CAMPBELL BIOLOGY IN FOCUS

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6

An Introduction to Metabolism

Lecture Presentations by
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SECOND EDITION

The Energy of Life

- The living cell is a miniature chemical factory where thousands of reactions occur
- The cell extracts energy and applies energy to perform work
- Some organisms even convert energy to light, as in bioluminescence

Figure 6.1

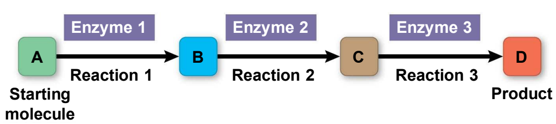
Concept 6.1: An organism's metabolism transforms matter and energy

- **Metabolism** is the totality of an organism's chemical reactions
- Metabolism is an emergent property of life that arises from interactions between molecules within the cell

Metabolic Pathways

- A **metabolic pathway** begins with a specific molecule and ends with a product
- Each step is catalyzed by a specific enzyme

Figure 6.UN01



- **Catabolic pathways** release energy by breaking down complex molecules into simpler compounds
- One example of catabolism is cellular respiration, the breakdown of glucose and other organic fuels to carbon dioxide and water

- **Anabolic pathways** consume energy to build complex molecules from simpler ones
- The synthesis of proteins from amino acids is an example of anabolism
- **Bioenergetics** is the study of how energy flows through living organisms

Forms of Energy

- **Energy** is the capacity to cause change
- Energy exists in various forms, some of which can perform work

- **Kinetic energy** is energy associated with motion
- **Thermal energy** is kinetic energy associated with random movement of atoms or molecules
- **Heat** is thermal energy in transfer from one object to another
- Light is another type of energy that can be harnessed to perform work

- **Potential energy** is energy that matter possesses because of its location or structure
- **Chemical energy** is potential energy available for release in a chemical reaction
- Energy can be converted from one form to another

Animation: Energy Concepts

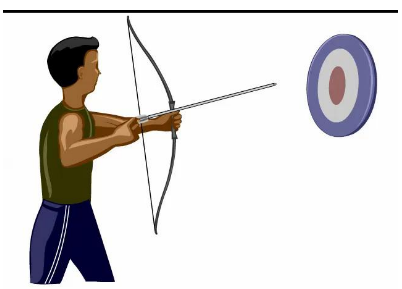


Figure 6.2

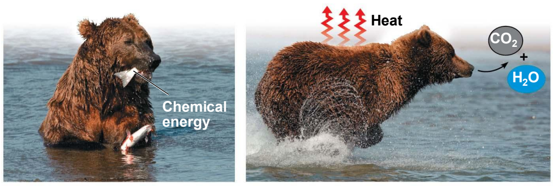
The Laws of Energy Transformation

- **Thermodynamics** is the study of energy transformations
- In an open system, energy and matter can be transferred between the system and its surroundings
- In an isolated system, exchange with the surroundings cannot occur
- Organisms are open systems

The First Law of Thermodynamics

- According to the **first law of thermodynamics**, the energy of the universe is constant
  - *Energy can be transferred and or transformed, but it cannot be created or destroyed*
- The first law is also called the *principle of conservation of energy*

Figure 6.3



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

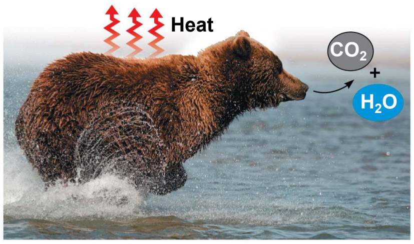
Figure 6.3-1

(a) First law of thermodynamics

The Second Law of Thermodynamics

- During every energy transfer or transformation, some energy is lost as heat
- According to the **second law of thermodynamics**
  - *Every energy transfer or transformation increases the entropy of the universe*
- **Entropy** is a measure of disorder, or randomness

Figure 6.3-2



(b) Second law of thermodynamics

- Living cells unavoidably convert organized forms of energy to heat
- **Spontaneous processes** occur without energy input; they can happen quickly or slowly
  - *For a process to occur spontaneously, it must increase the entropy of the universe*

Biological Order and Disorder

- Cells create ordered structures from less ordered materials
- Organisms also replace ordered forms of matter and energy with less ordered forms
- Energy flows into an ecosystem in the form of light and exits in the form of heat

