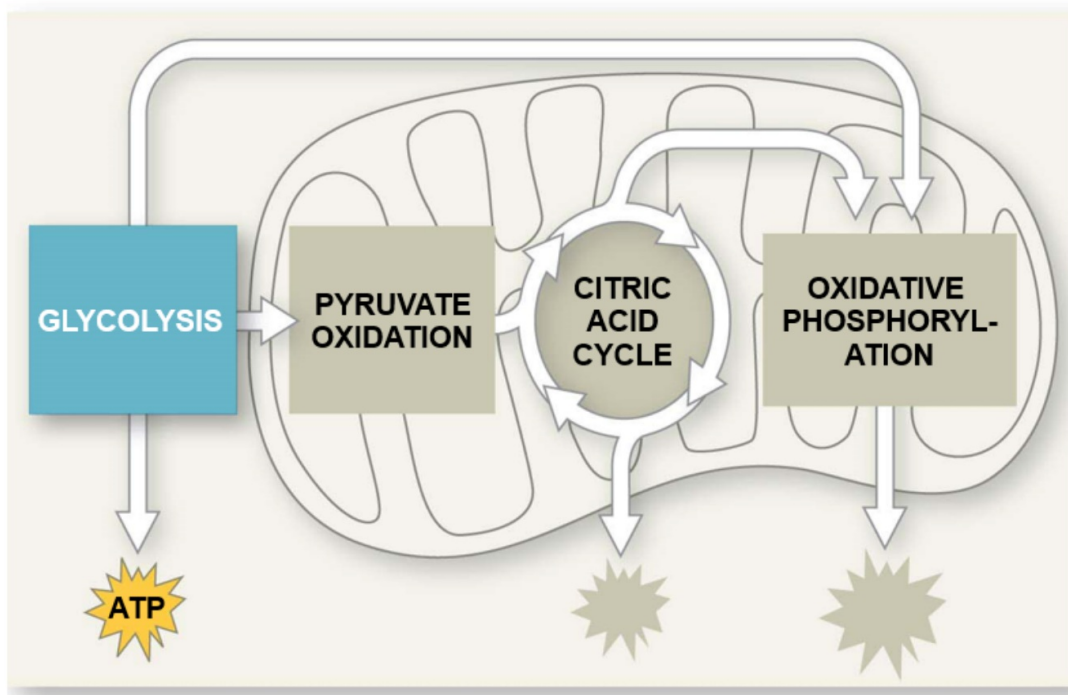
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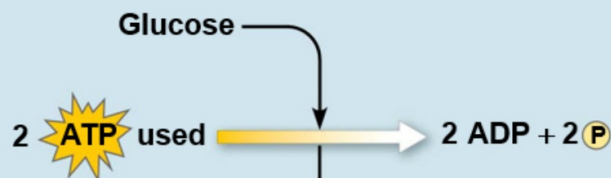
Concept 7.2: Glycolysis harvests chemical energy by oxidizing glucose to pyruvate

- Glycolysis (“sugar splitting”) breaks down glucose into two molecules of pyruvate
- Glycolysis occurs in the cytoplasm and has two major phases
 - Energy investment phase
 - Energy payoff phase
- The net energy yield is 2 ATP plus 2 NADH per glucose molecule
- Glycolysis occurs whether or not O₂ is present

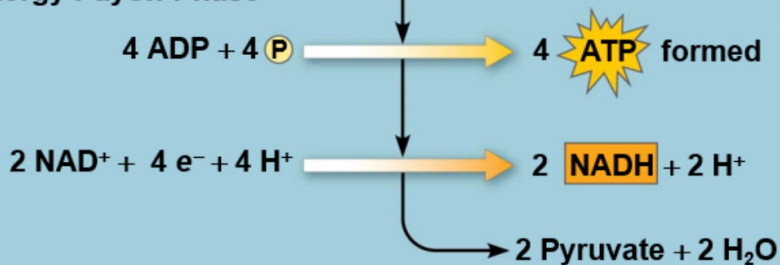
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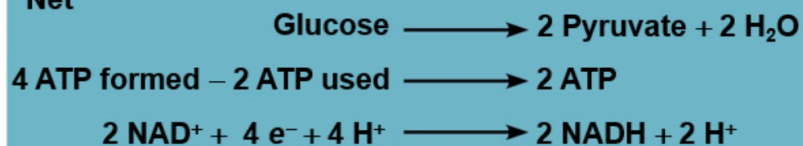
Energy Investment Phase



Energy Payoff Phase

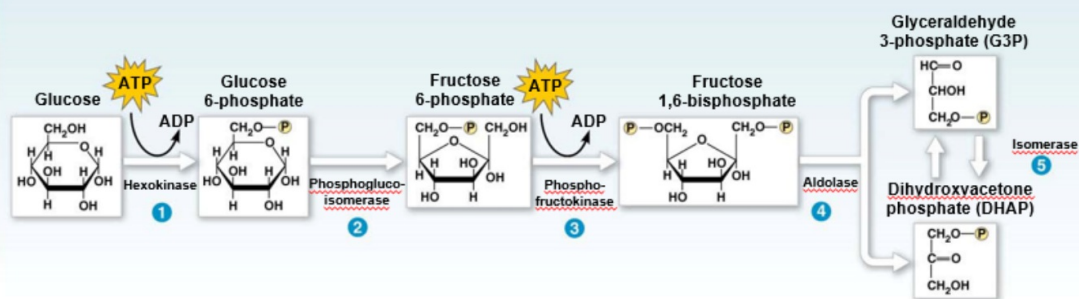


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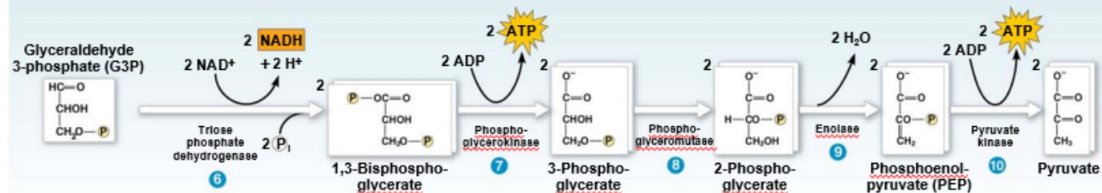


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GLYCOLYSIS: Energy Investment Phase



