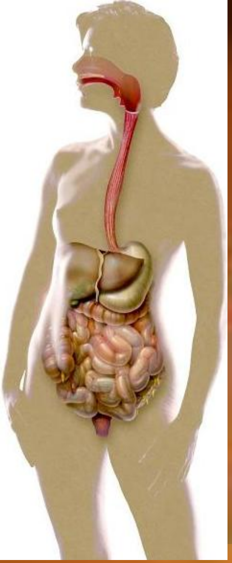

BIOLOGY I

Chapter 8: INTRODUCTION TO METABOLISM

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Instructor

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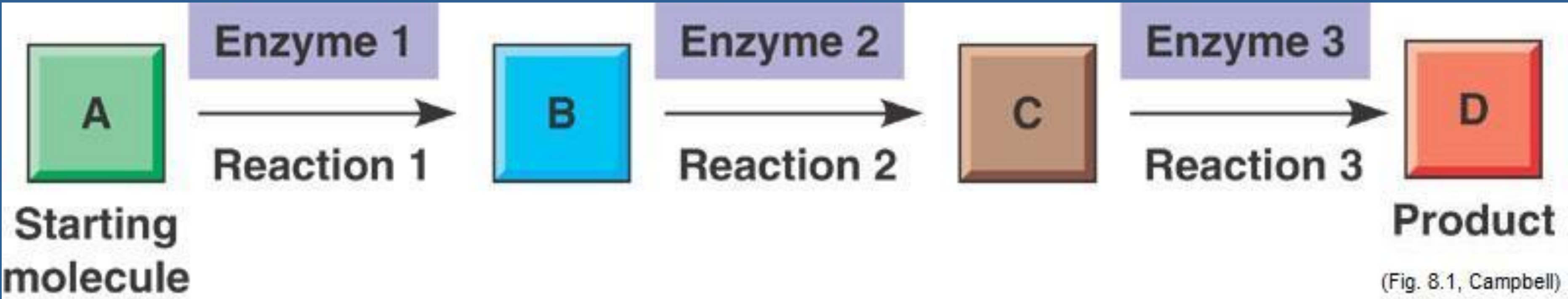
Metabolism: Basic Definitions

Metabolism	The sum of **all chemical reactions** within a living organism (from the Greek *metabole*, change). Metabolism as a whole manages the material and energy resources of the cell; it includes catabolism and anabolism.
Catabolism	All ***decomposition reactions***: chemical reactions that result in the **breakdown** of complex organic molecules into simpler substances. Catabolic, or ***degradative*** pathways or reactions: • are generally ***hydrolytic reactions (hydrolysis)***: chemical bond is broken through the addition of a water molecule. • are usually ***exergonic***: **produce** or **release** more energy than they consume.
Anabolism	All ***synthesis reactions***: chemical reactions in which simpler substances are combined to **build** more complex molecules. Anabolic, or ***biosynthetic*** pathways or reactions: • are usually ***dehydration synthesis reactions (condensation)***: release water. • are usually ***endergonic*****: consume** (require) more energy than they produce.

Organization of the Chemistry of Life into Metabolic Pathways

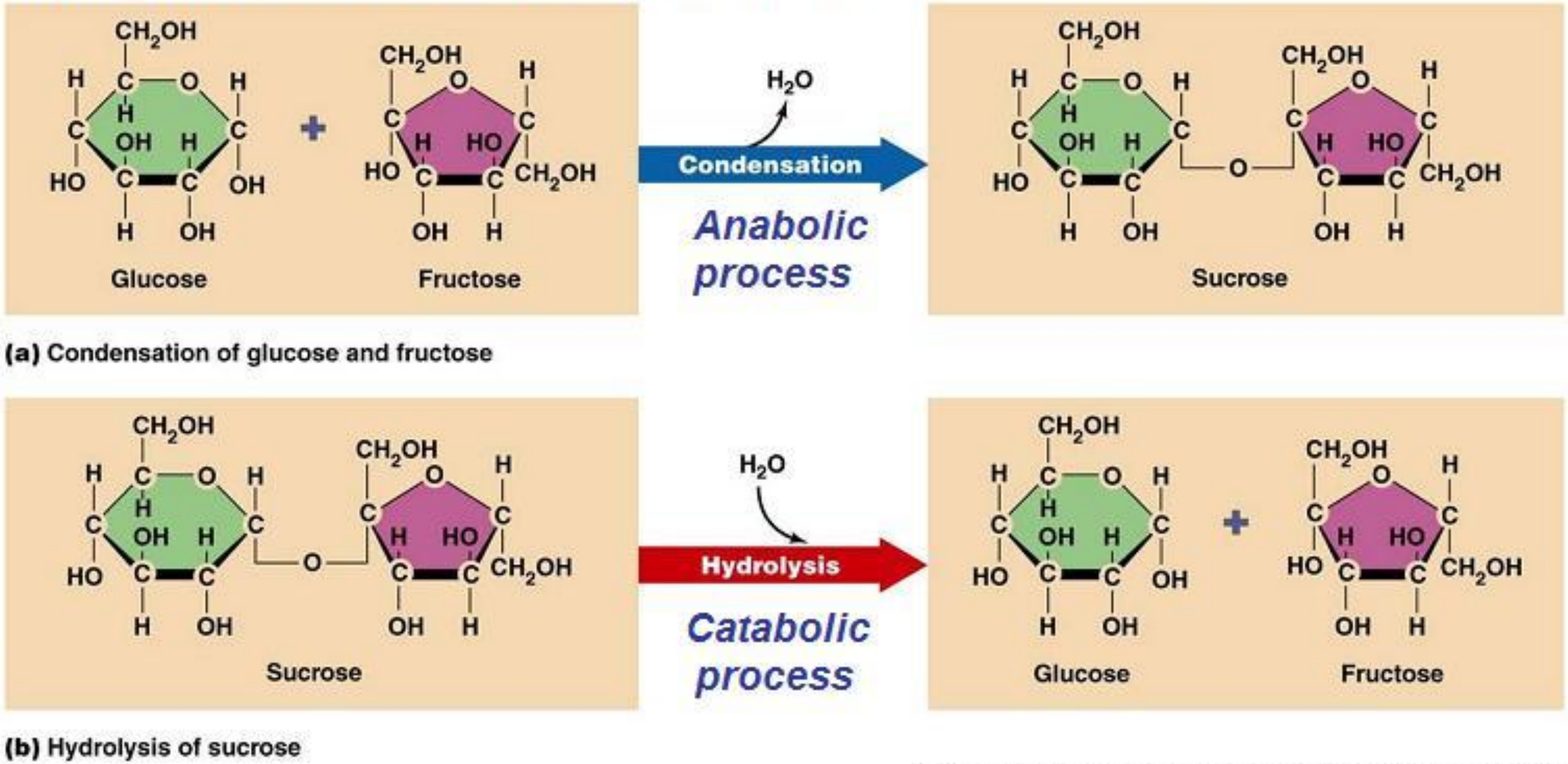
- A cell's metabolism is arranged like an elaborate road map of the thousands of chemical reactions that occur in a cell, in intersecting **metabolic pathways**.
- A ***metabolic pathway*** is a series of chemical reactions. Remember:
  - An ***anabolic pathway*** builds a complex molecule from simpler compounds.
  - A ***catabolic pathway*** breaks down a complex molecule into simpler compounds.
  - **Enzymes** are macromolecules serving as *catalysts*, chemical agents that speed up the rate of a reaction without being consumed by the reaction.



(Fig. 8.1, Campbell)

Metabolism: Anabolic and Metabolic Pathways

Figure 7.4. Anabolic and Catabolic Reactions



Life Requires Energy

- Biological molecules can combine to form complex cellular structures such as the various organelles in a eukaryotic cell. But is this enough to qualify as being alive? If the chemical building blocks of life were put into a container and water added, would you have life?
- Of course, the answer is no, in part because one important ingredient would be missing. **Life requires *energy*.** (*Presson & Jenner*, 2008)

Forms of Energy

Energy	Capacity to cause <u>change</u>, or do <u>work</u>. Energy is expressed in units of work—***kilojoules (kJ)*** or in units of heat energy—**kilocalories (kcal)**. One kilocalorie is equal to 4.184 kJ.
Kinetic energy	Energy associated with matter or objects in **motion**. • ***Mechanical energy*** performs work by moving **matter**---anything that has mass and takes up space.
Heat or thermal energy	Kinetic energy associated with the **random movement** of atoms or molecules. • Thermal energy flows from an object with a higher temperature to an object with a lower temperature.
Potential energy	Energy **stored** by matter due to its position, location or structure—its capacity to accomplish work is not being used at the moment. • Molecules possess energy because of the arrangement of their atoms.
Chemical energy	Form of potential energy that is stored in the **bonds** of compounds and molecules (such as in food), available for release in a chemical reaction.