Figure 6.4

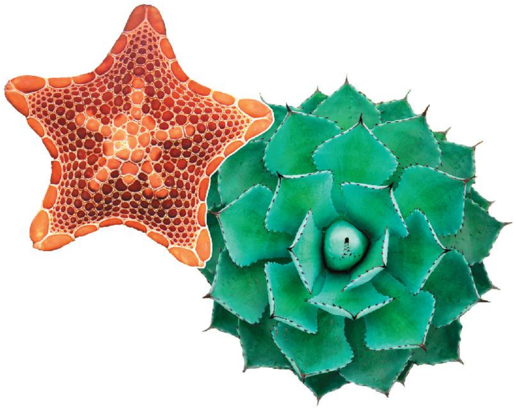


Figure 6.4-1

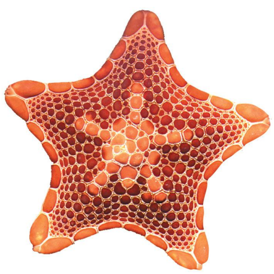
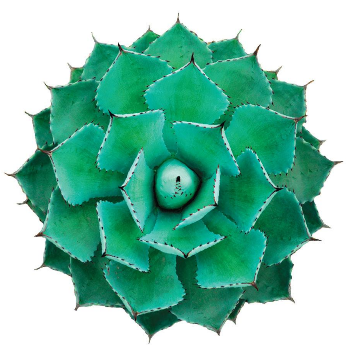


Figure 6.4-2



- The evolution of more complex organisms does not violate the second law of thermodynamics
- Entropy (disorder) may decrease in a system, but the universe's total entropy increases
- Organisms are islands of low entropy in an increasingly random universe

Concept 6.2: The free-energy change of a reaction tells us whether or not the reaction occurs spontaneously

- Biologists measure changes in free energy to help them understand the chemical reactions of life

Free-Energy Change (ΔG), Stability, and Equilibrium

- A living system's **free energy** is energy that can do work when temperature and pressure are uniform, as in a living cell

- The change in free energy (ΔG) during a chemical reaction is the difference between the free energy of the final state and the free energy of the initial state

$$\Delta G = G_{\text{final state}} - G_{\text{initial state}}$$

- Only processes with a negative ΔG are spontaneous
- Spontaneous processes can be harnessed to perform work

- Free energy is a measure of a system's instability, its tendency to change to a more stable state
- During a spontaneous change, free energy decreases and the stability of a system increases

Figure 6.5

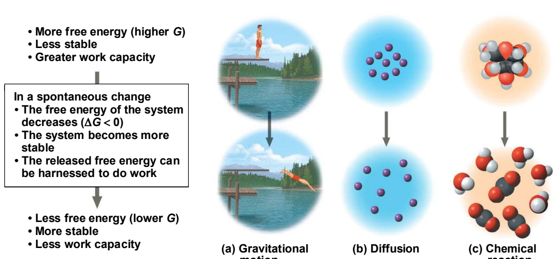


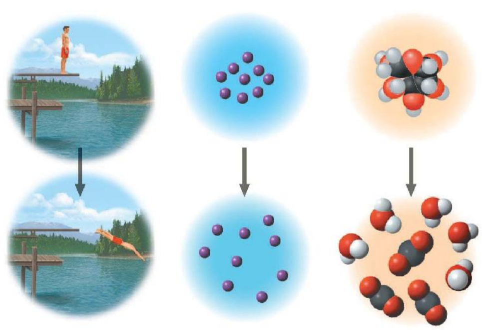
Figure 6.5-1

- More free energy (higher *G*)
- Less stable
- Greater work capacity

In a spontaneous change
- The free energy of the system decreases ($\Delta G < 0$)
- The system becomes more stable
- The released free energy can be harnessed to do work

- Less free energy (lower *G*)
- More stable
- Less work capacity

Figure 6.5-2



(a) Gravitational motion (b) Diffusion (c) Chemical reaction

- At equilibrium, forward and reverse reactions occur at the same rate; it is a state of maximum stability
  - *A process is spontaneous and can perform work only when it is moving toward equilibrium*

Free Energy and Metabolism

- The concept of free energy can be applied to the chemistry of life's processes

Exergonic and Endergonic Reactions in Metabolism

- An **exergonic reaction** proceeds with a net release of free energy and is spontaneous; ΔG is negative
- The magnitude of ΔG represents the maximum amount of work the reaction can perform

Figure 6.6

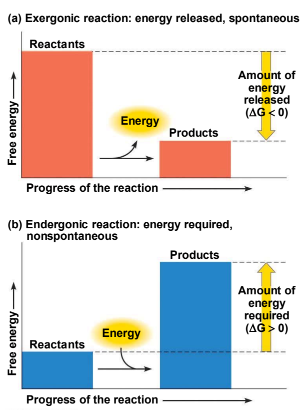
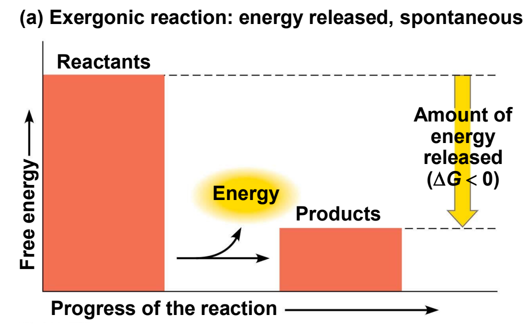
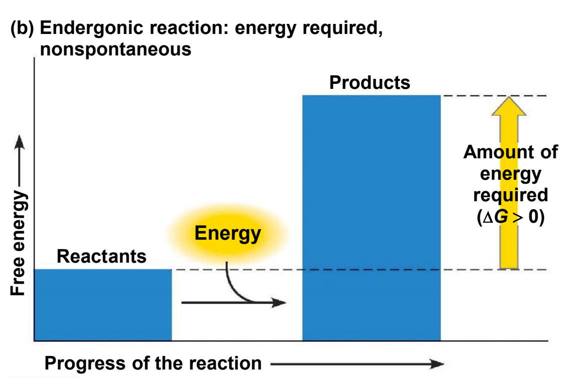


