

6

An Introduction to Metabolism

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

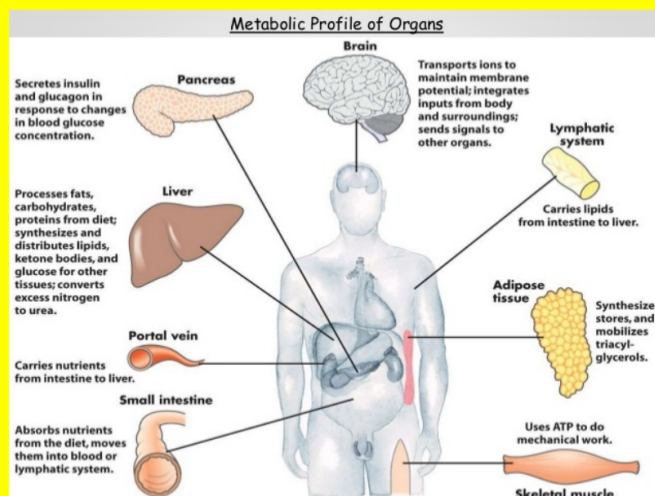


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Concept 6.1: An organism's metabolism transforms matter and energy

*NO MASS
NO volume*

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

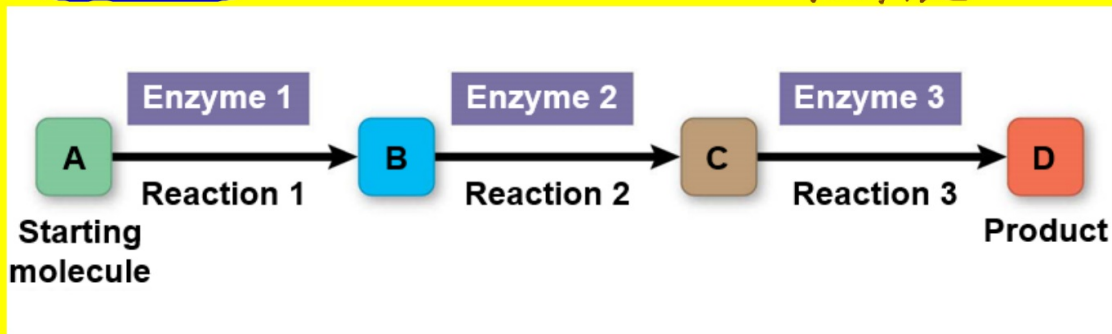


Metabolic Pathways

ase
rxn specific
named for
reactants
ASSIS

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

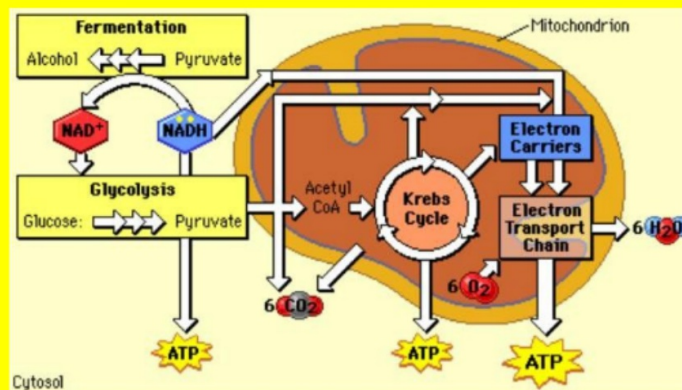
proteins - specific 3D structure = function



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catabolism

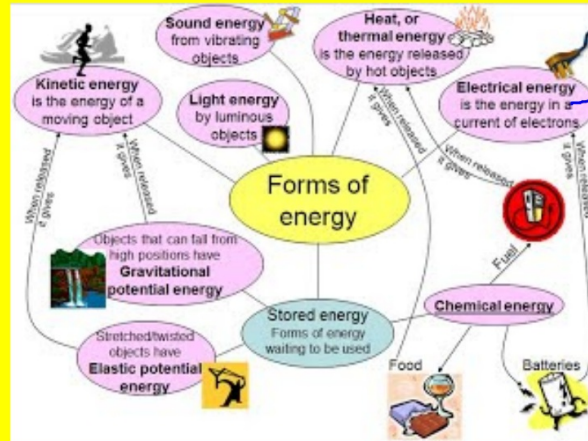
- **Catabolic pathways** release energy by breaking down complex molecules into simpler compounds
- One example of catabolism is cellular respiration, the breakdown of glucose and other organic fuels to carbon dioxide and water



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- Stored Energy
 Potential energy is energy that matter possesses because of its location or structure
- potential EMs
Ch
combdy
 Chemical energy is potential energy available for release in a chemical reaction → FOOD, FUELS,
- Energy can be converted from one form to another

↓
NOT 100% efficient



Animation: Energy Concepts

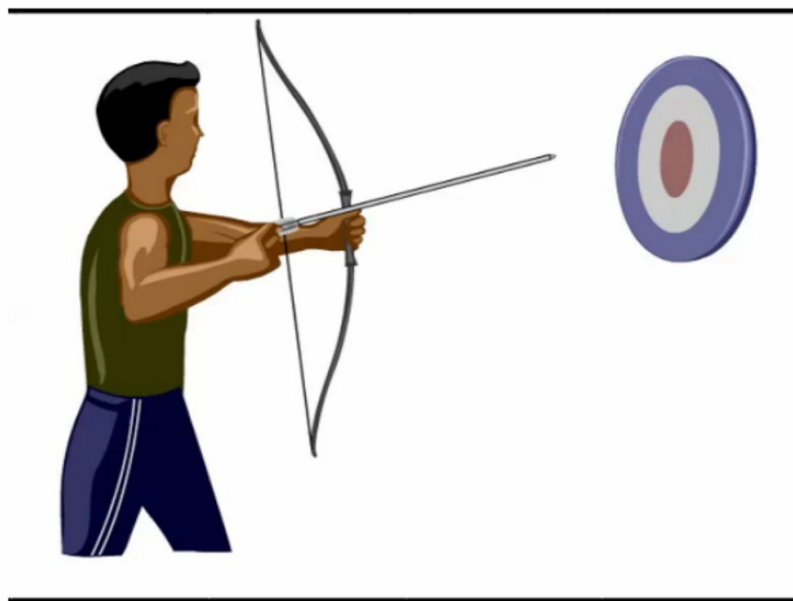


Figure 6.2

A diver has more potential energy on the platform.

Diving converts potential energy to kinetic energy.



Climbing up converts the kinetic energy of muscle movement to potential energy.

A diver has less potential energy in the water.

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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

- FOOD

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

↓
Heat

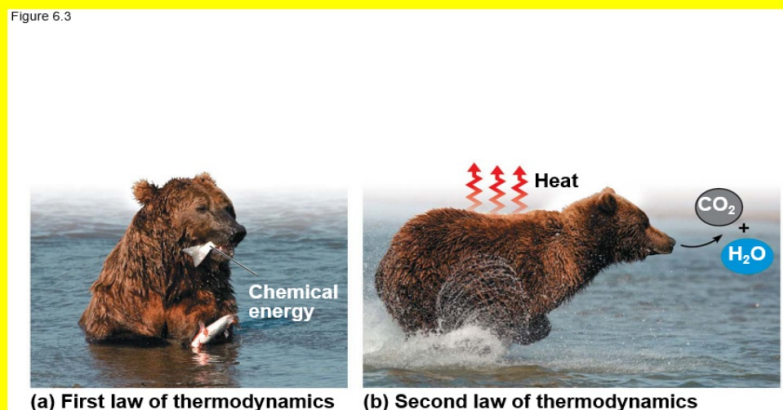
- FOOD

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The Second Law of Thermodynamics

