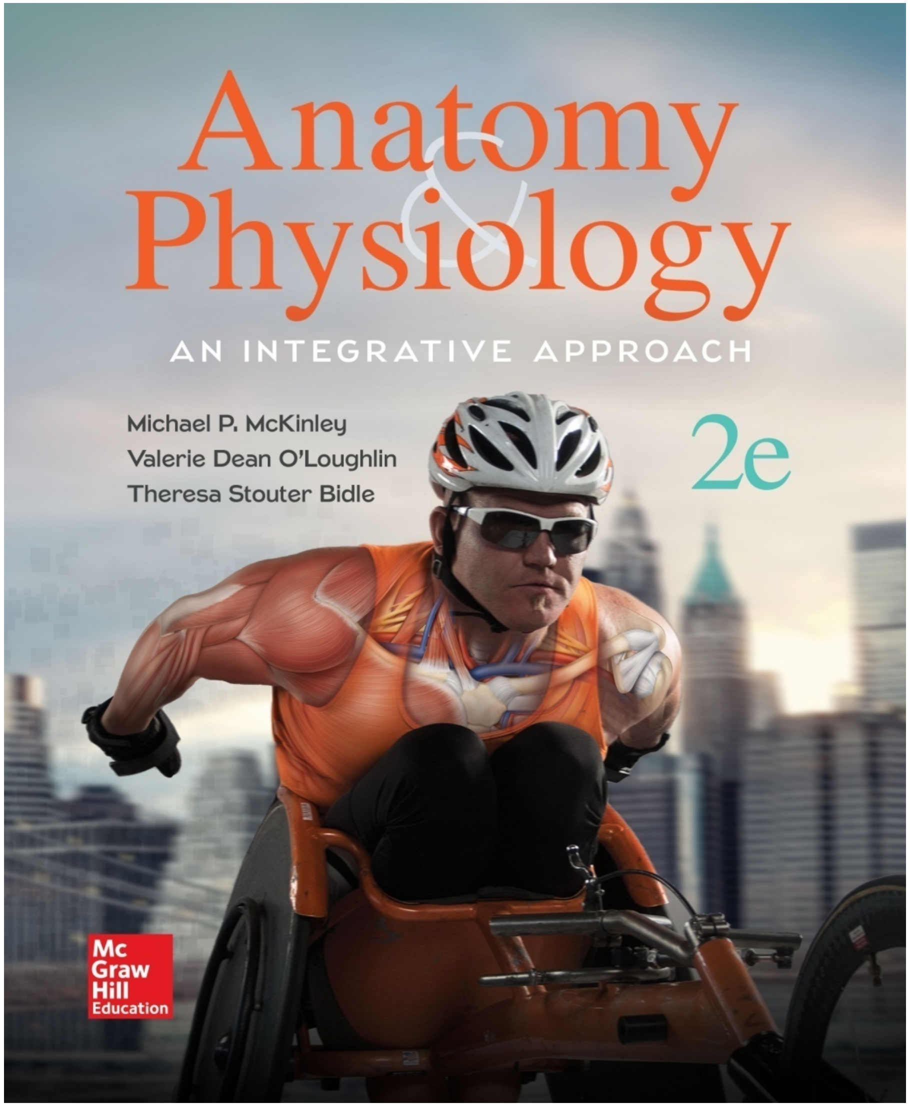
Chapter 03
Lecture Outline

See separate PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes.



Energy, Chemical Reactions, and Cellular Respiration

- All living organisms require energy to
  - Power muscle
  - Pump blood
  - Absorb nutrients
  - Exchange respiratory gases
  - Synthesize new molecules
  - Establish cellular ion concentrations
- Glucose broken down through metabolic pathways
  - Forms ATP, the “energy currency” of cells

3.1 Energy

Learning Objectives:

1. Describe the two classes of energy.
2. Describe chemical energy (one form of potential energy) and the various forms of kinetic energy.
3. List the three important molecules within the body that function primarily in chemical energy.
4. State the first law and second law of thermodynamics.
5. Explain why energy conversion is always less than 100%.

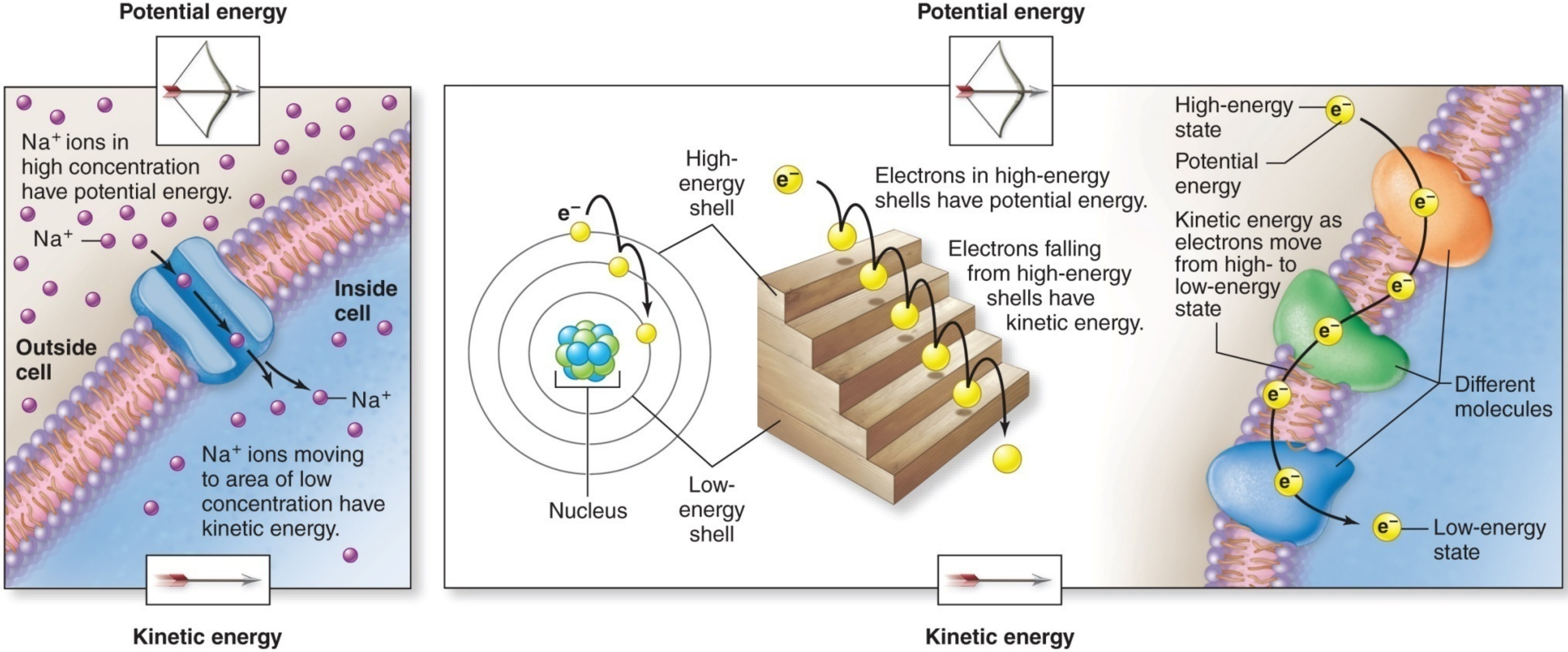
3.1a Classes of Energy

- **Energy**
  - Capacity to do work
  - Two classes of energy
    - **Potential energy—**stored energy (energy of position)
    - **Kinetic energy—**energy of motion
  - Both can be converted from one class to the other

3.1a Classes of Energy

- Potential energy and the plasma membrane
  - Concentration gradient exists across plasma membrane
    - Boundary between inside and outside of cell
- Potential energy and electron shells
  - Electrons move from a higher- to lower-energy shell
  - Kinetic energy can be harnessed to do work
- Potential energy must be converted to kinetic energy before it can do work

Conversion of Potential Energy to Kinetic Energy



(a) Concentration gradients

(b) Movement of electrons

Figure 3.1

3.1b Forms of Energy

- **Chemical energy**
  - One form of potential energy
  - Energy stored in a molecule's chemical bonds
  - Most important form of energy in the human body
  - Used for
    - Movement
    - Molecule synthesis
    - Establishing concentration gradients
  - Present in all chemical bonds
  - Released when bonds are broken during reactions

3.1b Forms of Energy

- **Chemical energy** (*continued*)
  - Molecules that function in chemical energy storage
    - Triglycerides (long term energy storage in adipose tissue)
    - Glucose (glycogen stores in liver and muscle)
    - ATP (stored in all cells; produced continuously and used immediately)
  - Protein
    - Stored chemical energy and can be used as a fuel molecule
    - Has more important structural and functional role in body

3.1b Forms of Energy

- Kinetic energy forms
  - **Electrical energy:** movement of charged particles
    - E.g., electricity or the movement of ions across the plasma membrane of a neuron
  - **Mechanical energy:** exhibited by objects in motion due to applied force
    - E.g., muscle contraction for walking
  - **Sound energy:** molecule compression caused by a vibrating object
    - E.g., sound waves causing vibration of the eardrum in the ear

3.1b Forms of Energy

- Kinetic energy forms (*continued*)
  - **Radiant energy:** energy of electromagnetic waves
    - Vary in wavelength and frequency
    - Higher frequencies with greater radiant energy
    - Frequencies higher than visible light
      - Penetrate body and mutate DNA
      - Cells protected by melanin
    - Visible light detected by retinal cells of the eye
      - Relayed along optic nerve to brain
  - **Heat:** kinetic energy of random motion
    - Usually not available to do work
    - Measured as the **temperature** of a substance

The Electromagnetic Spectrum

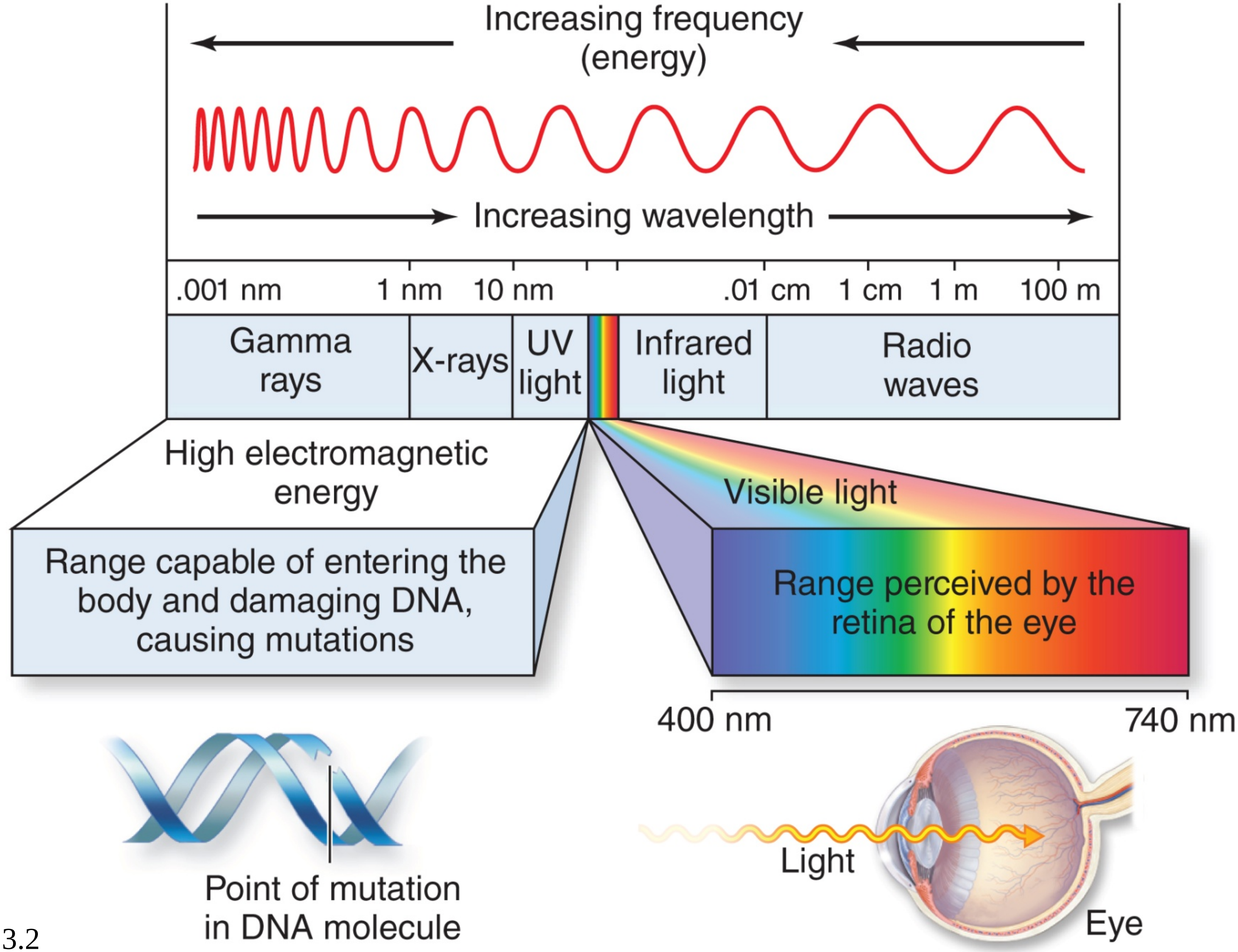


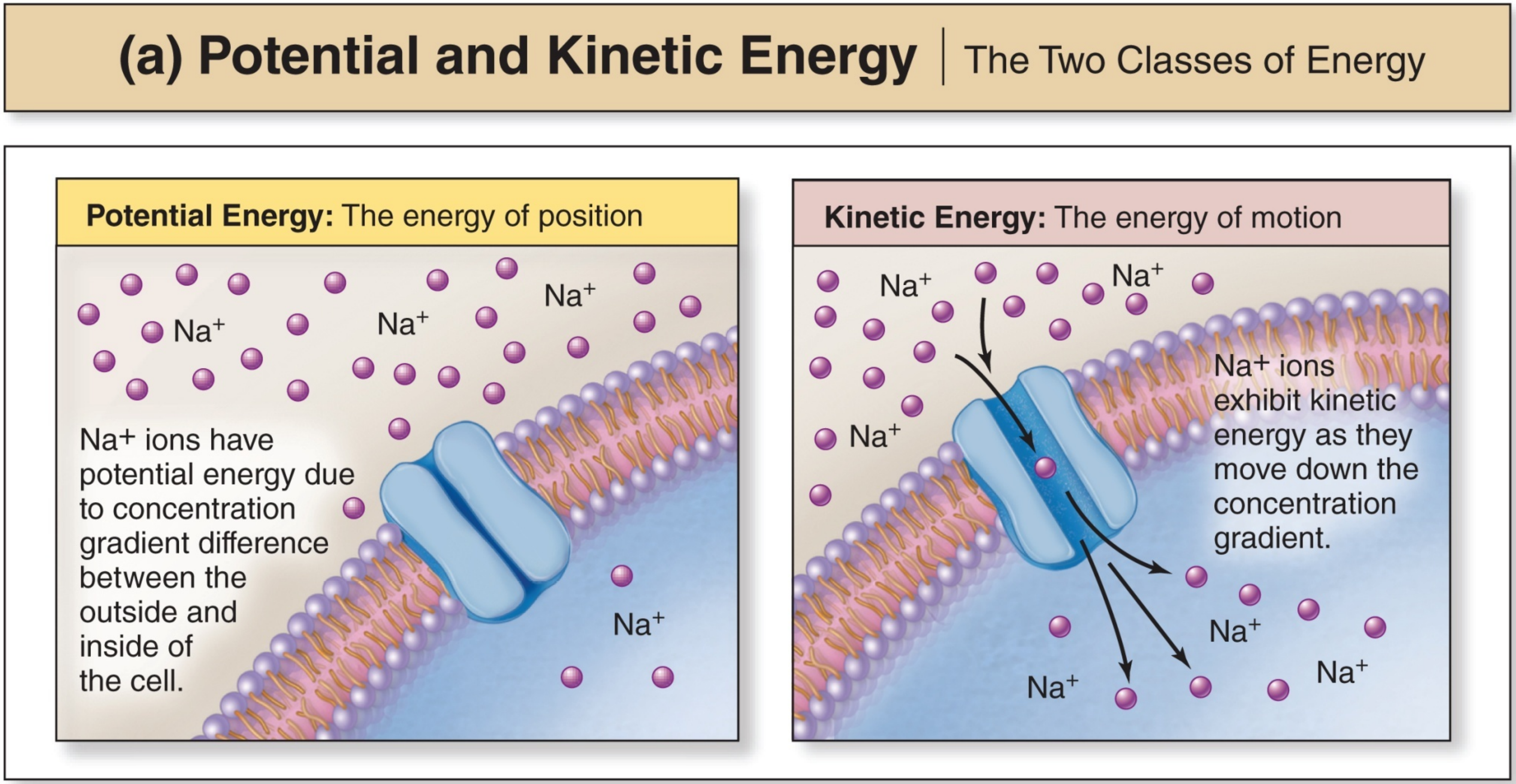
Figure 3.2

3.1c Laws of Thermodynamics

- Energy can change forms, for example
  - A burning candle converts chemical energy to light and heat energy
  - Retinal cells convert light energy into electrical energy of a nerve impulse
  - Chemical energy in food converted to another chemical form, then into mechanical energy
- **Thermodynamics—**study of energy transformations