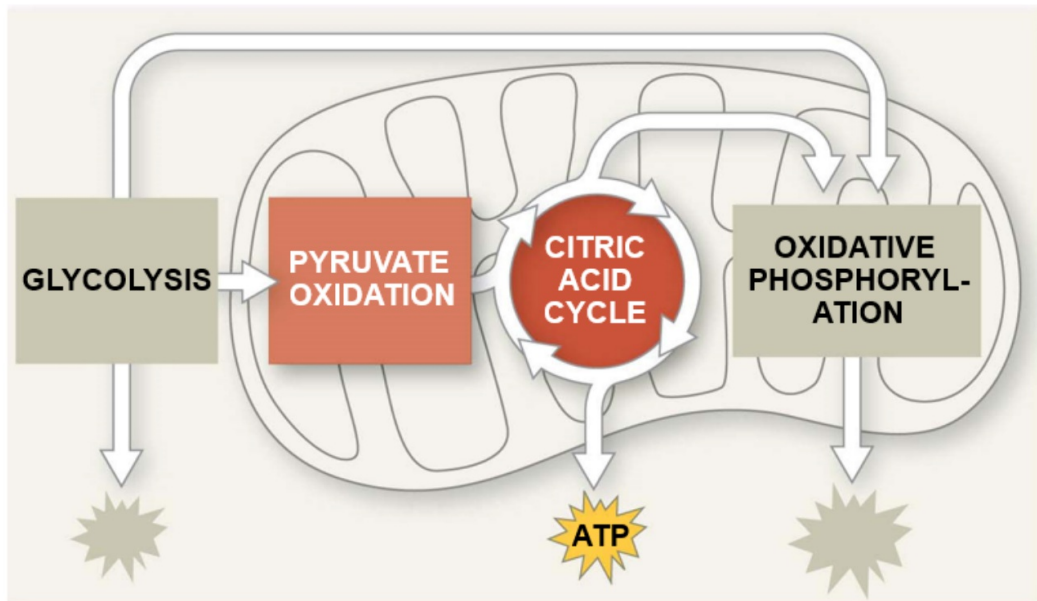
GLYCOLYSIS: Energy Payoff Phase

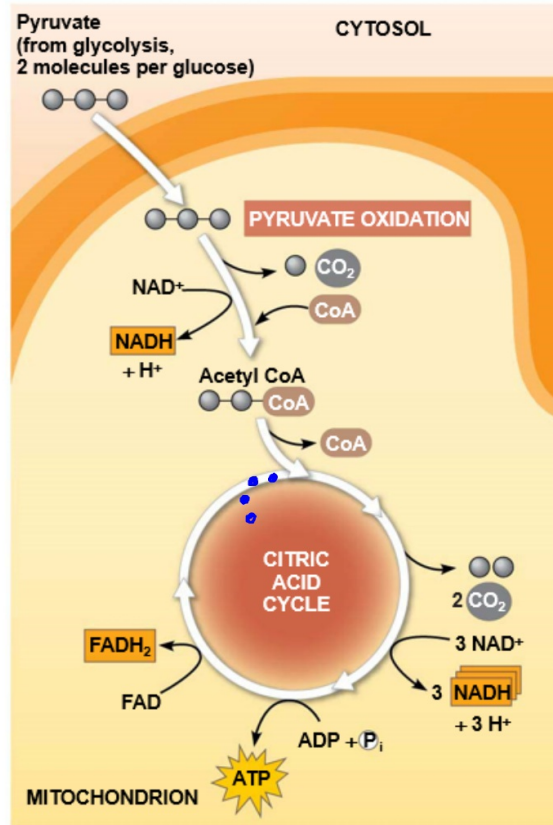


Concept 7.3: After pyruvate is oxidized, the citric acid cycle completes the energy-yielding oxidation of organic molecules

- In the presence of O_2 , pyruvate enters the mitochondrion (in eukaryotic cells), where the oxidation of glucose is completed
- Before the citric acid cycle can begin, pyruvate must be converted to acetyl coenzyme A (**acetyl CoA**), which links glycolysis to the citric acid cycle

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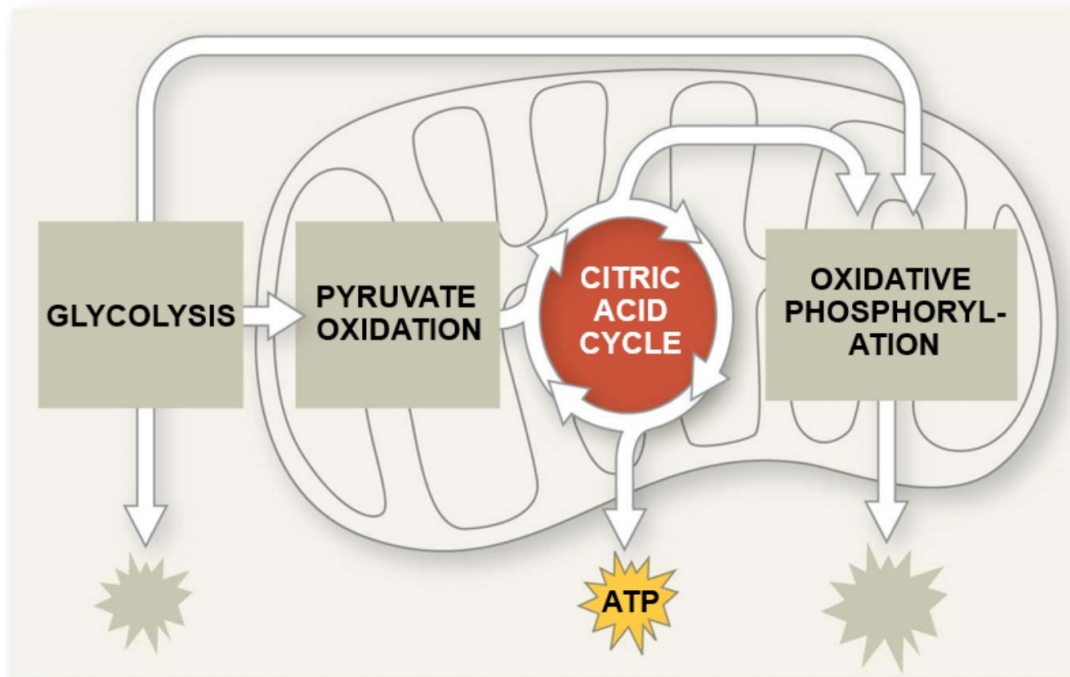