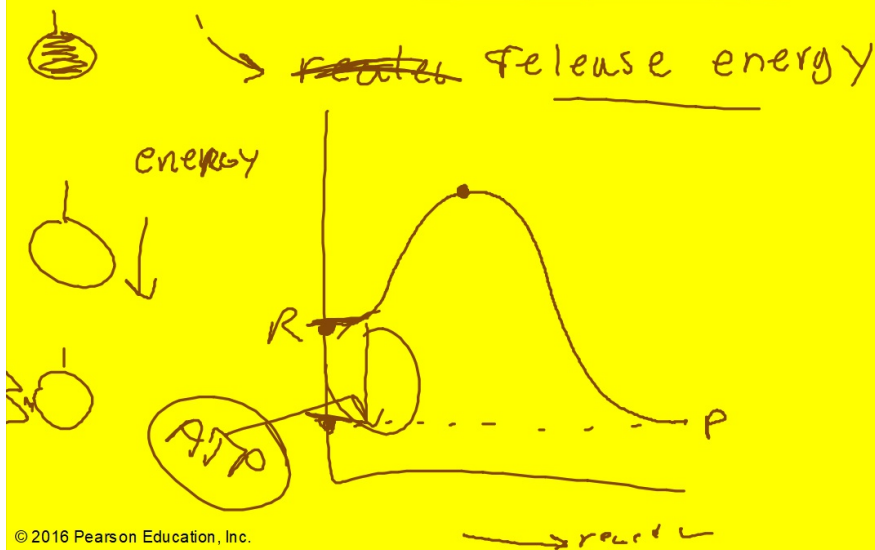
- During every energy transfer or transformation, some energy is lost as heat
- According to the **second law of thermodynamics**
 - Every energy transfer or transformation increases the entropy of the universe
- Entropy is a measure of disorder, or randomness

Figure 6.3



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- Living cells unavoidably convert organized forms of energy to heat — *“Energetically Favorable”*
- 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*



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Biological Order and Disorder

- Cells create ordered structures from less ordered materials — *requires energy (↓ entropy)*
- Organisms also replace ordered forms of matter and energy with less ordered forms *Energetically favorable*
- Energy flows into an ecosystem in the form of light and exits in the form of heat

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- 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

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Concept 6.2: The free-energy change of a reaction tells us whether or not the reaction occurs spontaneously (*Energetically favorable*)

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

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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

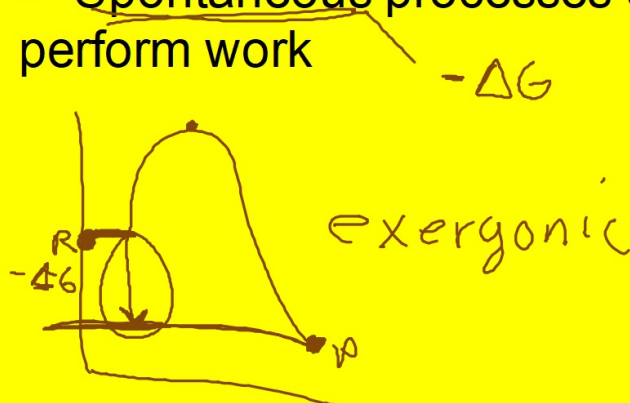
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- The change in free energy (ΔG) during a chemical reaction is the difference between the free energy of the final state and the free energy of the initial state

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

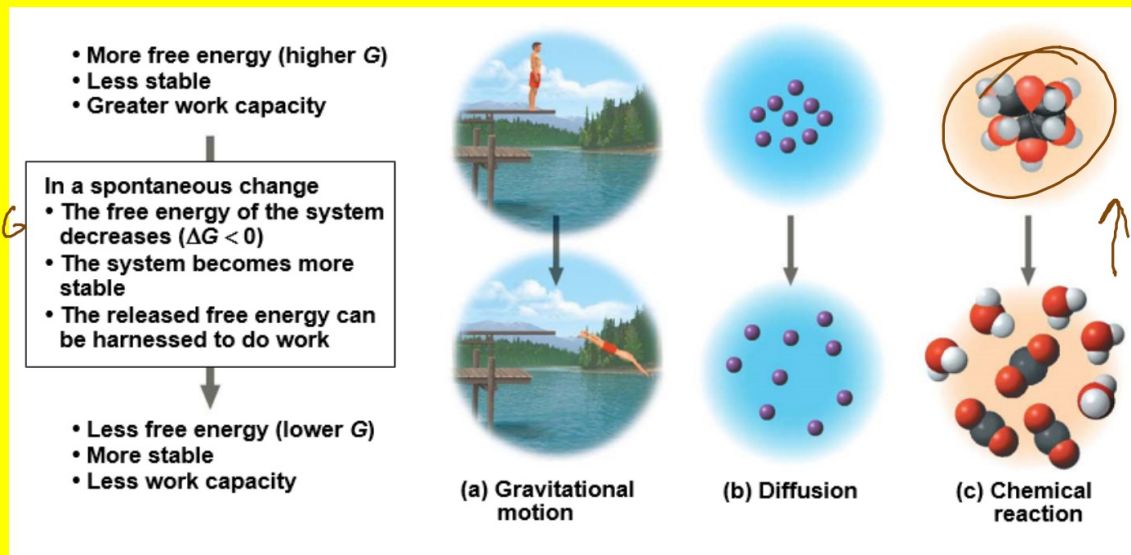
- Only processes with a negative ΔG are spontaneous
- Spontaneous processes can be harnessed to perform work



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- 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

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- 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*

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Free Energy and Metabolism

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

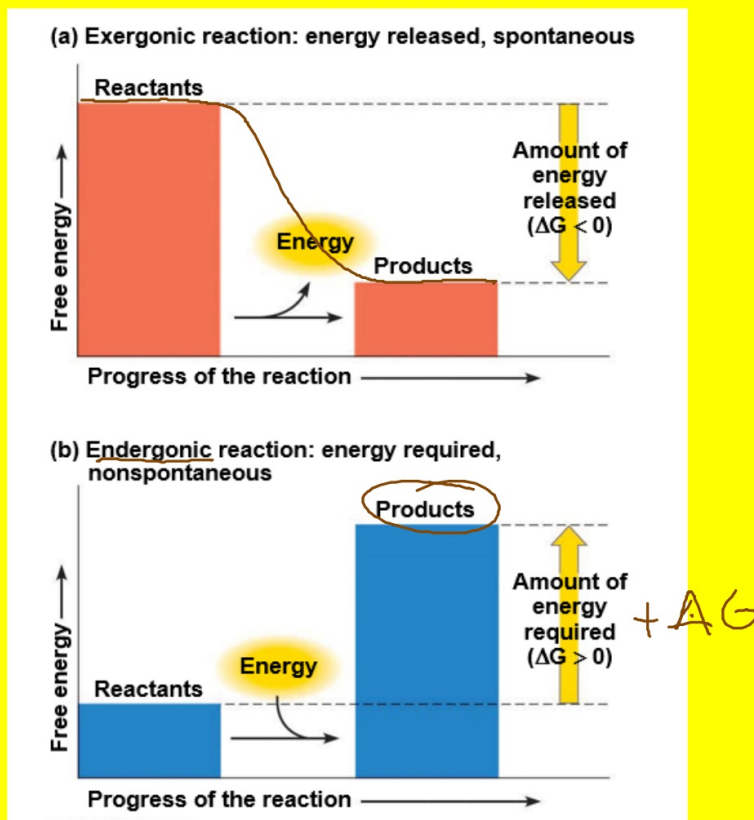
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Exergonic and Endergonic Reactions in Metabolism

(exit)

- 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

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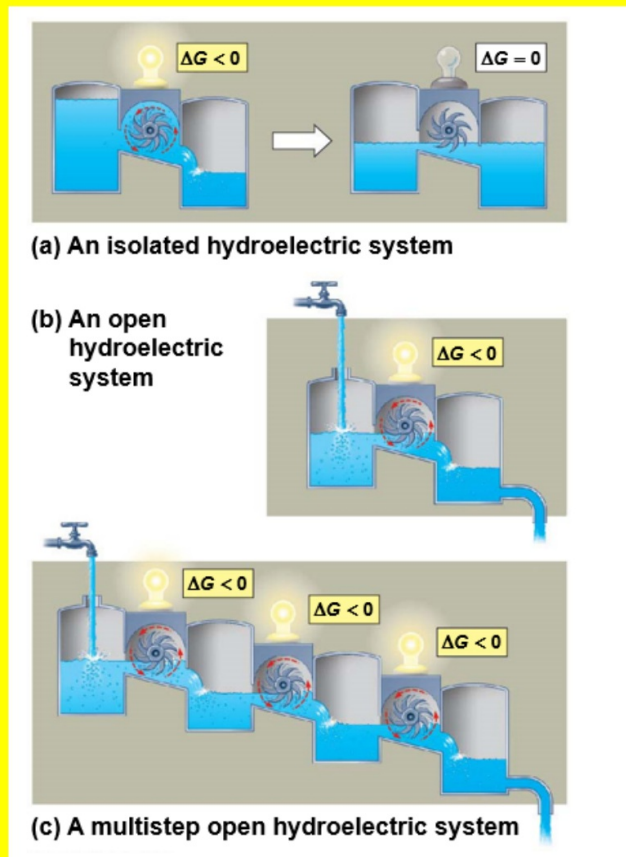
- An **endergonic reaction** absorbs free energy from its surroundings and is nonspontaneous; ΔG is positive
- The magnitude of ΔG is the quantity of energy required to drive the reaction

