

## Chapter 8

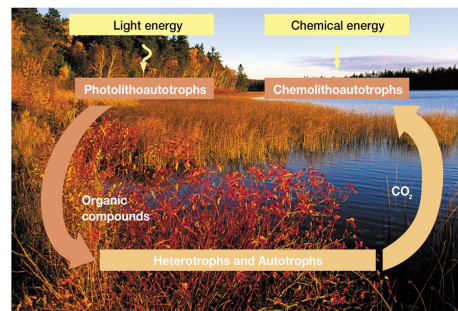
### Metabolism: Energy, Enzymes, and Regulation

## Energy and Work

- ✓ energy
  - capacity to do work or to cause particular changes

### Types of work carried out by organisms

- ✓ chemical work
  - synthesis of complex molecules
- ✓ transport work
  - take up of nutrients, elimination of wastes, and maintenance of ion balances
- ✓ mechanical work
  - movement of organisms or cells and movement of internal structures



The processes used by organisms to obtain energy and to do chemical work are the basis of the functioning of ecosystems.

## Energy currency of cells

- ✓ ATP
  - used to transfer energy from cell's energy-conserving systems to the systems that carry out cellular work

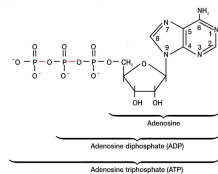
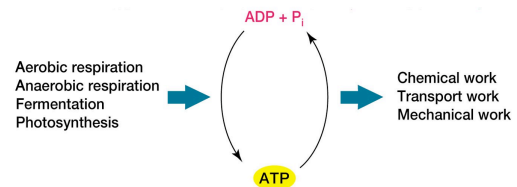


Figure 8.2

## The cell's energy cycle



## The Laws of Thermodynamics

### ✓ thermodynamics

- a science that analyzes energy changes in a collection of matter called a system (e.g., a cell)
- all other matter in the universe is called the surroundings

## Energy units

### ✓ calorie (cal)

- amount of heat energy needed to raise 1 gram of water from 14.5 to 15.5°C

### ✓ joules (J)

- units of work capable of being done by a unit of energy
- 1 cal of heat is equivalent to 4.1840 J of work

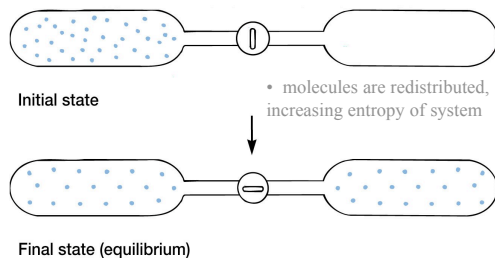
## First law of thermodynamics

- ✓ energy can be neither created nor destroyed
- ✓ total energy in universe remains constant
  - however energy may be redistributed either within a system or between the system and its surroundings

## Second law of thermodynamics

- ✓ entropy
  - amount of disorder in a system
- ✓ physical and chemical processes proceed in such a way that the disorder of the universe increases to the maximum possible

## Second law in action...



## Free Energy and Reactions

$$\Delta G = \Delta H - T \cdot \Delta S$$

- expresses the change in energy that can occur in chemical reactions and other processes
- used to indicate if a reaction will proceed spontaneously

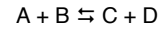
$$\Delta G = \Delta H - T \cdot \Delta S$$

- $\Delta G$ 
  - free energy change
  - amount of energy that is available to do work
- $\Delta H$ 
  - change in enthalpy (heat content)
- T
  - temperature in Kelvin
- $\Delta S$ 
  - change in entropy

## Chemical equilibrium

✓ equilibrium

consider the chemical reaction



- reaction is at equilibrium when rate of forward reaction = rate of reverse reaction

✓ equilibrium constant ( $K_{eq}$ )

- expresses the equilibrium concentrations of products and reactants to one another

## Standard free energy change ( $\Delta G^\circ$ )

- free energy change defined at standard conditions of concentration, pressure, temperature, and pH

$\Delta G^\circ$

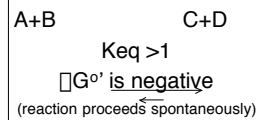
□ standard free energy change at pH 7

□ directly related to  $K_{eq}$

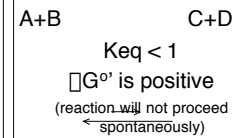
$$\Delta G^\circ = -2.303RT \cdot \log K_{eq}$$

