CAMPBELL
BIOLOGY IN FOCUS

Chapter 6
An Introduction to Metabolism

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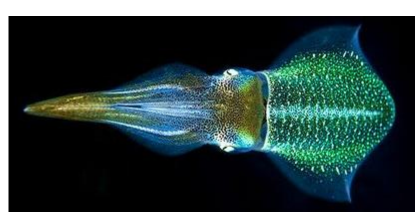
Overview: The Energy of Life

- 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 the energy stored in organic molecules to light, as in bioluminescence

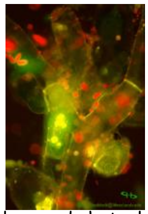


https://www.pinterest.com/deyzel/group-bioluminescence-living-lights-shows/?lp=true

BIOLUMINESCENCE

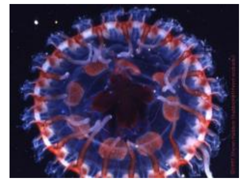
Light produced by a chemical reaction which originates in an organism

octopod



algae and phytoplankton.

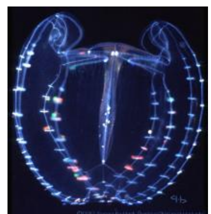
Tuscaridium cygneum



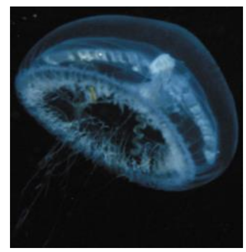
Atolla vanhoeffeni

Paraphyllina

ctenophore



Deiopea



Aequorea victoria

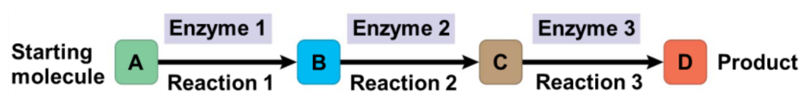
http://www.lifesci.ucsb.edu/~biolum/organism/photo.html

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 via a series of defined steps.
- Each step is catalyzed by a specific enzyme



- **Catabolic pathways** release energy by breaking down complex molecules into simpler compounds
- Cellular respiration, the breakdown of glucose in the presence of oxygen, is an example of a pathway of catabolism
- **Anabolic pathways** consume energy to build complex molecules from simpler ones
- The synthesis of protein from amino acids is an example of anabolism
- **Bioenergetics** is the study of how organisms manage their energy resources

Forms of Energy

- **Energy** is the capacity to cause change

  E.g. gravity and friction: move matter against opposing forces.

- Energy exists in various forms, some of which can perform work
- Life depends on the ability of cells to transform energy from one form to another.

- **Kinetic energy** is energy associated with motion of objects.

- E.g. Water gushing through a dam turns turbines,

- the contraction of leg muscles pushes bicycle pedals.

- **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 powering photosynthesis in green plants

- **Potential energy** is energy that matter possesses because of its location or structure even an object is not moving.

- Water behind a dam possesses energy because of its altitude above sea level.
- Molecules possess energy because of the arrangement of electrons in the bonds between their atoms.

- **Chemical energy** is potential energy available for release in a chemical reaction

- Energy can be converted from one form to another

\- Catabolic pathways release energy by breaking down complex molecules (e.g. glucose) and resulting in lower-energy breakdown products.

\- Hydrocarbons of gasoline react explosively with oxygen, releasing the energy that pushes the pistons and producing exhaust.

\- Food + O_2 $\longrightarrow$ Energy + CO_2 +H_2O

- Biochemical pathways, carried out in the context of cellular structures, enable cells to release chemical energy from food molecules and use the energy to power life processes.

PLAY Animation: Energy Concepts

Figure 6.2

The Laws of Energy Transformation

- **Thermodynamics** is the study of energy transformations that occur in a collection of matter
- An isolated system, such as that approximated by liquid in a thermos, is isolated from its surroundings and cannot exchange either energy or matter with its surroundings.
- In an open system, energy and matter can be transferred between the system and its surroundings
- Organisms are open systems can absorb energy (light energy or chemical energy) in the form of organic molecules—and release heat and metabolic waste products (carbon dioxide) to the surroundings.