Figure 6.6-1



- An **endergonic reaction** absorbs free energy from its surroundings and is nonspontaneous; ΔG is positive
- The magnitude of ΔG is the quantity of energy required to drive the reaction

Figure 6.6-2



Equilibrium and Metabolism

- Hydroelectric systems can serve as analogies for chemical reactions in living systems
- Reactions in an isolated system eventually reach equilibrium and can then do no work

Figure 6.7

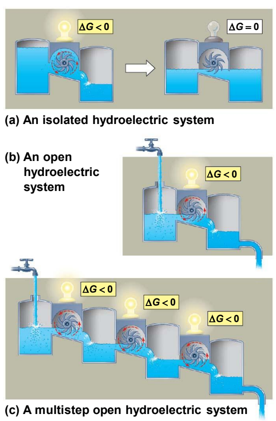
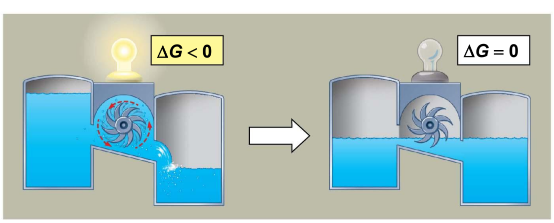


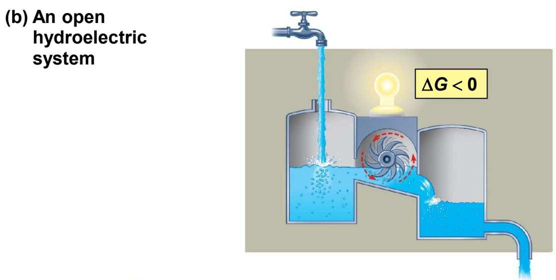
Figure 6.7-1



(a) An isolated hydroelectric system

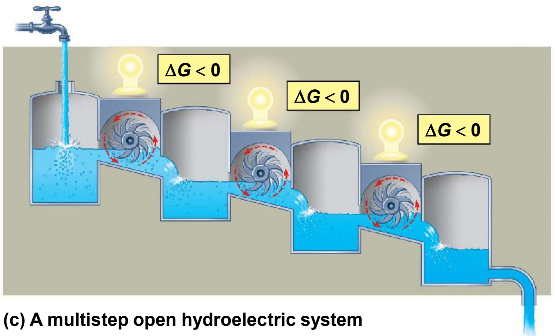
- Cells are not in equilibrium; they are open systems experiencing a constant flow of materials

Figure 6.7-2



- A catabolic pathway in a cell releases free energy in a series of reactions
- The product of each reaction is the reactant for the next, preventing the system from reaching equilibrium

Figure 6.7-3



(c) A multistep open hydroelectric system

Concept 6.3: ATP powers cellular work by coupling exergonic reactions to endergonic reactions

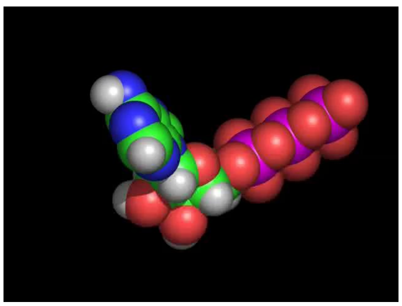
- A cell does three main kinds of work
  - Chemical
  - Transport
  - Mechanical

- To do work, cells manage energy resources by **energy coupling**, the use of an exergonic process to drive an endergonic one
- Most energy coupling in cells is mediated by ATP

The Structure and Hydrolysis of ATP

- **ATP** (**adenosine triphosphate**) is composed of ribose (a sugar), adenine (a nitrogenous base), and three phosphate groups
- In addition to its role in energy coupling, ATP is also used to make RNA

