CHAPTER 5

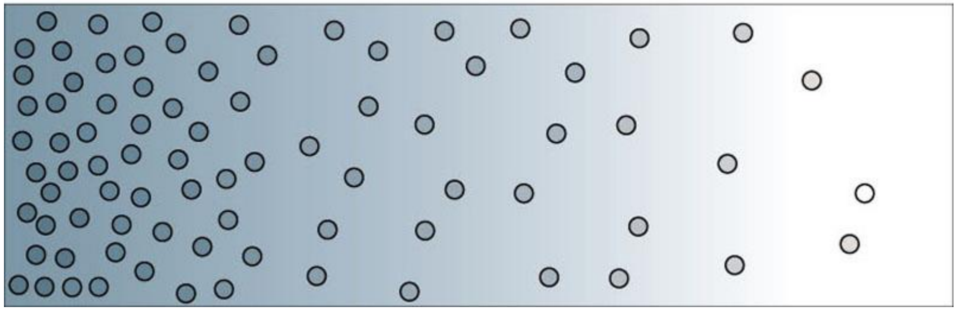
The Working Cell

Getting Through Membranes

- Diffusion
- Facilitated diffusion
- Osmosis
- Active transport
- Endocytosis
- Exocytosis

Diffusion

- Molecules are in constant, random motion.
- Molecules move from where they are most concentrated to where they are less concentrated.
  - This is called diffusion.
  - Involves a concentration gradient (diffusion gradient)
    - No concentration gradient=dynamic equilibrium



The Rate of Diffusion

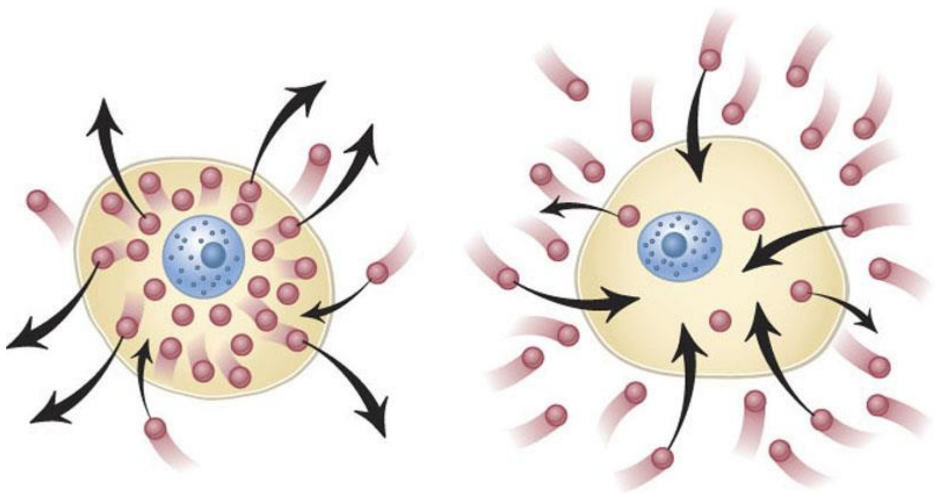
- Depends on
  - The size of the molecule
    - Smaller molecules diffuse faster.
  - The size of the concentration gradient
    - The greater the concentration difference, the faster the diffusion.

Diffusion in Cells

- Diffusion can only happen if there is no barrier to the movement of molecules.
- Can only happen across a membrane if the membrane is permeable to the molecule
  - Membranes are semi-permeable; they only allow certain molecules through.
  - Membrane permeability depends on the molecules size, charge, and solubility.

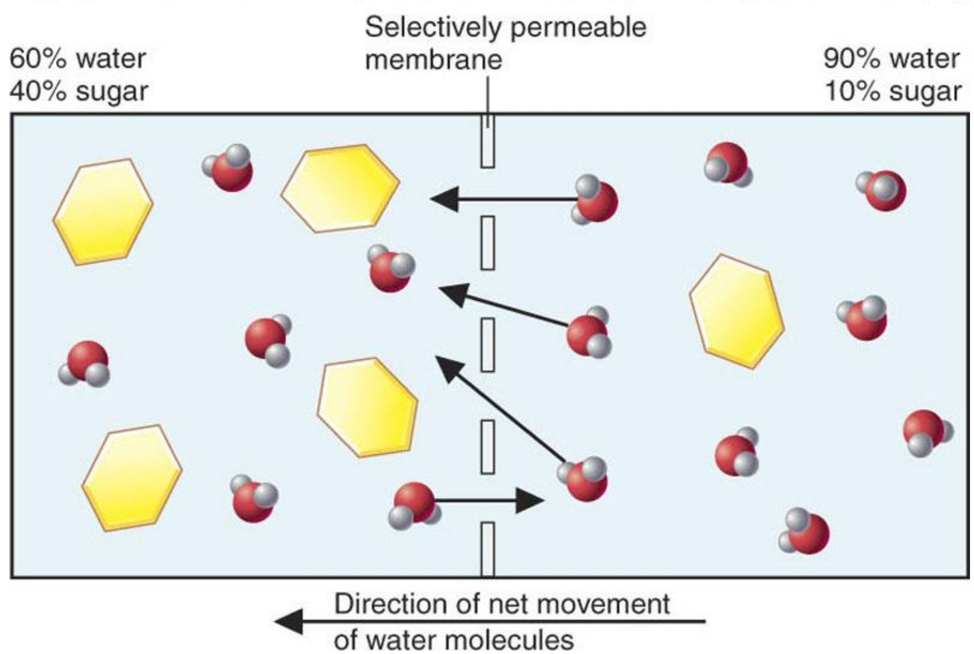
The Direction of Diffusion

- Determined solely by the concentration gradient
- Diffusion that does not require energy input is passive.
- Example:
  - Oxygen diffusion

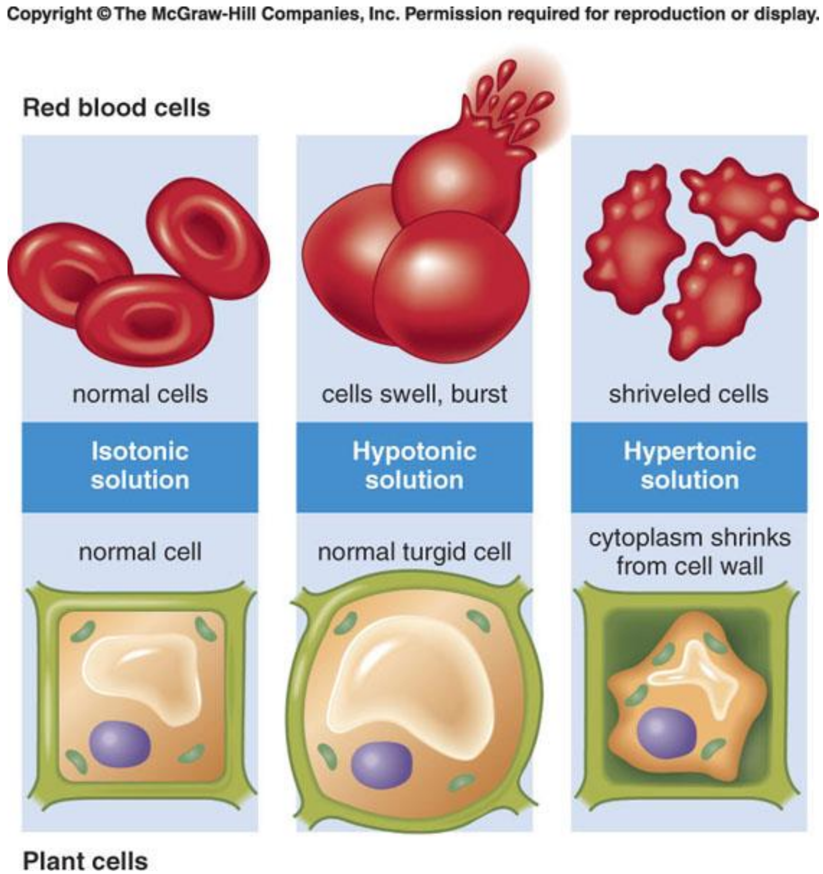


Osmosis

- The diffusion of water through a selectively-permeable membrane
- Occurs when there is a difference in water concentration on opposite sides of the membrane.
- Water will move to the side where there is less water
  - Or more solute



Osmotic Influences on Cells



Osmotic Influences on Cells

- If a cell has less water (more solute) than its environment
  - It is hypertonic to its surroundings.
- If a cell has more water (less solute) than its environment
  - It is hypotonic to its surroundings.
- If a cell has equal amounts of water (and solute) as its environment
  - It is isotonic to its surroundings.

Osmosis in Animal and Plant Cells

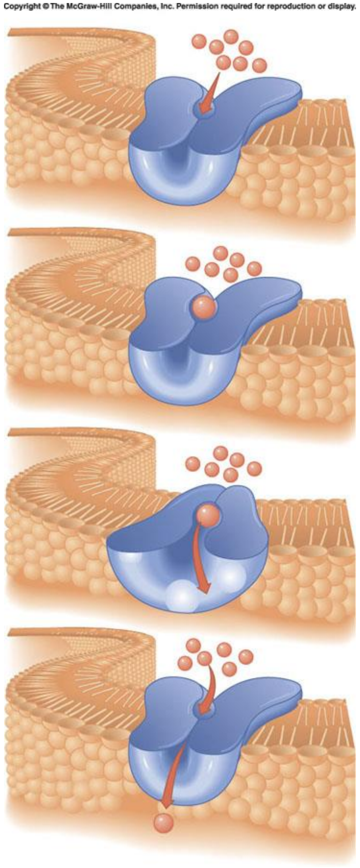
TABLE 4.1

Effects of Osmosis on Various Cell Types

Cell Type	What Happens When Cell Is Placed in Hypotonic Solution	What Happens When Cell Is Placed in Hypertonic Solution
With cell wall (e.g., bacteria, fungi, plants)	Water enters the cell, causing it to swell and generate pressure. However, the cell does not burst because the presence of an inelastic cell wall on the outside of the plasma membrane prevents the membrane from stretching and rupturing.	Water leaves the cell and the cell shrinks. The plasma membrane pulls away from inside the cell wall; the cell contents form a small mass.
Without cell wall (e.g., human red blood cells)	Water enters the cell and it swells, causing the plasma membrane to stretch and rupture.	Water leaves the cell and it shrinks into a compact mass.

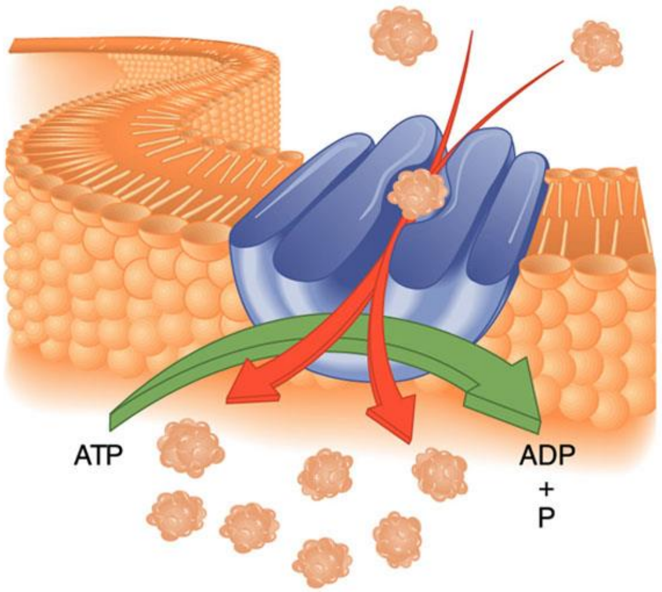
Facilitated Diffusion

- Some molecules have to be carried across the membrane.
  - Accomplished by carrier proteins
- Still involves diffusion
  - Follows a concentration gradient
  - Is passive transport



Active Transport

- Opposite of diffusion
- Moves molecules across a membrane UP their concentration gradient
- Uses transport proteins in the membrane
  - Specific proteins pump specific molecules
- Requires the input of energy



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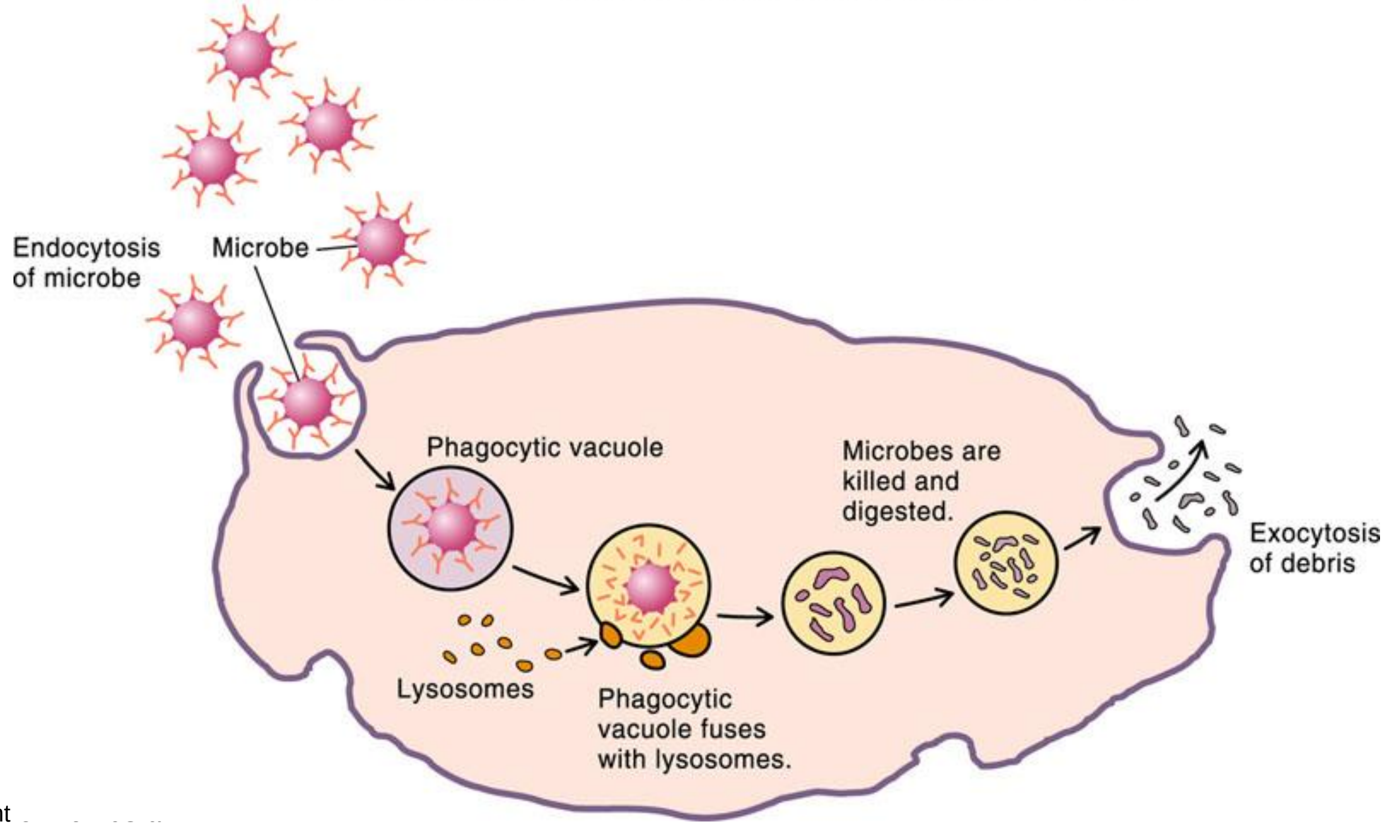
Endocytosis and Exocytosis