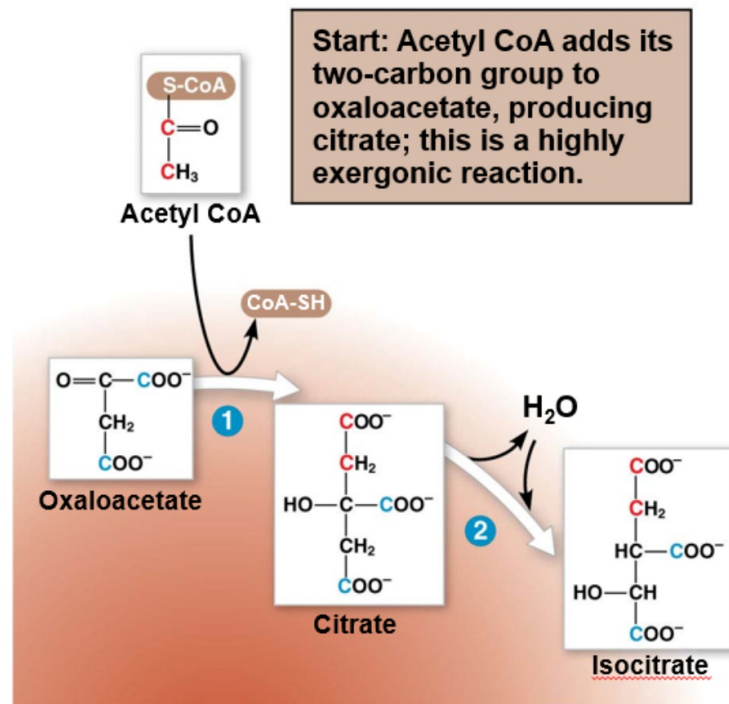
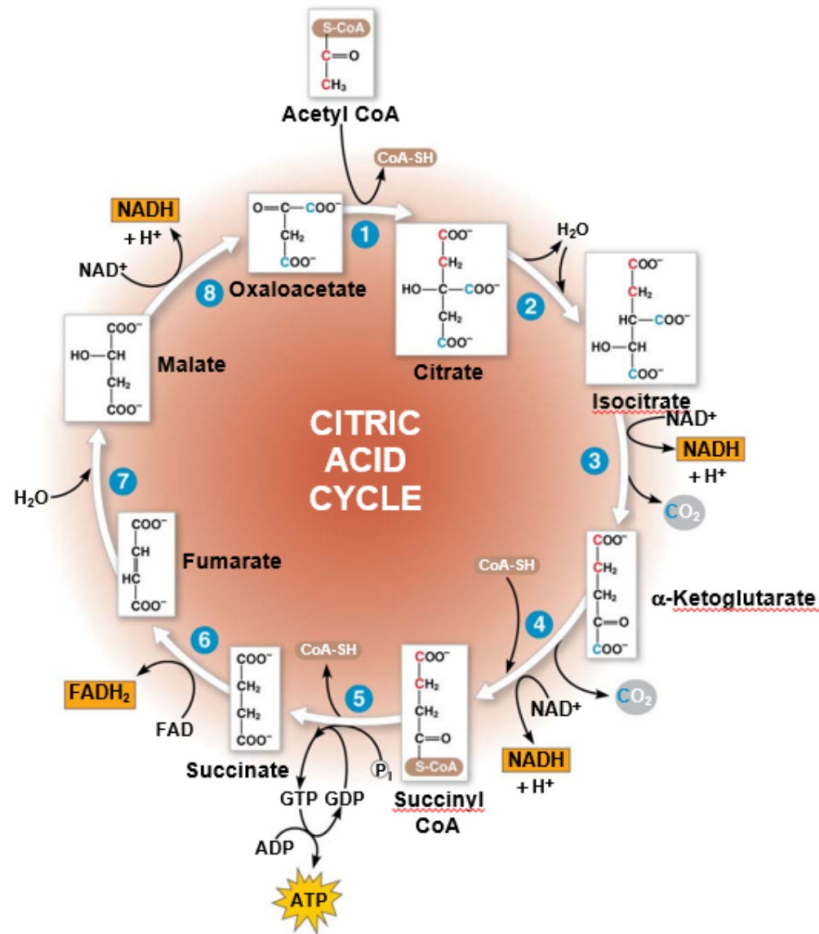


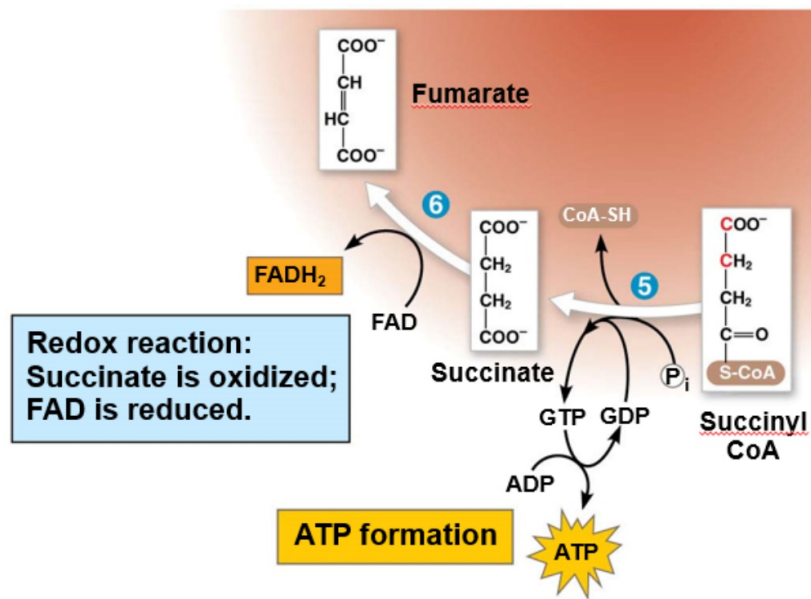
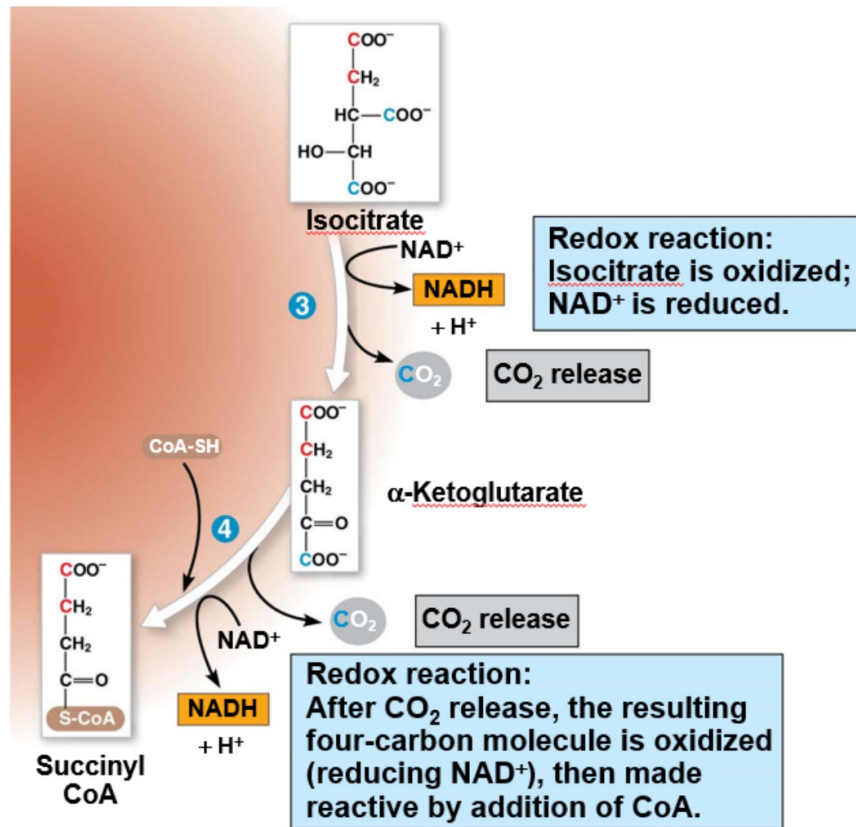
- The citric acid cycle, also called the Krebs cycle, completes the breakdown of pyruvate to CO₂
- The cycle oxidizes organic fuel derived from pyruvate, generating 1 ATP, 3 NADH, and 1 FADH₂ per turn

