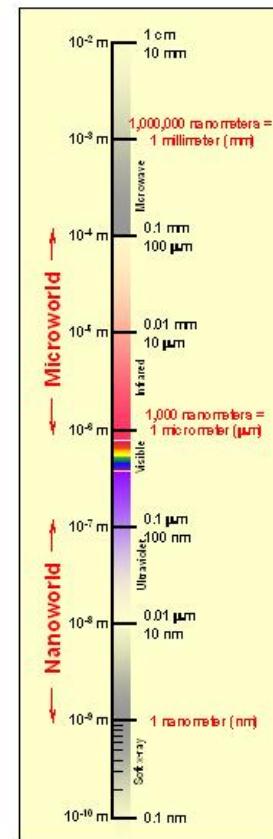
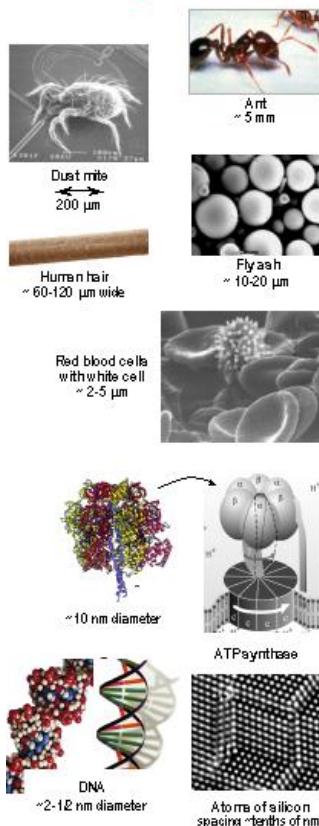


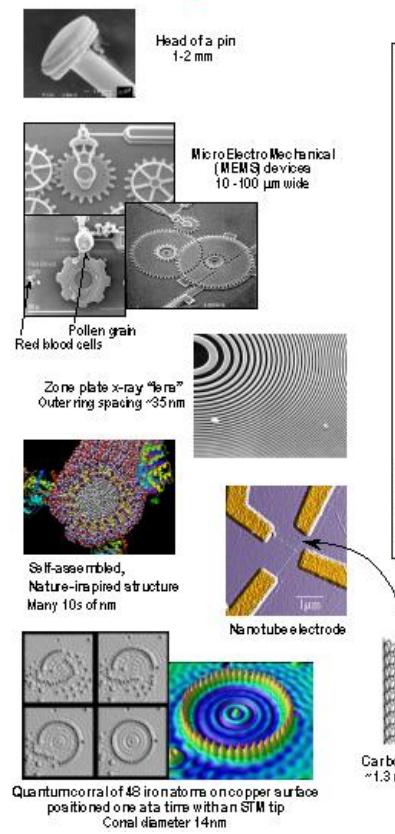
# What is nano?

## The Scale of Things – Nanometers and More

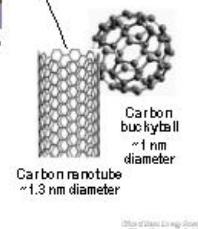
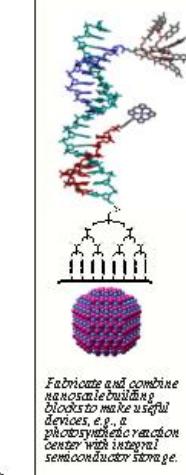
### Things Natural



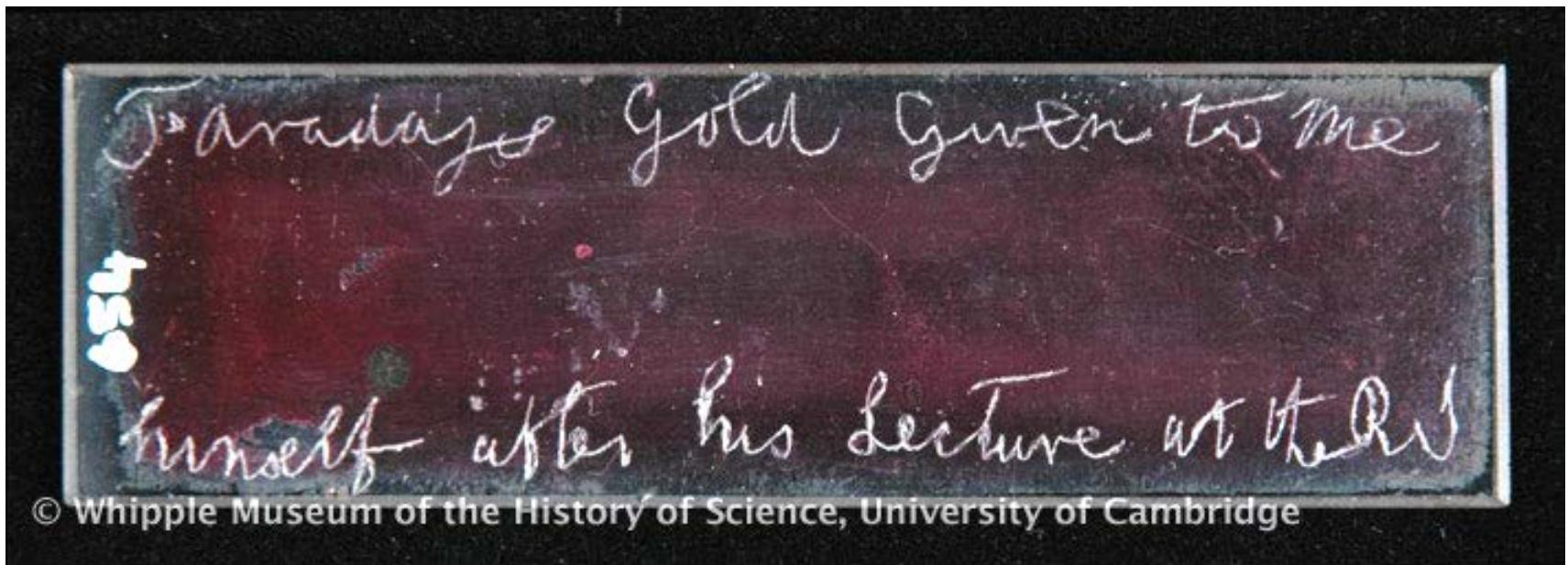
### Things Manmade



### The Challenge



# Faraday's Gold Sol



© Whipple Museum of the History of Science, University of Cambridge

1856  
20-40 nm gold

# Topics

## Fundamental Knowledge and Current Literatures

- Analytical Chemistry
- Spectroscopic tools
- Microarray
- Cell-surface interaction
- Ultrasensitive detection
- Physical Chemistry
- Single molecular behavior (Optical and AFM)
- Optical properties of Q-dot
- SERS
- Surface plasmon
- Material Chemistry:
- Nanomaterials: Q-dot, nanoparticle, DNA assembly
- Surface functionalization
- Drug delivery
- DNA, Protein, Cell interactions

# Review of General Chemistry, Biochemistry and Cell Biology

# Synthesis of Nanoparticles and Surface Modifications

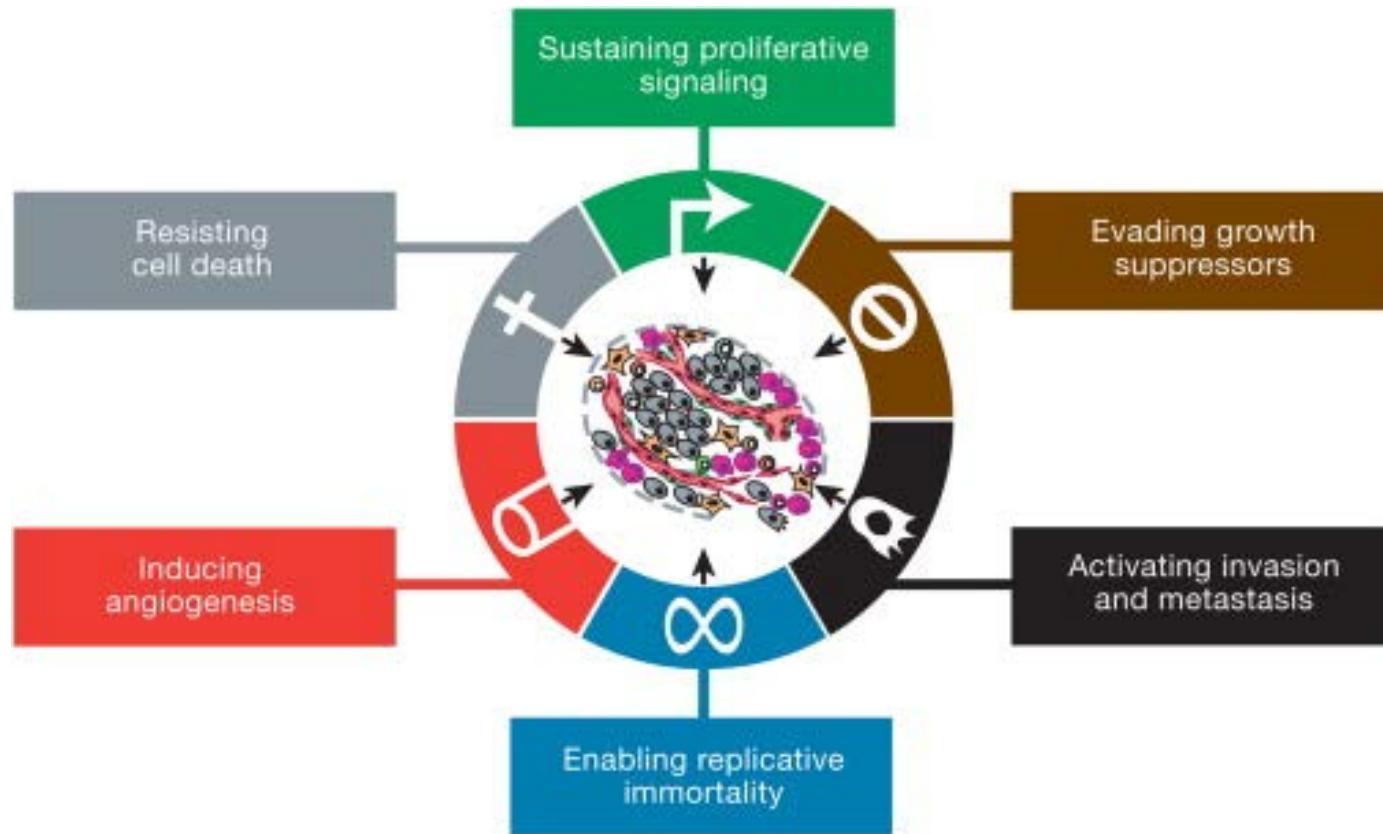
# Properties of Nanomaterials

# Nanomaterials for Biodiagnostic

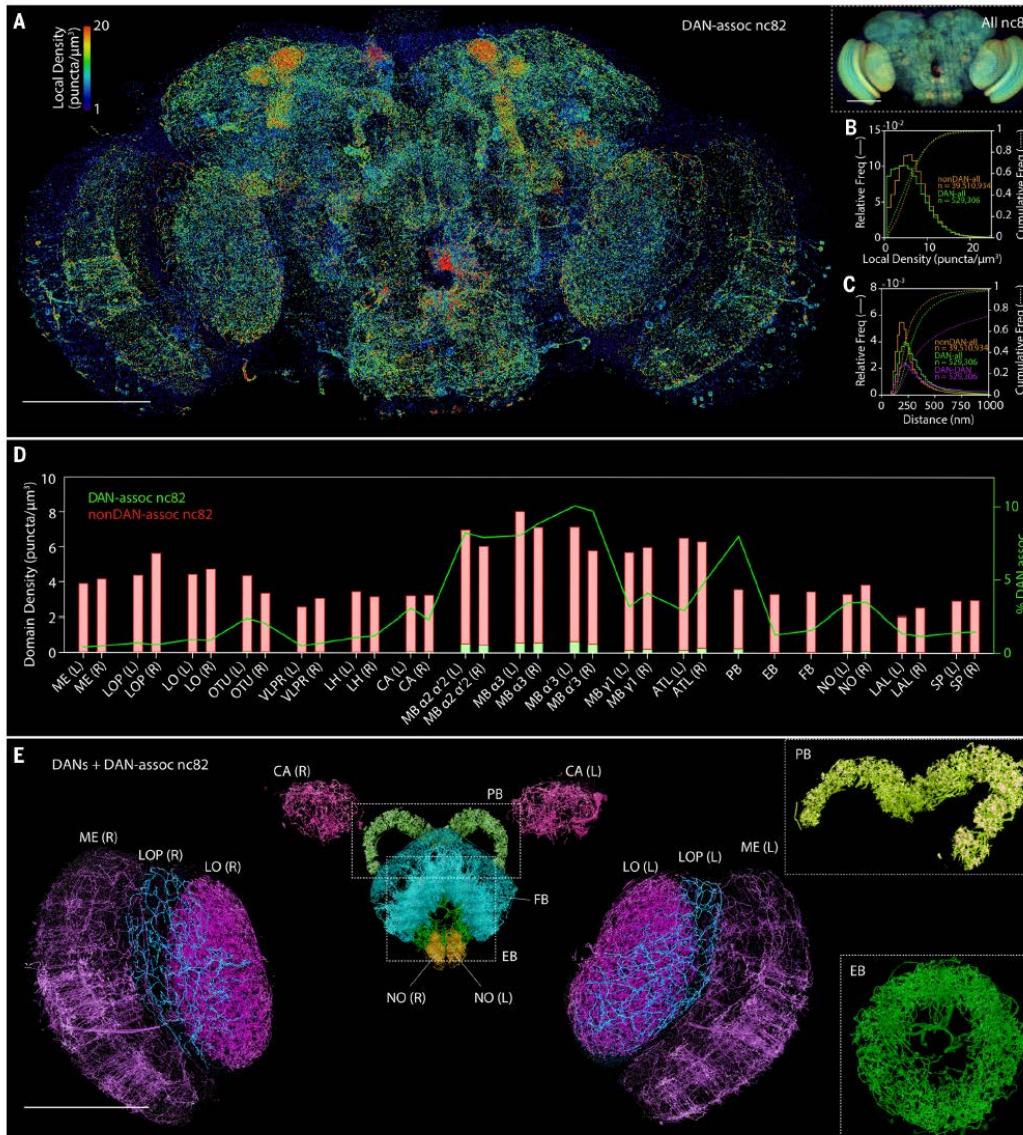
- Nucleic Acid
  - Genetic information for identification
  - Diseases, bacterium, virus, pathogen
  - PCR with molecular fluorophore, State of the Art
  - Expansive, Non-portable, Non-multiplexing
- Proteins
  - Cancers and diseases, unusual high concentration of marker
  - ELISA (~pM) with molecular fluorophore
  - No PCR version