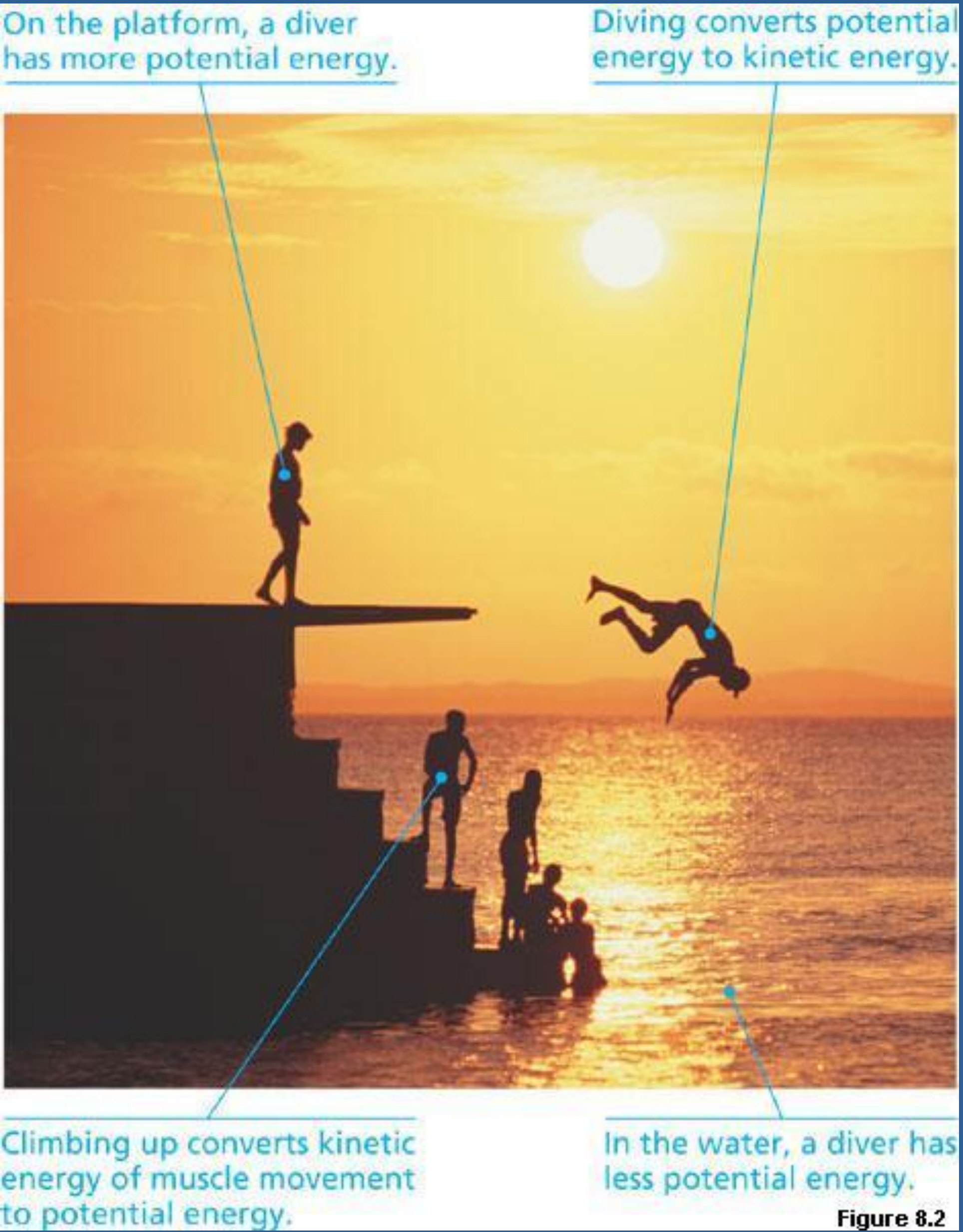


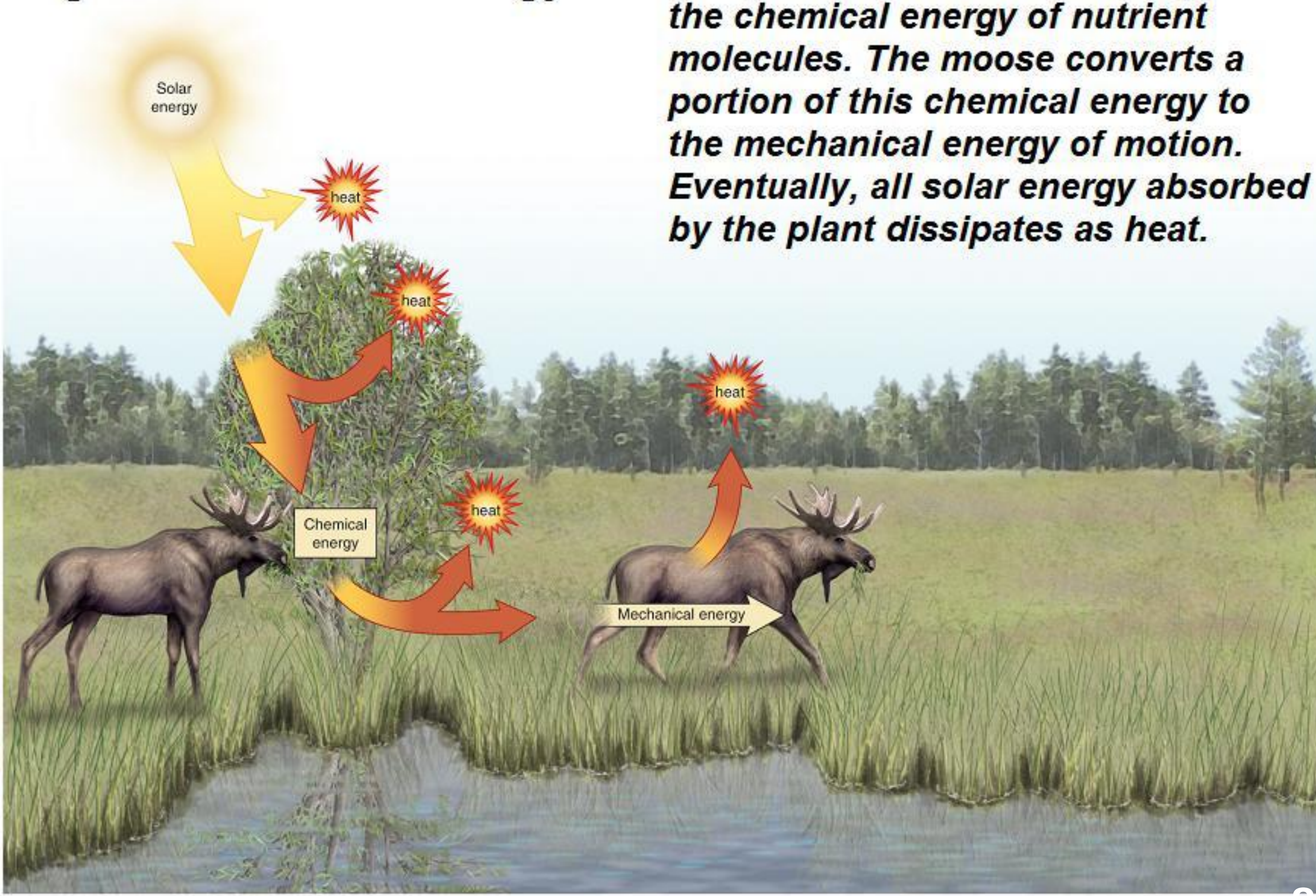
Figure 8.2

Forms of Energy

- **Organisms are energy transformers.**
- The man climbing the steps to the diving platform is releasing *chemical energy* from the food he ate for lunch and using some of that energy to perform the work of climbing. Climbing up transforms *kinetic energy* of muscle movement into *potential energy* due to his increasing height above water.
- The man diving is converting his *potential energy* to *kinetic energy*, which is then transferred to the water as he enters it. A small amount of energy is lost as heat due to friction.

Figure 6.1. Flow of energy.

The plant converts solar energy to the chemical energy of nutrient molecules. The moose converts a portion of this chemical energy to the mechanical energy of motion. Eventually, all solar energy absorbed by the plant dissipates as heat.



The Laws of Energy Transformation (Thermodynamics)

- **Thermodynamics** is the study of **energy** and its ***transformations*** that occur in a collection of matter.
- ***System*** refers to the matter under study.
- ***Surroundings*** refer to everything outside the system—the rest of the universe.
  - ***Isolated system*** = unable to exchange either energy or matter with its surroundings. *Example*: liquid in a thermos bottle.
  - ***Closed system*** = able to exchange energy (heat and work) but not matter with its environment. *Example*: a greenhouse (exchanges heat but not work with its environment). In reality no system can be completely closed; there are only varying degrees of closure.
  - ***Open system*** = able to exchange energy or matter with its surroundings. *Example*: organisms (they absorb light or chemical energy and release heat and metabolic waste products).

The Laws of Energy Transformation (Thermodynamics)

- **First law of thermodynamics = law or principle of conservation of energy:**
  - Energy can be **transferred and transformed**, but it **cannot be created or destroyed**.
    - ✓ Organisms must capture energy from the environment and ***transform it*** to a form that can be used for biological work.
- **Second law of thermodynamics:**
  - Every energy transfer or transformation **increases the entropy of the universe**. ***Entropy*** is a measure of disorder (disorganization), or randomness.
    - ✓ This law also explains that during energy transfer or transformation, some energy becomes *unusable energy*, unavailable to do work.

The Laws of Energy Transformation (Thermodynamics)

a) **First law of thermodynamics (conservation of energy):** ***Energy can be transferred or transformed but neither created nor destroyed*.** For example, the chemical (potential) energy in food will be converted to the kinetic energy of the cheetah's movement in (b).

b) **Second law of thermodynamics:** ***Every energy transfer or transformation increases the disorder (entropy) of the universe*.** For example, disorder is added to the cheetah's surroundings in the form of heat and the small molecules that are the by-products of metabolism.

(a) First law of thermodynamics (b) Second law of thermodynamics Figure 8.3

Energy Transfer in Metabolism

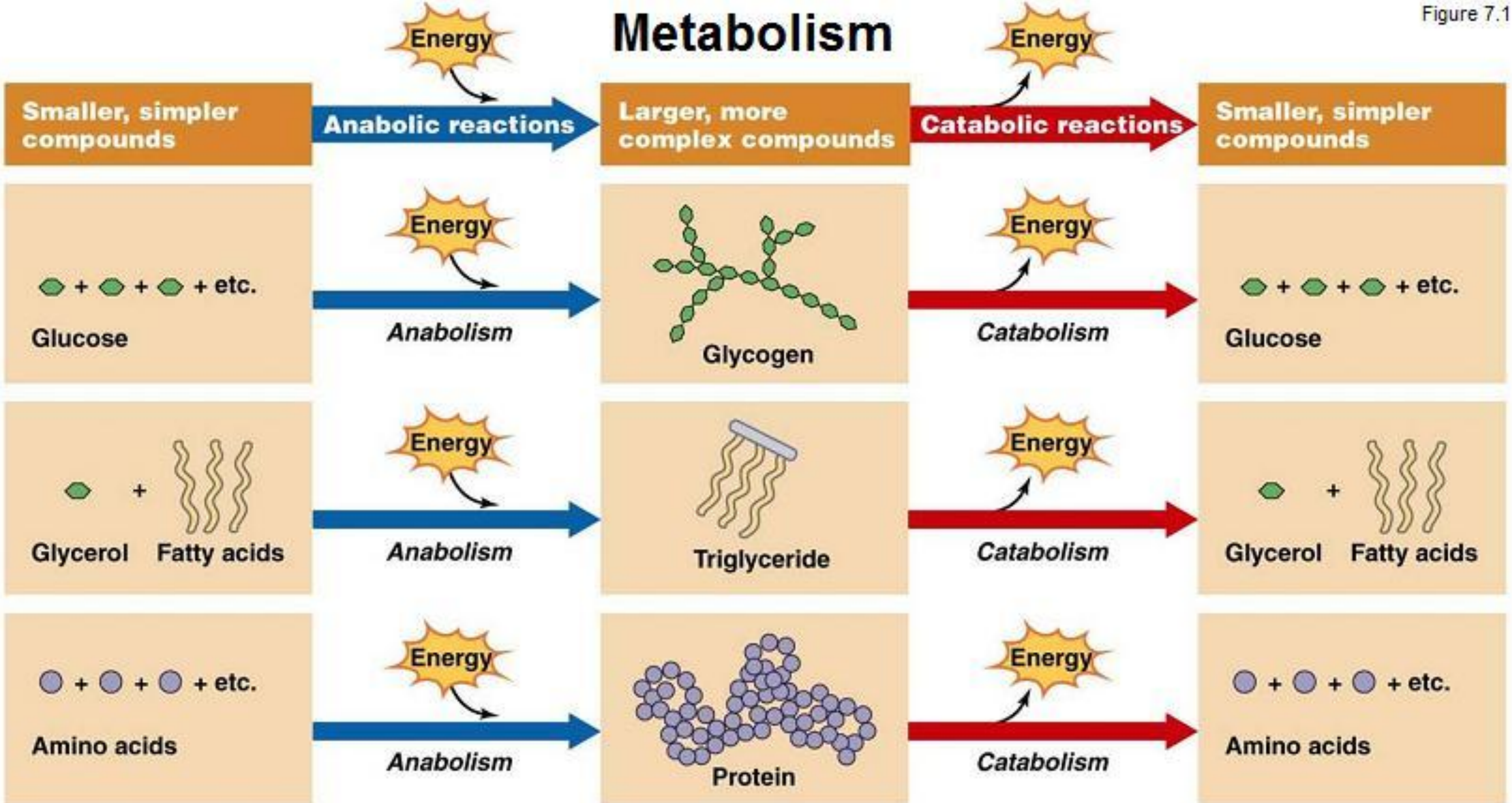
- Cells manage energy in the form of chemical reactions that change molecules. Some cellular reactions release energy, and others require it to proceed.
- **Endergonic reactions** ("energy inward"): ***Absorb*** or require more energy than they release. Endergonic reactions are driven forward with the addition of energy.

$$\text{Energy} + A + B \xrightarrow{\text{Enzyme}} C$$

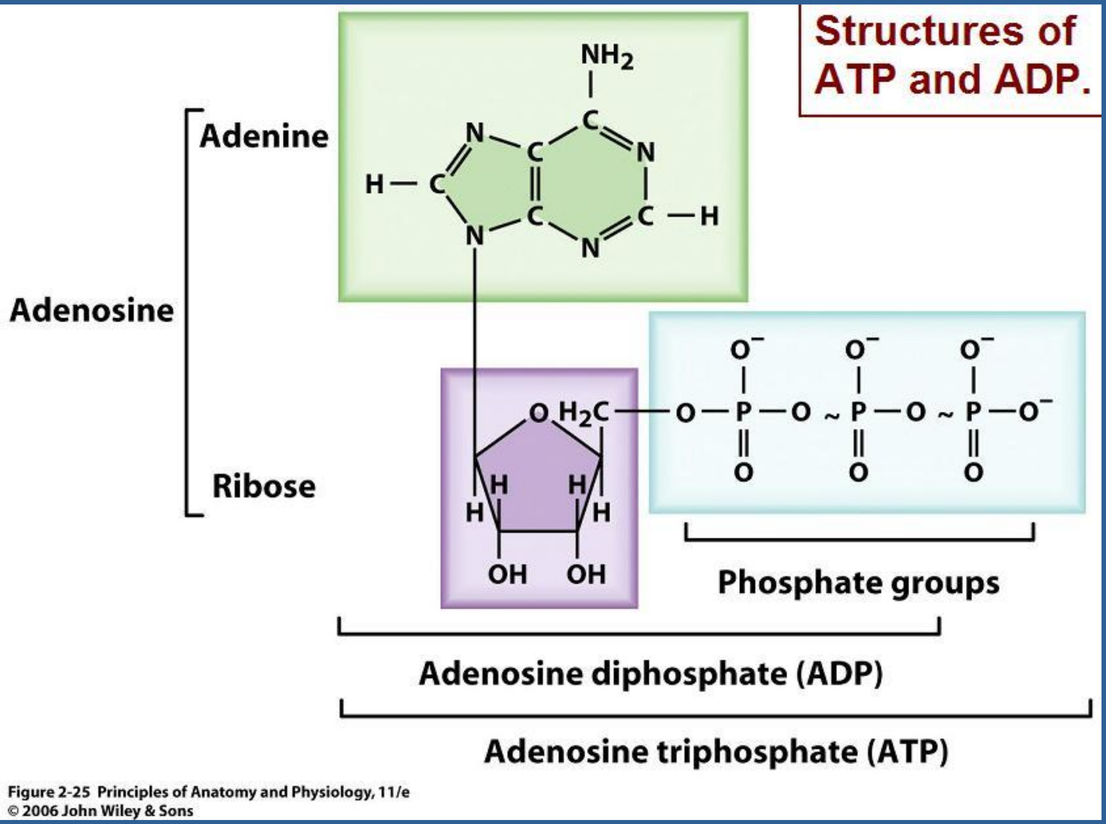
- **Exergonic reactions** ("energy outward"): ***Release*** more energy than they absorb as they go forward.

$$X + Y \xrightarrow{\text{Enzyme}} Z + \text{Energy}$$

Metabolism: Endergonic and Exergonic Reactions



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



- 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.

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.

Figure 8.9 Hydrolysis of ATP.

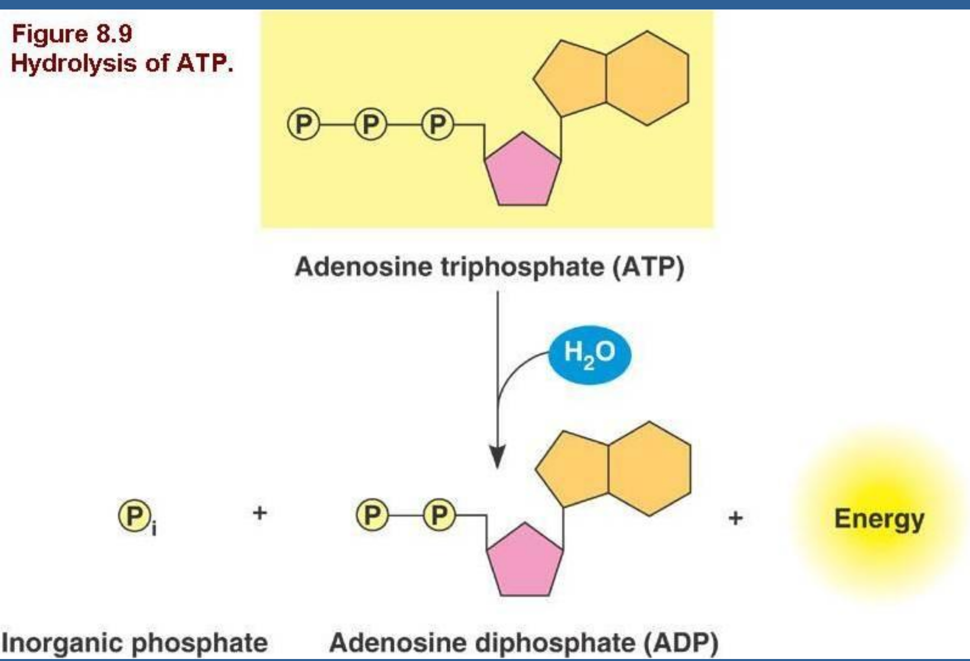
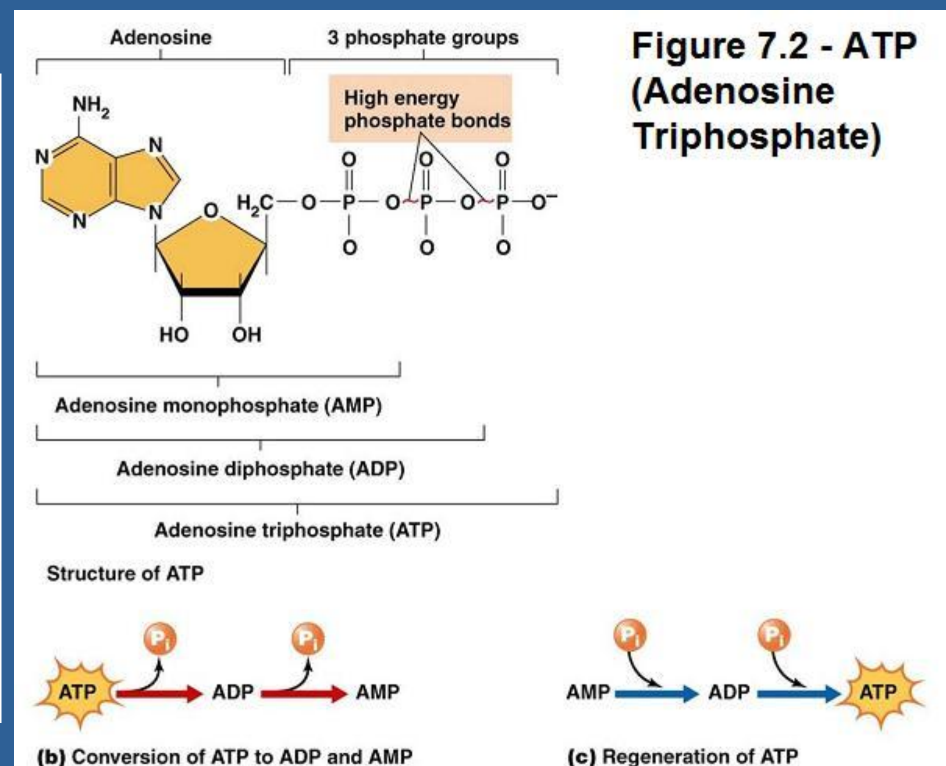