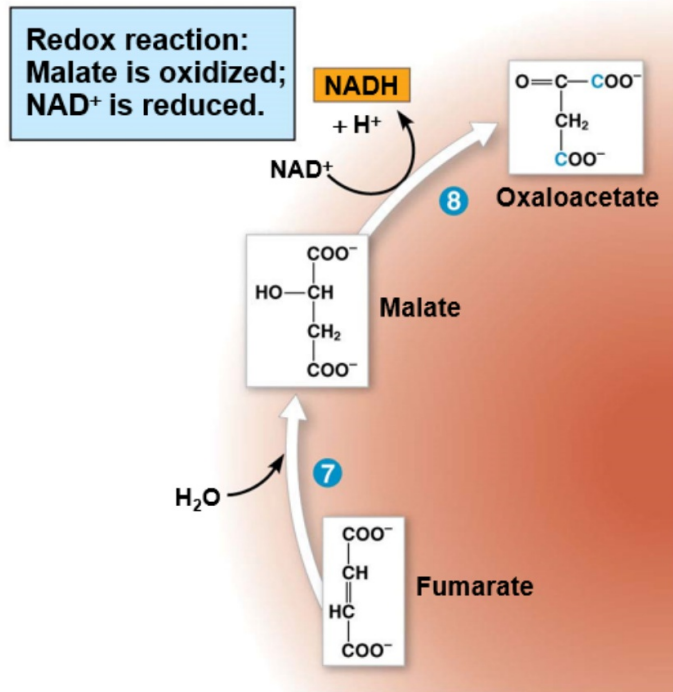
- The citric acid cycle has eight steps, each catalyzed by a specific enzyme
- The acetyl group of acetyl CoA joins the cycle by combining with oxaloacetate, forming citrate
- The next seven steps decompose the citrate back to oxaloacetate, making the process a cycle
- The NADH and FADH₂ produced by the cycle relay electrons extracted from food to the electron transport chain

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Concept 7.4: During oxidative phosphorylation, chemiosmosis couples electron transport to ATP synthesis

- Following glycolysis and the citric acid cycle, NADH and FADH₂ 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

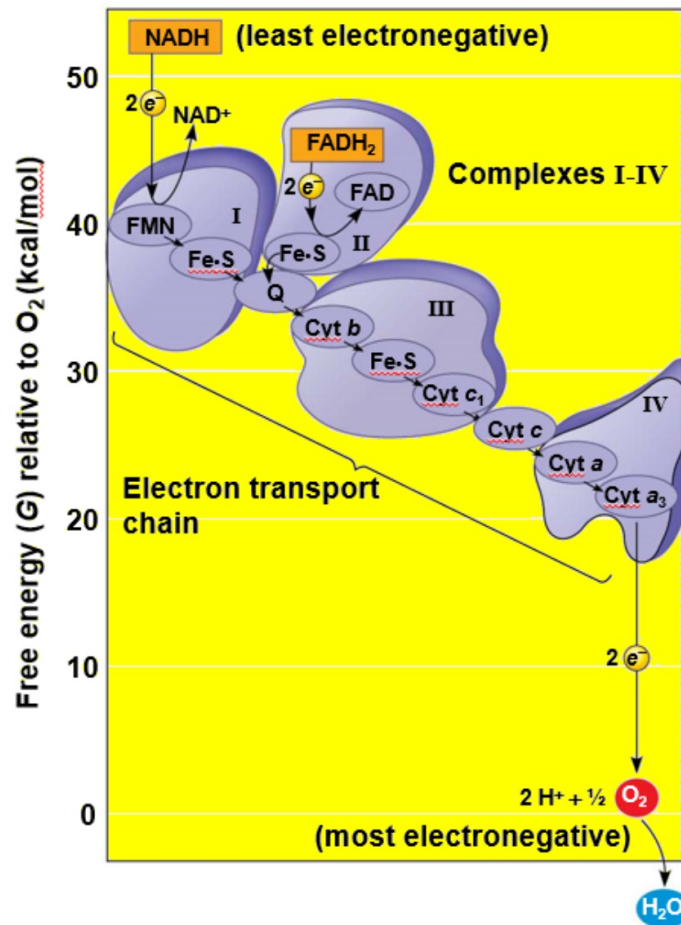
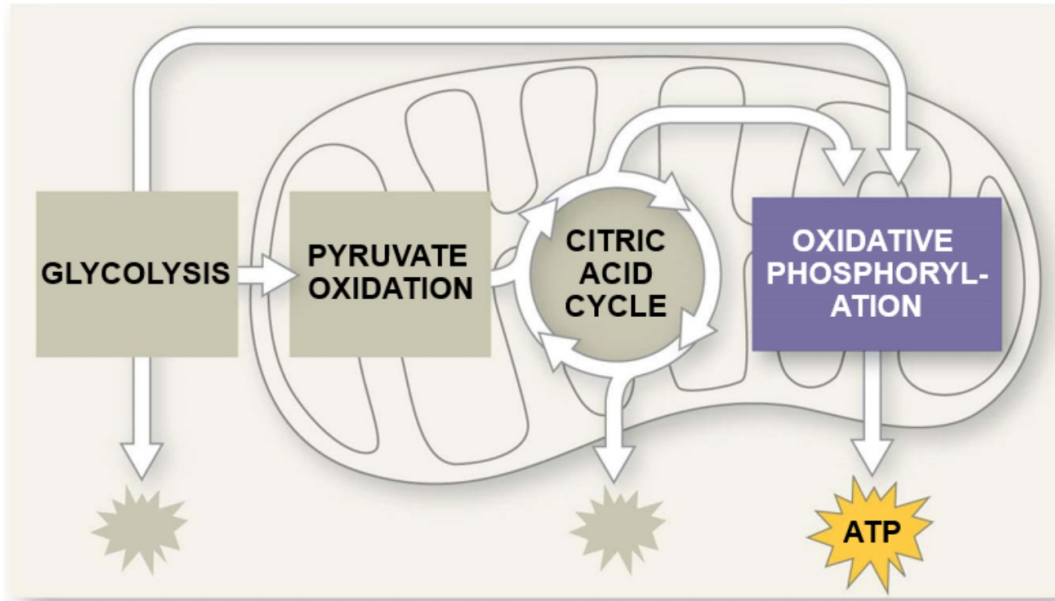
- The electron transport chain is located in the inner membrane (cristae) of the mitochondrion
- Most of the chain's components are proteins, which exist in multiprotein complexes
- The carriers alternate reduced and oxidized states as they accept and donate electrons
- Electrons drop in free energy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