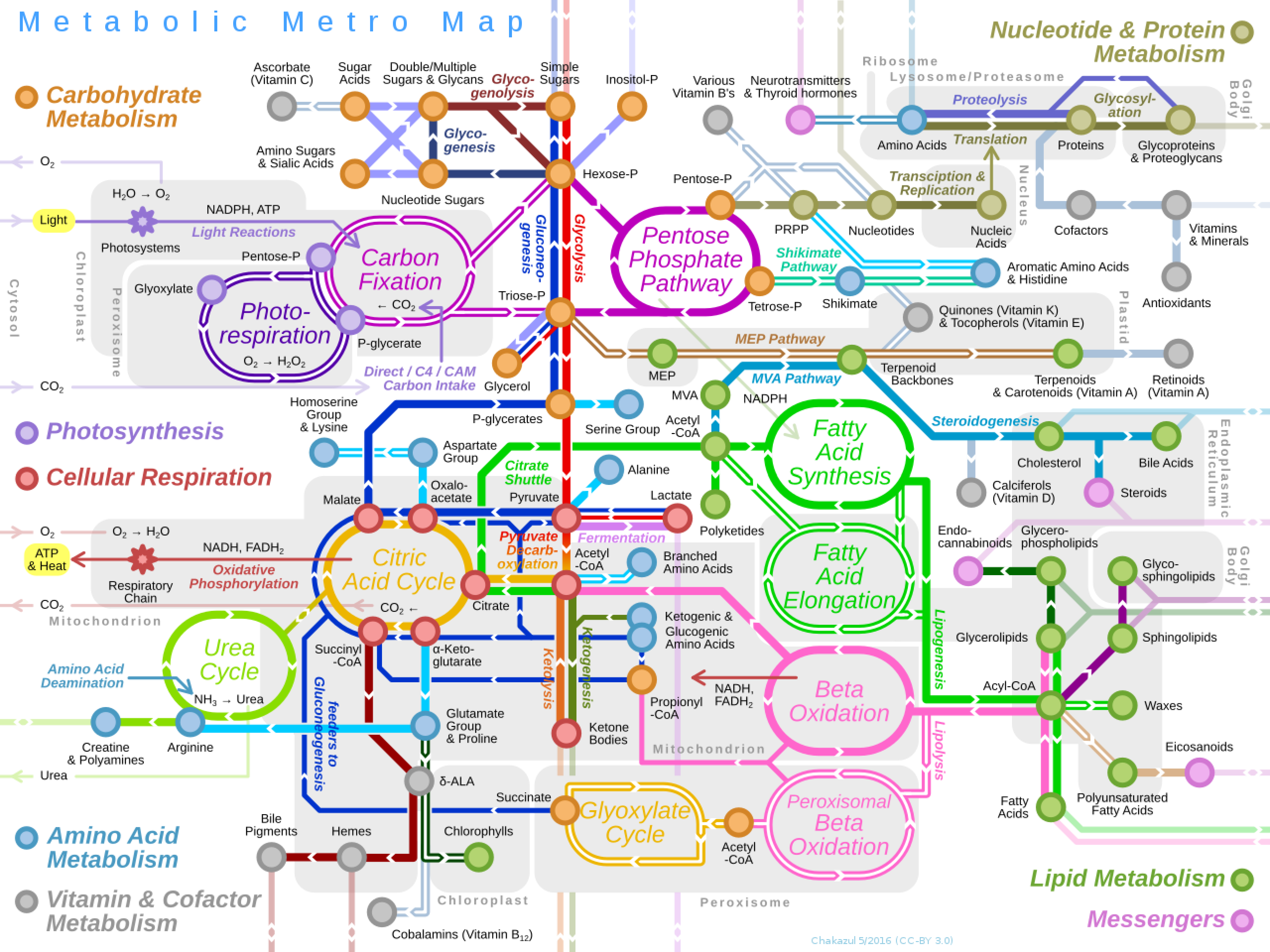


Endocytosis

- Moves large molecules or sets of molecules into the cell
  - Phagocytosis
    - Cell eating
    - Food engulfed by the membrane
    - Material enters the cell in a vacuole.
  - Pinocytosis
    - Cell drinking
    - Just brings fluid into the cell
  - Receptor-mediated endocytosis
    - Molecules entering the cell bind to receptor proteins first.

Exocytosis

- Moves large molecules or sets of molecules out of the cell
- Vesicles containing the molecules to be secreted fuse with the plasma membrane.
  - Contents are dumped outside the cell.



Metabolic Metro Map
Carbohydrate Metabolism
Photosynthesis
Cellular Respiration
Amino Acid Metabolism
Vitamin & Cofactor Metabolism
Nucleotide & Protein Metabolism
Lipid Metabolism
Messengers
Ascorbate (Vitamin C)
Sugar Acids
Double/Multiple Sugars & Glycans
Glycogenolysis
Simple Sugars
Inositol-P
Amino Sugars & Sialic Acids
Glycogenesis
Nucleotide Sugars
Hexose-P
Gluconeogenesis
Glycolysis
O_2
$H_2O \rightarrow O_2$
Light
NADPH, ATP
Photosystems
Light Reactions
Chloroplast
Peroxisome
Cytosol
Pentose-P
Glyoxylate
Carbon Fixation
$\leftarrow CO_2$
Photorespiration
$O_2 \rightarrow H_2O_2$
P-glycerate
Triose-P
Glycerol
CO_2
Direct / C4 / CAM Carbon Intake
Various Vitamin B's
Neurotransmitters & Thyroid hormones
Ribosome
Lysosome/Proteasome
Proteolysis
Glycosylation
Golgi Body
Amino Acids
Translation
Proteins
Glycoproteins & Proteoglycans
Transcription & Replication
Nucleus
Pentose-P
PRPP
Nucleotides
Nucleic Acids
Cofactors
Vitamins & Minerals
Antioxidants
Pentose Phosphate Pathway
Shikimate Pathway
Aromatic Amino Acids & Histidine
Tetrose-P
Shikimate
Quinones (Vitamin K) & Tocopherols (Vitamin E)
Plastid
MEP Pathway
MEP
Terpenoid Backbones
Terpenoids & Carotenoids (Vitamin A)
Retinoids (Vitamin A)
MVA
MVA Pathway
NADPH
Homoserine Group & Lysine
P-glycerates
Serine Group
Acetyl-CoA
Fatty Acid Synthesis
Steroidogenesis
Cholesterol
Bile Acids
Endoplasmic Reticulum
Calciferols (Vitamin D)
Steroids
Aspartate Group
Citrate Shuttle
Alanine
Oxaloacetate
Pyruvate
Lactate
Malate
Polyketides
Fatty Acid Elongation
Endocannabinoids
Glycerophospholipids
Glycosphingolipids
Golgi Body
O_2
$O_2 \rightarrow H_2O$
ATP & Heat
NADH, $FADH_2$
Respiratory Chain
Oxidative Phosphorylation
Citric Acid Cycle
Pyruvate Decarboxylation
Fermentation
Acetyl-CoA
Branched Amino Acids
CO_2
$CO_2 \leftarrow$
Citrate
Mitochondrion
Ketogenic & Glucogenic Amino Acids
Glycerolipids
Sphingolipids
Lipogenesis
Urea Cycle
Amino Acid Deamination
$NH_3 \rightarrow$ Urea
Succinyl-CoA
α-Ketoglutarate
Ketolysis
Ketogenesis
Propionyl-CoA
NADH, $FADH_2$
Beta Oxidation
Acyl-CoA
Waxes
Creatine & Polyamines
Arginine
feeders to Gluconeogenesis
Glutamate Group & Proline
Ketone Bodies
Mitochondrion
Lipolysis
Eicosanoids
Urea
δ-ALA
Succinate
Glyoxylate Cycle
Acetyl-CoA
Peroxisomal Beta Oxidation
Fatty Acids
Polyunsaturated Fatty Acids
Bile Pigments
Hemes
Chlorophylls
Chloroplast
Peroxisome
Cobalamins (Vitamin B_{12})
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The Instantaneous Reaction Rate

- Consider the following reaction

$$A + B \rightarrow C$$

- Define the instantaneous rate of consumption of reactant A, ν_A

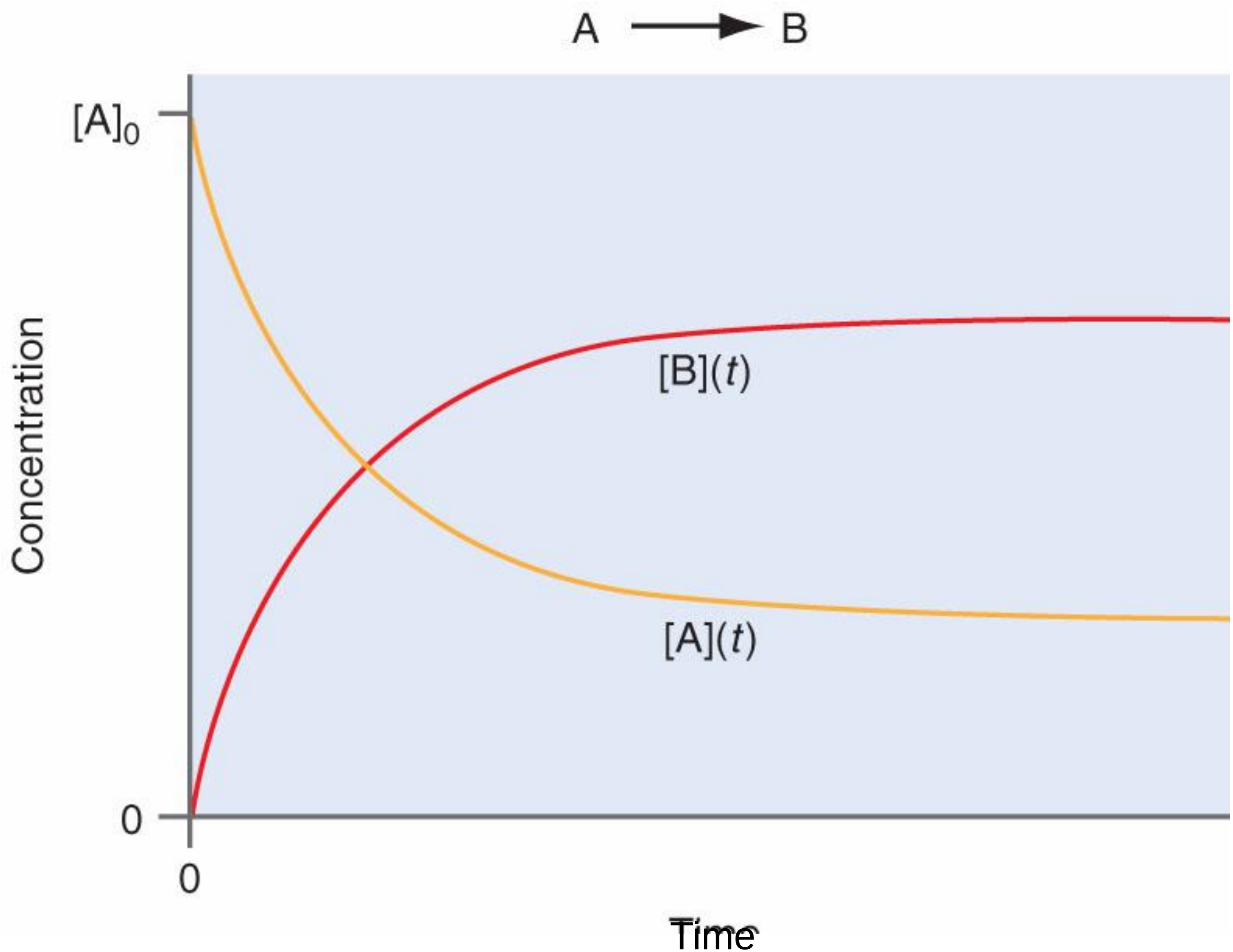
$$\nu_A = -\frac{d[A]}{dt}$$

Reaction Rates and Reaction Stoichiometry

- Look at the reaction

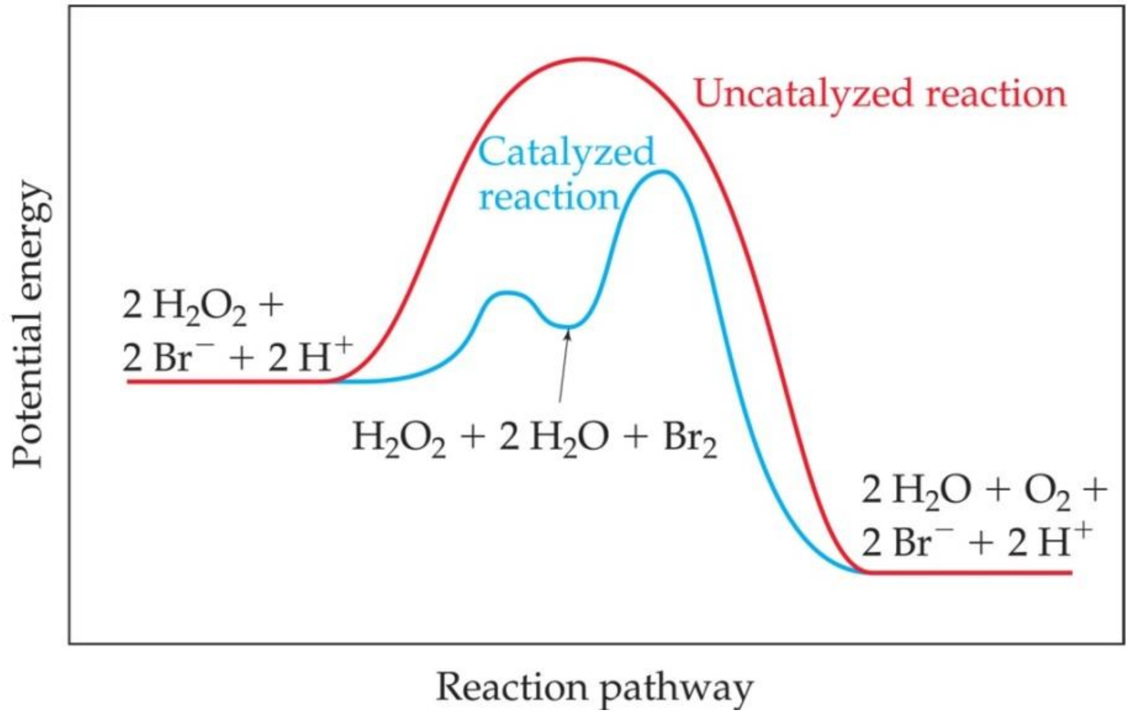
$$O_3(g) + NO(g) \rightarrow NO_2(g) + O_2(g)$$

$$\boxed{rate = -\frac{d[O_3]}{dt} = -\frac{d[NO]}{dt} = +\frac{d[NO_2]}{dt} = +\frac{d[O_2]}{dt}}$$


A → B
[A]0
0
0
Concentration
Time
[B](t)
[A](t)

Catalysts

- Catalysts increase the rate of a reaction by decreasing the activation energy of the reaction.
- Catalysts change the mechanism by which the process occurs.