Figure 7.2 - ATP (Adenosine Triphosphate)



How ATP Performs Work

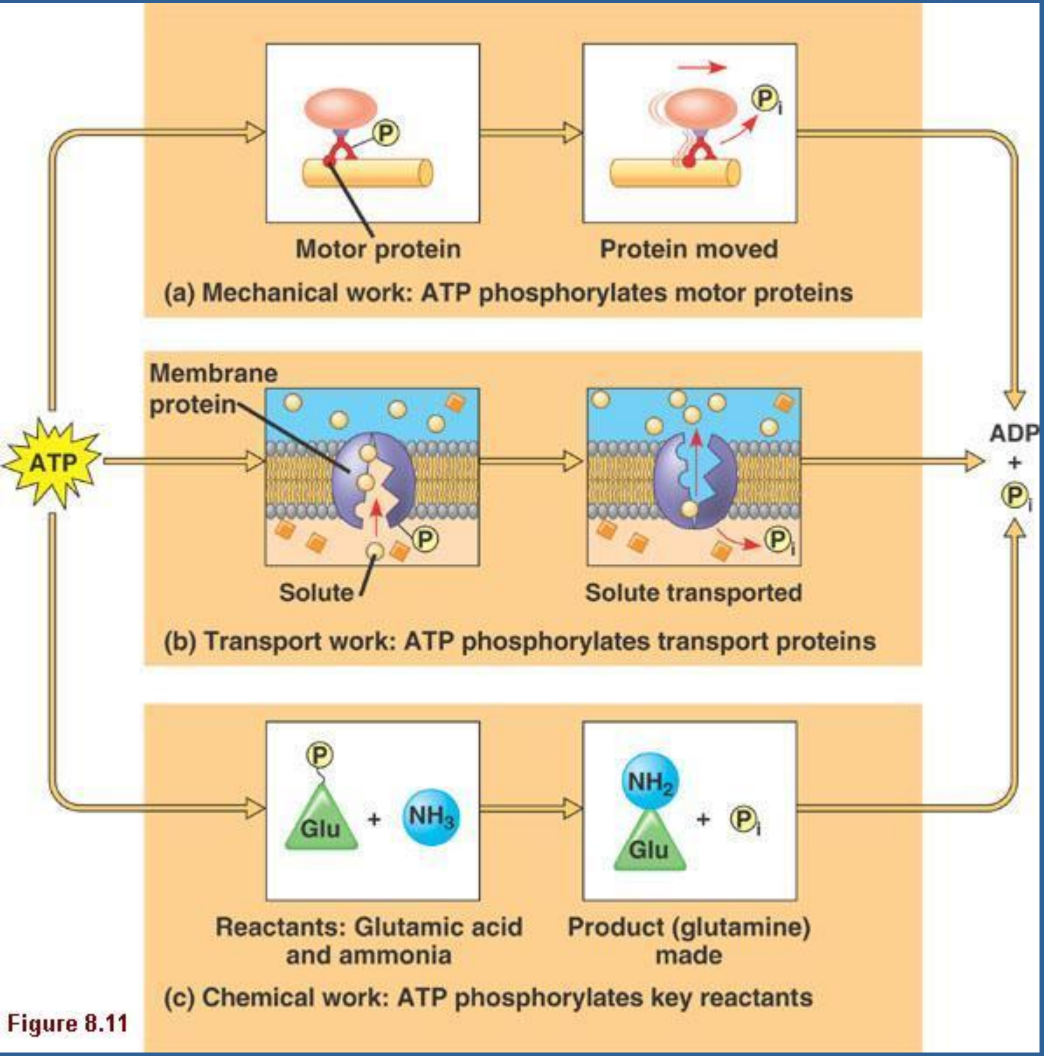


Figure 8.11

- **ATP** hydrolysis causes changes in the shapes and binding affinities of proteins.
- This can occur *directly*, by **phosphorylation** (phosphate group transfer; as shown for membrane proteins involved in active transport of solutes) or *indirectly*, via **noncovalent binding** of ATP and its hydrolytic products (as in the case for motor proteins that move vesicles and organelles along cytoskeletal “tracks” in the cell).

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.

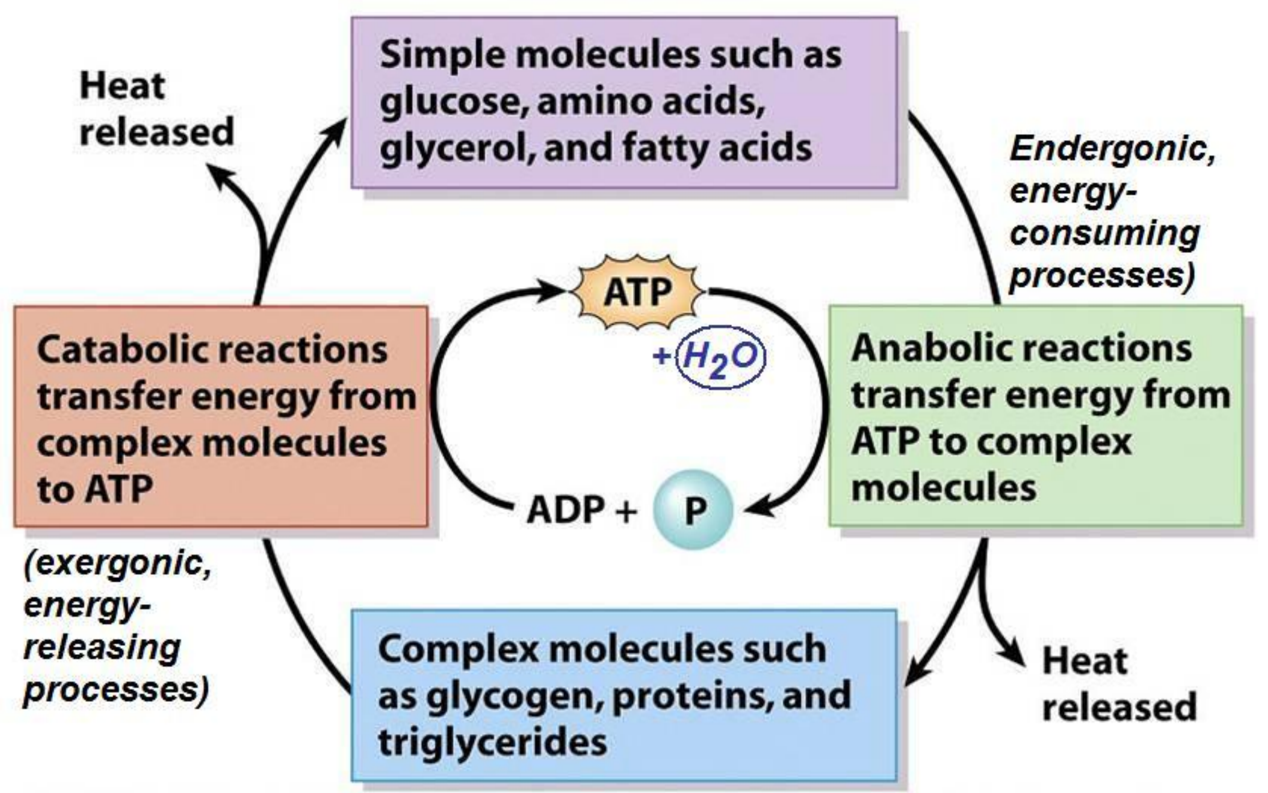


FIGURE 25.1 - Role of ATP in linking anabolic and catabolic reactions.

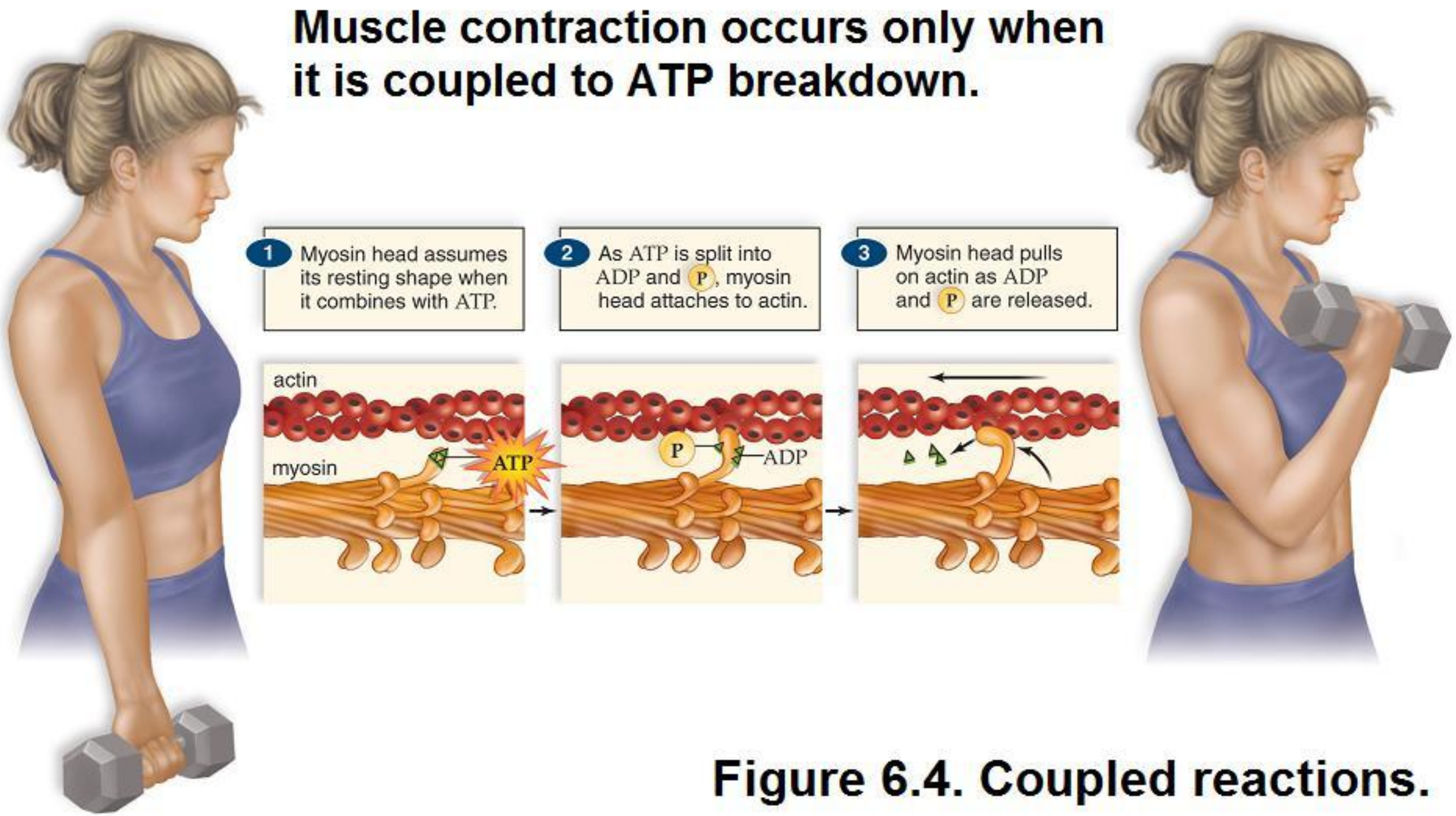


Figure 6.4. Coupled reactions.

Through coupled reactions, ATP drives forward energetically unfavorable processes that must occur to create the high degree of order essential for life.

Enzymes Speed Up Metabolic Reactions By Lowering Energy Barriers (Activation Energy)

- **Enzymes** are biological *catalysts*, substances that ***accelerate chemical reactions*** of life without becoming part of the products or being consumed in the reaction.
- Some important properties of enzymes:
  - ***Highly specific.*** Each particular enzyme binds only to a specific **substrate**—the reactant molecule on which the enzyme acts.
  - ***Very efficient and fast.*** An enzyme speeds up a chemical reaction without being altered or consumed.
  - ***Regulated.*** Enzymes are subject to cellular controls.
  - **Most enzymes are proteins**, but some types of RNA (ribonucleic acid)—called ***riboenzymes***, have catalytic activity.