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- 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

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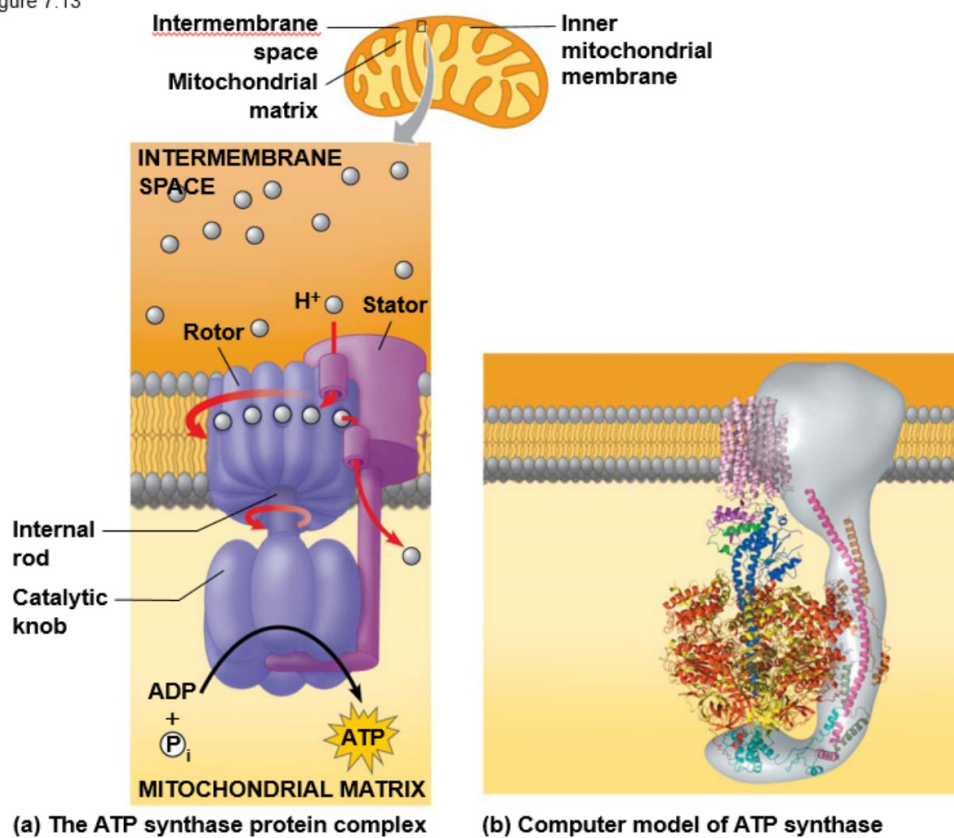


Chemiosmosis: The Energy-Coupling Mechanism

- 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 the protein complex, **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

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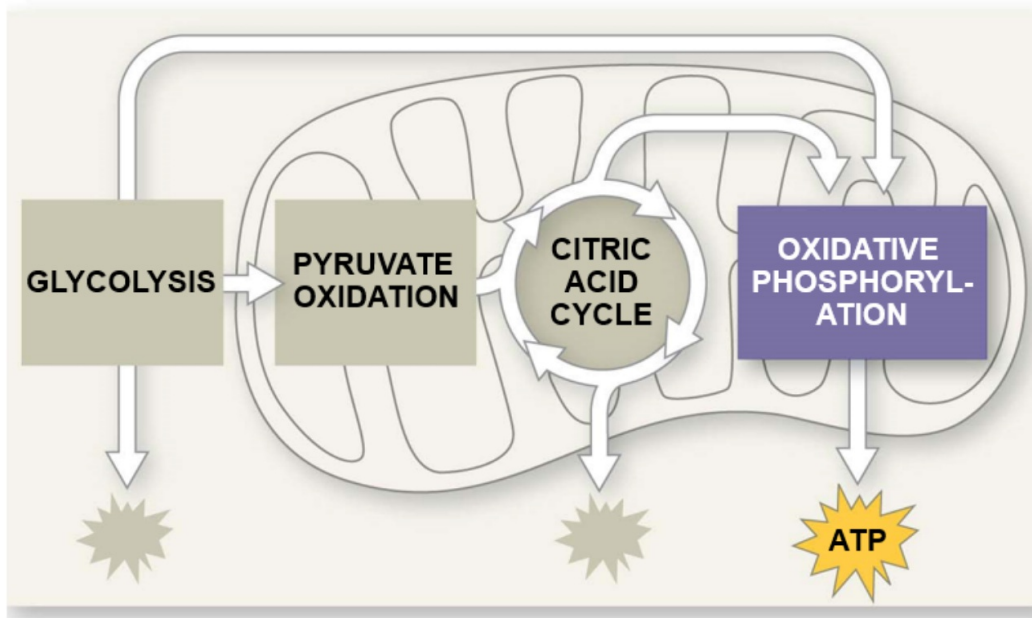
Figure 7.13