Enzyme Catalysis

- Consider the reaction

$$H_2O_2 \longrightarrow H_2O + O_2$$

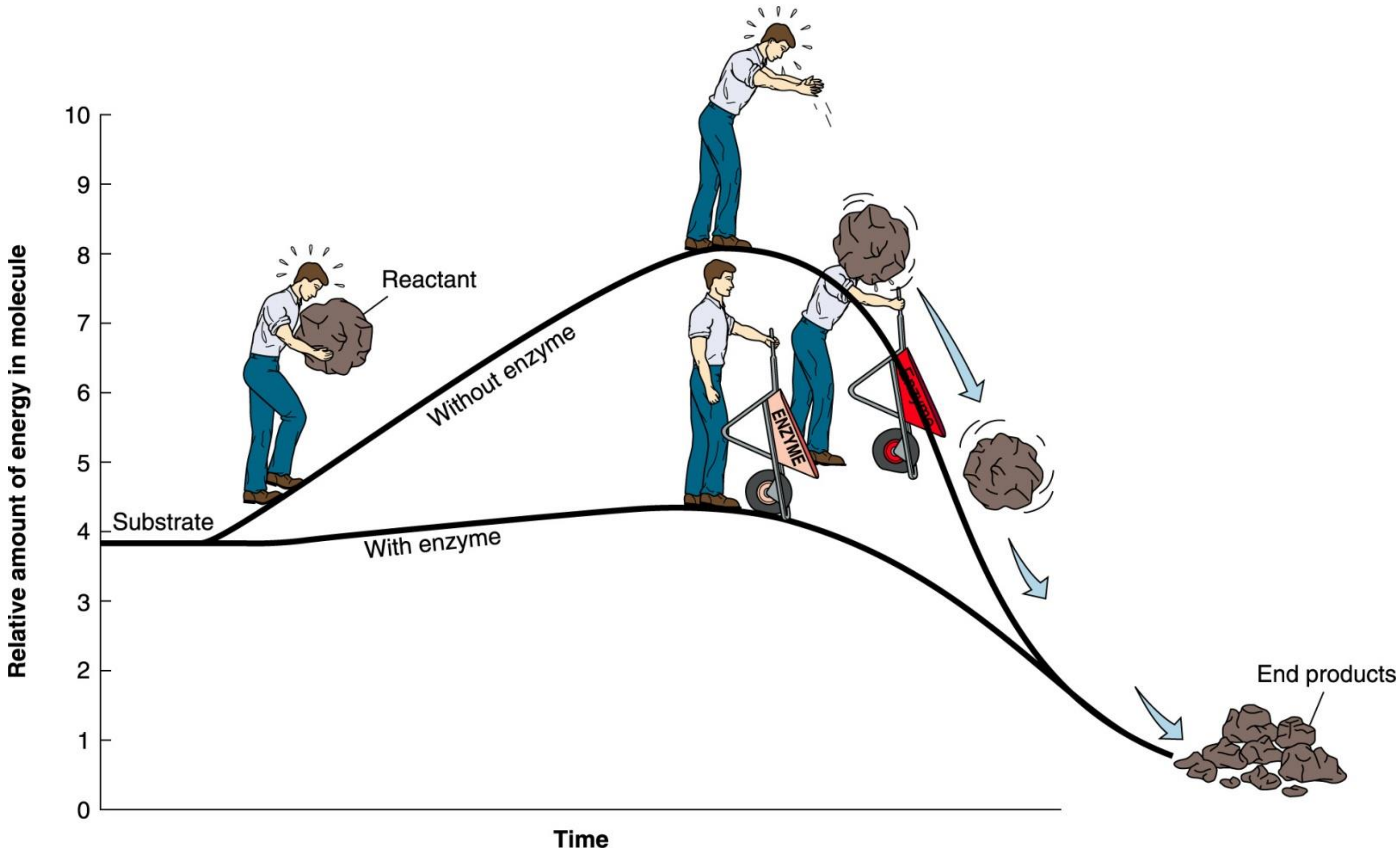
Table 6.1

Lowering of the Activation Energy of Hydrogen Peroxide Decomposition by Catalysts

Reaction Conditions	Activation Free Energy kJmol^{-1}	Activation Free Energy kcal mol^{-1}	Relative Rate
No catalyst	75.2	18.0	1
Platinum surface	48.9	11.7	2.77×10^4
Catalase	23.0	5.5	6.51×10^8

Rates are given in arbitrary units relative to a value of 1 for the uncatalyzed reaction at 37°C.

Lowering Activation Energy



Binding of a substrate to an enzyme at the active site

Chymotrypsin with bound substrate in red.

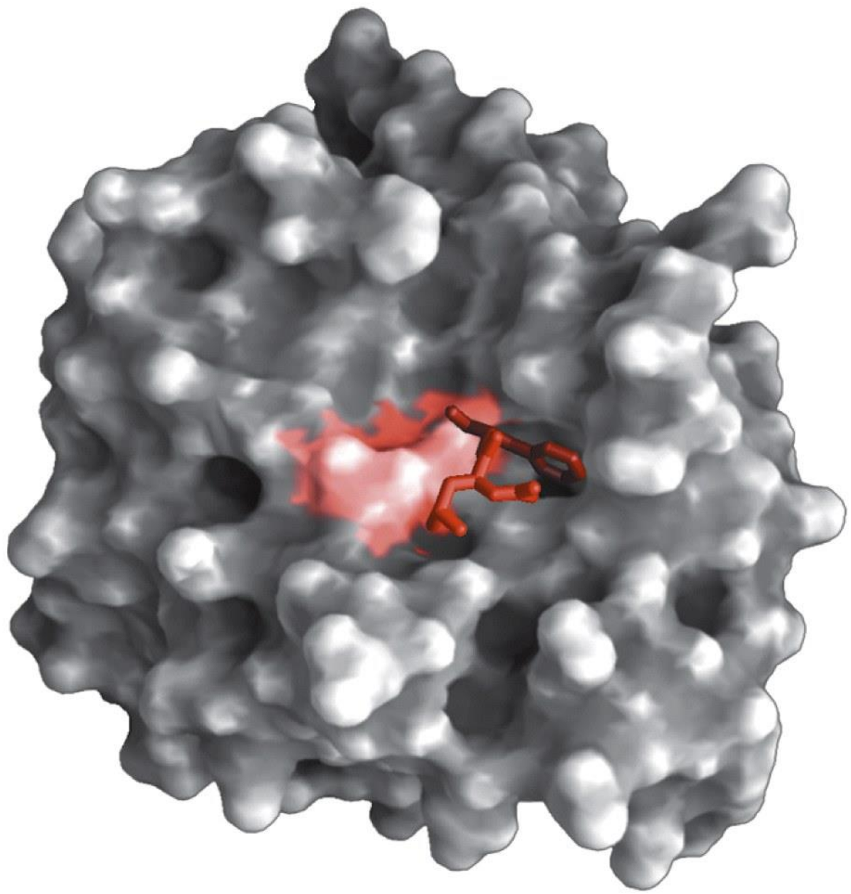
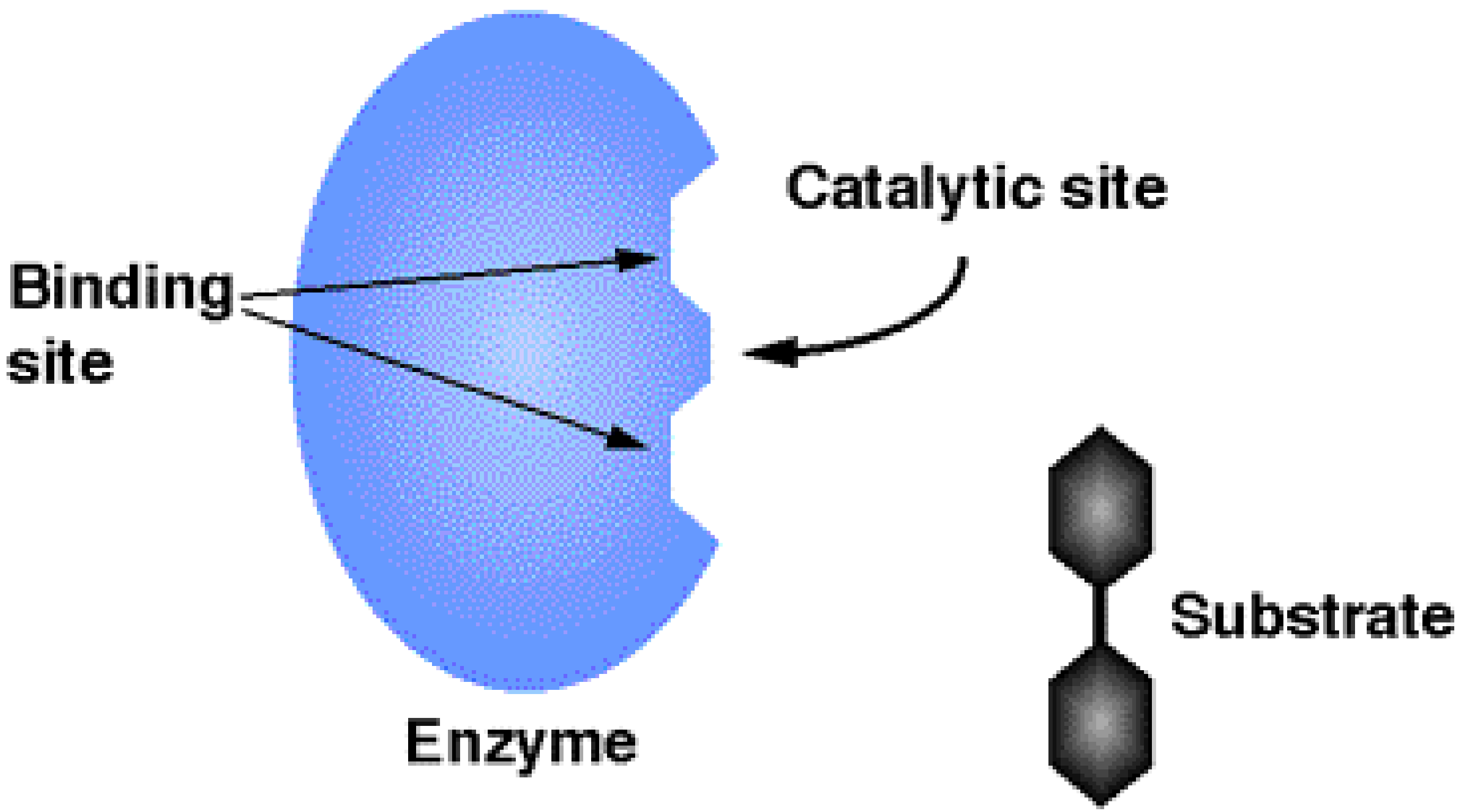
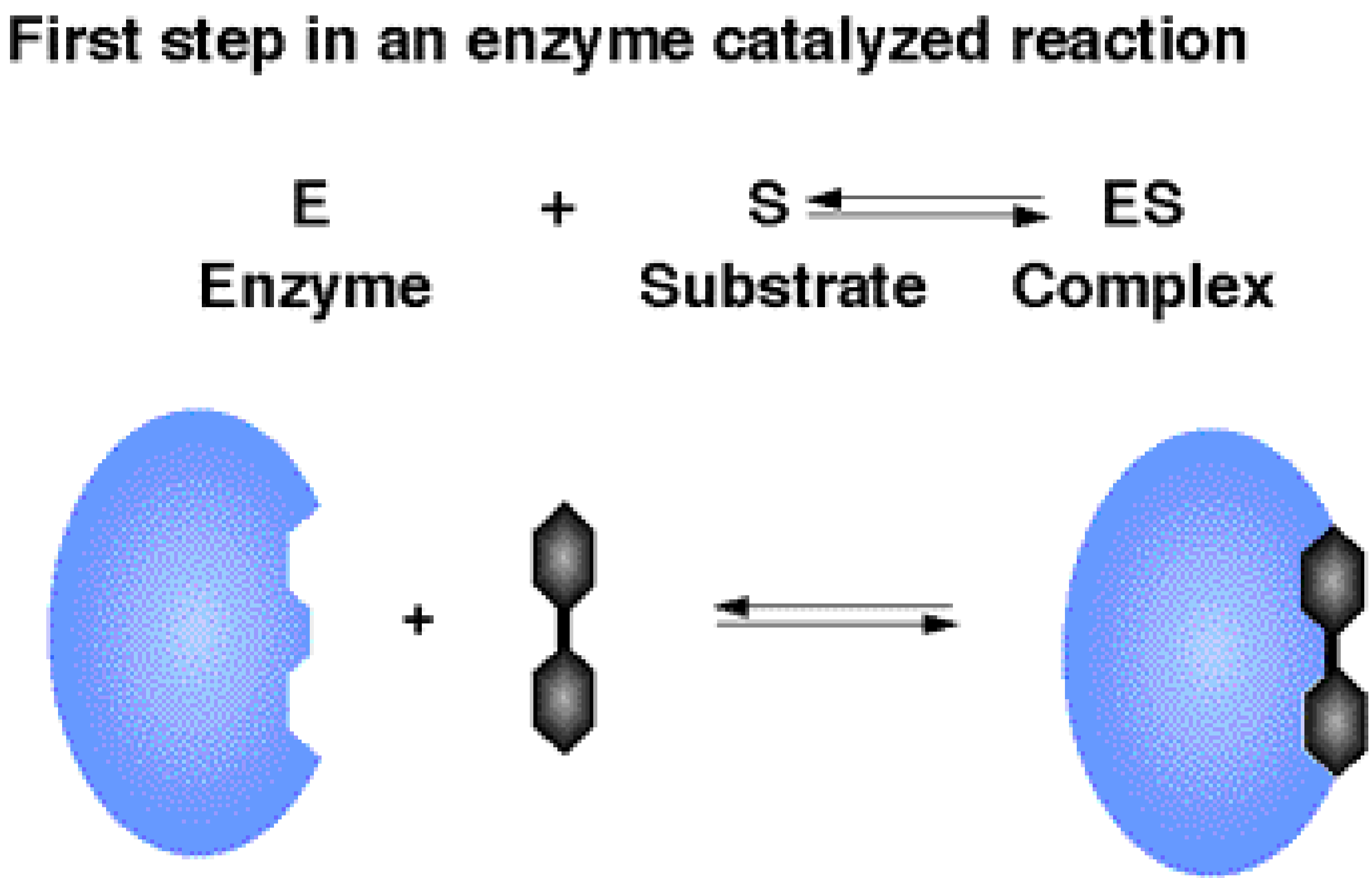