TABLE 8.1 Checklist of Enzyme Characteristics

- Most composed of protein; may require cofactors
- Act as organic catalysts to speed up the rate of cellular reactions
- Lower the activation energy required for a chemical reaction to proceed
- Have unique characteristics such as shape, specificity, and function
- Enable metabolic reactions to proceed at a speed compatible with life
- Have an active site for target molecules called substrates
- Are much larger in size than their substrates
- Associate closely with substrates but do not become integrated into the reaction products
- Are not used up or permanently changed by the reaction
- Can be recycled, thus function in extremely low concentrations
- Are greatly affected by temperature and pH
- Can be regulated by feedback and genetic mechanisms

Enzymes Speed Up Metabolic Reactions By Lowering Energy Barriers

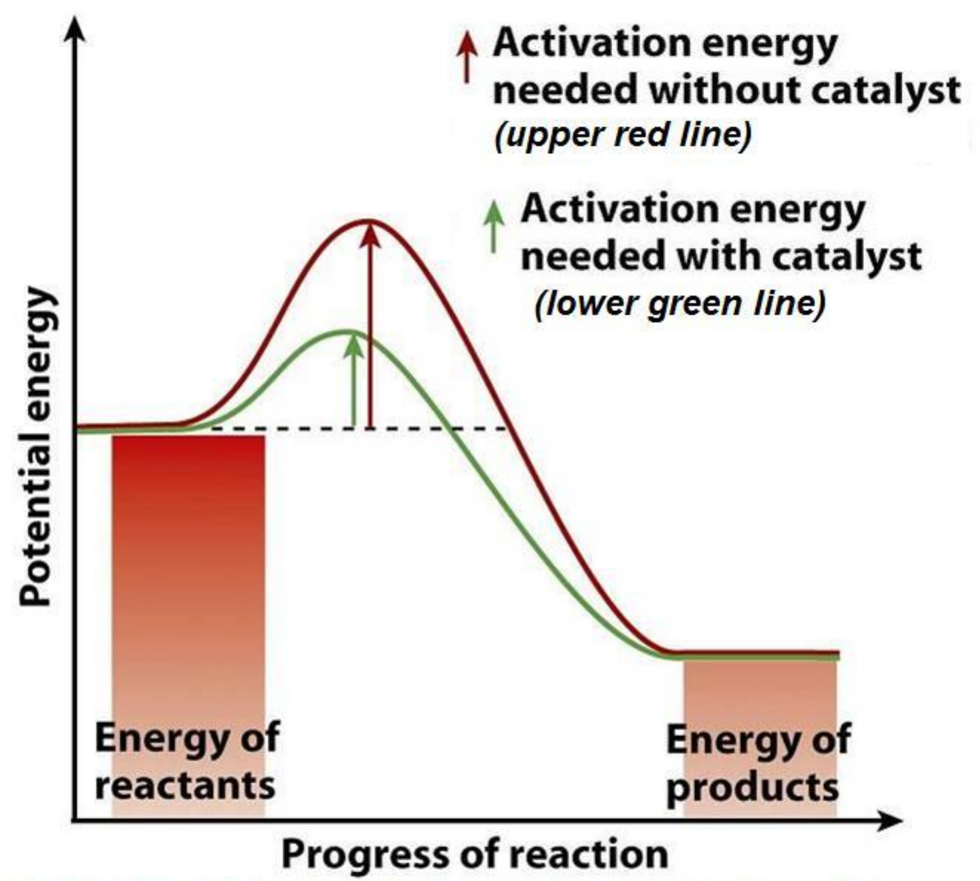


FIGURE 2.10 - Catalysts and chemical reactions.

- **Enzymes** are **catalysts**, chemical compounds that *speed up chemical reactions* by lowering the ***activation energy (E_A)***, the minimum amount of energy required for a chemical reaction to begin (to break the bonds in the reactants).
- A catalyst helps to *properly orient the colliding particles* so they can interact at the spots that make the reaction happen.
- **Enzymes** are the most important catalysts in the body.

The Effect of an Enzyme on Activation Energy (E_A)

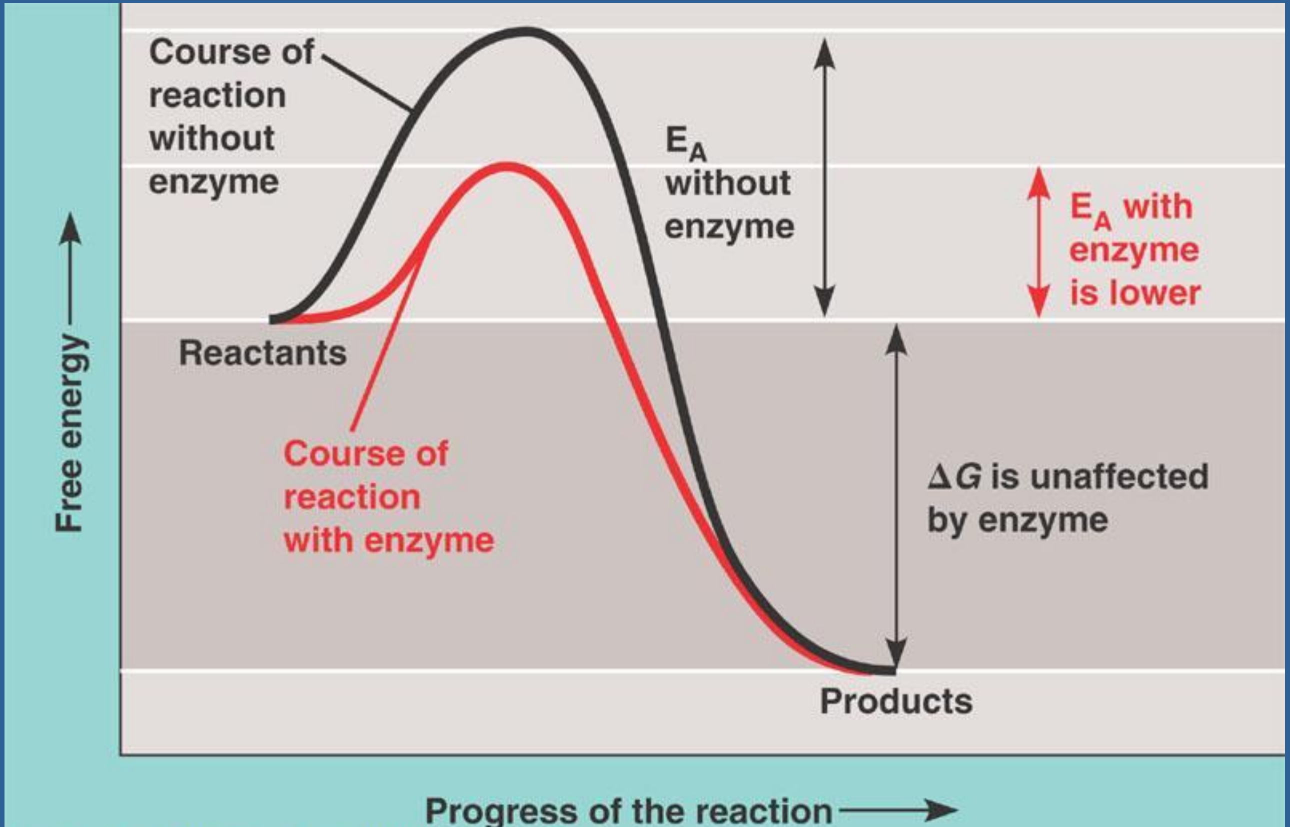


Figure 8.15. The effect of an enzyme on activation energy.

- ***ΔG* is the *change in free energy*.** Free energy is the portion of a biological system's energy that can perform work when temperature and pressure are uniform throughout the system. (The change in free energy of a system is calculated by the equation $\Delta G = \Delta H - T\Delta S$, where H is enthalpy [in biological systems, equivalent to total energy], T is absolute temperature, and S is entropy.)

Animation: Enzymes and Activation Energy

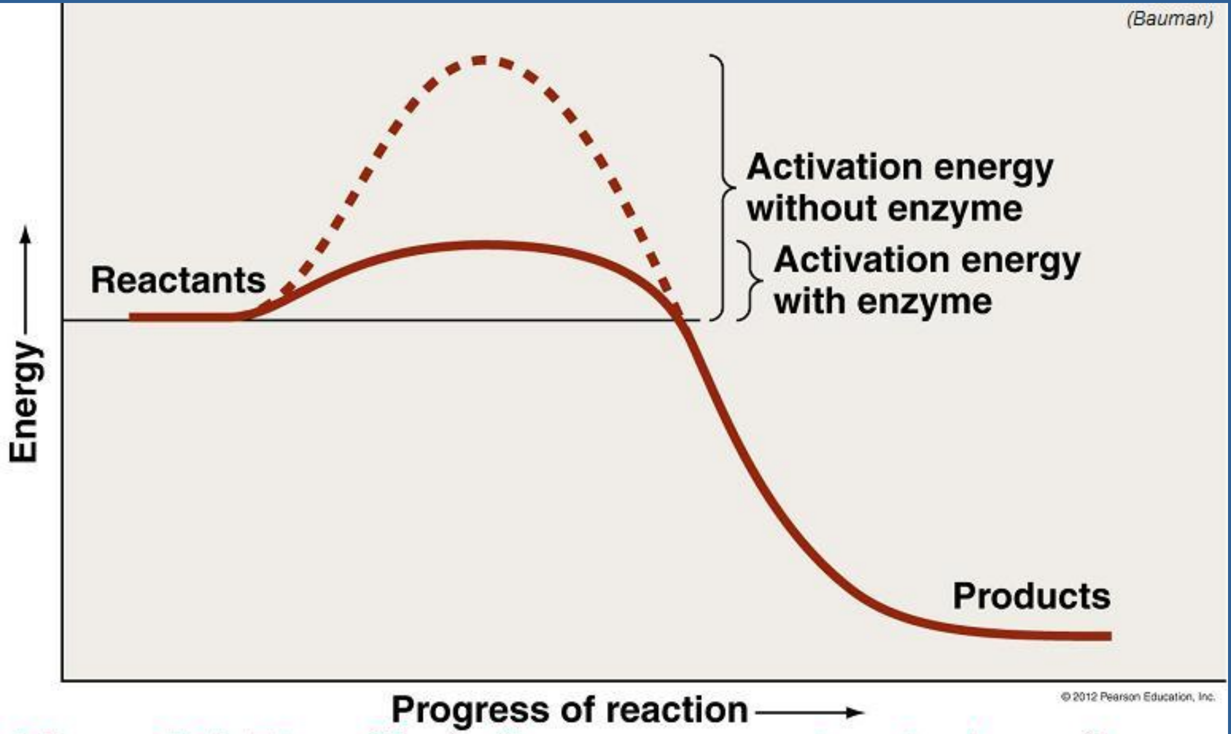


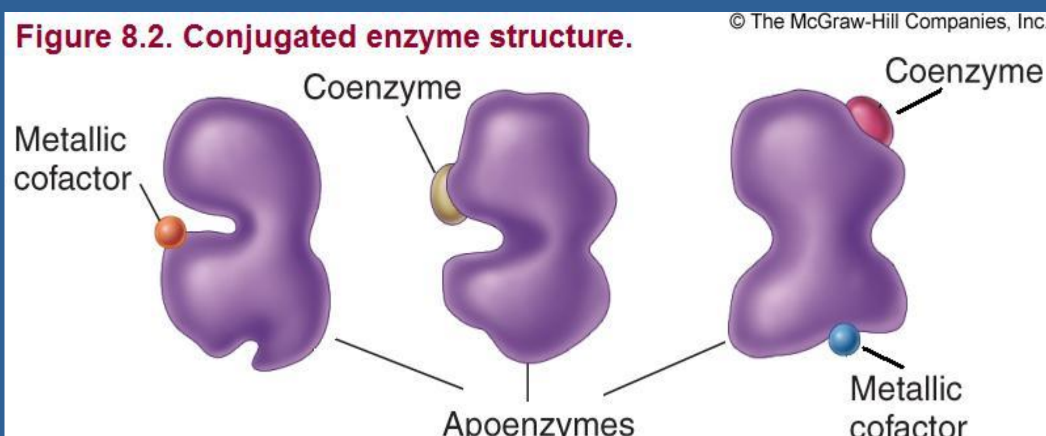
Figure 5.4. The effect of enzymes on chemical reactions.

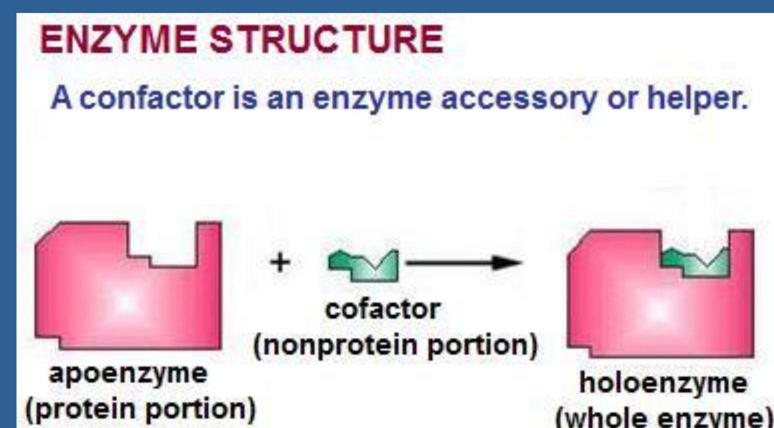
CLICK
TO PLAY

** Note: Animations can be seen only during class. Students can look for similar animations in the book's website or other biology websites.*

Enzyme Structure

- Most enzymes are ***proteins*** and can be classified as:
  - **Simple enzyme:** consists of protein alone.
  - **Conjugated enzyme = holoenzyme:** contains protein and nonprotein molecules; it is a combination of:
    - ✓ A protein, called the **apoenzyme**, and one or more **cofactors**, or ***nonprotein helpers***. Many enzymes require cofactors, which may be bound tightly to the enzyme as permanent residents, or they may bind loosely and reversibly along with the substrate.
    - ✓ **Metallic cofactors:** inorganic elements—metal ions.
    - ✓ **Coenzymes:** organic molecules, including vitamins.