# Nanomedicine

## Cancer Hallmark



# Bioimaging



# Review of General Chemistry

1	<b>H</b>	IA	0
2	<b>Li</b>	IIA	<b>He</b>
3	<b>Mg</b>	11	2
4	<b>Ca</b>	12	<b>Ne</b>
5	<b>Rb</b>	13	3
6	<b>Cs</b>	14	18
7	<b>Fr</b>	15	<b>Ar</b>
8	<b>Ra</b>	16	
9	<b>+Ac</b>	17	
10	<b>Rf</b>	18	
11	<b>Ha</b>	19	
12	<b>106</b>	20	
13	<b>107</b>	21	
14	<b>108</b>	22	
15	<b>109</b>	23	
16	<b>110</b>	24	
17		25	
18		26	
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79		87	
80		88	
81		89	
82		104	
83		105	
84		106	
85		107	
86		108	
87		109	
88		110	

\* Lanthanide Series

58	59	60	61	62	63	64	65	66	67	68	69	70	71
<b>Ce</b>	<b>Pr</b>	<b>Nd</b>	<b>Pm</b>	<b>Sm</b>	<b>Eu</b>	<b>Gd</b>	<b>Tb</b>	<b>Dy</b>	<b>Ho</b>	<b>Er</b>	<b>Tm</b>	<b>Yb</b>	<b>Lu</b>

+ Actinide Series

90	91	92	93	94	95	96	97	98	99	100	101	102	103
<b>Th</b>	<b>Pa</b>	<b>U</b>	<b>Np</b>	<b>Pu</b>	<b>Am</b>	<b>Cm</b>	<b>Bk</b>	<b>Cf</b>	<b>Es</b>	<b>Fm</b>	<b>Md</b>	<b>No</b>	<b>Lr</b>

Legend - click to find out more...

H - gas



Non-Metals

Li - solid



Transition Metals

Br - liquid



Rare Earth Metals

Tc - synthetic



Halogens

Alkali Metals



Alkali Earth Metals



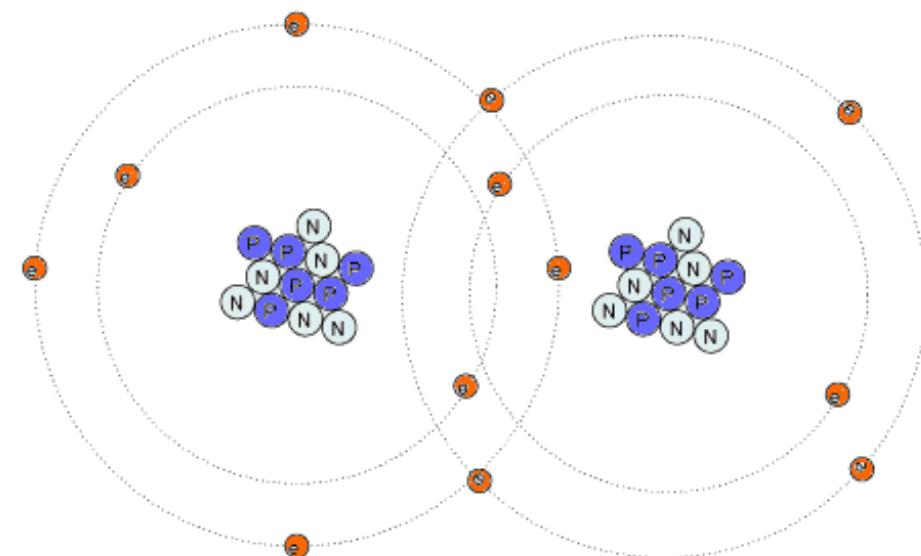
Other Metals



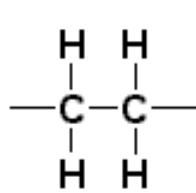
Inert Elements

# Chemical bond

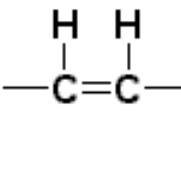
Hydrogen	$\text{H}^\bullet$	$\text{H}^\bullet$
Carbon	$\cdot\ddot{\text{C}}\cdot$	$\cdot\ddot{\text{C}}\cdot$
Water	$\text{H}:\ddot{\text{O}}:\text{H}$	$\text{H}-\ddot{\text{O}}-\text{H}$
Ethylene	$\begin{array}{c} \text{H} \ \text{H} \\   \ \   \\ \text{C} \ \text{:} \ \text{C} \\   \ \   \\ \text{H} \ \text{H} \end{array}$	$\begin{array}{c} \text{H} \ \text{H} \\   \ \   \\ \text{C} = \text{C} \\   \ \   \\ \text{H} \ \text{H} \end{array}$
Acetylene	$\text{H}:\ddot{\text{C}}\equiv\ddot{\text{C}}:\text{H}$	$\text{H}-\text{C}\equiv\text{C}-\text{H}$



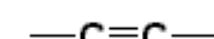
# Functional Groups



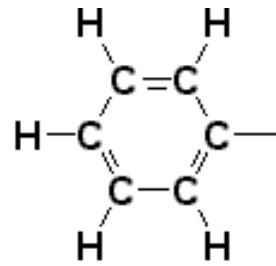
alkane



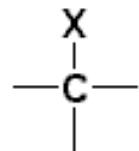
alkene



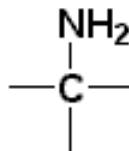
alkyne



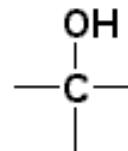
phenyl



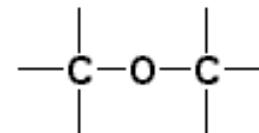
alkyl halide  
(X = F, Cl, Br, I)



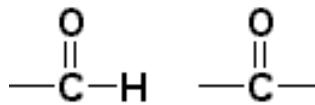
amine



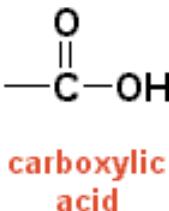
alcohol



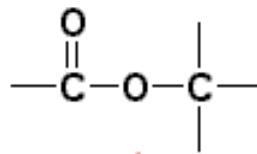
ether



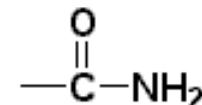
aldehyde



ketone



carboxylic acid



ester



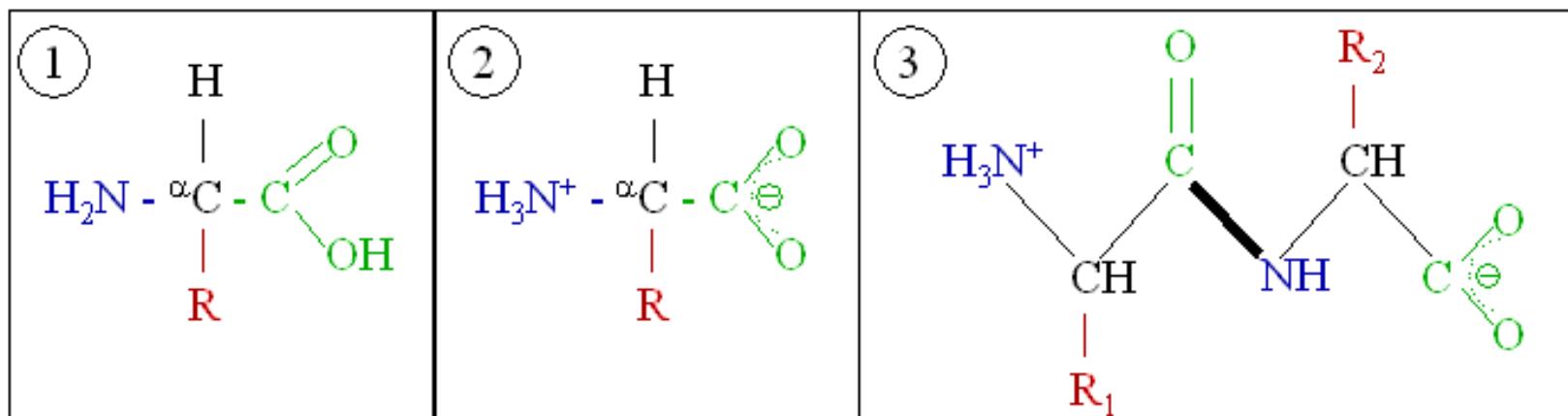
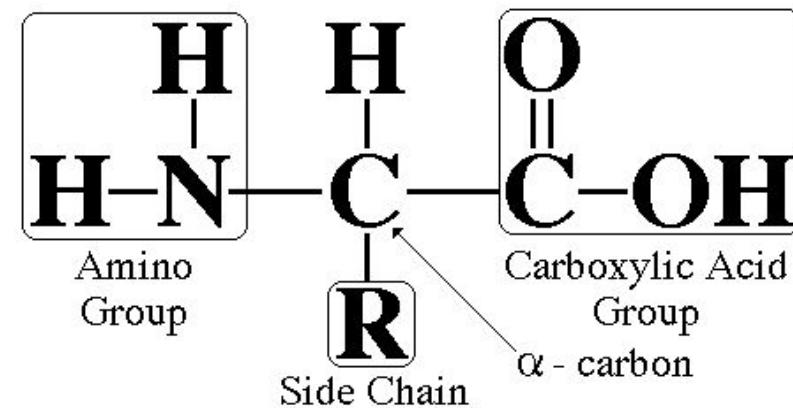
amide

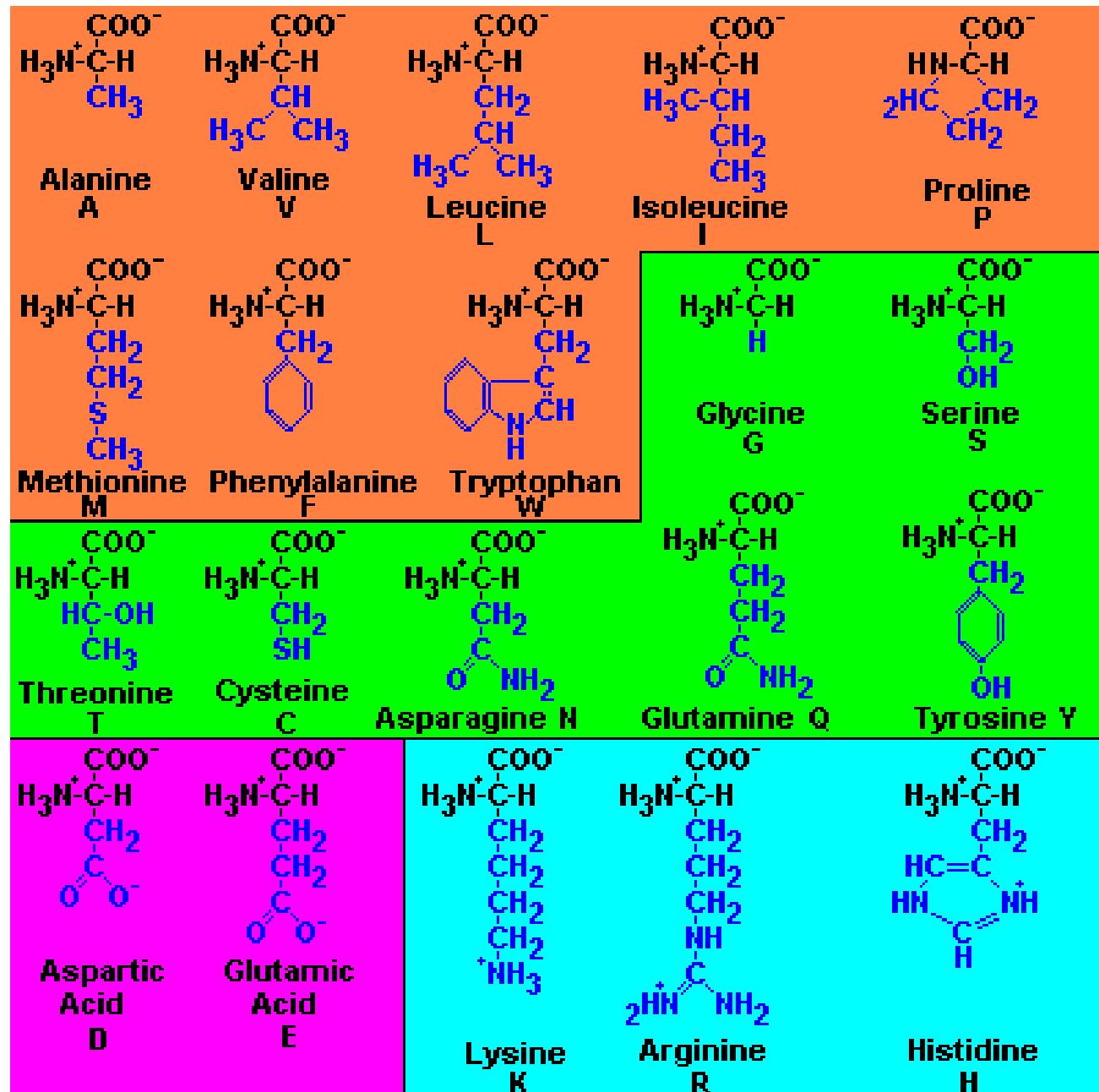
TABLE 18.1 Functional Groups of Importance in Biochemical Molecules