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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

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

- 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

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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

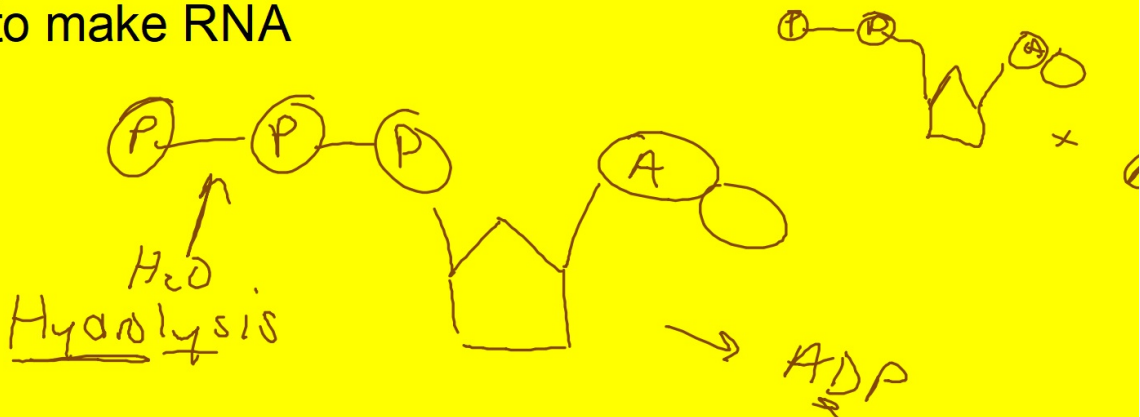
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- To do work, cells manage energy resources by **energy coupling**, the use of an exergonic process to drive an endergonic one
- Most energy coupling in cells is mediated by ATP

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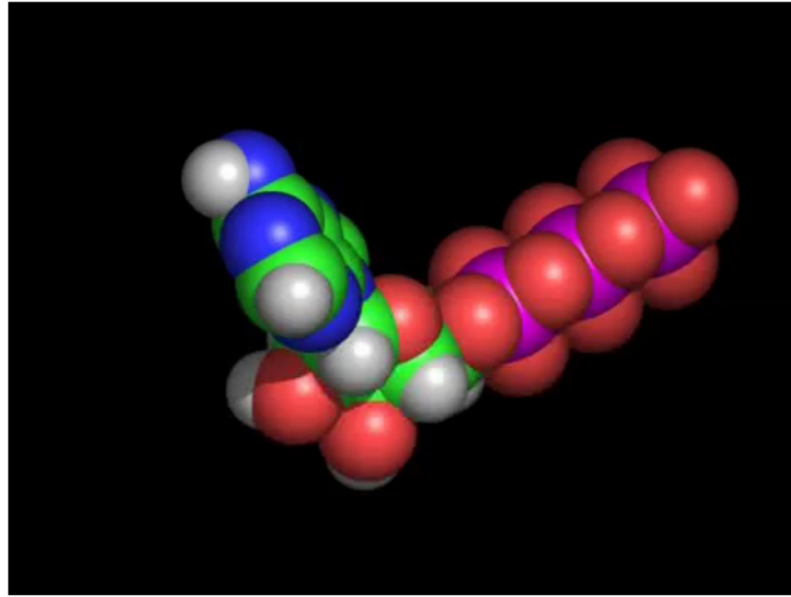
The Structure and Hydrolysis of ATP

- **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



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Video: ATP Space-filling Model



Video: ATP Stick Model

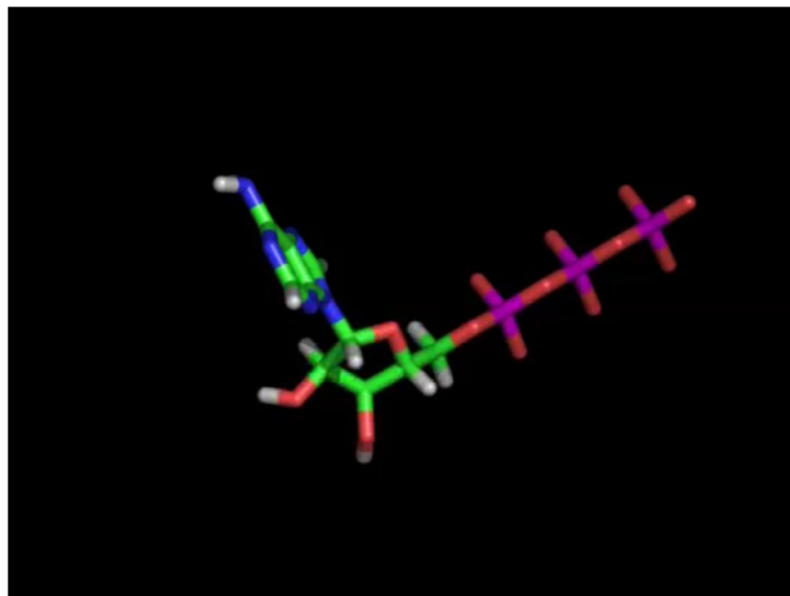
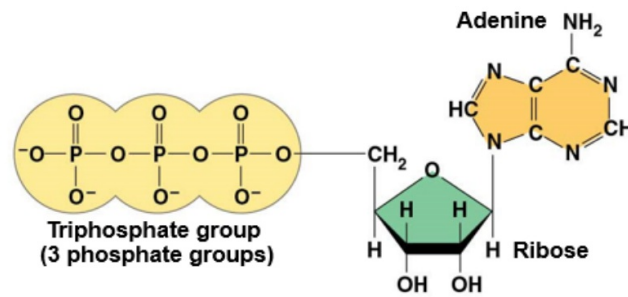
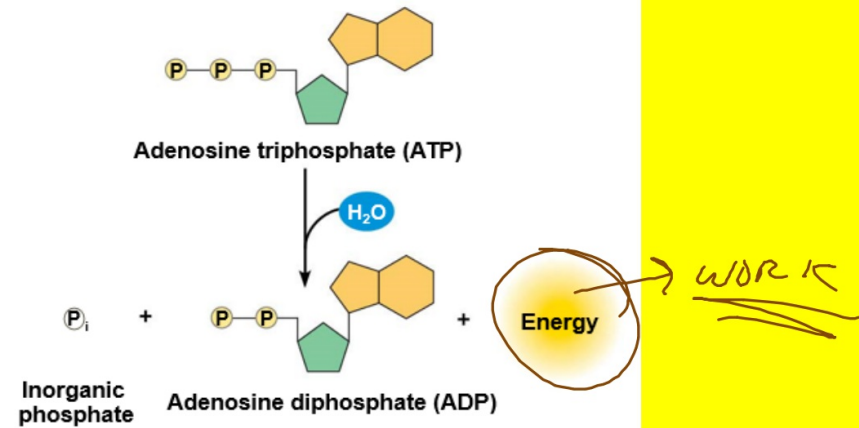


Figure 6.8



(a) The structure of ATP



(b) The hydrolysis of ATP

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- 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

- 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

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How the Hydrolysis of ATP Performs Work