Enzyme Structure

TABLE 8.2 Selected Enzymes, Catalytic Actions, and Cofactors

Enzyme	Action	Metallic Cofactor Required
Catalase	Breaks down hydrogen peroxide	Iron (Fe)
Oxidase	Adds electrons to oxygen	Iron (Fe), copper (Cu)
Hexokinase	Transfers phosphate to glucose	Magnesium (Mg)
Urease	Splits urea into an ammonium ion	Nickel (Ni)
Nitrate reductase	Reduces nitrate to nitrite	Molybdenum (Mo)
DNA polymerase complex	Synthesis of DNA	Zinc (Zn) and magnesium (Mg)

- A **cofactor** is an accessory molecule that acts as an enzyme helper.
- Inorganic cofactors are, for example, the **metal atoms** copper, iron, magnesium, and zinc.
- If the cofactor is an organic molecule, it is called a ***coenzyme***.
- Most **vitamins** are coenzymes or raw materials from which coenzymes are made (example: niacin and riboflavin-vitamin B_6).

Substrate Specificity of Enzymes: *The Active Site*

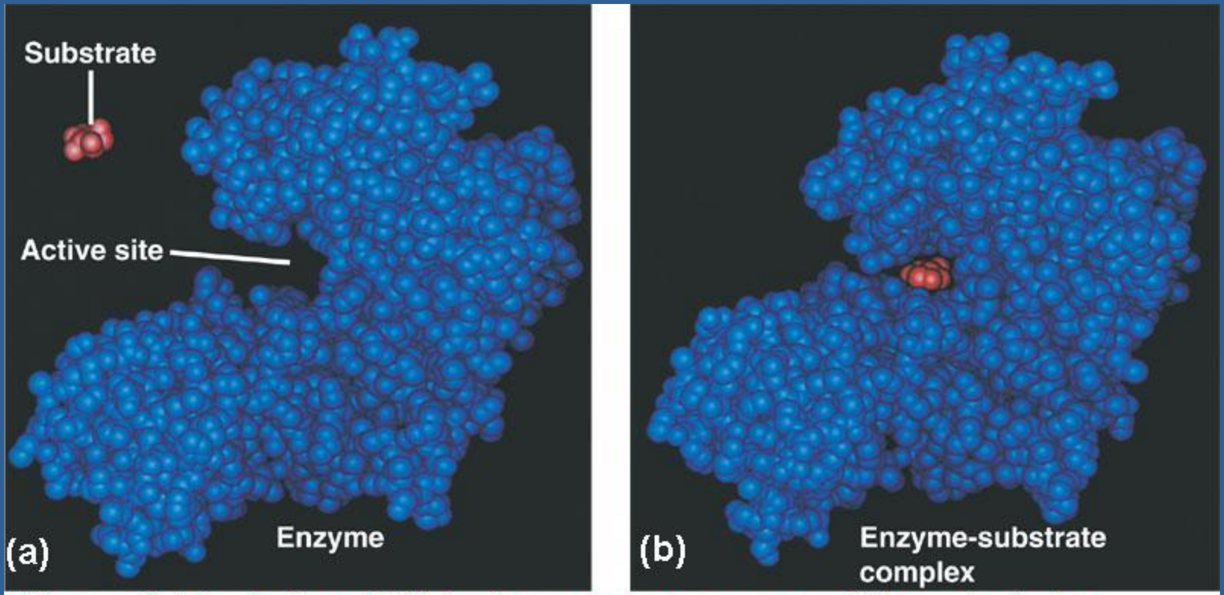


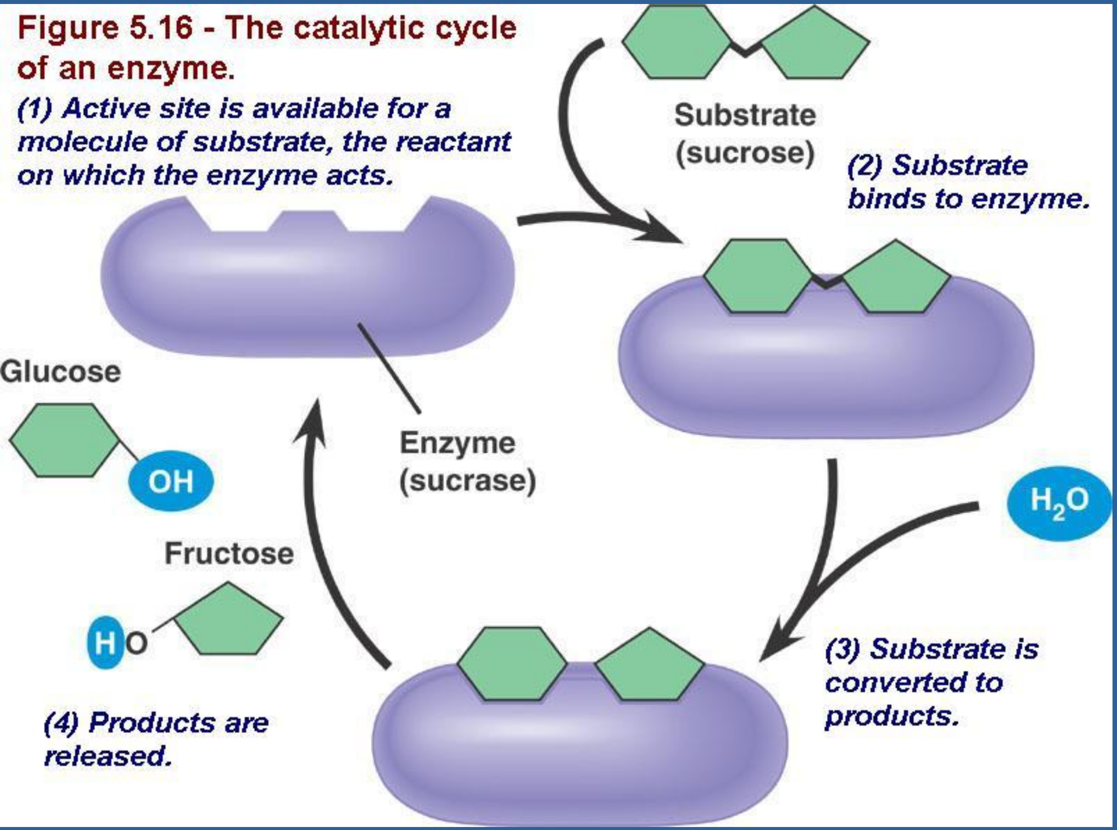
Figure 8.16 - Induced fit between an enzyme and its substrate.

- The reactant an enzyme acts on is referred to as the enzyme's **substrate**. The enzyme binds to its substrate (or substrates) through a groove called the **active** or **catalytic site**, forming an **enzyme-substrate complex**.

a) In this computer graphic model, the **active site** of this enzyme (*hexokinase*, shown in blue) forms a groove on its surface. Its substrate is glucose (red).

b) When the substrate enters the active site, it induces a temporary **change in the shape** of the protein (***induced fit*** or ***"lock and key fit"***). This change allows more weak bonds to form, causing the active site to enfold the substrate and hold it in place.

Mechanism of Action of Enzymes



The enzyme ***sucrase*** accelerates hydrolysis of **sucrose** into glucose and fructose. Acting as a catalyst, the sucrase protein is not consumed during the cycle, but is available for further catalysis.

- The reactant an enzyme acts on is its **substrate**.
- The enzyme has an **active site**, the region on the surface of the enzyme where the substrate binds and where the reaction occurs.
- Each type of enzyme has a unique active site that **combines specifically with its substrate**. The enzyme changes shape slightly when it binds the substrate ("***induced fit***").
- The substrate binds to the enzyme, is **converted to products** and the products are released. Then the **enzyme is available again**.

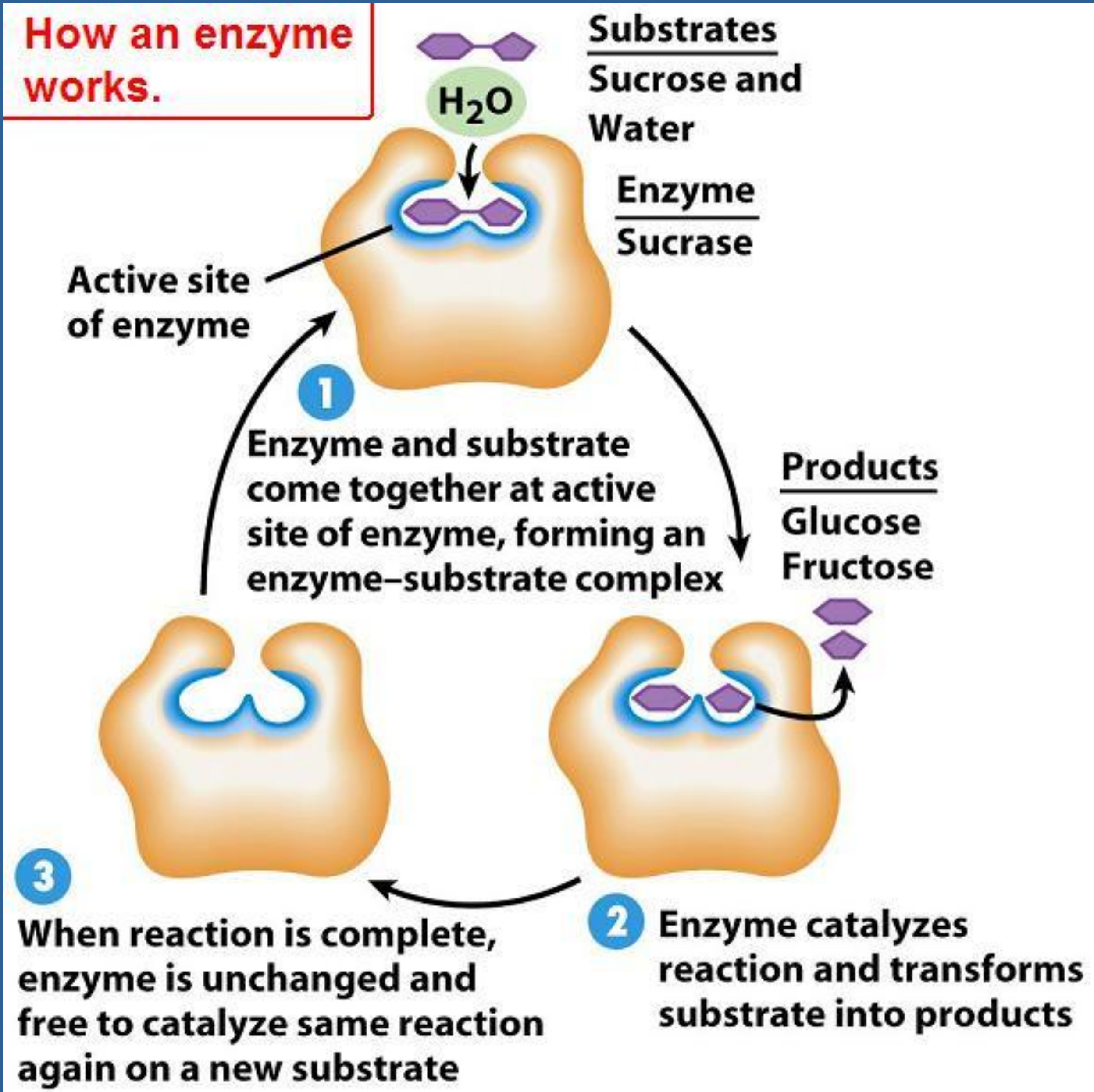


Figure 2-23 Principles of Anatomy and Physiology, 11/e

The Mechanism of Action of an Enzyme

- **Substrate:** The reactant molecule on which the enzyme acts.
- **Active site:** The specific portion of an enzyme that binds the substrate by means of multiple weak interactions and that forms the pocket in which catalysis occur.