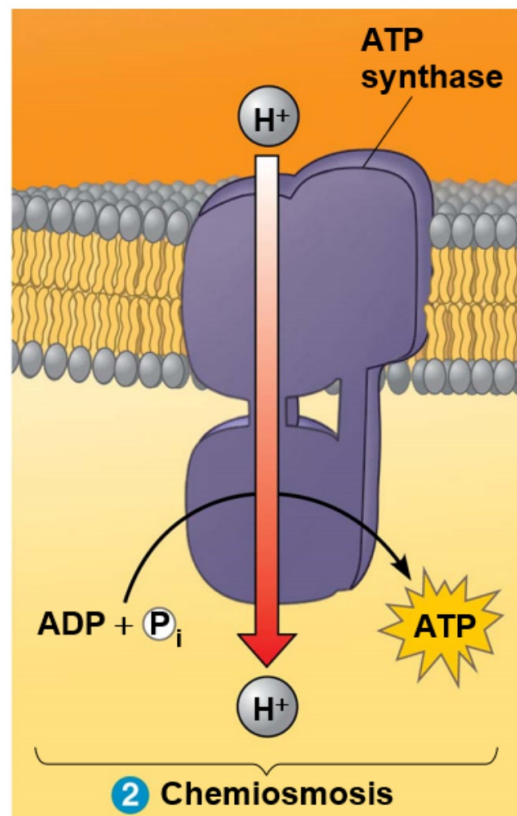
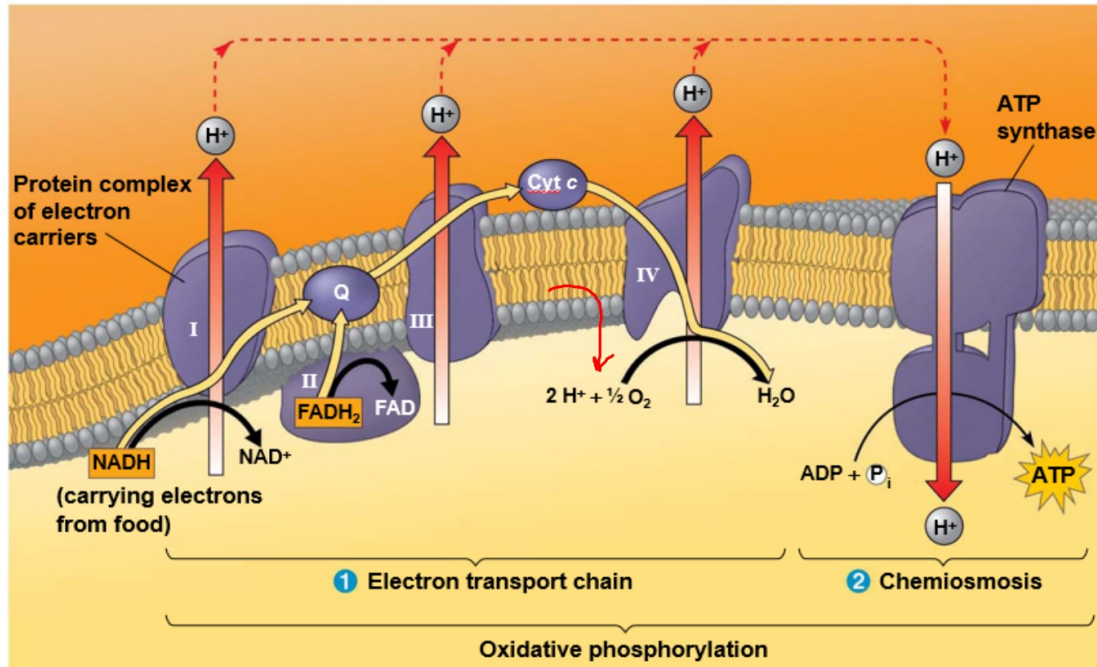


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- The energy stored in a H^+ gradient across a membrane couples the redox reactions of the electron transport chain to ATP synthesis (H⁺)
- The H^+ gradient is referred to as a proton-motive force, emphasizing its capacity to do work

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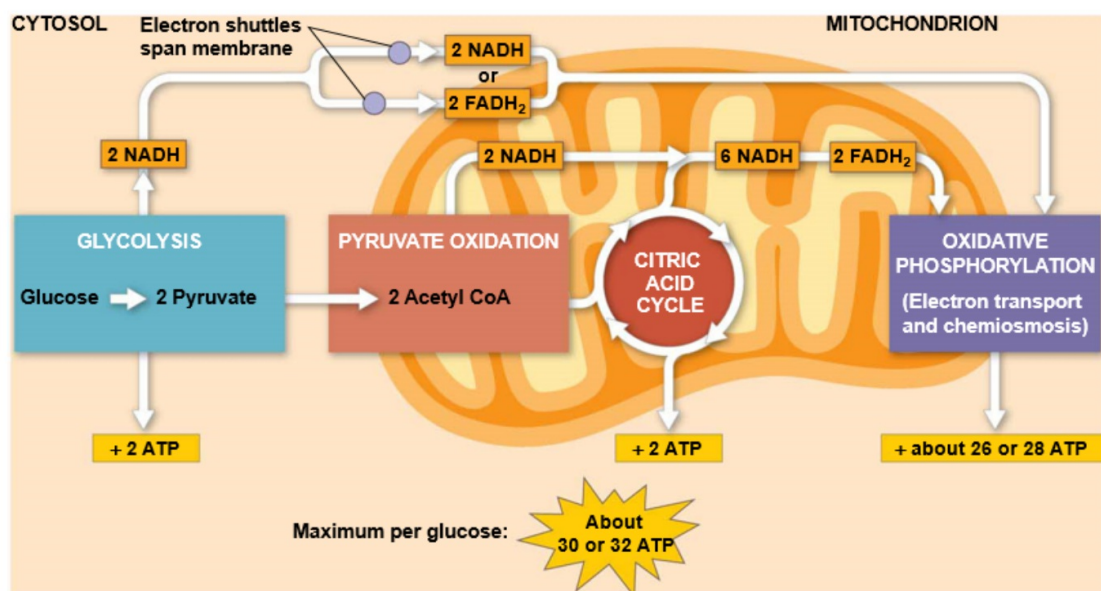




An Accounting of ATP Production by Cellular Respiration

- During cellular respiration, most energy flows in the following sequence:
 - glucose \square NADH \square electron transport chain \square proton-motive force \square 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 molecules is not known exactly

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Concept 7.5: 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

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- 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

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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

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- In **alcohol fermentation**, pyruvate is converted to ethanol in two steps
 - The first step releases CO_2 from pyruvate, and the second step reduces the resulting acetaldehyde to ethanol
 - Alcohol fermentation by yeast is used in brewing, winemaking, and baking

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Animation: Fermentation Overview