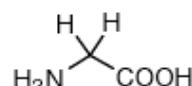
Functional Group	Structure	Type of Biomolecule
Amino group	$-\text{NH}_3^+$ , $-\text{NH}_2$	Amino acids and proteins (Sections 18.3, 18.7)
Hydroxyl group	$-\text{OH}$	Monosaccharides (carbohydrates) and glycerol: a component of triacylglycerols (lipids) (Sections 22.4, 24.2)
Carbonyl group	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}- \end{array}$	Monosaccharides (carbohydrates); in acetyl group ( $\text{CH}_3\text{CO}$ ) used to transfer carbon atoms during catabolism (Sections 22.4, 21.4, 21.8)
Carboxyl group	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{OH}, -\text{C}-\text{O}^- \end{array}$	Amino acids, proteins, and fatty acids (lipids) (Sections 18.3, 18.7, 24.2)
Amide group	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{N}- \end{array}$	Links amino acids in proteins; formed by reaction of amino group and carboxyl group (Section 18.7)
Carboxylic acid ester	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{O}-\text{R} \end{array}$	Triacylglycerols (and other lipids); formed by reaction of carboxyl group and hydroxyl group (Section 24.2)
Phosphates, mono-, di-, tri-	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{O}-\text{P}(\text{O})-\text{O}^- \end{array}$ $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{O}-\text{P}(\text{O})-\text{O}-\text{P}(\text{O})-\text{O}^- \end{array}$ $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{O}-\text{P}(\text{O})-\text{O}-\text{P}(\text{O})-\text{O}-\text{P}(\text{O})-\text{O}^- \end{array}$	ATP and many metabolism intermediates (Sections 17.8, 21.5, and throughout metabolism sections)
Hemiacetal group	$\begin{array}{c}   \\ -\text{C}-\text{OH} \\   \\ \text{OR} \end{array}$	Cyclic forms of monosaccharides; formed by a reaction of carbonyl group with hydroxyl group (Sections 16.7, 22.4)
Acetal group	$\begin{array}{c}   \\ -\text{C}-\text{OR} \\   \\ \text{OR} \end{array}$	Connects monosaccharides in disaccharides and larger carbohydrates; formed by reaction of carbonyl group with hydroxyl group (Sections 16.7, 22.7, 22.9)

# Amino Acid

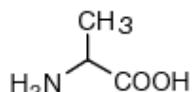
# Amino Acid Structure



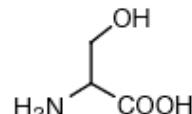


**Small**

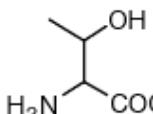
Glycine (Gly, G)  
MW: 57.05



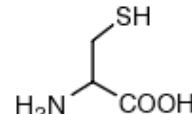
Alanine (Ala, A)  
MW: 71.09

**Nucleophilic**

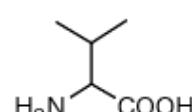
Serine (Ser, S)  
MW: 87.08,  $pK_a \sim 16$



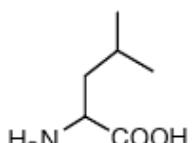
Threonine (Thr, T)  
MW: 101.11,  $pK_a \sim 16$



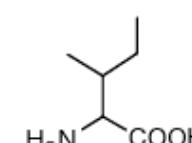
Cysteine (Cys, C)  
MW: 103.15,  $pK_a = 8.35$

**Hydrophobic**

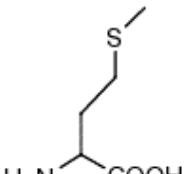
Valine (Val, V)  
MW: 99.14



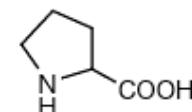
Leucine (Leu, L)  
MW: 113.16



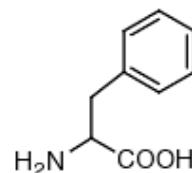
Isoleucine (Ile, I)  
MW: 113.16



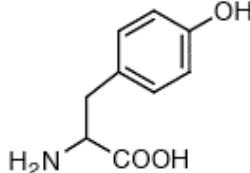
Methionine (Met, M)  
MW: 131.19



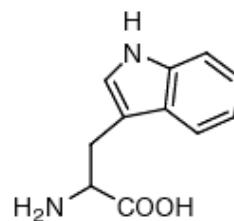
Proline (Pro, P)  
MW: 97.12

**Aromatic**

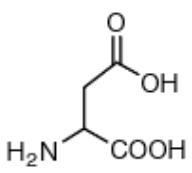
Phenylalanine (Phe, F)  
MW: 147.18



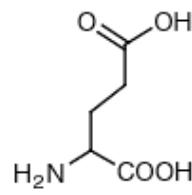
Tyrosine (Tyr, Y)  
MW: 163.18



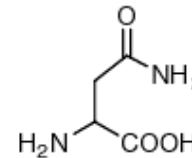
Tryptophan (Trp, W)  
MW: 186.21

**Acidic**

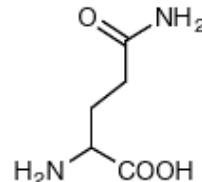
Aspartic Acid (Asp, D)  
MW: 115.09,  $pK_a = 3.9$



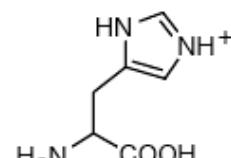
Glutamic Acid (Glu, E)  
MW: 129.12,  $pK_a = 4.07$

**Amide**

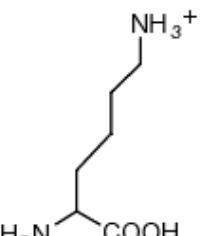
Asparagine (Asn, N)  
MW: 114.11



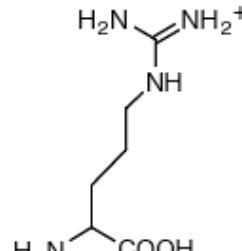
Glutamine (Gln, Q)  
MW: 128.14

**Basic**

Histidine (His, H)  
MW: 137.14,  $pK_a = 6.04$



Lysine (Lys, K)  
MW: 128.17,  $pK_a = 10.79$

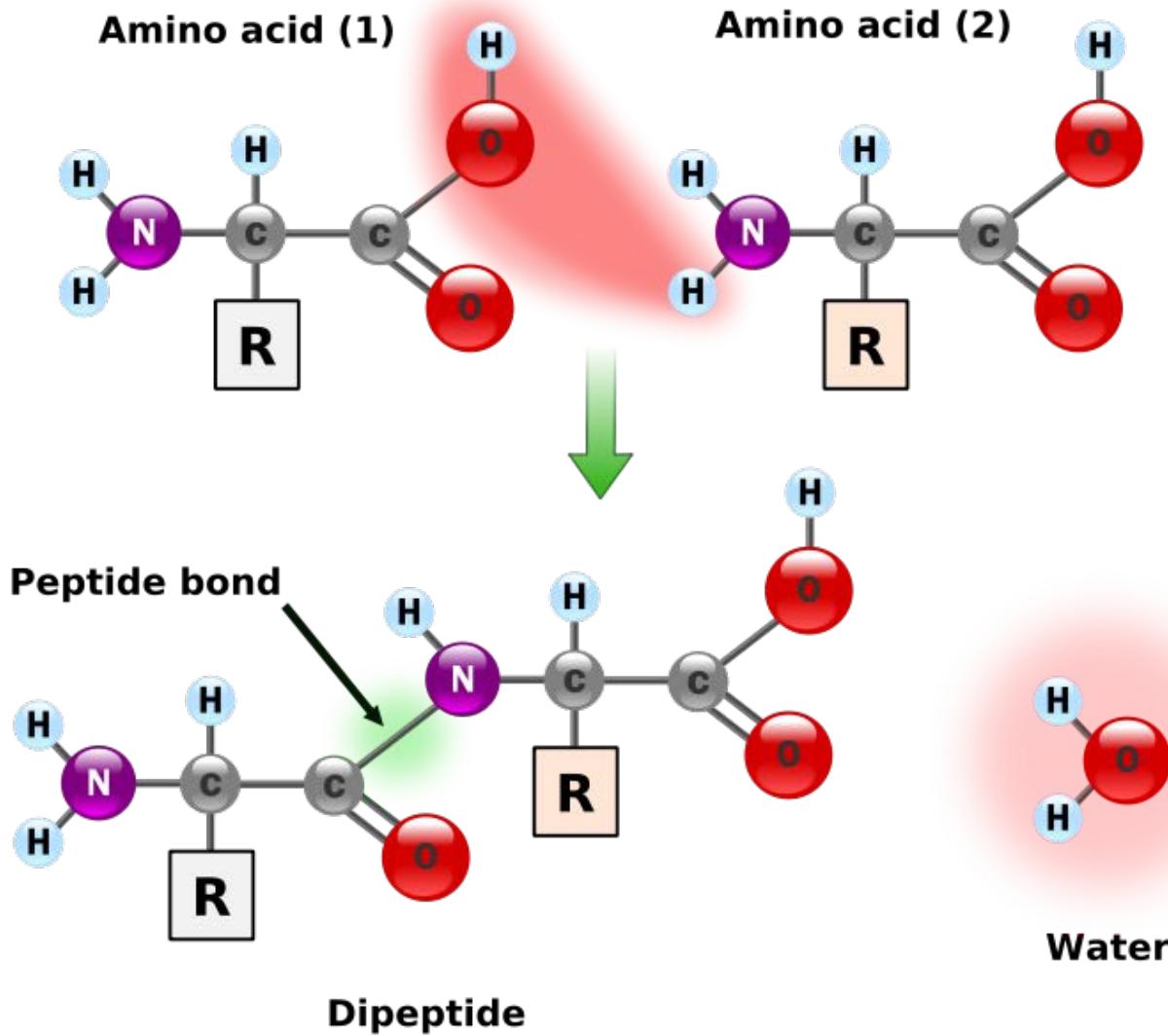


Arginine (Arg, R)  
MW: 156.19,  $pK_a = 12.48$

# Protein Structure and Function

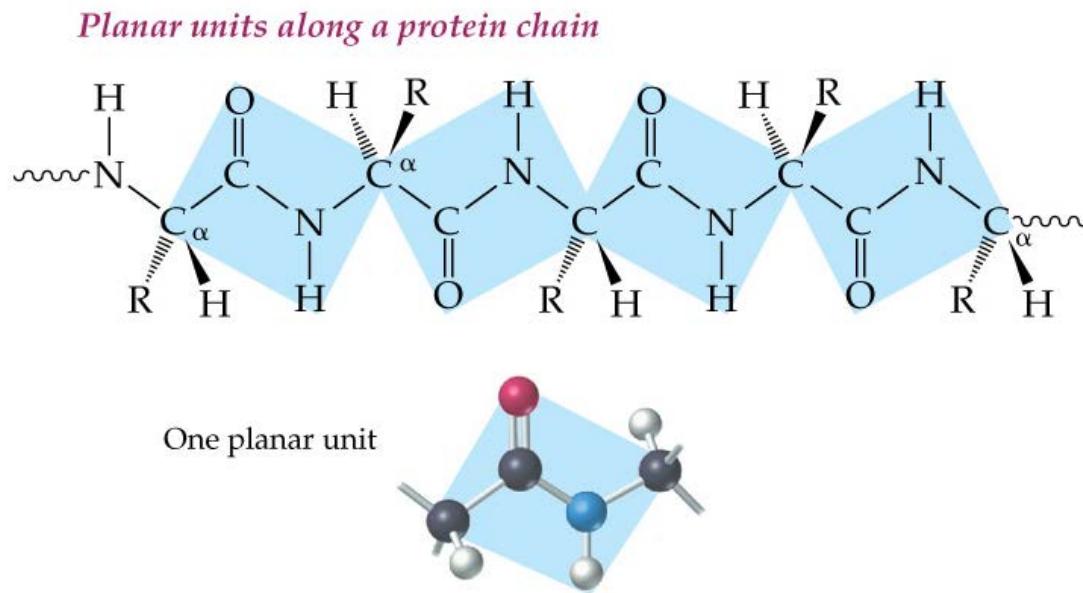
- Proteins are **polymers** of amino acids.
- Each amino acids in a protein contains a amino group,  $-\text{NH}_2$ , a carboxyl group,  $-\text{COOH}$ , and an R group, all bonded to the central carbon atom. The R group may be a hydrocarbon or they may contain functional group.
- All amino acids present in a proteins are  **$\alpha$ -amino acids** in which the amino group is bonded to the carbon next to the carboxyl group.
- Two or more amino acids can join together by forming amide bond, which is known as a **peptide bond** when they occur in proteins.

