BIOLOGY I

Chapter 9:
CELLULAR RESPIRATION:
Harvesting Chemical Energy

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2012

INTRODUCTION: Defining Cellular Respiration

- *** **Cellular respiration** is a major biochemical pathway by which cells release the chemical-bond energy from organic molecules (food) and convert it into a usable form: **ATP** (adenosine triphosphate).
- A simplified definition:
  - A process by which living cells obtain **energy** from organic molecules.

INTRODUCTION: Review

- In order to function, living things must acquire **energy** by breaking down nutrient molecules obtained from outside sources or internal metabolic pathways.
- **Organic molecules** that the cells break down for their metabolism are:
  - Carbohydrates, lipids, proteins
- **Carbohydrates** are the main source of energy for most cells, especially ***glucose***.
  - When using other organic molecules as energy sources, cells usually first convert the molecules to glucose or other compounds that enter the pathways of glucose metabolism.

Review of Carbohydrates

- Organic compounds composed of **carbon, hydrogen,** and **oxygen** in the approximate ratio of 1:2:1, $(CH_2O)_n$.
- Perform several major functions in living things, including **energy storage** and **structural** function (building material).
  - *** Carbohydrates are the main source of energy (fuel) for most living things.**
- Carbohydrates include: **sugars** (such as glucose, fructose and sucrose)**, starch, glycogen,** and **cellulose.**

TABLE 2.6 Major Carbohydrate Groups

Type of Carbohydrate	Examples
Monosaccharides (Simple sugars that contain from 3 to 7 carbon atoms.)	Glucose (the main blood sugar). Fructose (found in fruits). Galactose (in milk sugar). Deoxyribose (in DNA). Ribose (in RNA).
Disaccharides (Simple sugars formed from the combination of two monosaccharides by dehydration synthesis.)	Sucrose (table sugar) = glucose + fructose. Lactose (milk sugar) = glucose + galactose. Maltose = glucose + glucose.
Polysaccharides (From tens to hundreds of monosaccharides joined by dehydration synthesis.)	Glycogen (the stored form of carbohydrates in animals). Starch (the stored form of carbohydrate in plants and main carbohydrate in food). Cellulose (part of cell walls in plants that cannot be digested by humans but aids movement of food through intestines).

Table 2-6 Principles of Anatomy and Physiology, 11/e

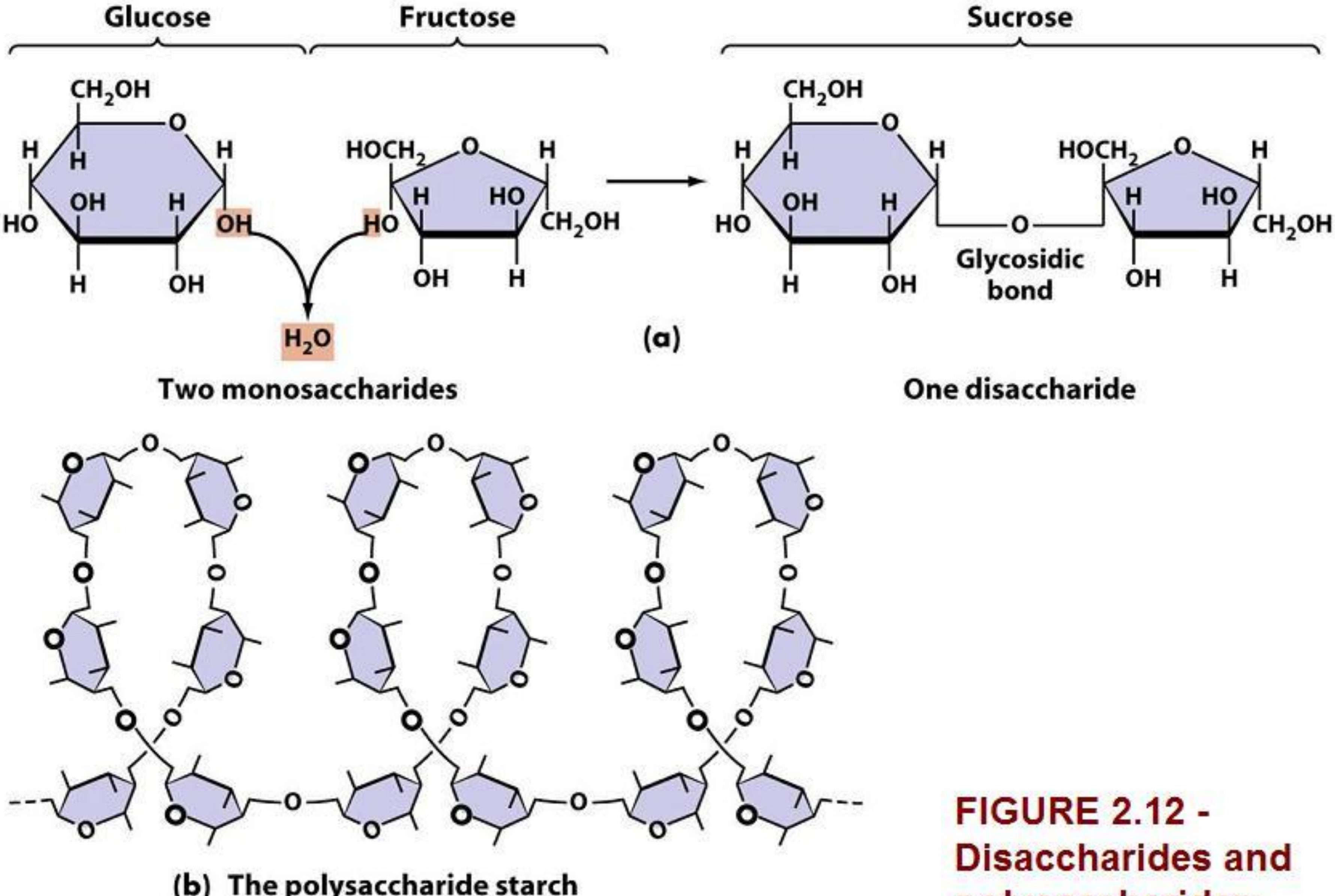
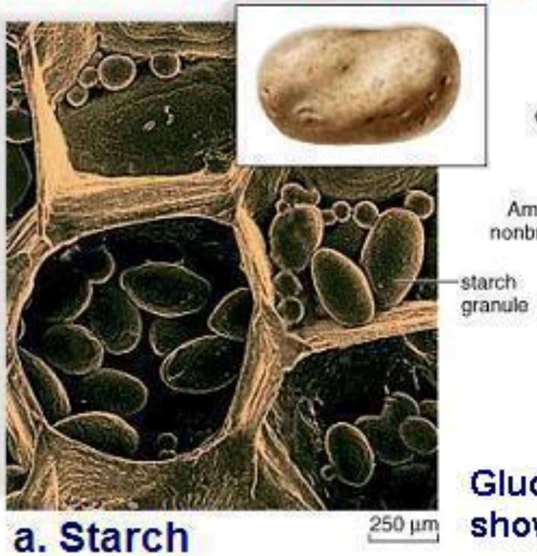
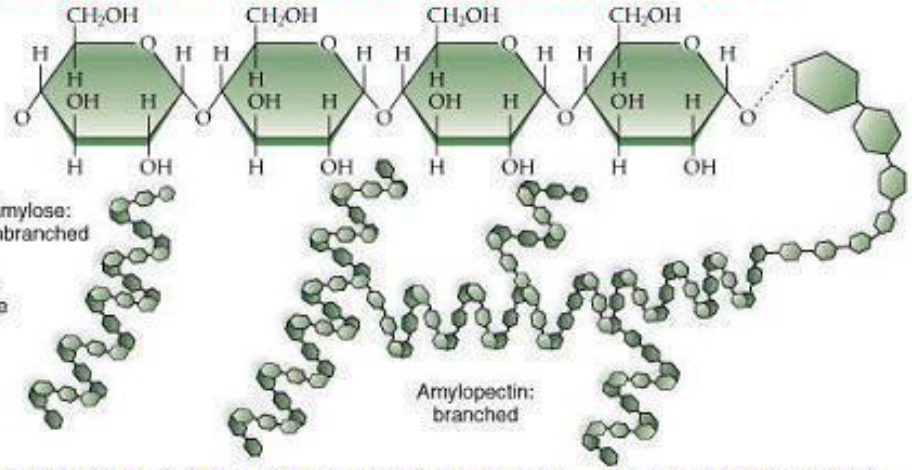


Figure 2-12 Microbiology, 6/e

FIGURE 2.12 - Disaccharides and polysaccharides.

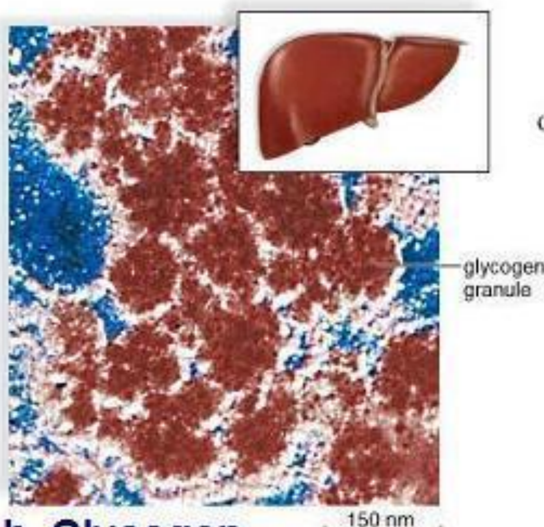
FIGURE 3.8 - Starch and glycogen (storage polysaccharides)

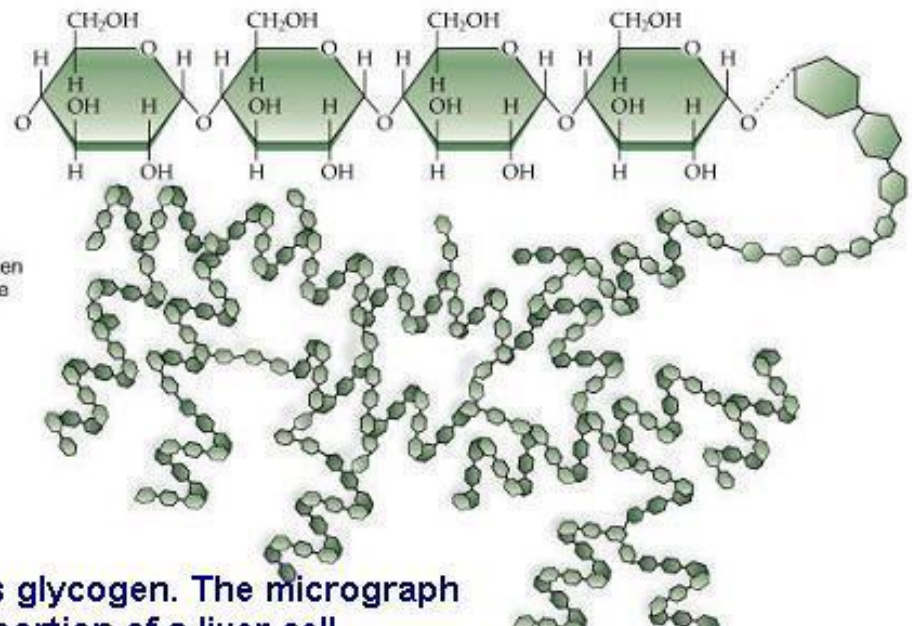




a. Starch

Glucose is stored in plants as starch. The micrograph shows the location of starch in plant cells.

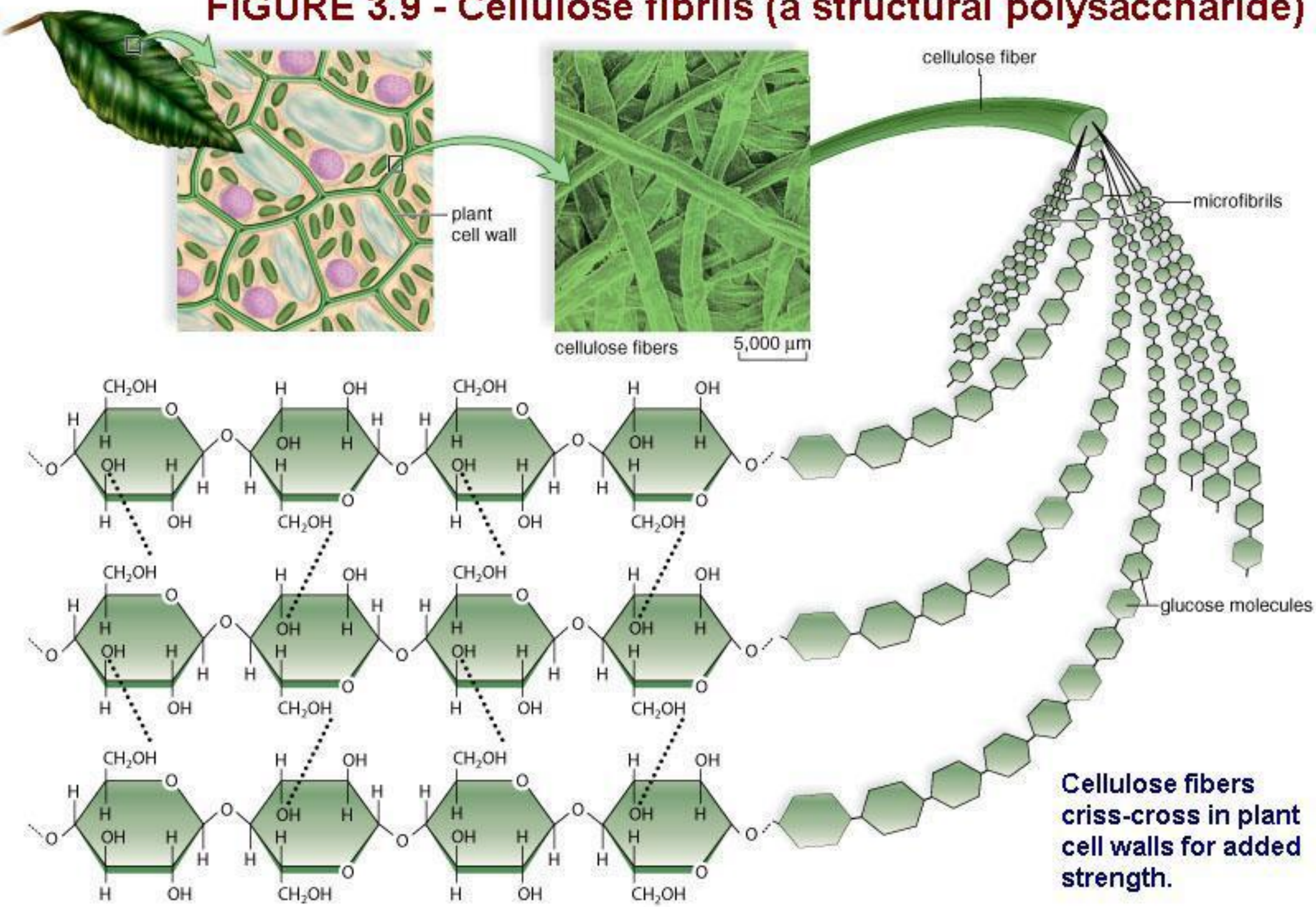




b. Glycogen

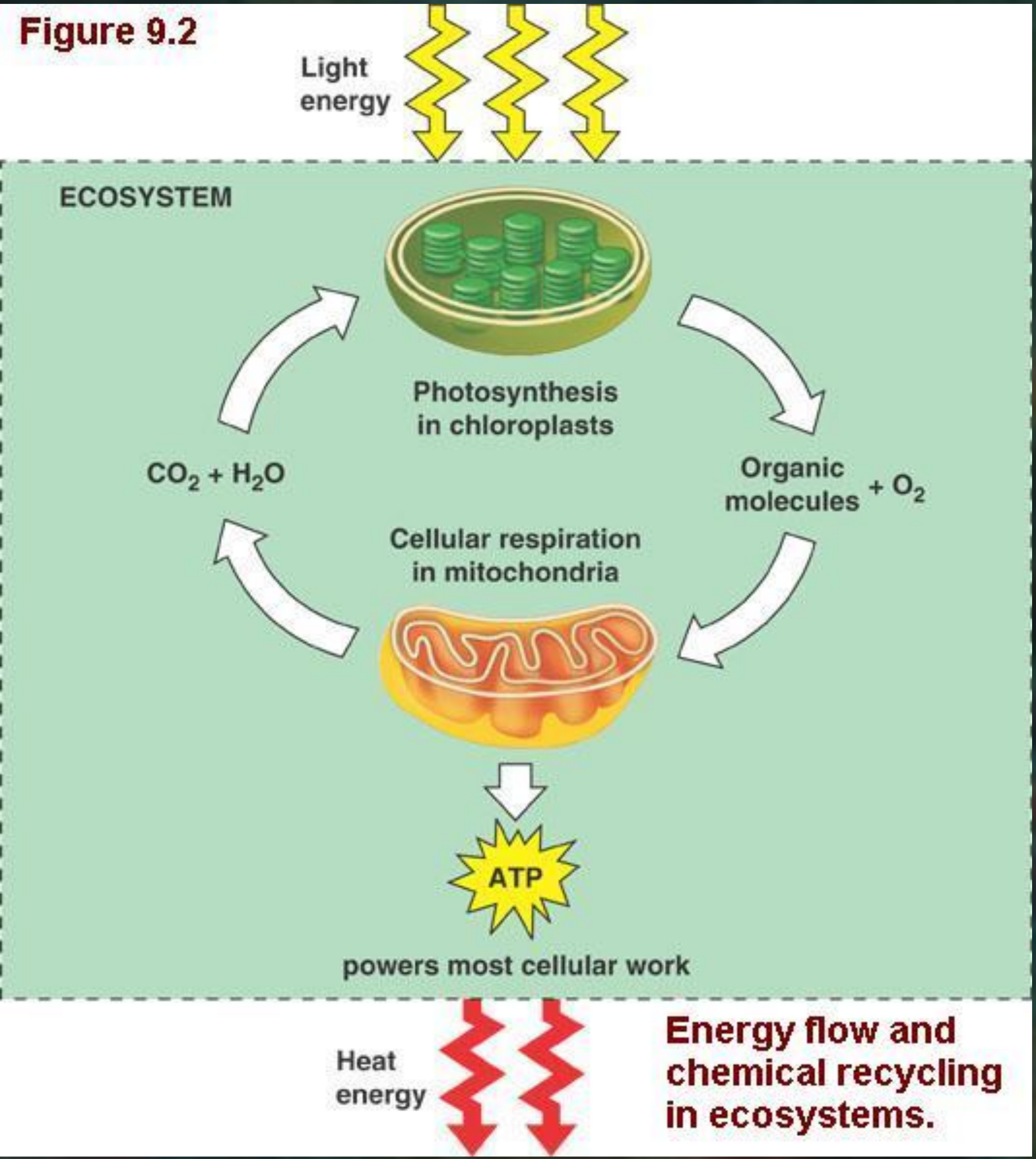
Glucose is stored in animals as glycogen. The micrograph shows glycogen deposits in a portion of a liver cell.

FIGURE 3.9 - Cellulose fibrils (a structural polysaccharide)



Cellulose fibers criss-cross in plant cell walls for added strength.

Figure 9.2



Energy flow and chemical recycling in ecosystems.

Life is Work: Photosynthesis and Cellular Respiration

- Energy flows into an ecosystem as sunlight and ultimately leaves as heat, while the chemical elements essential to life are recycled.
- **Photosynthesis** (by plants and algae) generates **oxygen** and **organic molecules** used by the mitochondrion of eukaryotic organisms as fuel for **cellular respiration**. Respiration breaks this fuel down, generating **ATP**. The waste products of respiration, **carbon dioxide** and **water**, are the raw materials for photosynthesis.

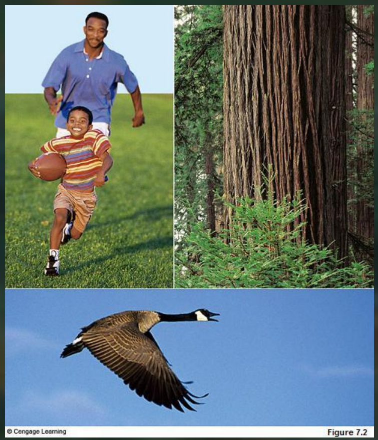
The Metabolic Pathways

Catabolism: Getting Materials and Energy

- Nutrient processing is extremely varied, especially in bacteria, yet in most cases it is based on three basic catabolic pathways. Frequently, the main nutrient is **glucose**. The most common pathway for break down of glucose is **glycolysis**.
  - **Aerobic respiration:** A series of reactions (glycolysis, Krebs cycle, electron transport chain) which convert **glucose** to **CO_2** and consume **oxygen** as final electron acceptor, producing a relatively large amount of **ATP** (energy). It is used by many bacteria, fungi, protists, and animals.
  - **Anaerobic respiration:** Respiration in which the final electron acceptor in the electron transport chain is ***not oxygen***; instead it is an inorganic molecule such as nitrate, nitrite, sulfate, or carbonate.
  - **Fermentation:** Anaerobic breakdown of glucose that results in a small amount of ATP **without an electron transport chain**, producing a characteristic end product such as ethyl alcohol or lactic acid.

Comparison of Main Types of Energy-Releasing Pathways

- All organisms make **ATP** by the breakdown of ***glucose*** and other organic compounds.
- **Glycolysis**, the initial breakdown of one glucose to two **pyruvate** molecules, takes place in the cell's **cytoplasm**. It is the first stage of all the main energy-releasing pathways, and it *doesn't require free oxygen*.
- **Anaerobic pathways** (such as fermentation) end in the cytoplasm, and the net yield of ATP is small.
- An oxygen-requiring pathway called **aerobic respiration** continues in mitochondria in eukaryotes, and it releases far more ATP energy from glucose.