3.1c Laws of Thermodynamics

- **First law of thermodynamics**
  - Energy can neither be created nor destroyed; it can only change in form
- **Second law of thermodynamics**
  - When energy is transformed, some energy is lost to heat
    - The amount of usable energy decreased
    - E.g., moving around to warm up on a cold day
    - As chemical energy converts to mechanical energy, heat is produced



(a) Potential and Kinetic Energy | The Two Classes of Energy
Potential Energy: The energy of position
Na+
Na+
Na+
Na+ ions have potential energy due to concentration gradient difference between the outside and inside of the cell.
Na+
Kinetic Energy: The energy of motion
Na+
Na+
Na+
Na+ ions exhibit kinetic energy as they move down the concentration gradient.
Na+
Na+
Na+

Figure 3.3a

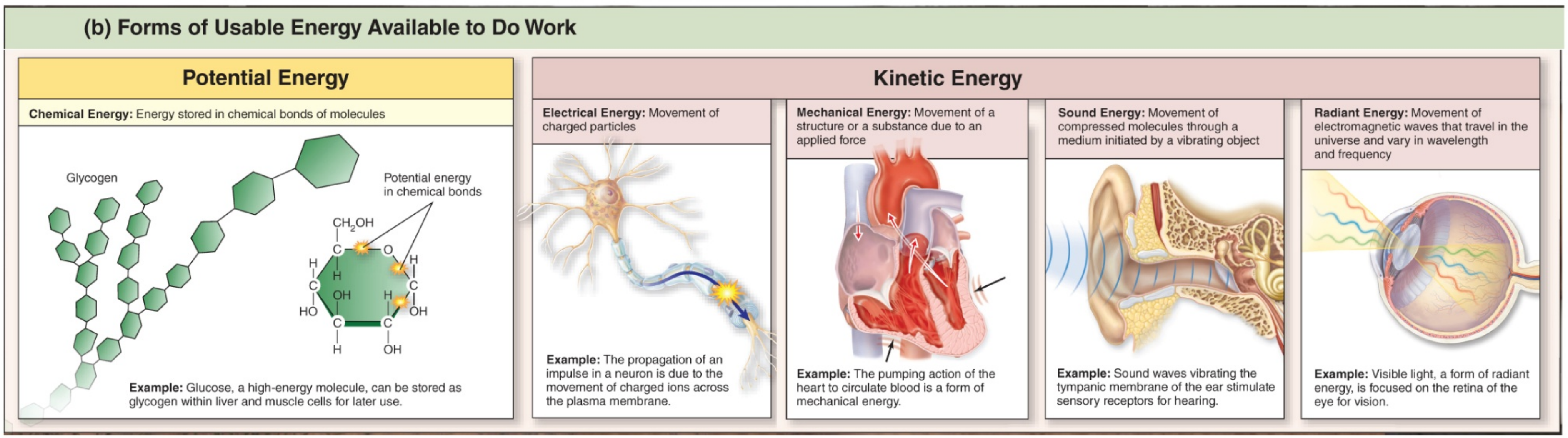
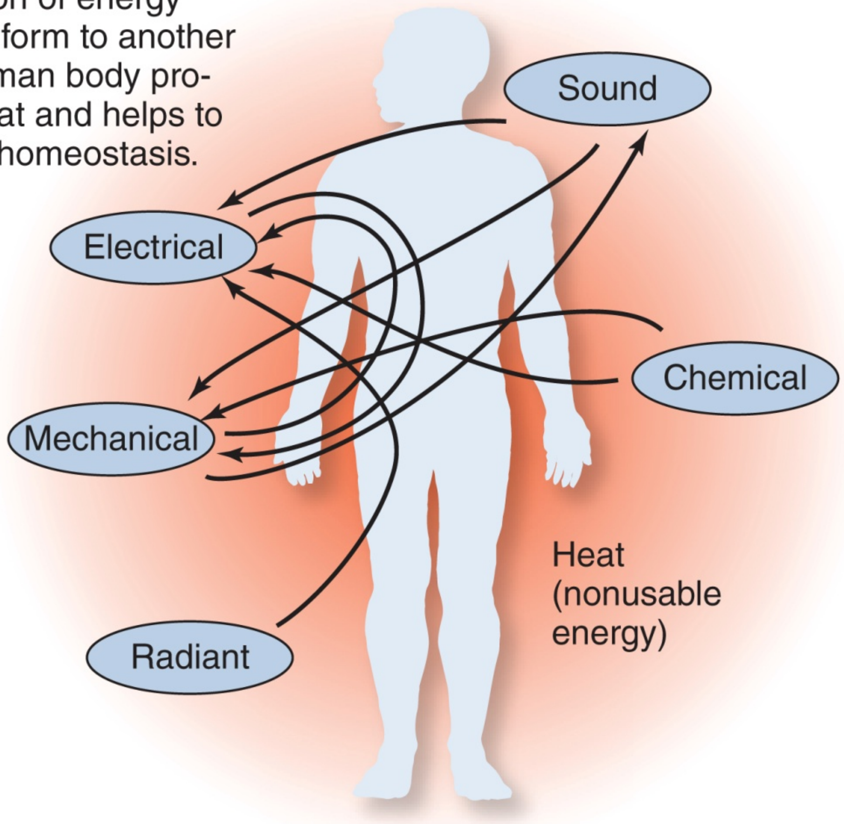

(b) Forms of Usable Energy Available to Do Work
Potential Energy
Chemical Energy: Energy stored in chemical bonds of molecules
Glycogen
Potential energy in chemical bonds
CH2OH
Example: Glucose, a high-energy molecule, can be stored as glycogen within liver and muscle cells for later use.
Kinetic Energy
Electrical Energy: Movement of charged particles
Example: The propagation of an impulse in a neuron is due to the movement of charged ions across the plasma membrane.
Mechanical Energy: Movement of a structure or a substance due to an applied force
Example: The pumping action of the heart to circulate blood is a form of mechanical energy.
Sound Energy: Movement of compressed molecules through a medium initiated by a vibrating object
Example: Sound waves vibrating the tympanic membrane of the ear stimulate sensory receptors for hearing.
Radiant Energy: Movement of electromagnetic waves that travel in the universe and vary in wavelength and frequency
Example: Visible light, a form of radiant energy, is focused on the retina of the eye for vision.

Figure 3.3b

(c) Laws of Energy

Conversion of energy from one form to another in the human body produces heat and helps to maintain homeostasis.



First Law of Thermodynamics

Energy cannot be created or destroyed, it can only be converted from one form to another.

Second Law of Thermodynamics

Every time energy is transformed from one form to another, some of that energy is converted to heat.

Figure 3.3c

What did you learn?

- A sodium ion moving down its concentration gradient is an example of what kind of energy?

- Muscle contraction is an example of what kind of energy?

3.2 Chemical Reactions

Learning Objectives:

1. Explain what occurs in a chemical reaction.
2. Distinguish between reactants and products.
3. Describe the three classifications of chemical reactions.
4. Distinguish between catabolism and anabolism.

3.2 Chemical Reactions (*continued*)

Learning Objectives:

5. Discuss the exchange that takes place in an oxidation reduction reaction.
6. Explain ATP cycling.
7. Define chemical reaction rate.
8. Explain activation energy.

3.2a Chemical Equations

- **Metabolism**
  - All biochemical reactions in living organisms
- **Chemical reactions**
  - Occur when chemical bonds in existing molecular structures are broken
  - New bonds formed
  - Expressed as **chemical equation**
    - Reactants
    - Products

3.2a Chemical Equations

- **Reactants**
  - Substances present prior to start of a chemical reaction
  - Written on left side of equation
- **Products**
  - Substances formed by the reaction
  - Written on right side of equation

$$A + B \rightarrow C$$

    - A and B are reactants
    - C is the product
    - Arrow indicates reaction direction
  - In a balanced equation, number of elements are equal on both sides of the reaction

3.2b Classification of Chemical Reactions

- Chemical reactions are classified based on three criteria
  1. Changes in chemical structure,
  2. Changes in chemical energy
  3. Whether the reaction is irreversible or reversible

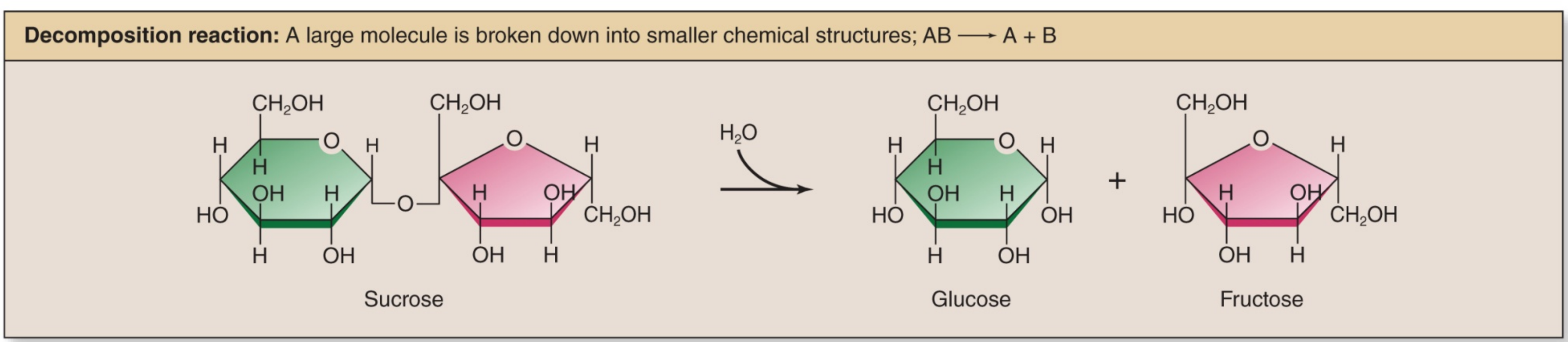
- Changes in chemical structure
  - Decomposition reactions
  - Synthesis reactions
  - Exchange reactions

3.2b Classification of Chemical Reactions

- **Decomposition reaction**
  - Initial large molecule broken down into smaller structures

$$AB \rightarrow A + B$$

    - E.g., hydrolysis reaction of sucrose into glucose and fructose
  - All decomposition reactions in the body are referred to as **catabolism** or *catabolic reactions*



(a)

Figure 3.4a

3.2b Classification of Chemical Reactions

- **Synthesis reaction**
  - Two or more structures combined to form a larger structure

$$A + B \rightarrow AB$$

    - E.g., *dehydration synthesis* reaction forming a dipeptide
    - **Anabolism** is the collective term for all synthesis reactions in the body

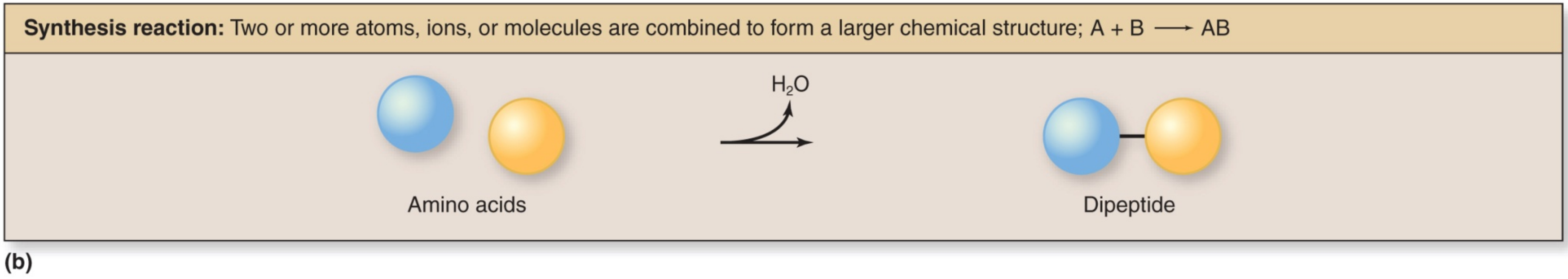


Figure 3.4b

3.2b Classification of Chemical Reactions

- **Exchange reaction**
  - Groups exchanged between two chemical structures
    - Has both decomposition and synthesis components
    - Most prevalent in human body

$$AB + C \rightarrow A + BC$$

    - E.g., production of ATP in muscle tissue

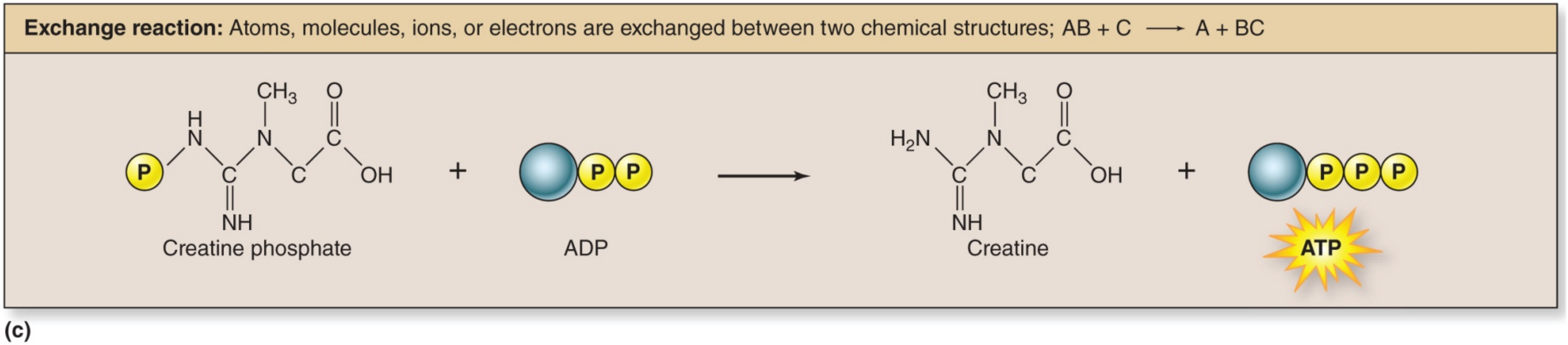


Figure 3.4c

3.2b Classification of Chemical Reactions

- **Oxidation-reduction reaction** (*redox reaction*)
  - Electrons moved from one chemical structure to another
  - Structure that loses an electron, **oxidized** during **oxidation**
  - Structure that gains an electron, **reduced** during **reduction**
  - Reactions always occur together
    - Electrons may be moved alone or with a hydrogen ion

3.2b Classification of Chemical Reactions

- **Nicotinamide adenine dinucleotide (NAD^+)**
  - Modified dinucleotide containing nicotinamide
  - Important in ATP synthesis
- Electrons can be harnessed to do work
  - Electrons in oxidation-reduction reactions represent energy transfer

3.2b Classification of Chemical Reactions

- Energy-rich molecule (glucose) is oxidized
  - Gives off two hydrogen atoms
- NAD^+ reduced
  - Gains both a hydrogen ion and two electrons

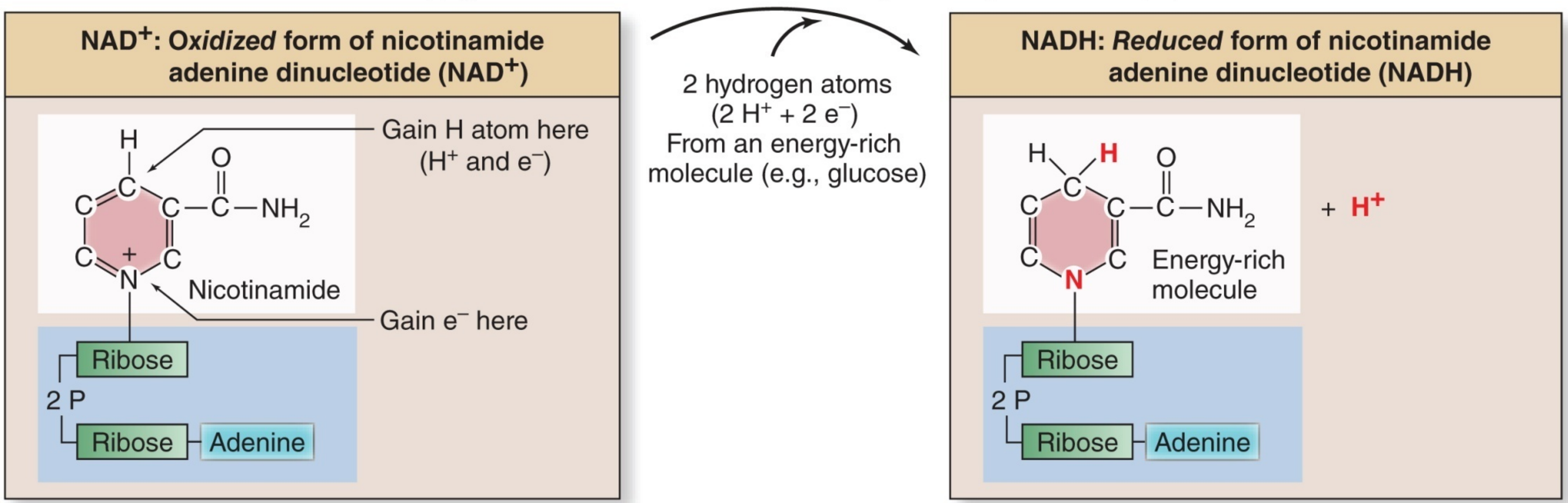


Figure 3.5

3.2b Classification of Chemical Reactions

- **Exergonic reactions**
  - Reactants with more energy within their chemical bonds than products
  - Energy released with net decrease in potential energy
    - E.g., decomposition reactions
- **Endergonic reactions**
  - Reactants with less energy within their chemical bonds than products
  - Energy supplied with a net increase in potential energy
    - E.g., synthesis reactions