# Peptide bond



# Primary Protein Structure

- Primary structure of a proteins is the sequence of amino acids connected by peptide bonds. Along the backbone of the proteins is a chain of alternating peptide bonds and  $\alpha$ -carbons and the amino acid side chains are connected to these



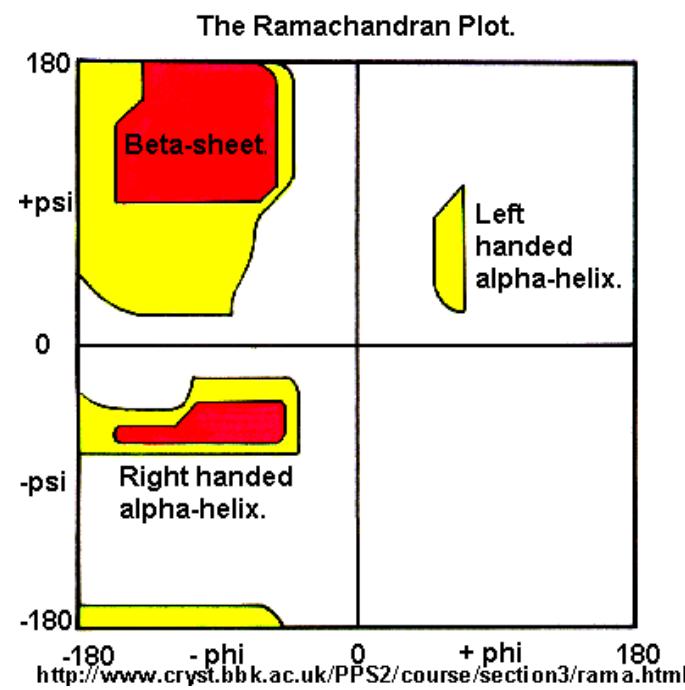
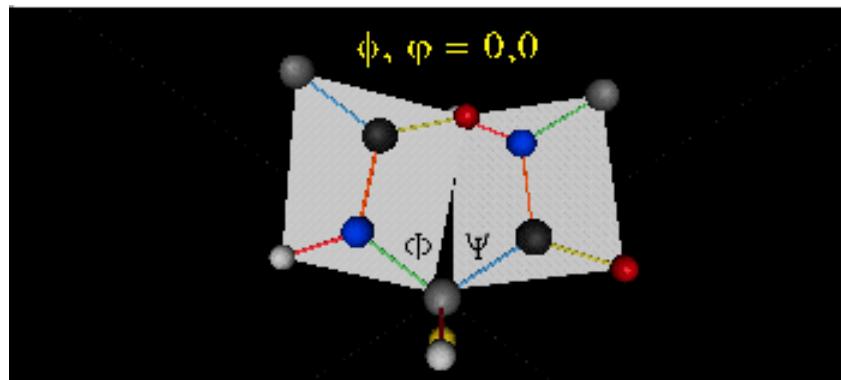
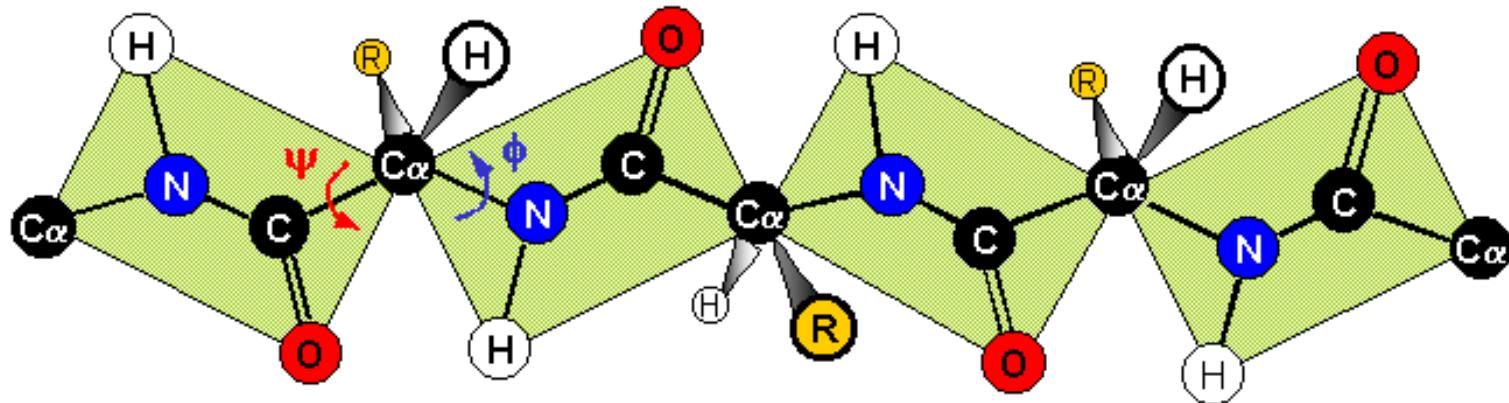
- By convention, peptides and proteins are always written with the amino terminal amino acid (N-terminal) on the left and carboxyl-terminal amino acid (C-terminal) on the right.

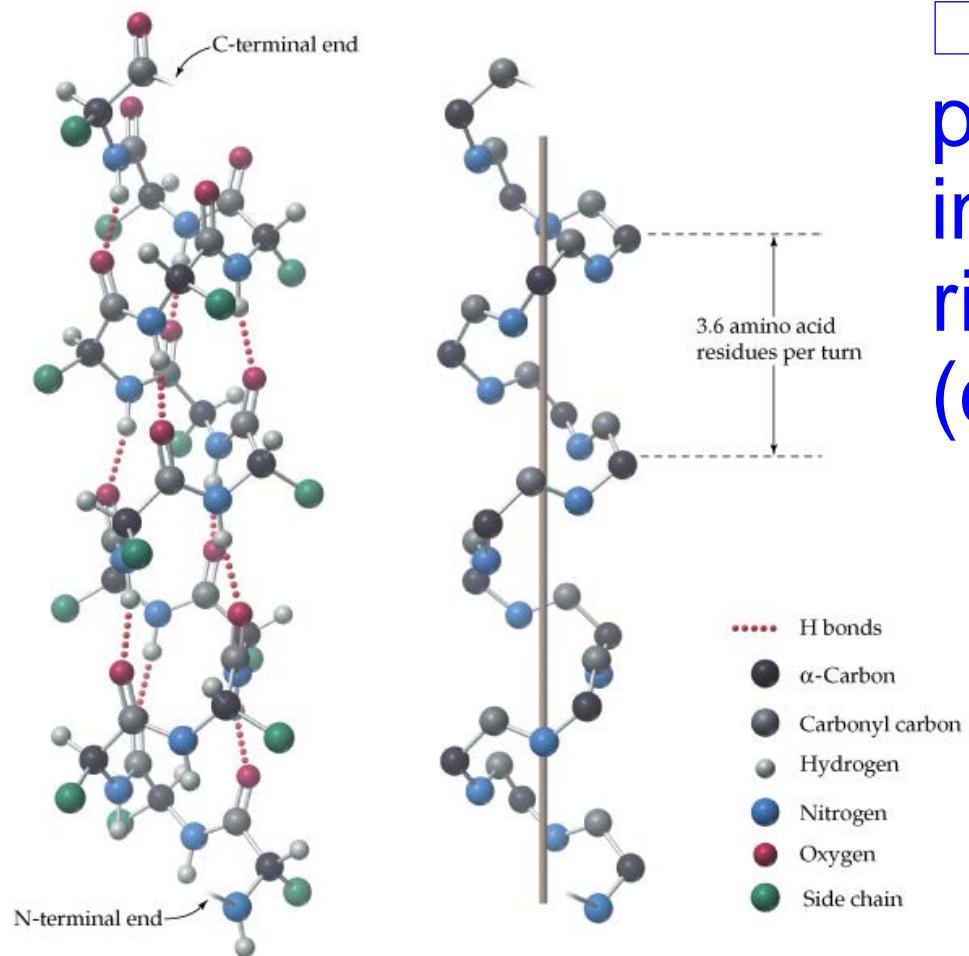
N  C

# Secondary Protein Structure

- Secondary structure of a protein is the arrangement of polypeptide backbone of the protein in space. The secondary structure includes two kinds of repeating pattern known as the  *$\alpha$ -helix* and  *$\beta$ -sheet*.
- Hydrogen bonding between backbone atoms are responsible for both of these secondary structures.

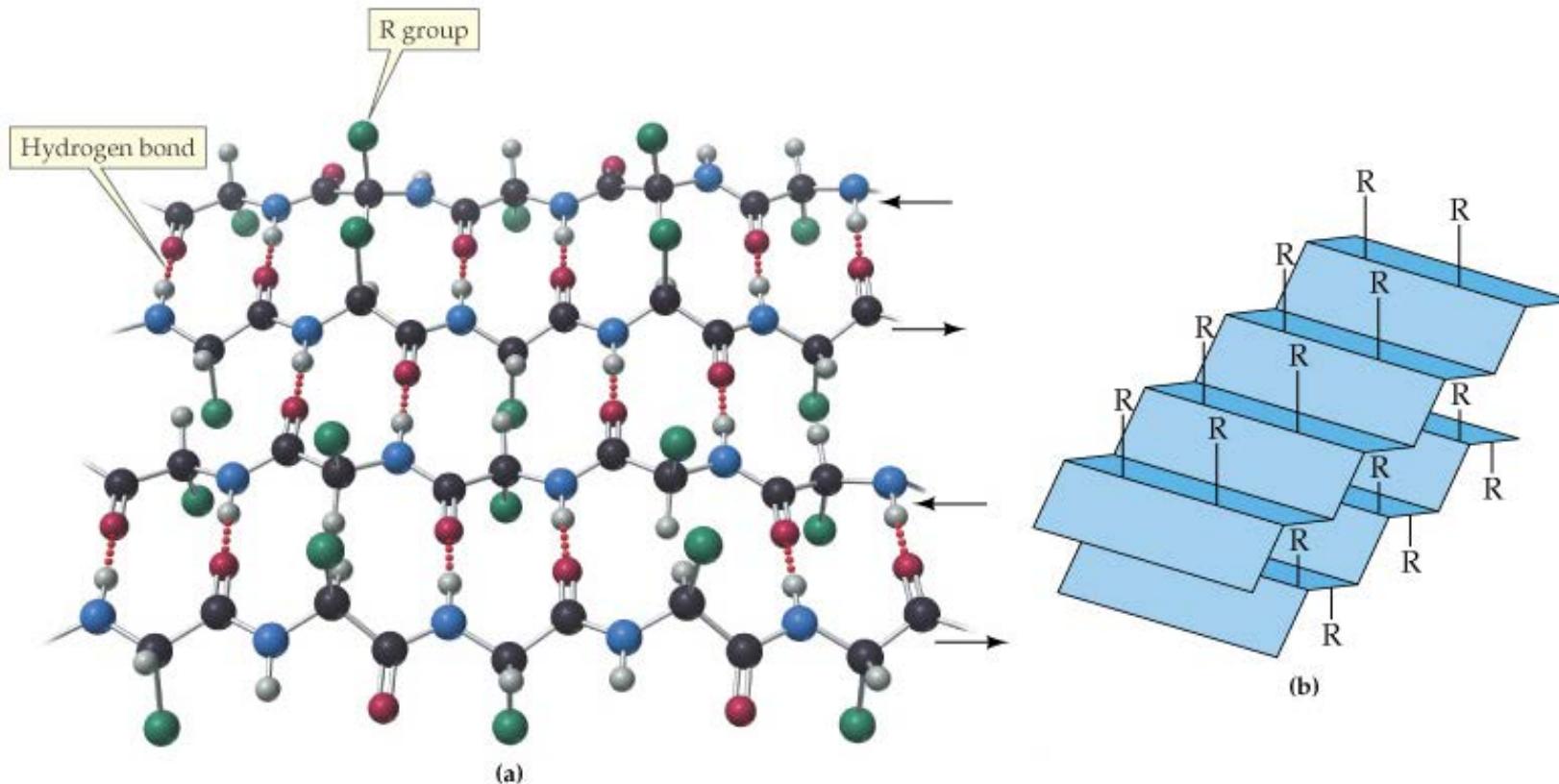
## FULLY EXTENDED POLYPEPTIDE CHAIN





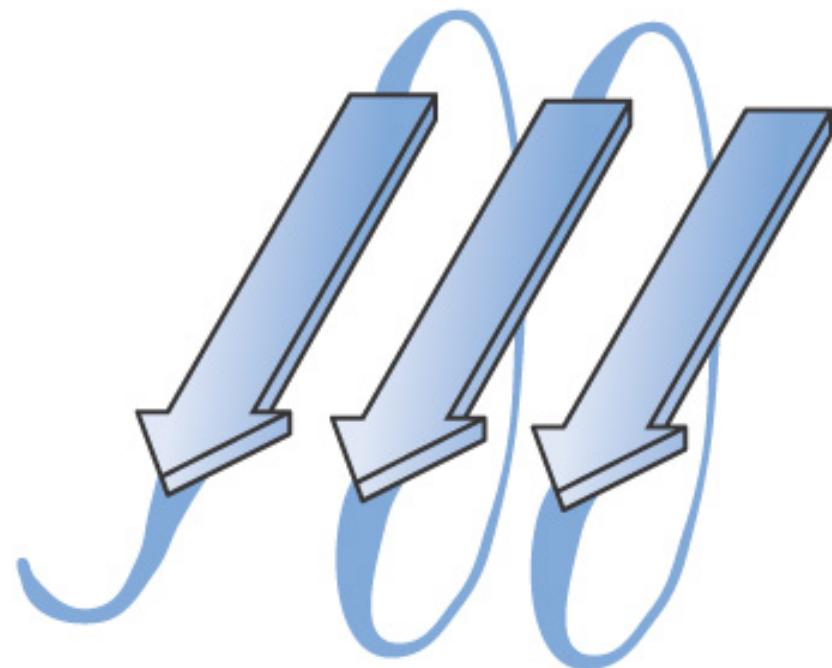
□  **$\alpha$ -Helix:** A single protein chain coiled in a spiral with a right-handed (clockwise) twist.