## The relationship...

Exergonic reactions

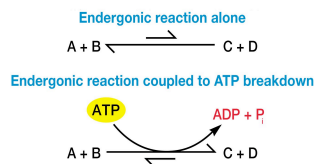


Endergonic reactions



## The Role of ATP in Metabolism

- ✓ exergonic breakdown of ATP is coupled with endergonic reactions to make them more favorable



## Oxidation-Reduction Reactions and Electron Carriers

- ✓ many metabolic processes involve oxidation-reduction reactions (electron transfers)
- ✓ electron carriers are often used to transfer electrons from an electron donor to an electron acceptor

## Oxidation-reduction (redox) reactions

- ✓ transfer of electrons from a donor to an acceptor
  - reducing agent or reductant = electron donor
  - oxidizing agent or oxidant = electron acceptor
- ✓ can result in energy release, which can be conserved and used to form ATP

## Standard reduction potential ( $E_0$ )

- ✓ equilibrium constant for an oxidation-reduction reaction
- ✓ a measure of the tendency of the reducing agent to lose electrons

more negative  $E_0$  □ better electron donor  
 more positive  $E_0$  □ better electron acceptor

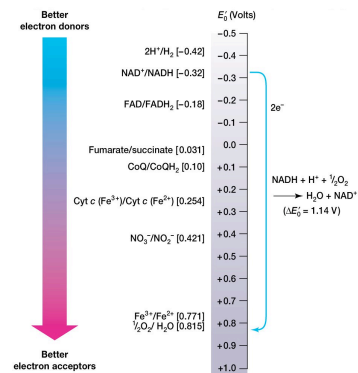
**Table 8.1** Selected Biologically Important Redox Couples

Redox Couple	$E_0$ (Volts) <sup>a</sup>
$2\text{H}^+ + 2\text{e}^- \longrightarrow \text{H}_2$	-0.42
Ferredoxin( $\text{Fe}^{3+}$ ) + $\text{e}^- \longrightarrow$ ferredoxin ( $\text{Fe}^{2+}$ )	-0.42
$\text{NAD(P)}^+ + \text{H}^+ + 2\text{e}^- \longrightarrow \text{NAD(P)H}$	-0.32
$\text{S} + 2\text{H}^+ + 2\text{e}^- \longrightarrow \text{H}_2\text{S}$	-0.274
Acetaldehyde + $2\text{H}^+ + 2\text{e}^- \longrightarrow$ ethanol	-0.197
Pyruvate <sup>-</sup> + $2\text{H}^+ + 2\text{e}^- \longrightarrow$ lactate <sup>2-</sup>	-0.185
$\text{FAD} + 2\text{H}^+ + 2\text{e}^- \longrightarrow \text{FADH}_2$	-0.18 <sup>b</sup>
Oxaloacetate <sup>2-</sup> + $2\text{H}^+ + 2\text{e}^- \longrightarrow$ malate <sup>2-</sup>	-0.166
Fumarate <sup>2-</sup> + $2\text{H}^+ + 2\text{e}^- \longrightarrow$ succinate <sup>2-</sup>	0.031
Cytochrome <i>b</i> ( $\text{Fe}^{3+}$ ) + $\text{e}^- \longrightarrow$ cytochrome <i>b</i> ( $\text{Fe}^{2+}$ )	0.075
Ubiquinone + $2\text{H}^+ + 2\text{e}^- \longrightarrow$ ubiquinone $\text{H}_2$	0.10
Cytochrome <i>c</i> ( $\text{Fe}^{3+}$ ) + $\text{e}^- \longrightarrow$ cytochrome <i>c</i> ( $\text{Fe}^{2+}$ )	0.254
$\text{NO}_3^- + 2\text{H}^+ + 2\text{e}^- \longrightarrow \text{NO}_2^- + \text{H}_2\text{O}$	0.421
$\text{NO}_3^- + 8\text{H}^+ + 6\text{e}^- \longrightarrow \text{NH}_4^+ + 2\text{H}_2\text{O}$	0.44
$\text{Fe}^{3+} + \text{e}^- \longrightarrow \text{Fe}^{2+}$	0.771
$\text{O}_2 + 4\text{H}^+ + 4\text{e}^- \longrightarrow 2\text{H}_2\text{O}$	0.815

<sup>a</sup> $E_0$  is the standard reduction potential at pH 7.0.