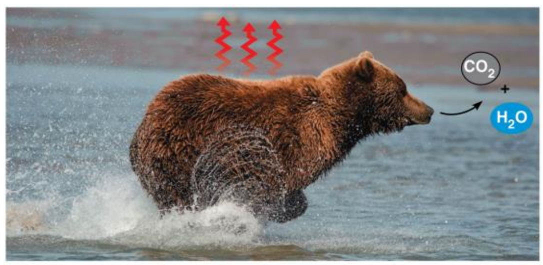
The First Law of Thermodynamics

- According to the **first law of thermodynamics**, the energy of the universe is constant
- *Energy can be transferred and transformed, but it cannot be created or destroyed*
- The first law is also called the *principle of conservation of energy*
- *By converting sunlight to chemical energy, a plant acts as an energy transformer, not an energy producer.*

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

The Second Law of Thermodynamics

- During every energy transfer or transformation, some energy is unusable and is often lost as heat
- According to the **second law of thermodynamics**
  - *Every energy transfer or transformation increases the entropy **(disorder)** of the universe*
- **Entropy** is a measure of disorder, or randomness. The more randomly arranged a collection of matter is, the greater its entropy.



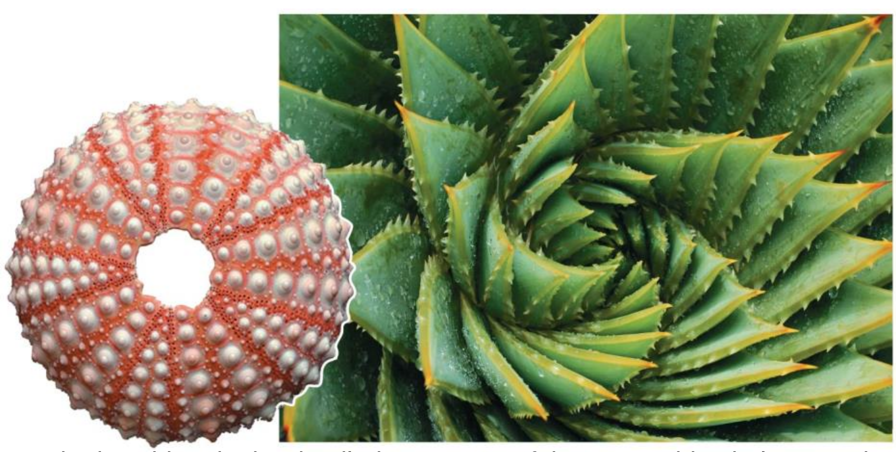
- Living cells unavoidably convert organized forms of energy to heat
- **Spontaneous processes** occur without energy input; they can happen quickly (an explosion) or slowly (rusting of an old car over time)
- *For a process to occur without energy input, it must increase the entropy of the universe*

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

Figure 6.4

Order as a characteristic of life



Order is evident in the detailed structures of the sea urchin skeleton and the succulent plant shown here. As open systems, organisms can increase their order as long as the order of their surroundings decreases.

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

- Biologists want to know which reactions occur spontaneously and which require input of energy
- To do so, they need to determine energy changes that occur in chemical reactions