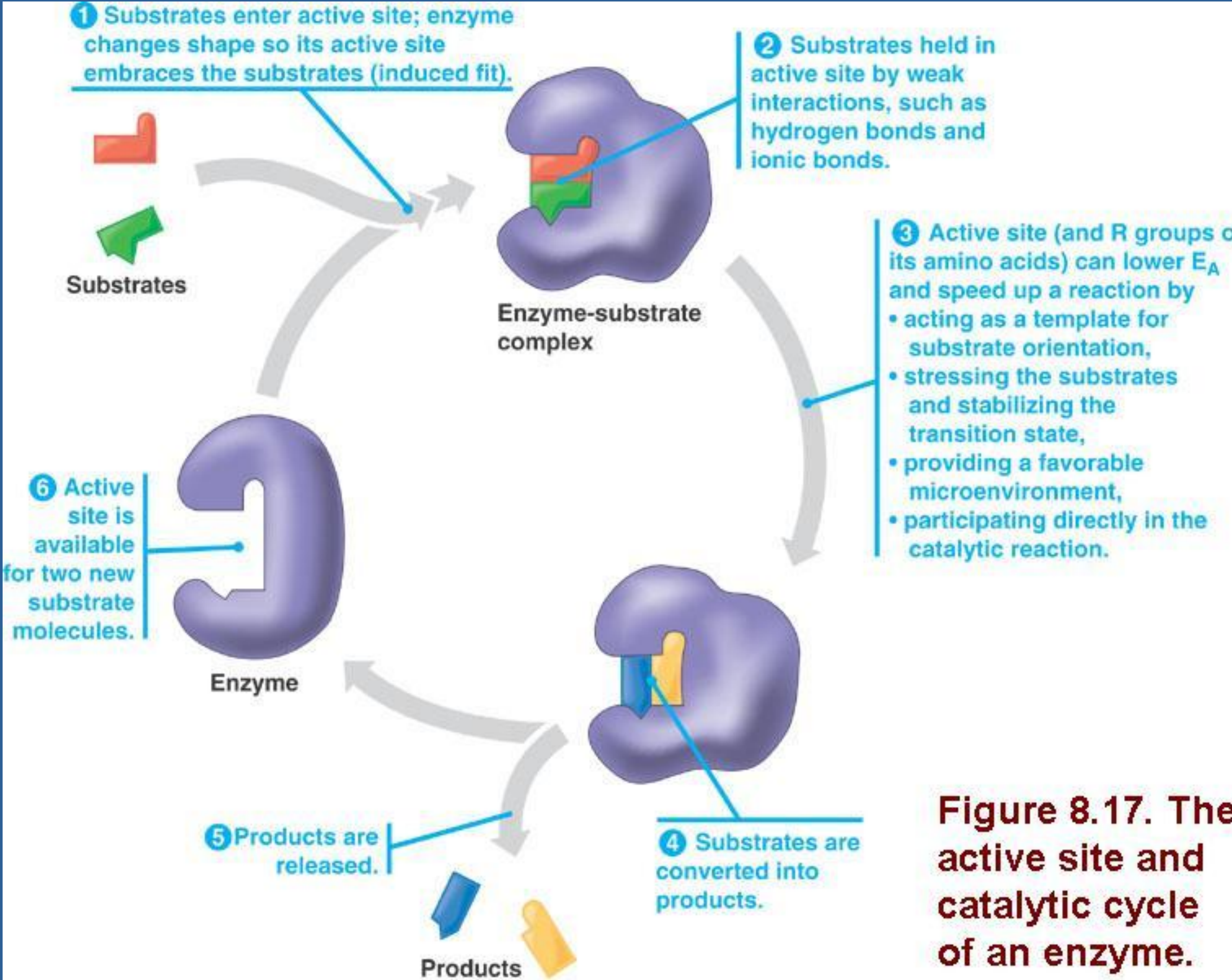
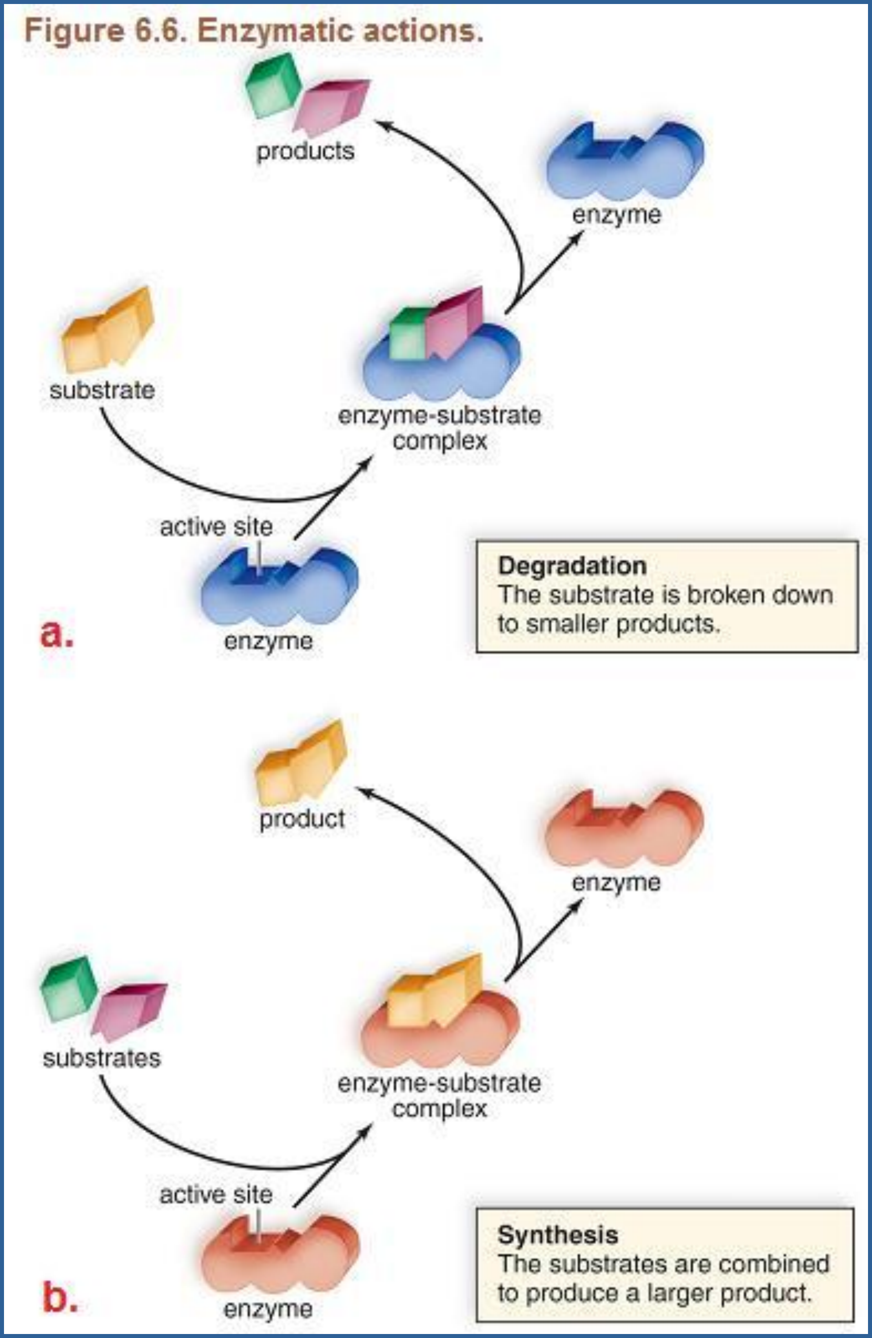


Figure 8.17. The active site and catalytic cycle of an enzyme.



Enzymatic Actions

- Enzymes have an **active site** where the **substrate(s)** and the enzyme fit together so the reaction will occur.
- Following the reaction, the product(s) is released, and the enzyme is free to act again.
- Certain enzymes carry out ***(a)*** degradation and others carry out ***(b)*** synthesis.

Example of an Enzyme-Catalyzed Reaction

- Hydrolysis of **sucrose** (table sugar, a carbohydrate) by the enzyme ***sucrase***.
  - Sucrose is hydrolyzed to glucose and fructose by the enzyme (***sucrase***) within seconds.
  - In the absence of regulation by enzymes, chemical traffic through the pathways of metabolism would become terribly congested because many chemical reactions would take such a long time.

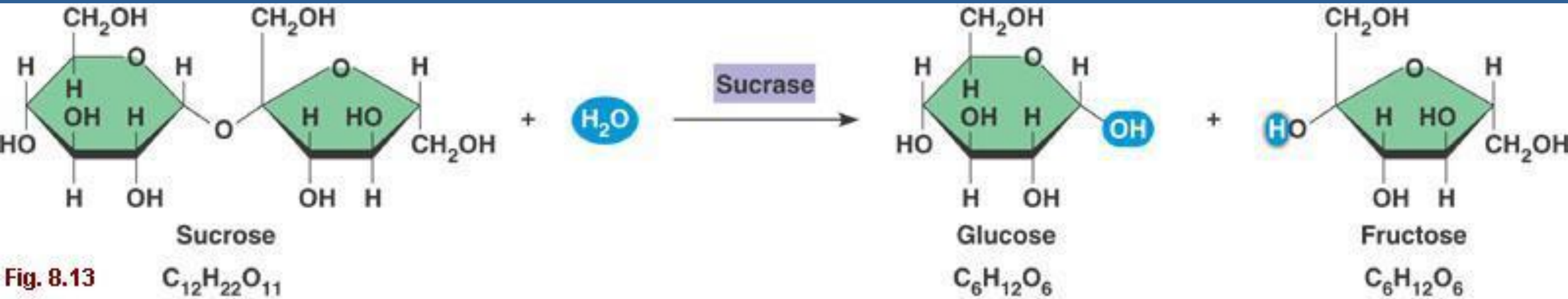
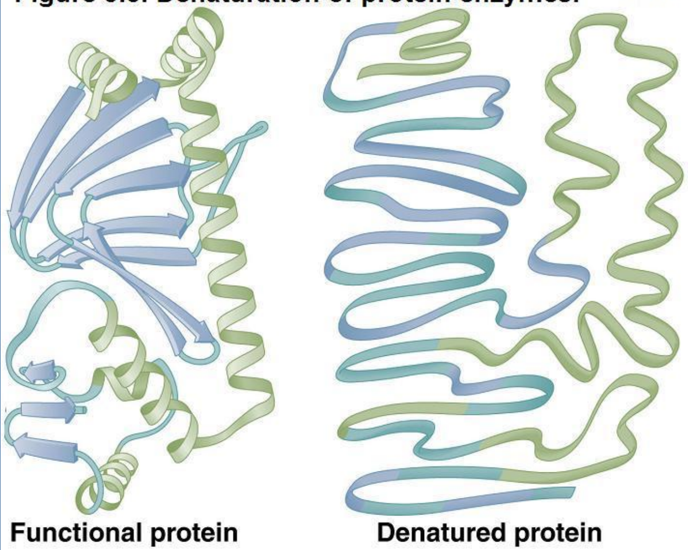


Fig. 8.13

Factors that Affect Enzyme Activity

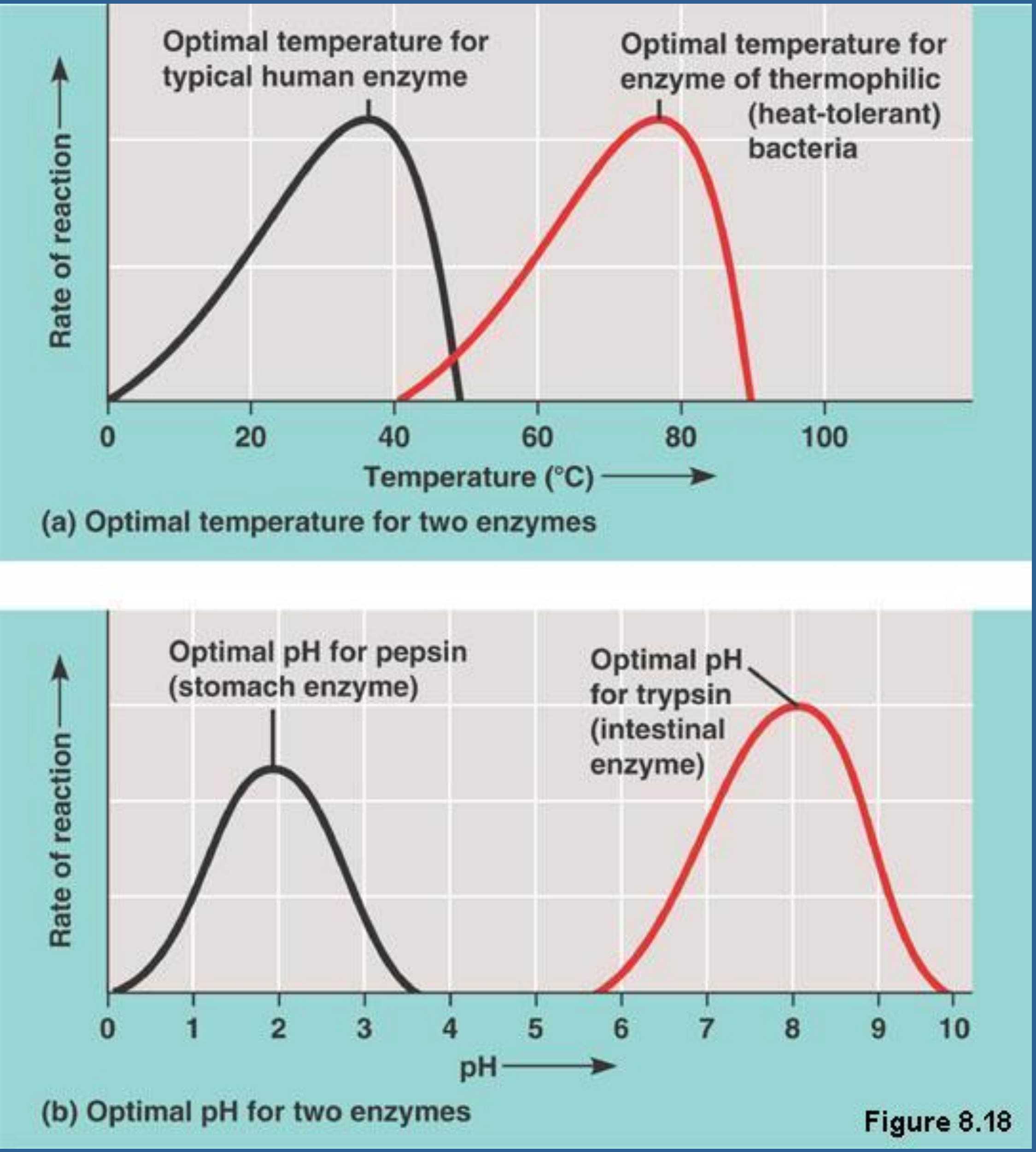
- **Cellular and environmental factors** that affect enzyme activity (or the rate of enzymatic reactions) include:
  - Cofactors (enzyme helpers), enzyme concentration, substrate concentration, enzyme activators and inhibitors, temperature, pH (degree of acidity or concentration of hydrogen ions in a solution), osmotic pressure (influenced by the amount of water and solutes)
- When enzymes are subjected to changes in normal conditions, they tend to be chemically unstable, or **labile**.
- **Denaturation** is a process by which the weak bonds that collectively maintain the native shape of an enzyme are broken. The enzyme is distorted and cannot bind its substrate.
  - Enzymes can be denatured and rendered nonfunctional, for example, by high temperatures.

Figure 5.8. Denaturation of protein enzymes. (Bauman)



Effects of Local Conditions on Enzyme Activity (Environmental Factors)

- Temperature
  - Each enzyme has an **optimal temperature** for activity.
  - In general, the **rate of an enzymatic reaction increases with increasing temperature to certain point** (molecules move around faster and substrates collide with active sites more frequently).
  - ***Increasing temperature too much*** may lead to a **disruption** in enzyme-substrate interactions, and the reaction speed declines rapidly because the enzyme is ***denatured*** (its native shape is altered) and it no longer functions.
  - Most human enzymes have optimal temperatures of about 35-40°C (close to human body temperature).
- pH
  - All enzymes have an **optimal pH** at which they are most active.
  - Most enzymes work best between pH 6 to 8, but there are exceptions.
    - ✓ Pepsin, an enzyme in the human stomach works best at a pH 2.