□  **$\beta$ -Sheet:** The polypeptide chain is held in place by hydrogen bonds between pairs of peptide units along neighboring backbone segments.





$\alpha$  helix



$\beta$  sheet

# Tertiary Protein Structure

- ***Tertiary Structure of a protein*** The overall three dimensional shape that results from the folding of a protein chain. Tertiary structure depends mainly on attractions of amino acid side chains that are far apart along the same backbone. Non-covalent interactions and disulfide covalent bonds govern tertiary structure.
- A protein with the shape in which it exists naturally in living organisms is known as a *native protein*.

# Shape-Determining Interactions in Proteins

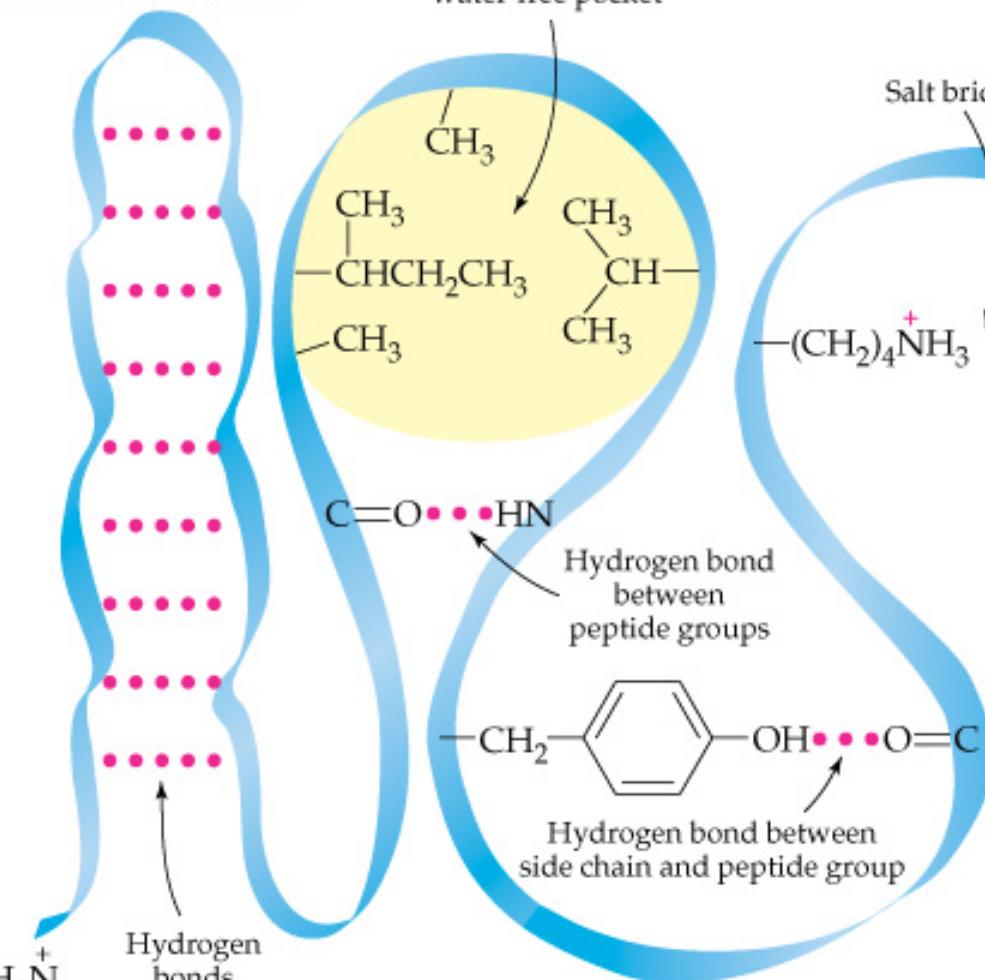
- The essential structure-function relationship for each protein depends on the polypeptide chain being held in its necessary shape by the interactions of atoms in the side chains.

- Protein shape determining interactions are summarized below:
- Hydrogen bond between neighboring backbone segments.
- Hydrogen bonds of side chains with each other or with backbone atoms.
- Ionic attractions between side chain groups or salt bridge.
- Hydrophobic interactions between side chain groups.
- Covalent sulfur-sulfur bonds.

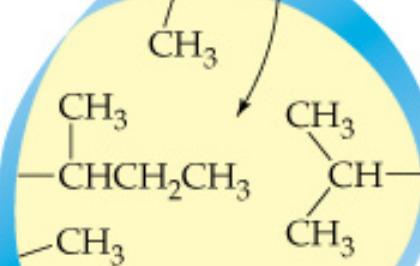


Pleated sheet structure

$\text{H}_3\text{N}^+$



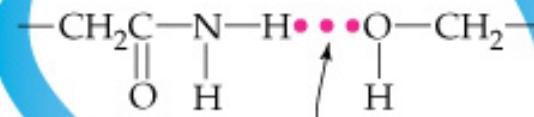
Hydrophobic interactions—  
water-free pocket



Salt bridge

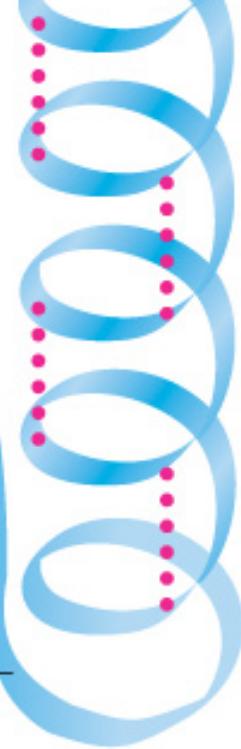


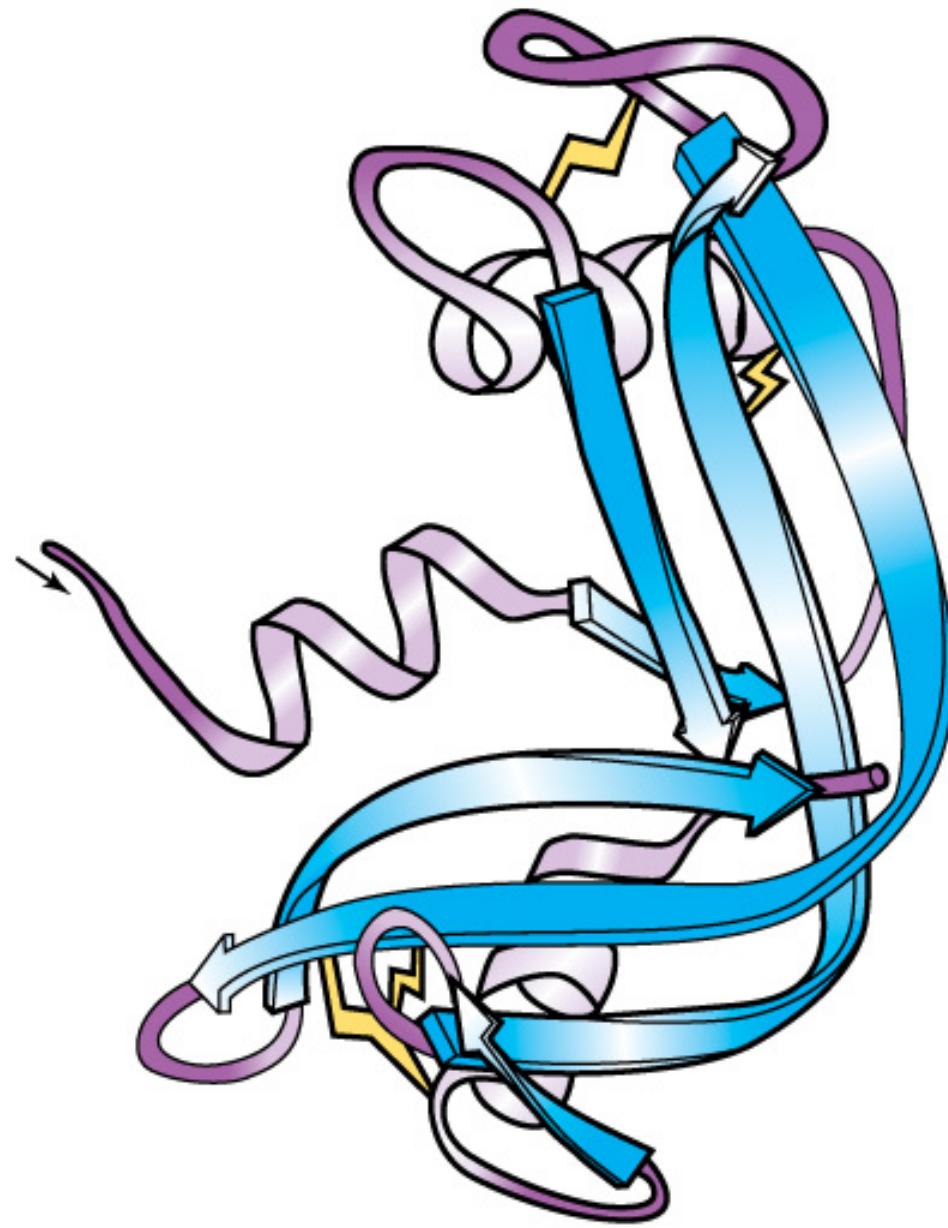
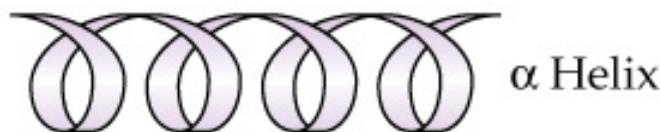
Hydrogen bond  
between side chains