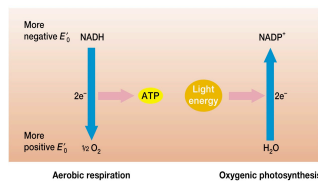
<sup>b</sup>The value for FAD/FADH<sub>2</sub> applies to the free cofactor because it can vary considerably when bound to an apoenzyme.

The greater the difference between the  $E_0$  of the donor and the  $E_0$  of the acceptor □ the more negative the  $\Delta G^\circ$



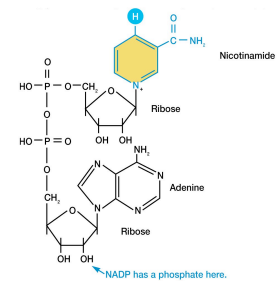
## Energy and electron flow in metabolism

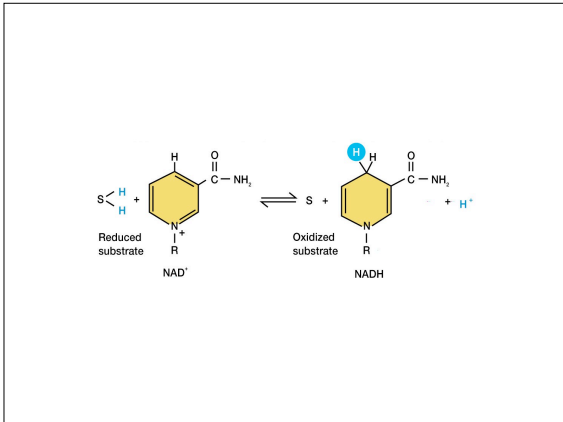
- ✓ flow of electrons down the tower releases energy
- ✓ light energy is used to drive electrons up the tower during photosynthesis



## Electron carriers

- ✓ NAD
  - nicotinamide adenine dinucleotide
- ✓ NADP
  - nicotinamide adenine dinucleotide phosphate





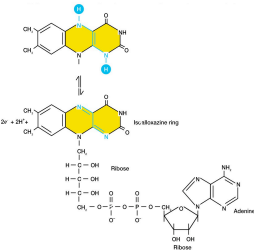
## Electron carriers

### ✓ FAD

- flavin adenine dinucleotide

### ✓ FMN

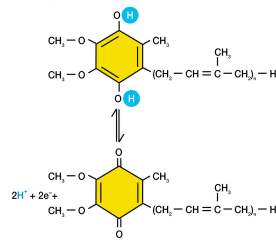
- flavin mononucleotide
- riboflavin phosphate



## Electron carriers

### ✓ coenzyme Q (CoQ)

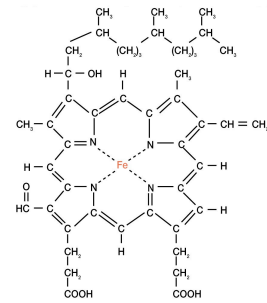
- a quinone
- also called ubiquinone



## Electron carriers

### ✓ cytochromes

- use iron to transfer electrons
- iron is part of a heme group



## Electron carriers

### ✓ nonheme iron proteins

- e.g., ferredoxin
- use iron to transport electrons
- iron is not part of a heme group

## Enzymes

### ✓ protein catalysts

- have great specificity for the reaction catalyzed and the molecules acted on

### ✓ catalyst

- substance that increases the rate of a reaction without being permanently altered

### ✓ substrates

- reacting molecules

### ✓ products

- substances formed by reaction

## Structure and Classification of Enzymes

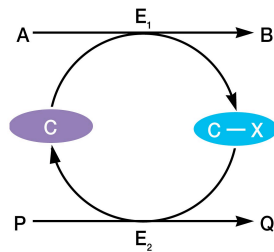
- ✓ one or more polypeptides
- ✓ one or more polypeptides and nonprotein components

## Enzyme structure

- ✓ apoenzyme
  - protein component of an enzyme
- ✓ cofactor
  - nonprotein component of an enzyme
    - ☞ prosthetic group – firmly attached
    - ☞ coenzyme – loosely attached
- ✓ holoenzyme = apoenzyme + cofactor