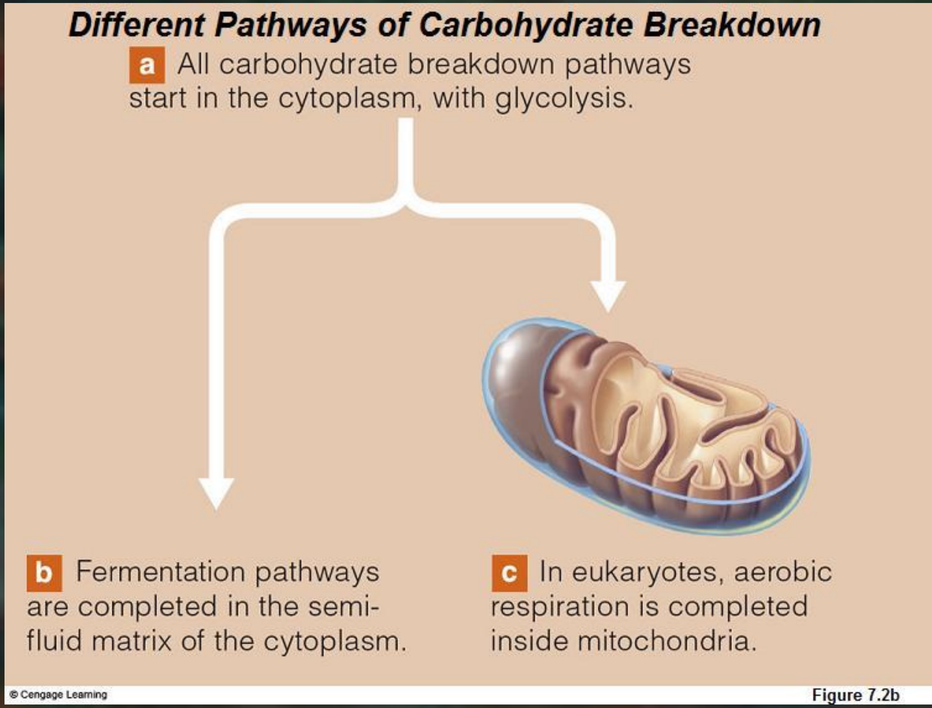
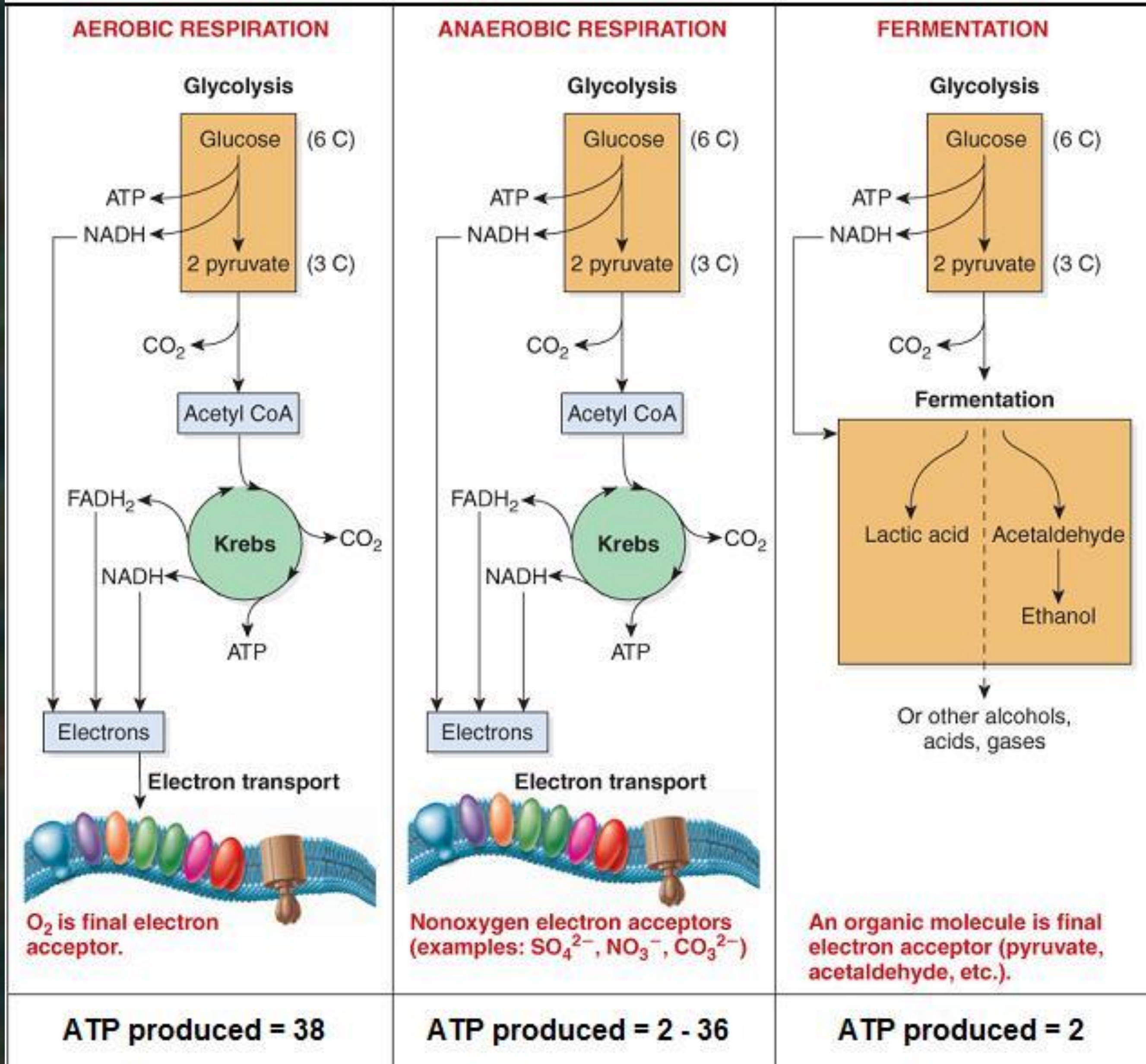


Figure 8.15. Summary of the most common pathways of glucose metabolism.



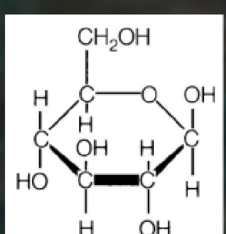
Catabolic Pathways and Production of ATP

- **Aerobic cellular respiration** is the most prevalent and efficient catabolic pathway for production of **ATP**, in which ***oxygen*** is consumed as a reactant along with the ***organic fuel***, and carbon dioxide and water are released.

Organic Compounds + Oxygen → Carbon Dioxide + Water + Energy (ATP & Heat)

- Carbohydrates, fats, and proteins can all be processed and consumed as fuels. However, carbohydrates are more readily processed. The sugar **glucose** is the fuel that cells most often use.
- The breakdown of **glucose** is ***exergonic***, it releases energy. It is summarized by this ***chemical equation***:

$$C_6H_{12}O_6 + 6\ O_2 + 36\ ADP + 36\ P_i \rightarrow 6\ CO_2 + 6\ H_2O + 36\ ATP$$



Coupling of Catabolism and Anabolism by ATP: **The Structure of ATP**

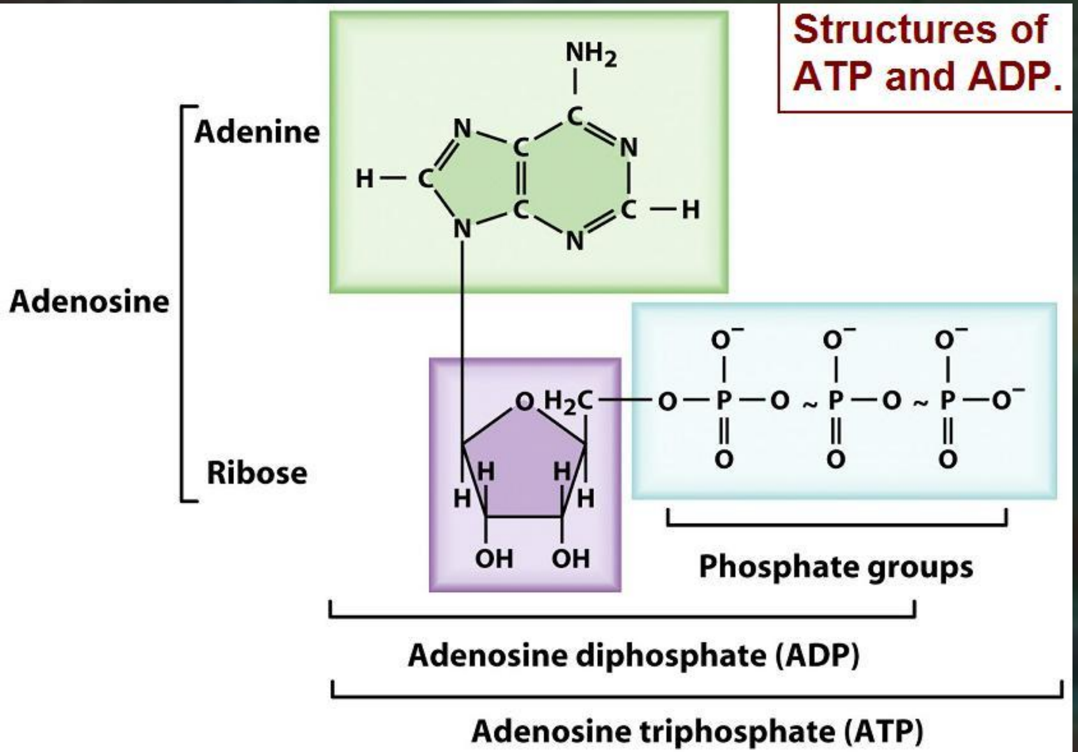


Figure 2-25 Principles of Anatomy and Physiology, 11/e

- When ATP breaks down to ADP and inorganic phosphate, a large amount of chemical energy is release for use in other chemical reactions.
- High-energy phosphate bonds are indicated by wavy lines.

- **ATP (*adenosine triphosphate*)** is a *nucleotide* that consists of adenine (a nitrogenous base), ribose (a sugar), and three phosphate groups.
- ATP is the main **energy-carrying molecule** (the energy currency) of the cell; it transfers energy from one molecule to another.
- ATP is involved in energy-demanding reactions, such as synthesis of proteins and carbohydrates.

ATP Powers Cellular Work by Coupling Catabolism to Anabolism

- When complex molecules are split apart (**catabolism**, left), some of the energy is transferred to form ATP and the rest is given off as heat.
- When simple molecules are combined to form complex molecules (**anabolism**, right), ATP provides the energy for synthesis, and again some energy is given off as heat.

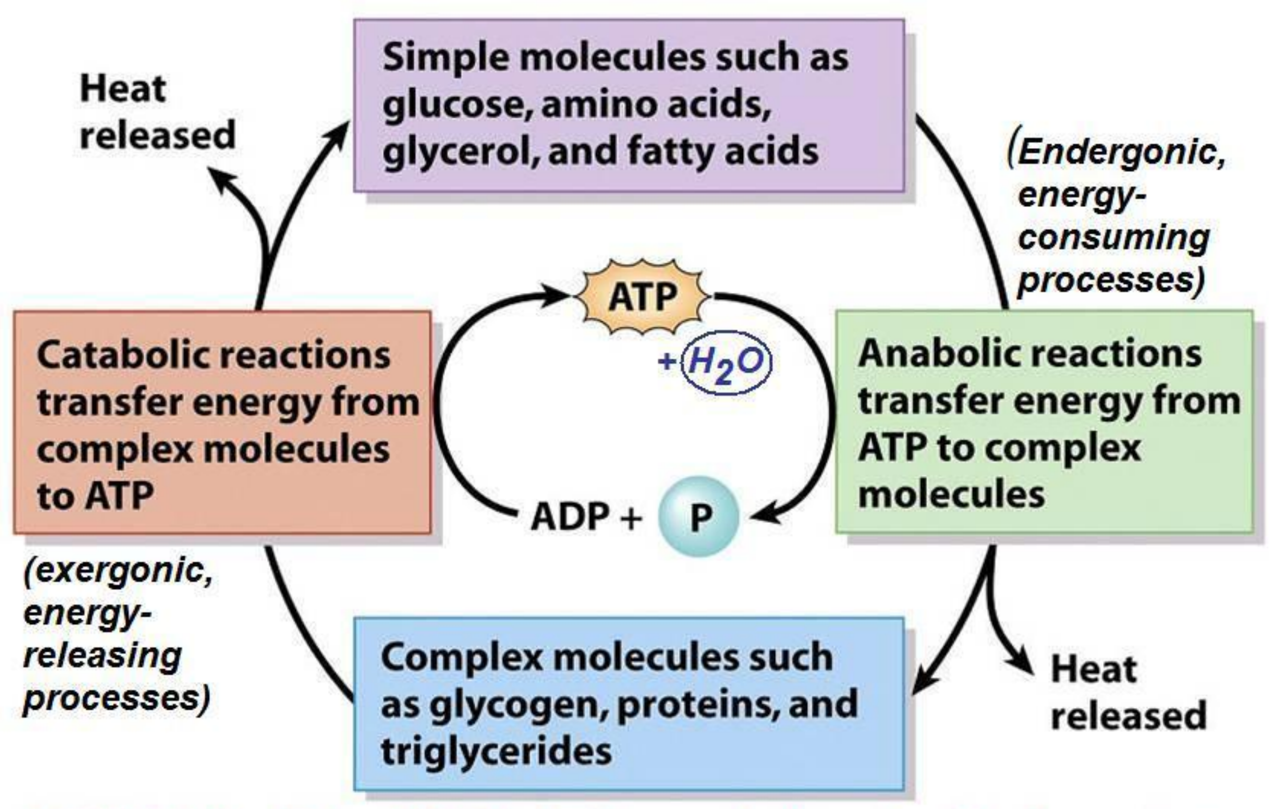


FIGURE 25.1 - Role of ATP in linking anabolic and catabolic reactions.

ENERGY PRODUCTION: **The Generation of ATP**

- Energy released during certain metabolic reactions can be trapped to form **ATP** (adenosine triphosphate) from ADP (adenosine diphosphate) and phosphate (P).
- **Phosphorylation:** The addition of a phosphate group (P) to an organic molecule.

ADP **ATP**

Adenosine—P ~ P + Energy + P → Adenosine—P ~ P ~ P

Mechanisms of ATP Generation

ADP + P = ATP

- Organisms use three mechanisms of **phosphorylation** to generate ATP.

1) **Substrate-level phosphorylation:** Synthesis of **ATP** by direct transfer of a high-energy phosphate group from an intermediate metabolic compound (a substrate) to ADP. In eukaryotic cells, it occurs in the *cytosol* (through **glycolysis**).
2) **Oxidative phosphorylation:** Production of **ATP** coupled with electron transport (redox reactions); it transfers electrons from organic compounds through a group of electron carriers, called the ***electron transport chain***, to molecules of oxygen (O_2). Some of the released energy is used to generate **ATP** from ADP (through ***chemiosmosis***). In eukaryotic cells, it occurs in the *inner mitochondrial membrane* of cells as the final major stage of cellular respiration.
3) **Photophosphorylation:** Production of **ATP** from ADP and phosphate through a series of sunlight-driven reactions in photosynthetic organisms such as *plants* and *certain bacteria* (they contain light-absorbing pigments such as chlorophyll).

Mechanisms of ATP Generation: ***Substrate-Level Phosphorylation***

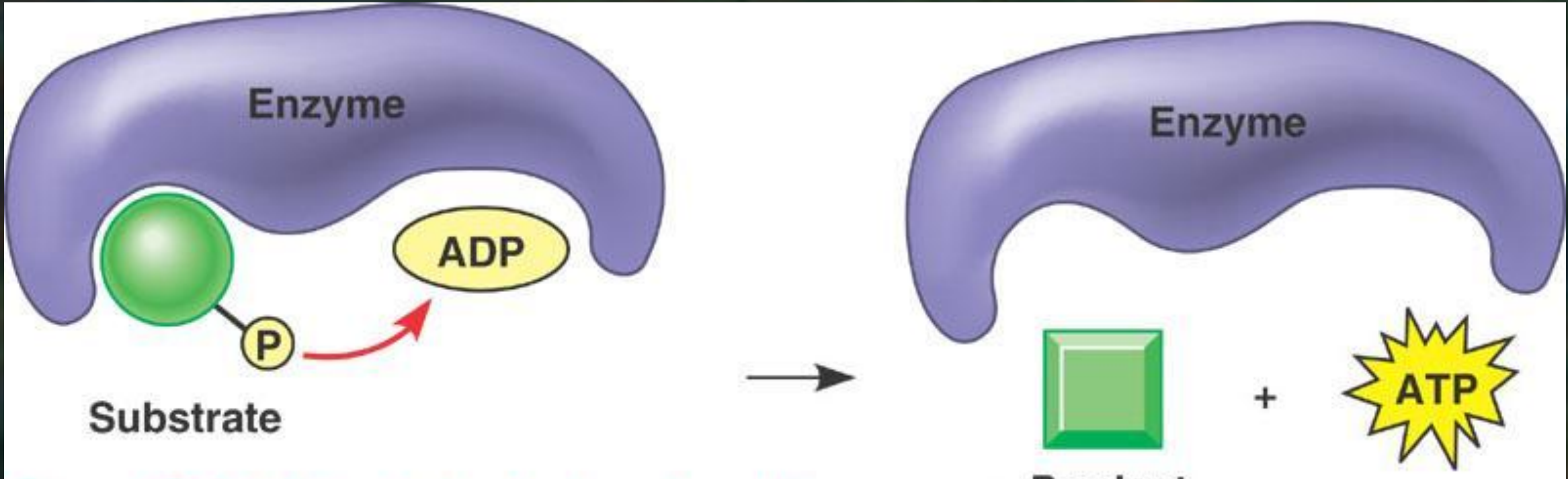


Figure 9.7. Substrate-level phosphorylation.

- Some **ATP** is made by direct transfer of a phosphate group from an organic substrate to ADP by an enzyme (for example in glycolysis, the breakdown of glucose).

Figure 8.14. ATP formation by substrate-level phosphorylation.

The Structure, Hydrolysis and Regeneration of ATP

- The **bonds** between the **phosphate groups** of ATP can be broken by ***hydrolysis*** (water is required).
- The reaction of ATP and water yields inorganic phosphate (P_i) and ADP and ***releases energy*** (is exergonic).
- ATP is a renewable resource that can be regenerated by the addition of **phosphate** to ADP (**phosphorylation**).

Figure 8.9 Hydrolysis of ATP.

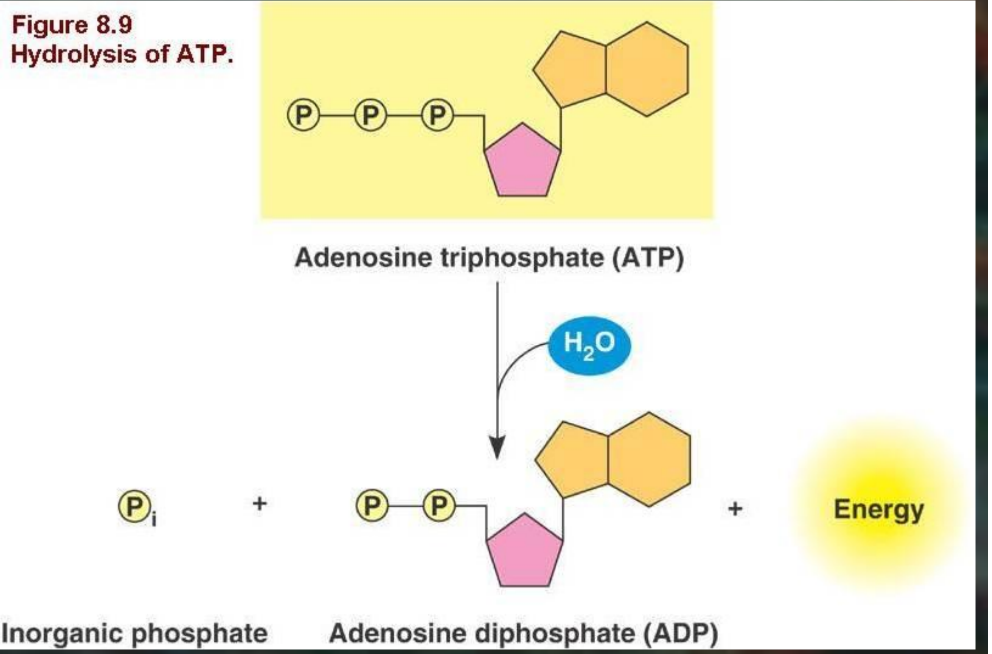
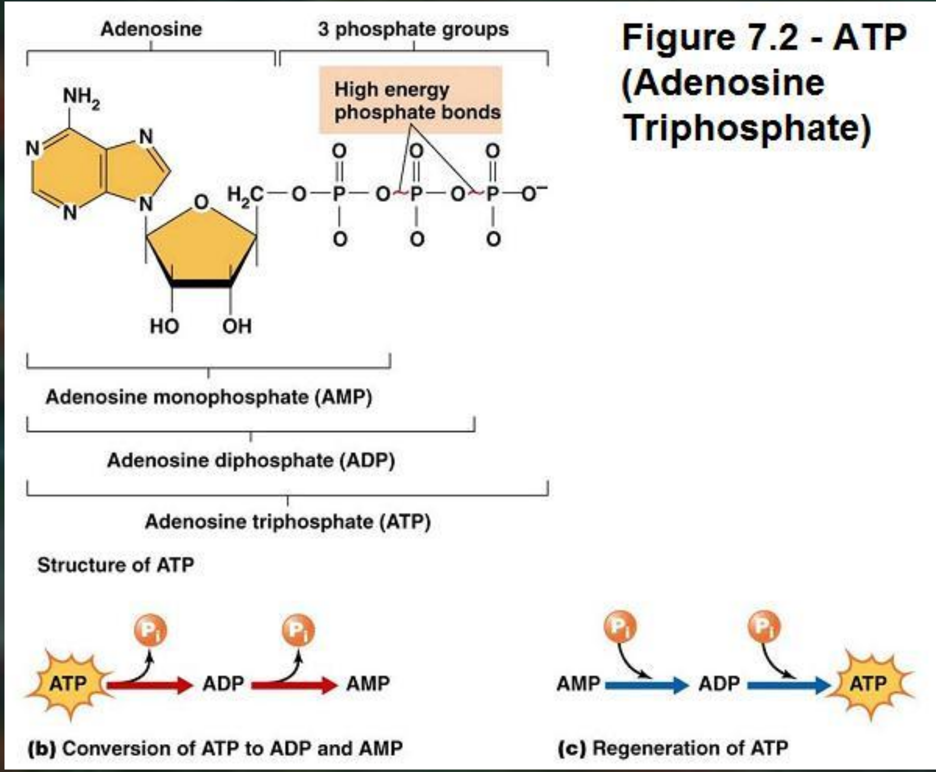
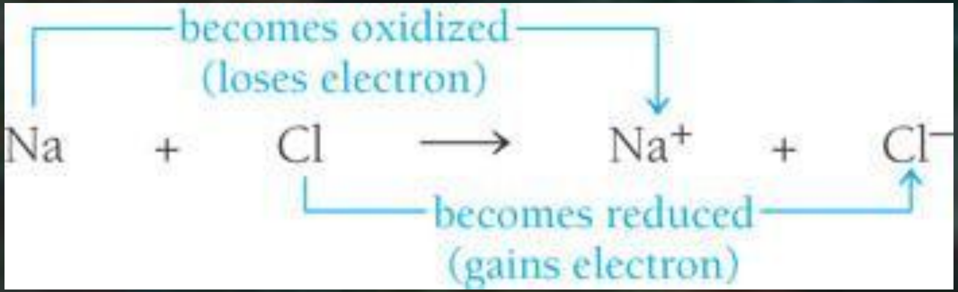


Figure 7.2 - ATP (Adenosine Triphosphate)

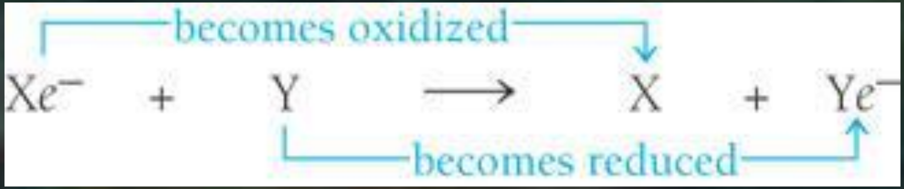


REDOX REACTIONS: **Oxidation and Reduction**

- The **relocation of electrons (*e*⁻)** ***releases energy*** stored in organic molecules, and this energy ultimately is used to synthesize ATP.
- **Oxidation:** The **removal** of electrons from a molecule (substrate, the ***electron donor***), a reaction that often *produces energy* (decreases the potential, or stored, energy of the molecule).
- **Reduction:** The **addition** of electrons to a molecule (the ***electron acceptor***). Negatively charged electrons added to an atom ***reduce*** the amount of positive charge of that atom. It results in an increase in the potential energy of the molecule.



Generalized Redox Reaction



REDOX REACTIONS: **Oxidation and Reduction**

- **Oxidation and reduction reactions are always coupled**; each time one substance is ***oxidized*** (loses electrons), another is simultaneously ***reduced*** (gains electrons). An electron transfer requires both a donor and an acceptor. Such paired reactions are called **redox reactions**.
- In this generalized reaction, substance ***A***, the electron donor, is the **reducing agent**; it reduces ***B***, which accepts the donated electron.
- Substance ***B***, the electron acceptor, is the **oxidizing agent**; it oxidizes ***A*** by removing its electron.