Exergonic and Endergonic Reactions

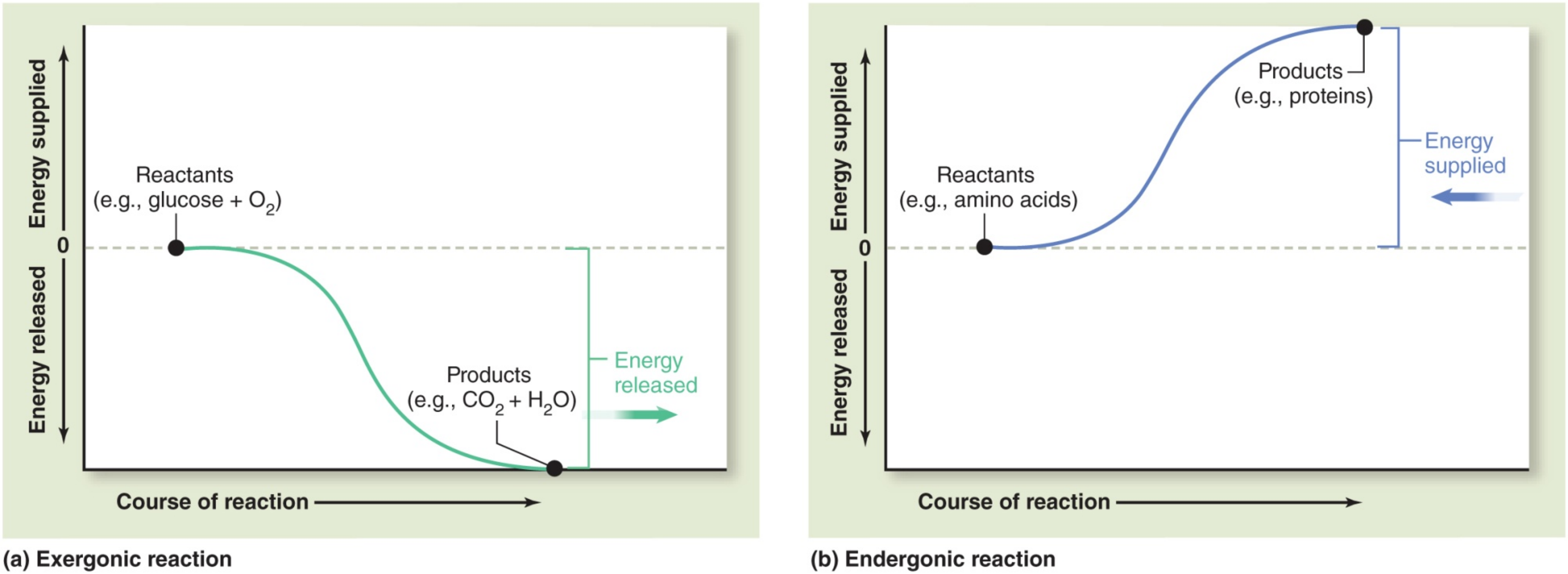


Figure 3.6

3.2b Classification of Chemical Reactions

- **ATP cycling**
  - Continuous formation and breakdown of ATP
  - ATP formed when energy is released in exergonic reactions
    - Fuel molecules from food are oxidized
    - Energy in their bonds transferred to ADP and free phosphate to form ATP
  - ATP oxidized
    - Released energy used for energy-requiring processes
  - Only a few seconds worth of ATP present at a time
    - Formation of ATP occurs continuously to provide energy

ATP Cycling

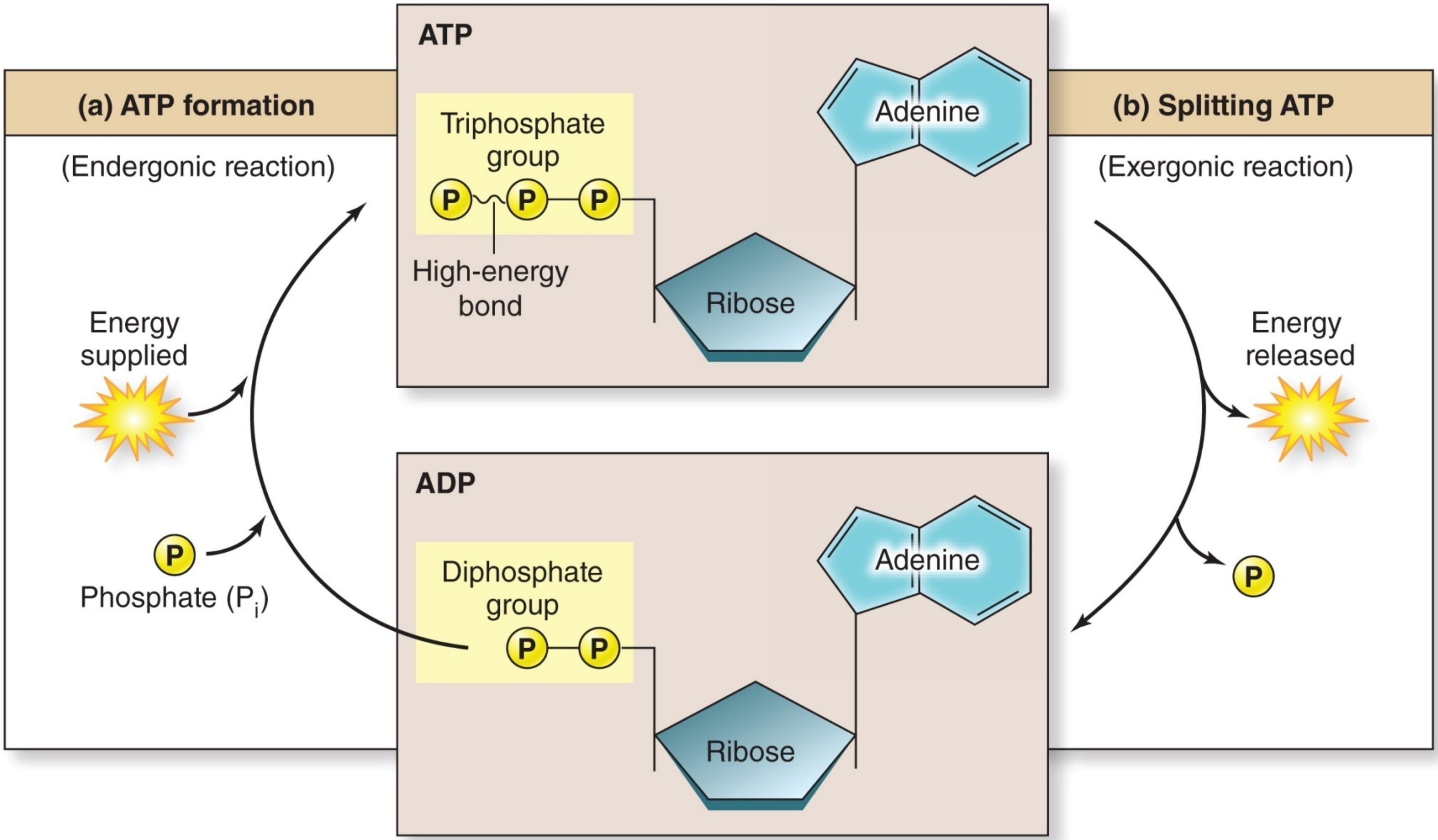


Figure 3.7

3.2b Classification of Chemical Reactions

- **Irreversible reaction**
  - Net loss of reactants and a net gain in products

$$A + B \rightarrow AB \quad \text{or} \quad AB \rightarrow A + B$$

- **Reversible reaction**
  - Does not proceed only to the right
  - Reactants become products and products become reactants at equal rate
  - No net change in concentration of either reactants or products—equilibrium

$$A + B \leftrightarrows AB$$

3.2b Classification of Chemical Reactions

- **Reversible reaction** (*continued*)
  - Remains in equilibrium if left undisturbed
    - Increase in reactants or decrease in products drives equation to the right
      - Additional product formed until new equilibrium reached
    - Decrease in reactants or increase in products drives equation to the left
      - Additional reactants formed until new equilibrium reached

3.2b Classification of Chemical Reactions

- **Reversible reaction** (*continued*)
  - E.g., carbon dioxide reacts water to form carbonic acid

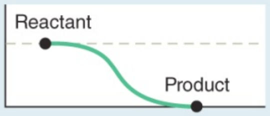
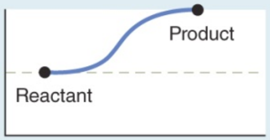
$$CO_2 + H_2O \leftrightarrows H_2CO_3$$

  - Carbonic acid dissociates to yield bicarbonate ion and hydrogen ion

$$CO_2 + H_2O \leftrightarrows H_2CO_3 \leftrightarrows H^+ + HCO_3^-$$

  - Important reaction in blood transport of carbon dioxide and maintaining acid-base balance

Table 3.1 Classification of Chemical Reactions

Type of Chemical Reaction	Definition	Example
CHANGE IN CHEMICAL STRUCTURE		
Decomposition	Complex chemical structure broken down into simpler structures	Sucrose → glucose and fructose 
Synthesis	Simple chemical structures bonded together into a more complex structure	Amino acids → dipeptide 
Exchange	Atoms, molecules, ions, or electrons exchanged between two chemical structures	Creatine phosphate + ADP → Creatine + ATP 
CHANGES IN CHEMICAL ENERGY		
Exergonic	Energy released	Glucose and oxygen → carbon dioxide and water 
Endergonic	Energy required	Amino acids → dipeptide 
NET DIRECTION OF REACTION		
Irreversible	Net change of reactants to products	Most chemical reactions **A + B → AB, or AB → A + B**
Reversible	Formation of products = formation of reactants (once equilibrium is reached)	$CO_2 + H_2O \leftrightarrows H_2CO_3 \leftrightarrows H^+ + HCO_3^-$

3.2c Reaction Rates and Activation Energy

- **Reaction rate**
  - Measure of how quickly a chemical reaction takes place
- **Activation energy (E_a)**
  - Energy required to break existing chemical bonds
  - A primary factor determining reaction rate
- Overcoming the activation energy
  - In a lab, increasing temperature provides energy to break bonds
  - Significant temperature increase in a cell would denature proteins
    - Protein catalysts called enzymes are used instead

What did you learn?

- Is the formation of a dipeptide a decomposition or synthesis reaction?
- Is it exergonic or endergonic?
- Is it an example of anabolism or catabolism?
- What molecule is formed from exergonic reactions and used as the energy currency for endergonic reactions and other energy-requiring processes in the cell?
- What is the term for the energy required to break existing chemical bonds?

3.3 Enzymes

Learning Objectives:

1. Describe the general function of enzymes.
2. Describe the key structural components of enzymes.
3. Identify the places in the body where enzymes may be found.
4. Explain the steps by which an enzyme catalyzes a reaction.
5. Describe cofactors and their role in reactions.

3.3 Enzymes (*continued*)

Learning Objectives:

6. Identify the six major classes of enzymes and the general functions of enzymes in each class.
7. Describe the naming conventions for enzymes.
8. Define how enzyme and substrate concentration affect reaction rates.
9. Explain the effect of temperature on enzymes.
10. Describe how pH changes affect enzymes.

3.3 Enzymes (*continued*)

Learning Objectives:

11. Describe how competitive and noncompetitive inhibitors control enzyme action.
12. Distinguish between a metabolic pathway and a multienzyme complex.
13. Explain the role of negative feedback in enzyme regulation.
14. Identify and explain the processes involving phosphate that commonly are used to regulate enzymes.

3.3a Function of Enzymes

- **Enzymes**
  - **Catalysts** that accelerate normal physiologic activities
  - Decrease activation energy of cellular reactions
  - **Uncatalyzed—**no enzyme present
  - **Catalyzed—**enzyme present
  - Only facilitate reactions that would already occur
  - Increase rate of product formation

Activation of Energy (E_a)

- Exergonic reaction
- Sucrose has higher potential energy than total potential energy of products
- Activation energy required to initiate reaction
- Presence of enzyme lovers required E_a

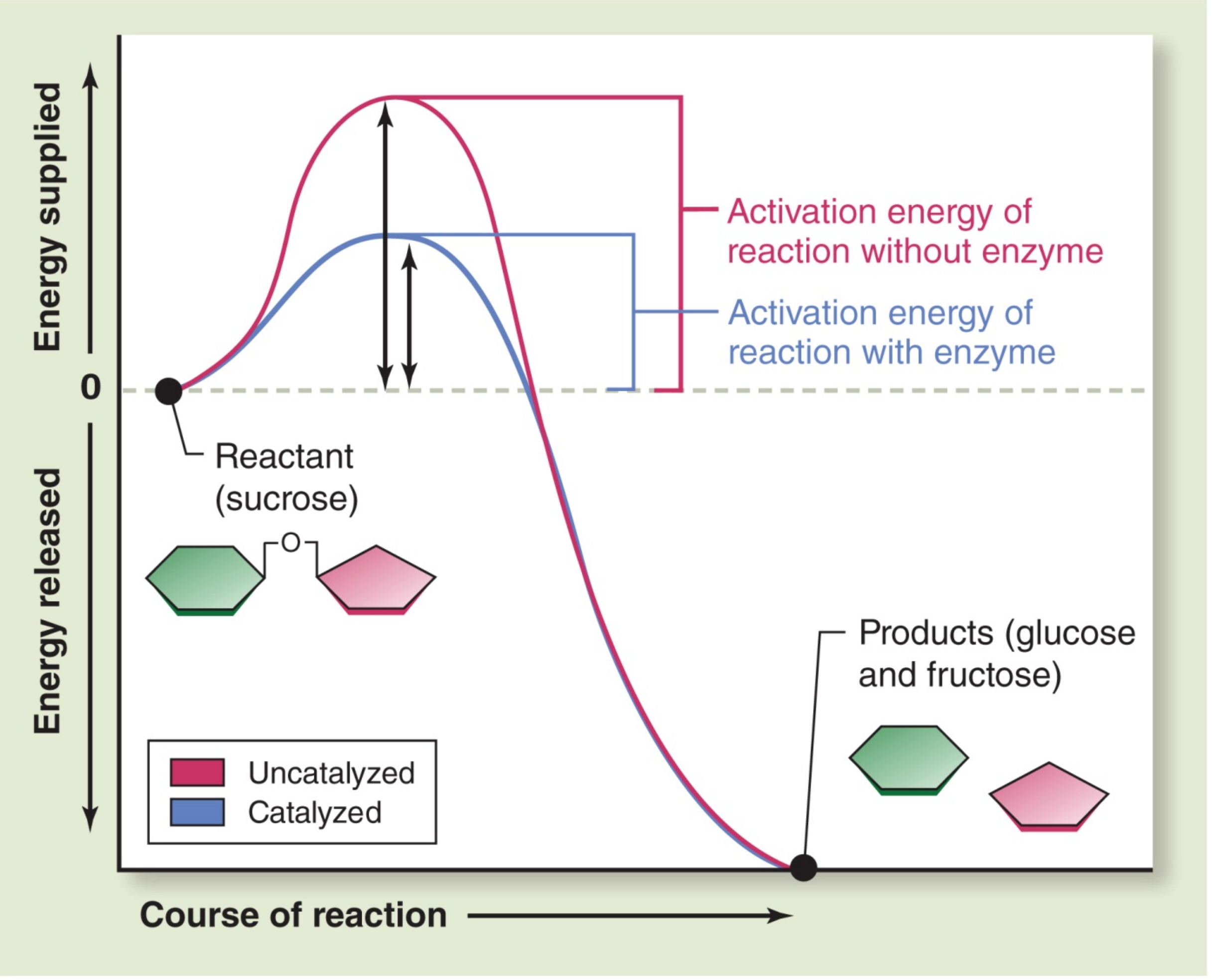


Figure 3.8

3.3b Enzymes Structure and Location

- Most enzymes are **globular proteins**
  - Range in size from small (60 amino acids) to large (2500 amino acids)
  - Unique 3-dimensional structure in protein chain called **active site**
  - Temporarily forms **enzyme-substrate complex**

3.3 b Enzymes Structure and Location

- Active site's **specificity** of shape
  - Permits only a single substrate to bind
  - Helps catalyze only one specific reaction