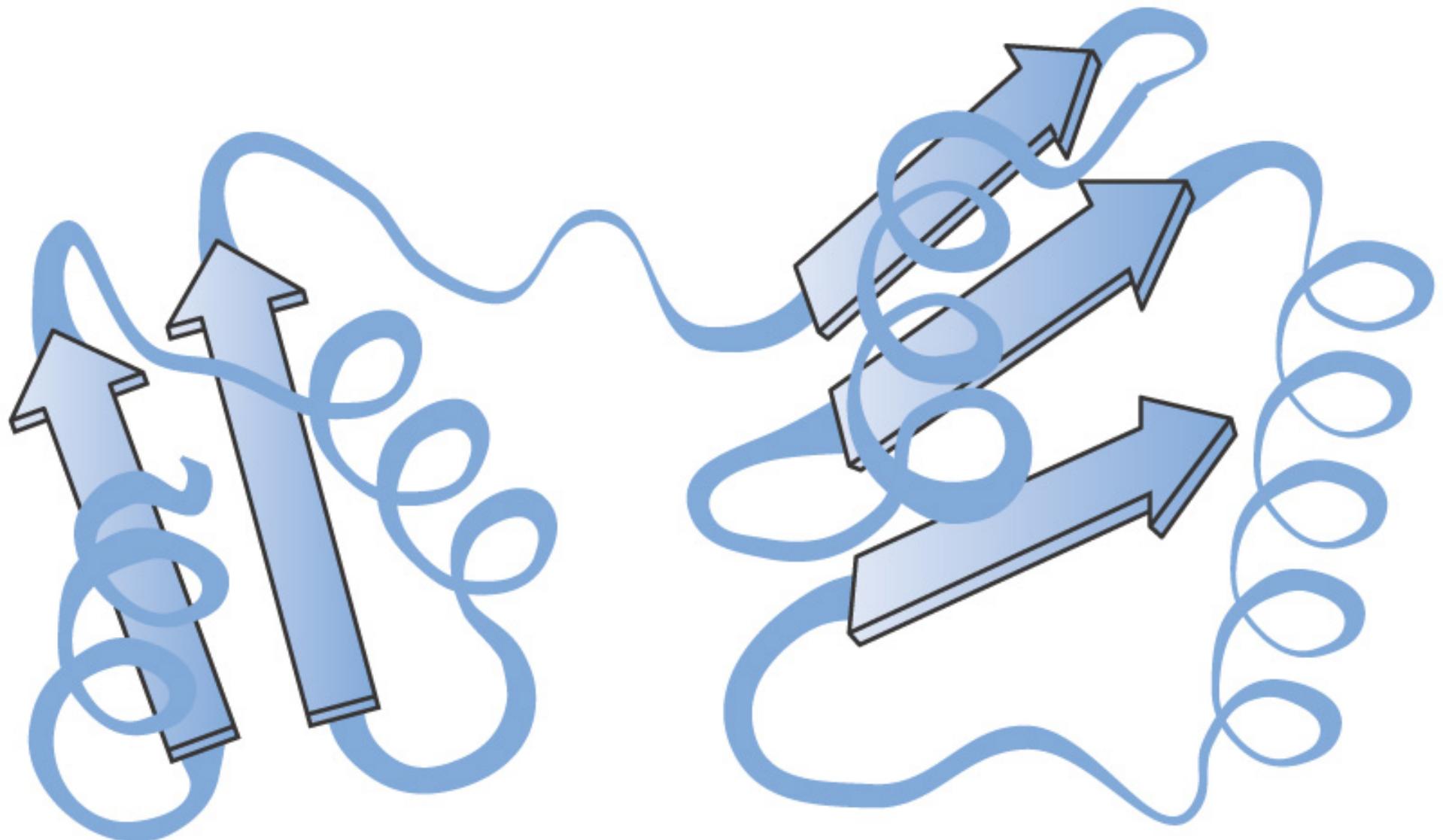


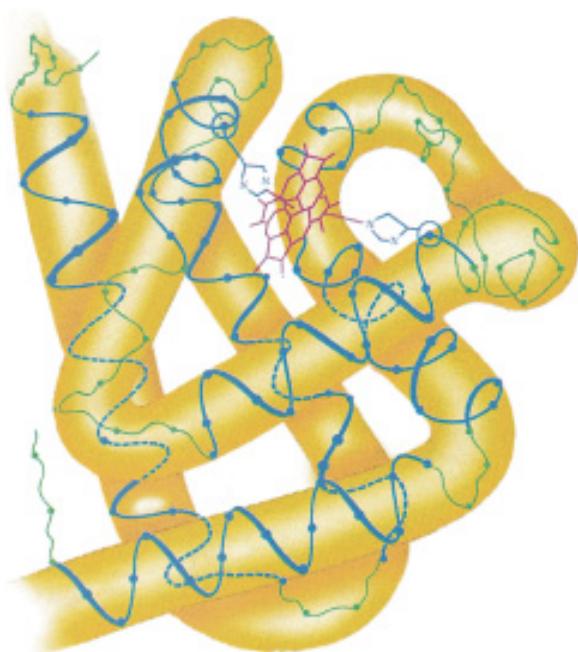
$\text{COO}^-$

Helical structure

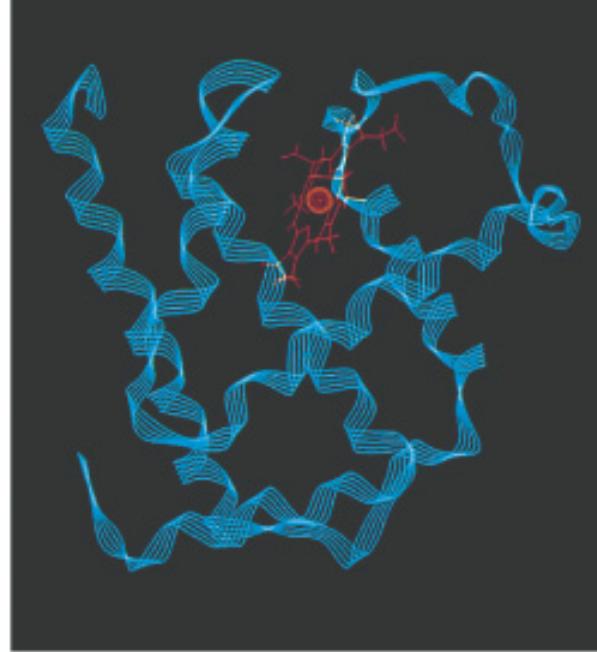




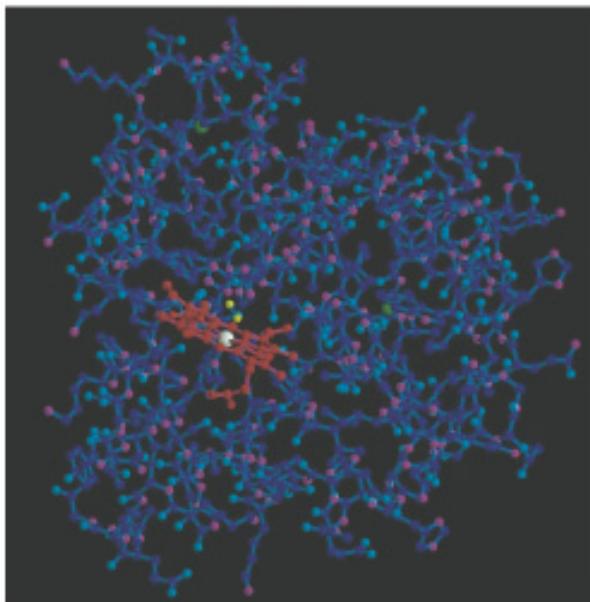




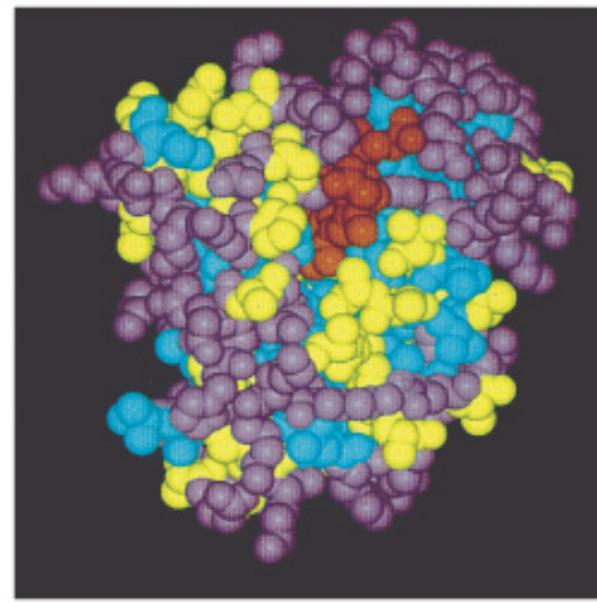
(a)



(b)



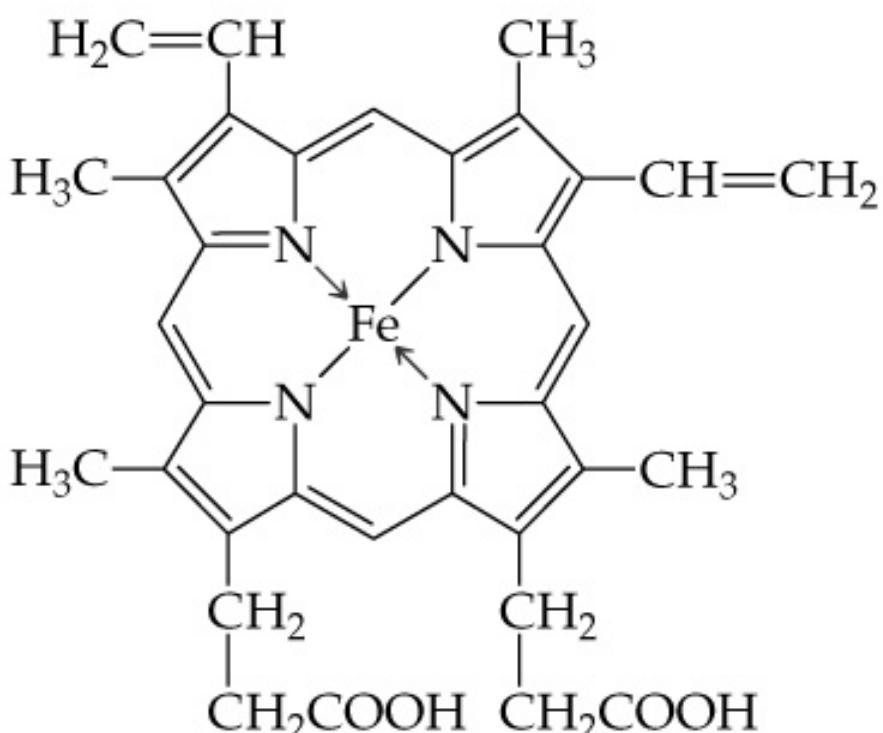
(c)



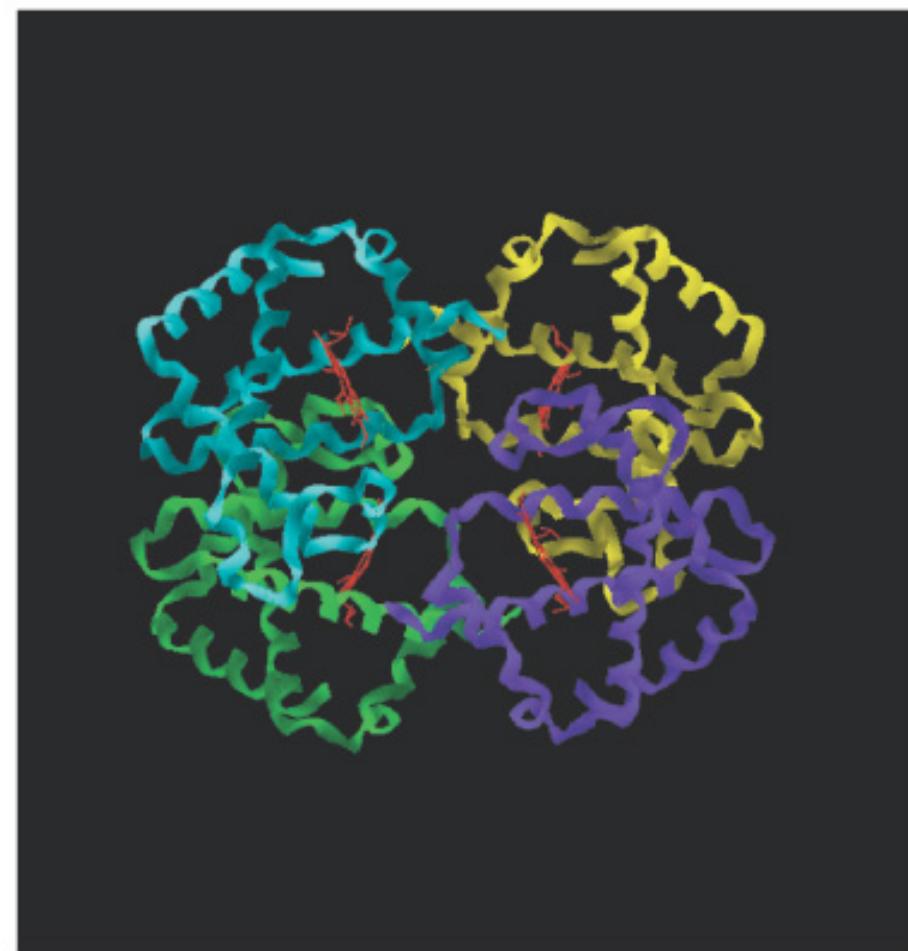
(d)

# Quaternary Protein Structure

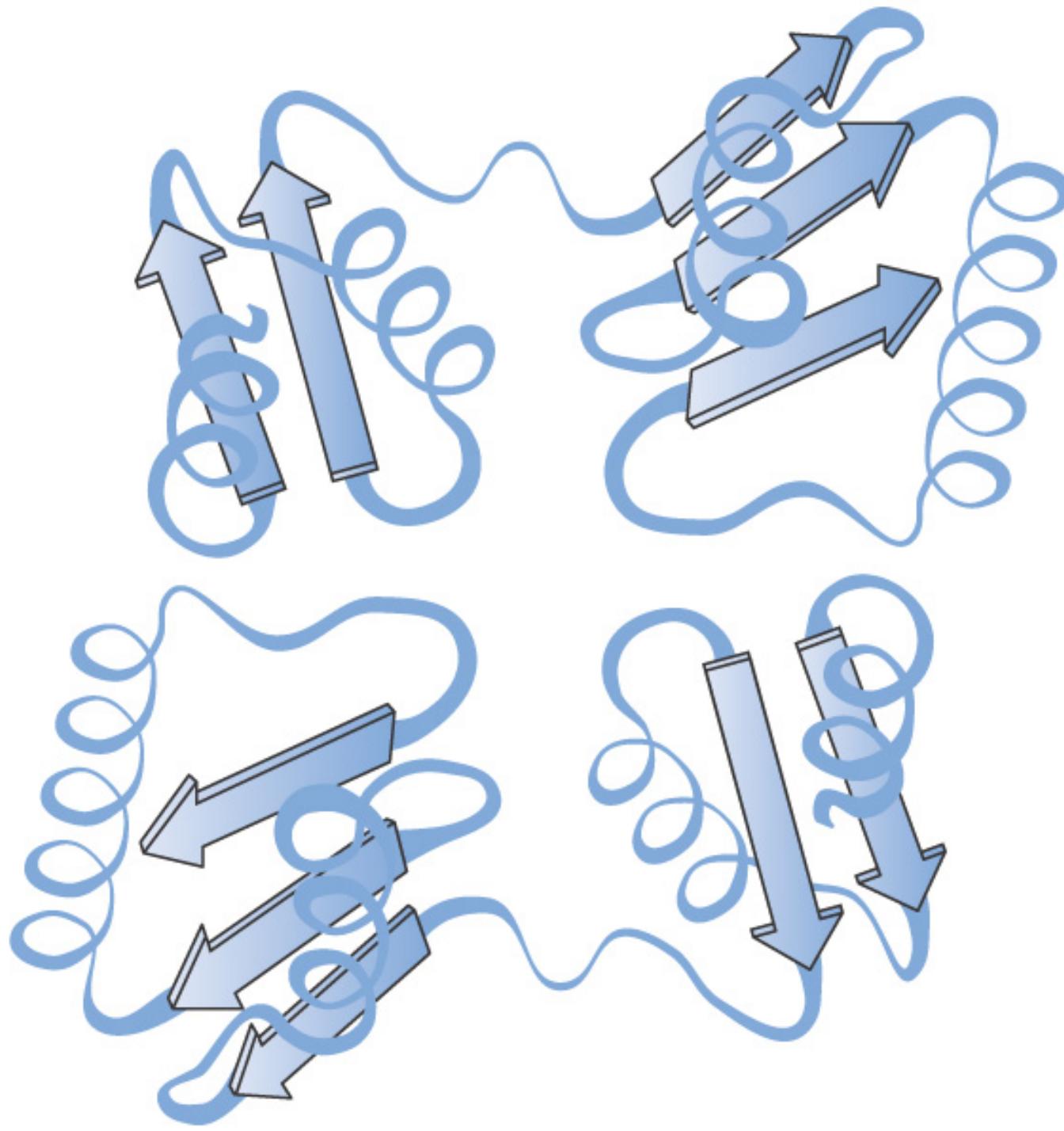
- ***Quaternary protein structure:*** The way in which two or more polypeptide sub-units associate to form a single three-dimensional protein unit. Non-covalent forces are responsible for quaternary structure essential to the function of proteins.