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

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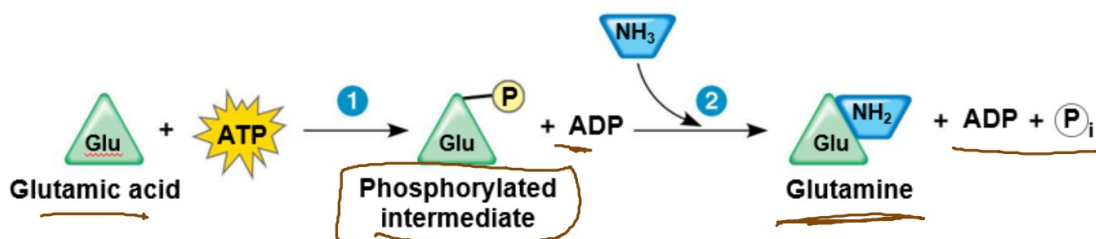
- ATP drives endergonic reactions by phosphorylation, transferring a phosphate group to some other molecule, such as a reactant
- The recipient molecule is now called a phosphorylated intermediate
- Overall, the coupled reactions are exergonic

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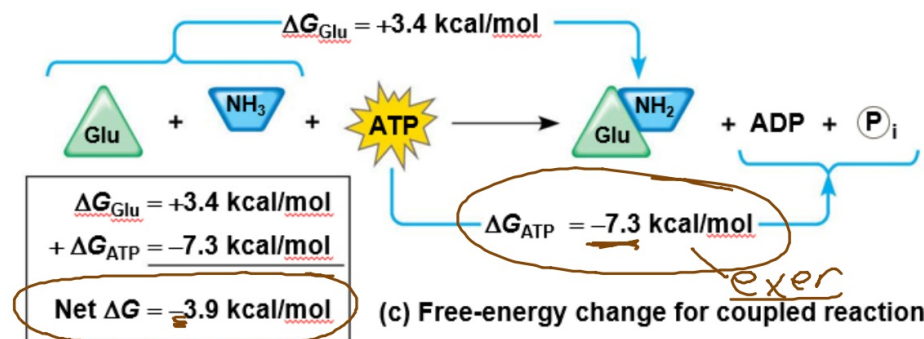
Figure 6.9



(a) Glutamic acid conversion to glutamine



(b) Conversion reaction coupled with ATP hydrolysis



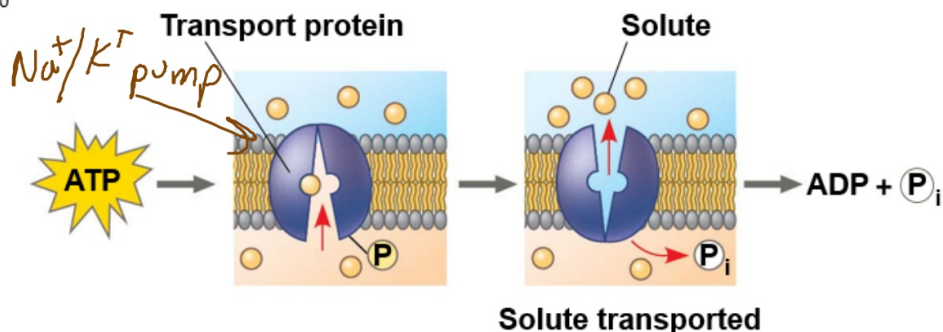
(c) Free-energy change for coupled reaction

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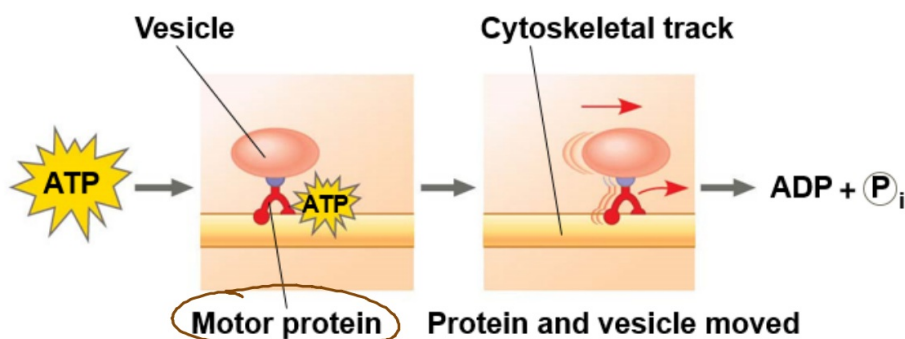
- Transport and mechanical work in the cell are powered by ATP hydrolysis
- ATP hydrolysis leads to a change in a protein's shape and often its ability to bind to another molecule

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Figure 6.10



(a) Transport work: ATP phosphorylates transport proteins.

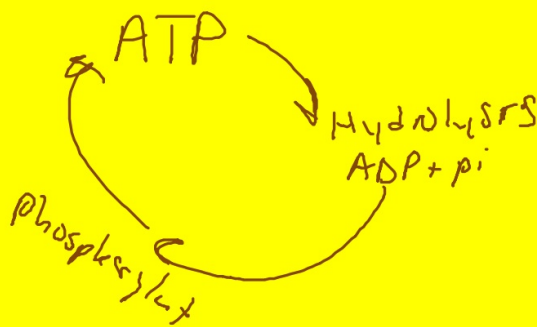


(b) Mechanical work: ATP binds noncovalently to motor proteins and then is hydrolyzed.

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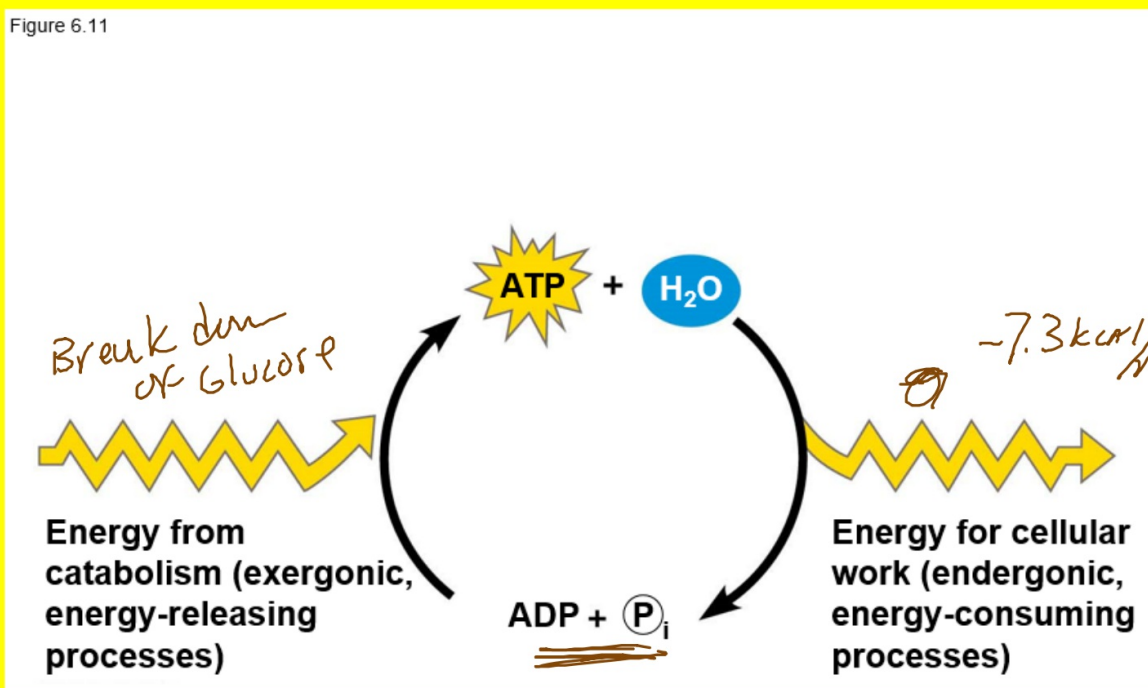
The Regeneration of ATP

- ATP is a renewable resource that is regenerated by addition of a phosphate group to adenosine diphosphate (ADP) – *Cell respiration*
- 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



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Figure 6.11



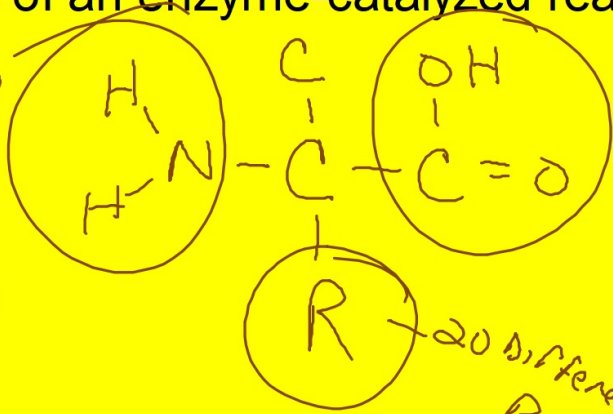
Concept 6.4: Enzymes speed up metabolic reactions by lowering energy barriers

- 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

proteins
species
spec.