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

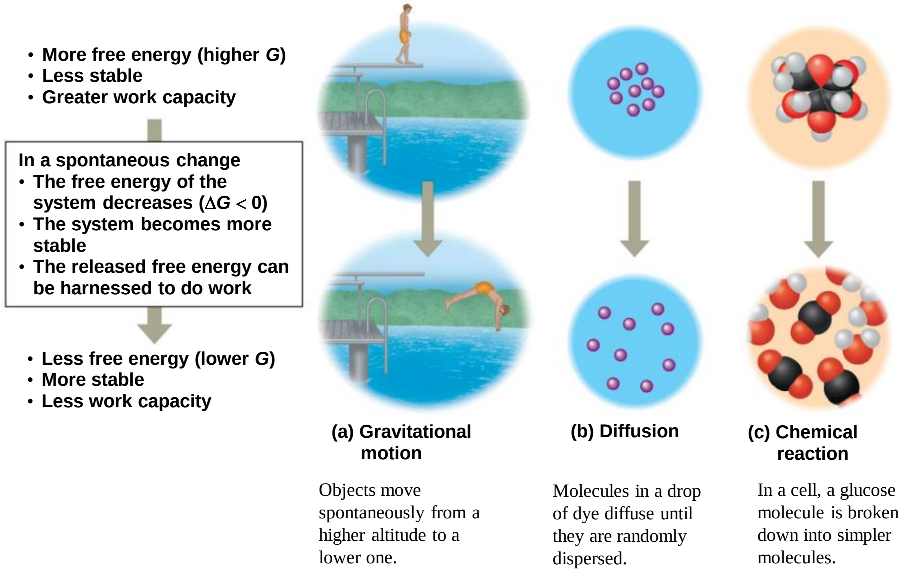
$$\Delta G = G_{\text{final state}} - G_{\text{initial state}}$$

- Only processes with a negative ΔG are spontaneous
- For a reaction to have a negative ΔG, the system must lose free energy during the change from initial state to final state.

- 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
- 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

Figure 6.5

The relationship of free energy to stability, work capacity, and spontaneous change



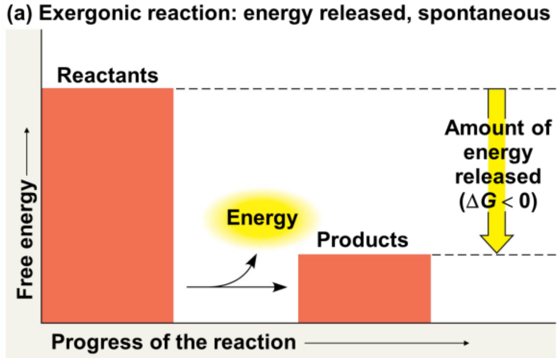
Free Energy and Metabolism

- The concept of free energy can be applied to the chemistry of life's processes
- Based on their free-energy changes, chemical reactions can be classified as either **exergonic** ("energy outward") or **endergonic** ("energy inward").

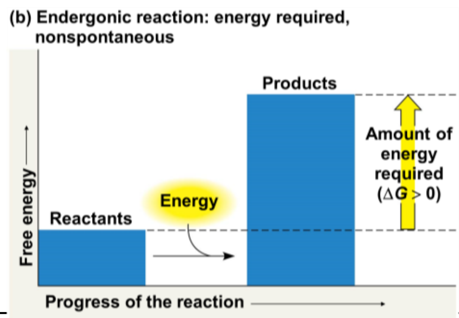
Exergonic and Endergonic Reactions in Metabolism

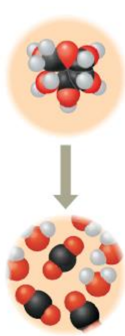
- An **exergonic reaction** proceeds with a net release of free energy and is spontaneous; ΔG is negative
- The magnitude of ΔG represents the maximum amount of work the reaction can perform
- The greater the decrease in free energy, the greater the amount of work that can be done.

(a) Exergonic reaction: energy released, spontaneous



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





exergonic reaction

$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$

ΔG = −686 kcal/mol (−2,870 kJ/mol)

endergonic reaction

$C_6H_{12}O_6 + 6\ O_2 \leftarrow 6\ CO_2 + 6\ H_2O$

ΔG = 686 kcal/mol (−2,870 kJ/mol)

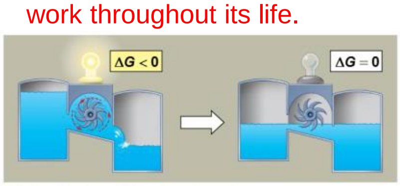
686 kcal (2,870 kJ) of energy are made available for work for each mole (180 g) of glucose broken down by respiration under "standard conditions", or 686 kcal of energy is required to form glucose.