## Coenzymes

- ✓ often act as carriers, transporting substances around the cell



**Table 8.2** Enzyme Classification

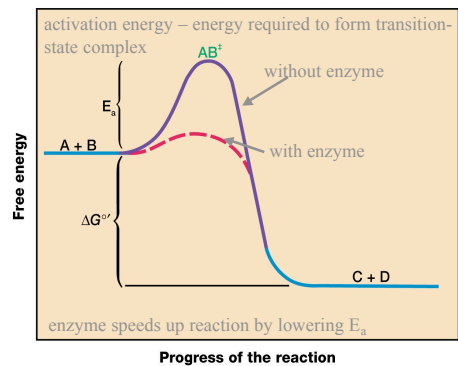
Type of Enzyme	Reaction Catalyzed by Enzyme	Example of Reaction
Oxidoreductase	Oxidation-reduction reactions	Lactate dehydrogenase: Pyruvate + NADH + H <sup>+</sup> ⇌ lactate + NAD <sup>+</sup>
Transferase	Reactions involving the transfer of groups between molecules	Aspartate carbamoyltransferase: Aspartate + carbamoylphosphate ⇌ carbamoylaspartate + phosphate
Hydrolase	Hydrolysis of molecules	Glucose-6-phosphatase: Glucose 6-phosphate + H <sub>2</sub> O → glucose + P <sub>i</sub>
Lyase	Removal of groups to form double bonds or addition of groups to double bonds	Fumarate hydratase: l-malate ⇌ fumarate + H <sub>2</sub> O
Isomerase	Reactions involving isomerizations	Alanine racemase: l-alanine ⇌ D-alanine
Ligase	Joining of two molecules using ATP energy (or that of other nucleoside triphosphates)	Glutamine synthetase: Glutamate + NH <sub>3</sub> + ATP → glutamine + ADP + P <sub>i</sub>

## The Mechanism of Enzyme Reactions

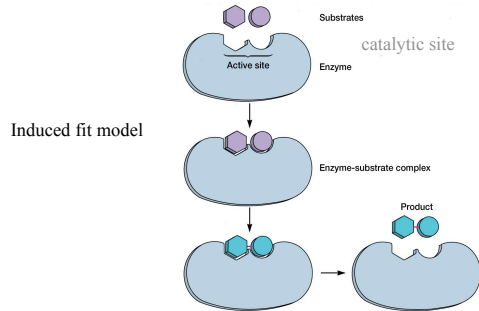
a typical exergonic reaction



↑  
transition-state complex –  
resembles both the substrates and the products



## Interaction of enzyme and substrate



## How enzymes lower $E_a$

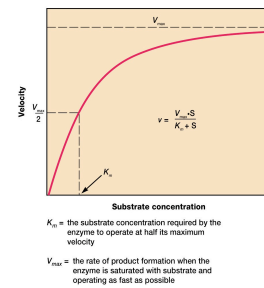
- ✓ by increasing concentrations of substrates at active site of enzyme
- ✓ by orienting substrates properly with respect to each other in order to form the transition-state complex

## The Effect of Environment on Enzyme Activity

- ✓ enzyme activity is significantly impacted by substrate concentration, pH, and temperature

## Effect of [substrate]

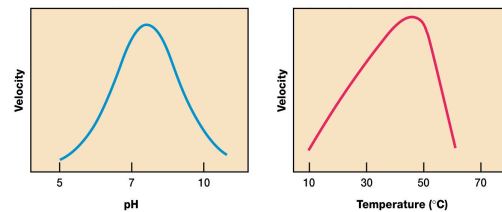
- ✓ rate increases as [substrate] increases
- ✓ no further increase occurs after all enzyme molecules are saturated with substrate



## Effect of pH and temperature

- ✓ each enzyme has specific pH and temperature optima
- ✓ denaturation
  - loss of enzyme's structure and activity when temperature and pH rises too much above optima

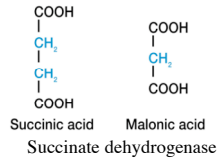
## Enzyme activity (pH and temperature)



## Enzyme Inhibition

- **competitive inhibitor**

–directly competes with binding of substrate to active site



- **uncompetitive inhibitor**

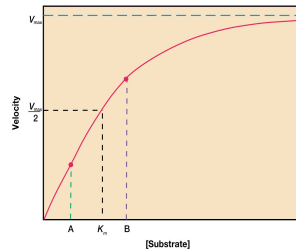
–binds enzyme at site other than active site; changes enzyme's shape so that it becomes less active