(a) Optimal temperature for two enzymes

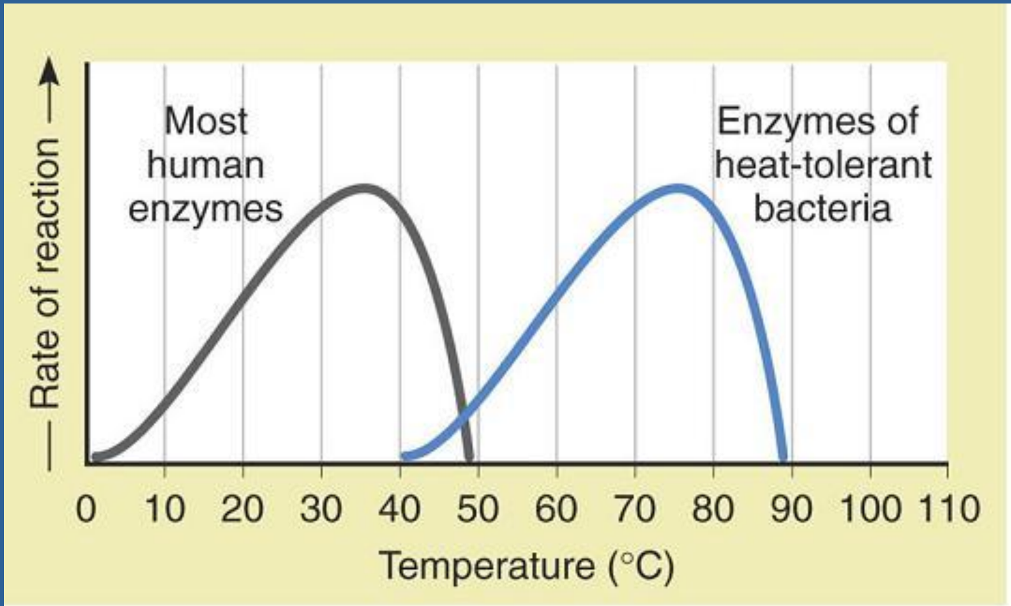
(b) Optimal pH for two enzymes

Figure 8.18

Environmental Factors Affecting Enzyme Activity

- Each enzyme has an optimal temperature ***(a)*** and pH ***(b)***, that favor the most active shape of the protein molecule.
- Other factors affecting enzyme action are *enzyme concentration*, *salt concentration*, *substrate concentration*, *cofactors* (nonprotein helpers), and *enzyme inhibitors* and *activators*.

Animation: Effect of Temperature on Enzyme Activity



(a) Generalized curves for the effect of temperature on enzyme activity. As temperature increases, enzyme activity increases until it reaches an optimal temperature. Enzyme activity abruptly falls after it exceeds the optimal temperature because the enzyme, being a protein, denatures.

Figure 7-12a.

CLICK
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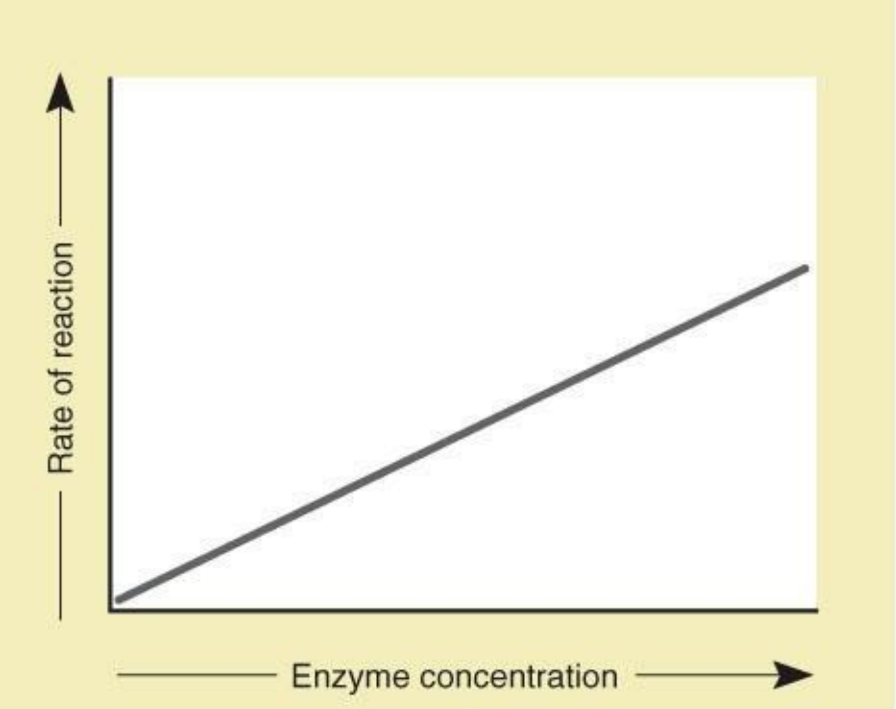
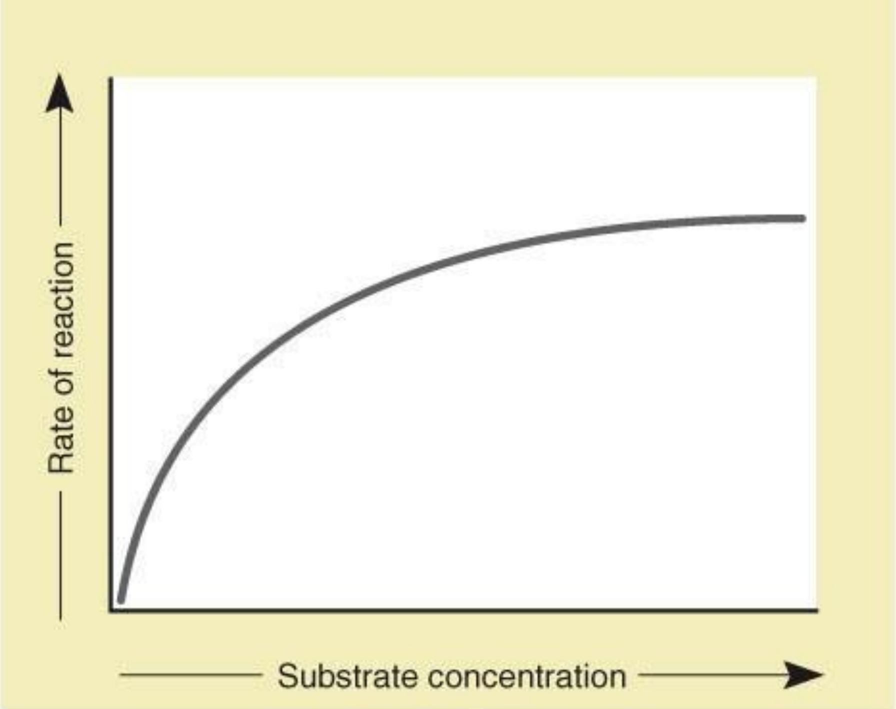
Regulation of Enzymes and Effects of Local Conditions on Enzyme Activity (Environmental Factors)

- Cells regulate enzymatic activity by:
  - Controlling the ***amount of enzyme*** produced.
    - ✓ A specific **gene** (segment of DNA) directs the synthesis of each type of enzyme. The gene, in turn, may be switched on by a signal molecule (such as a hormone).
    - ✓ The rate of the reaction can be affected by ***enzyme concentration*** or ***substrate concentration***.
  - Regulating metabolic conditions that influence the ***shape of the enzyme***.
    - ✓ In their inactive form, the active sites of the enzyme are inappropriately shaped, so the substrates do not fit.

Regulation of Enzymes and Effects of Local Conditions on Enzyme Activity (Environmental Factors)



(a) In this example, the rate of reaction is measured at different enzyme concentrations, with an excess of substrate present. (Temperature and pH are constant.) The rate of the reaction is directly proportional to the enzyme concentration.



(b) In this example, the rate of the reaction is measured at different substrate concentrations, and enzyme concentration, temperature, and pH are constant. If the substrate concentration is relatively low, the reaction rate is directly proportional to substrate concentration. However, higher substrate concentrations do not increase the reaction rate, because the enzymes become saturated with substrate.

Figure 7-14. The effects of enzyme concentration and substrate concentration on the rate of a reaction.

Effects of Local Conditions on Enzyme Activity and Regulation of Enzymatic Activity

- **Enzyme inhibitors** are chemicals that selectively inhibit (prevent) the action of specific enzymes.
- **Competitive inhibitor:** reduces the activity of an enzyme by *entering the active site* in place of the substrate whose structure it mimics (it blocks the active site for the substrate).
- **Noncompetitive (allosteric) inhibitor:** binds to an **allosteric** site (a location *remote from the active site*), changing the conformation of the enzyme so that it no longer binds to the substrate (it does not directly compete with the substrate).

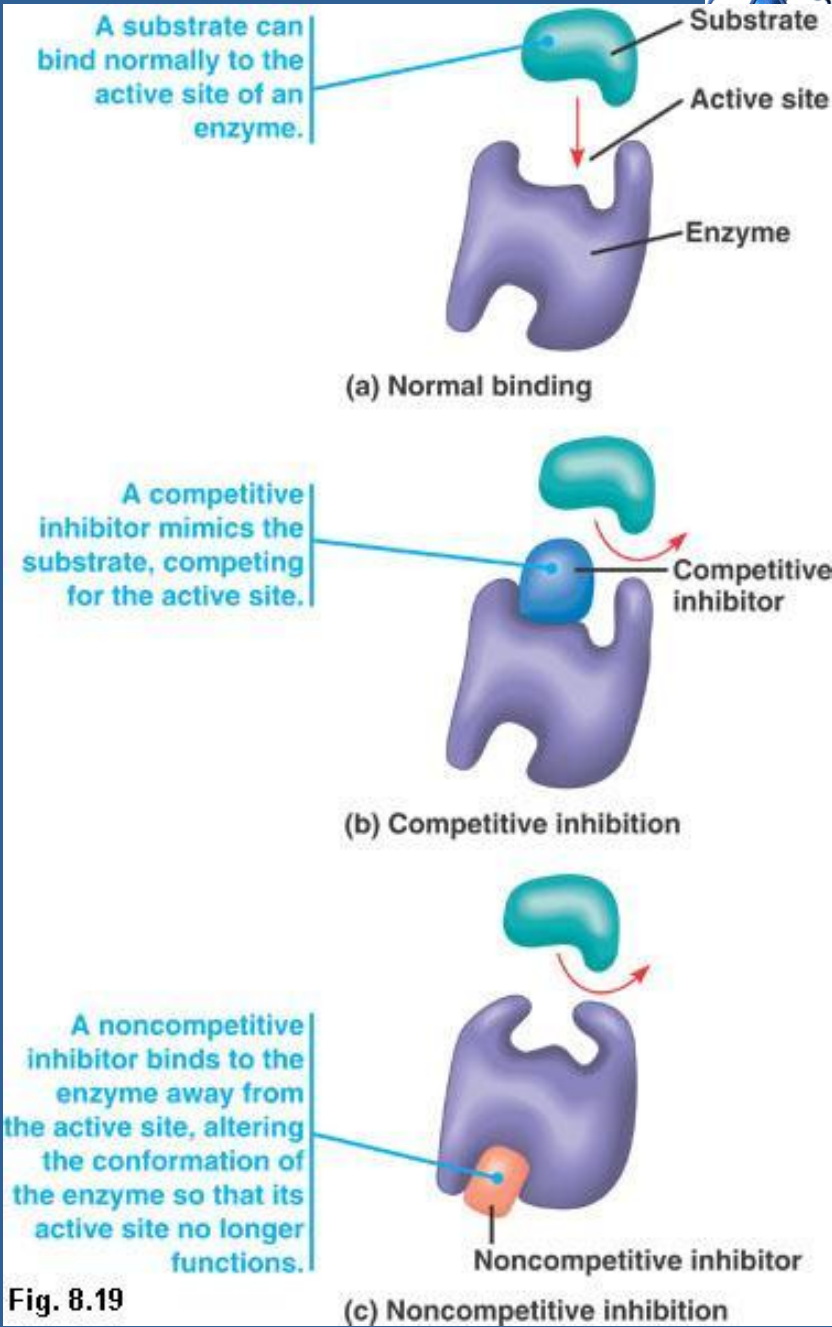
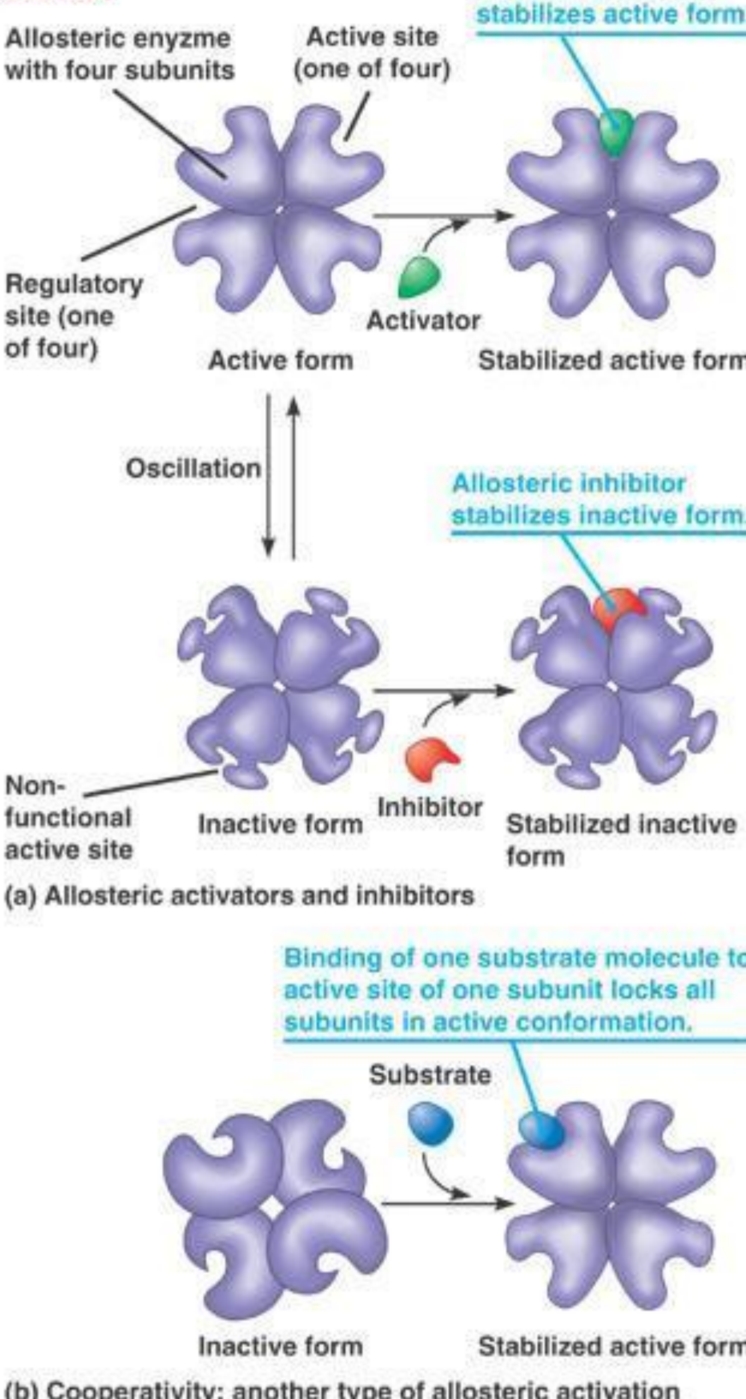