JOB
Spec.

General
Structure
of an
amino
acid



20 different
R-groups

DNA → RNA → protein

polypeptide

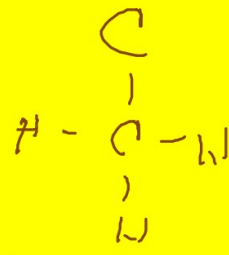
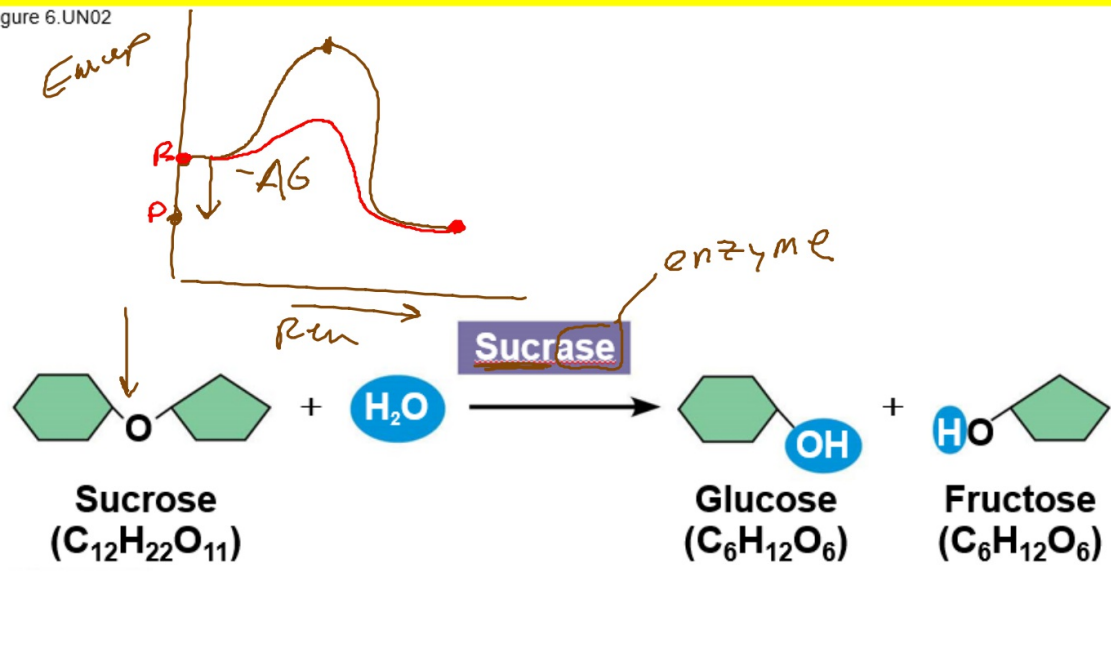


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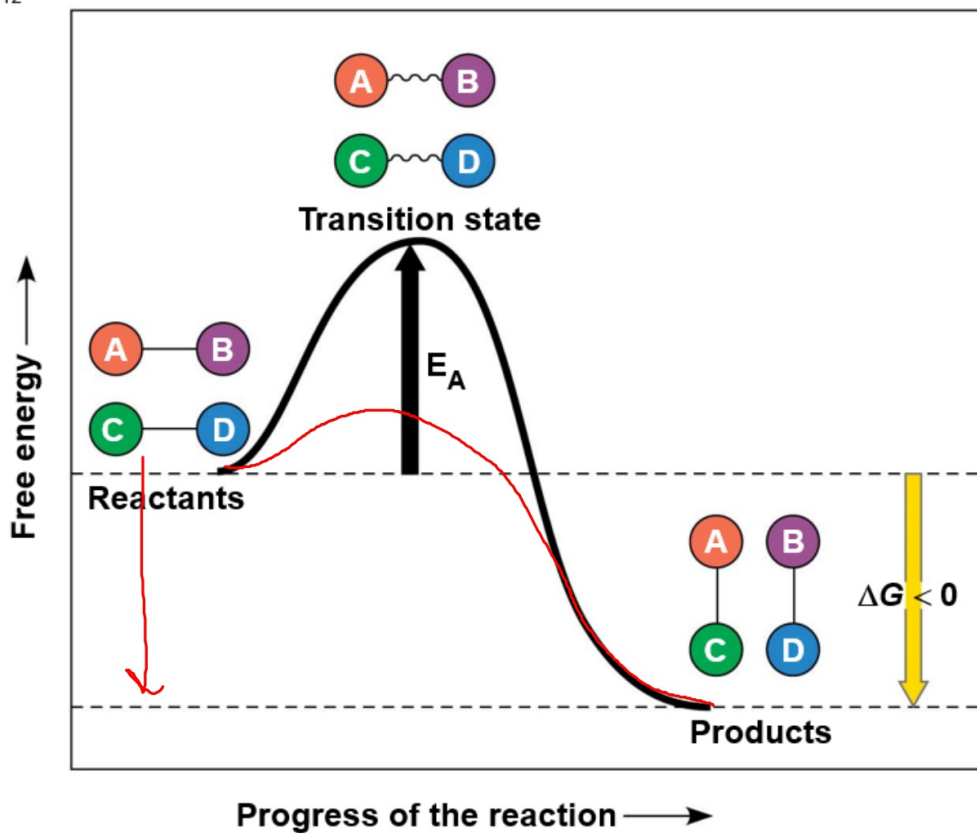


The Activation Energy Barrier

- 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

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Figure 6.12



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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

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Animation: How Enzymes Work

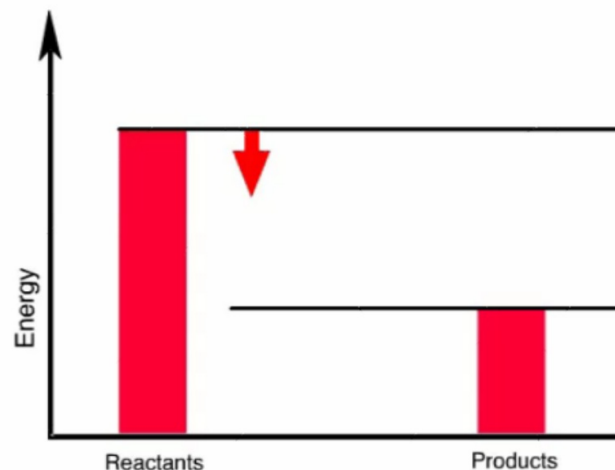
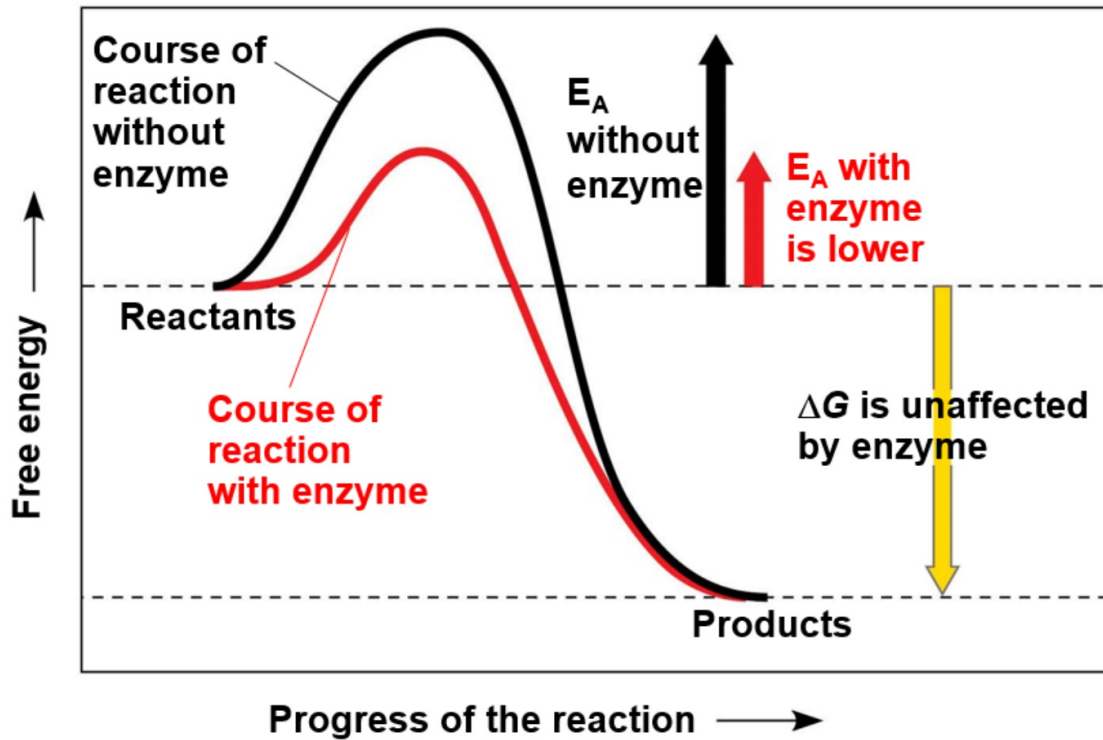