Equilibrium and Metabolism

- Reactions in a closed system eventually reach equilibrium and then do no work
- Cells are not in equilibrium; they are open systems experiencing a constant flow of materials
- A defining feature of life is that metabolism is never at equilibrium

Equilibrium and work in isolated and open systems

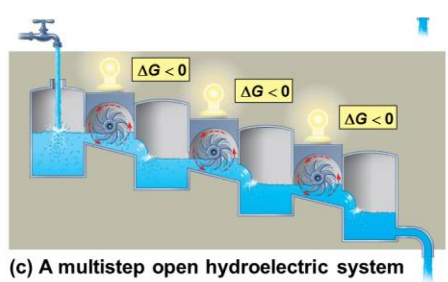
- A catabolic pathway in a cell releases free energy in a series of reactions
- Closed and ope hydroelectric systems can serve as analogies
- The constant flow of materials in and out of the cell keeps the metabolic pathways from ever reaching equilibrium, and the cell continues to do work throughout its life.



(a) An isolated hydroelectric system
Water flowing downhill turns a turbine that drives a generator providing electricity to a lightbulb, but only until the system reaches equilibrium. In biosystem, metabolism as a whole is never at equilibrium.

(b) An open hydroelectric system

Flowing water keeps driving the generator because intake and outflow of water keep the system from reaching equilibrium.



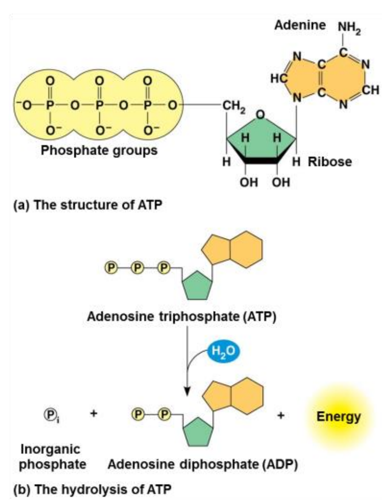
(c) A multistep open hydroelectric system
Cellular respiration is analogous to this system: Glucose is broken down in a series of exergonic reactions that power the work of the cell. The product of each reaction is used as the reactant for the next, so no reaction reaches equilibrium.

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

- A cell does three main kinds of work
  - ✓ **Chemical:** the pushing of endergonic reactions
  - ✓ **Transport:** the pumping of substances across membranes against the direction of spontaneous movement
  - ✓ **Mechanical:** the beating of cilia (see Chapter 4), the contraction of muscle cells, and the movement of chromosomes during cellular reproduction
- 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
- 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



PLAY Video: ATP Space-filling Model

PLAY Video: ATP Stick Model

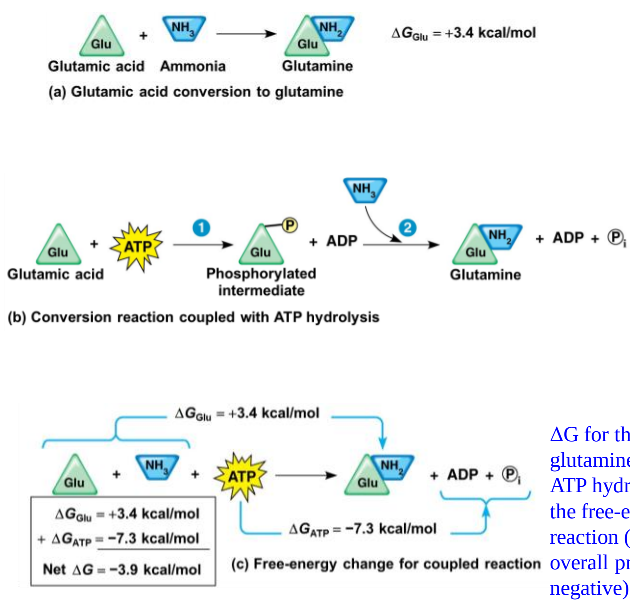
$ATP + H_2O \rightarrow ADP + P_i$

$\Delta G = -7.3$ kcal/mol (-30.5 kJ/mol)