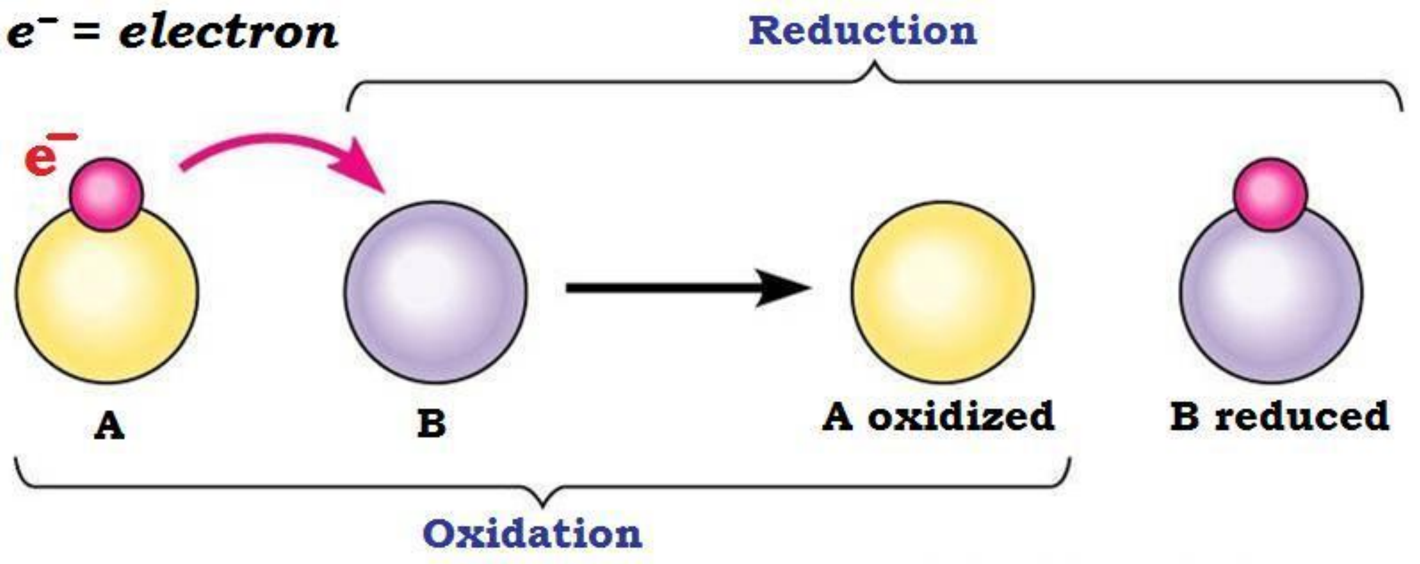
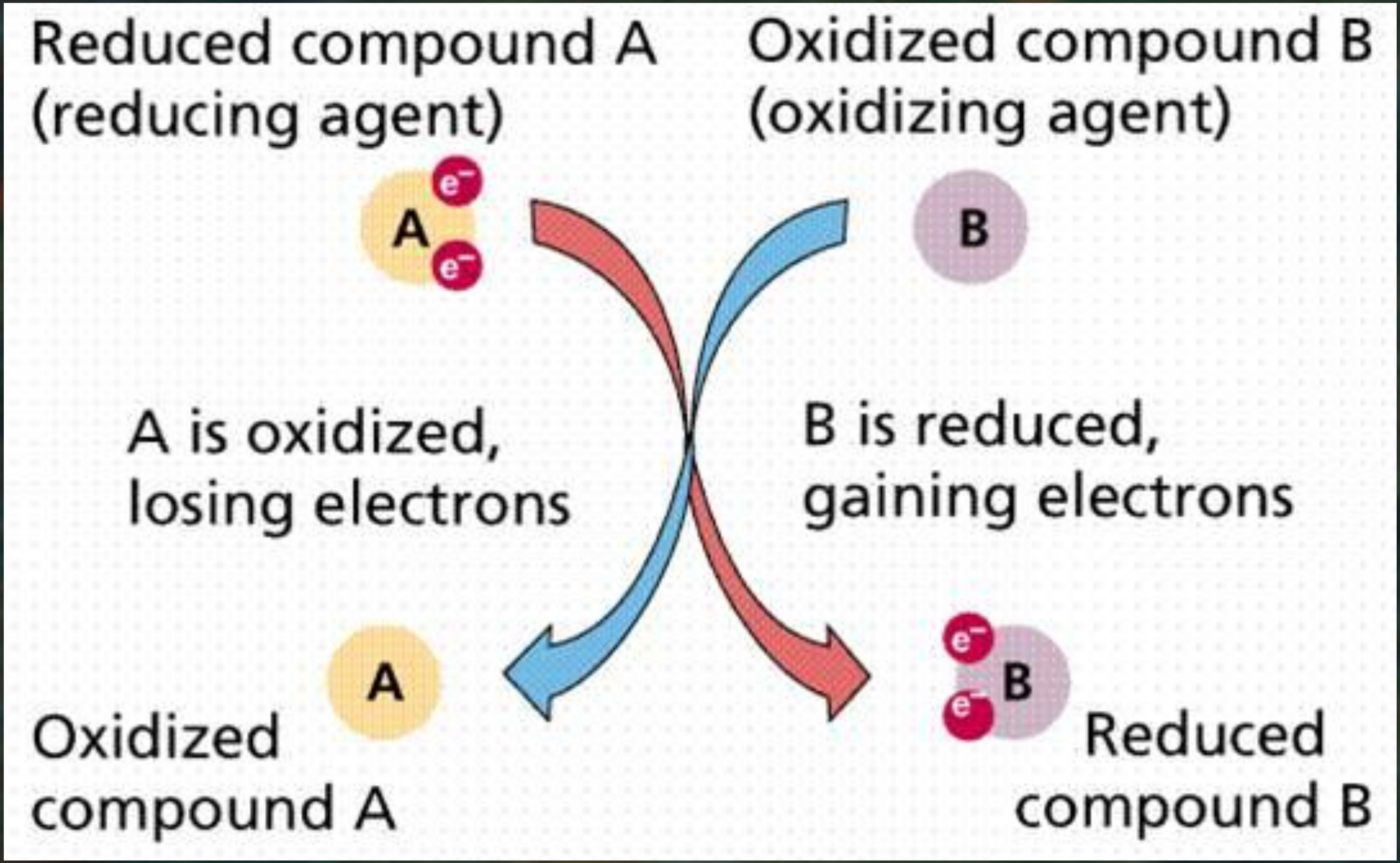


Figure 5.9 - Oxidation-reduction.

REDOX REACTIONS: **Oxidation and Reduction**



Example: When we burn foods we exchange electrons in our cells.

Oxidation of Organic Fuel Molecules During Cellular Respiration

- During aerobic cellular respiration, **glucose is oxidized to carbon dioxide** and **oxygen is reduced to water.** The electrons lose potential energy during their transfer to ***oxygen***, and **energy** is released.
- In general, organic molecules that have an abundance of hydrogen are excellent fuels because their bonds are a source of "hilltop" electrons, whose energy may be released as these electrons "fall" down an energy gradient when they are transferred to oxygen. The energy state of electrons changes as hydrogen (with its electron) is transferred to oxygen.
- By oxidizing glucose, respiration liberates stored energy from glucose and makes it available for **ATP synthesis**.

becomes oxidized

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

glucose

becomes reduced

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

- Glucose and other organic fuels are broken down in a series of steps, each one catalyzed by its own enzyme.
- In oxidation reactions, each electron travels with a **proton**—thus, as a **hydrogen atom** (*dehydrogenation*; a hydrogen atom consists of a proton and an electron). Released hydrogen atoms are transferred immediately by coenzymes to another compound.
- Two coenzymes are commonly used by cells to carry electrons and hydrogen atoms.
  - **NAD^+ (nicotinamide adenine dinucleotide),** a derivative of the B vitamin niacin.
  - **FAD (flavin adenine dinucleotide),** a derivative of vitamin B_2 (riboflavin). It is sometimes used instead of NAD^+.
- When the two coenzymes are carrying electrons and hydrogen, they are in a reduced form and may be abbreviated NADH and $FADH_2$.

REDOX REACTIONS: **NAD^+ as an Electron Shuttle**

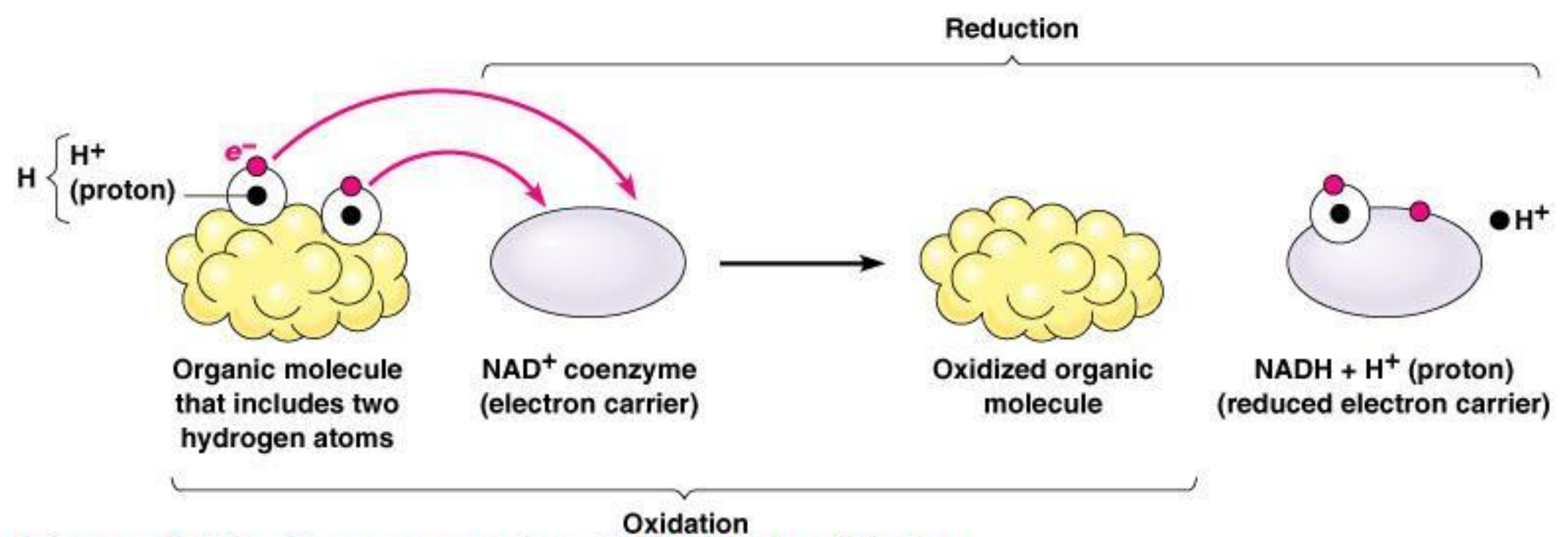


Figure 5.10 - Representative biological oxidation.

- **Representative biological oxidation.** *Electrons from organic compounds are usually passed first to NAD^+, reducing it to NADH.* Two electrons and two protons (altogether equivalent to two hydrogen atoms) are transferred from an organic substrate molecule to a coenzyme, **NAD^+**. NAD^+ actually receives one hydrogen atom and one electron, and one proton is released into the medium. NAD^+ is reduced to NADH, which is a more energy-rich molecule. NADH passes the electrons to an **electron transport chain**, which conducts them to O_2 in energy-releasing steps. The energy released is used to make ATP.

REDOX REACTIONS: NAD^+ as an Electron Shuttle

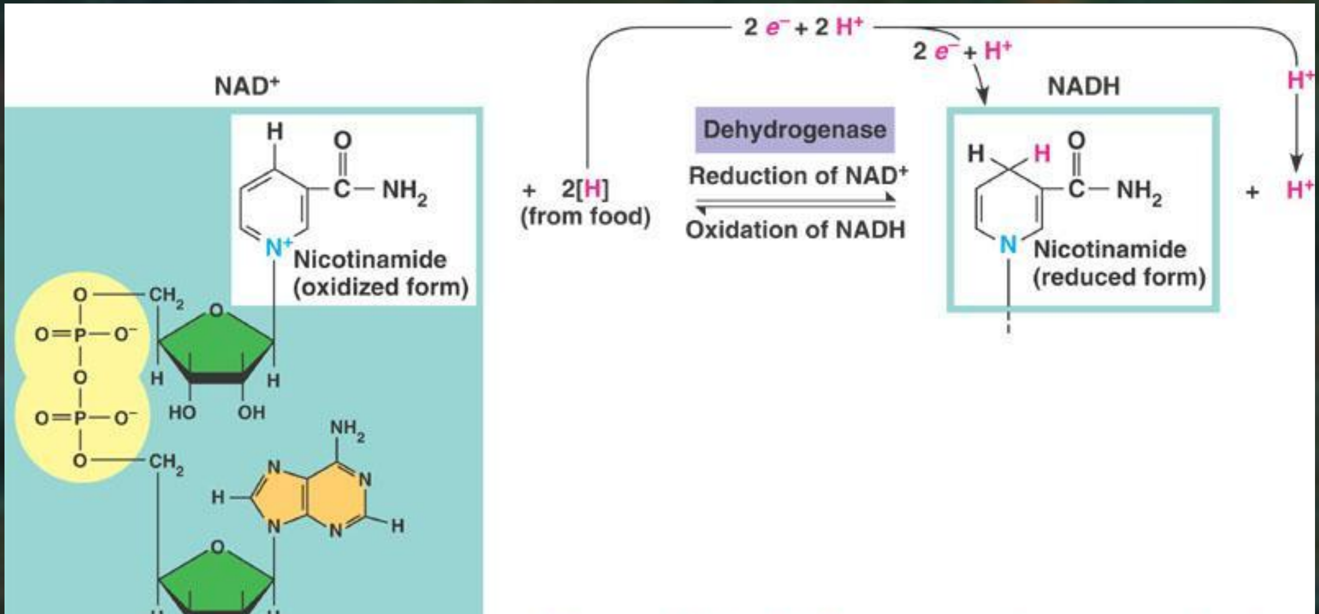


Figure 9.4. NAD+ as an electron shuttle.

- The full name for **NAD^+**, **nicotinamide adenine dinucleotide**, describes its structure; the molecule consists of two nucleotides joined together at their phosphate groups (shown in yellow). (Nicotinamide is a nitrogenous base, although not one that is present in DNA or RNA.) The enzymatic transfer of two electrons and one proton (H^+) from an organic molecule in food to NAD^+ reduces the NAD^+ to NADH, the second proton (H^+) is released. Most of the electrons removed from food are transferred initially to NAD^+.

REDOX REACTIONS: **FAD in Oxidation and Reduction**

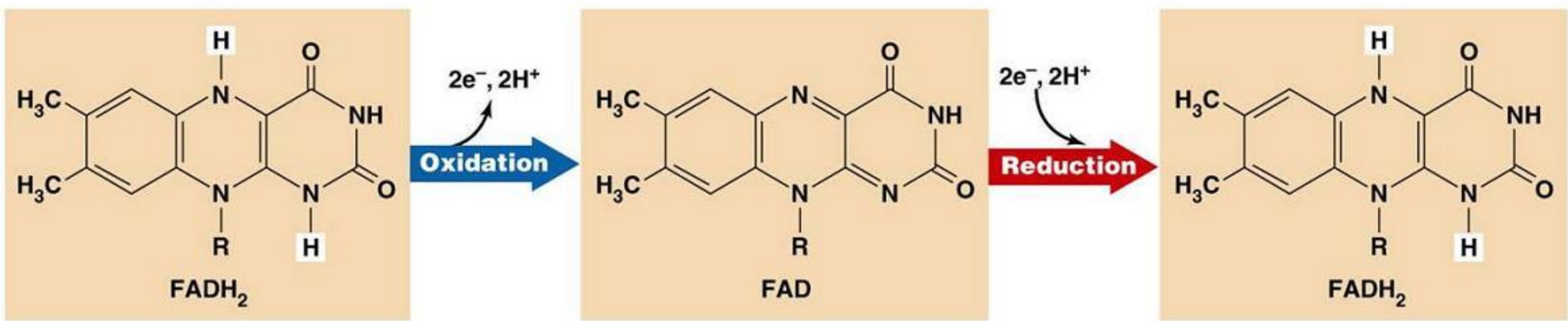
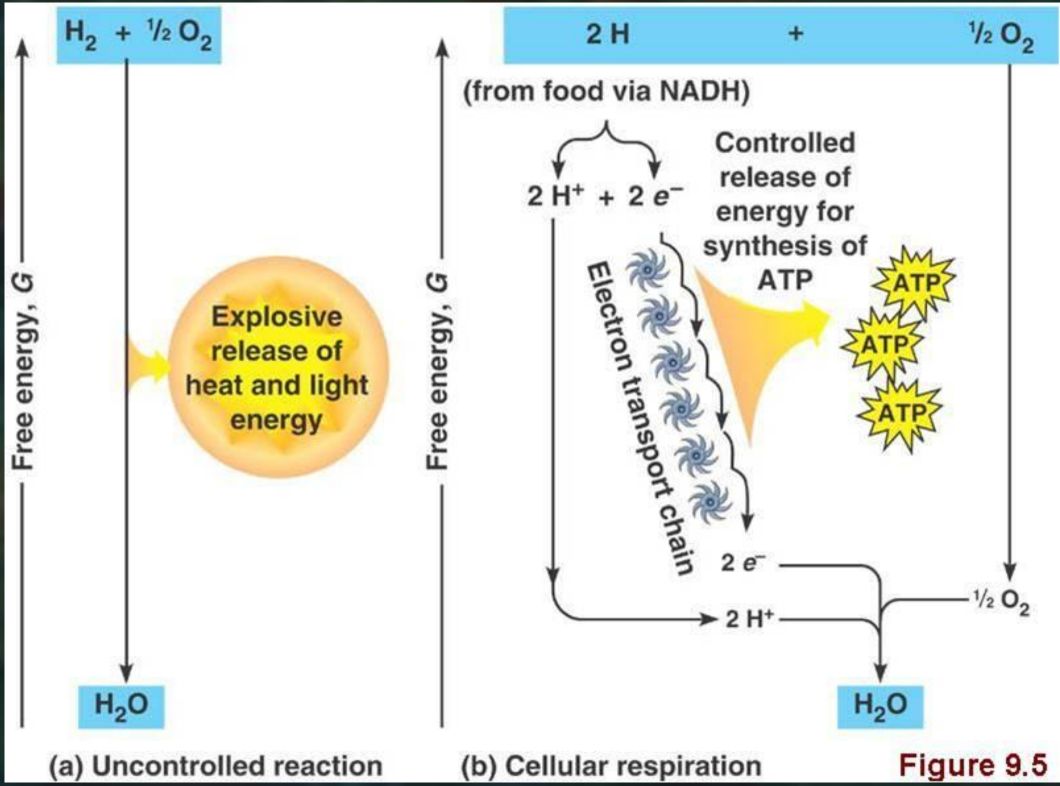


Figure 7.5. Oxidation and Reduction

- **FAD** (flavin adenine dinucleotide), another coenzyme of oxidation-reduction, is sometimes used instead of NAD^+. FAD accepts two electrons and two hydrogen ions (H^+) to become **$FADH_2$**.

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

- How do electrons that are extracted from glucose and stored as potential energy in NADH finally reach oxygen?



- **Figure 9.5: An introduction to electron transport chains.**

(a) The one-step exergonic reaction of hydrogen with oxygen to form water releases a large amount of energy in the form of heat and light: an explosion.

(b) In **cellular respiration**, the same reaction occurs in **stages**: An electron transport chain breaks the "fall" of electrons in this reaction into a series of smaller steps and stores some of the released energy in a form that can be used to make ATP. (The rest of the energy is released as heat.)

The Stages of Aerobic Cellular Respiration: ***A Preview***

1) **Glycolysis:** (*glyco* = sugar; *lysis* = splitting)

- **Glucose** is broken down in the cell's **cytoplasm** to **two** molecules of **pyruvate**. Oxidation by the removal of hydrogen atoms results in **NADH** and provides enough energy for the net yield of **two molecules of ATP** by *substrate phosphorylation*.
- Glycolysis is **anaerobic**, it does not require oxygen. It occurs in nearly all organisms.

The Stages of Aerobic Cellular Respiration: ***A Preview***

2) **Krebs Cycle (**also called **Citric Acid Cycle** or **Tricarboxylic Acid Cycle**):

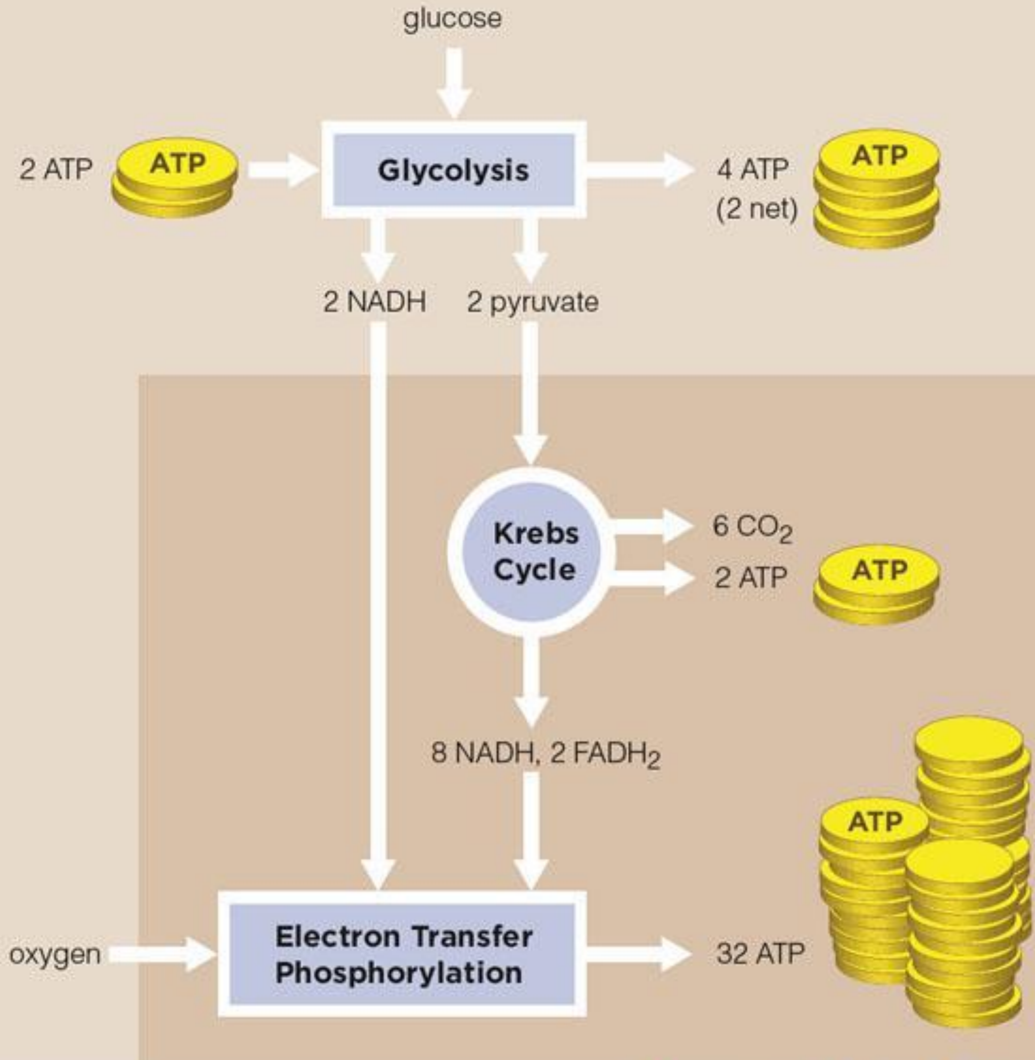
   a) ***Acetyl-CoA Formation (Preparatory [Prep] Reaction):*** Pyruvate enters a **mitochondrion** and is converted to a compound called acetyl-coenzyme A, or **acetyl-CoA**. **NADH** is formed; and the waste product **CO_2** is removed. Since glycolysis ends with two molecules of pyruvate, the prep reaction **occurs *twice* per glucose molecule**.

   b) ***Krebs Cycle:*** Series of oxidation reactions in the **matrix of the mitochondrion** that result in **NADH** and **$FADH_2$.** In addition, **CO_2** is given off and one **ATP** is produced. The **citric acid cycle turns twice** because two acetyl CoA molecules enter the cycle per glucose molecule. Altogether, the citric acid cycle accounts for **two immediate ATP** molecules per glucose molecule.

The Stages of Aerobic Cellular Respiration: *A Preview*

3) Oxidative Phosphorylation: *Electron Transport and Chemiosmosis* (*Electron Transfer Phosphorylation*):

- A series of **electron carriers** in the **inner mitochondrial membrane** (and the plasma membrane of aerobic prokaryotes) accept the electrons (from **NADH** and **$FADH_2$**) removed from glucose and pass them along from one carrier to the next until they are finally received by oxygen (**O_2**), which then combines with the hydrogen ions and becomes **water**.
- As the electrons pass from a higher-energy to a lower-energy state, energy is released and later used for **ATP** synthesis by **chemiosmosis**. The electrons from one glucose result in **32 or 34 ATP**, depending on certain conditions.