Figure 6-1
Lehninger Principles of Biochemistry, Fifth Edition

The Players

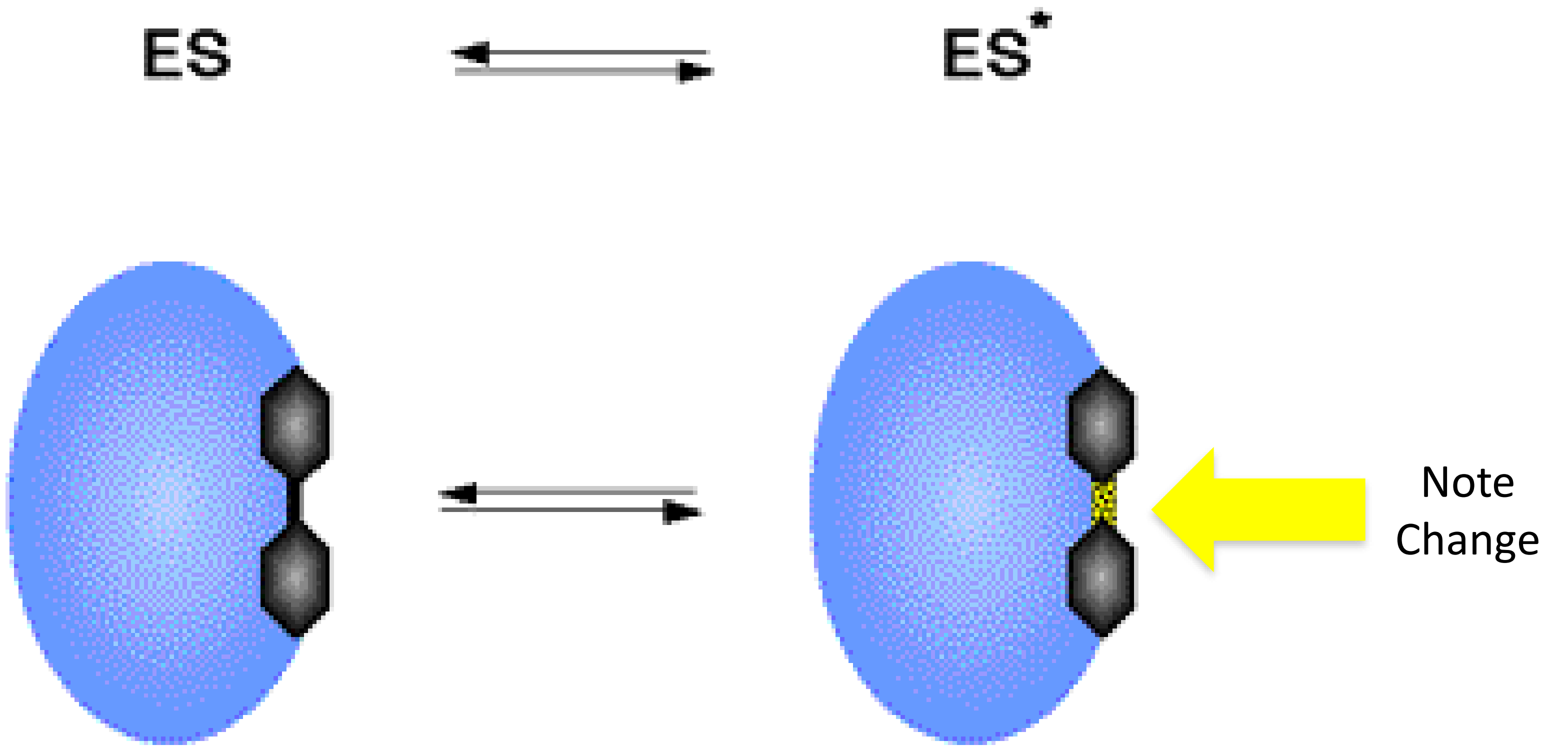


Formation of Enzyme-Substrate Complex

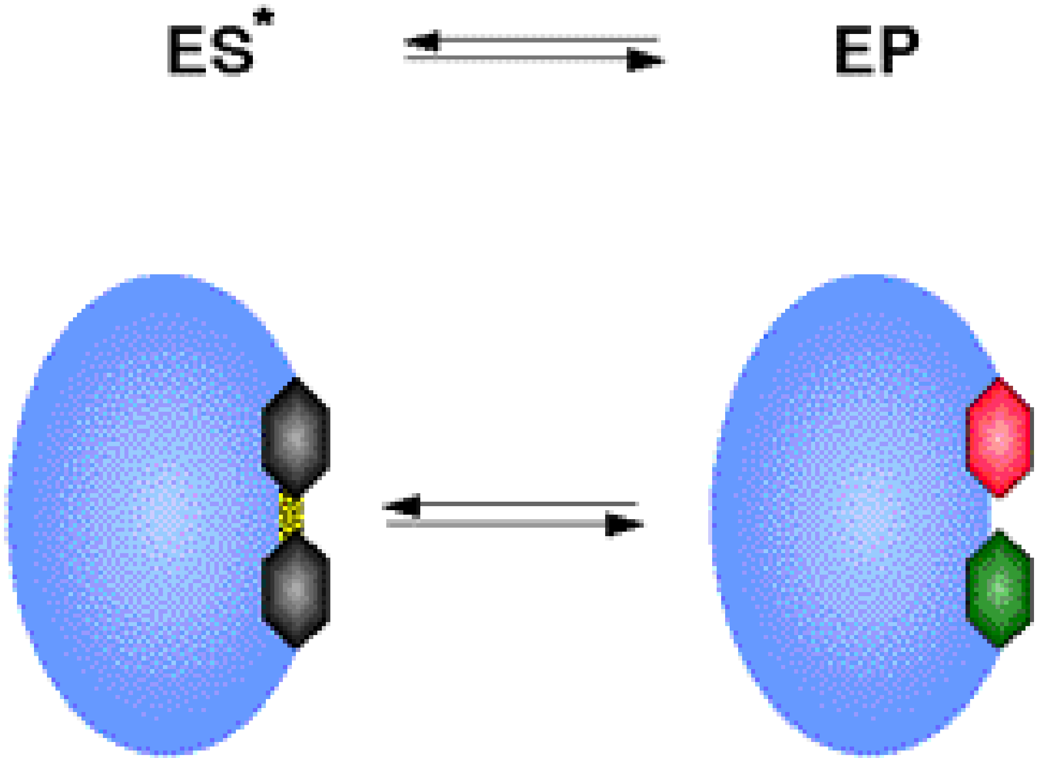


Formation of Transition State Intermediate

An intermediate species is then formed.



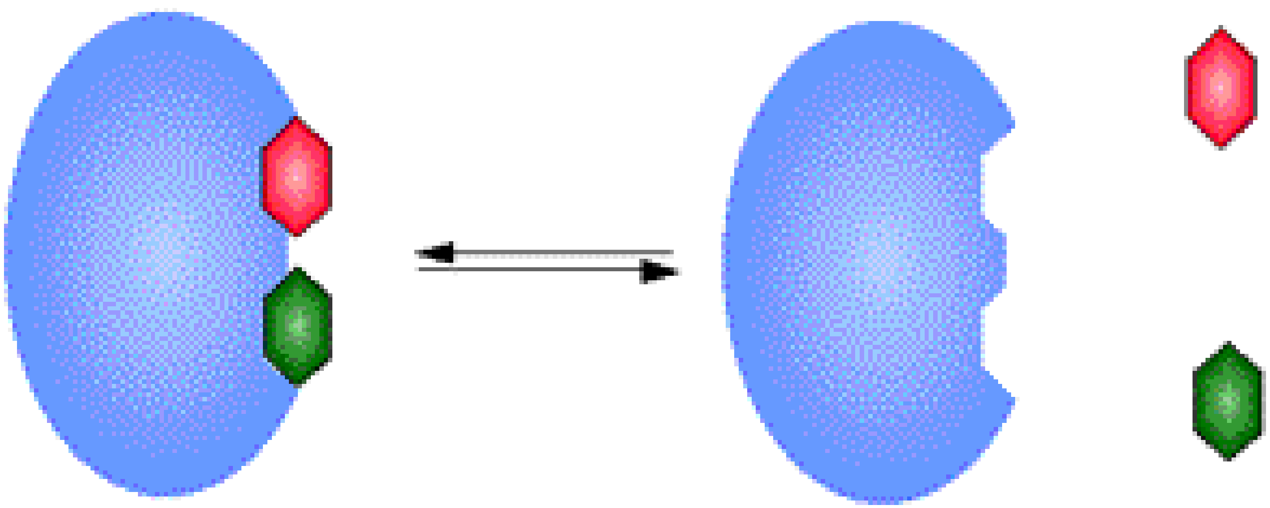
Enzyme-Product Complex is Formed



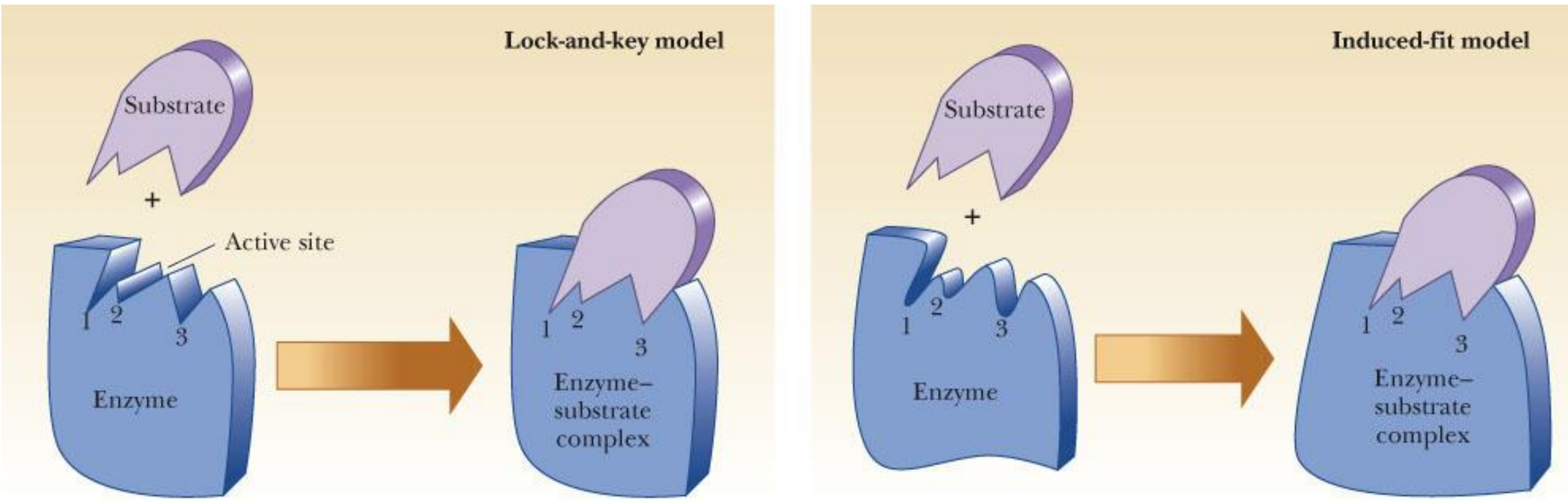
Product Released

The product is finally made and the enzyme is ready for another substrate.

$$EP \rightleftharpoons E + P$$

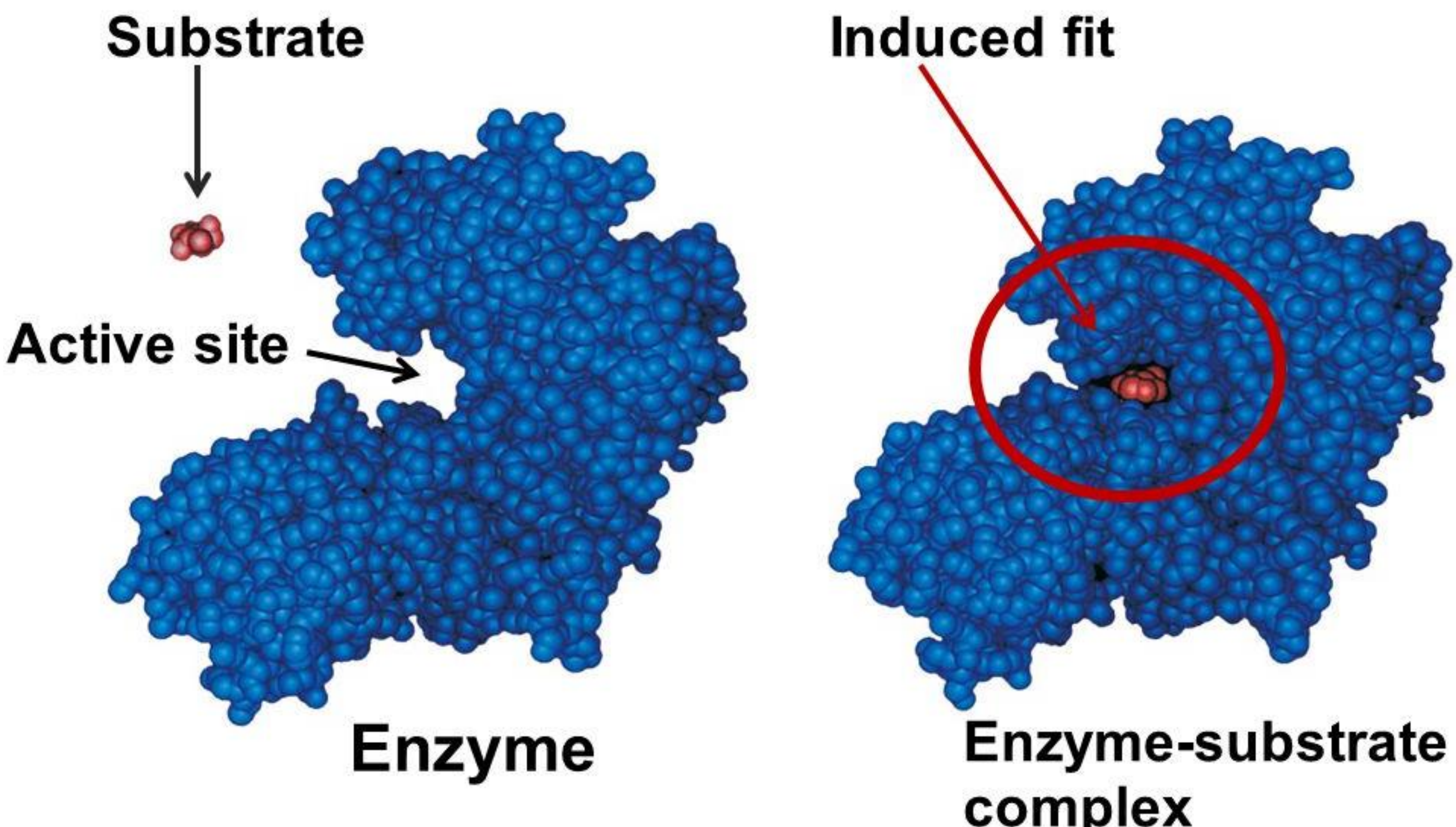


2 Modes of E-S Complex Formation

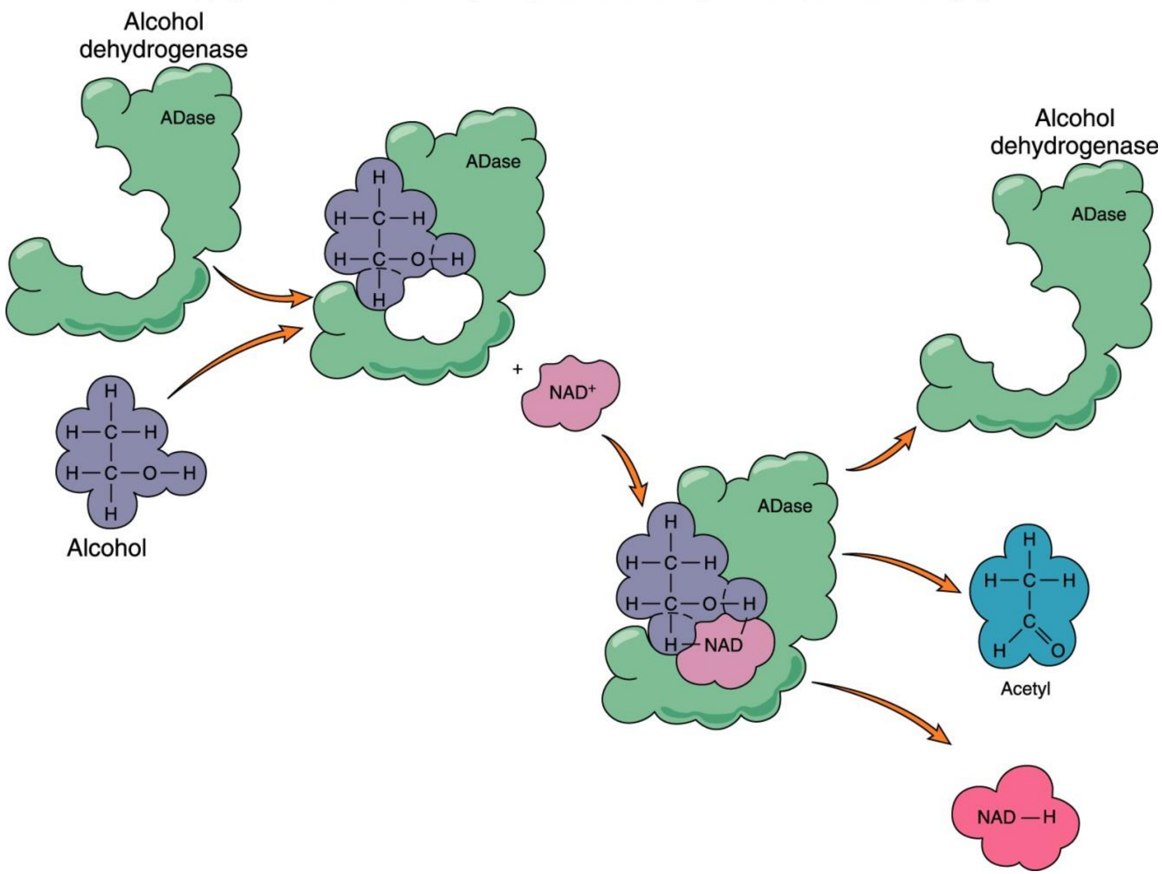


A In the lock-and-key model, the shape of the substrate and the confirmation of the active site are complementary to one another.