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 an endergonic reaction
- Overall, the coupled reactions are exergonic

How ATP drives chemical work: energy coupling using ATP hydrolysis



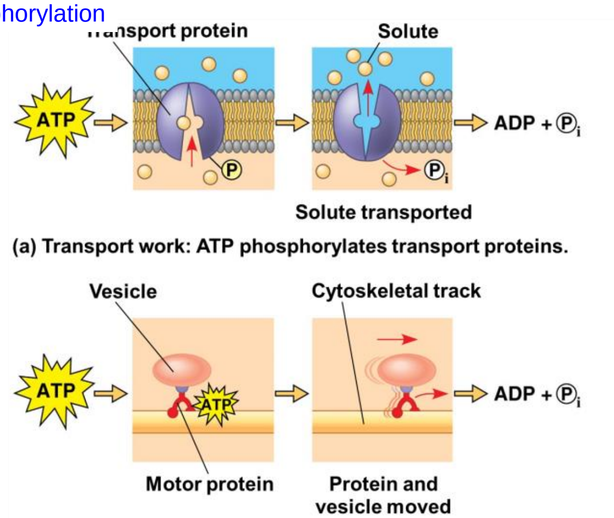
Not spontaneous.

In the cell, glutamine synthesis occurs in two steps, coupled by a **phosphorylated intermediate**. ATP phosphorylates glutamic acid, making it less stable. Ammonia displaces the phosphate group, forming glutamine. ATP hydrolysis leads to a change in a protein's shape and often its ability to bind to another molecule

ΔG for the glutamic acid conversion to glutamine (+3.4 kcal/mol) plus ΔG for ATP hydrolysis (–7.3 kcal/mol) gives the free-energy change for the overall reaction (–3.9 kcal/mol). Because the overall process is exergonic (net ΔG is negative), it occurs spontaneously.

How ATP drives transport and mechanical work?

directly, by phosphorylation



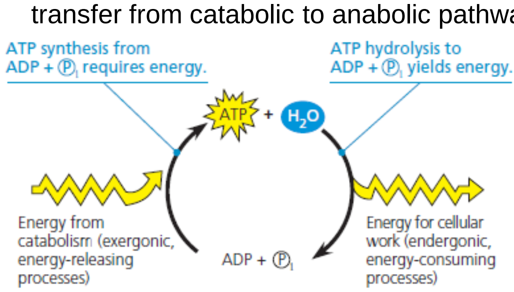
(a) Transport work: ATP phosphorylates transport proteins.

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

Indirectly, via noncovalent binding of ATP and its hydrolytic products

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
- Energy released by breakdown reactions (catabolism) in the cell is used to phosphorylate ADP, regenerating ATP. Chemical potential energy stored in ATP drives most cellular work.
- The ATP cycle is a revolving door through which energy passes during its transfer from catabolic to anabolic pathways

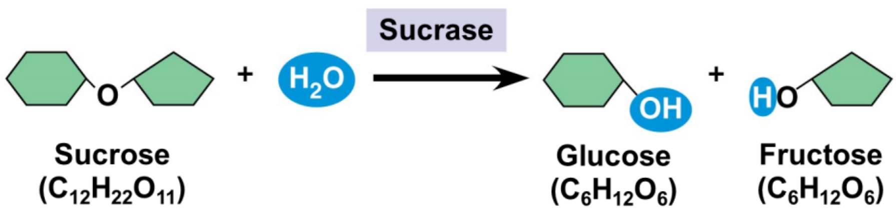


Both directions of a reversible process cannot be downhill, the regeneration of ATP from ADP and Pi is necessarily endergonic:

ADP + P i → ATP + H_2O
ΔG = +7.3 kcal/mol (+30.5 kJ/mol)
(standard conditions)

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
- Without regulation by enzymes, chemical traffic through the pathways of metabolism would become terribly congested because many chemical reactions would take such a long time.
- Hydrolysis of sucrose by the enzyme sucrase is an example of an enzyme-catalyzed reaction