Cytoplasm

a The first stage, glycolysis, occurs in the cell's cytoplasm. Enzymes convert a glucose molecule to 2 pyruvate for a net yield of 2 ATP. During the reactions, 2 NAD^+ pick up electrons and hydrogen atoms, so 2 NADH form.

Mitochondrion

b The second stage, the Krebs cycle and a few steps before it, occurs inside mitochondria. The 2 pyruvates are broken down to CO_2, which leaves the cell. During the reactions, 8 NAD^+ and 2 FAD pick up electrons and hydrogen atoms, so 8 NADH and 2 $FADH_2$ form. 2 ATP also form.

c The third and final stage, electron transfer phosphorylation, occurs inside mitochondria. 10 NADH and 2 $FADH_2$ donate electrons and hydrogen ions at electron transfer chains. Electron flow through the chains sets up H^+ gradients that drive ATP formation. Oxygen accepts electrons at the end of the chains.

Figure 7.3. Overview of Aerobic Respiration.

Review: Cell Structures: **Cytoplasm**

- The thick, aqueous, semitransparent, and elastic substance or contents of a cell inside the plasma membrane (excluding the nucleus in eukaryotic cells); site of metabolic processes.
- The *fluid portion* of the cytoplasm is called the **cytosol**.
- About 80% water and contains proteins (enzymes), carbohydrates, lipids, inorganic ions, and many low-molecular-weight compounds.

FIGURE 5-3 - A generalized animal cell (an eukaryotic cell)

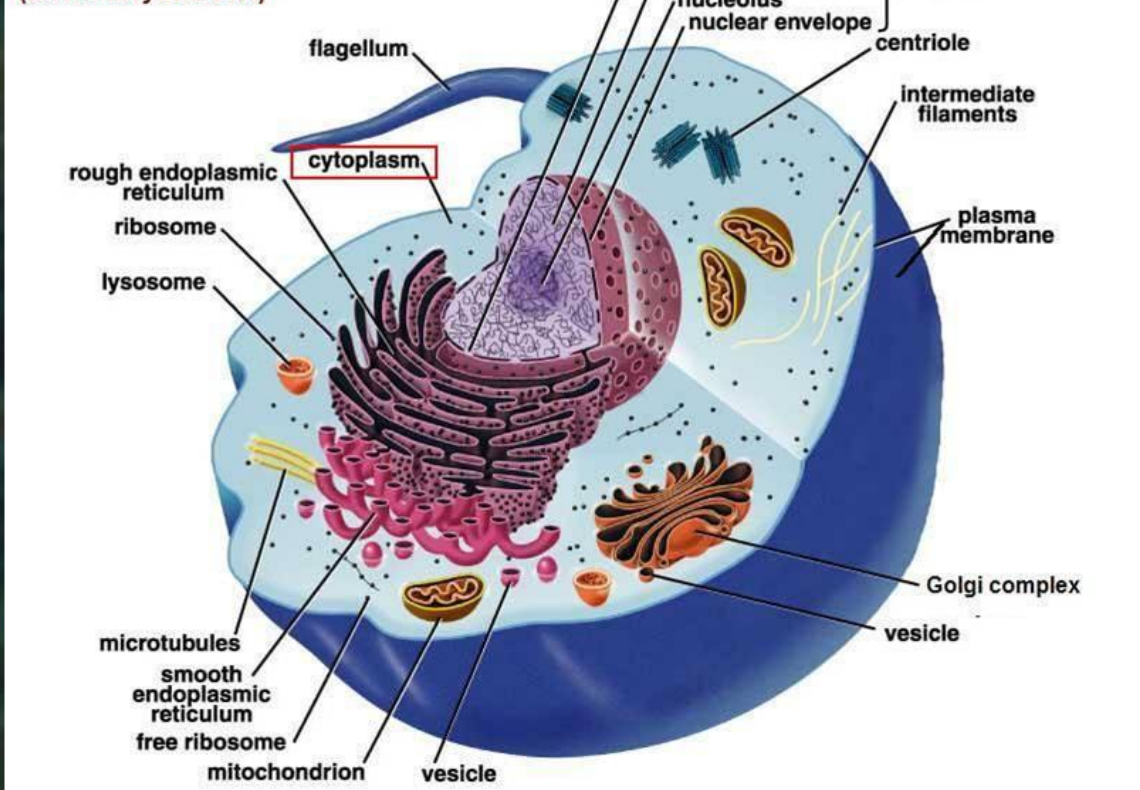
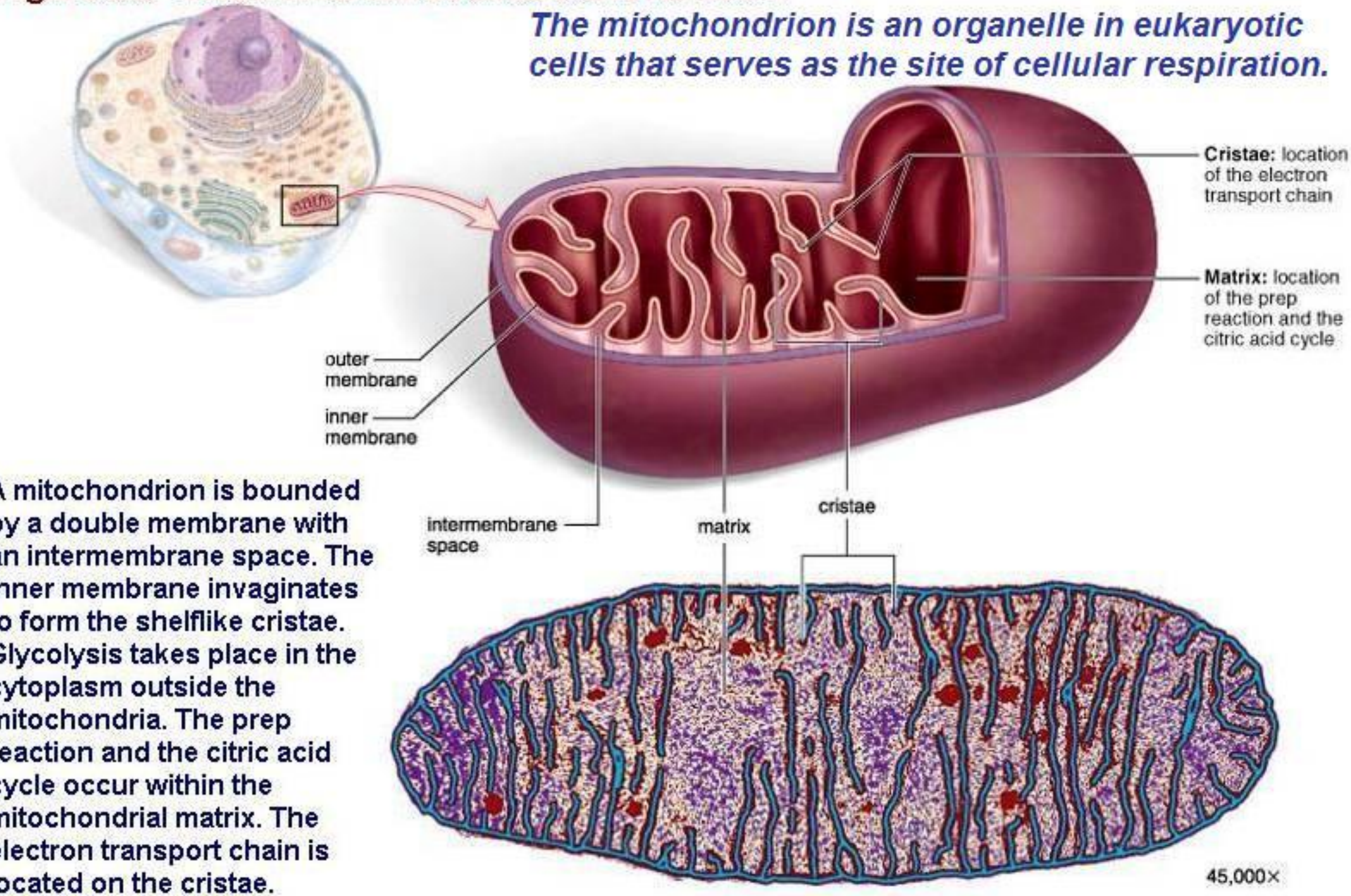
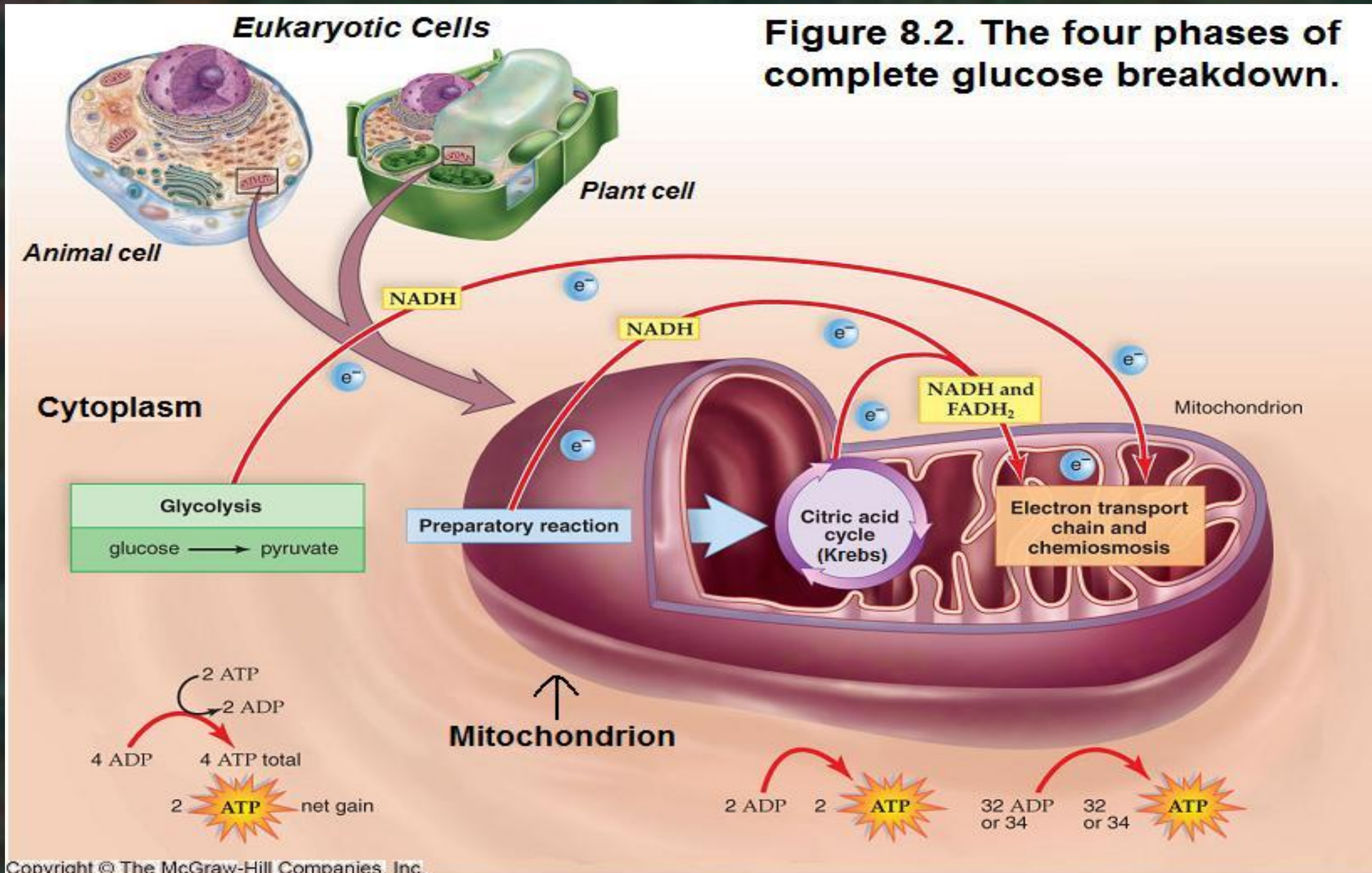


Figure 8.5 - Mitochondrion structure and function.

The mitochondrion is an organelle in eukaryotic cells that serves as the site of cellular respiration.



A mitochondrion is bounded by a double membrane with an intermembrane space. The inner membrane invaginates to form the shelflike cristae. Glycolysis takes place in the cytoplasm outside the mitochondria. The prep reaction and the citric acid cycle occur within the mitochondrial matrix. The electron transport chain is located on the cristae.

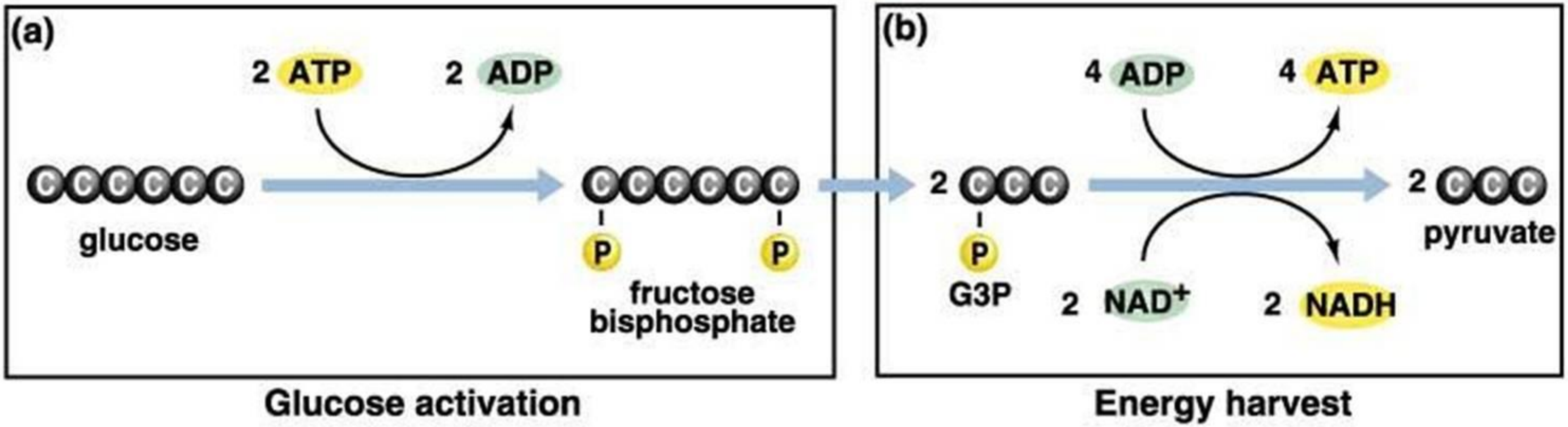


PHASES OF AEROBIC CELLULAR RESPIRATION

The complete **breakdown of glucose** consists of four phases. **Glycolysis** in the cytoplasm produces pyruvate, which enters the mitochondria if oxygen is available. The **preparatory reaction** and the **citric acid (Krebs) cycle** that follow occur inside the mitochondria. Also, inside the mitochondria, the **electron transport chain** receives the electrons that were removed from glucose breakdown products. The result of glucose breakdown is **36 or 38 ATP**, depending on the particular cell.

Stages of Cellular Respiration: **(1) Glycolysis (Summarized)**

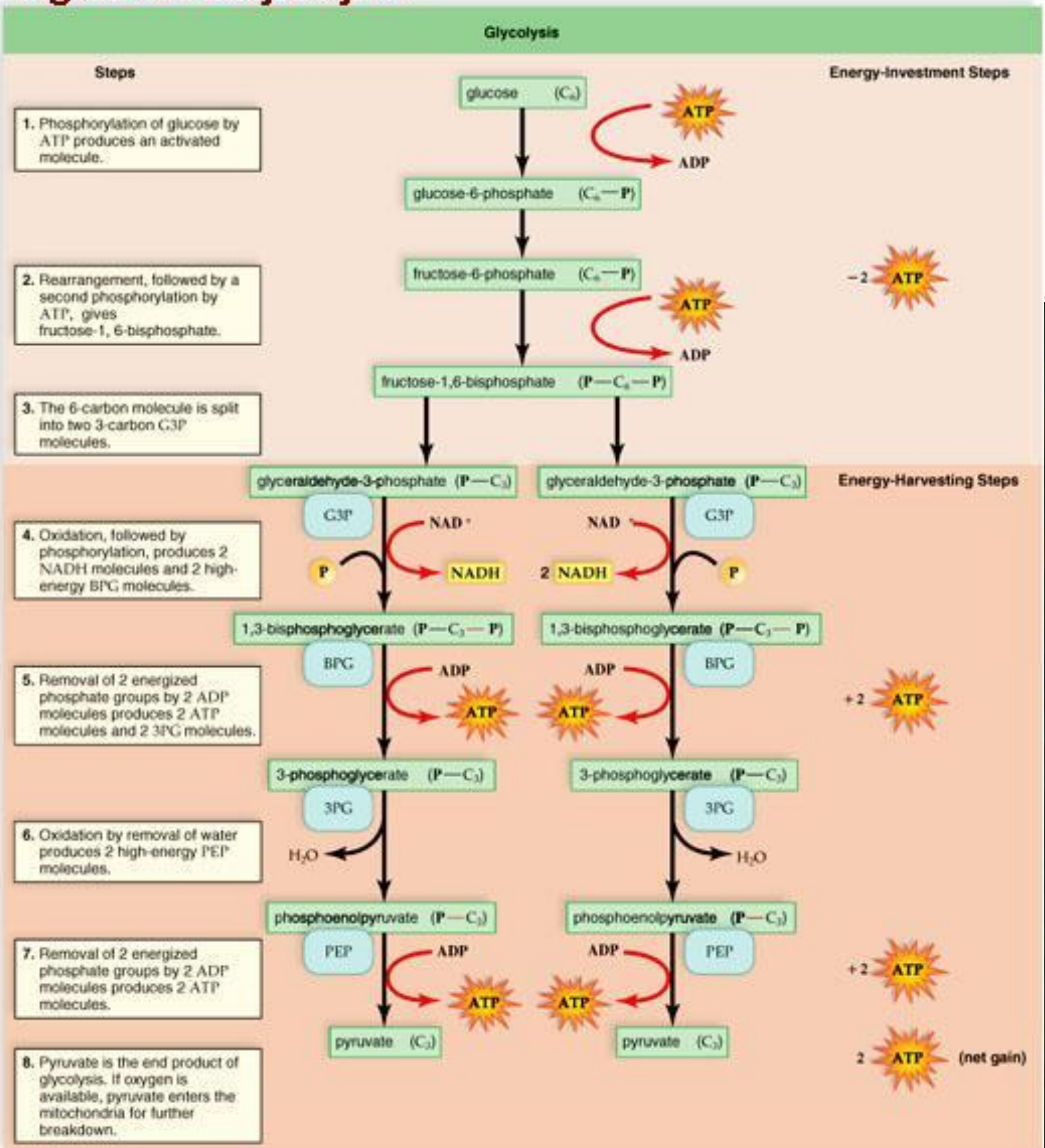
FIGURE 8-2. The Essentials of Glycolysis.



a) **Energy investment phase (glucose activation):** The energy of two ATP molecules is used to convert glucose to the highly reactive fructose bisphosphate, which splits into two reactive molecules of **G3P**.

b) **Energy payoff phase (ATP harvest or generation):** The two G3P molecules undergo a series of reactions that generate four ATP and two NADH molecules. Thus, glycolysis results in a net production of **two ATP**, **two NADH** and two **pyruvate** molecules per glucose molecule.

Figure 8.4. Glycolysis



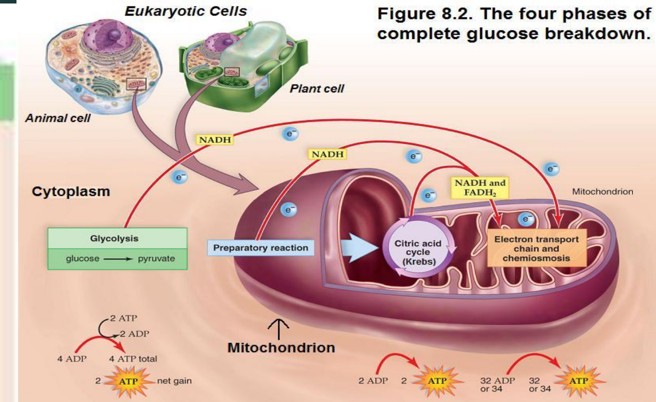


Figure 8.2. The four phases of complete glucose breakdown.

(1) Glycolysis

- The metabolic pathway begins with **glucose** and ends with **pyruvate**. Net gain of **two ATP** molecules can be calculated by subtracting those expended during the energy-investment steps from those produced during the energy-harvesting steps.