Video: ATP Space-filling Model



Video: ATP Stick Model

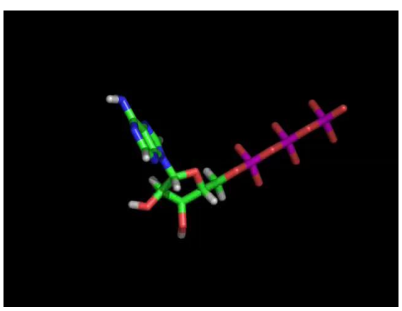


Figure 6.8

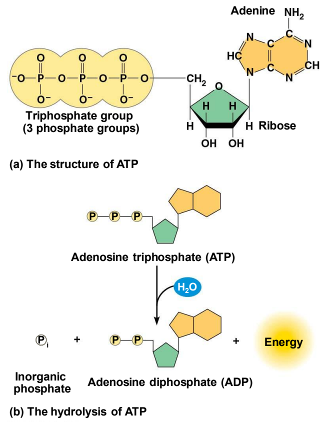
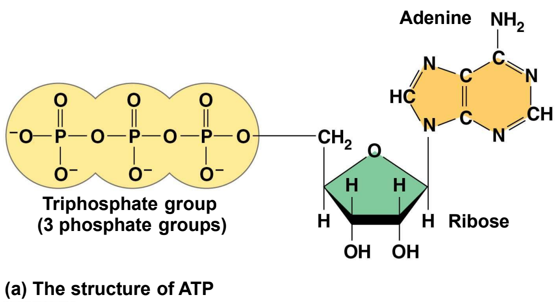
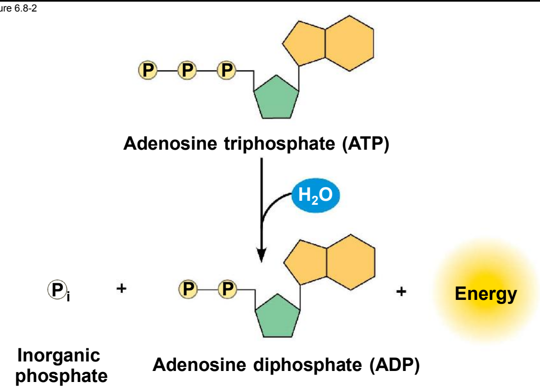


Figure 6.8-1



- The bonds between the phosphate groups of ATP can be broken by hydrolysis
- Energy is released from ATP when the terminal phosphate bond is broken
- This release of energy comes from the chemical change to a state of lower free energy, not from the phosphate bonds themselves

Figure 6.8-2



(b) The hydrolysis of ATP

- ATP hydrolysis releases a lot of energy due to the repulsive force of the three negatively charged phosphate groups
- The triphosphate tail of ATP is the chemical equivalent of a compressed spring

How the Hydrolysis of ATP Performs Work

- The three types of cellular work (mechanical, transport, and chemical) are powered by the hydrolysis of ATP
- In the cell, the energy from the exergonic reaction of ATP hydrolysis can be used to drive endergonic reactions

- ATP drives endergonic reactions by phosphorylation, transferring a phosphate group to some other molecule, such as a reactant
- The recipient molecule is now called a **phosphorylated intermediate**
- Overall, the coupled reactions are exergonic

Figure 6.9

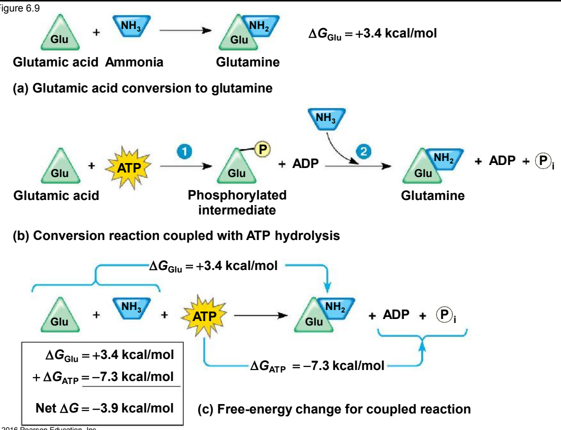


Figure 6.9-1

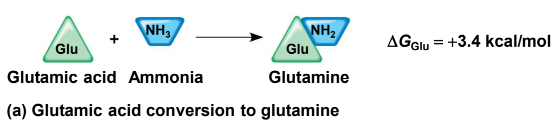
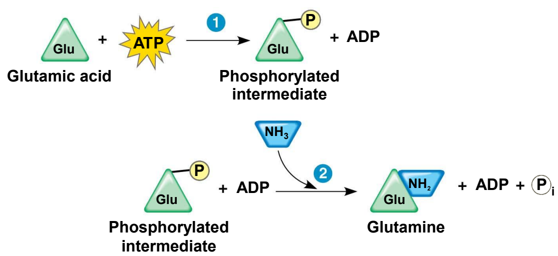
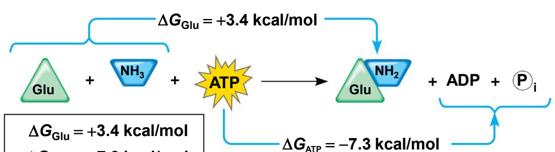