Figure 6.13



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** = reactants
- 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

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Video: Enzyme Induced Fit

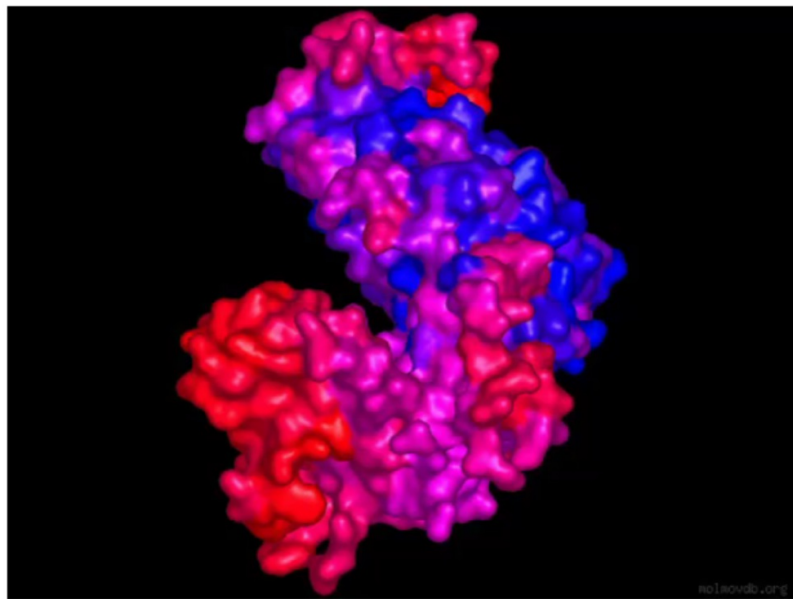
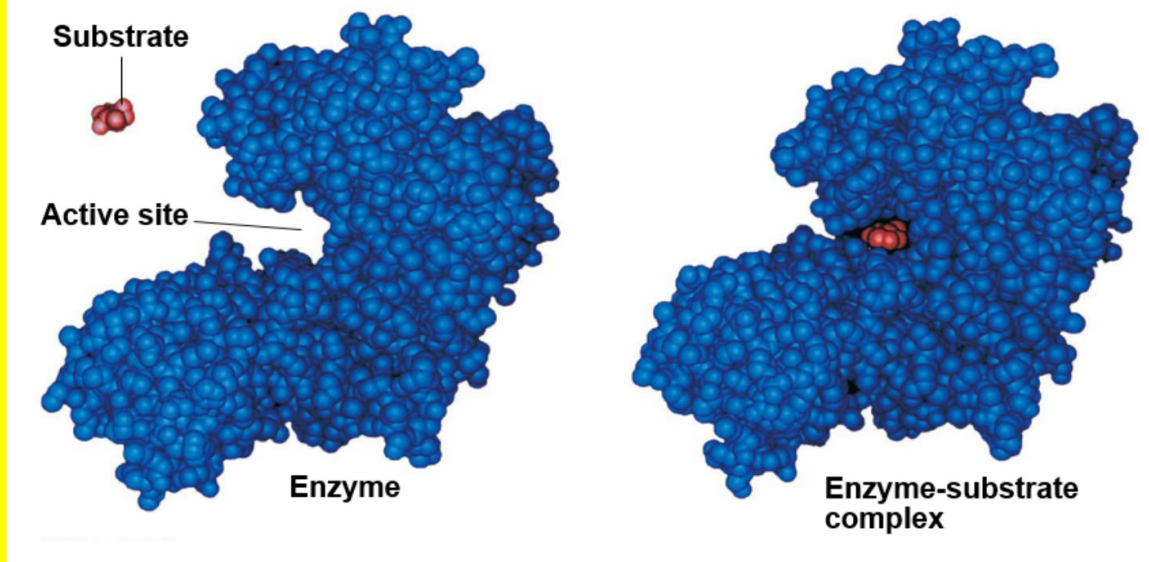


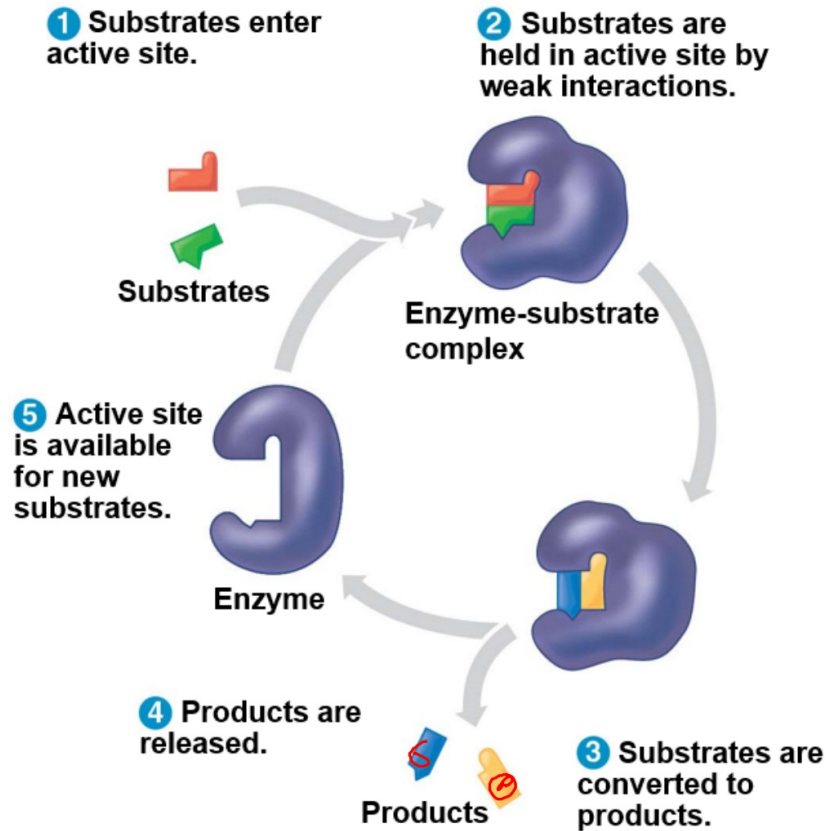
Figure 6.14



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-s4



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- 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

20 molecules \longleftrightarrow 2 enzymes \rightarrow 20012

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

Globular proteins

- Susceptible
→ to changes in pH & temp

7.4

Denaturing

2

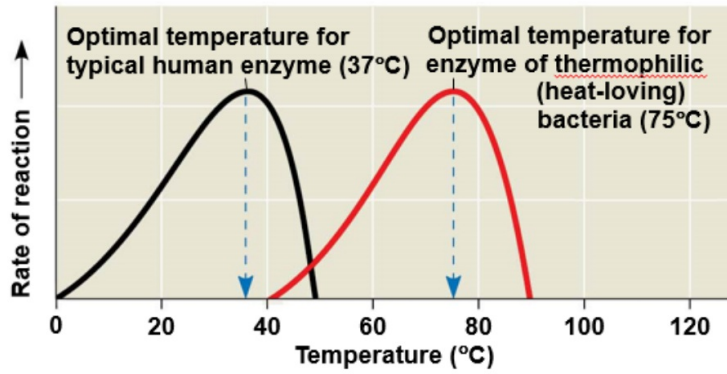
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Effects of Temperature and pH