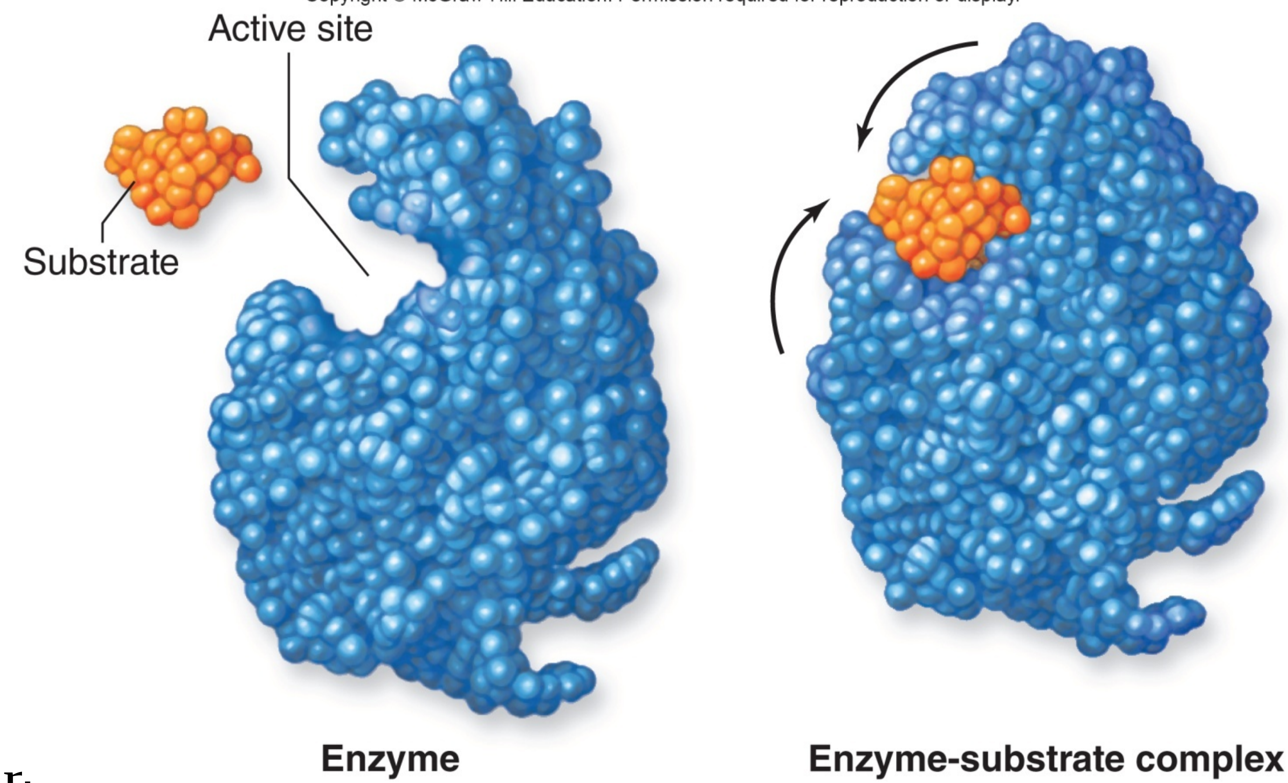


Figure 3.9

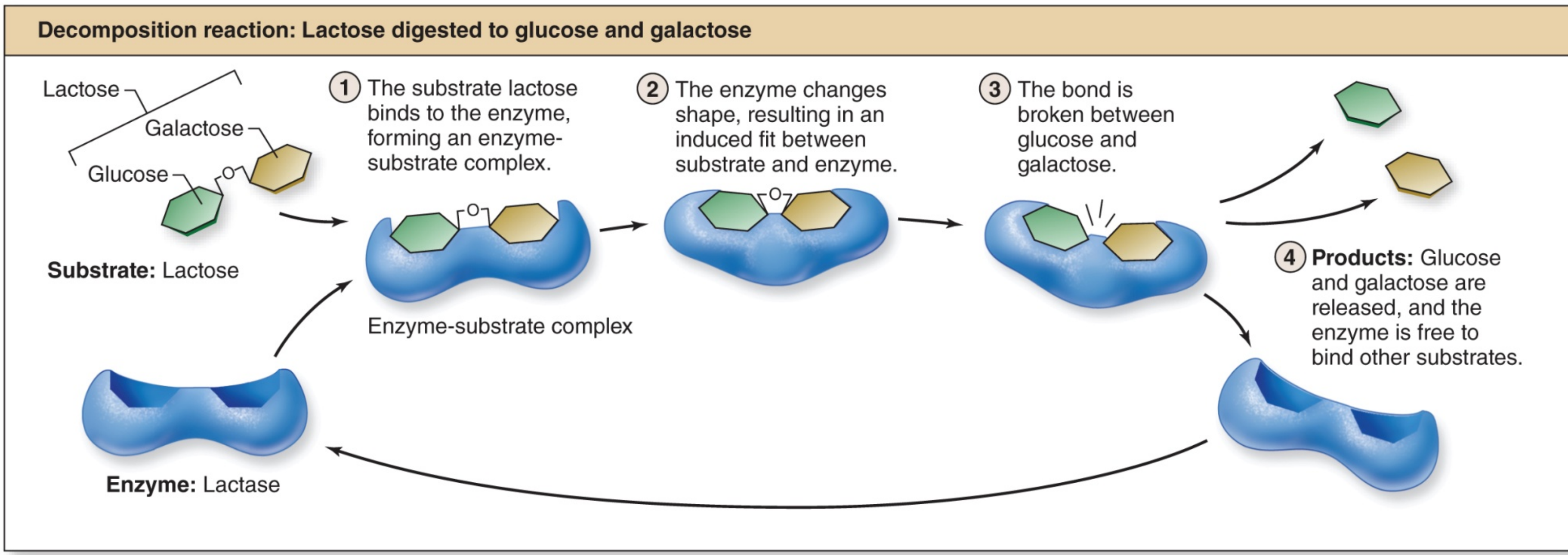
3.3b Enzymes Structure and Location

- Location of enzymes
  - Some remain within cells
    - E.g., DNA polymerase, which helps form new DNA
  - Some become embedded in plasma membrane
    - E.g., lactase in walls of small intestine cells helps digest lactose
  - Some are secreted from the cell
    - E.g., pancreatic amylase released from pancreas to participate in starch digestion

3.3c Mechanism of Enzyme Action

- Enzyme catalysis
  1. Substrate enters active site, forming enzyme-substrate complex
  2. Enzyme changes shape slightly, resulting in even closer fit (*induced fit model*)
  3. Change in enzyme shape stresses chemical bonds, permitting new bonds to be formed
  4. Products are released; enzyme may repeat process.

Mechanism of Action for Enzymes in Decomposition Reaction



(a)

Figure 3.10a

Mechanism of Action for Enzymes in Synthesis Reaction

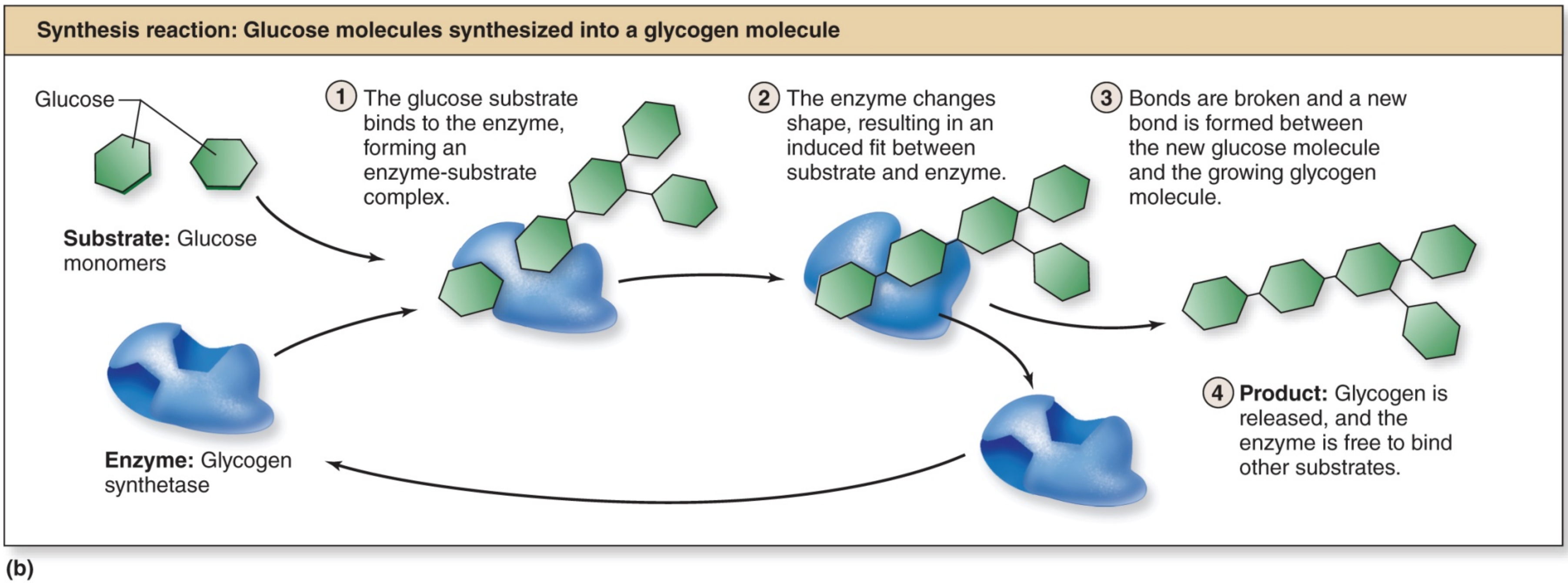


Figure 3.10b

3.3c Mechanism of Enzyme Action

- **Cofactors**
  - Molecules or “helper” ions required to ensure that a reaction occurs
  - Associated with particular enzyme
  - *Nonprotein* organic or inorganic structure
    - Inorganic cofactors attach to enzyme
      - E.g., zinc ion required for carbonic anhydrase to function
    - Organic cofactors called **coenzymes**
      - E.g., vitamins or modified nucleotides serving as coenzymes

3.3d Classification and Naming of Enzymes

- Enzymes are organized into six major functional classes
  1. Oxidoreductase
     - E.g., enzymes in this class participate in oxidation-reduction reactions
     - **Dehydrogenase**
  2. Transferase
     - E.g., all enzymes in this class transfer atoms or molecules between chemical structures
     - **Kinase**
  3. Hydrolase
  4. Isomerase
  5. Ligase
  6. Lyase

Table 3.2 Major Classes of Enzymes

Enzyme Class	Description	Examples
Oxidoreductase	Transfers electrons from one substance to another	Dehydrogenase uses NAD^+ or a molecule other than oxygen as electron acceptor. Peroxidase uses hydrogen peroxide (H_2O_2) as electron acceptor.
Transferase	Transfers a functional group	Phosphorylase transfers a phosphate (PO_4^{3-}) to a different substance. Kinase transfers a phosphate (PO_4^{3-}), usually from ATP to a different substance.
Hydrolase	Splits a chemical bond using water	Phosphatase removes phosphate. Protease digests proteins. Lipase splits lipids (e.g., triglyceride). Sucrase splits sucrose.
Isomerase	Converts one isomer to another	Mutase transfers atoms within a molecule.
Ligase	Bonds two molecules together	Synthetase bonds two molecules using ATP.
Lyase	Splits a chemical bond in the absence of water	Decarboxylase cleaves a molecule to release carbon dioxide.

3.3d Classification and Naming of Enzymes

- Enzyme names based on
  - Name of substrate or product
  - Subclass
  - Suffix –*ase*
    - E.g., **pyruvate dehydrogenase** transfers hydrogen from pyruvate
    - E.g., **DNA polymerase** helps form DNA
    - E.g., **lactase** digests lactose

3.3e Enzymes and Reaction Rates

Conditions that influence reaction rates

- Rate of a chemical reaction may be accelerated by
  - Increase in enzyme concentration
  - Increase in substrate concentration
    - Increases only up to point of saturation
    - **Saturation—**so much substrate is present that all enzyme molecules are engaged in reaction

Environmental Conditions That Influence Reaction Rates of Enzymes

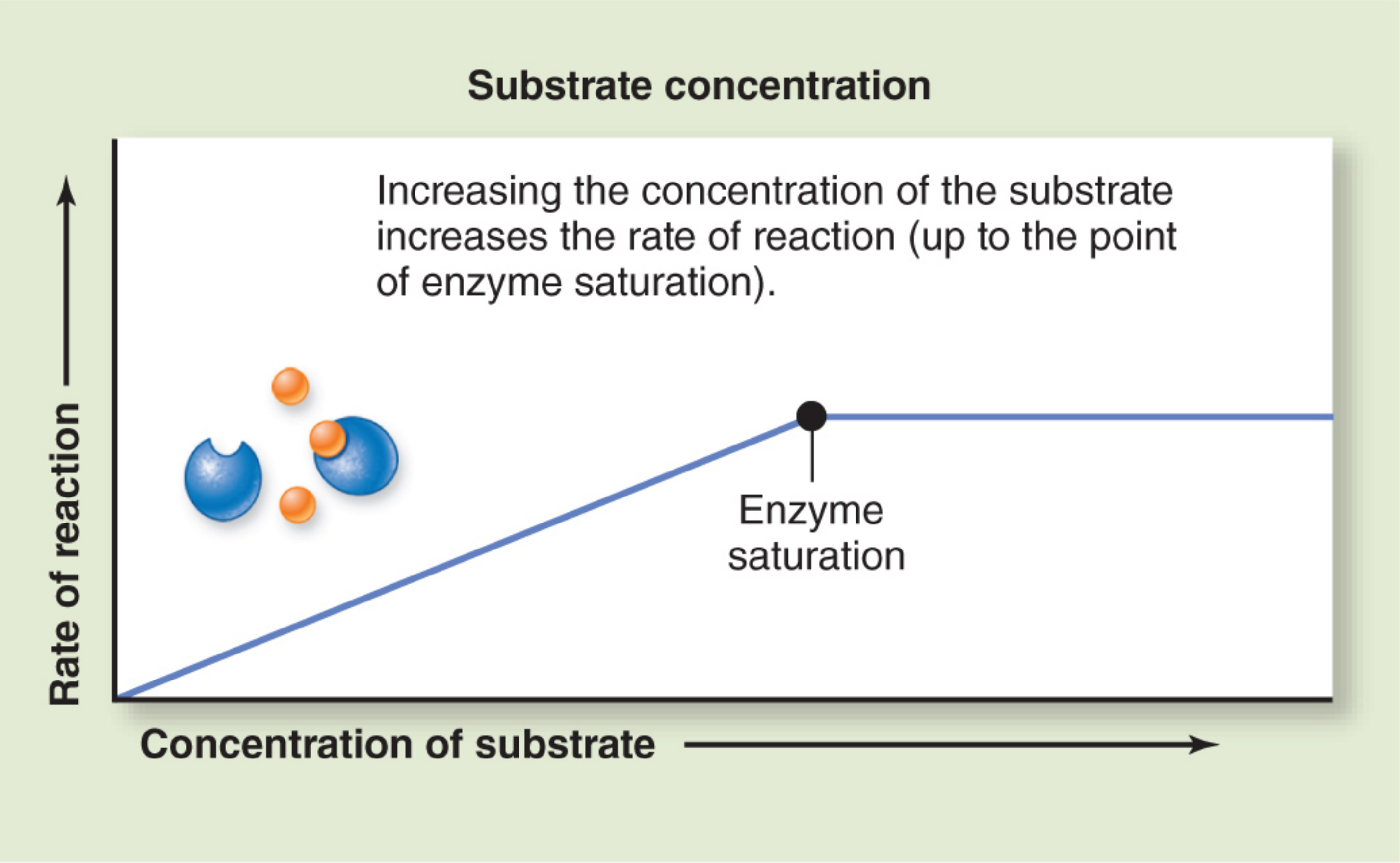


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Figure 3.11a

3.3e Enzymes and Reaction Rates

Conditions that influence reaction rates (*continued*)

- 3-dimensional shape of enzymes dependent on temperature
  - Human enzymes function best at **optimal temperature**
    - Usually 37ºC (98.6ºF)
  - Moderate fever
    - Results in more efficient enzyme activity
  - Severe increases in temperature
    - Cause protein denaturation with loss of function