Figure 6.9-2



(b) Conversion reaction coupled with ATP hydrolysis

Figure 6.9-3



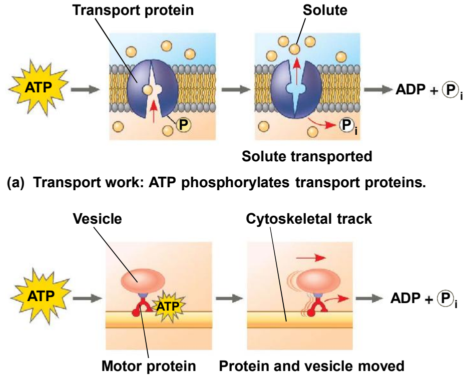
$\Delta G_{Glu} = +3.4$ kcal/mol
$+\Delta G_{ATP} = -7.3$ kcal/mol

Net $\Delta G = -3.9$ kcal/mol

(c) Free-energy change for coupled reaction

- Transport and mechanical work in the cell are powered by ATP hydrolysis
- ATP hydrolysis leads to a change in a protein's shape and often its ability to bind to another molecule

Figure 6.10



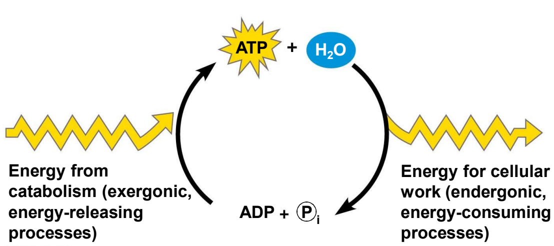
(a) Transport work: ATP phosphorylates transport proteins.

(b) Mechanical work: ATP binds noncovalently to motor proteins and then is hydrolyzed.

The Regeneration of ATP

- ATP is a renewable resource that is regenerated by addition of a phosphate group to adenosine diphosphate (ADP)
- The energy to phosphorylate ADP comes from catabolic reactions in the cell
- The ATP cycle is a revolving door through which energy passes during its transfer from catabolic to anabolic pathways

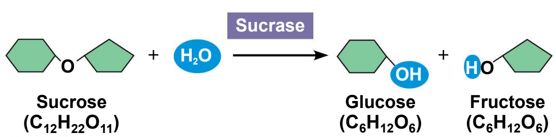
Figure 6.11



Concept 6.4: Enzymes speed up metabolic reactions by lowering energy barriers

- A **catalyst** is a chemical agent that speeds up a reaction without being consumed by the reaction
- An **enzyme** is a catalytic protein
- Hydrolysis of sucrose by the enzyme sucrase is an example of an enzyme-catalyzed reaction

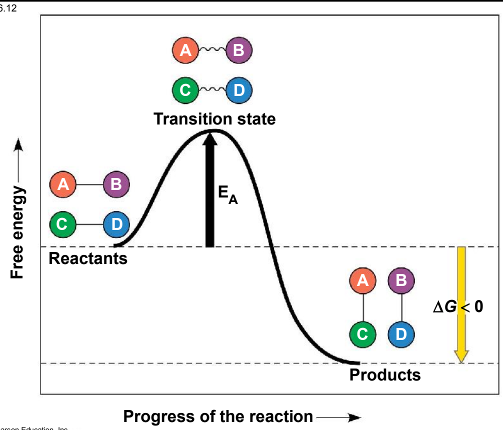
Figure 6.UN02



The Activation Energy Barrier

- Every chemical reaction between molecules involves bond breaking and bond forming
- The initial energy needed to start a chemical reaction is called the free energy of activation, or **activation energy** (E_A)
- Activation energy often occurs in the form of heat that reactant molecules absorb from the surroundings

Figure 6.12



How Enzymes Speed Up Reactions

- Instead of relying on heat, organisms carry out **catalysis** to speed up reactions
- A catalyst (for example, an enzyme) can speed up a reaction by lowering the E_A barrier without itself being consumed
- Enzymes do not affect the change in free energy (ΔG); instead, they hasten reactions that would occur eventually

Animation: How Enzymes Work

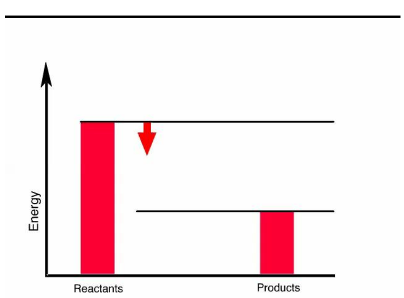
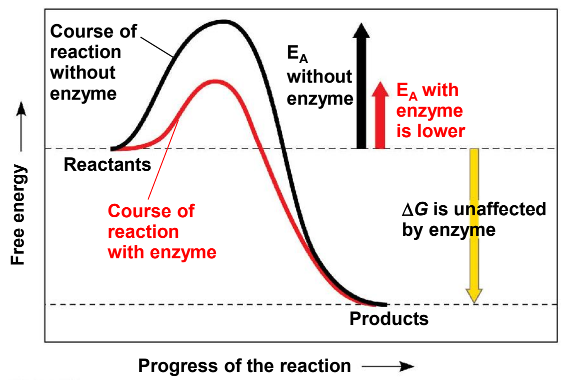