Stages of Cellular Respiration: **(1) Glycolysis**

- *When oxygen is available*, the end product of glycolysis, **pyruvate**, enters the mitochondria, where it undergoes further breakdown.
- If oxygen is not available, **fermentation** occurs in the cytoplasm and pyruvate undergoes reduction. In fermentation, glucose is incompletely metabolized to lactic acid (lactate) or to carbon dioxide and alcohol, depending on the organism (lactic acid in humans).
- Altogether, the inputs and outputs of glycolysis are as follows:

Glycolysis

Inputs (Reactants)	Outputs (Products)
glucose	**2 pyruvate**
2 NAD^+	**2 NADH**
2 ATP	2 ADP
4 ADP + 4 P	**4 ATP total**
	2 ATP net gain

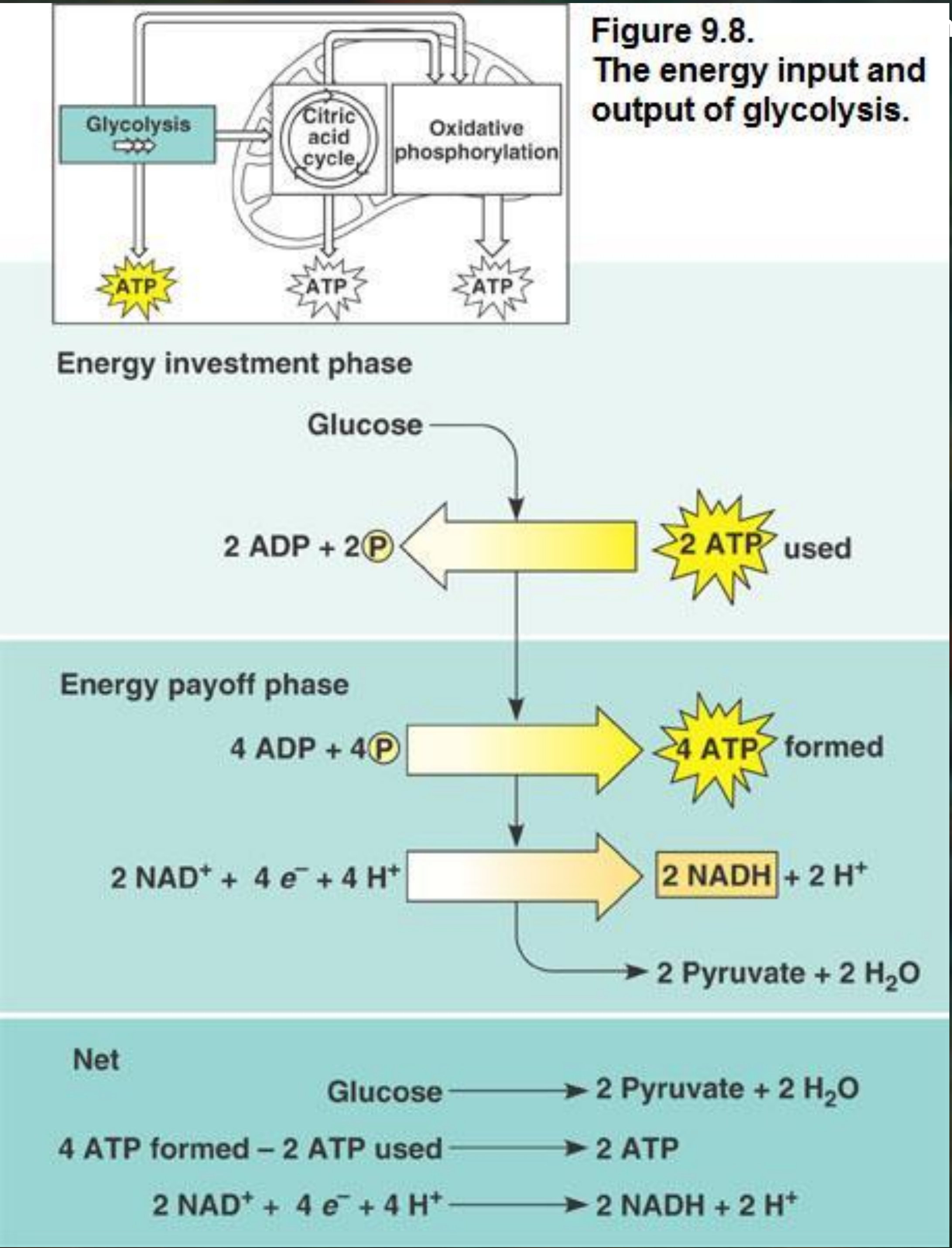
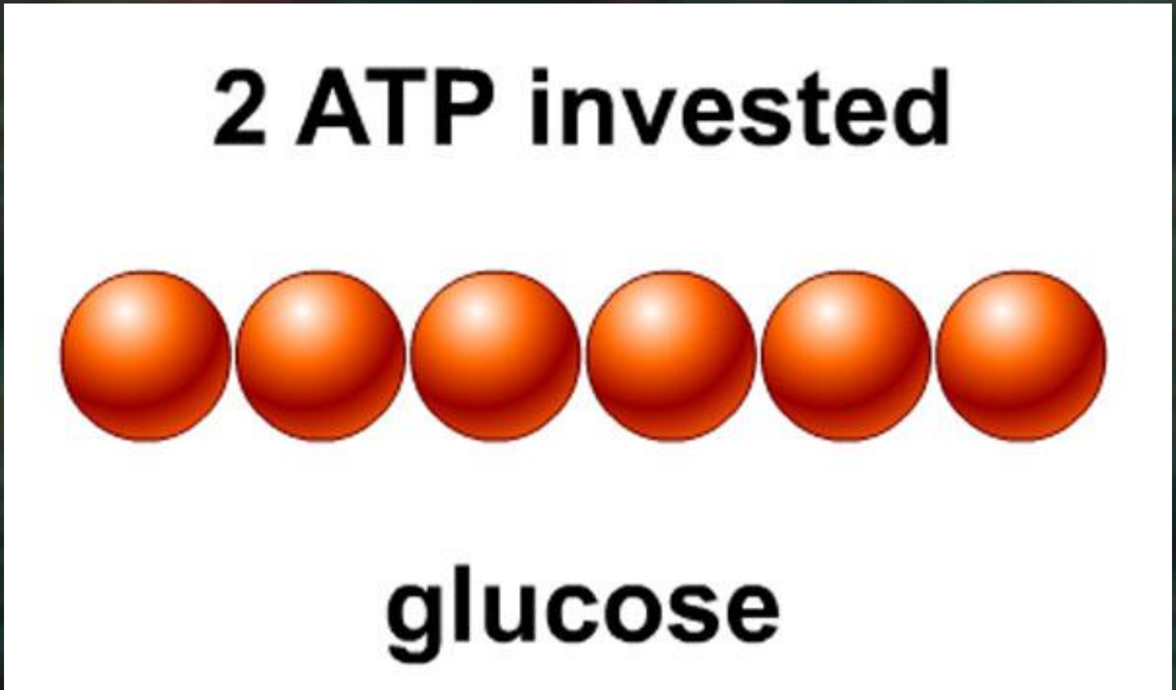


Figure 9.8. The energy input and output of glycolysis.

The Energy Input and Output of Glycolysis

- Glycolysis can be divided into two phases: *energy investment* and *energy payoff*.
- During the **energy investment phase**, the cell spends ATP. This investment is repaid with interest during the **payoff phase**, when ATP is produced.
- The net energy yield from glycolysis, per glucose molecule, is **2 ATP** plus **2 NADH**.

Animation: The Overall Reactions of Glycolysis



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Stages of Cellular Respiration: **(2-a) Conversion of Pyruvate to Acetyl CoA (*Preparatory Reaction* or *Pyruvate Oxidation*)**

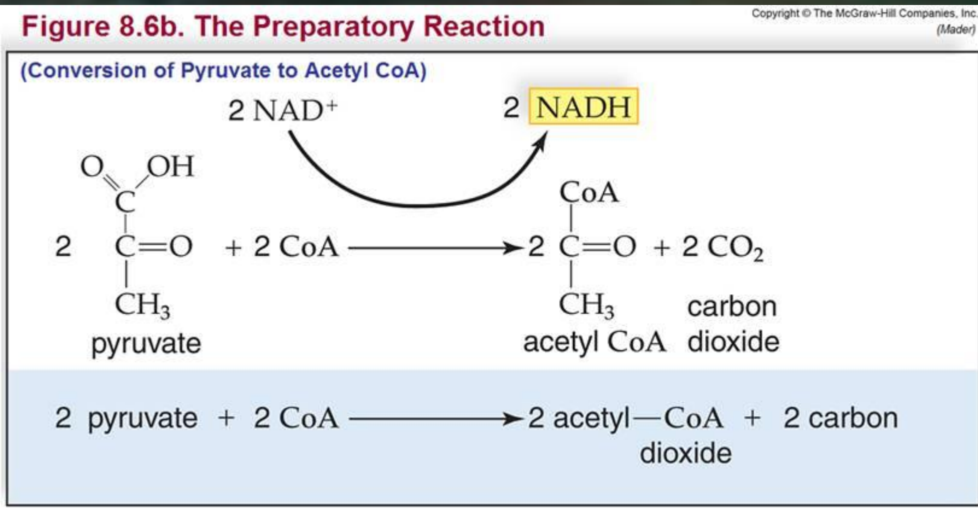


Figure 8.6b. The Preparatory Reaction

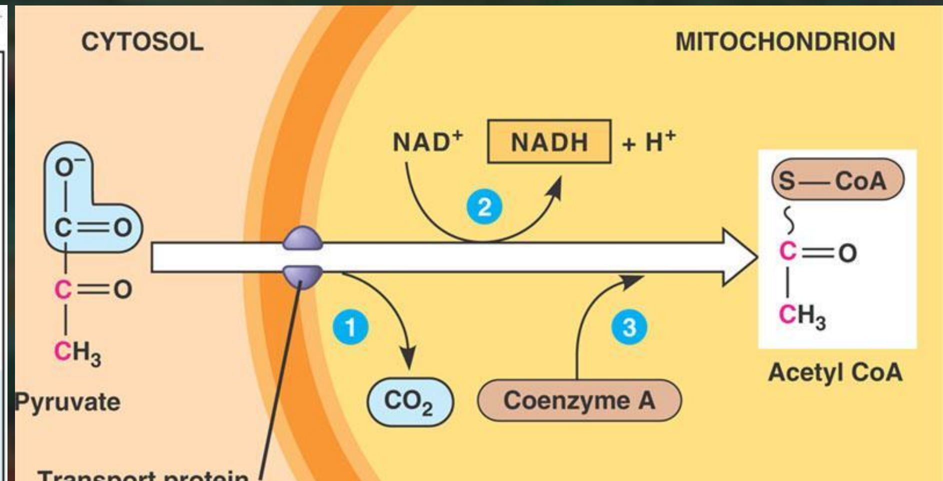
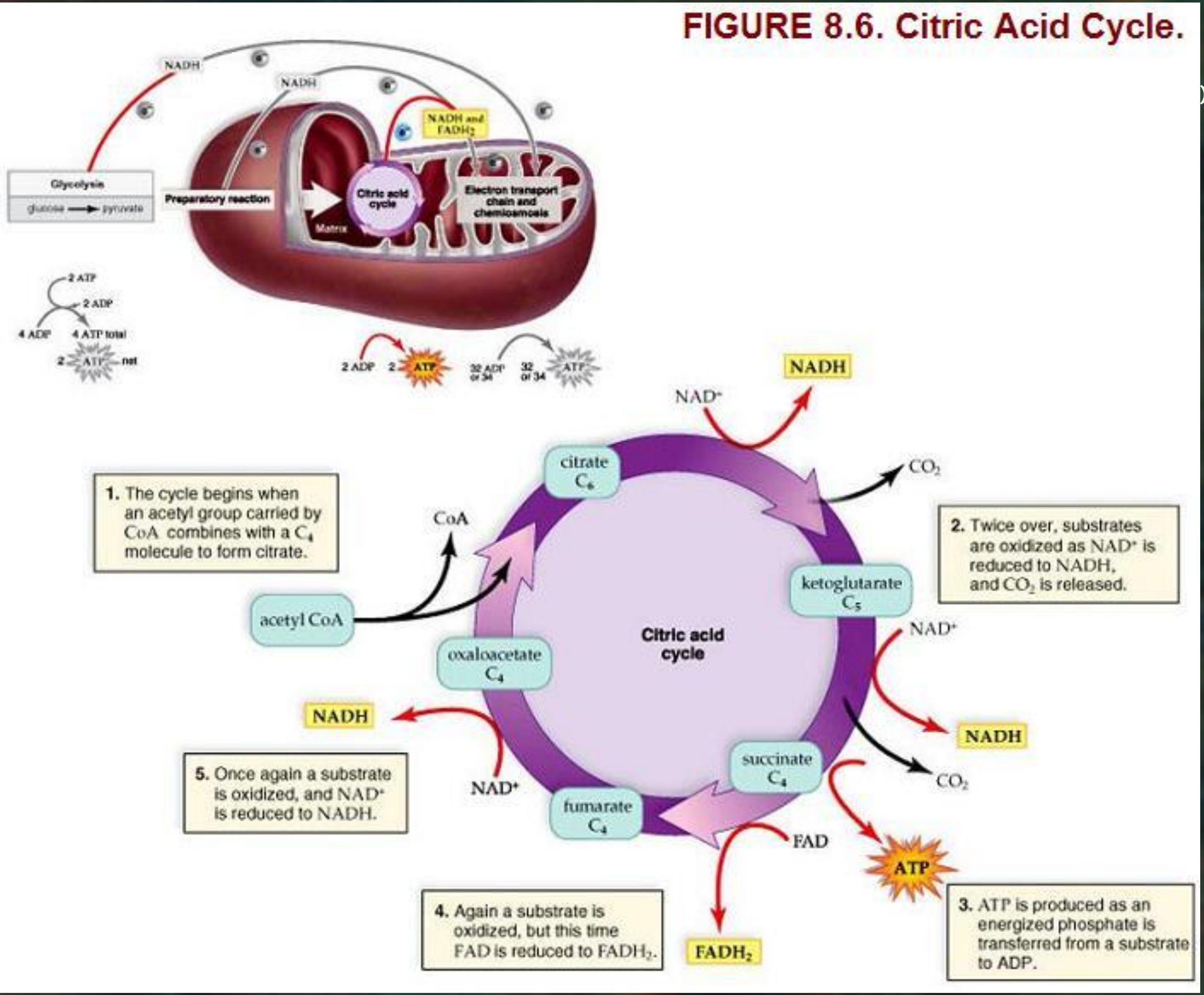


Figure 9.10. Conversion of pyruvate to acetyl CoA.

- The **preparatory (prep) reaction *(acetyl-CoA formation)*** is so called because it occurs before the Krebs cycle. In this reaction, **pyruvate** enters the mitochondrion with the help of a transport protein. Next, a complex of several enzymes (the pyruvate dehydrogenase complex) catalyze the three numbered steps (***formation of CO_2, NADH***, and ***acetyl CoA***). Pyruvate is converted to a **2-carbon (C_2) *acetyl group*** attached to ***coenzyme A***, or **CoA**, and **CO_2** is given off. This is an oxidation reaction in which electrons are removed from pyruvate by NAD^+, and NAD^+ goes to $NADH + H^+$ as **acetyl CoA** forms. This reaction **occurs twice** per glucose molecule. The **acetyl group** of acetyl CoA will enter the **Krebs cycle**. The CO_2 molecule will diffuse out of the cell.

Stages of Cellular Respiration: **(2-b) Citric Acid Cycle (Krebs Cycle)**



- The net result of this cycle is the oxidation of an **acetyl group** to **two** molecules of **CO_2** and the formation of **three** molecules of **NADH** and **one** molecule of **$FADH_2$**. **One ATP** molecule also results. *This cycle turns twice per glucose molecule*.

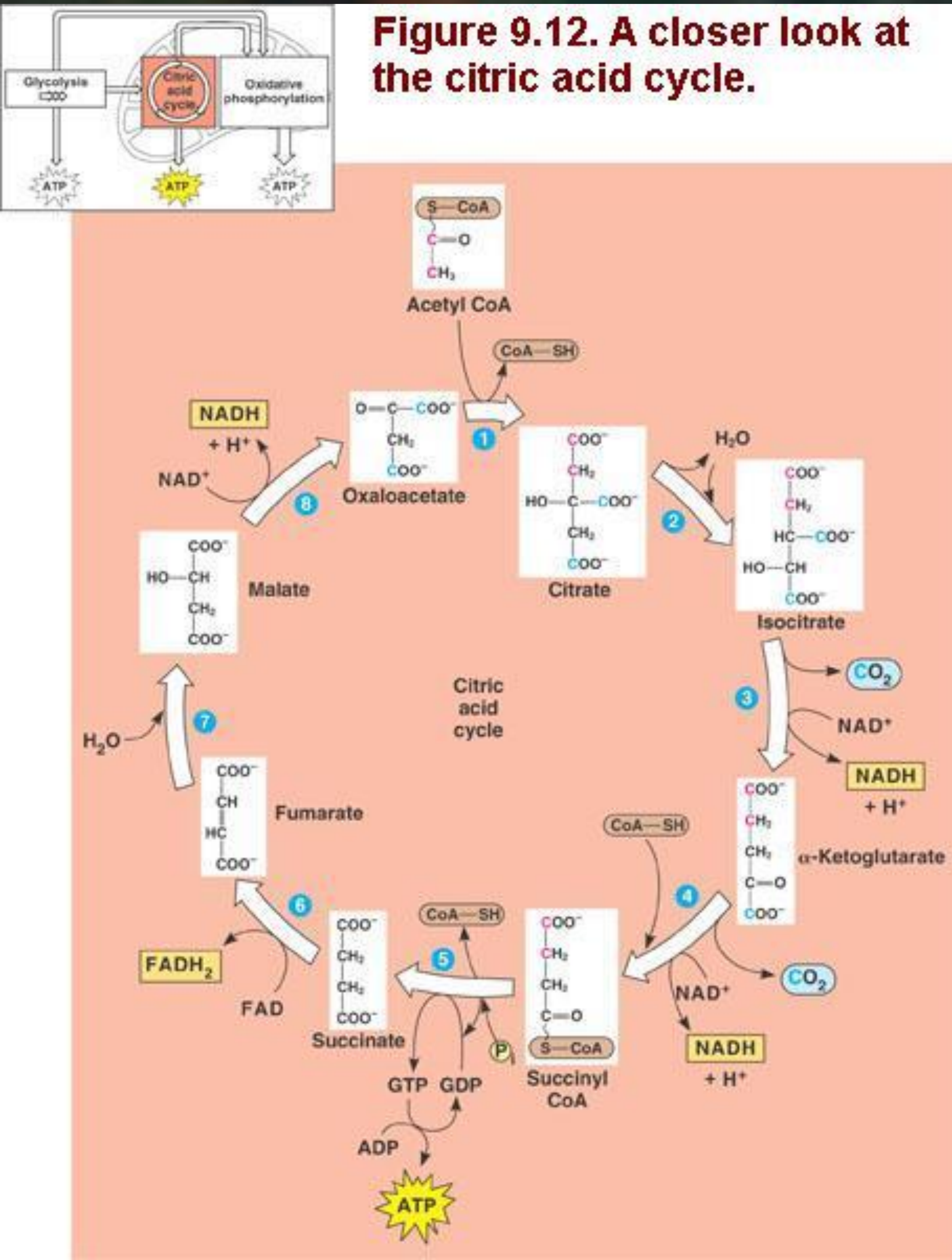


Figure 9.12. A closer look at the citric acid cycle.

A Closer Look at the Krebs Cycle (Citric Acid Cycle)

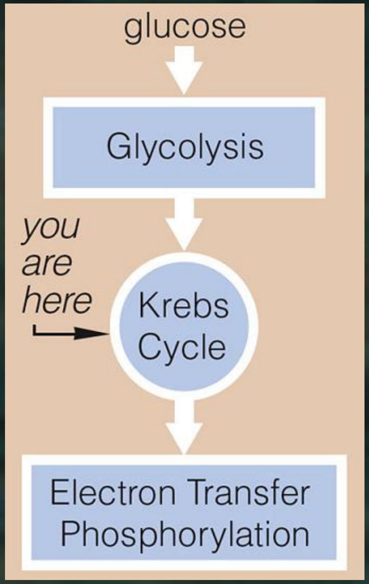
- The citric acid cycle has *eight steps*, each catalyzed by a specific enzyme. This process takes place in the cytoplasm of bacteria and in the mitochondrial matrix in eukaryotes.
- For each turn of the citric acid cycle, two carbons (red) enter in the relatively reduced form of an **acetyl group** (step 1), and two different carbons (blue) leave in the completely oxidized form of **CO_2** molecules (steps 3 and 4). The acetyl group of acetyl CoA joins the cycle by combining with oxaloacetate, forming citrate (1).
- The next 7 steps regenerate *citrate* back to *oxaloacetate*. *Note the production of **NADH**, **$FADH_2$**, and **ATP**.

Stages of Cellular Respiration: **(2) Citric Acid Cycle (Krebs Cycle)**

- Because the citric acid cycle ***turns twice*** for each original glucose molecule, the inputs and outputs of the citric acid cycle per glucose molecule are as follows:

Citric acid cycle

Inputs	Outputs
2 acetyl groups	4 **CO_2**
6 NAD^+	**6 NADH**
2 FAD	**2 $FADH_2$**
2 ADP + 2 **P**	2 **ATP**



- The six carbon atoms originally located in a glucose molecule have now become CO_2. The prep reaction produces two CO_2, and the Krebs cycle produces four CO_2 per glucose molecule.

Summary of Aerobic Cellular Respiration so Far (Before Oxidative Phosphorylation)

Process	Location	Reactions	Electron Carriers Formed	ATP Yield (per glucose molecule)
Glycolysis	Cytoplasm	Glucose broken down into 2 pyruvates	**2 NADH**	**2 ATP**
Acetyl CoA formation *(Prep reaction)*	*Mitochondria Matrix*	Pyruvate combined with CoA to form acetyl CoA and CO_2	**2 NADH**	
Krebs Cycle *(Citric Acid Cycle)*	*Mitochondria Matrix*	Acetyl group of acetyl CoA metabolized to 2 CO_2	**6 NADH, 2 $FADH_2$**	**2 ATP**

Stages of Cellular Respiration: **(3) Oxidative Phosphorylation (Electron Transport Chain and Chemiosmosis)**

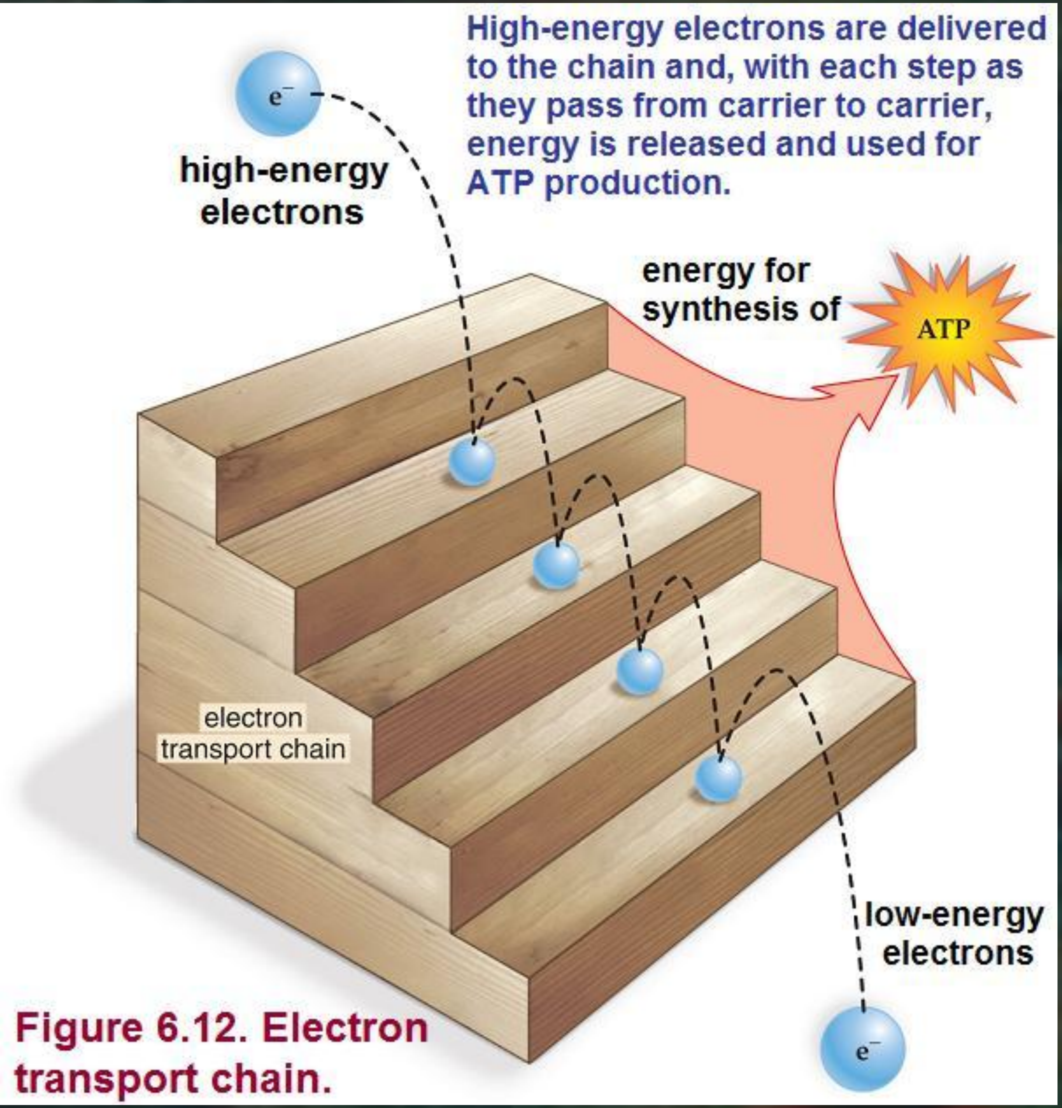


Figure 6.12. Electron transport chain.

- An **electron transport chain (ETC)** is a series of membrane-bound carriers that pass electrons from one carrier to another.
- *High-energy electrons* are delivered to the chain, and *low-energy electrons* leave it.
- If a hot potato were passed from one person to another, it would lose heat with each transfer. In the same manner, every time electrons are transferred to a new carrier, **energy is released**. The cell is able to capture the released energy and use it to produce **ATP** molecules.