Environmental Conditions That Influence Reaction Rates of Enzymes

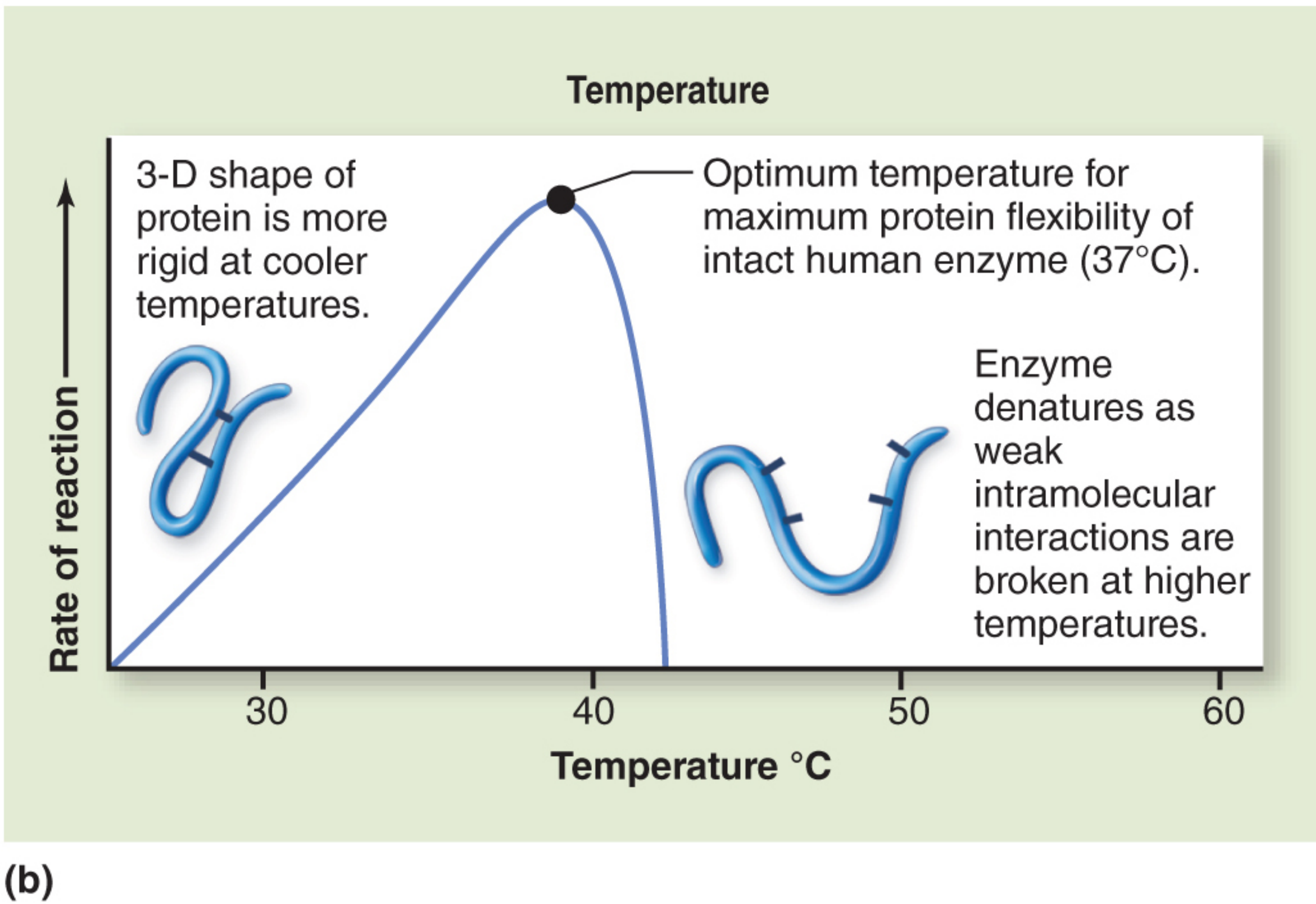

Figure 3.11b

3.3e Enzymes and Reaction Rates

Conditions that influence reaction rates (*continued*)

- Effect of pH
- Enzymes function best at **optimal pH**
  - Between pH of 6 and 8 for most enzymes
  - Changes in H^+ disrupt electrostatic interactions
  - Enzyme loss of shape, denaturation
  - Optimal pH may differ
    - E.g., enzymes working in the lower pH of the stomach

Environmental Conditions That Influence Reaction Rates of Enzymes

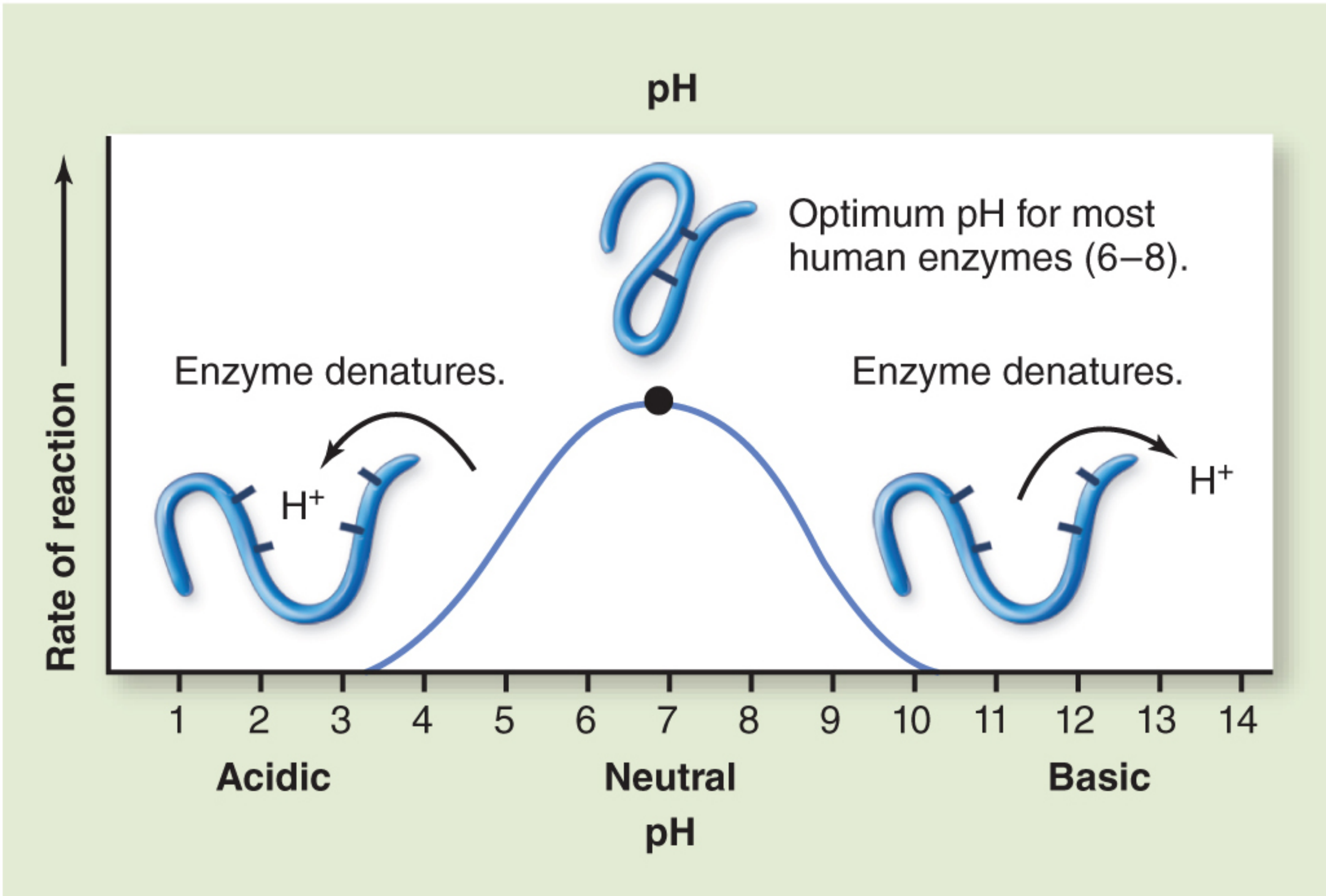

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Figure 3.11c

3.3f Controlling Enzymes

- **Inhibitors** bind enzymes and prevent enzymatic catalysis
  - Prevents overproduction of product
  - Later release of inhibitor allows it to function and catalysis continues
  - Inhibitors can be competitive or noncompetitive

3.3f Controlling Enzymes

- **Competitive inhibitor**
  - Resembles substrate and binds to active site of enzyme
  - Compete for occupation of active site
  - With greater substrate
    - Less likely competitive inhibitor will occupy site
  - With more substrate
    - More likely inhibitor will occupy site

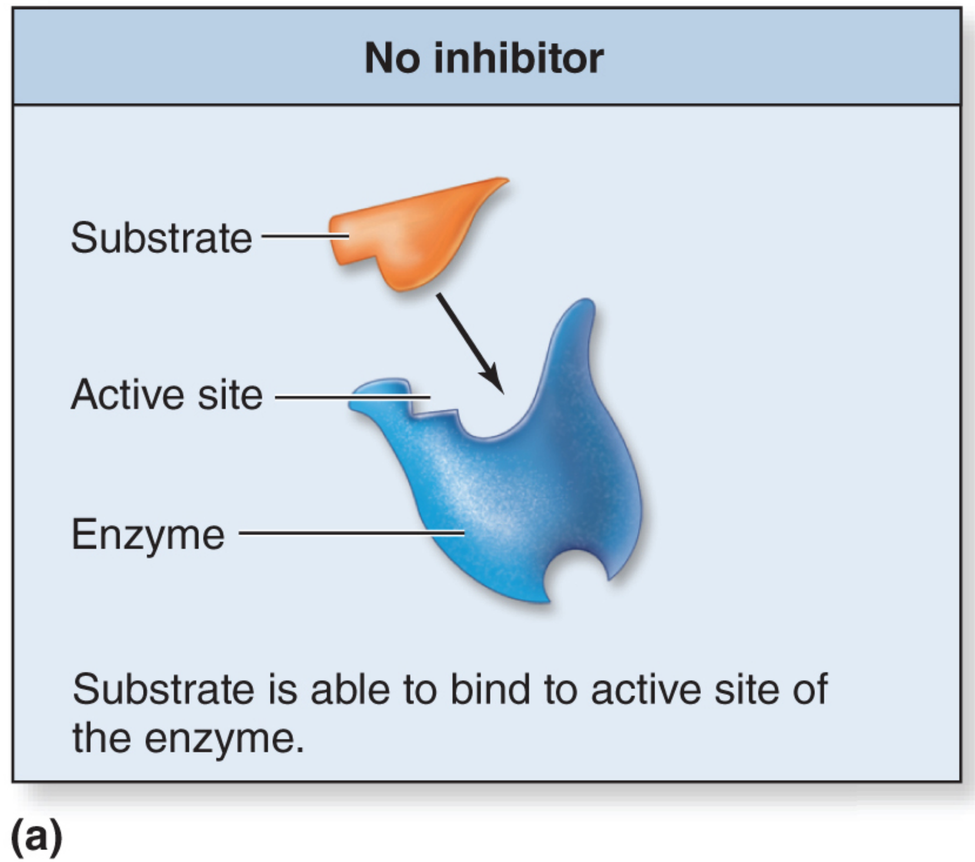


Figure 3.12a

3.3f Controlling Enzymes

- **Noncompetitive inhibitors**
  - Do not resemble substrate
  - Bind a site other than active site **(allosteric site)**
  - Induce conformational change to enzyme and active site
  - Also called **allosteric inhibitors**
  - Not influenced by concentration of substrate

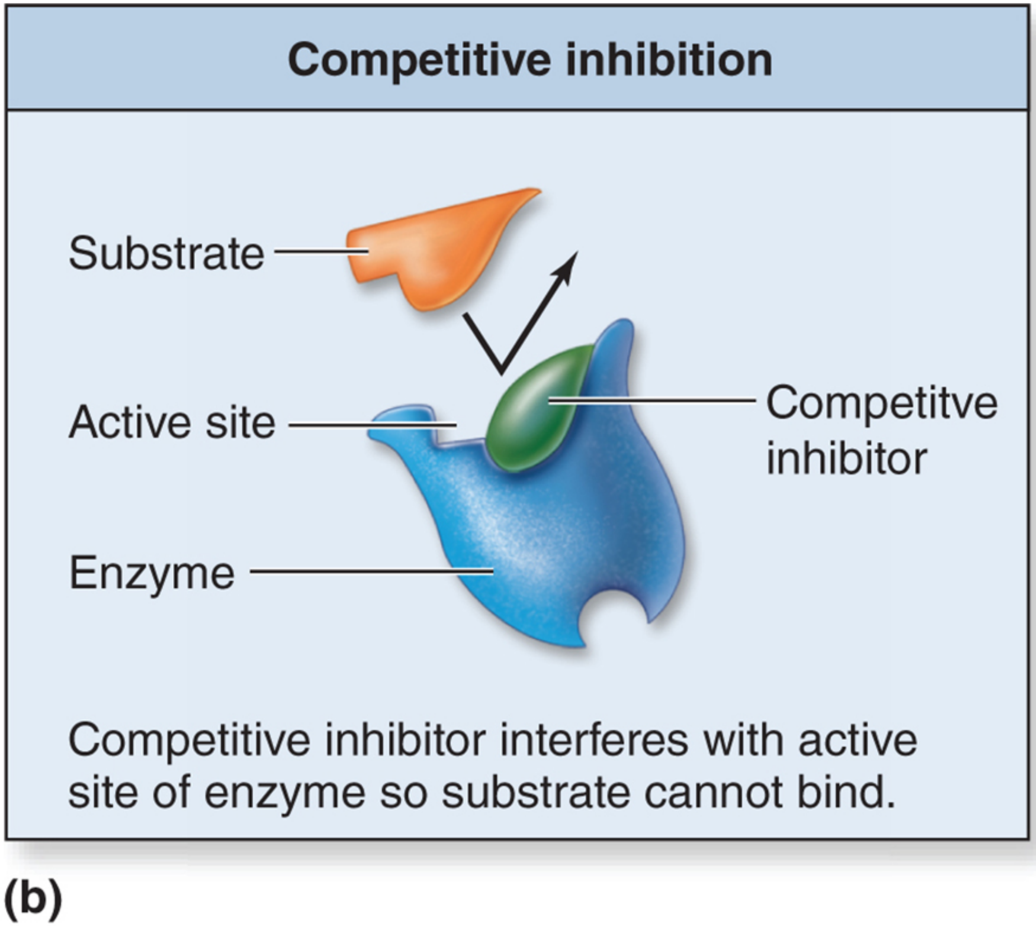


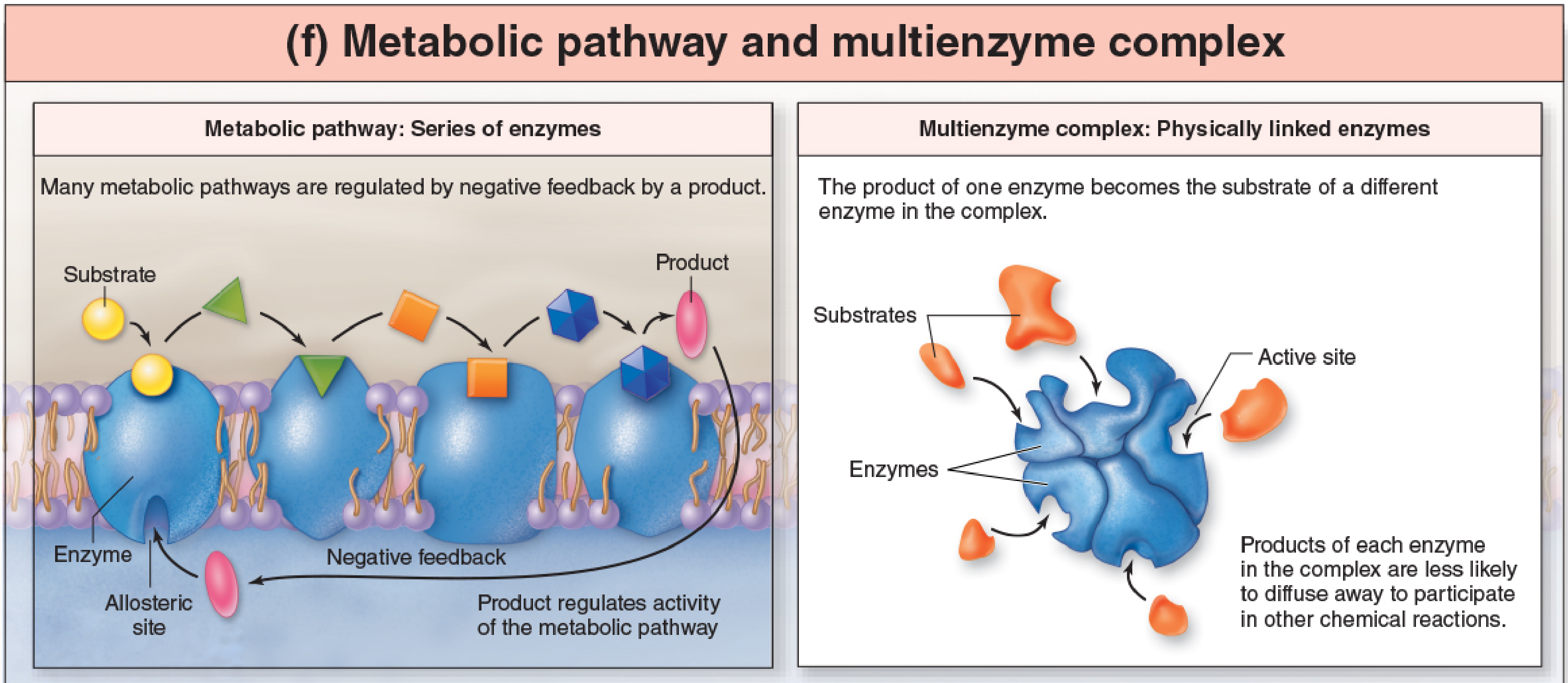
Figure 3.12b

3.3g Metabolic Pathways and Multienzyme Complexes

- Multiple enzymes usually required to convert initial substrate to final product
- **Metabolic pathway**
  - Series of enzymes
  - Product of one enzyme becomes substrate of the next
    - E.g., chemical breakdown of glucose
- **Multienzyme complex**
  - Group of attached enzymes
  - Work in a sequence of reactions
    - E.g., pyruvate dehydrogenase

3.3g Metabolic Pathways and Multienzyme Complexes

- Multienzyme complex advantages
  - Less likely substance will diffuse away into different biochemical pathway
  - Single complex can be regulated rather than individual enzymes
- Pathways regulated through negative feedback
  - Product from metabolic pathway acts as an allosteric inhibitor
    - Turns off enzyme early in pathway
    - As more product accumulates, less product formed
    - As less product accumulates, more product formed



(f) Metabolic pathway and multienzyme complex
Metabolic pathway: Series of enzymes
Many metabolic pathways are regulated by negative feedback by a product.
Substrate
Product
Enzyme
Allosteric site
Negative feedback
Product regulates activity of the metabolic pathway
Multienzyme complex: Physically linked enzymes
The product of one enzyme becomes the substrate of a different enzyme in the complex.
Substrates
Active site
Enzymes
Products of each enzyme in the complex are less likely to diffuse away to participate in other chemical reactions.