Fig. 8.19

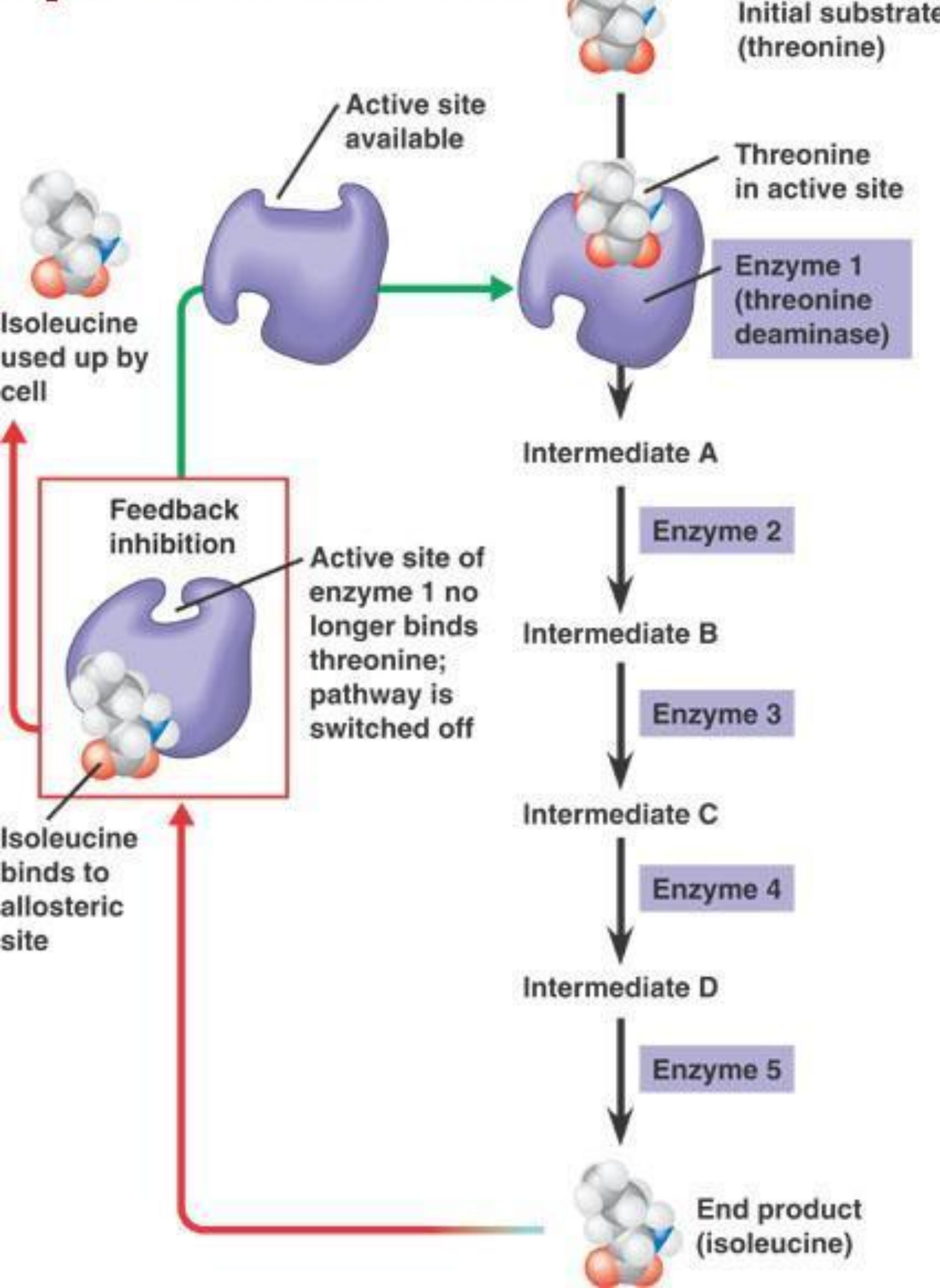
Figure 8.20



Allosteric Regulation of Enzyme Activity Helps Control Metabolism

- **Allosteric regulation** is the binding of a regulatory molecule to an enzyme at an ***allosteric site***, a region other than the active site of the enzyme, affecting its shape and function.
- The regulatory molecules can be either **activators** or **inhibitors**.
- In **cooperativity**, binding of one substrate molecule can stimulate binding or activity at other active sites; it is a type of allosteric activation.

Figure 8.21 Feedback Inhibition.



Regulation of Enzyme Activity Helps Control Metabolism

- **Feedback inhibition** is a method of metabolic control and enzyme regulation in which the ***end product*** of a metabolic pathway acts as an ***inhibitor*** of an enzyme for a previous step or reaction in the metabolic pathway.
- In the figure, the end product (isoleucine) binds to an allosteric site (a region other than the active site) on the enzyme to inhibit it and the pathway is switched off.

Animation: Feedback Inhibition

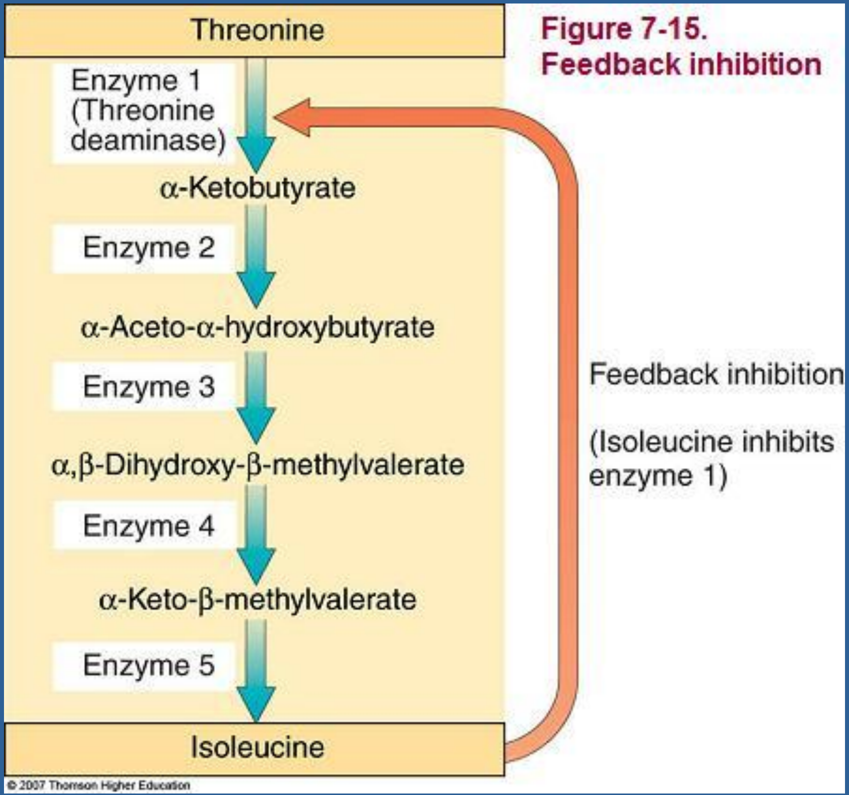
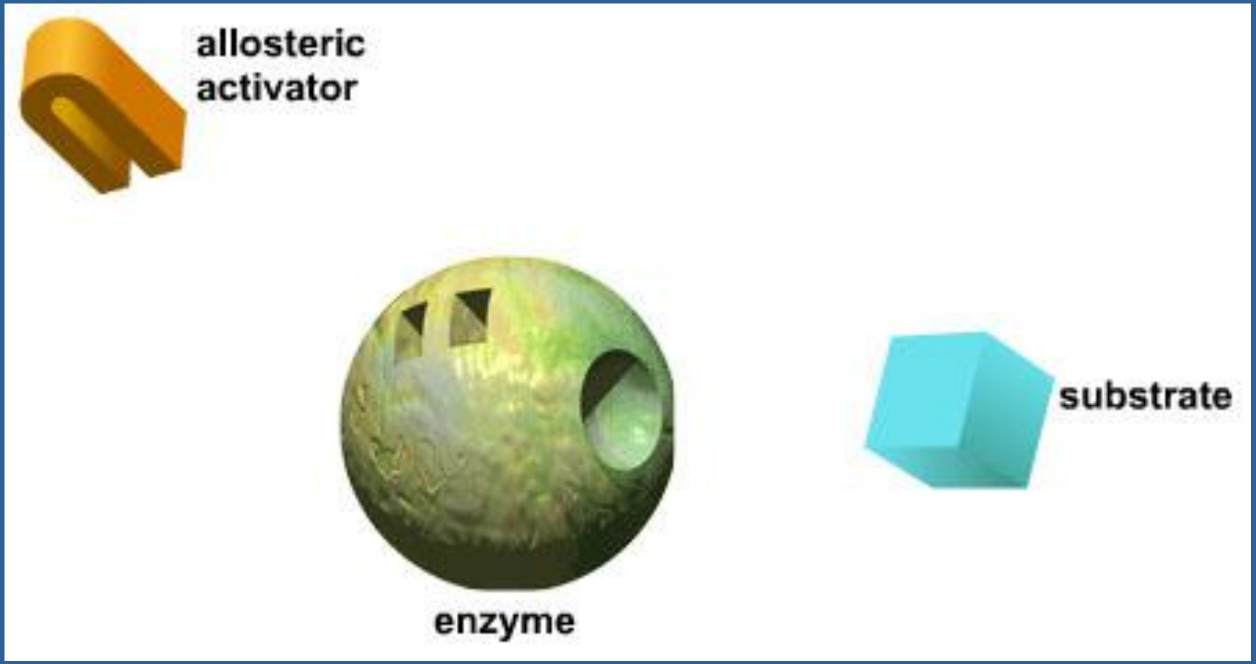


Figure 7-15. Feedback inhibition

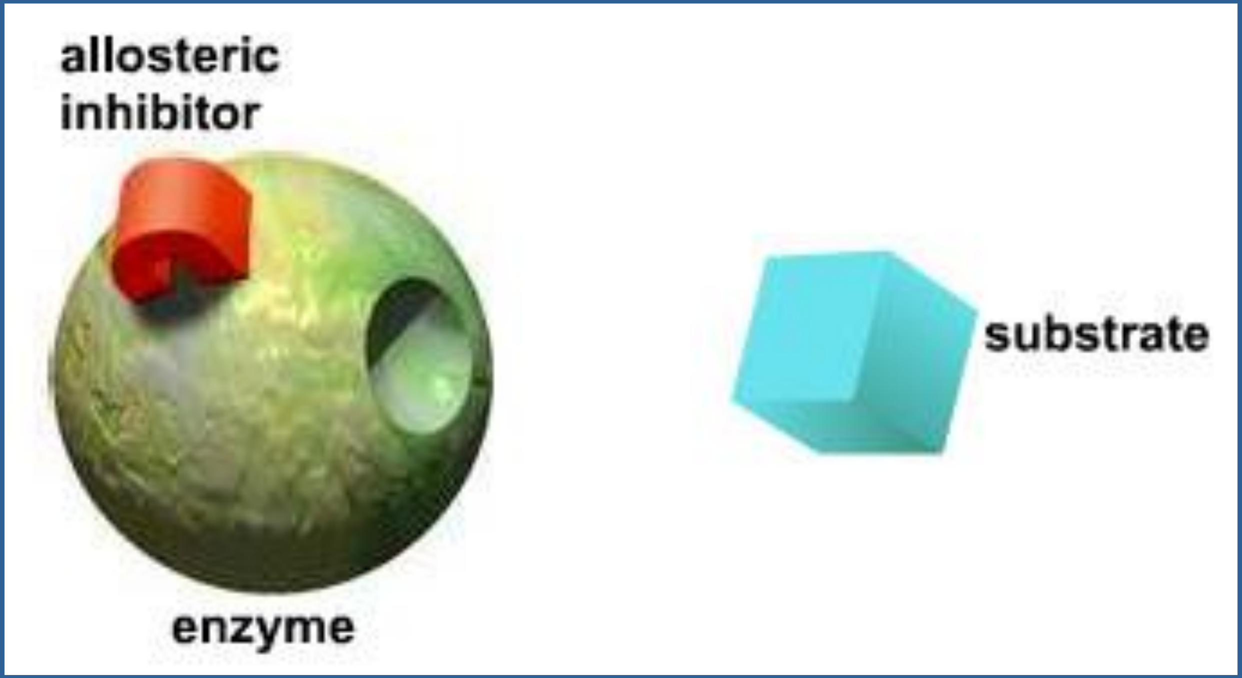
CLICK
TO PLAY

Animation: Allosteric Regulation: *Activator*



CLICK
TO [PLAY]

Animation: Allosteric Regulation: *Inhibitor*



CLICK
TO PLAY

Table 5.1 Key Players in Metabolic Reactions

Reactant	Substance that enters a metabolic reaction or pathway; also called a substrate of an enzyme
Intermediate	Any substance that forms in a reaction or pathway, between the reactants and the end products
Product	Substance at the end of a reaction or pathway
Enzyme	A catalytic protein, one that enhances the rate of a reaction; a few RNAs are catalytic
Cofactor	Molecule or metal ion that assists enzymes. May carry electrons, hydrogen, or functional groups to other reaction sites. NAD^+ is an example
Energy carrier	Mainly ATP; couples reactions that release energy with different reactions that require energy
Transport protein	Protein that passively assists or actively pumps specific solutes across a cell membrane

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