Stages of Cellular Respiration: **(3) Electron Transport Chain**

- The ETC is made up of **multiprotein complexes** (designated **I** to **IV**) and other **electron carrier molecules**.
  - **Complex I:** NADH dehydrogenase (reductase)
  - **Complex II:** succinate reductase
  - **Complex III:** cytochrome $b\text{-}c_1$
  - **Complex IV:** cytochrome oxidase
  - **Flavoprotein:** has FMN (flavin mononucleotide)
  - **Iron-sulfur protein (Fe·S):** with iron and sulfur tightly bound
  - **Ubiquinone (Q):** not a protein; a small molecule that is mobile within the membrane (also called **coenzyme Q** or **CoQ**)
  - **Cytochromes:** have a heme group and an iron atom

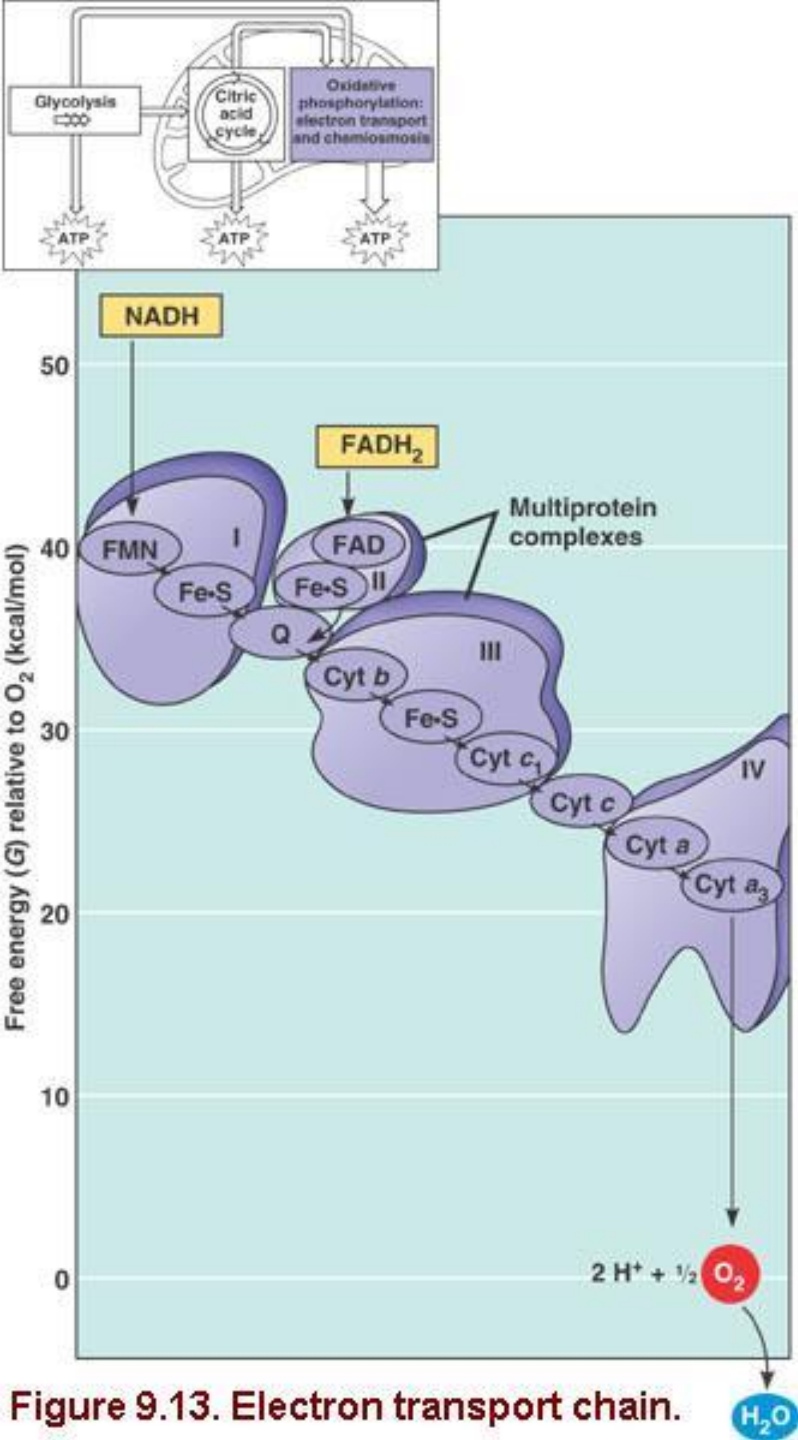


Figure 9.13. Electron transport chain.

Electron Transport Chain (ETC)

- Electrons from **NADH** are transferred to FMN and Fe-S in complex I.
- The electrons are then transferred to ubiquinone (Q), which is mobile.
- From Q, electrons pass to cytochromes and Fe-S in complex III.
- From complex III, the electrons are transferred to cytochromes in complex IV.
- Cyt a_3 in complex IV passes its electrons to oxygen.
- Each oxygen atom also picks up a pair of hydrogen ions, forming water.
- **$FADH_2$** is also a source of electrons. It passes its electron to complex II, then to the rest of the chain.

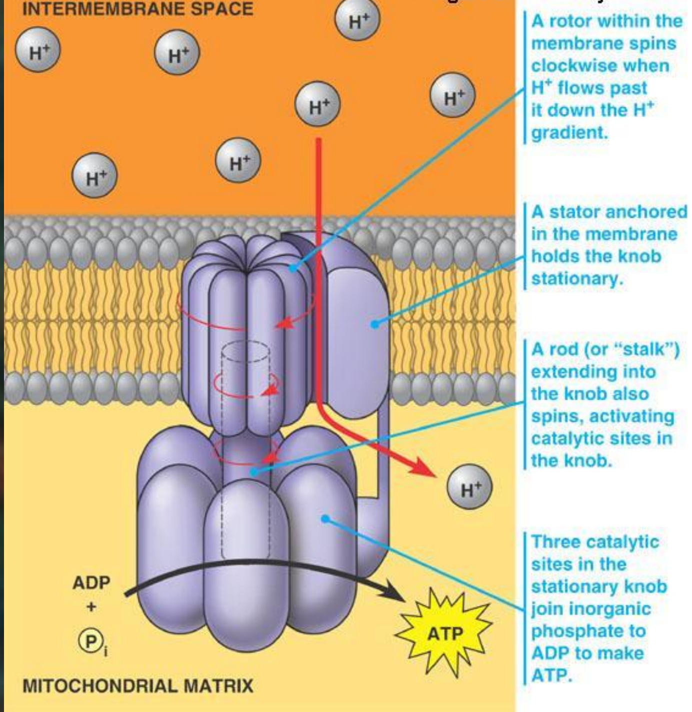
Stages of Cellular Respiration: **(3) Electron Transport Chain**

- *The electron transport chain makes **no ATP directly***. Its function is to ease the fall of electrons from food to oxygen, breaking a large free-energy drop into a series of smaller steps that **release energy in manageable amounts**.
- How does the mitochondrion couple this electron transport and energy release to **ATP synthesis**?
  - Answer: through a process called **chemiosmosis**, an energy-coupling mechanism that uses energy stored in the form of a ***hydrogen ion (H^+) gradient*** across a membrane to drive cellular work, such as the synthesis of ATP. (*** See next slides.)

Chemiosmosis: ATP Production

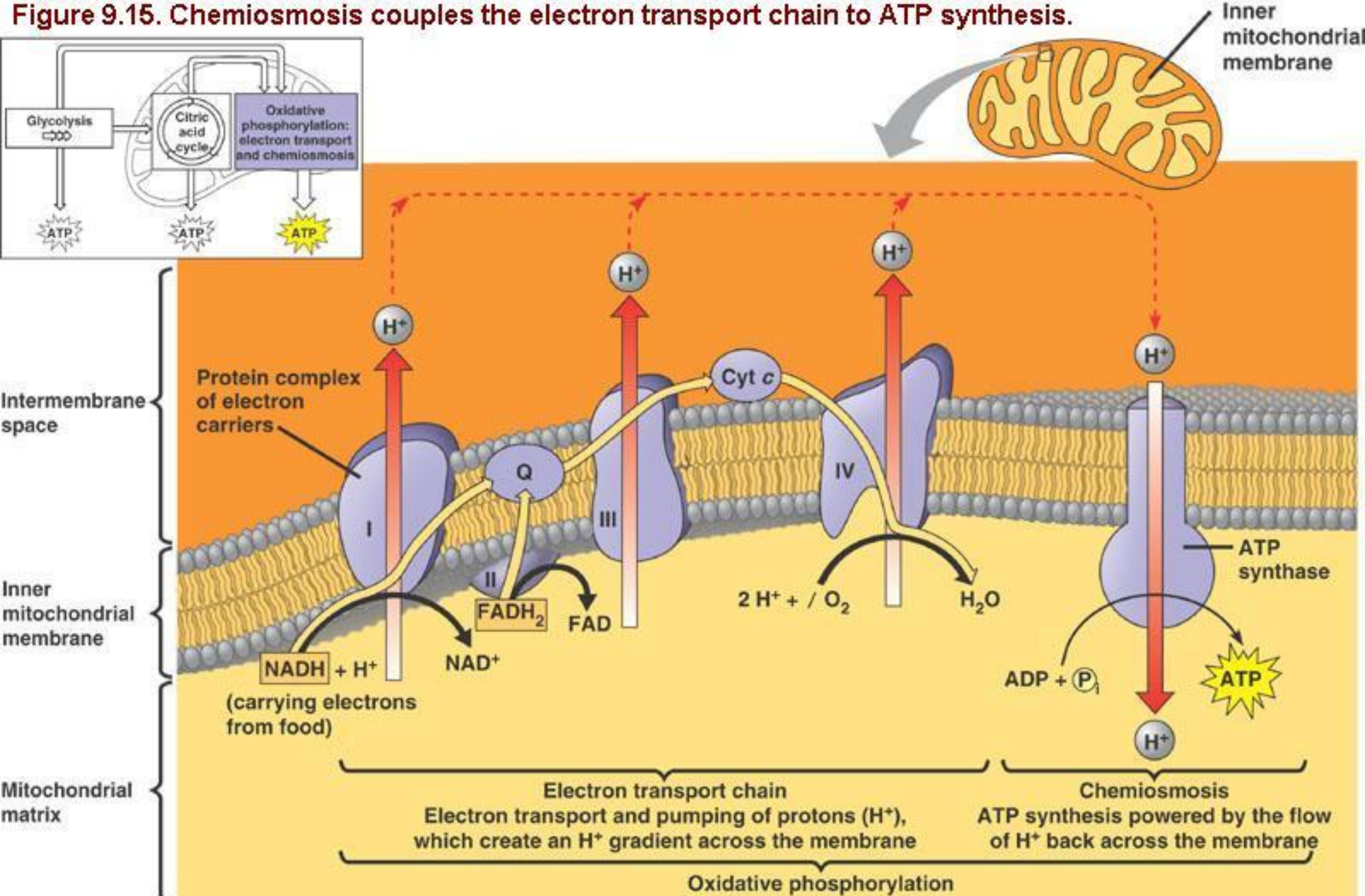
- At certain steps along the electron transport chain, electron transfer causes protein complexes to move **hydrogen ions (H^+)** from the mitochondrial matrix to the **intermembrane space,** storing energy as an **electrochemical gradient** (**proton-motive force** or **proton gradient**).
- As H^+ diffuses back into the matrix through **ATP synthase**, this enzyme synthesizes **ATP** from **ADP + phosphate (P_i)** (*phosphorylation*). This process is called **chemiosmosis** because ATP production is tied to the establishment of an H^+ gradient.
- Once formed, ATP moves out of mitochondria and is used to perform cellular work.

Figure 9.14. ATP synthase.



The production of ATP using energy derived from the redox reactions of an electron transport chain is called **oxidative phosphorylation**.

Figure 9.15. Chemiosmosis couples the electron transport chain to ATP synthesis.



*** **Figure 9.15** – Chemiosmosis couples the electron transport chain to ATP synthesis. ***

- NADH and $FADH_2$ shuttle high-energy electrons extracted from food during glycolysis and the citric acid cycle to an electron transport chain built into the inner mitochondrial membrane. The yellow arrow traces the transport of electrons, which finally pass to oxygen at the "downhill" end of the chain, forming water. As Figure 9.13 showed, most of the electron carriers of the chain are grouped into four complexes. Two mobile carriers, ubiquinone (Q) and cytochrome *c* (Cyt *c*), move rapidly along the membrane, ferrying electrons between the large complexes. As complexes I, III and IV accept and then donate electrons, they pump hydrogen ions (protons) from the mitochondrial matrix into the intermembrane space. (Note that $FADH_2$ deposits its electrons via complex II and so results in fewer protons being pumped into the intermembrane space than NADH.) Chemical energy originally harvested from food is transformed into a proton-motive force, a gradient of H^+ across the membrane. The hydrogen ions flow back down their gradient through a channel in an ATP synthase, another protein complex built into the membrane. The ATP synthase harnesses the proton-motive force to phosphorylate ADP, forming ATP. The use of an H^+ gradient (proton-motive force) to transfer energy from redox reactions to cellular work (ATP synthesis, in this case) is called chemiosmosis. Together, electron transport and chemiosmosis compose <u>oxidative phosphorylation</u>.

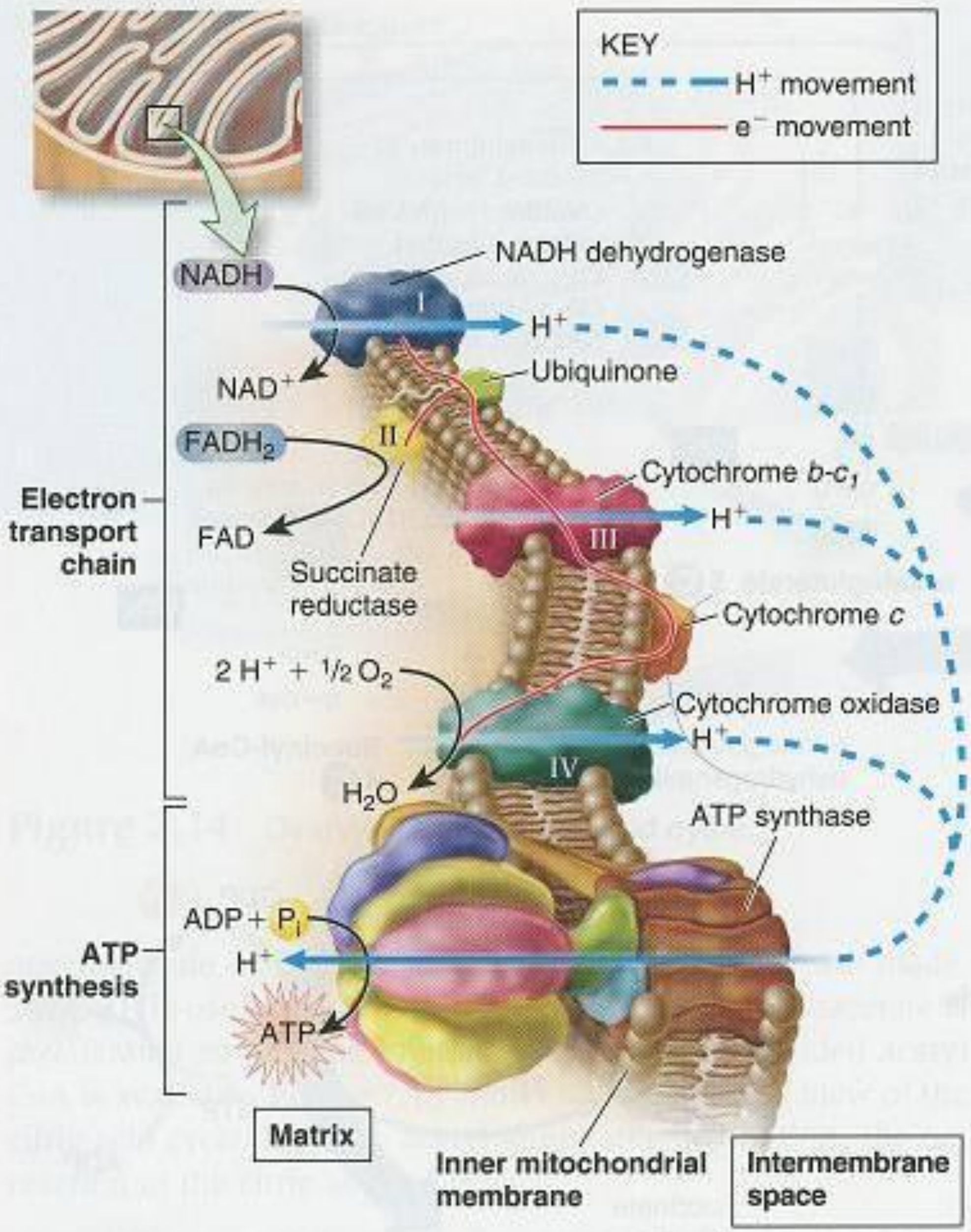


Figure 7.16. Oxidative phosphorylation (Electron transport chain & chemiosmosis)

Oxidative Phosphorylation

- This process consists of two distinct events involving the **electron transport chain** and the **ATP synthase**.
- The electron transport chain removes electrons from NADH or $FADH_2$ and pumps H^+ across the inner mitochondrial membrane.
- The ATP synthase uses the energy in the electrochemical gradient of H^+ (hydrogen ions) to synthesize ATP (chemiosmosis).

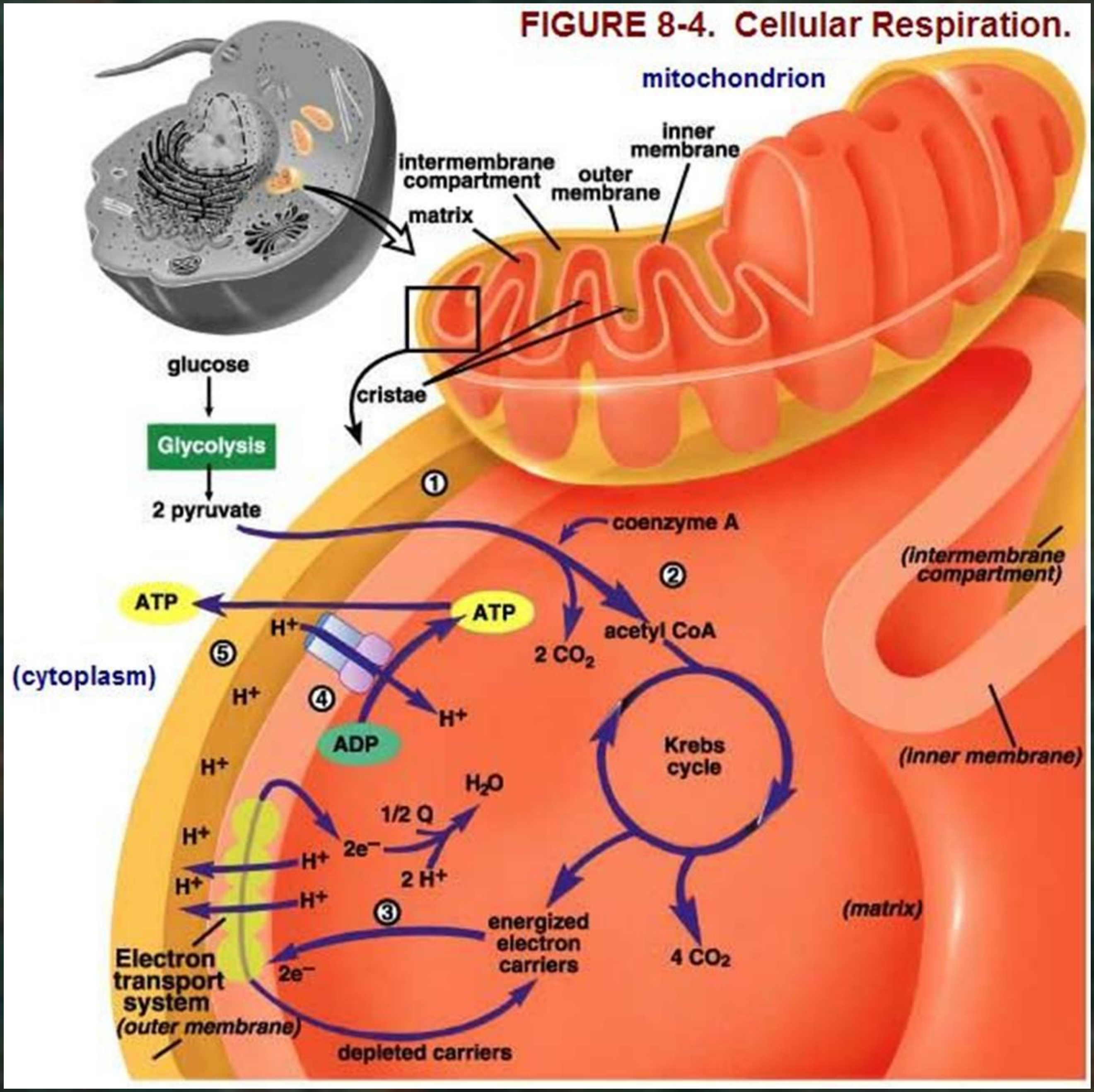


FIGURE 8-4. Cellular Respiration.
mitochondrion
inner membrane
intermembrane compartment
outer membrane
matrix
cristae
glucose
Glycolysis
2 pyruvate
①
coenzyme A
②
(intermembrane compartment)
ATP
ATP
H+
acetyl CoA
2 CO2
⑤
(cytoplasm)
H+
④
H+
Krebs cycle
ADP
H+
(inner membrane)
H2O
1/2 O
H+
H+
2e–
H+
2 H+
H+
H+
③
energized electron carriers
(matrix)
Electron transport system
(outer membrane)
2e–
4 CO2
depleted carriers

Summary of Main Events of Cellular Respiration

- Figure 8-4 details (previous slide):

1) The two molecules of pyruvate produced by **glycolysis** (in the cytoplasm) are transported across both mitochondrial membranes and into the matrix.
2) Each **pyruvate** is split into CO_2 and a two-carbon acetyl group (**acetyl-CoA**) (prep reaction), which enters the ***citric acid cycle (Krebs cycle)*** (in the mitochondrion). This cycle releases the remaining carbons as CO_2, produces **one ATP from each pyruvate**, and donates energetic electrons to several **electron-carrier molecules** (**NADH** and **$FADH_2$**).
3) The electron carriers donate their energetic electrons to the **electron transport chain** of the mitochondrial inner membrane. There the energy of the electrons is used to transport **H^+** from the matrix to the intermembrane compartment. At the end of the chain, the electrons combine with **O_2** and **H^+** to form H_2O. Depleted carriers are reused in the Krebs cycle.
4) In **chemiosmosis**, the **hydrogen ion gradient** created by the electron transport chain discharges through **ATP-synthesizing enzymes** in the inner membrane, and the energy is used to produce **ATP**.
5) **ATP** is transported out of the mitochondrion into the fluid of the cytoplasm, where it provides energy for cellular activities.

Table 8-1 Summary of Glycolysis and Cellular Respiration of a Molecule of Glucose

Process	Location	Reactions	Electron Carriers Formed	ATP Yield (per glucose molecule)
Glycolysis	Fluid cytoplasm	Glucose broken down into two pyruvates	2 NADH	2 ATP
Cellular Respiration	Mitochondria			
Acetyl CoA formation	Matrix	Pyruvate combined with CoA to form acetyl CoA and CO_2	2 NADH	
Krebs cycle	Matrix	Acetyl group of acetyl CoA metabolized to two CO_2	6 NADH, 2 $FADH_2$	2 ATP
Electron transport	Inner membrane and intermembrane compartment	Energetic electrons from NADH and $FADH_2$ used to create a H^+ gradient, which is used to synthesize ATP **(chemiosmosis)**		32 or 34 ATP*

* Glycolysis produces two NADH molecules in the fluid portion of the cytoplasm. The electrons from these two NADH molecules must be transported into the matrix before they can enter the electron transport chain. In most eukaryotic cells, the energy of 1 ATP molecule is used to transport the electrons from each NADH molecule into the matrix. Thus, the 2 "glycolytic NADH" molecules net only 2 ATPs, not the usual 3, during electron transport. The heart and liver cells of mammals, however, use a different transport chain, one that does not consume ATP. In these cells, the 2 NADH molecules produced during glycolysis net 3 ATPs apiece, just as the "mitochondrial NADH" molecules do.