Figure 3.14f

3.3g Metabolic Pathways and Multienzyme Complexes

- Regulation of enzymes
  - **Phosphorylation**
    - Addition of phosphate group
    - Performed by **protein kinases**
    - Turns on some enzymes; turns off others
  - **Dephosphorylation**
    - Removal of phosphate group
    - Performed by **phosphatases**
    - Turns on some enzymes; turns off others

What did you learn?

- What is the relationship between enzymes and activation energy?
- What is the active site of an enzyme?
- Increasing the concentration of a substrate increases the rate of reaction up until what point?
- Which type of inhibitor resembles the substrate and binds to the enzyme active site?
- What two processes involve phosphate and are commonly used to regulate enzymes in a metabolic pathway or a multienzyme complex?

Clinical View: Drugs as Enzyme Inhibitors

- Drugs increase or decrease specific enzyme activity
  - E.g., penicillin targets a bacterial enzyme, slowing spread of infection
  - E.g., Sildenafil (Viagra) inhibits phosphodiesterase type 5
    - Treats erectile dysfunction by vasodilation of blood vessels of the penis

Clinical View: Lactose Intolerance

- Caused by a deficiency in lactase or abnormal lactase
  - Lactase is required to break bond in lactose into glucose and galactose
- Common in older adults
- Common symptoms: abdominal upset, nausea, diarrhea, bloating, gas
- Treated with lactase enzymes, avoidance of milk, or drinking lactose-free milk

3.4 Cellular Respiration

Learning Objectives:

1. Write the overall formula for glucose oxidation.
2. Name the two pathways that generate ATP.
3. List the four stages of glucose oxidation and where each stage occurs within a cell.
4. Summarize the metabolic pathway of glycolysis, including (a) where it occurs in a cell, (b) if it requires oxygen, (c) the initial substrate and final product, and (d) the molecules formed during energy transfer.

3.4 Cellular Respiration (*continued*)

Learning Objectives:

5. Explain the enzymatic reaction of the intermediate stage, including (a) where it occurs in a cell, (b) if it requires oxygen, (c) the initial substrate and final product, and (d) the molecules formed during energy transfer.
6. Define decarboxylation.
7. Summarize the metabolic pathway of the citric acid cycle including (a) where it occurs in a cell, (b) if it requires oxygen, (c) the initial substrate and final product, and (d) the molecules formed during energy transfer.
8. Describe the importance of NADH and $FADH_2$ in energy transfer.

3.4 Cellular Respiration (*continued*)

Learning Objectives:

9. Explain the actions that take place in the electron transport system.
10. Calculate the number of ATP molecules produced in cellular respiration if oxygen is not available and if oxygen is available.
11. Explain the fate of pyruvate when oxygen is in short supply.
12. Describe the impact on ATP production if there is insufficient oxygen.
13. Describe the entry point in the metabolic pathway of cellular respiration for both fatty acids and amino acids.

3.4 Cellular Respiration

- Exergonic multistep metabolic pathway
- Organic molecules oxidized and disassembled by a series of enzymes
- Potential energy in chemical bonds released
- Energy used to make ATP (endergonic process)
- Oxygen required

3.4a Overview of Glucose Oxidation

- **Glucose oxidation**
  - Step-by-step breakdown of glucose with energy release
  - Carbon dioxide and water formed
- Glucose
  - Energy-rich molecule with many C—C, C—H, C—O bonds
- Net chemical reaction

$$C_6H_{12}O_2 + 6\ O_2 \longrightarrow 6\ CO_2 + 6\ H_2O$$

3.4a Overview of Glucose Oxidation

- Pathways for ATP production
  - Energy from broken bonds used to attach phosphate group to ADP
  - Energy can be used directly
    - Least common
    - **Substrate level phosphorylation**
  - Energy can be used indirectly
    - Most common
    - Energy first released to coenzymes
    - Then energy transferred to form ATP
    - **Oxidative phosphorylation**

3.4a Overview of Glucose Oxidation

- **Cellular location of glucose oxidation**
  - 20 different enzymes required
  - Enzymes found in both
    - **Cytosol—**semifluid cell contents of the cell
    - **Mitochondria—**small cellular organelles

Cellular Structures Required for Cellular Respiration

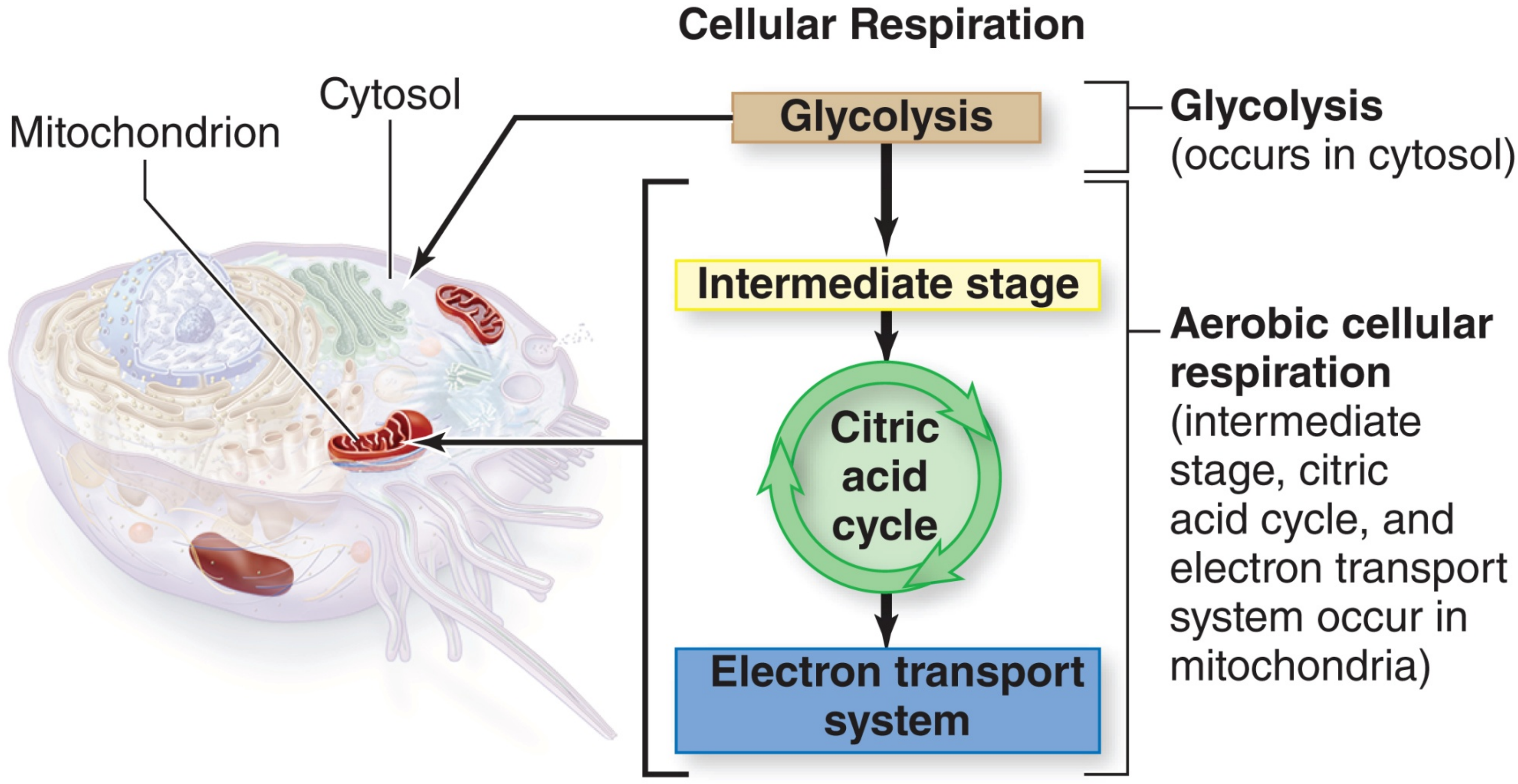


Figure 3.15

3.4a Overview of Glucose Oxidation

- Four stages of glucose oxidation
  1. Glycolysis
     - Occurs in cytosol
     - Does not require oxygen
  2. Intermediate stage
  3. Citric acid cycle
  4. Electron transport system

  – Stages 2, 3, and 4
     - Occur in mitochondria
     - Require oxygen

3.4b Glycolysis

- **Glycolysis**
  - Does not require oxygen
  - Ten enzymes in cytosol participate
  - Glucose broken down into two pyruvate molecules
  - Net production of 2 ATP and 2 NADH molecules

- **Glycolysis: Steps 1–5**
  - Glucose split into two molecules of glyceraldehye 3-phosphate (G3P)
  - ATP "invested" at steps 1 and 3
    - o Phosphate groups transferred to break down products of glucose

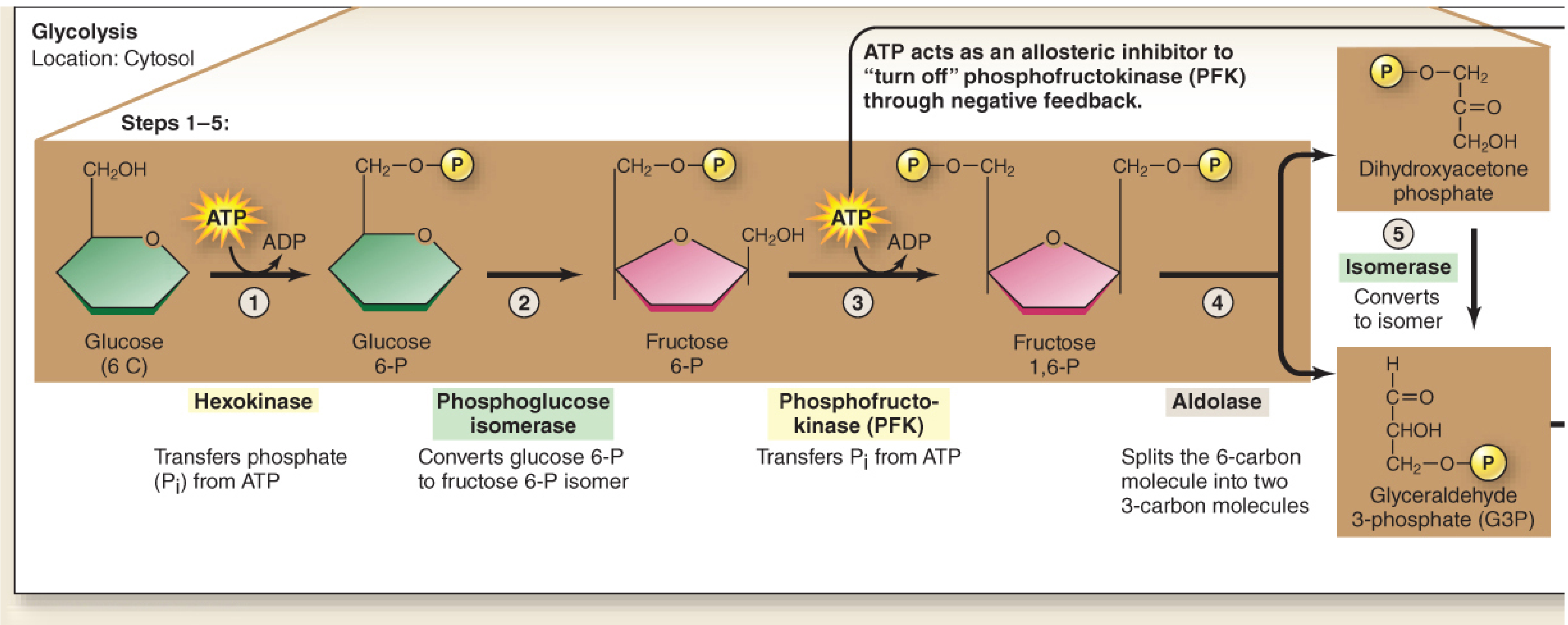


Figure 3.16b

- **Glycolysis: Steps 6–7**
  - Occur twice in glucose oxidation
  - Step 6: Unattached P_i added to substrate; two hydrogen atoms released to NAD^+
  - Step 7: P_i transferred to ADP to form ATP

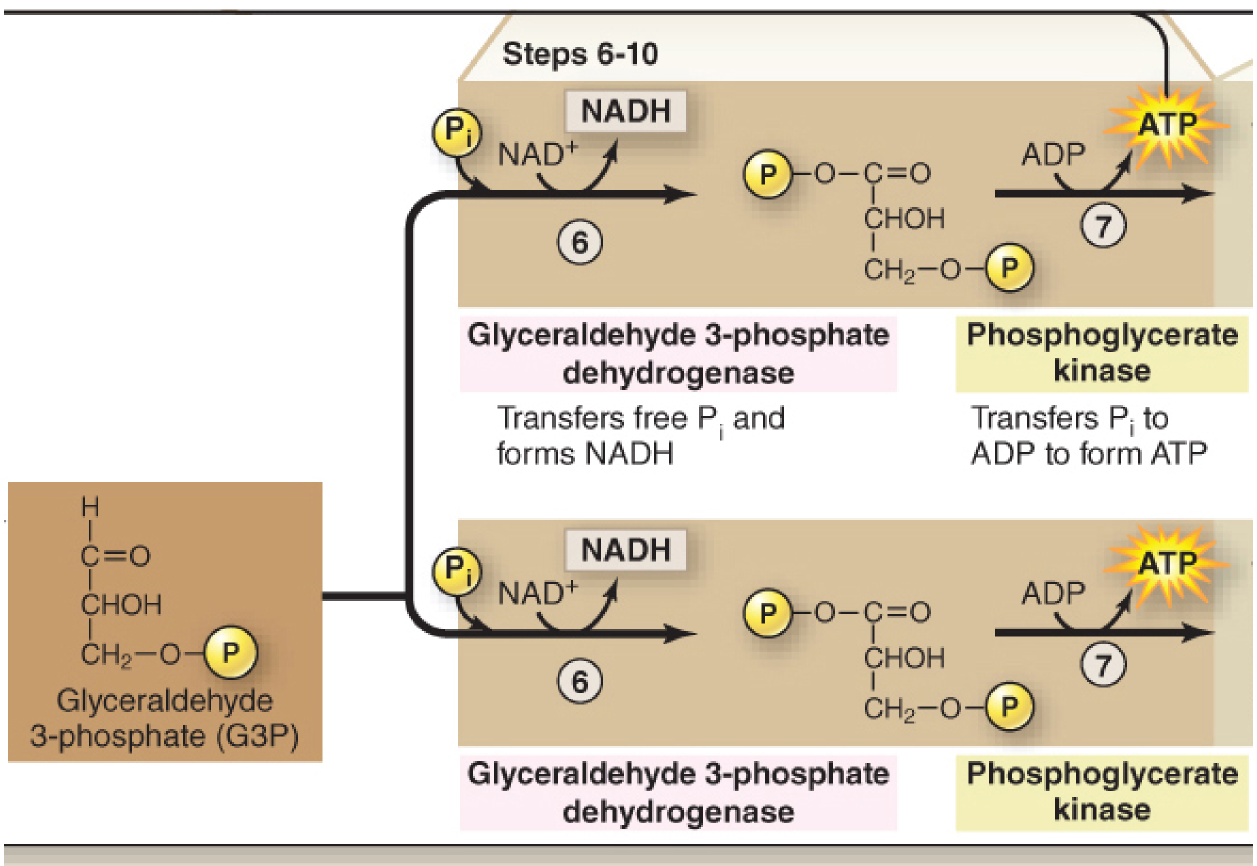


Figure 3.16b

- **Glycolysis: Steps 8–10**
  - Occur twice in glucose oxidation
  - Step 8: molecule from step 7 converted to an isomer
  - Step 9: loss of water molecule
  - Step 10: P_i transferred to form ATP