The Activation Energy Barrier

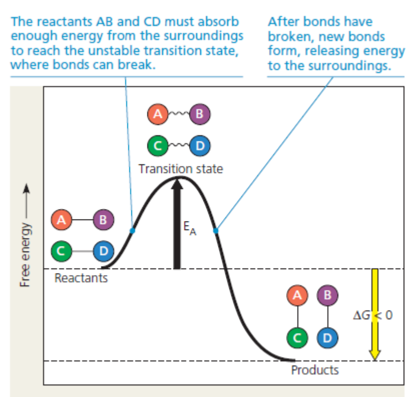
- Every chemical reaction between molecules involves bond breaking and bond forming
- The initial energy needed to start a chemical reaction is called the **free energy of activation, or activation energy** (E_A)
- Activation energy is often supplied in the form of thermal energy that the reactant molecules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

To reach the top of the activation energy barrier

before the reaction can occur.

$$AB + CD \rightarrow AC + BD$$

Reactants Products

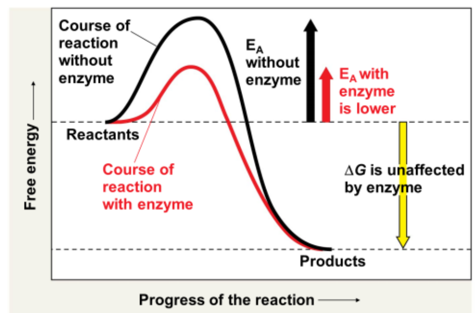


Energy profile of an exergonic reaction

How Enzymes Speed Up Reactions

- Enzymes catalyze reactions by lowering the E_A barrier enabling the reactant molecules to absorb enough energy to reach the transition state even at moderate temperatures.
- Enzymes do not affect the change in free energy (ΔG); instead, they hasten reactions that would occur eventually.
- Enzyme makes it possible for the cell to have a dynamic metabolism,

routing chemicals smoothly through the cell's metabolic pathways at any particular time .



PLAY Animation: How Enzymes Work

Substrate Specificity of Enzymes

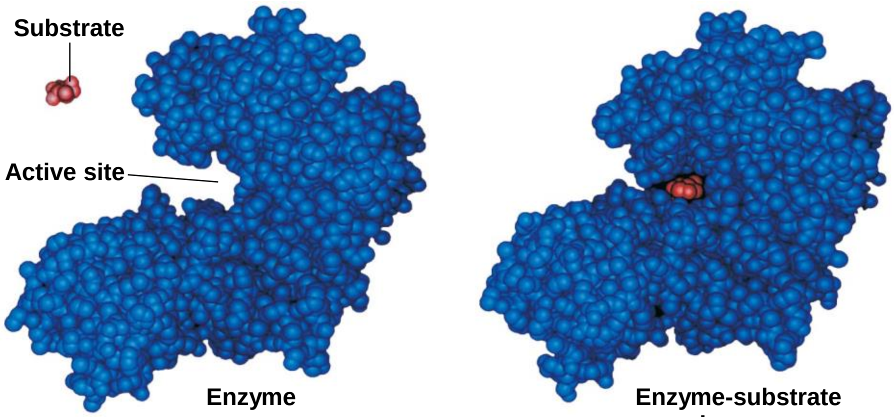
- Enzymes are proteins macromolecules with unique three-dimensional configurations. The specificity of an enzyme results from its shape
- The reactant that an enzyme acts on is called the enzyme's **substrate**
- The enzyme binds to its substrate, forming an **enzyme-substrate complex**
- The **active site** is the region on the enzyme where the substrate binds
- Enzyme specificity results from the complementary fit between the shape of its active site and the substrate shape
- 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 into positions that enhance their ability to catalyze the reaction

$$\text{Enzyme + Substrate(s)} \rightleftharpoons \text{Enzyme-substrate complex} \rightleftharpoons \text{Enzyme + Product(s)}$$

PLAY Video: Enzyme Induced Fit

Figure 6.14

Induced fit between an enzyme and its substrate



(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 forms weak bonds with the enzyme, inducing a change in the shape of the enzyme. This change allows additional weak bonds to form, causing the active site to enfold the substrate and hold it in place.