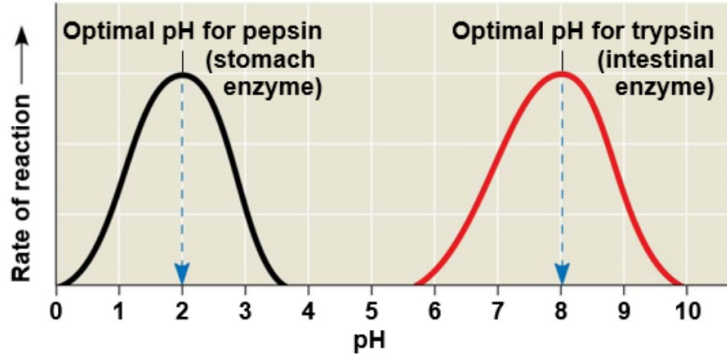
- Each enzyme has an optimal temperature and pH at which its reaction rate is the greatest

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Figure 6.16



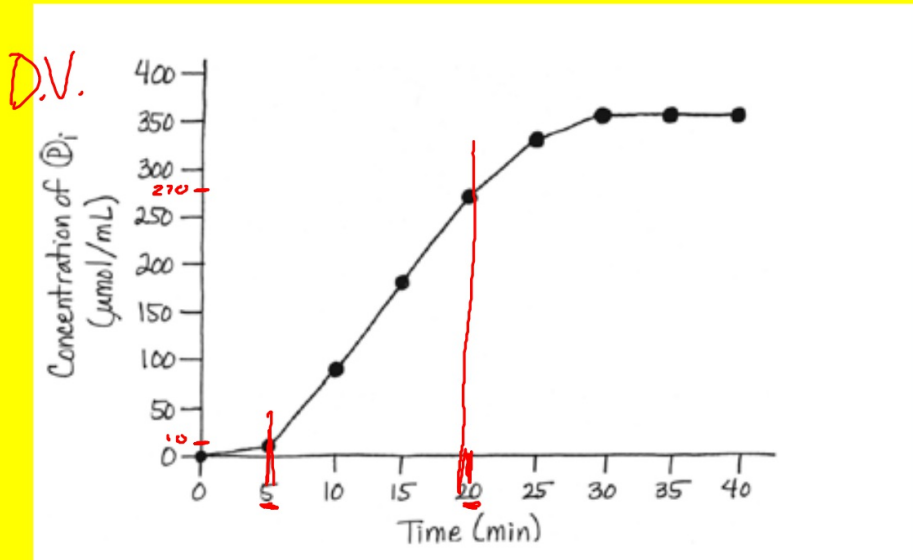
(a) Optimal temperature for two enzymes



(b) Optimal pH for two enzymes

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Science Skills Exercise ^{ASD}



$$\frac{260}{15} = 17.3 \mu\text{mol/mL} \cdot \text{min}$$

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

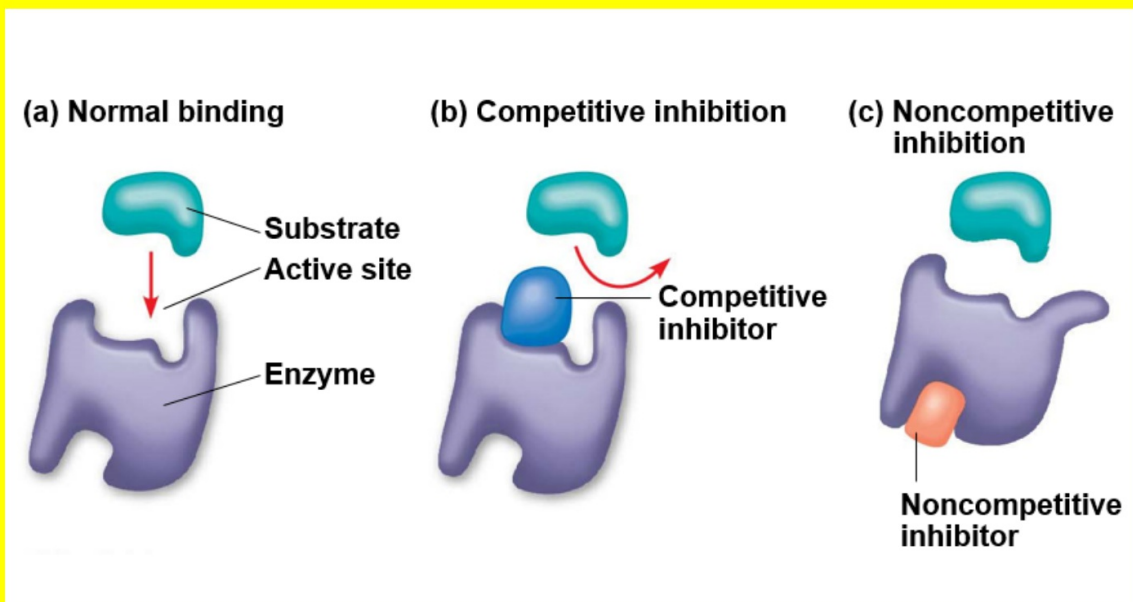
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Enzyme Inhibitors

- **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

penicillin

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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

SHAPE

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

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Allosteric Regulation of Enzymes

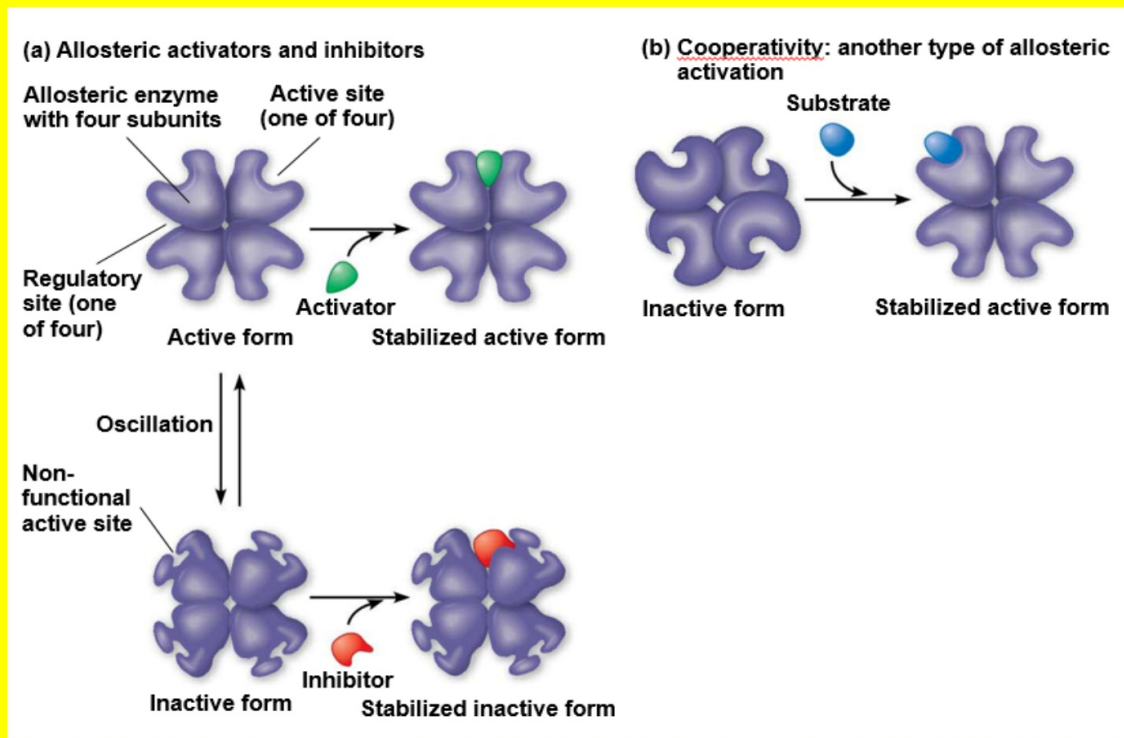
- **Allosteric regulation** may either inhibit or stimulate an enzyme's activity
- Allosteric regulation occurs when a regulatory molecule binds to a protein at one site and affects the protein's function at another site