Figure 6.13



Substrate Specificity of Enzymes

- Enzymes are very specific for the reactions they catalyze
- The reactant that an enzyme acts on is called the enzyme's **substrate**
- The enzyme binds to its substrate, forming an **enzyme-substrate complex**
- The **active site** is the region on the enzyme where the substrate binds

- Enzyme specificity results from the complementary fit between the shape of the enzyme's active site and the shape of the substrate
- Enzymes change shape due to chemical interactions with the substrate
- This **induced fit** of the enzyme to the substrate brings chemical groups of the active site together

Video: Enzyme Induced Fit

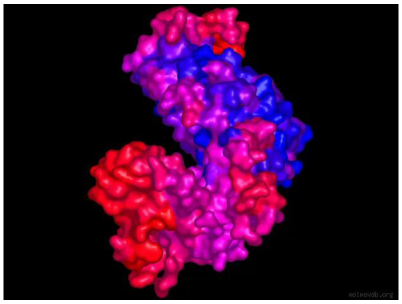
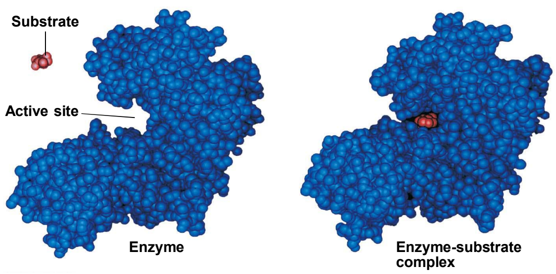


Figure 6.14



Catalysis in the Enzyme's Active Site

- In an enzymatic reaction, the substrate binds to the active site of the enzyme
- The active site can lower an E_A barrier by
  - Orienting substrates correctly
  - Straining substrate bonds
  - Providing a favorable microenvironment
  - Covalently bonding to the substrate

Figure 6.15-s1

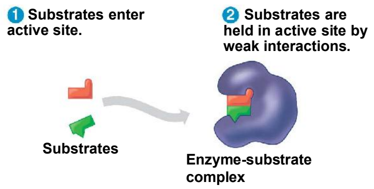


Figure 6.15-s2

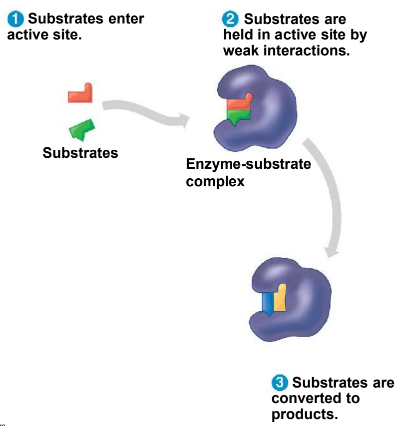


Figure 6.15-s3

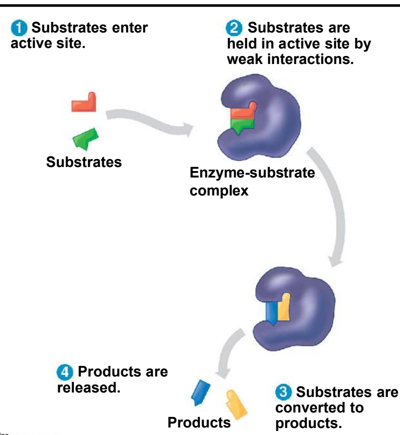
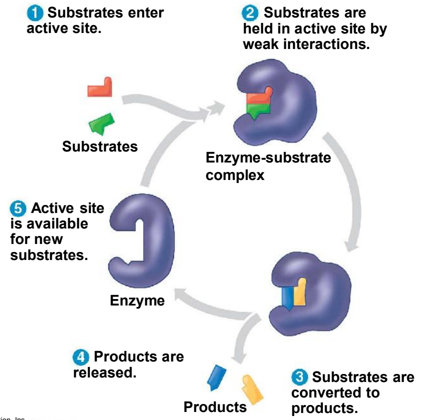


Figure 6.15-s4



- The rate of enzyme catalysis can usually be sped up by increasing the substrate concentration in a solution
- When all enzyme molecules in a solution are bonded with substrate, the enzyme is saturated
- At enzyme saturation, reaction speed can only be increased by adding more enzyme

Effects of Local Conditions on Enzyme Activity

- An enzyme’s activity can be affected by
  - General environmental factors, such as temperature and pH
  - Chemicals that specifically influence the enzyme

Effects of Temperature and pH

- Each enzyme has an optimal temperature and pH at which its reaction rate is the greatest