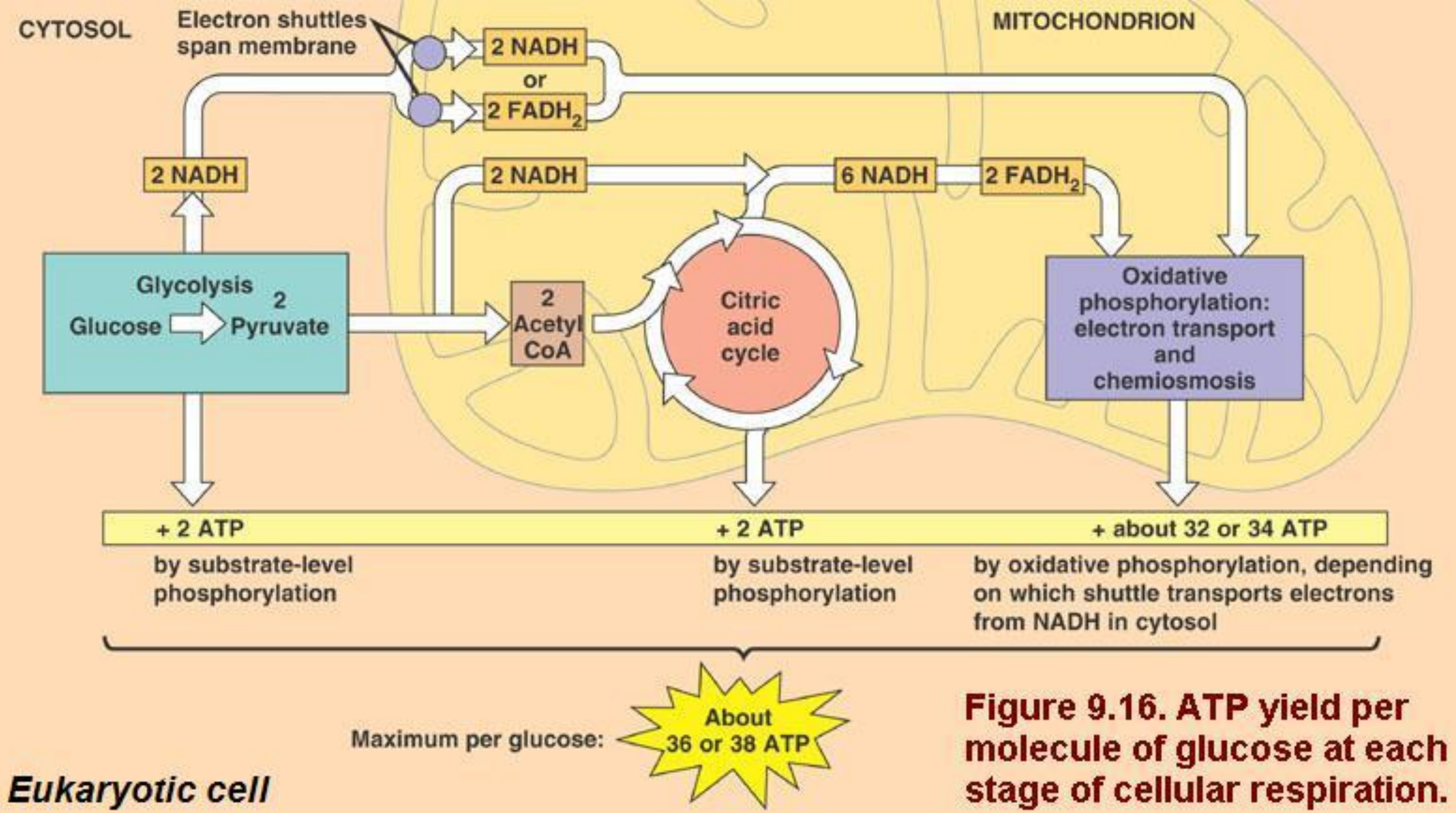
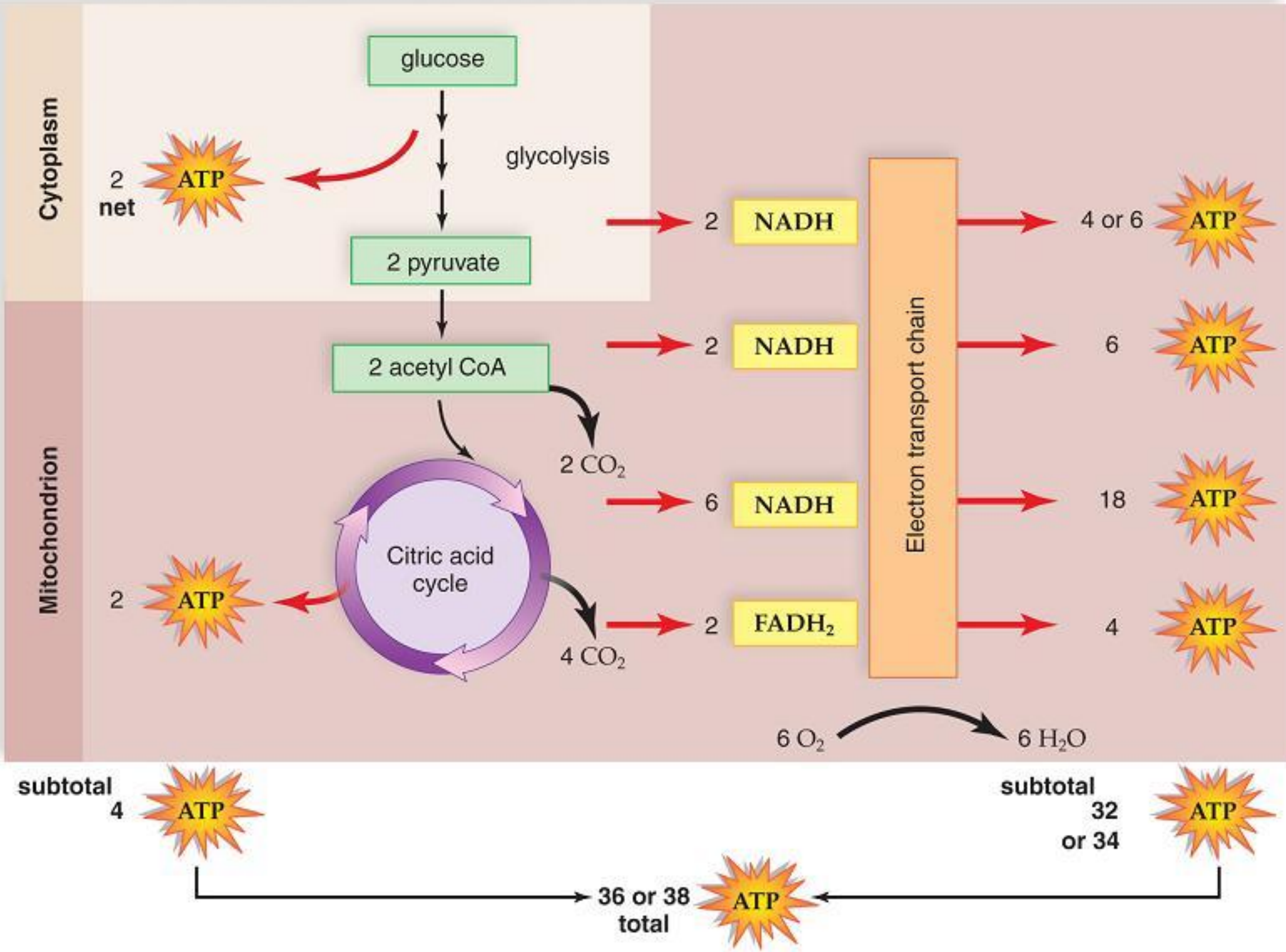


Figure 9.16. ATP yield per molecule of glucose at each stage of cellular respiration.

The two electrons of NADH captured in glycolysis must be conveyed into the mitochondrion by one of several electron shuttle systems. Depending on the type of shuttle in a particular cell type, the electrons are passed either to NAD^+ or to FAD in the mitochondrial matrix. If the electrons are passed to FAD, as in brain cells, only about 2 ATP can result from each cytosolic NADH. If the electrons are passed to mitochondrial NAD^+, as in liver cells and heart cells, the yield is about 3 ATP.

Figure 8.10. Energy yield per glucose molecule breakdown.



Anaerobic Catabolism of Glucose: **Anaerobic Respiration and Fermentation**

- In cellular respiration, **glycolysis** generates **2 ATP** whether oxygen is present or not—that is, whether conditions are ***aerobic*** or ***anaerobic*** (from the Greek *"aer"*, air, and "*bios"*, life; the prefix *an-* means without).
- **Anaerobic respiration** is used by certain prokaryotic organisms (anaerobic bacteria) that live in environments without oxygen. These organisms have an electron transport chain but ***do not use oxygen*** as a final electron acceptor. Compounds such as nitrate, nitrite, or sulfate serve this function.
- **Fermentation** is the *anaerobic* breakdown of glucose that results in the end products **ethanol (ethyl alcohol)** or acid, such as **lactic acid (lactate)**, with a gain of **2 ATP.** Fermentation ***does not use oxygen or an electron transport chain***.
  - **Pyruvate**, the end product of glycolysis, is reduced by NADH to either **alcohol** and **carbon dioxide** or to **lactic acid (lactate)**.

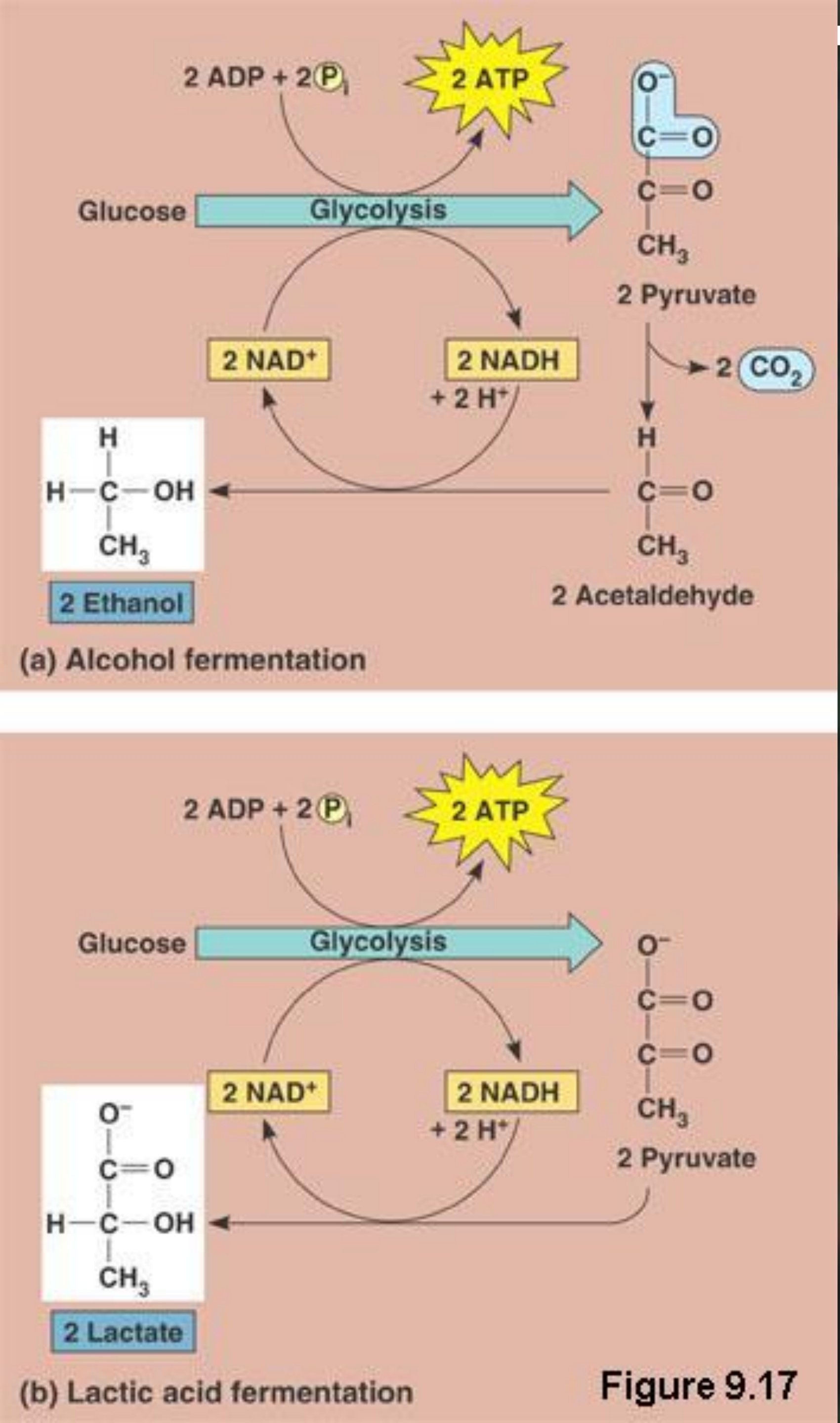
Anaerobic Catabolism of Glucose: Fermentation

1. Alcoholic Fermentation

- Produces ethanol (ethyl alcohol) and CO_2 from sugars.
- Used by many bacteria and yeast (a fungus).
- Used to make bread and alcoholic beverages (beer, wine, etc.).

2. Lactic Acid Fermentation

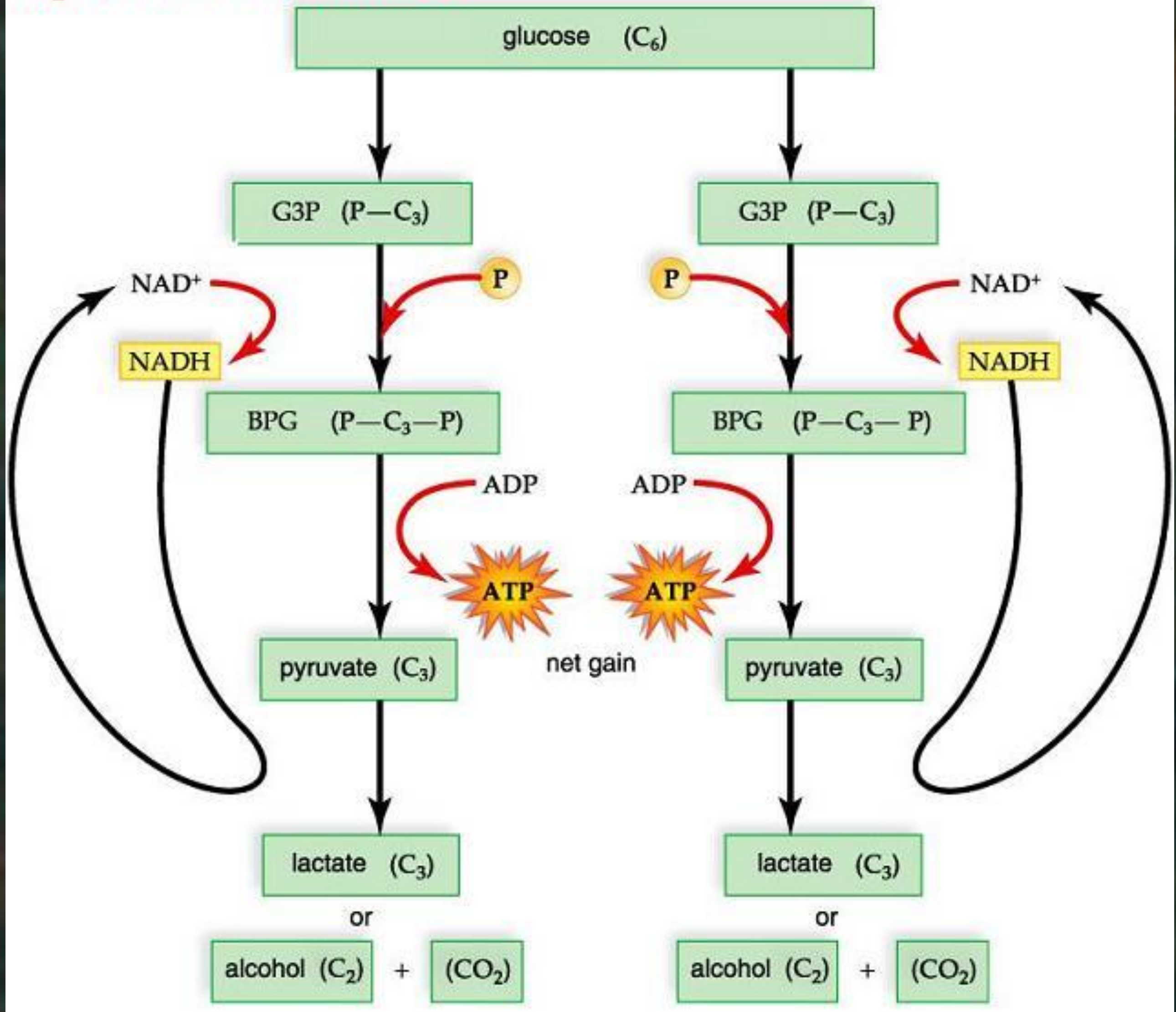
- Produces lactic acid (lactate) as the sole or primary product.
- Used by animals (including humans), certain bacteria, and fungi.
- Animal muscle tissue ferments pyruvate to lactate when oxygen is not being delivered to cells.
- Lactic acid fermentation by certain fungi and bacteria is used in the production of cheese, sour cream, yogurt, and sauerkraut.



Fermentation

- In the absence of oxygen, many cells use **fermentation** to produce ATP by substrate-level phosphorylation.
- **Pyruvate (pyruvic acid)**, the end product of ***glycolysis***, serves as an electron acceptor for oxidizing NADH back to NAD^+, which can then be reused in glycolysis.
- Two of the common end products formed from fermentation are ***(a)*** **ethanol** and ***(b)*** **lactate**, the ionized form of lactic acid.

Figure 8.10 - Fermentation



- **Fermentation** consists of *glycolysis* followed by a reduction of *pyruvate*. This "frees" NAD^+ and it returns to the glycolytic pathway to pick up more electrons.

Fermentation

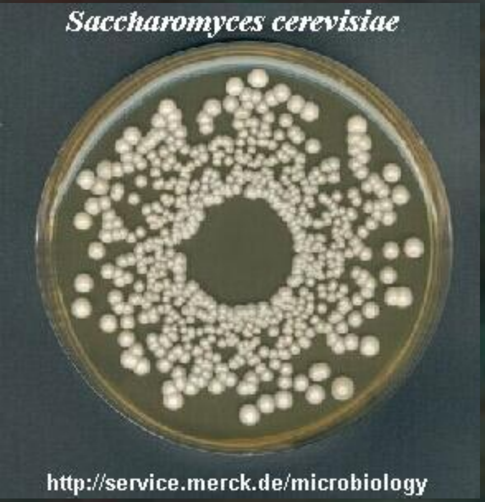
Figure 8-3a. Fermentation (Audesirk)

a) During a sprint, a runner's respiratory and circulatory systems cannot supply oxygen to her leg muscles fast enough to keep up with the demand for energy, so **glycolysis** must provide some of the ATP. In muscles, **lactic acid fermentation** follows glycolysis when oxygen is unavailable.

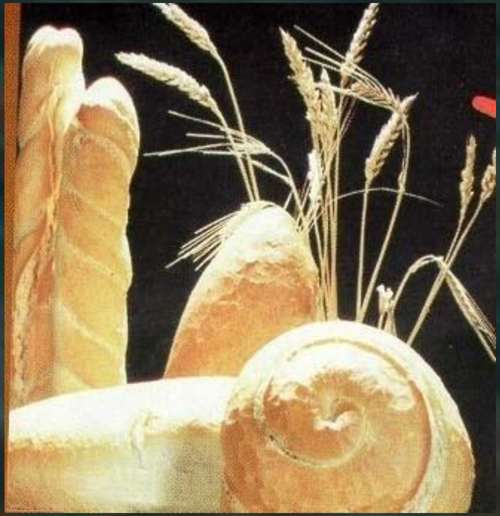
Figure 8.3b. Fermentation (Audesirk)

b) Bread rises as carbon dioxide (**CO_2**) is liberated by *fermenting yeast*, which converts **glucose** to **ethanol** (**alcoholic fermentation**). The dough on the left rose to the level on the right in a few hours.

Fermentation for Food Production



The **yeast** ***Saccharomyces cerevisiae*** (a fungus) also known as **"baker's yeast"** and **"brewer's yeast"**, is used for industrial production of diverse **foods** and **beverages**: beer, wine, breads, enzymes, etc.



Products from Fermentation

- Fermentation helps make food products such as beer, bread, cheese, pickles, sour cream, soy sauce, vinegar, wine, and yogurt.
- Organisms that use fermentation are bacteria and fungi such as some molds and yeasts.


Figure 8A. Products from fermentation.

Figure 8A. Products from fermentation.

Figure 8A. Products from fermentation.

Anaerobic Catabolism of Glucose: **Fermentation**

- Fermentation is **less efficient** than the complete breakdown of glucose in production of energy.

Fermentation

Inputs (reactants)	Outputs (products)
glucose	2 **lactate (lactic acid)** or 2 **alcohol** and 2 CO_2
2 ADP + 2 P	**2 ATP net gain**

Fermentation and Aerobic Cellular Respiration Compared

Similarities	Differences
Both pathways use **glycolysis** to oxidize glucose and other organic fuels to *pyruvate*, with a net production of **2 ATP** by substrate-level phosphorylation.	Contrasting mechanisms for oxidizing NADH back to NAD^+, which is required to sustain glycolysis: **Fermentation:** its final electron acceptor is an organic molecule such as pyruvate (lactic acid fermentation) or acetaldehyde (alcohol fermentation). **Aerobic Cellular Respiration:** there is an electron transport chain where the final electron acceptor is **oxygen**.
In both, $\mathbf{NAD^+}$ is the oxidizing agent that accepts electrons from food during glycolysis.	More **ATP** comes from the oxidation of *pyruvate* in the **Krebs cycle (citric acid cycle)**, which is unique to respiration.
	Due to the Krebs cycle & oxidative phosphorylation, aerobic respiration yields much more ATP than fermentation: up to **38 ATP for respiration**, compared to **2 ATP in fermentation**.

Pyruvate as a Key Juncture in Catabolism

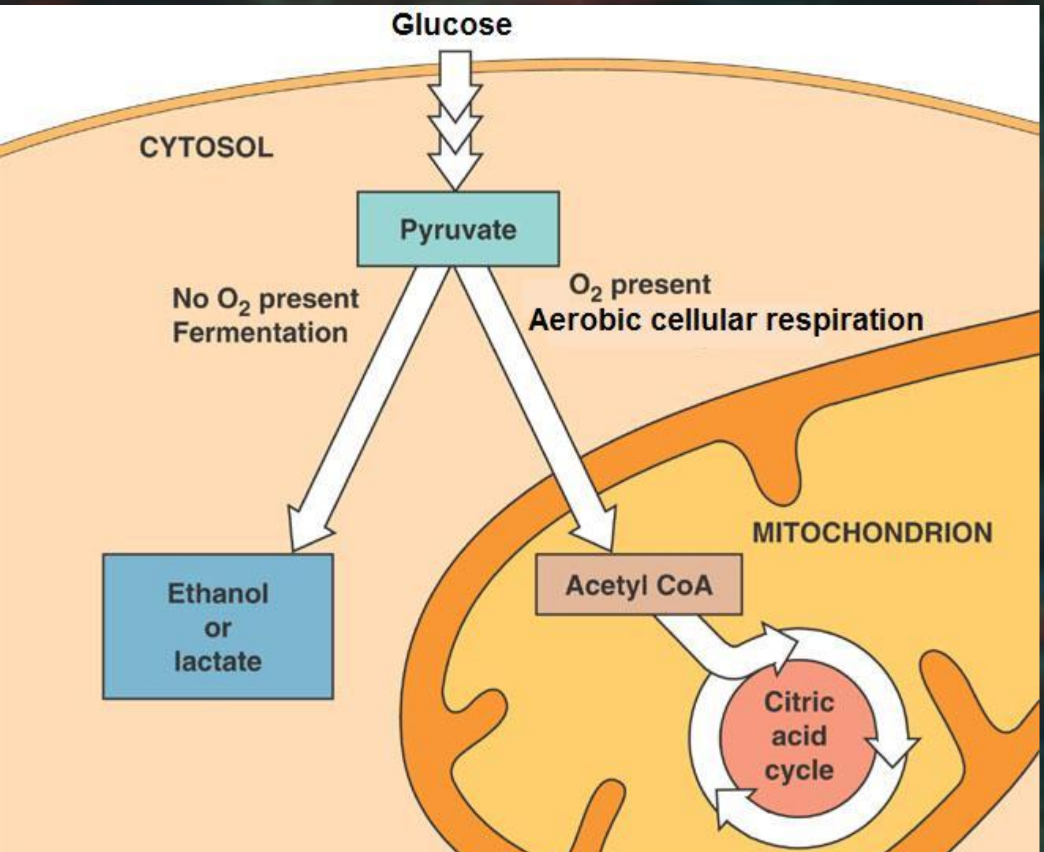


Figure 9.19. Pyruvate as a key juncture in catabolism.