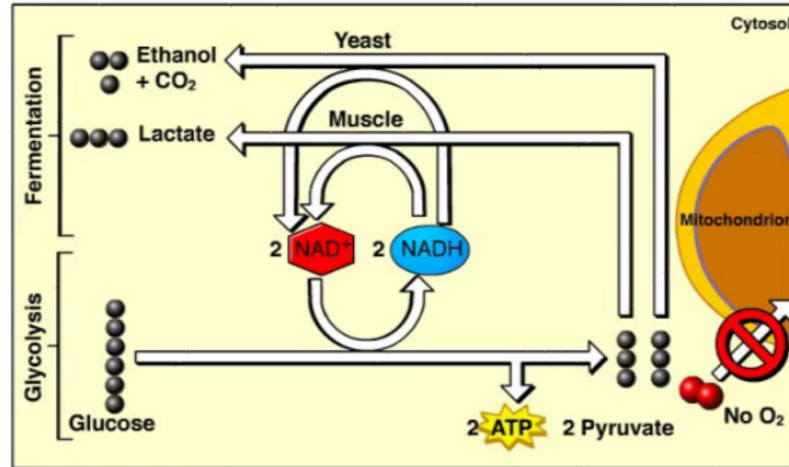
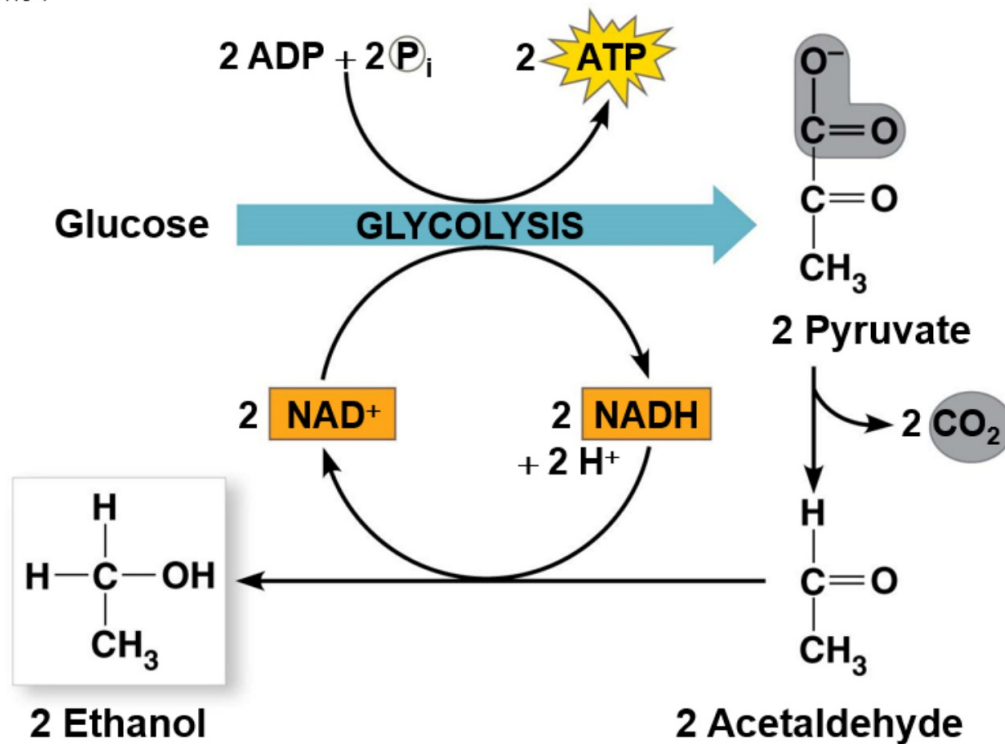


Figure 7.16-1

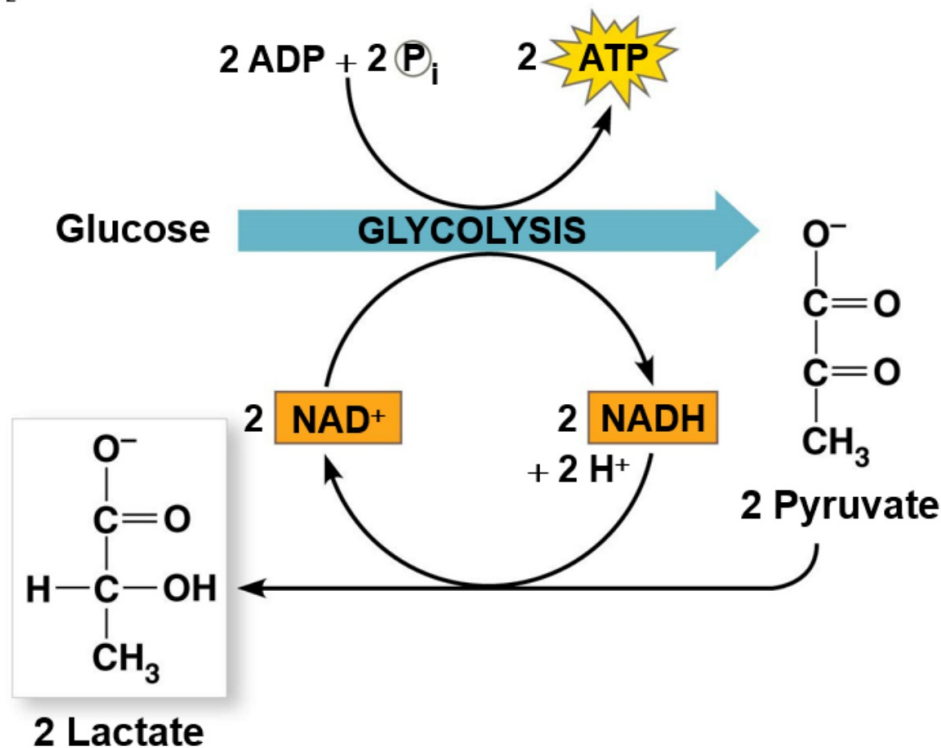


(a) Alcohol fermentation

- In **lactic acid fermentation**, pyruvate is reduced by 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

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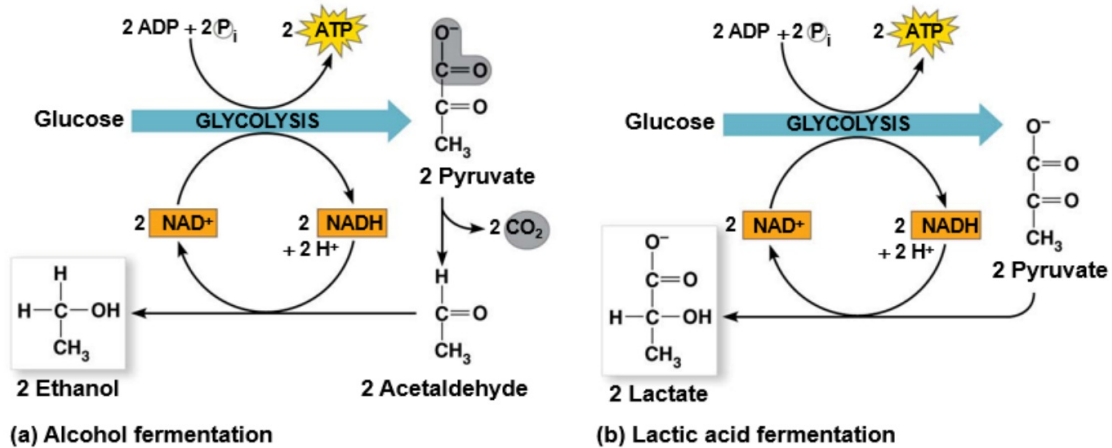
Figure 7.16-2



(b) Lactic acid fermentation

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Figure 7.16



Comparing Fermentation with Anaerobic and Aerobic Respiration

- All use glycolysis (net ATP = 2) to oxidize glucose and other organic fuels to pyruvate
 - In all three, NAD^+ is the oxidizing agent that accepts electrons from food during glycolysis
 - The mechanism of NADH oxidation differs
 - In fermentation the final electron acceptor is an organic molecule such as pyruvate or acetaldehyde
- Cellular respiration transfers electrons from NADH to a carrier molecule in the electron transport chain