Figure 6.16

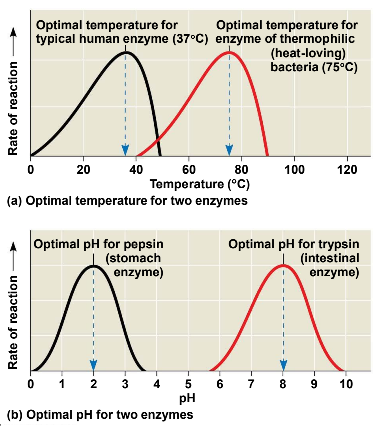


Figure 6.16-1

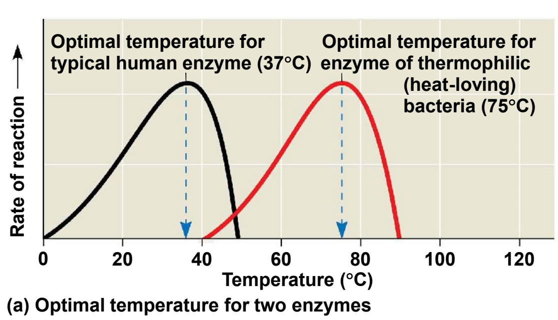
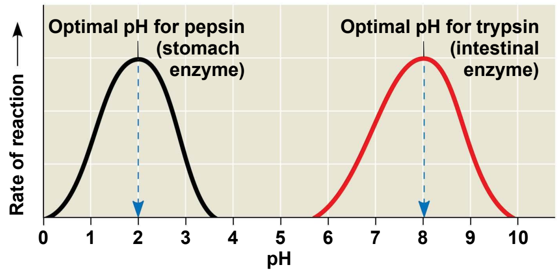


Figure 6.16-2



(b) Optimal pH for two enzymes

Figure 6.16-3

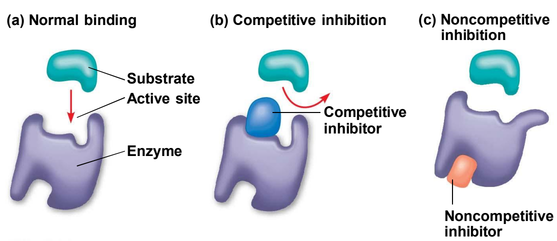
Cofactors

- **Cofactors** are nonprotein enzyme helpers
- Cofactors may be inorganic (such as a metal in ionic form) or organic
- An organic cofactor is called a **coenzyme**
- Most vitamins act as coenzymes or as the raw materials from which coenzymes are made

Enzyme Inhibitors

- **Competitive inhibitors** bind to the active site of an enzyme, competing with the substrate
- **Noncompetitive inhibitors** bind to another part of an enzyme, causing the enzyme to change shape and making the active site less effective
- Examples of inhibitors include toxins, poisons, pesticides, and antibiotics

Figure 6.17



The Evolution of Enzymes

- Most enzymes are proteins encoded by genes
- Changes (mutations) in genes lead to changes in amino acid composition of an enzyme
- Altered amino acids in enzymes may alter their activity or substrate specificity
- Under new environmental conditions a novel form of an enzyme might be favored

Concept 6.5: Regulation of enzyme activity helps control metabolism

- Chemical chaos would result if a cell's metabolic pathways were not tightly regulated
- A cell does this by switching on or off the genes that encode specific enzymes or by regulating the activity of enzymes

Allosteric Regulation of Enzymes

- **Allosteric regulation** may either inhibit or stimulate an enzyme's activity
- Allosteric regulation occurs when a regulatory molecule binds to a protein at one site and affects the protein's function at another site

Allosteric Activation and Inhibition

- Most allosterically regulated enzymes are made from polypeptide subunits
- Each enzyme has active and inactive forms
- The binding of an activator stabilizes the active form of the enzyme
- The binding of an inhibitor stabilizes the inactive form of the enzyme

Figure 6.18

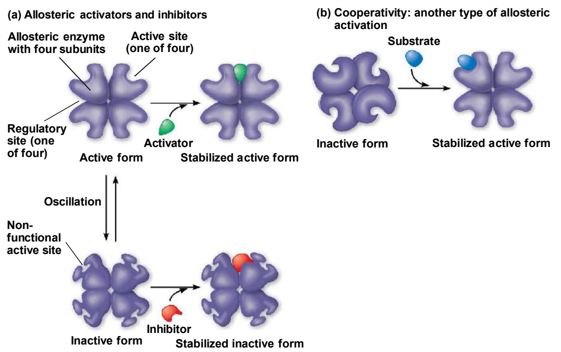
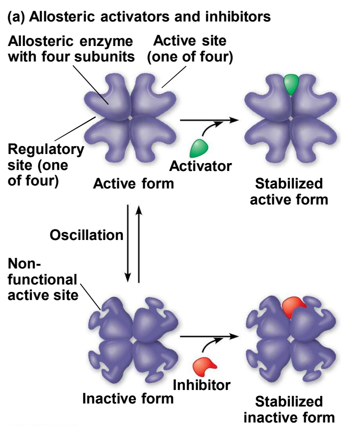
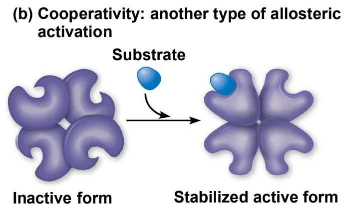