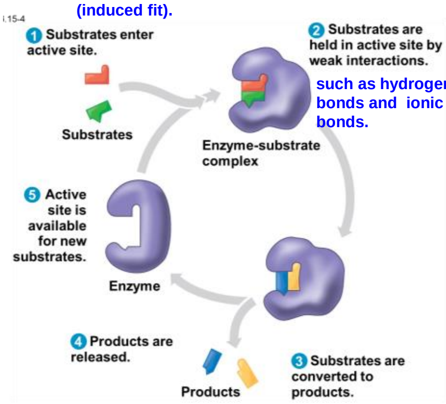
Catalysis in the Enzyme’s Active Site

- 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**

  as the active site of an enzyme clutches the bound substrates, the enzyme may stretch the substrate molecules toward their transition-state form, stressing And bending critical chemical bonds that must be broken during the reaction
  - **Providing a favorable microenvironment**

  For example, if the active site has amino acids with acidic R groups, the active site may be a pocket of low pH in an otherwise neutral cell. In such cases, an acidic amino acid may facilitate H+ transfer to the substrate as a key step in catalyzing the reaction.
  - **Covalently bonding to the substrate**

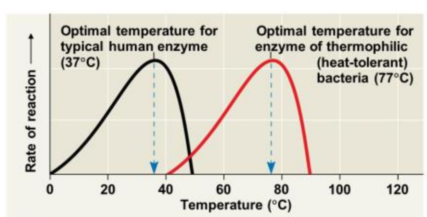
Enzyme changes shape such that its active site enfolds the substrates (induced fit).



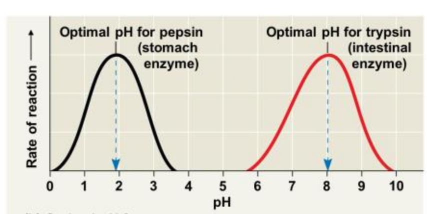
Effects of Local Conditions on Enzyme Activity

Effects of Temperature and pH on Enzyme Activity

- Each enzyme has an optimal temperature in which it can function
- Each enzyme has an optimal pH in which it can function
- Optimal conditions favor the most active shape for the enzyme molecule



(a) Optimal temperature for two enzymes



(b) Optimal pH for two enzymes

Cofactors

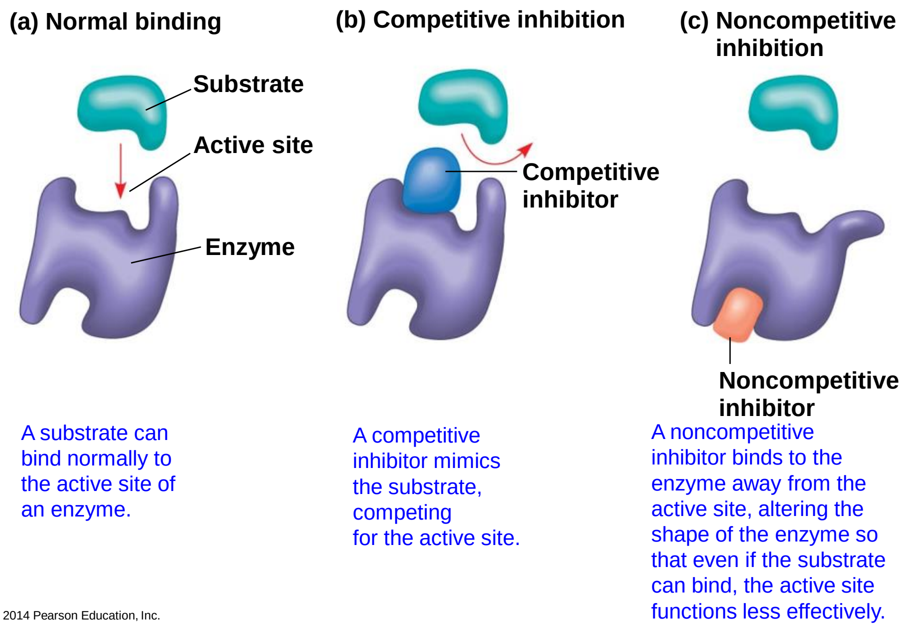
- **Cofactors** are nonprotein enzyme helpers
- Cofactors may be inorganic (metal atoms zinc, iron, and copper in ionic form) or organic.
- An organic cofactor is called a **coenzyme** include vitamins.
  - **cofactors**, may be bound tightly to the enzyme as permanent residents, or they may bind loosely and reversibly along with the substrate.