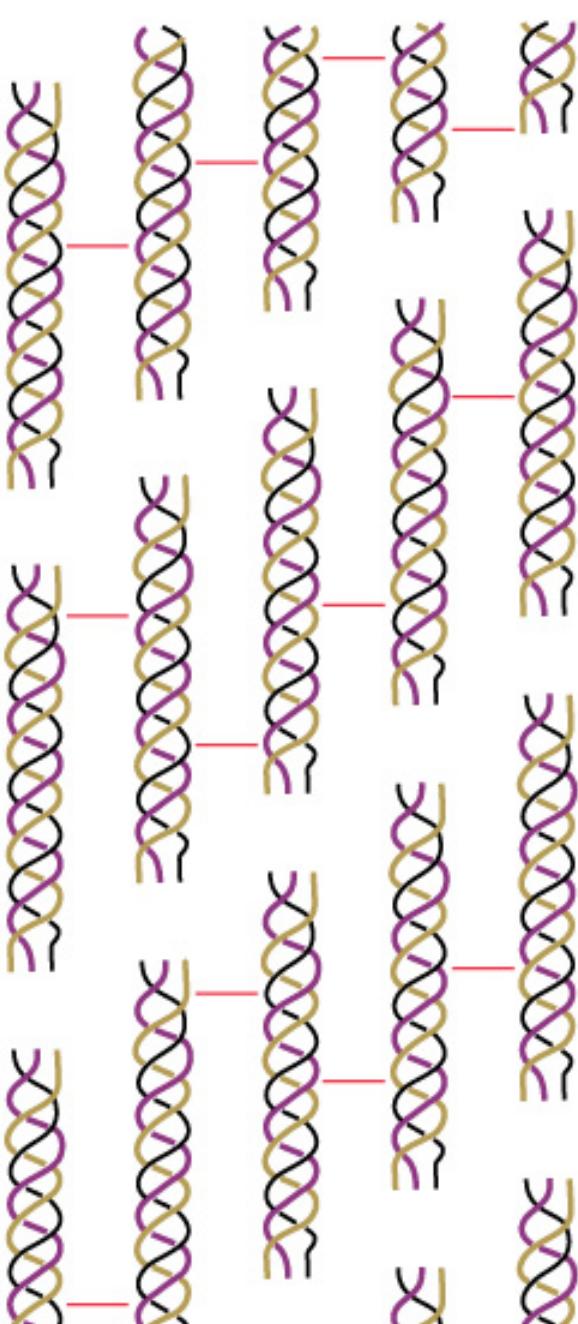
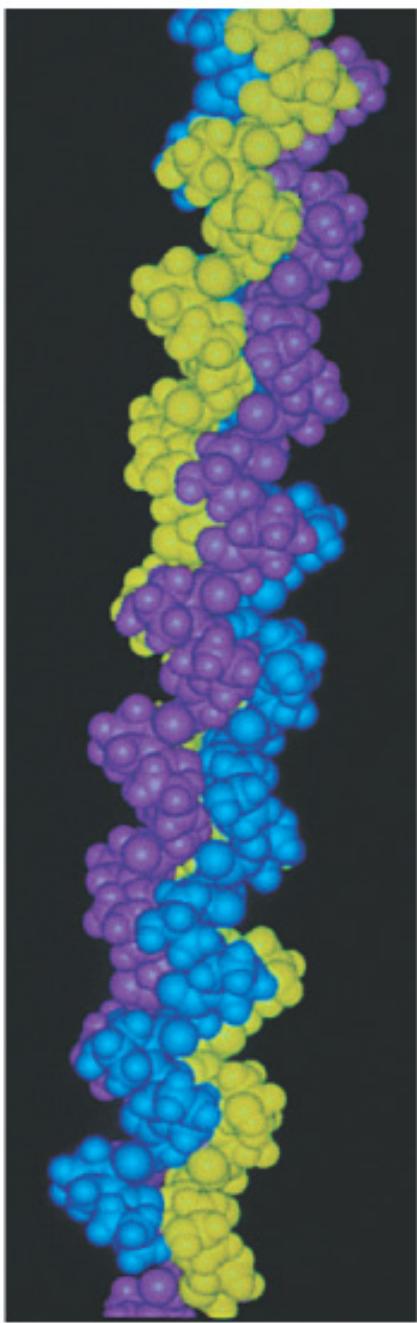
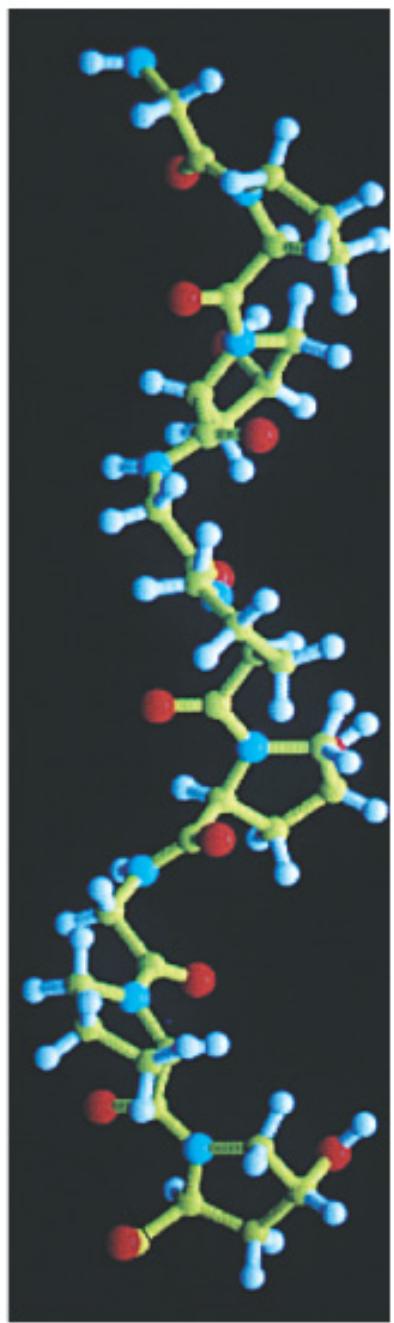


(a)



(b)



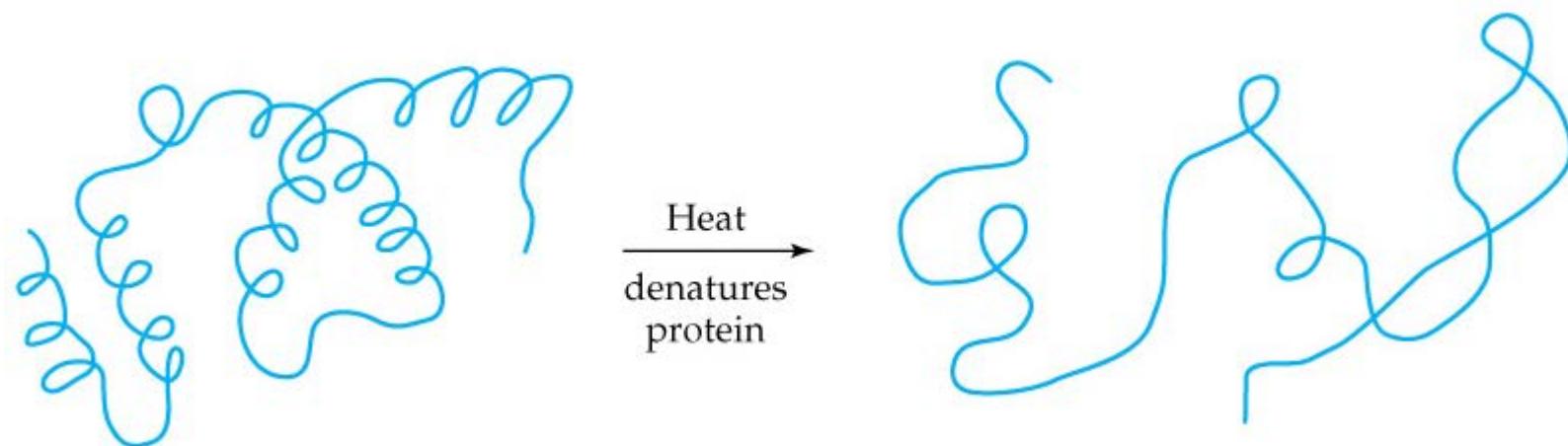


# Chemical Properties of Proteins

- *Protein hydrolysis:* In protein hydrolysis, peptide bonds are hydrolyzed to yield amino acids. This is reverse of protein formation.



- *Protein denaturation:* The loss of secondary, tertiary, or quaternary protein structure due to disruption of non-covalent interactions and or disulfide bonds that leaves peptide bonds and primary