B In the induced-fit model, the enzyme undergoes a conformational change upon binding to substrate. The shape of the active site becomes complementary to the shape of the substrate only after the substrate binds to the enzyme.


Substrate
Active site
Enzyme
Induced fit
Enzyme-substrate complex

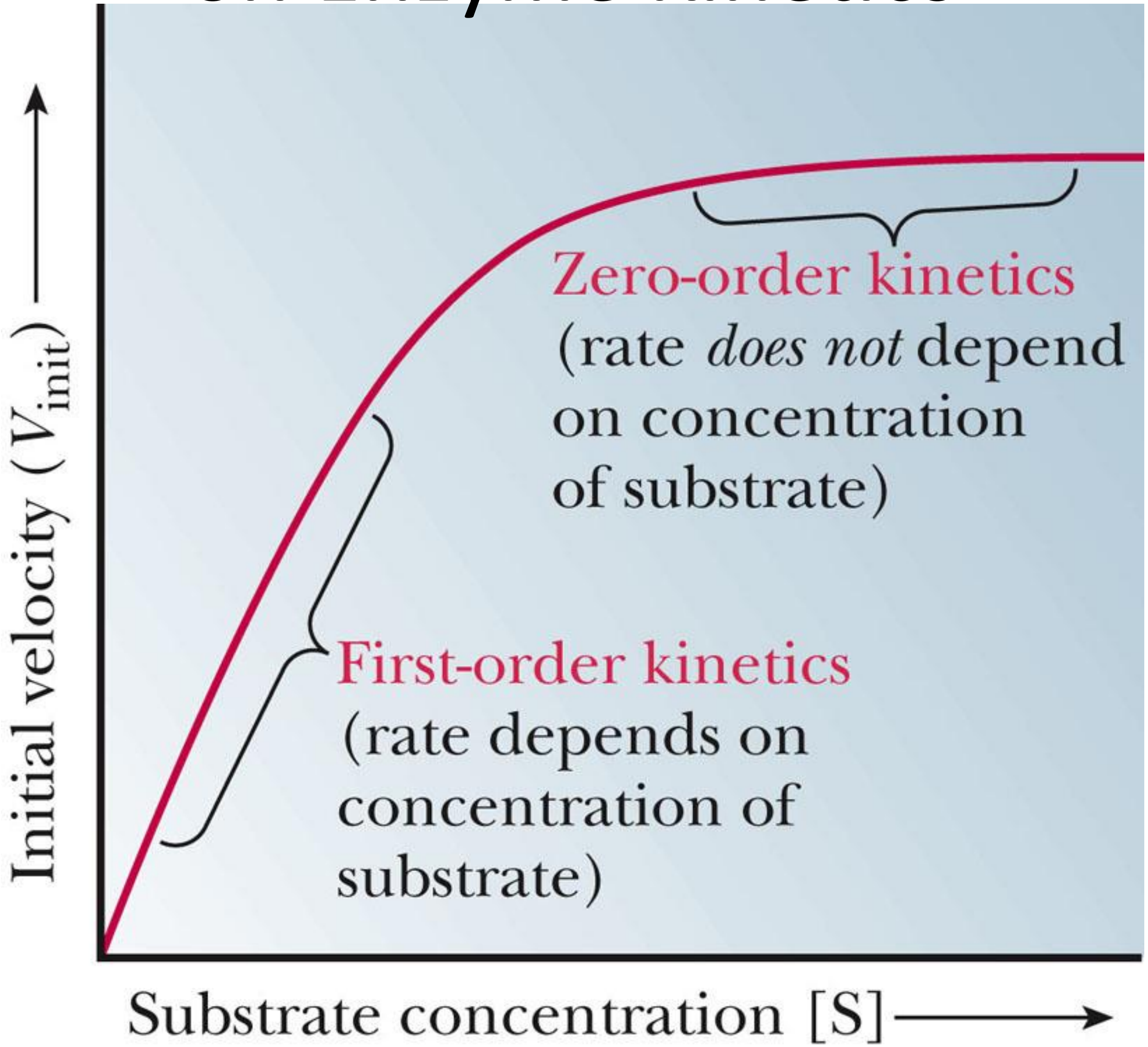
The Role of Coenzymes



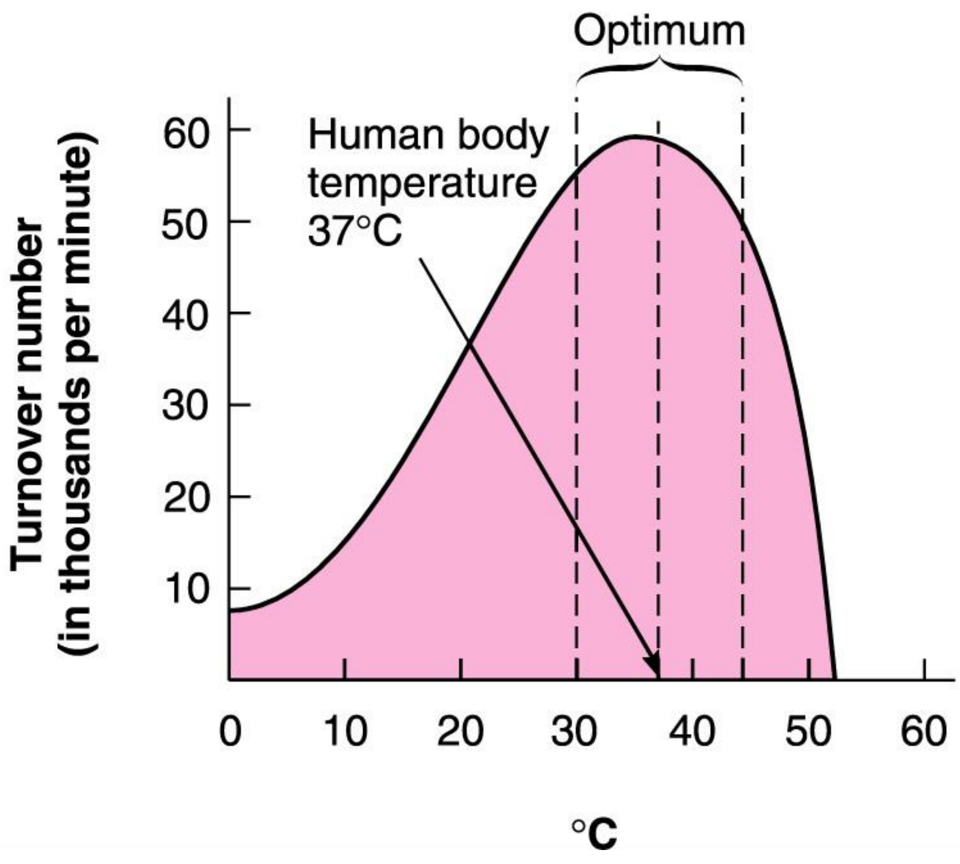
How Enzymes are Usually Named

- Since each enzyme catalyzes a specific reaction
  - Each has a unique name
- The first part of an enzyme's name
  - Is the name of the substrate
- The second part of an enzyme's name
  - Indicates the type of reaction it will catalyze
- All enzyme names end in the suffix
  - -ase
- Examples:
  - DNA polymerase
  - Glycogen synthetase

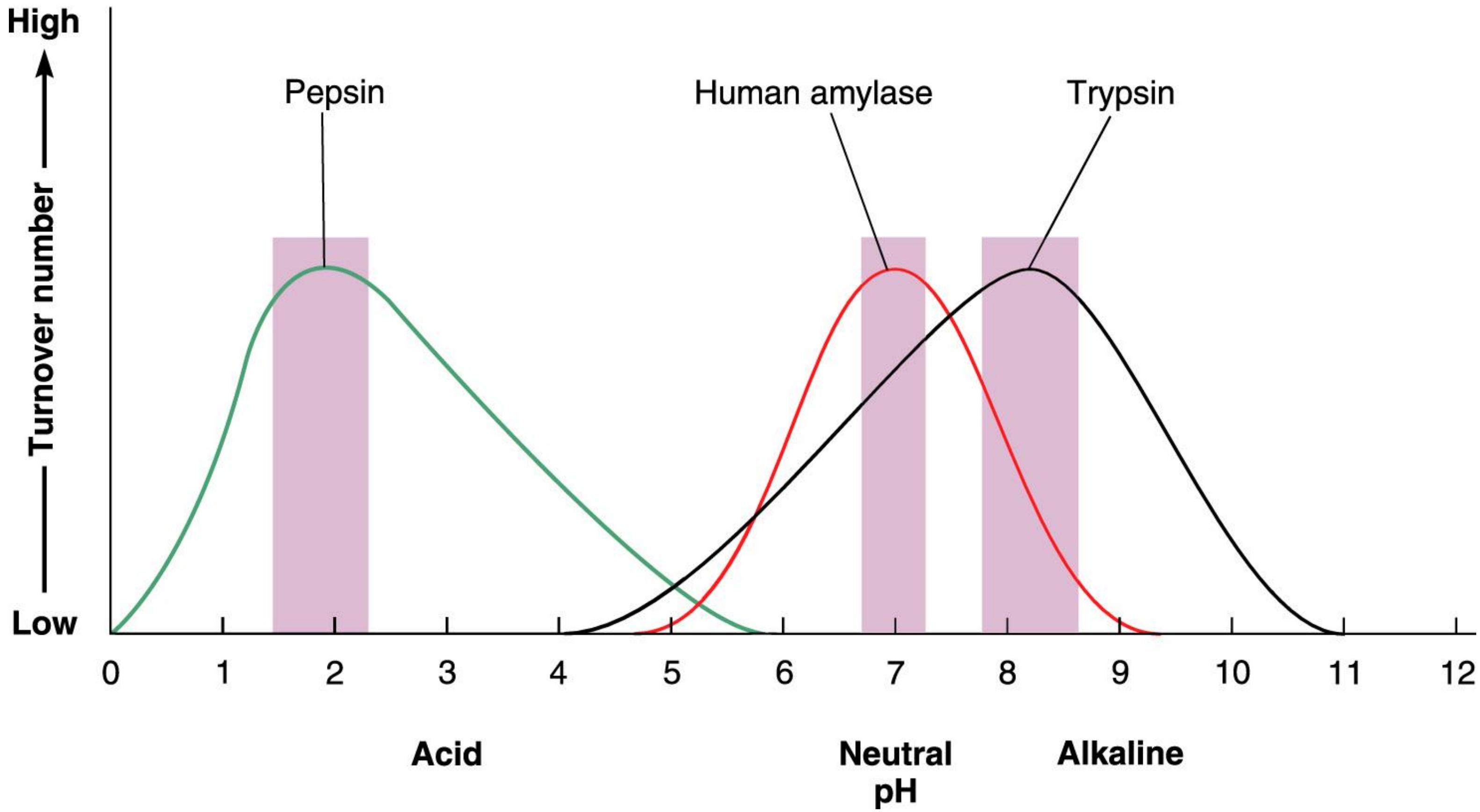
The Effect of Substrate Concentration on Enzyme Kinetics