## The Nature and Significance of Metabolic Regulation

- ✓ conservation of energy and materials
- ✓ maintenance of metabolic balance despite changes in environment
- ✓ three major mechanisms
  - metabolic channeling
  - control enzyme activity
  - control number of enzyme molecules present (discussed in Chapter 12)

## Metabolic Channeling

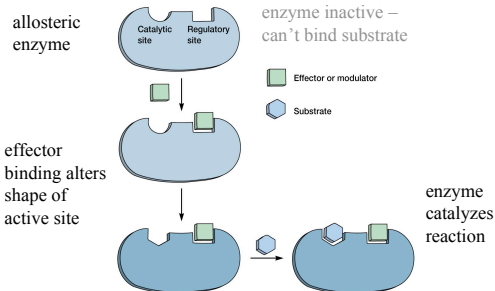
- ✓ differential localization of enzymes and metabolites
- ✓ compartmentation
  - differential distribution of enzymes and metabolites among separate cell structures or organelles



## Control of Enzyme Activity

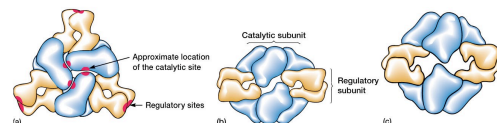
- ✓ allosteric regulation
- ✓ covalent modification

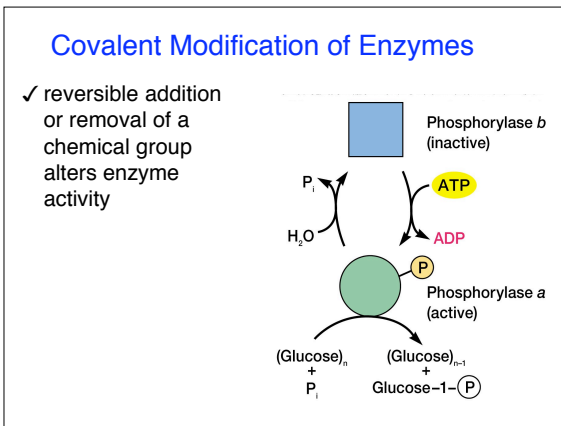
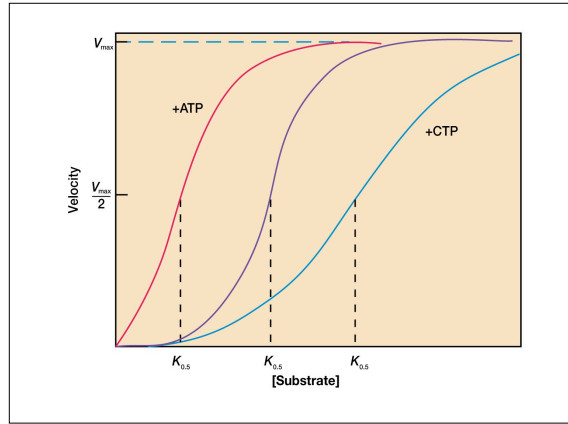
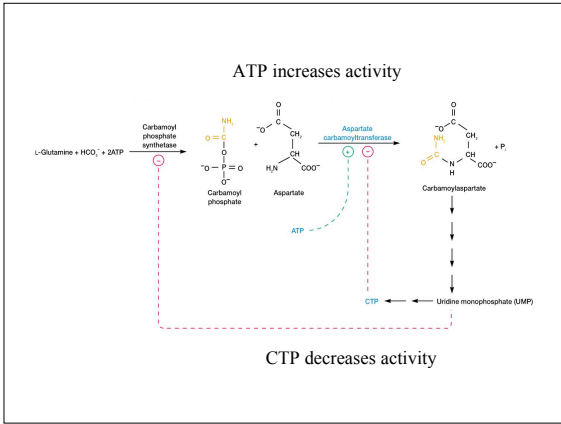
## Allosteric Regulation



## An example – aspartate carbamoyltransferase (ACTase) from *E. coli*

functions in pyrimidine synthesis





**Feedback Inhibition**

✓ also called end product inhibition

✓ inhibition of one or more critical enzymes in a pathway regulates entire pathway

- pacemaker enzyme
  - catalyzes the slowest or rate-limiting reaction in the pathway