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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

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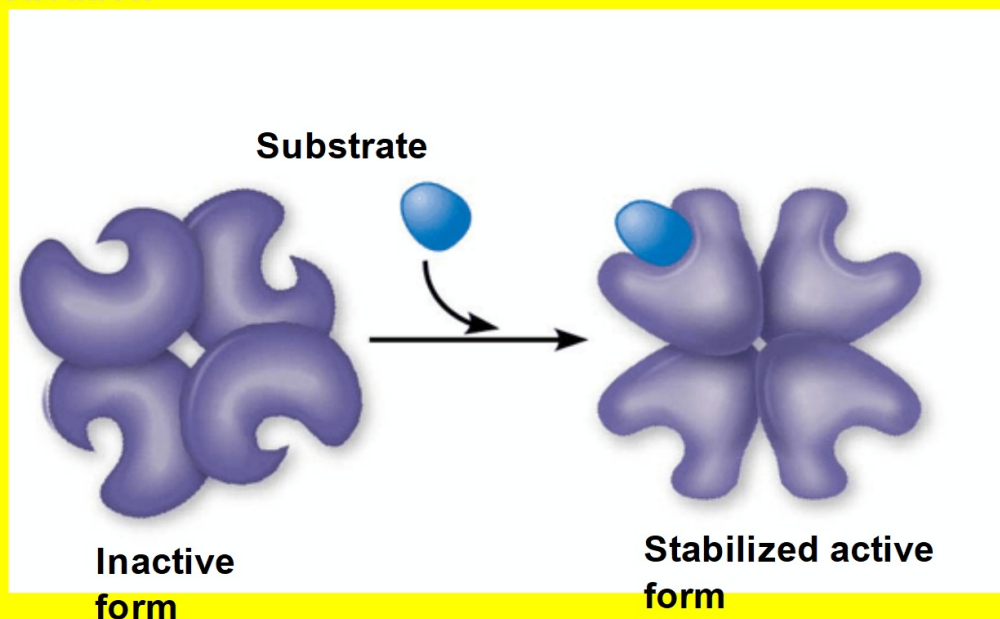


- **Cooperativity** is a form of allosteric regulation that can amplify enzyme activity
- One substrate molecule primes an enzyme to act on additional substrate molecules more readily
- Cooperativity is allosteric because binding by a substrate to one active site affects catalysis in a different active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

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Figure 6.18-2

(b) Cooperativity: another type of allosteric activation



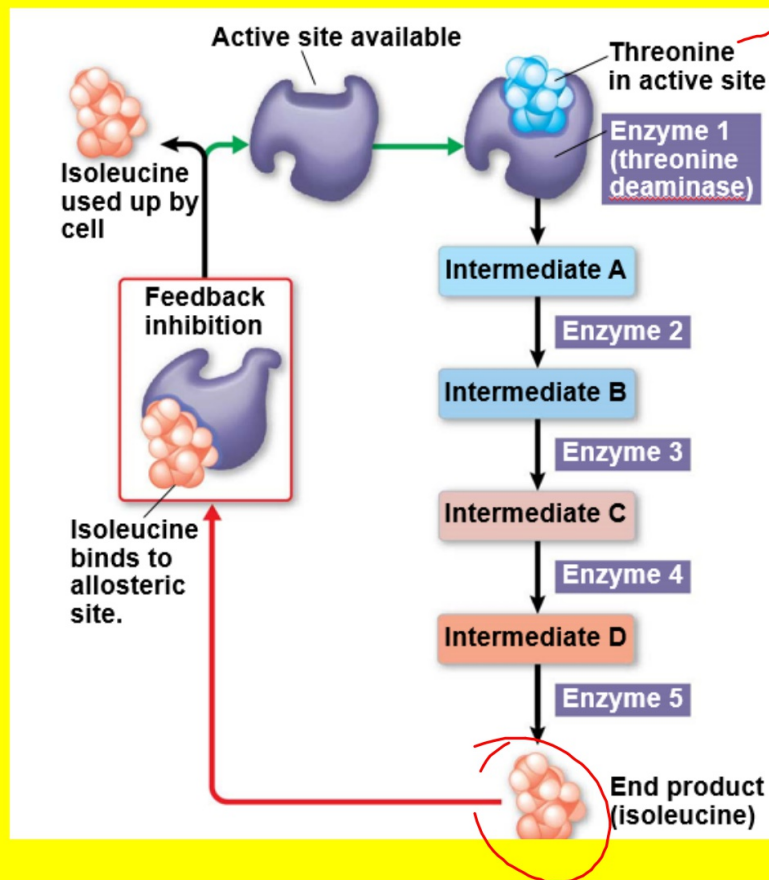
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Feedback Inhibition

- 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

Inhibitor to the original enzyme

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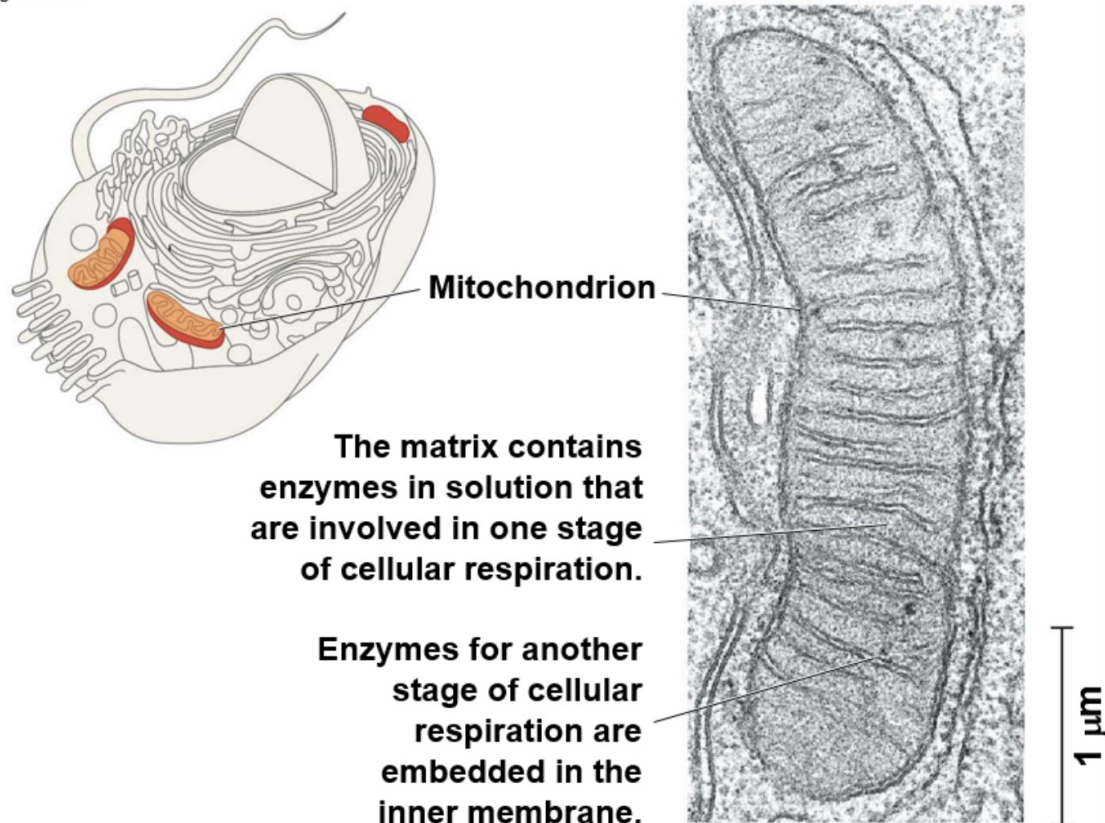
amino acids

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

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Figure 6.20



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