The Effect of Temperature on Turnover Number

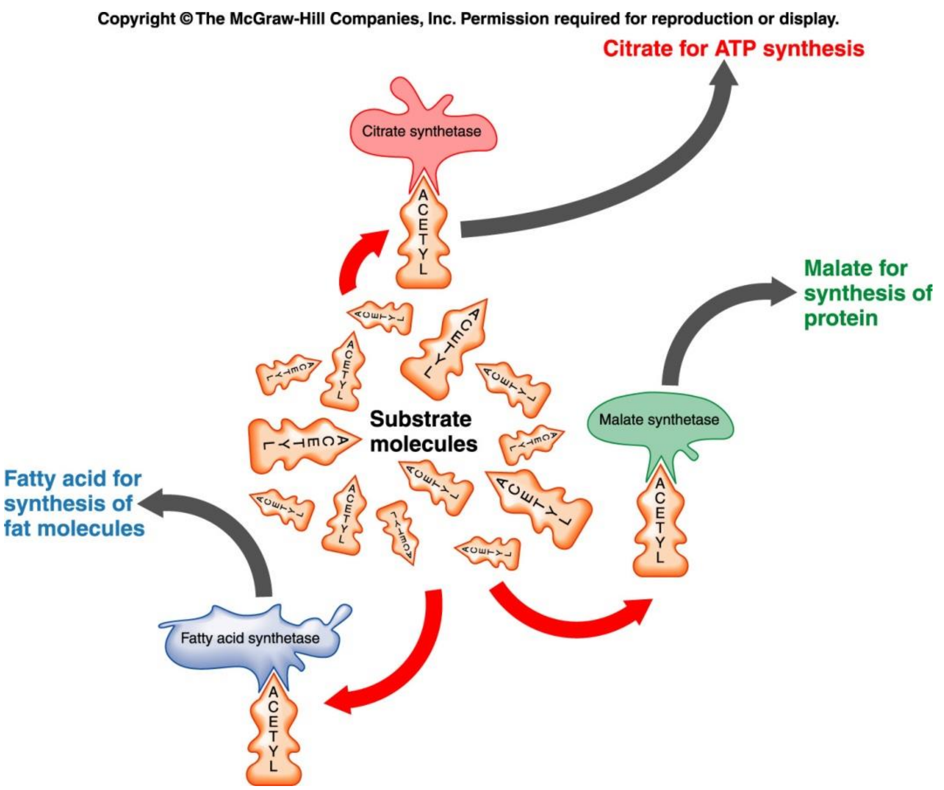


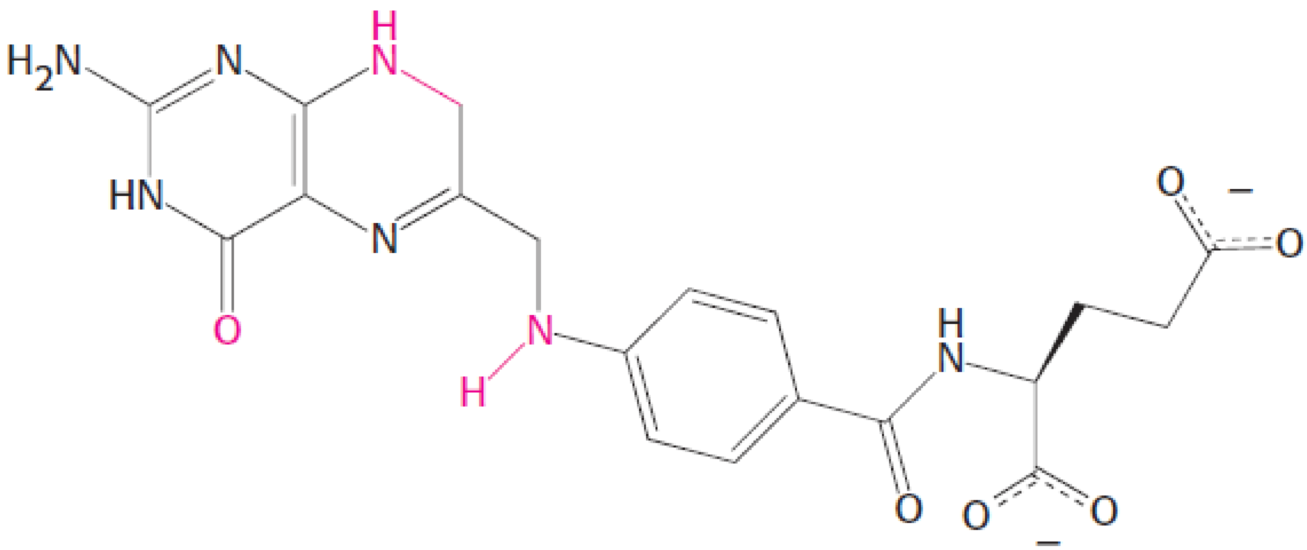
The Effect of pH on the Turnover Number



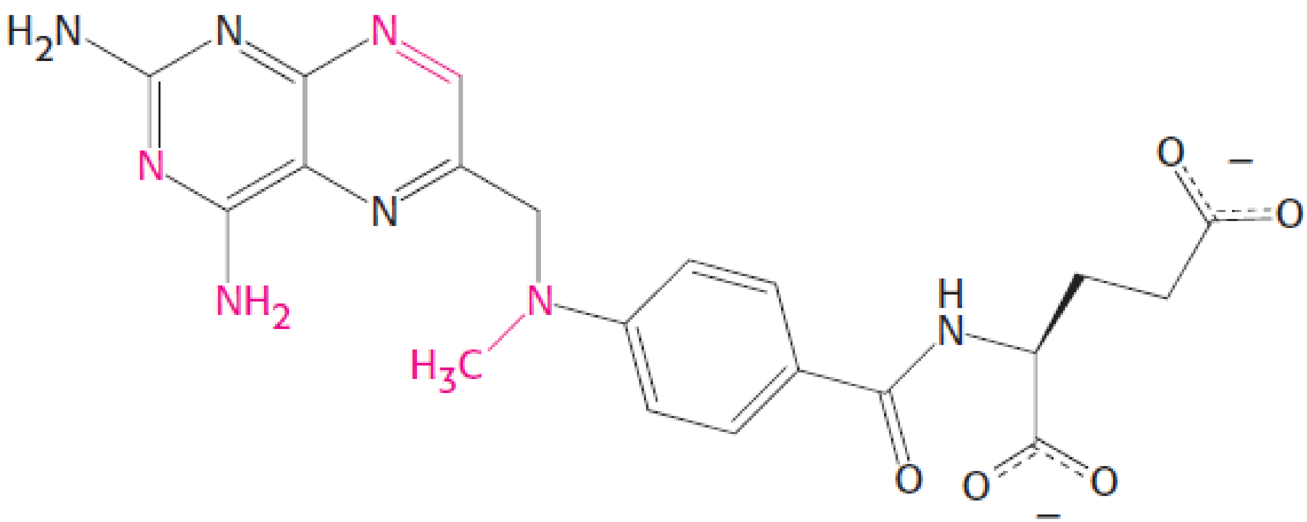
Enzymatic Competition for Substrate

- *Enzymatic competition*
  - Occurs when more than one enzyme interacts with the same substrate
- Each enzyme converts the substrate to a different product.
- The enzyme that "wins" is the one that is the most abundant at the time.





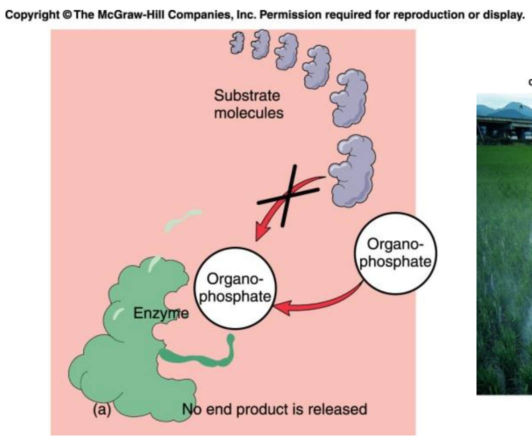
Dihydrofolate



Methotrexate

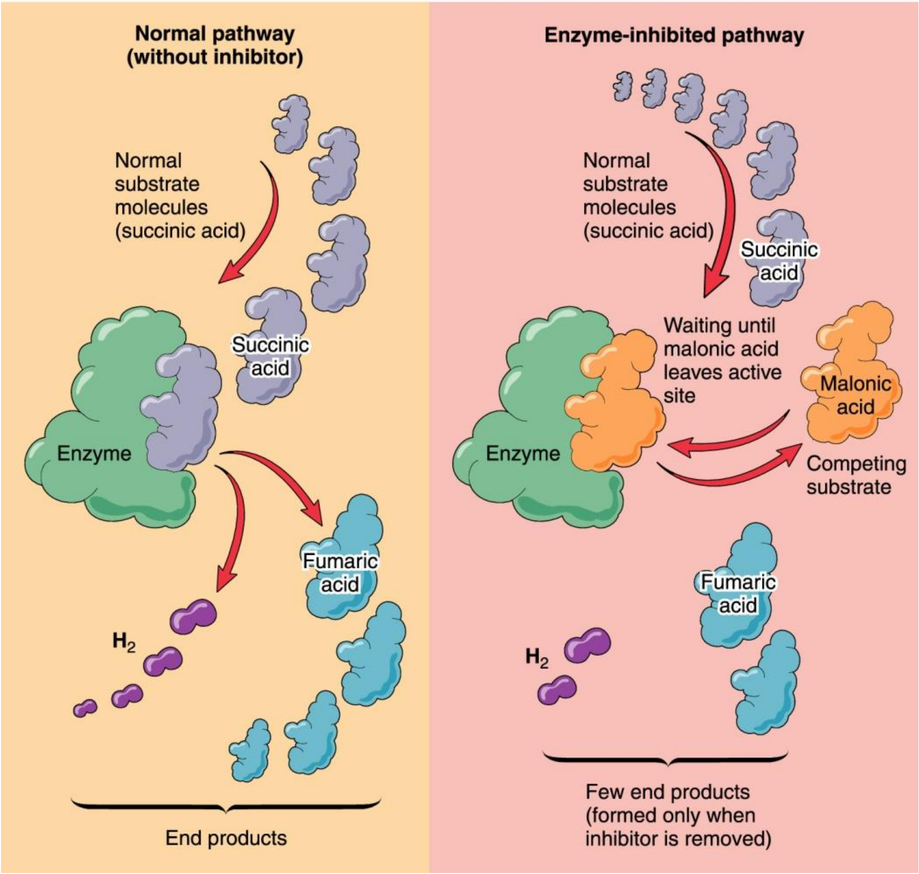
Enzyme Inhibition

- *Inhibitors* are molecules that attach to enzymes and make them unable to bind to substrate.
- Many drugs, pesticides and herbicides target enzymes.
- Types of inhibition
  - Competitive inhibition
  - Negative-feedback inhibition



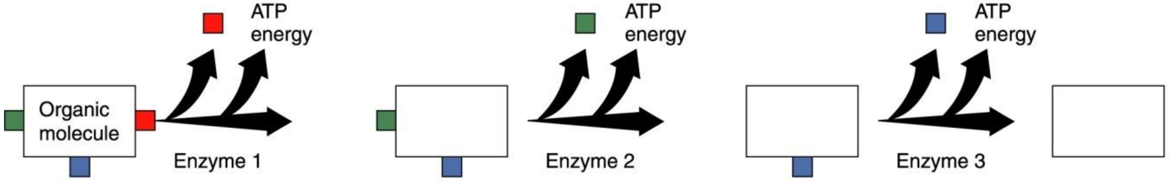
Competitive Inhibition

- Competitive inhibitors closely resemble the substrate.
  - Therefore, they bind to the active site of the enzyme.
  - They block the substrate from binding.
- Example:
  - Anti-herpes drugs

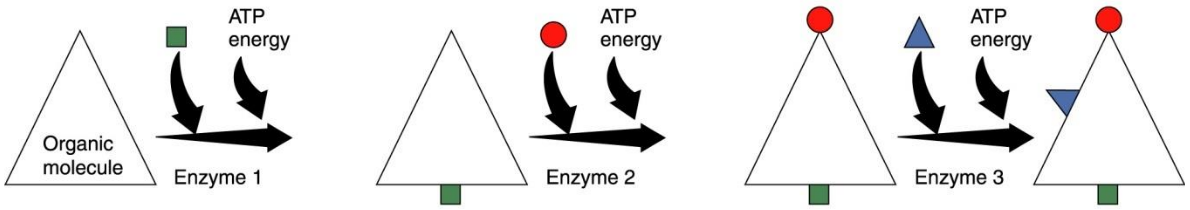


Biochemical Pathways

- A series of enzyme-catalyzed reactions
- Also called metabolic pathways
  - Catabolism-the breakdown of compounds
  - Anabolism-the synthesis of new, larger compounds
- Examples: photosynthesis, respiration, protein synthesis, etc.



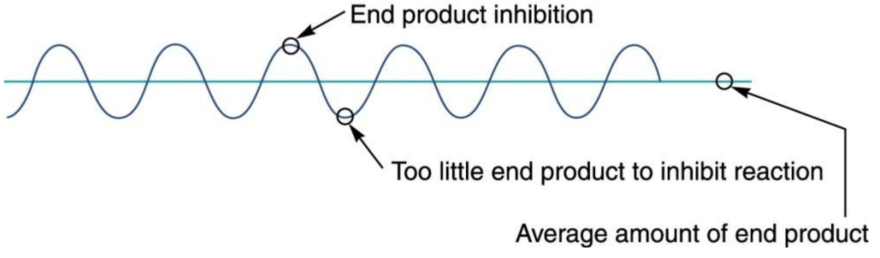
(a) A catabolic pathway breaks a large molecule into smaller molecules.



(b) An anabolic pathway combines smaller molecules to form a larger molecule.

Negative-Feedback Inhibition

- As the end-product of the sequence accumulates,
  - Those molecules *feedback* and bind to an enzyme early in the sequence.
  - They inhibit that enzyme, and stop the sequence.
  - This decreases the amount of end-product made.
- This functions to keep levels of the end-product within a certain range.



Enzyme: Salient features

- All are proteins except the catalytic RNA molecules
- Largest class of proteins
- Enzymes are catalysts that increase the rate of a chemical reaction without being changed themselves in the process (10^8 to 10^{20} fold)
- In the absence of an enzyme, the reaction

may hardly proceed

- Enzyme catalyzed reactions usually take place under relatively mild conditions
- Enzymes are also highly specific with respect to the substrate
- Enzyme activity can be regulated

How Enzymes Speed Chemical Reactions

- Enzymes lower the activation energy of biochemical reactions.
  - The reactants in an enzyme-catalyzed reaction are called *substrates.*
- Enzymes have a specific shape that fits with the substrate shape.
  - When the substrate and enzyme interact, an *enzyme-substrate complex* is formed.
  - This destabilizes the bonds in the substrate, speeding up the reaction.

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Steps in an Enzyme Reaction

1. Enzyme and substrate form a complex.
2. Complex goes through a transition state.
3. A complex of the enzyme and substrate, and enzyme and product is produced. (Reaction intermediates)
4. Enzyme and product separate

$$\mathbf{E + S \leftrightarrows E{\bullet}S \leftrightarrows E \bullet P \leftrightarrows E + P}$$

How Substrates Bind to Enzymes

- Enzymes only catalyze one or a few reactions.
  - They are specific because they have a particular shape that only fits particular substrates.
- The enzyme has a binding site for the substrate.
  - Called the *active site*
- Induced fit
  - When the substrate binds to the active site, the enzyme changes shape to fit it perfectly.

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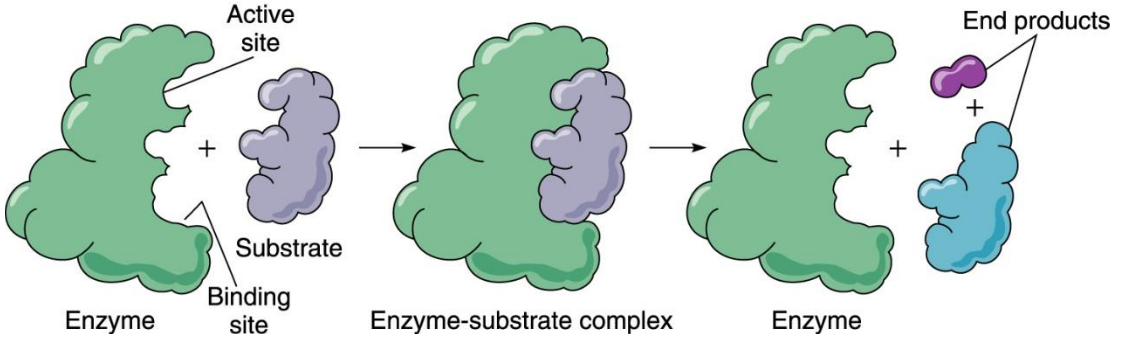


Why Enzymes Need Vitamins

- Some enzymes need special molecules to help them function correctly.
  - Called *cofactors*
- Cofactors can be inorganic ions, such as zinc or iron.
- Some cofactors are organic molecules.
  - Called *coenzymes*
- Vitamins are the precursors for many coenzymes.
  - Vitamin B2 is made into FAD.
  - Niacin is made into NAD.
- Vitamins must be acquired from the diet, since cells cannot make them.

How the Environment Affects Enzymes

- The rate at which an enzyme can bind to a substrate is called the *turnover number.*
- The turnover number of an enzyme is maximized under the ideal conditions for that enzyme.
- Each enzyme has ideal conditions that include:
  - Temperature
  - pH
  - Substrate concentration

Enzymes as Biomolecules

Large molecules–

Almost all are Proteins (12kDa - 1,000kDa)

(exception: Ribozymes-catalytic RNA molecules)

Active site -- specific region in enzyme which interacts with its substrate.