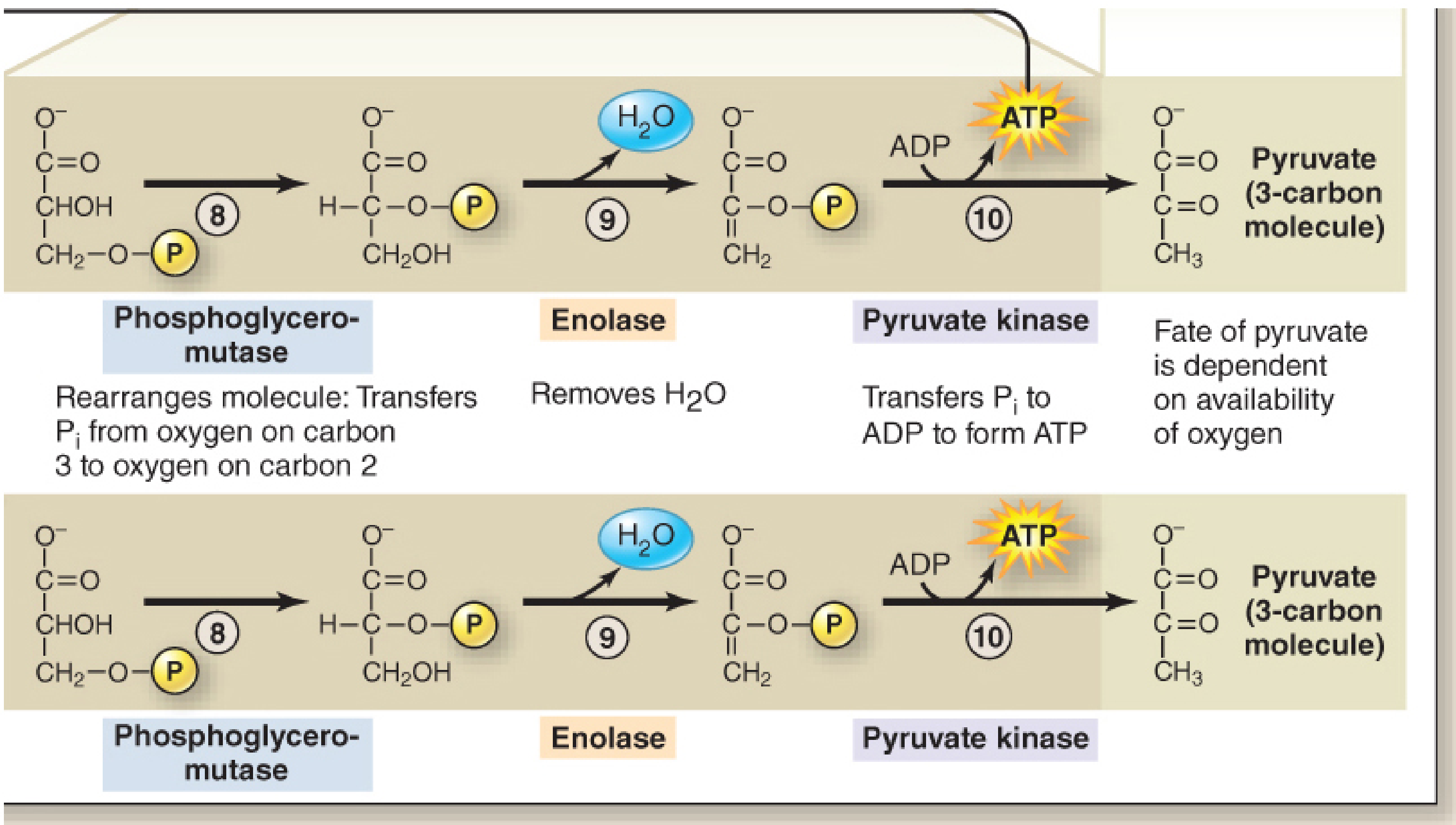


Figure 3.16b

3.4b Glycolysis

- Summary of Glycolysis
  - Metabolic process, occurs in cytosol, does not require oxygen
  - Glucose is the initial substrate
  - Pyruvate is the final product
  - Net 2 ATP formed (2 invested, 4 formed)
  - 2 NADH formed

Metabolic Pathway of Glycolysis

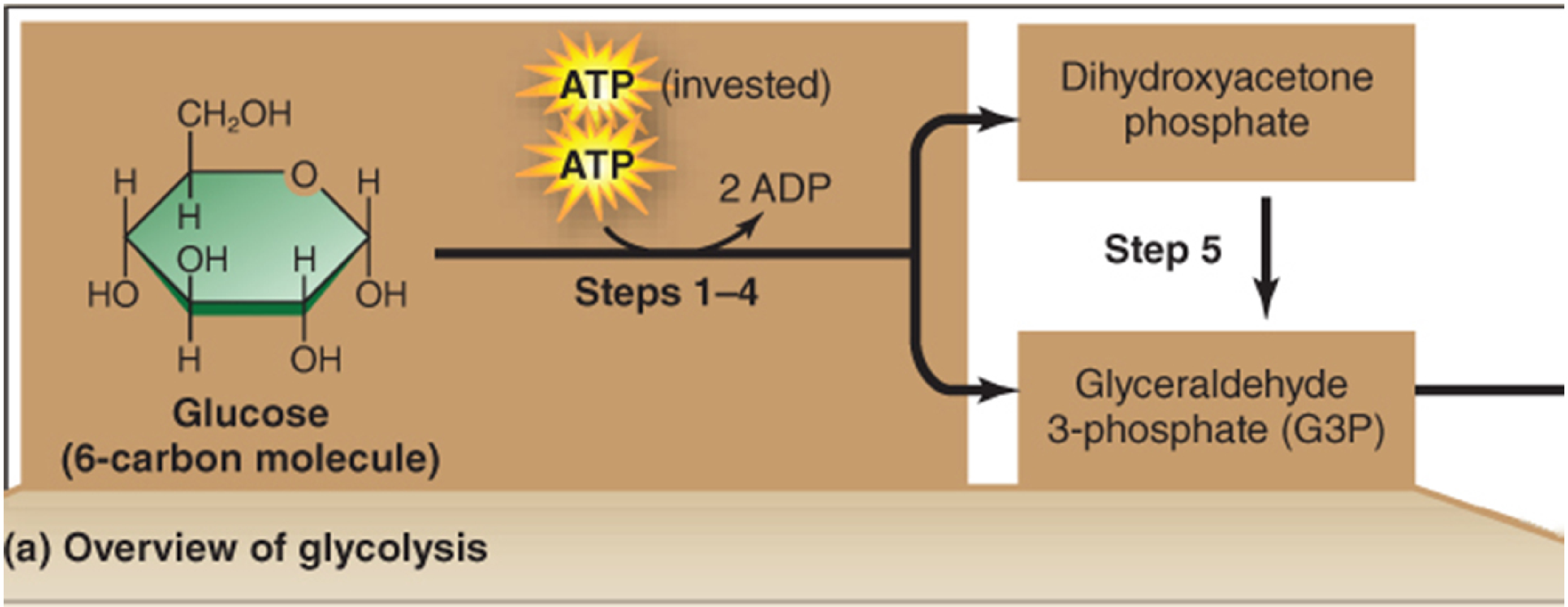


Figure 3.16a

3.4b Glycolysis

- Regulation of glycolysis
  - Through negative feedback
  - ATP acting as allosteric inhibitor to "turn off" phosphofructokinase (PFK)
  - As ATP increases, PFK inhibited
  - Glycolytic pathway progressively shut down
  - As ATP decreases, glycolysis increased
  - Glycolysis decreased by NADH, citrate, fatty acids, and other fuel molecules

3.4b Glycolysis

- **Pyruvate** is the final product of glycolysis
- Chemical changes made to pyruvate depend upon oxygen availability
  - If sufficient O_2 available, pyruvate enters mitochondria
  - If insufficient O_2 available, pyruvate converted to lactate

3.4c Intermediate Stage

- Remaining stages of cellular respiration
  - Intermediate stage
  - Citric acid cycle
  - Electron transport system
    - All aerobic and occur within mitochondria

3.4c Intermediate Stage

- Mitochondrion structure
  - Double membrane organelle
    - Outer membrane
    - Inner membrane
  - Space between membranes is the **outer compartment**
  - Innermost space is the **matrix**
    - Multienzyme complex of intermediate stage resides here
    - Enzymes of citric acid cycle reside here
  - Molecules of electron transport system embedded in cristae

3.4c Intermediate Stage

- **Intermediate Stage**
  - Link between glycolysis and citric acid cycle
  - Catalyzed by **pyruvate dehydrogenase**
    - Pyruvate and coenzyme A (CoA) combined to form acetyl CoA
  - During **decarboxylation,** a carboxyl group is released from pyruvate as CO_2
    - Energy released as NADH formed from NAD^+
    - Acetyl CoA enters citric acid cycle
  - Must occur twice
    - 2 NADH are produced from original glucose molecule

Intermediate Stage

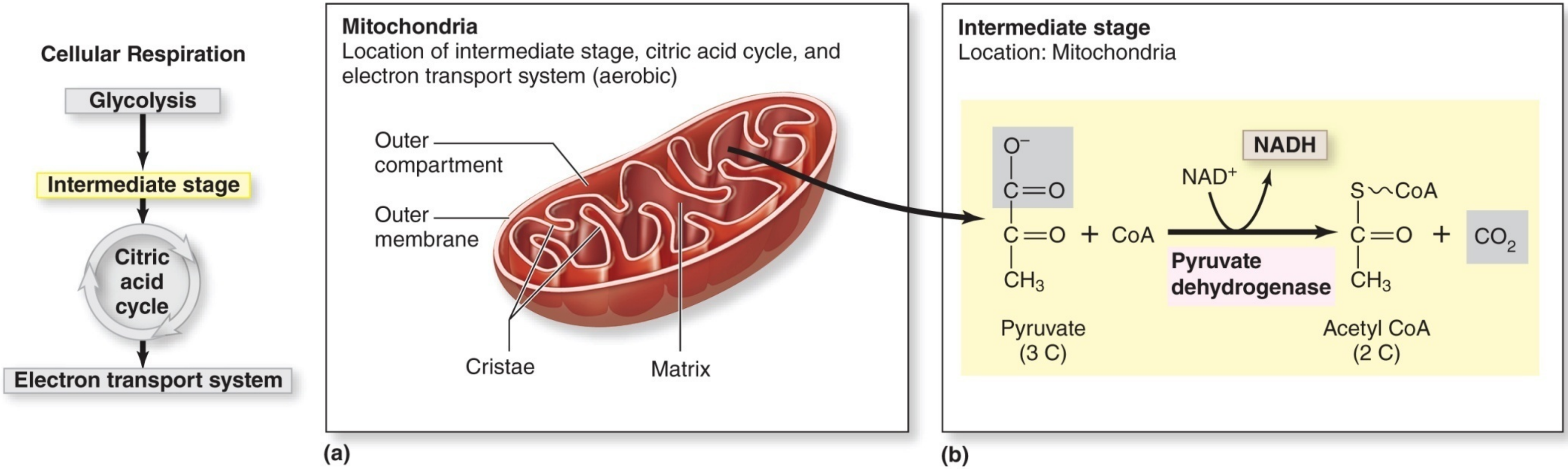
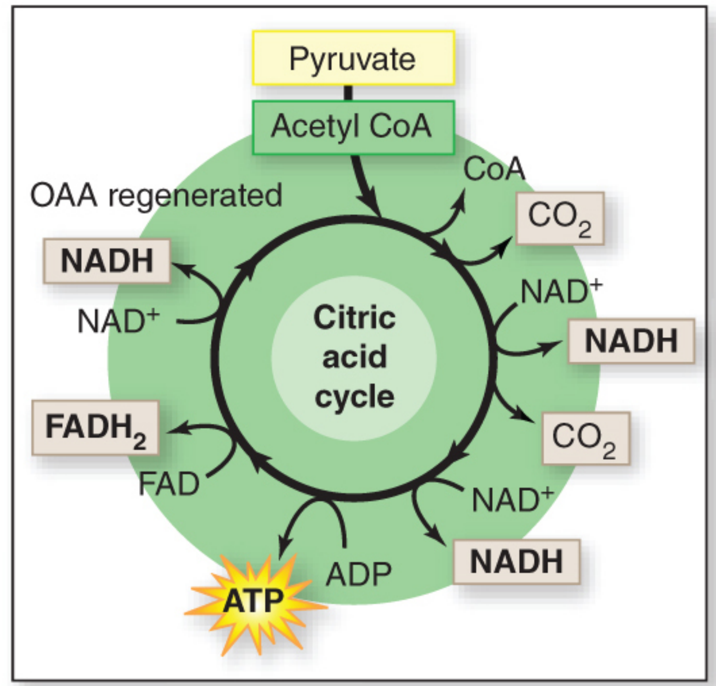


Figure 3.17

3.4d Citric Acid Cycle

- Cyclic metabolic pathway
  - Nine enzymes in the mitochondrial matrix
  - Acetyl CoA converted to two CO_2 molecules
  - CoA molecule released
  - ATP, 3 NADH, and 1 $FADH_2$ formed during one cycle



(a) Net chemical reaction of citric acid cycle

Figure 3.18a

3.4d Citric Acid Cycle

- Steps of the citric acid cycle

Step 1: Acetyl CoA combined with **oxaloacetate** to form **citrate**

Steps 2 and 3: Isomer formed by removing water molecule, then reattaching elsewhere

Steps 4 and 5: Transfer of hydrogen to NAD^+ to form NADH; CoA attached

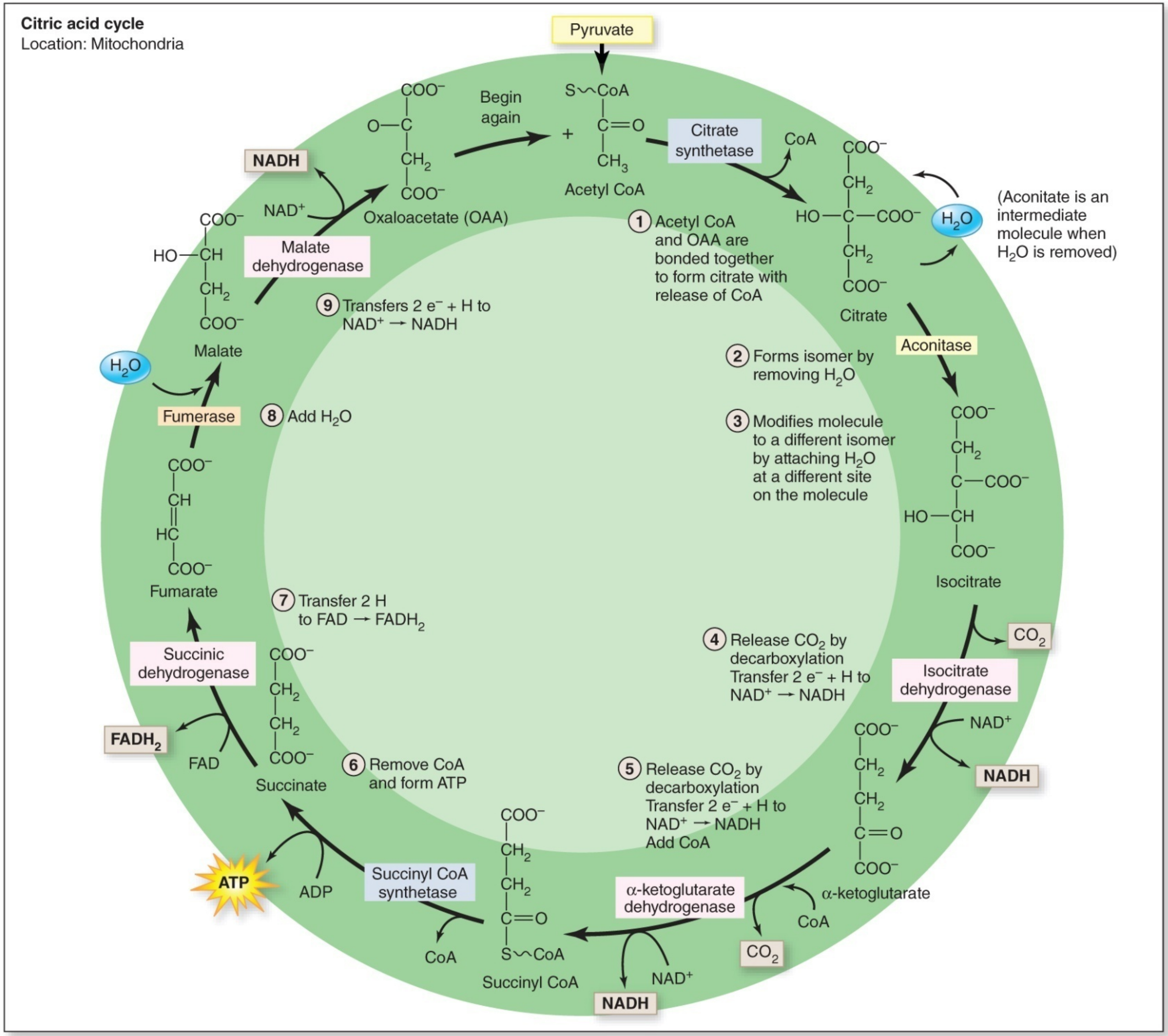
Step 6: Removal of CoA and the formation of ATP