Enzyme Inhibitors

- Certain chemicals selectively inhibit the action of specific enzymes. If the inhibitor attaches to the enzyme by covalent bonds, inhibition is usually irreversible.
- **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

Inhibition of enzyme activity



The Evolution of Enzymes

- 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 substrate specificity
- Under new environmental conditions a novel form of an enzyme might be favored

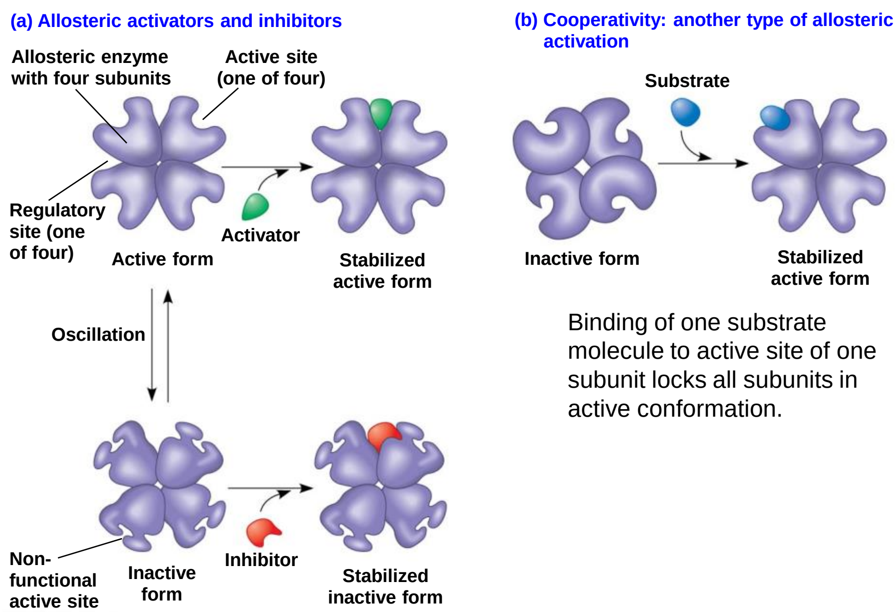
Concept 6.5: Regulation of enzyme activity helps control metabolism

- 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 (Inhibition) or stimulate (Activation) 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.
- 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

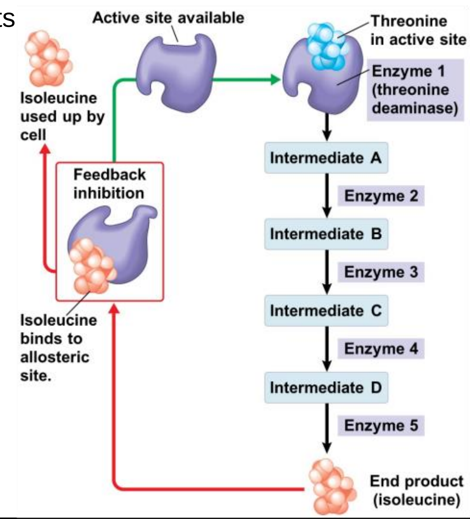
Figure 6.18



- **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

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



Specific Localization 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

Organelles and structural order in metabolism