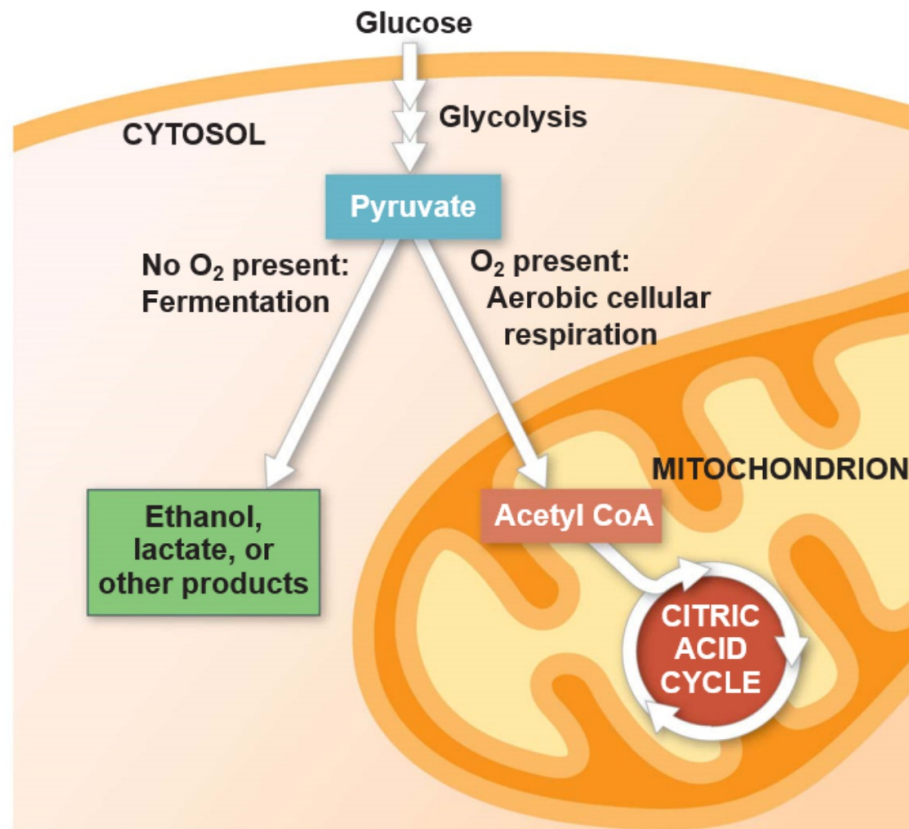
- Cellular respiration produces about 32 ATP per glucose molecule; fermentation produces 2 ATP per glucose molecule

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- **Obligate anaerobes** carry out only fermentation or anaerobic respiration and cannot survive in the presence of O₂
- 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

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Figure 7.17



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The Evolutionary Significance of Glycolysis

- Glycolysis is the most common metabolic pathway among organisms on Earth, indicating that it evolved early in the history of life
- Early prokaryotes may have generated ATP exclusively through glycolysis due to the low oxygen content in the atmosphere
- The location of glycolysis in the cytosol also indicates its ancient origins; eukaryotic cells with mitochondria evolved much later than prokaryotic cells

Concept 7.6: 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

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The Versatility of Catabolism

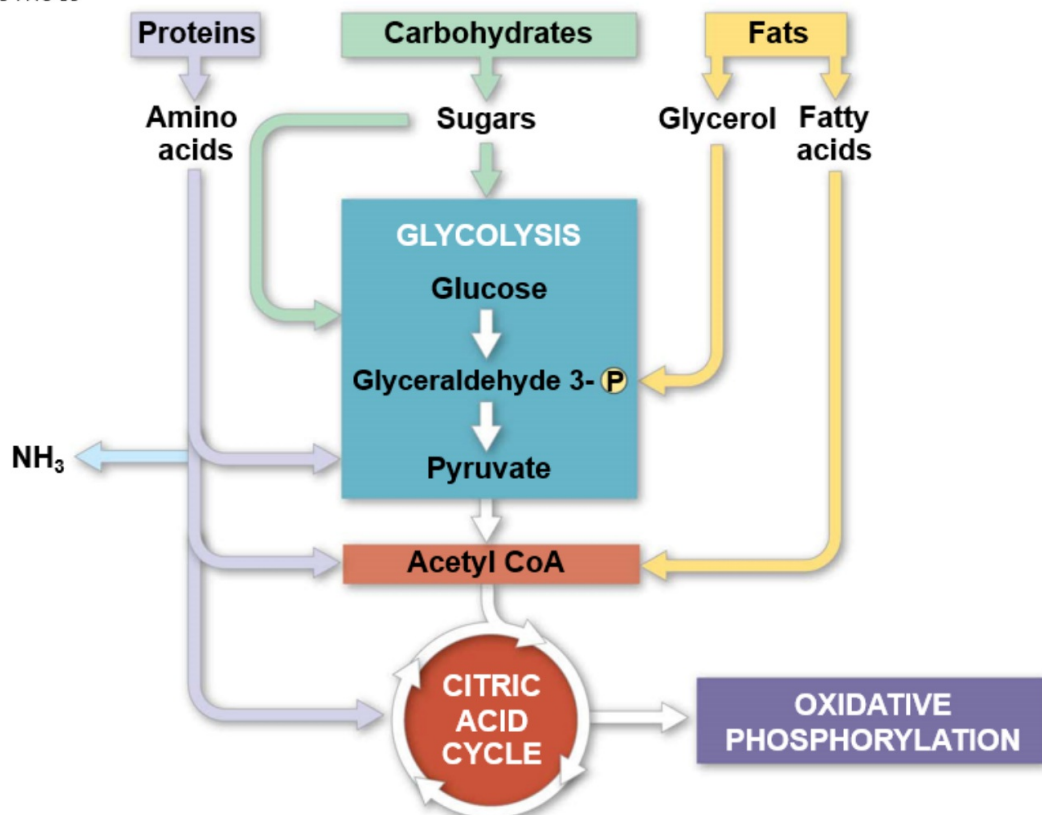
- Catabolic pathways funnel electrons from many kinds of organic molecules into cellular respiration
- Glycolysis accepts a wide range of carbohydrates
- Proteins must be digested to amino acids and amino groups must be removed before amino acids can feed glycolysis or the citric acid cycle

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- Fats are digested to glycerol (used in glycolysis) and fatty acids
- 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

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Figure 7.18-s5



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Biosynthesis (Anabolic Pathways)

- The body uses small molecules to build other substances
- Some of these small molecules come directly from food; others can be produced during glycolysis or the citric acid cycle

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Thyroid Hormone Level	Oxygen Consumption Rate [nmol O ₂ /(min · mg cells)]
Low	4.3
Normal	4.8
Elevated	8.7

Data from M. E. Harper and M. D. Brand, The quantitative contributions of mitochondrial proton leak and ATP turnover reactions to the changed respiration rates of hepatocytes from rats of different thyroid status, *Journal of Biological Chemistry* 268:14850–14860 (1993).

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