- ♦ both binding and catalytic reaction occur here.
- ♦ some residues involved in binding substrate
- ♦ others catalyze reaction

Temperature

- Temperature has two effects on enzymes.
  - Changes the rate of molecular motion
    - Increasing temperature increases molecular motion.
      - Increases the rate of catalysis
    - *Optimum temperature*–the temperature at which the enzyme has the highest rate of catalysis.
    - Decreasing temperature decreases molecular movement.
      - Decreases the rate of catalysis
  - Causes changes in the shape of an enzyme
    - Temperature changes above optimum will denature the enzyme.
    - This changes its shape, and it can no longer bind substrate and catalyze the reaction.
    - This is why a high fever is potentially dangerous.

pH

- In the three-dimensional shape of an enzyme
  - Some amino acid side chains are exposed to the environment.
- In a basic environment
  - The acidic side chains could donate protons.
- In an acidic environment
  - The basic side chains could accept protons.
- Both of these events will change the shape of the enzyme
  - Making it less able to bind substrate, thus less able to catalyze the reaction

Enzyme-Substrate Concentration

- The rate of catalysis increases as the amount of
  - Enzyme increases
  - Substrate increases
- However, once all of the enzymes are occupied, the rate of catalysis will not increase
  - Even if more substrate is added

How the Cell Controls Enzymes

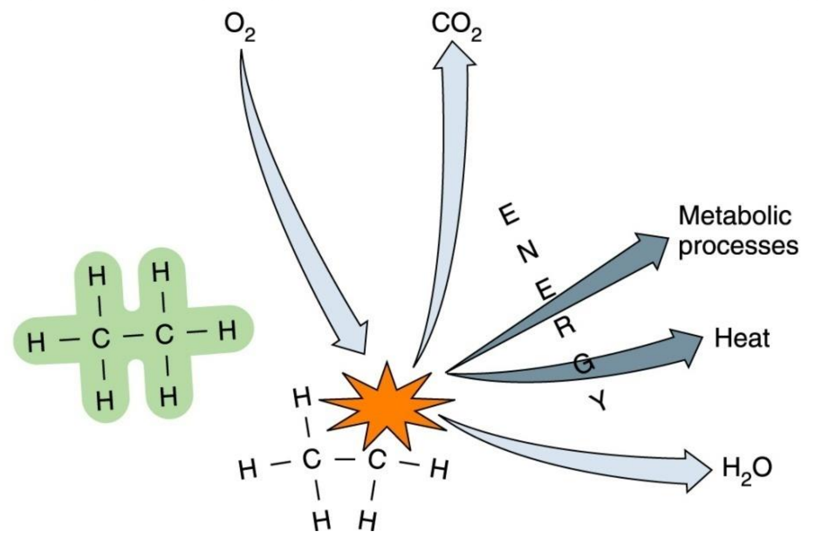
- A cell must be able to control when and how often its biochemical reactions take place.
  - It does this by controlling enzymes.
- *Coordination* ensures that reactions happen in the correct order.
- *Regulation* ensures that reactions happen at the correct rate and controls the amount of product that is made.
- Cells coordinate and regulate the activity of their enzymes by:
  - Enzymatic competition for substrate
  - Gene regulation
  - Enzyme inhibition

Gene Regulation

- Enzymes are proteins.
  - Protein production is controlled by genes.
- Certain chemicals in the cell turn particular enzyme-producing genes on or off depending on the situation.
  - Called gene-regulator proteins
    - Those that decrease the amount of an enzyme made are called gene-repressor proteins.
    - Those that increase the amount of an enzyme made are called gene-activator proteins.
    - Example: Malate synthetase

Cells Use Enzymes to Process Energy and Matter

- Organisms obtain energy through enzyme-catalyzed biochemical reactions.
  - These reactions break chemical bonds, releasing their internal potential energy.
  - Example: burning wood



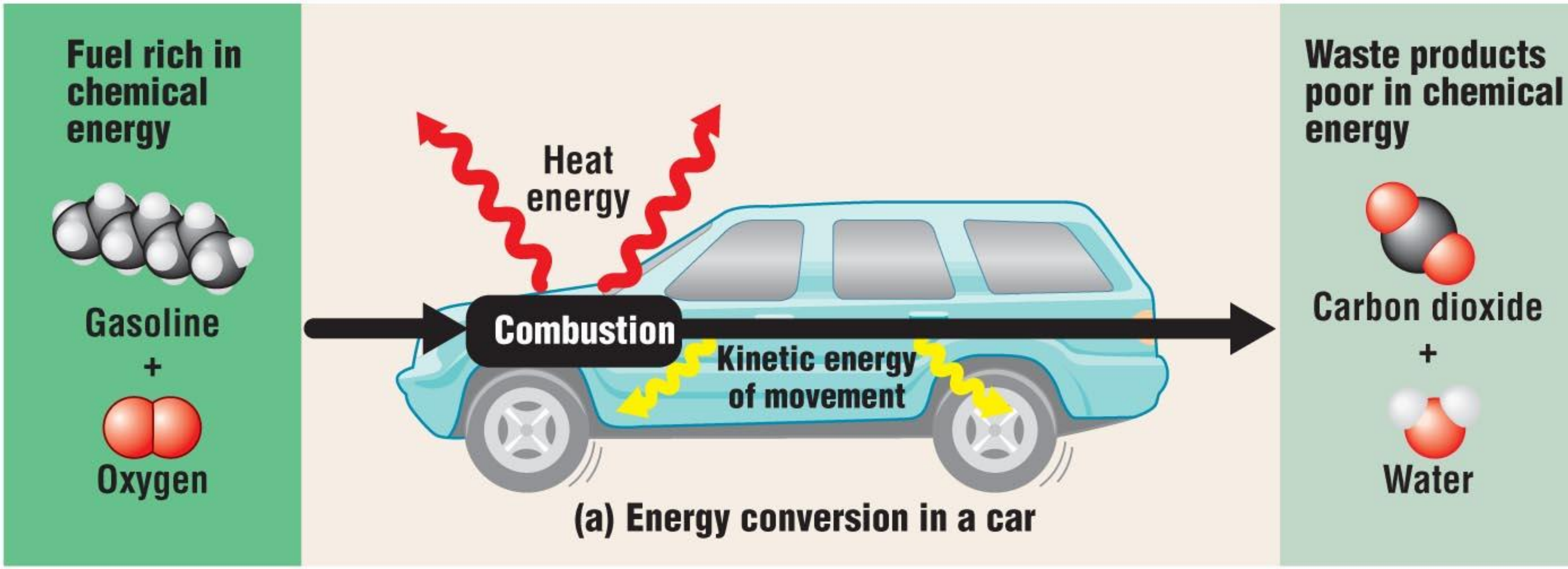

Fuel rich in chemical energy
Gasoline
+
Oxygen
Heat energy
Combustion
Kinetic energy of movement
Waste products poor in chemical energy
Carbon dioxide
+
Water
(a) Energy conversion in a car

Figure 5.3a

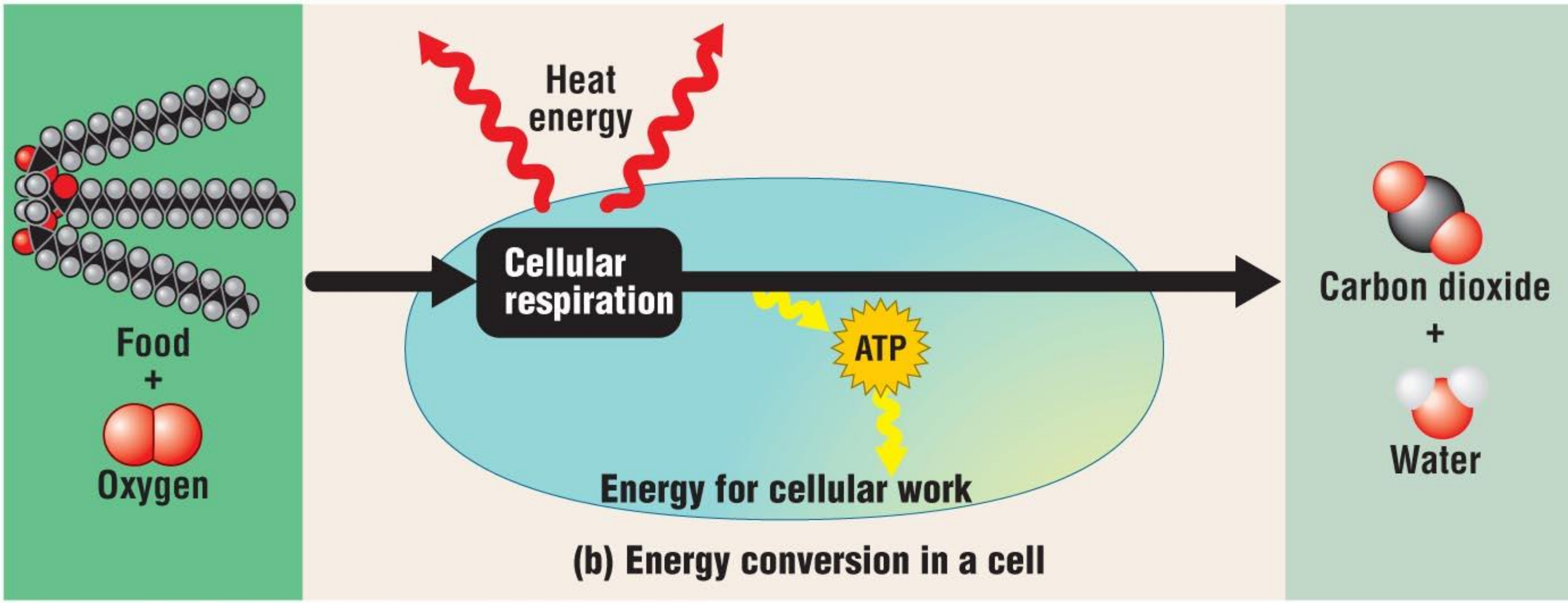

Heat
energy
Cellular
respiration
ATP
Energy for cellular work
Food
+
Oxygen
Carbon dioxide
+
Water
(b) Energy conversion in a cell

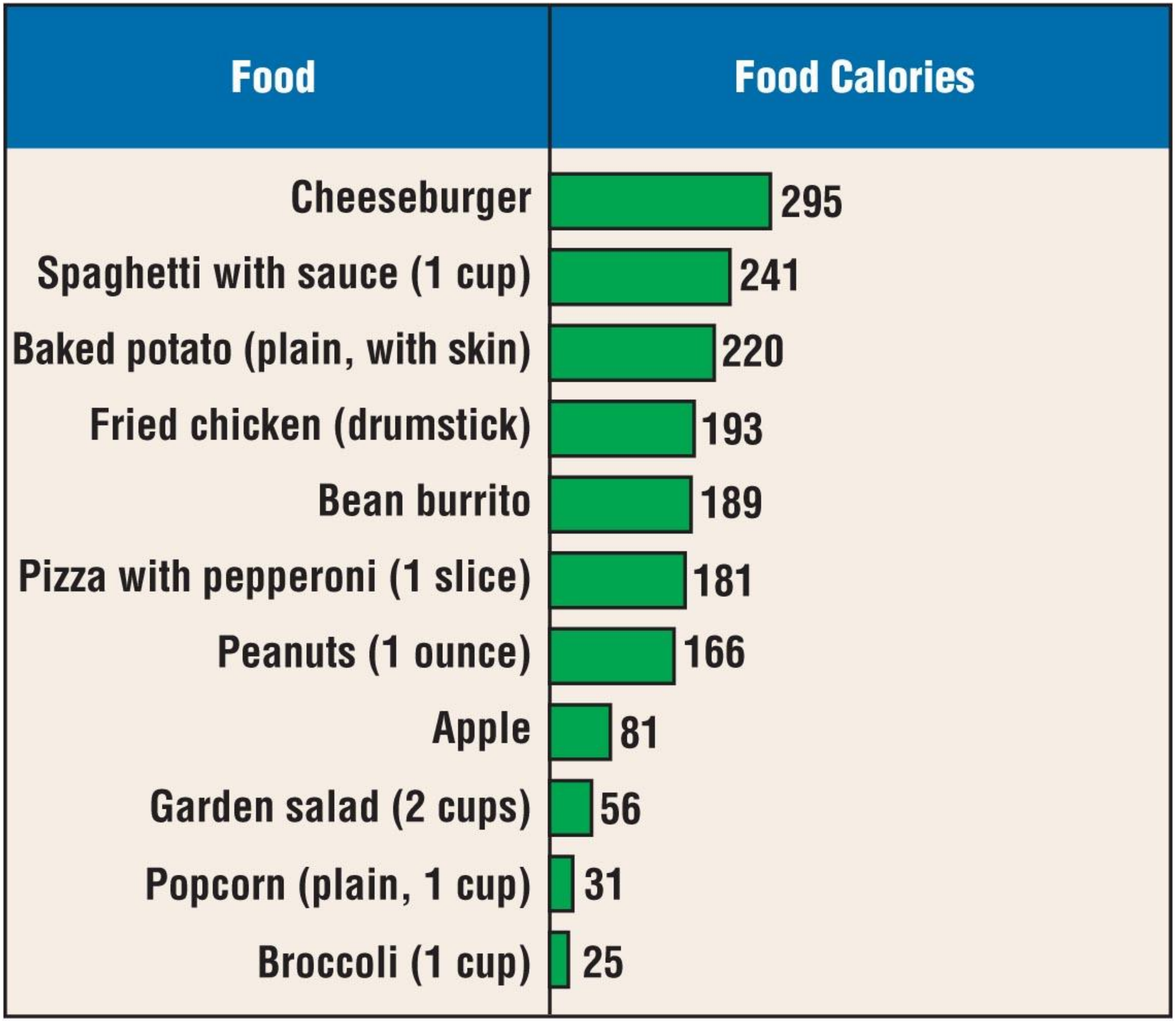
Figure 5.3b

- Cellular respiration
  - Is the energy-releasing chemical breakdown of fuel molecules.
  - Provides energy for the cell to do work.