Step 7: Dehydrogenase transfers hydrogens to form $FADH_2$

Step 8: Water removed

Step 9: Dehydrogenase transfers hydrogen to form NADH

Figure 3.18b



(b) Details of citric acid cycle

3.4d Citric Acid Cycle

- Summary of the citric acid cycle
  - Occurs in mitochondria
  - Requires oxygen
  - Acetyl CoA initial substrate
  - Two CO_2 and one CoA produced
  - 1 ATP, 3 NADH, 1 $FADH_2$ formed per cycle
  - Oxaloacetic acid involved in first step and regenerated in last step
  - Two “turns” for one glucose molecule
    - 2 ATP, 6 NADH, 2 $FADH_2$

3.4d Citric Acid Cycle

- Regulation of the citric acid cycle
  - Occurs at first step enzyme (citrate synthetase)
  - If energy demands high
    - Levels of NADH, ATP, and pathway intermediates low
    - Cycle activity increased
  - If energy demands low
    - Levels of substances higher
    - Cycle activity decreases
  - These adjustments maintain homeostasis

3.4d Citric Acid Cycle

- Completion of glucose digestion
  - Following glycolysis and two “turns” of the intermediate stage and citric acid cycle
    - Glucose completely digested
    - Six carbon atoms of glucose released as six carbon dioxide molecules

3.4d Citric Acid Cycle

Summary of the chemical breakdown of glucose

- Glycolysis
  - Occurs in the cytosol
  - Energy transferred to form 2 net ATP molecules and 2 NADH molecules
  - If oxygen available, pyruvate enters mitochondrion
- Intermediate stage
  - Occurs in mitochondrion
  - Pyruvate converted to acetyl CoA and 1 CO_2 molecule
  - 1 NADH molecule formed per pyruvate
  - 2 NADH molecules formed per glucose molecule

3.4d Citric Acid Cycle

Summary of the chemical breakdown of glucose (*continued*)

- Citric acid cycle
  - Completes breakdown of glucose in a mitochondrion
  - 2 CO_2 produced per turn of the cycle
  - 1 ATP, 3 NADH, 1 $FADH_2$ produced per cycle
  - Two acetyl CoA produced from one glucose molecule
  - Two cycles
  - 2 ATP, 6 NADH, 2 $FADH_2$

Table 3.3 Comparison of the First Three Stages of Glucose Breakdown

Characteristics	Glycolysis	Intermediate Stage	Citric Acid Cycle
Where it occurs	Cytosol	Mitochondria	Mitochondria
Requires oxygen (is aerobic)?	No	Yes (aerobic)	Yes (aerobic)
Substrate	Glucose	Pyruvate (2 pyruvates from each glucose)	Acetyl CoA (2 acetyl CoA from each glucose)
Product	2 pyruvate molecules	Acetyl CoA and 1 CO_2 per pyruvate	2 CO_2 per acetyl CoA
Pathway or complex	Metabolic pathway	Multienzyme complex	Metabolic pathway
Net energy molecules produced	2 ATP (net) and 2 NADH	1 NADH per pyruvate	1 ATP per acetyl CoA 3 NADH per acetyl CoA 1 $FADH_2$ per acetyl CoA
How lack of oxygen affects the stage	Lactate produced (to regenerate NAD^+ so glycolysis can continue)	Pathway inhibited by lack of oxygen	Pathway inhibited by lack of oxygen

3.4e The Electron Transport System

- What is the function of the **electron transport system?**
  - Transfer of electrons from NADH and $FADH_2$
    - Energy released used to make ATP
  - Located in the inner folded membrane of mitochondria (cristae)
    - H^+ pumps, electron carriers, ATP synthetase enzymes

3.4e The Electron Transport System

- Structures of the electron transport system
  - H^+ pump
    - Proteins that transport H^+ from matrix to outer membrane compartment
    - Maintains a H^+ gradient between outer compartment and mitochondrial matrix
    - Also binds and releases electrons
  - Electron carriers
    - Transport electrons between H^+ pumps
  - This series of H^+ pumps and electron carriers is called the **electron transport chain**
    - ATP synthetase allows passage of H^+

3.4e The Electron Transport System

- Steps of the electron transport system
  1. Electrons transferred from coenzymes to O_2
     - Coenzyme releases hydrogen and is oxidized
     - Electrons are passed through electron carriers to O_2
     - O_2 combines with 4 electrons and 4 H^+ to produce two molecules of H_2O
  2. Proton gradient established
     - As electrons are passed through the electron transport chain, kinetic energy harnessed by H^+ pumps
     - Move H^+ to outer compartment, maintaining proton gradient

3.4e The Electron Transport System

- Steps of the electron transport system (*continued*)

  3. Proton gradient harnessed to form ATP
     - H+ moves down its concentration gradient from outer compartment into matrix
       - Analogous to water of a dam turning water wheel
     - Kinetic energy of falling H^+ harnessed by ATP synthetase
     - New bond between ADP and P_i formed, producing ATP

3.4e The Electron Transport System

- **Oxidative phosphorylation**
  - Oxygen as final electron acceptor
  - ATP formed from phosphorylation of ADP
  - Distinguished from substrate-level phosphorylation
    - Forms ATP from energy directly released from a substrate
    - Occurs during glycolysis and citric acid cycle

The Electron Transport System

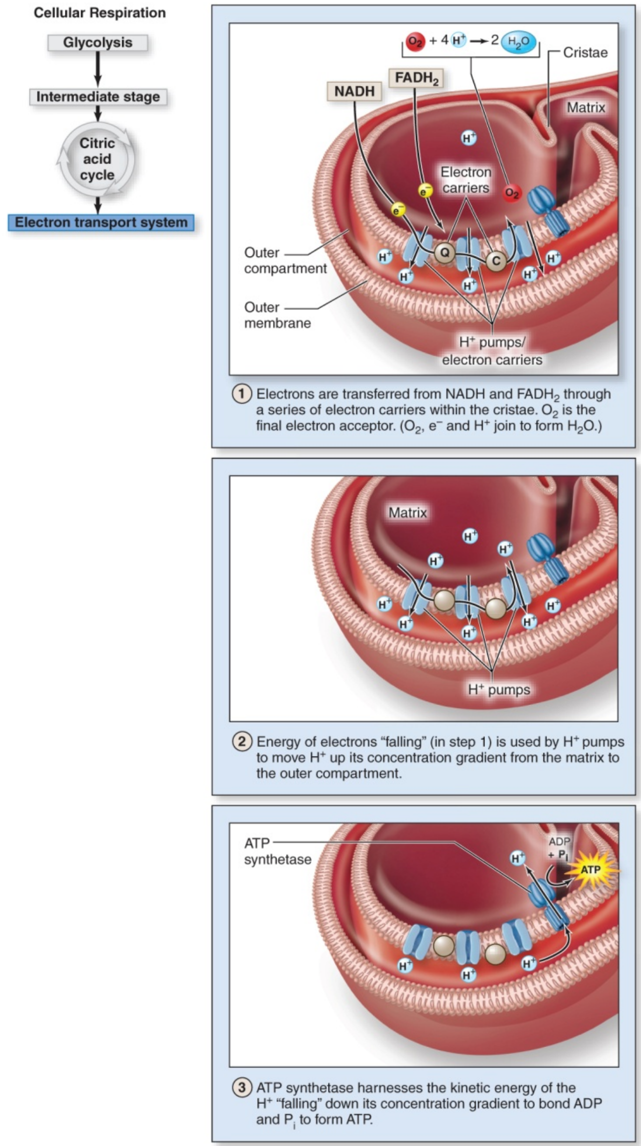


Figure 3.19

Summary of Stages of Cellular Respiration

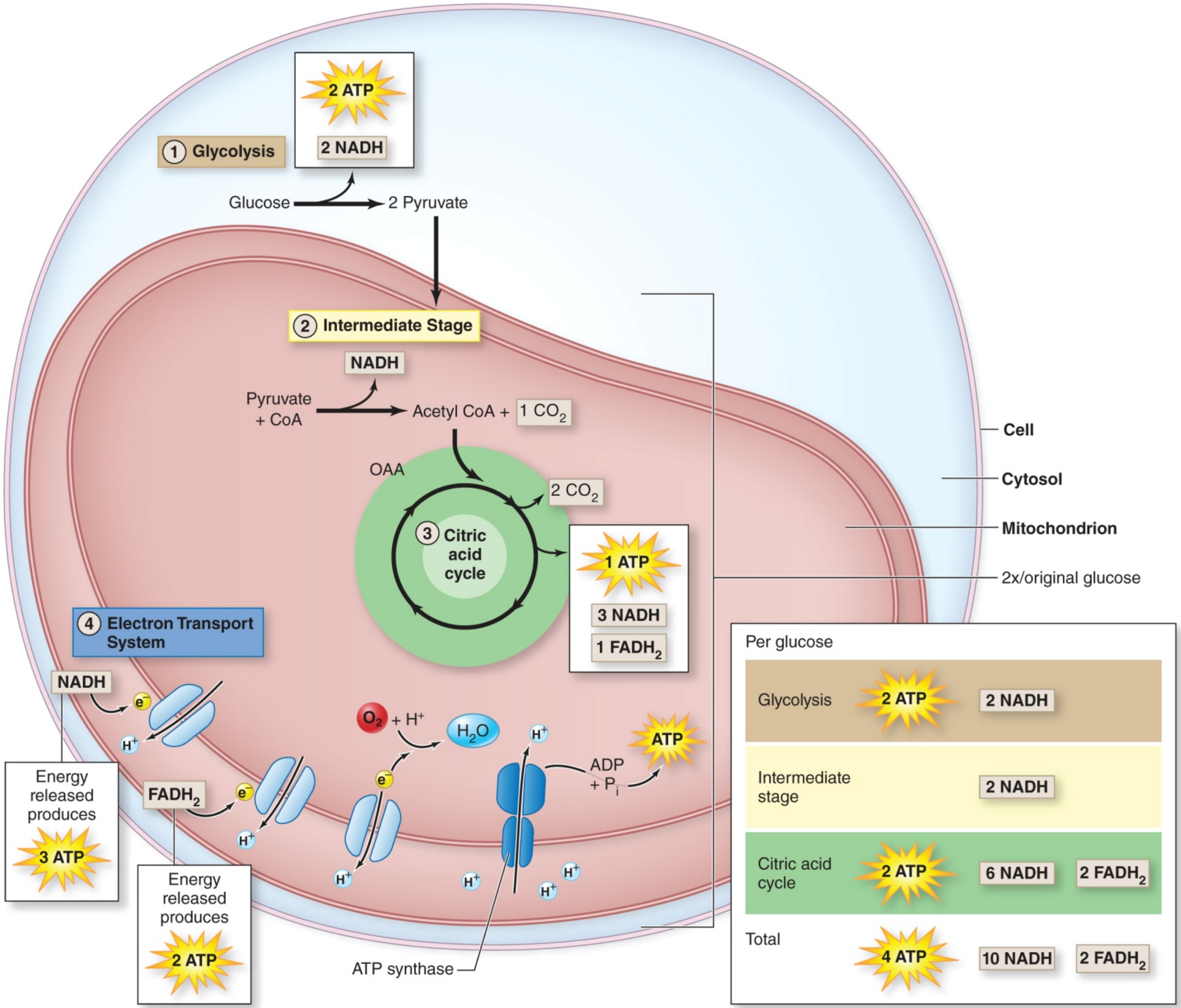


Figure 3.20

3.4f ATP Production

- Number of ATP molecules generated depends on entry point of electrons into the transport chain
  - Electrons from NADH enter at top
    - Passed through 3 H^+ pumps
    - Generates 3 ATP molecules
  - Electrons from $FADH_2$ enter at second pump
    - Generates 2 ATP molecules

3.4f ATP Production

- How can we calculate the specific number ATP molecules produced in the breakdown of a glucose molecule?
  - Number of energy molecules generated from glucose breakdown in each of first three stages of cellular respiration
  - Number of ATP generated by oxidation of each type of coenzyme in the electron transport system

3.4f ATP Production

- ATP in glucose breakdown

Stage/Total	**Substrate-level phosphorylation**	**Oxidative phosphorylation**
Glycolysis	2 ATP	2 NADH → 6 ATP
Intermediate Stage	—	2 NADH → 6 ATP
Citric Acid Cycle	2 ATP	6 NADH → 18 ATP
		2 FADH2 → 4 ATP
Total	**4 ATP**	**34 ATP**

Clinical View: Cyanide Poisoning

- Cyanide binds with a specific electron carrier of the electron transport system
  - Inhibits electron transport system and ATP production
  - Electrons unable to reach oxygen
  - Treat with cyanide- binding substances

3.4g The Fate of Pyruvate with Insufficient Oxygen

- Insufficient oxygen
  1. Activity of electron transport chain decreases
     - Levels of NADH and $FADH_2$ accumulate
     - Decreased levels of NAD^+ and FAD
  2. Cell becomes more dependent upon glycolysis
     - Requires NAD^+ to continue
  3. Glycolysis eventually shuts down
     - Due to lack of NAD^+
  4. NAD+ must be regenerated for glycolysis to continue

3.4g The Fate of Pyruvate with Insufficient Oxygen

- Regeneration of NAD^+
  - Hydrogen transferred from NADH to pyruvate
  - Pyruvate converted to lactate (lactic acid)
  - Enables glycolysis to continue
    - Only 2 ATP generated versus 30 with sufficient oxygen
    - Impacts individuals with decreased ability to deliver oxygen to cells
      - E.g., those with respiratory or cardiovascular disease

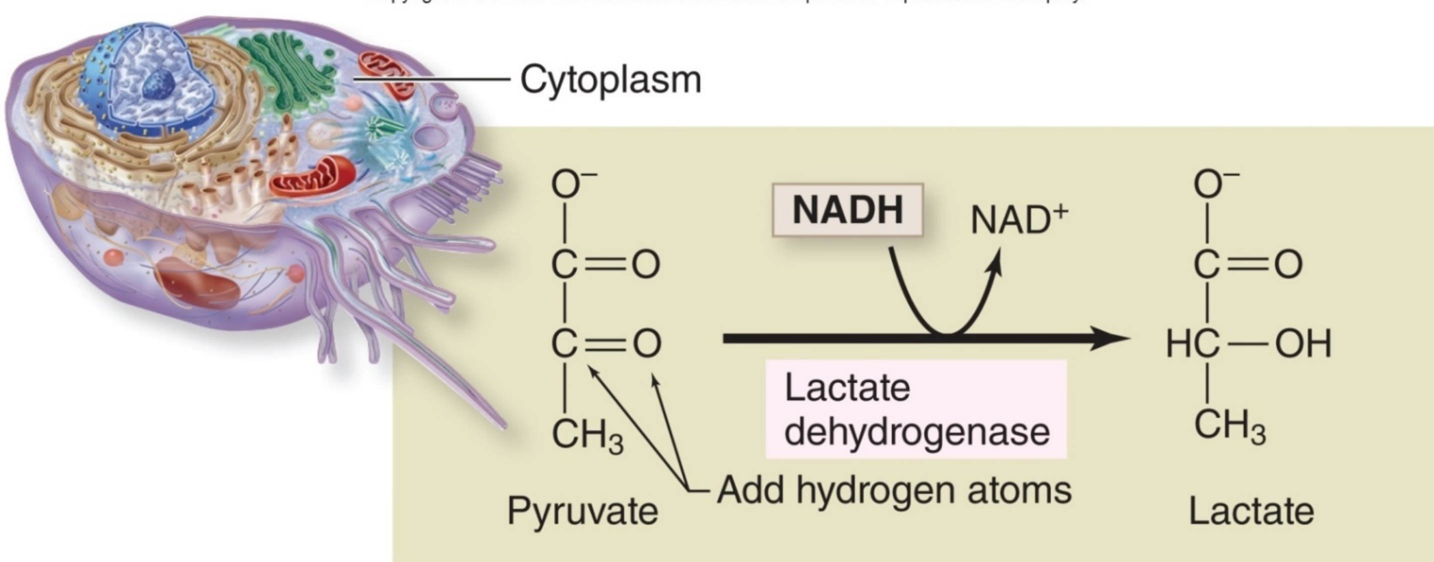


Figure 3.21

3.4h Other Fuel Molecules That Are Oxidized in Cellular Respiration

- Fatty acids
  - Enzymatically change two carbons at a time to form acetyl CoA—**beta oxidation**
  - Acetyl CoA the enters pathway at citric acid cycle
  - Can only be oxidized aerobically
- Amino acids
  - Different pathway if protein is used for fuel
  - Point of entry depends upon specific type
  - Amine group is a waste product
    - Converted to urea
    - Excreted by kidneys

What did you learn?

- What is the overall chemical reaction for glucose oxidation?
- What are the four stages of cellular respiration for glucose oxidation, and where does each occur?
- What are the final net products of glycolysis?
- What are the final net products the intermediate stage from one molecule of glucose?
- What energy molecules are produced in breaking down one molecule of glucose in the citric acid cycle?

What did you learn?

- What are the three primary steps that take place in the electron transport system?
- How many ATP are formed from a NADH molecule during oxidative phosphorylation? A $FADH_2$ molecule?
- Pyruvate is converted to what molecule if there is insufficient oxygen? Why is this done?
- Why is oxygen required to burn fatty acids?