- **Glycolysis** is common to fermentation and cellular respiration. ***Pyruvate***, the end product of glycolysis, represents a fork in the catabolic pathways of glucose oxidation. In a ***facultative anaerobe***, which is capable of both, aerobic cellular respiration and fermentation, pyruvate is committed to one of those two pathways, usually depending on whether or not oxygen is present.

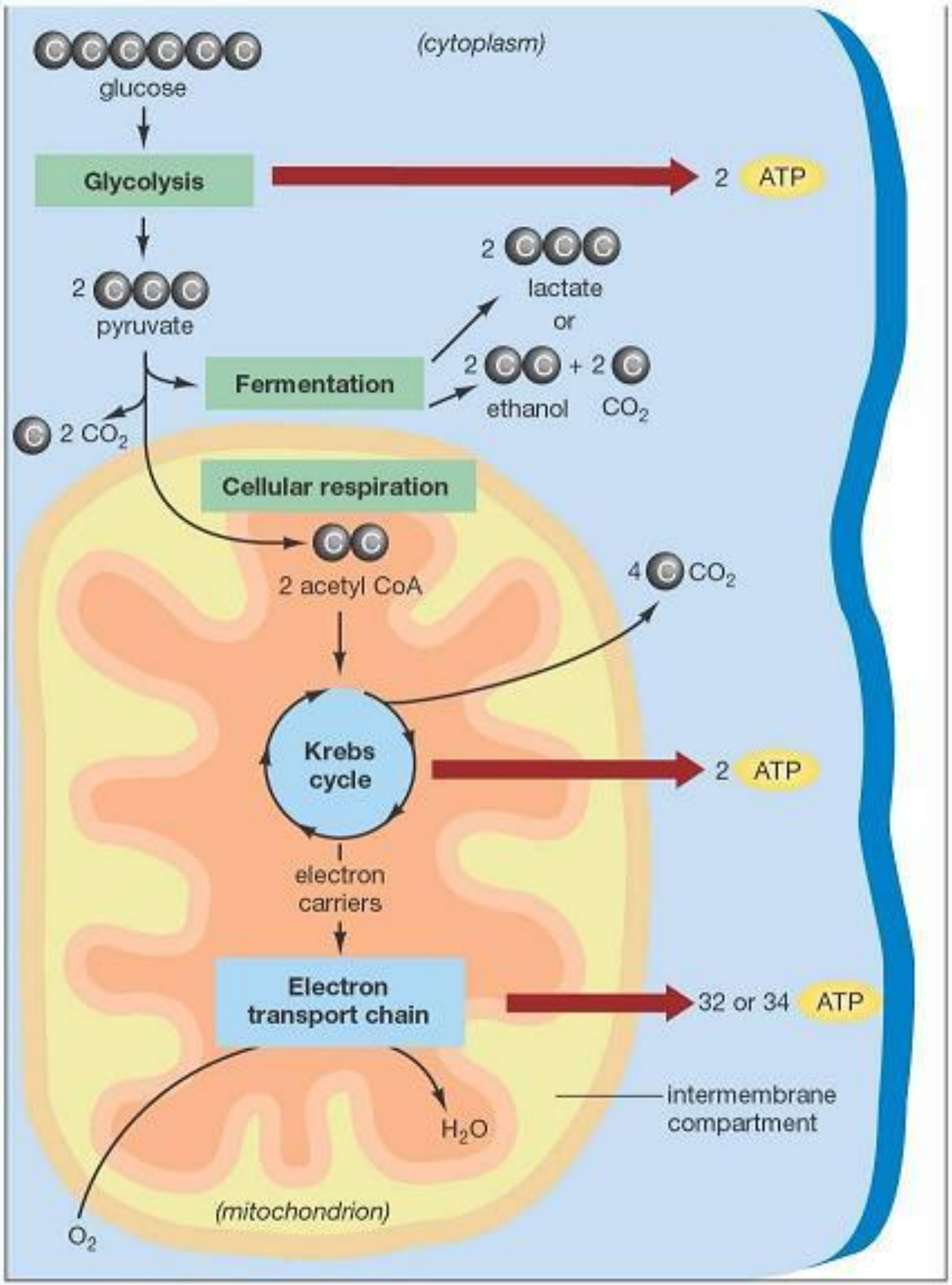
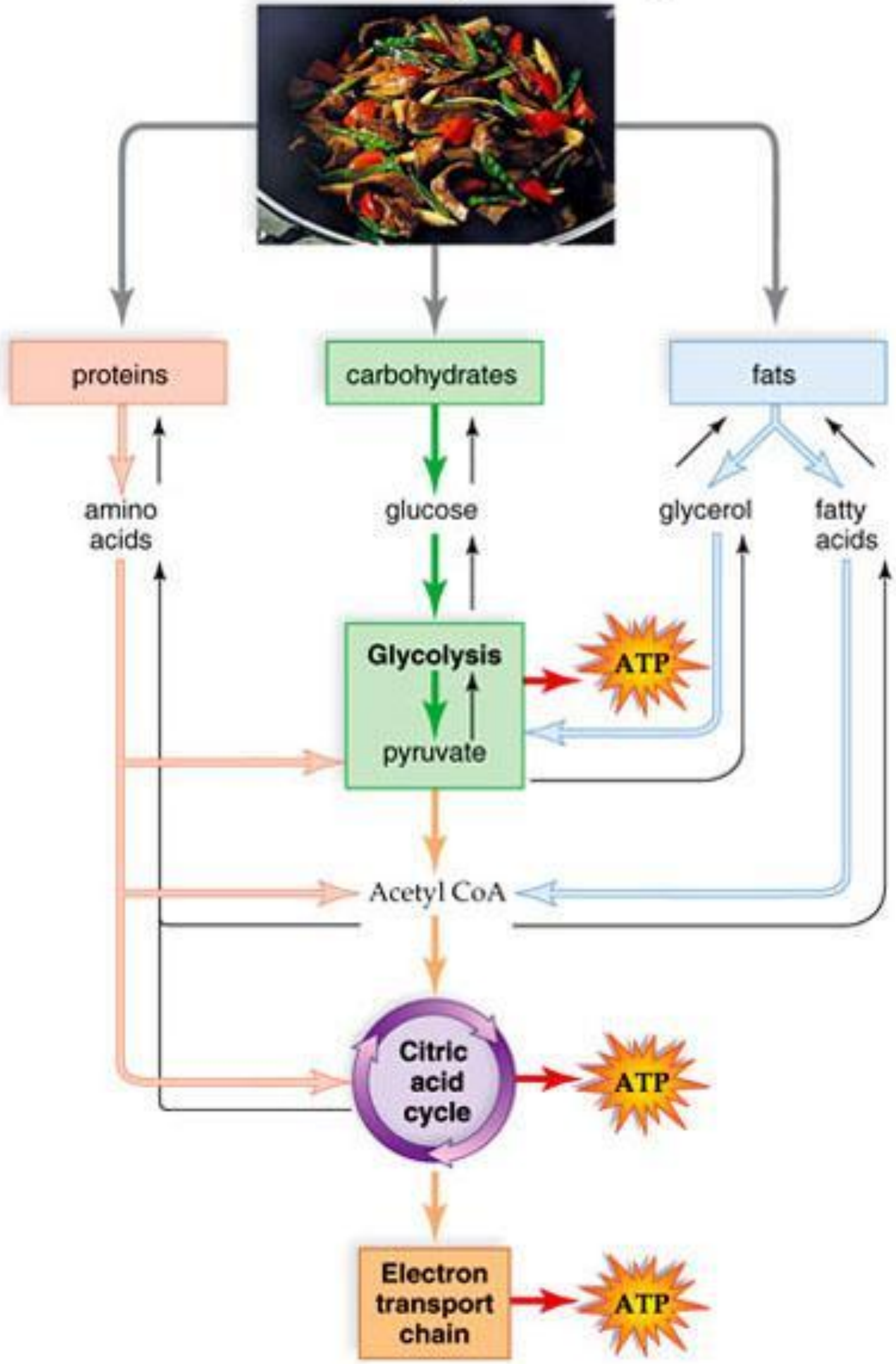


Figure 8-1. A summary of glucose metabolism

Summary of Glucose Metabolism

- Reactions of ***glycolysis*** occur in the fluid portion (cytosol) of the cell's cytoplasm. The other stages of ***cellular respiration*** occur in the mitochondria in eukaryotic organisms; in prokaryotes, they occur in the cell membrane.
- The breakdown of glucose occurs in stages, with energy captured in **ATP** along the way. Most ATP is produced in the mitochondria.

Figure 8.12. The metabolic pool concept.



Metabolic Pool: The Versatility of Catabolism

- **Carbohydrates**, **fats (lipids)**, and **proteins** can be used as energy sources, and they enter degradative pathways at specific points.
- **Catabolism** produces molecules that can also be used for **anabolism** of other compounds.
- Therefore, catabolism and anabolism both use the same pools of metabolites.

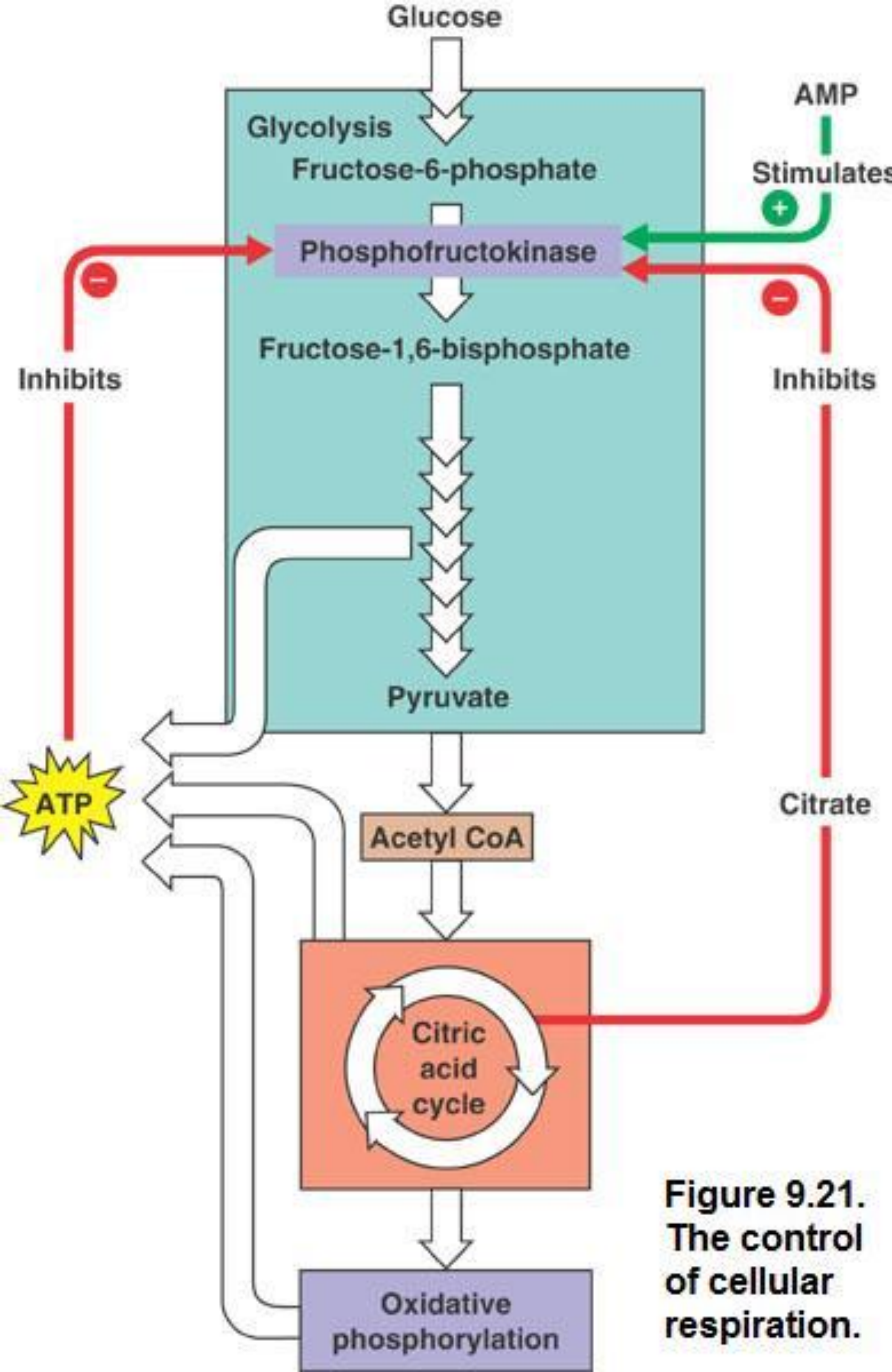
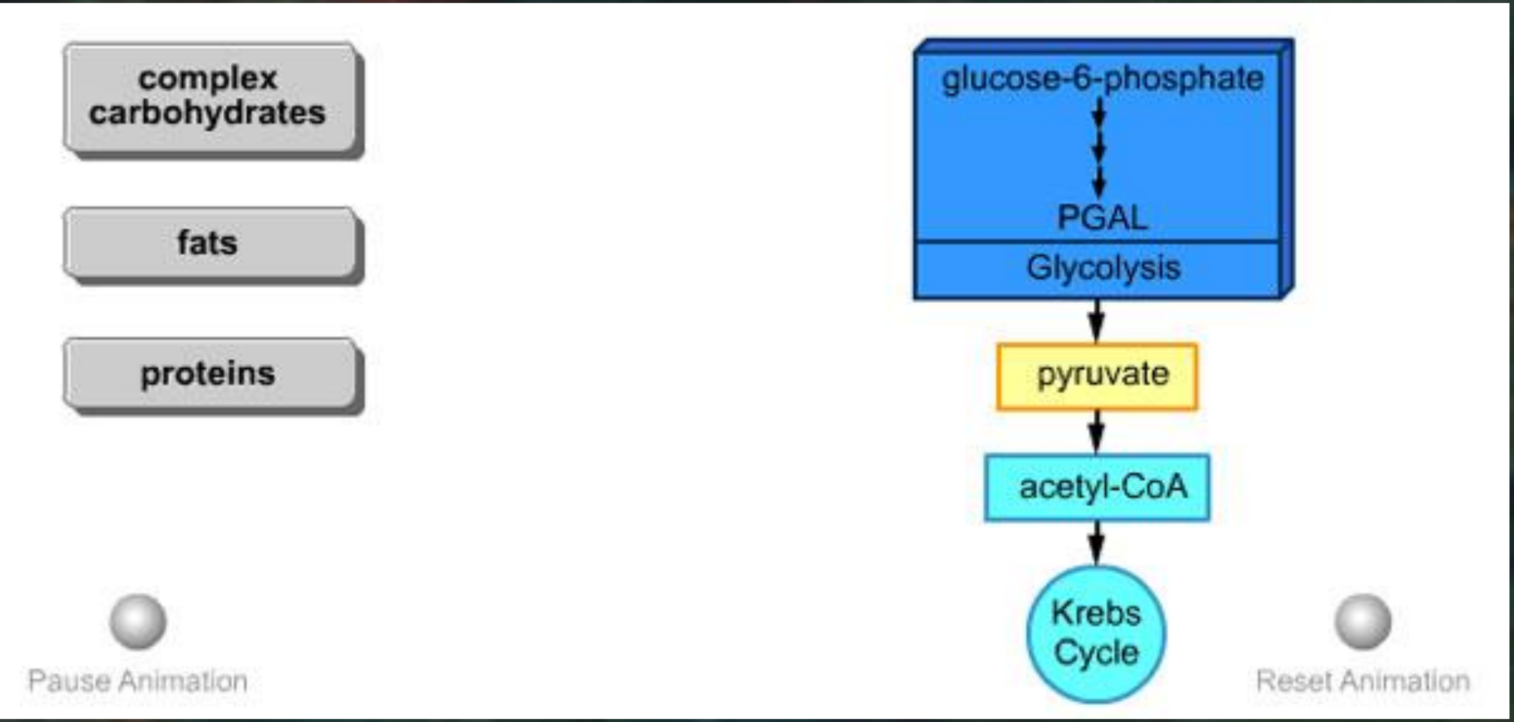


Figure 9.21. The control of cellular respiration.

Regulation of Cellular Respiration via Feedback Mechanisms

- **Enzymes** at certain points in the respiratory pathway respond to *inhibitors* and *activators* that help set the pace of glycolysis and the citric acid cycle.
- ***Phosphofructokinase***, which catalyzes an early step in glycolysis, is one such enzyme. It is stimulated by AMP (derived from ADP) but is inhibited by ATP and by citrate.
- This **feedback regulation** adjusts the rate of respiration as the cell's catabolic and anabolic demands change.

Animation: Alternative Energy Sources



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Summary of the Stages of Aerobic Cellular Respiration in Eukaryotic Cells

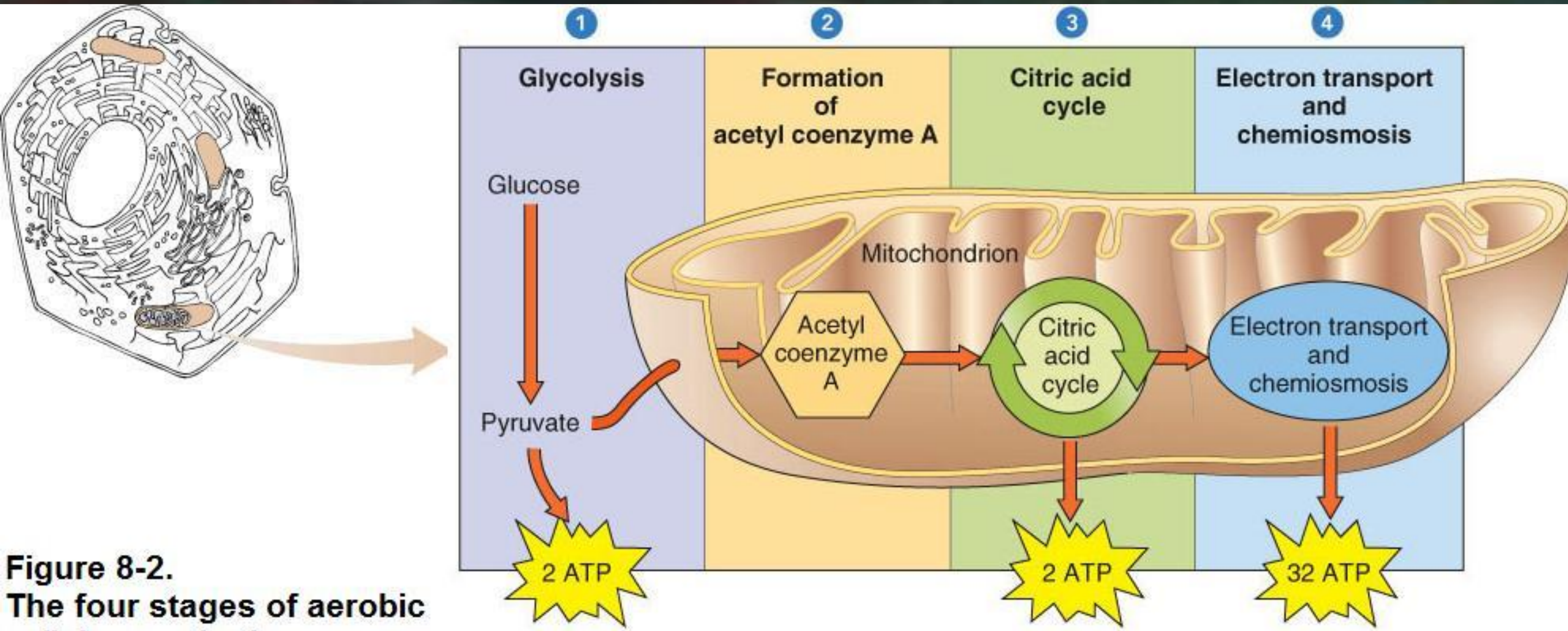

Figure 8-2.
The four stages of aerobic cellular respiration.

- **Glycolysis** occurs in the **cytosol** of the cell.
- **All other stages occur in the mitochondrion (in eukaryotes).**

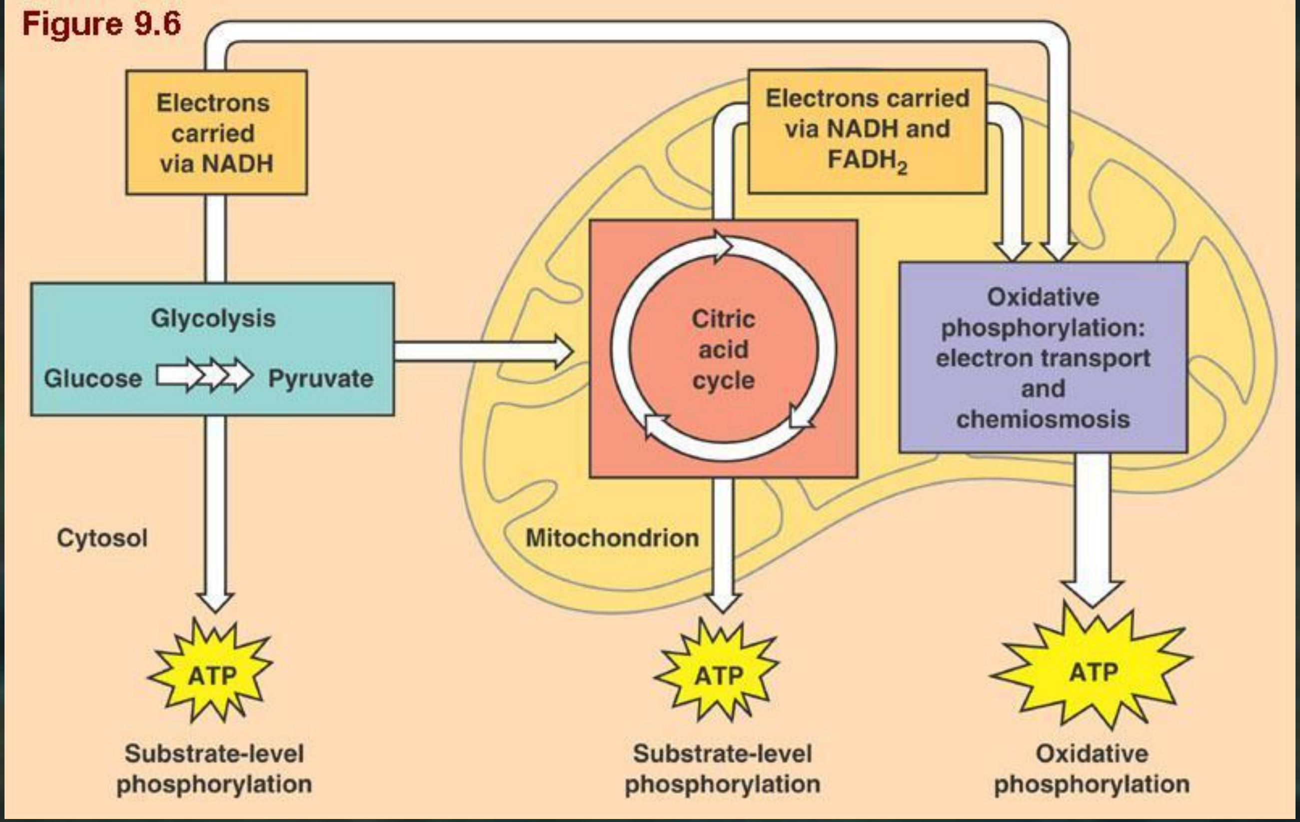

Figure 9.6: An overview of cellular respiration. (*Acetyl CoA formation not shown*)

- During **glycolysis**, each glucose molecule is broken down into two molecules of the compound *pyruvate*. The pyruvate enters the mitochondrion, where the **citric acid (Krebs) cycle** oxidizes it to *carbon dioxide*. The coenzymes *NADH* and *FADH$_2$* transfer electrons derived from glucose to electron transport chains, which are built into the inner mitochondrial membrane. During *oxidative phosphorylation*, **electron transport chains** convert the chemical energy to a form used for **ATP** synthesis in the process called **chemiosmosis**.

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