Figure 6.18-1



- **Cooperativity** is a form of allosteric regulation that can amplify enzyme activity
- One substrate molecule primes an enzyme to act on additional substrate molecules more readily
- Cooperativity is allosteric because binding by a substrate to one active site affects catalysis in a different active site

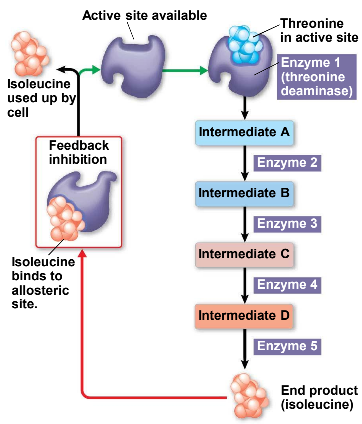
Figure 6.18-2



Feedback Inhibition

- In **feedback inhibition**, the end product of a metabolic pathway shuts down the pathway
- Feedback inhibition prevents a cell from wasting chemical resources by synthesizing more product than is needed

Figure 6.19



Organization of Enzymes Within the Cell

- Structures within the cell help bring order to metabolic pathways
- Some enzymes act as structural components of membranes
- In eukaryotic cells, some enzymes reside in specific organelles; for example, enzymes for cellular respiration are located in mitochondria

Figure 6.20

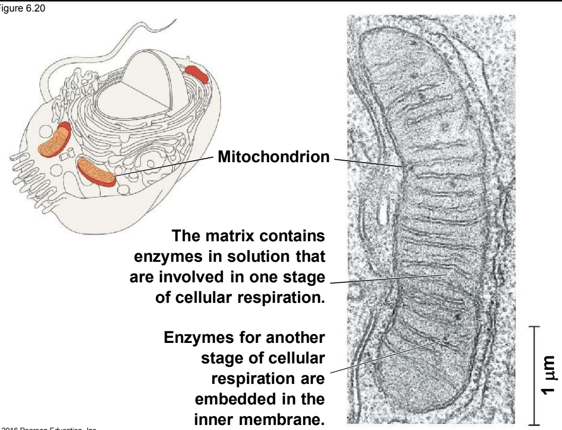


Figure 6.20-1

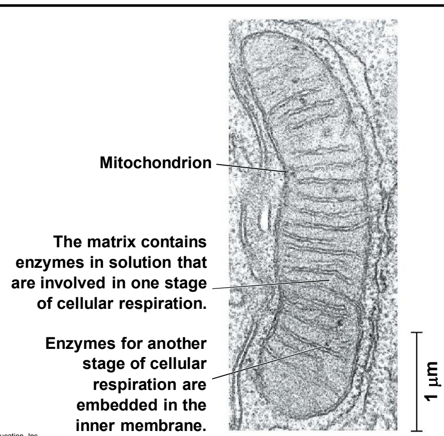


Figure 6.UN03a

Time (min)	Concentration of Ⓟi (µmol/mL)
0	0
5	10
10	90
15	180
20	270
25	330
30	355
35	355
40	355

Data from S. R. Commerford et al., Diets enriched in sucrose or fat increase gluconeogenesis and G-6-Pase but not basal glucose production in rats, *American Journal of Physiology—Endocrinology and Metabolism* 283:E545–E555 (2002).

Figure 6.UN03b

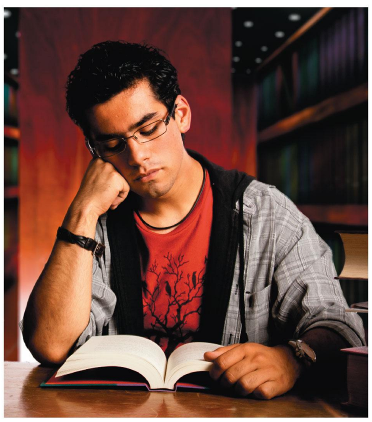


Figure 6.UN04

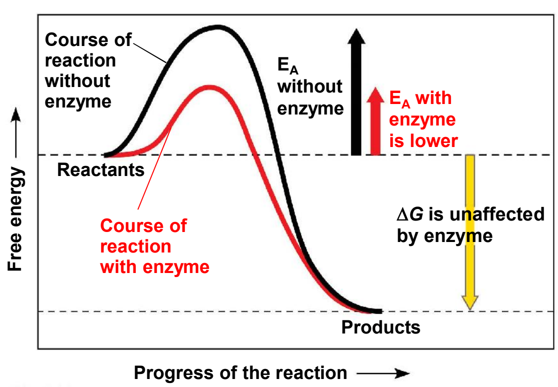


Figure 6.UN05