Food Calories

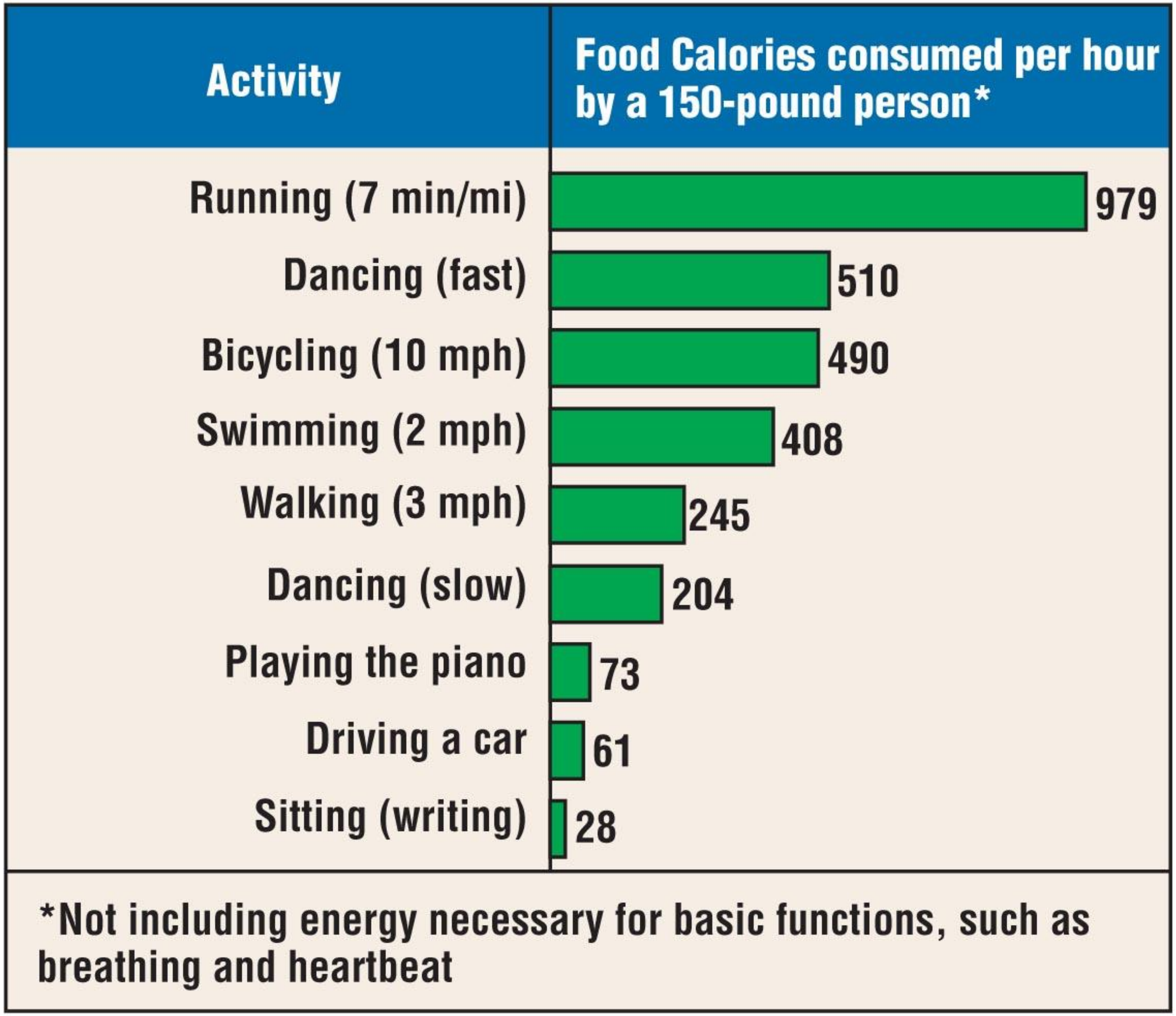
- A calorie is the amount of energy that raises the temperature of one gram of water by one degree Celsius.

- The kilocalorie is
  - 1,000 calories.
  - The unit used to measure the energy in food.



(a) Food Calories (kilocalories) in various foods

Figure 5.4a



(b) Food Calories (kilocalories) we burn in various activities

Figure 5.4b

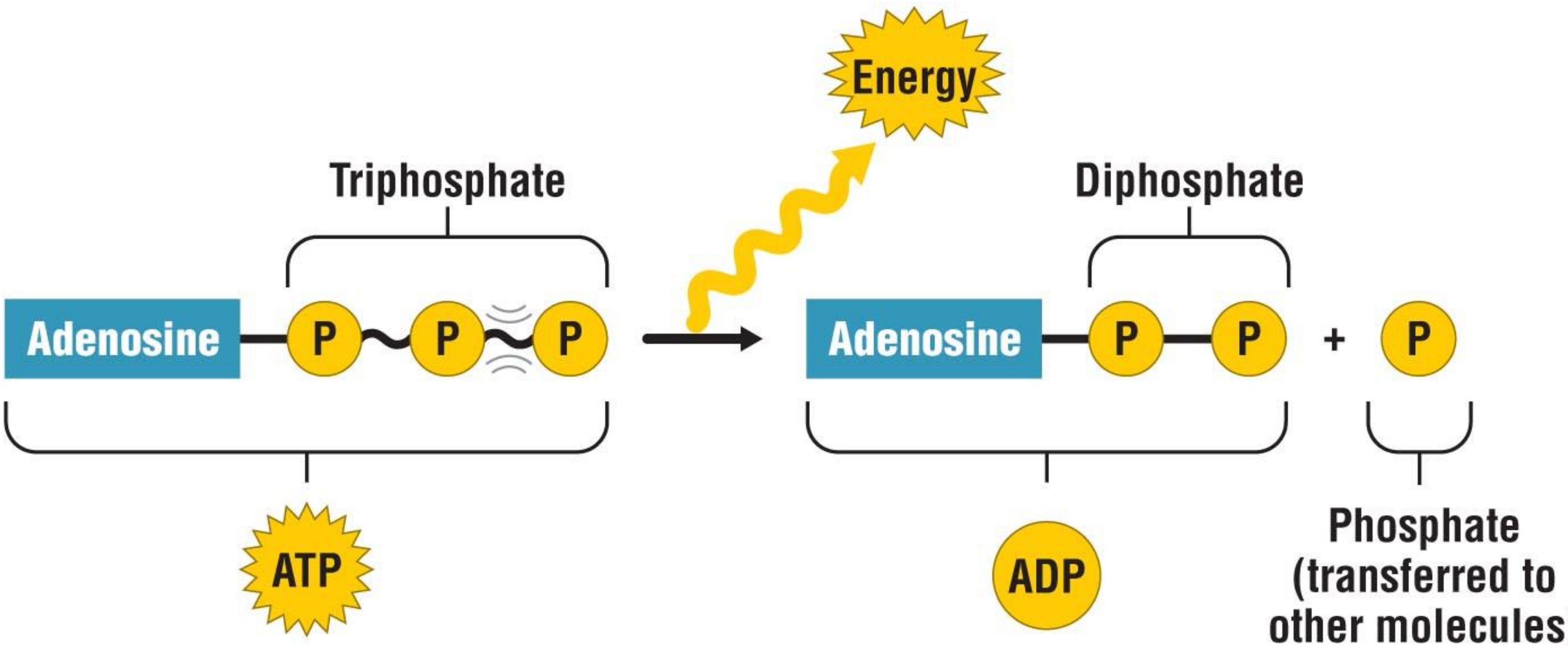
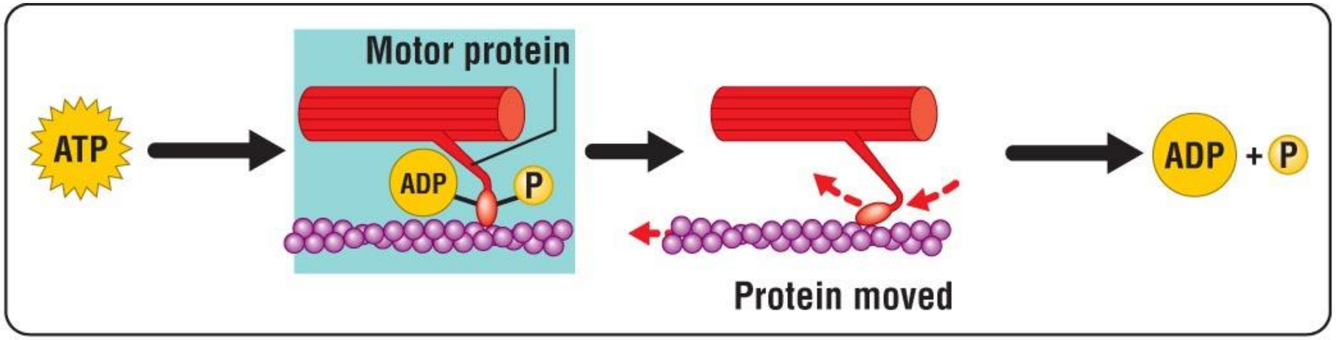

Energy
Triphosphate
Diphosphate
Adenosine
P
P
P
Adenosine
P
P
+
P
ATP
ADP
Phosphate
(transferred to
other molecules)

Figure 5.5

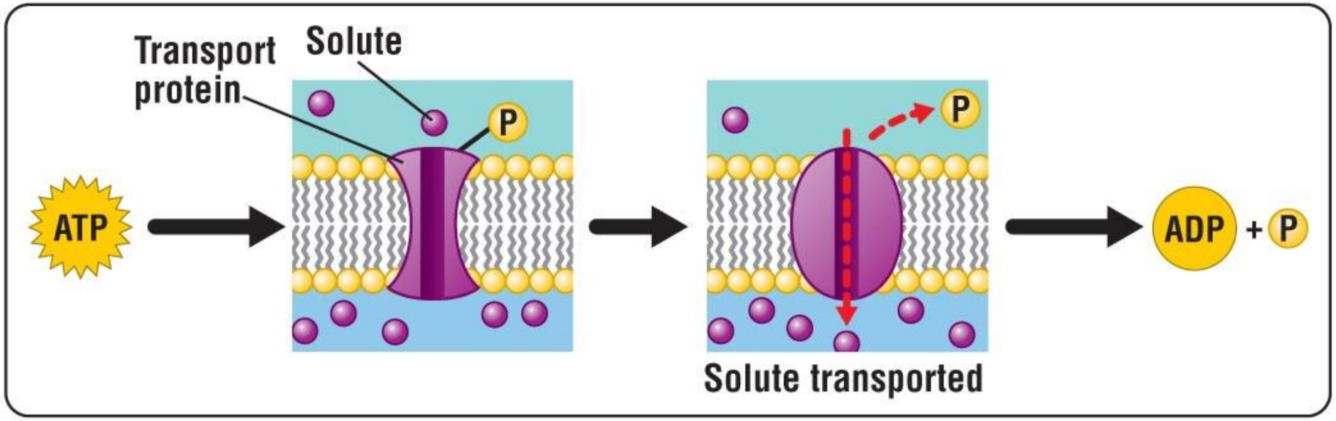
ATP and Cellular Work

– The chemical energy of organic molecules is released in cellular respiration to make ATP in the mitochondria.

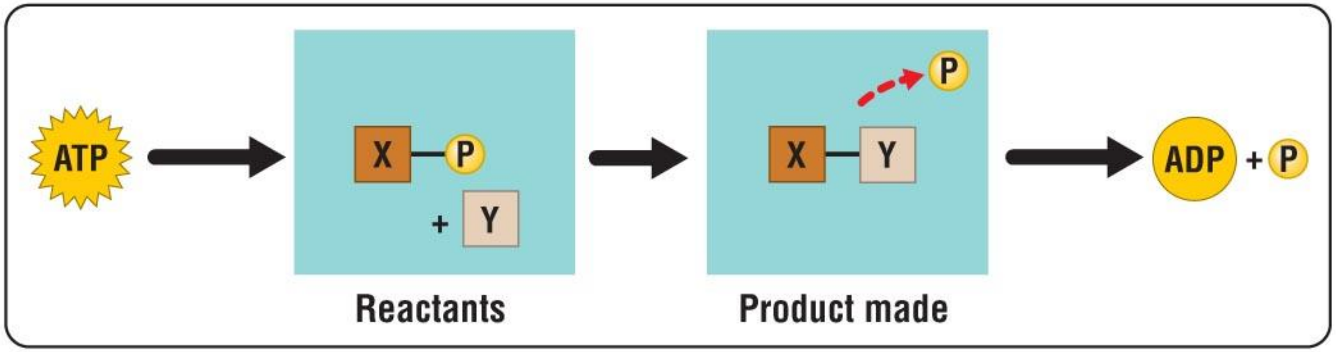
- ATP (adenosine triphosphate)
  - Consists of adenosine plus a tail of three phosphate groups.
  - Is broken down to ADP, accompanied by the release of energy.



(a) Mechanical work



(b) Transport work



(c) Chemical work

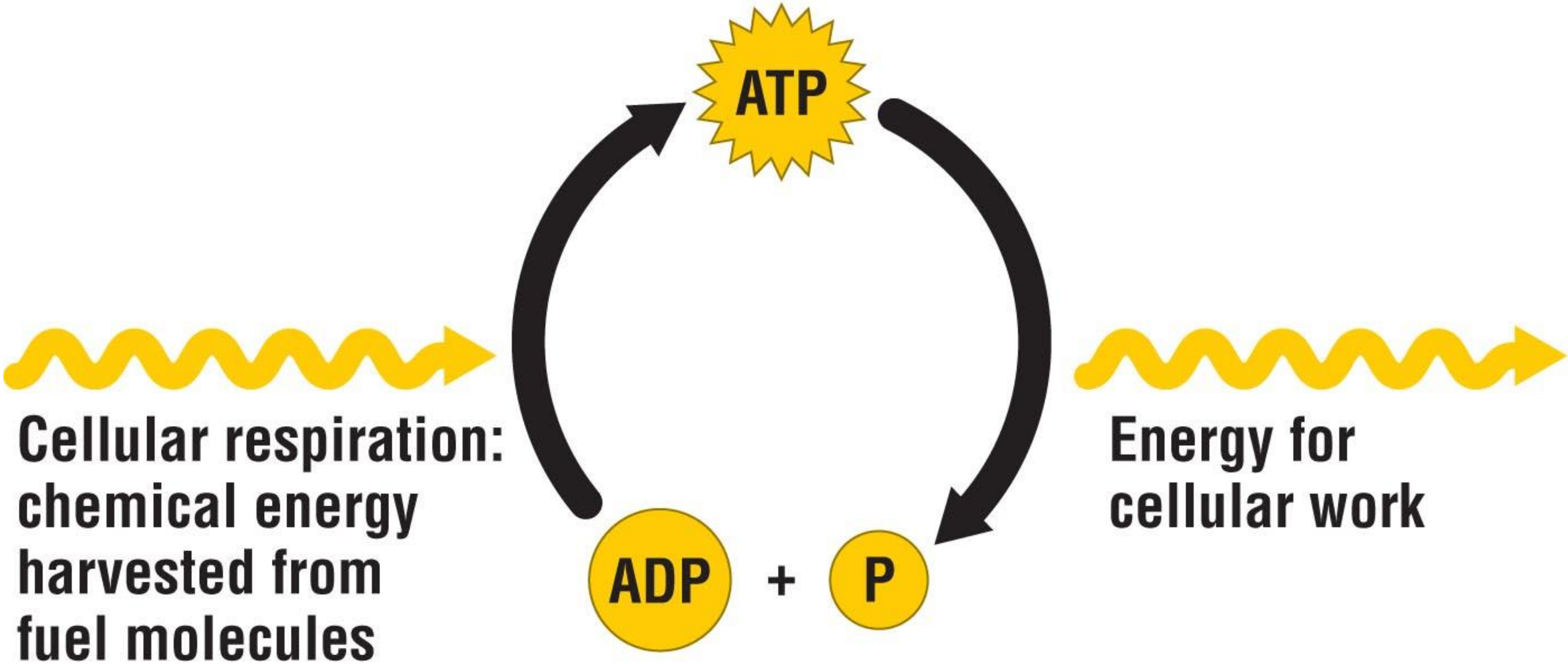

ATP
Cellular respiration: chemical energy harvested from fuel molecules
Energy for cellular work
ADP
+
P

Figure 5.7

The ATP Cycle

- Cellular work spends ATP.
- ATP is recycled from ADP and phosphate through cellular respiration.

- ATP can energize other molecules by transferring phosphate groups.
  - This energy can be used to drive cellular work.
- ATP functions in what is called energy coupling, or the ATP cycle.