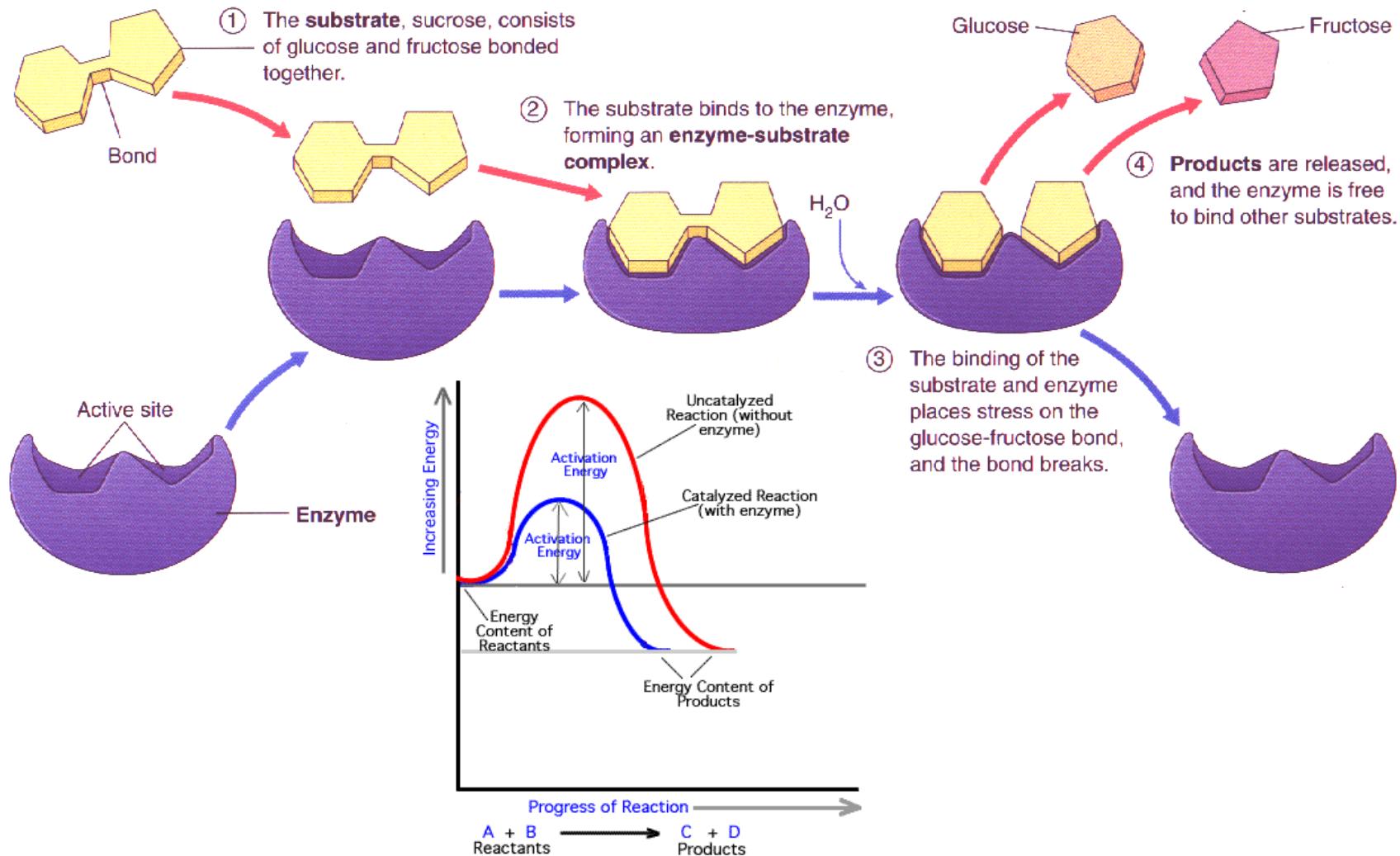


# Catalysis by Enzymes

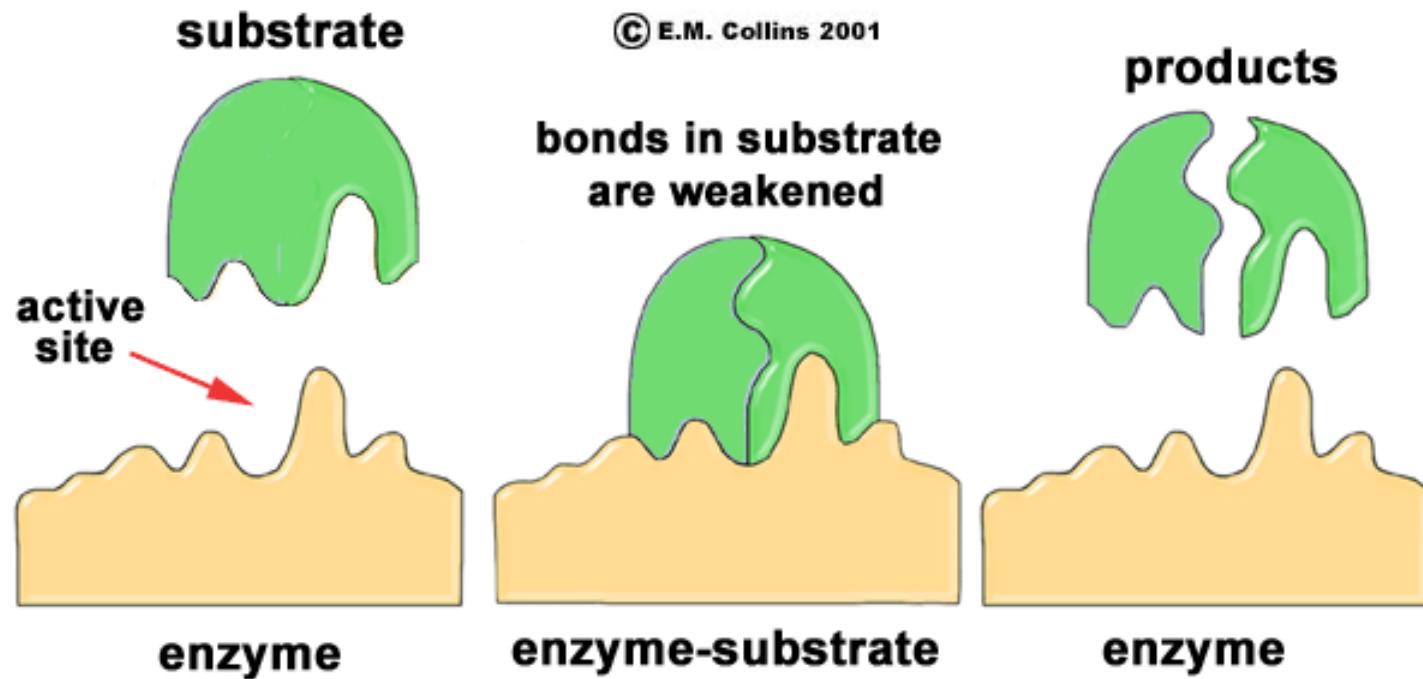
- **Enzyme** A protein that acts as a catalyst for a biochemical reaction.



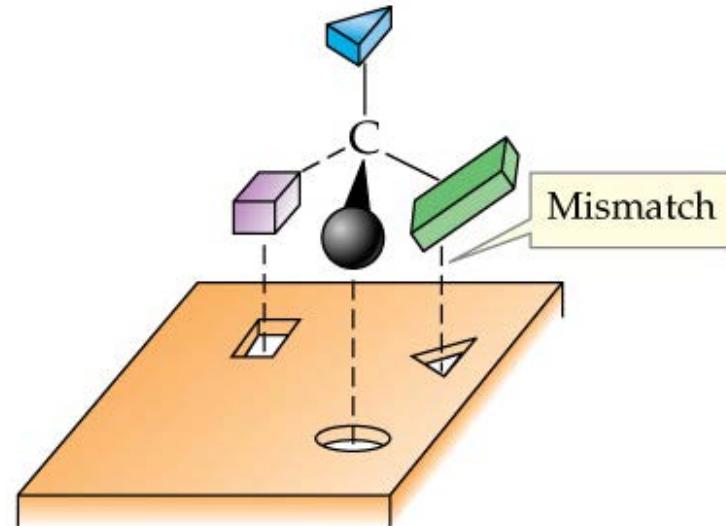
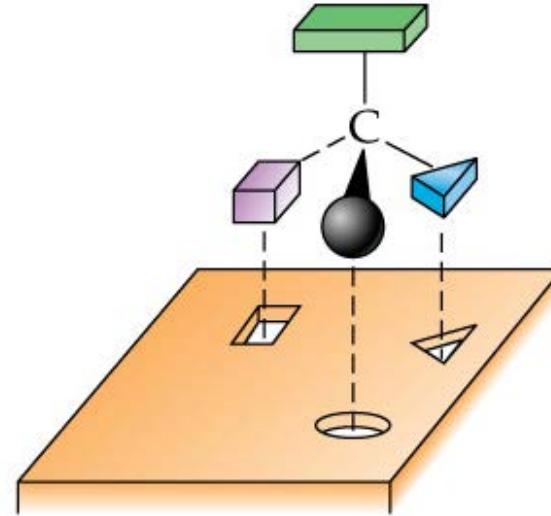
# Enzymatic Reaction



# Specificity



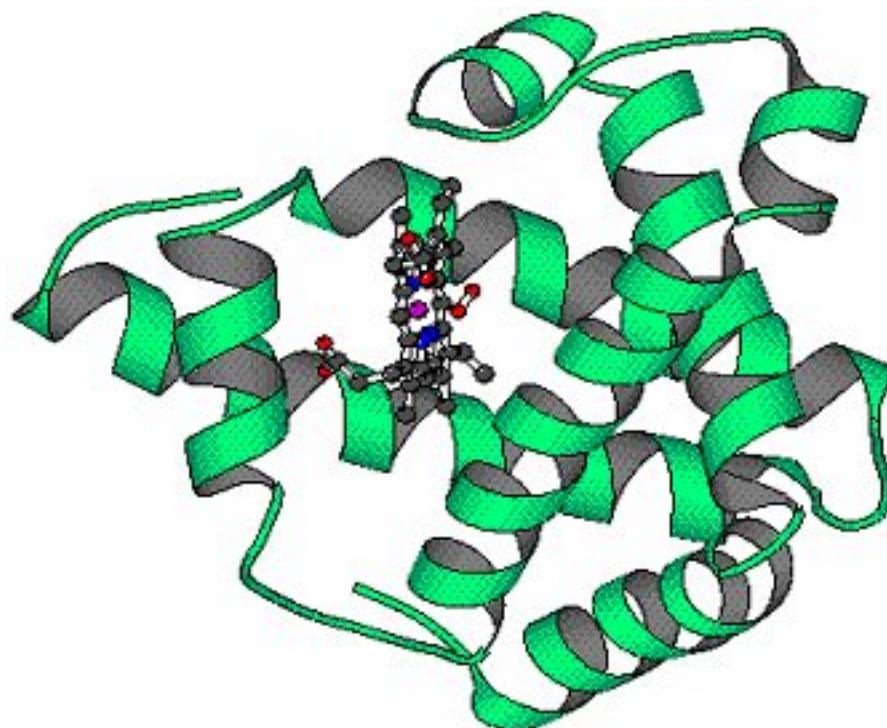
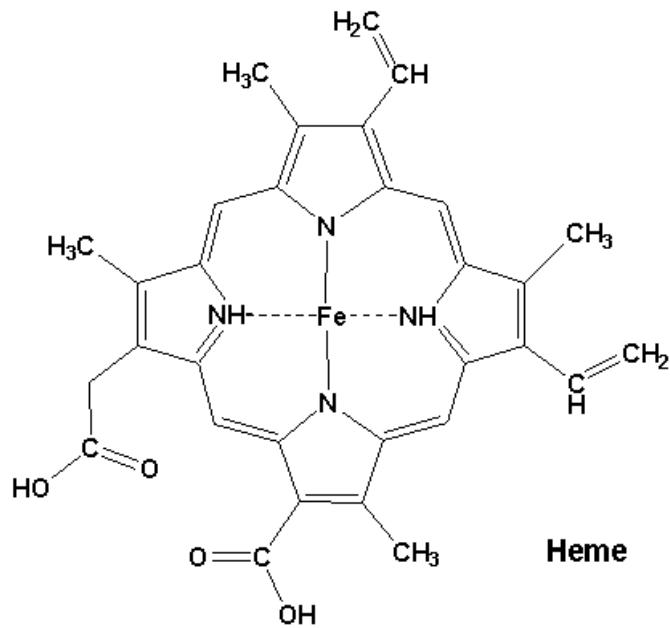
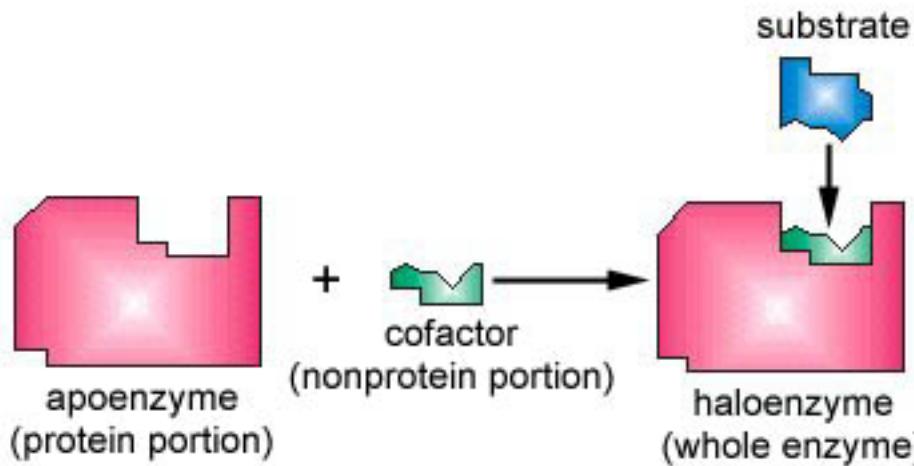
The specificity of an enzyme for one of two enantiomers is a matter of fit. One enantiomer fits better into the active site of the enzyme than the other enantiomer. Enzyme catalyzes reaction of the enantiomer that fits better into the active site of the enzyme.



# Enzyme Cofactors

- Many enzymes are conjugated proteins that require nonprotein portions known as **cofactors**.
- Some cofactors are metal ions, others are nonprotein organic molecules called **coenzymes**.
- An enzyme may require a metal-ion, a coenzyme, or both to function.

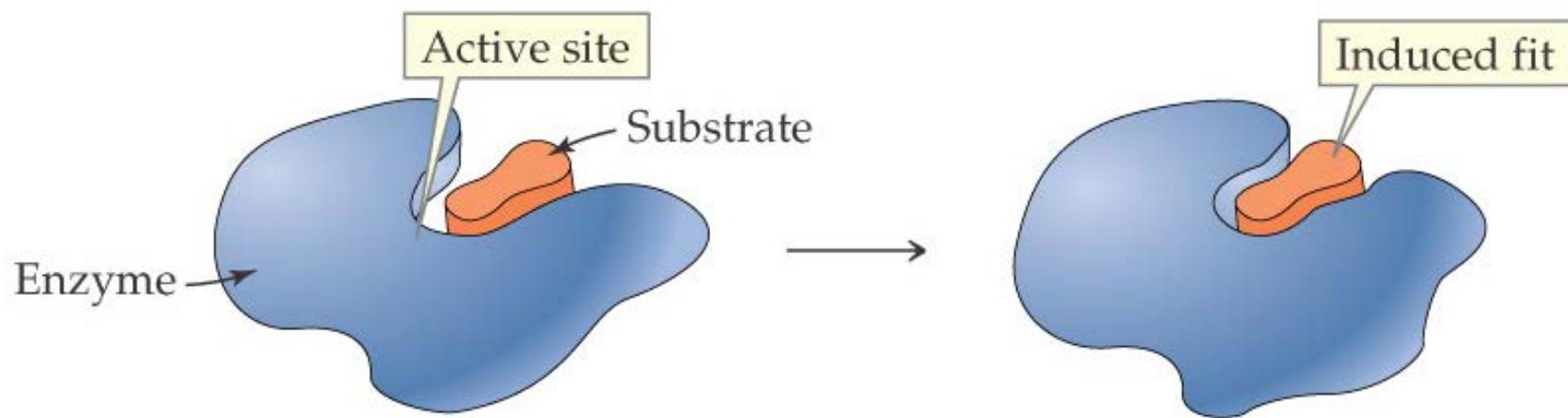
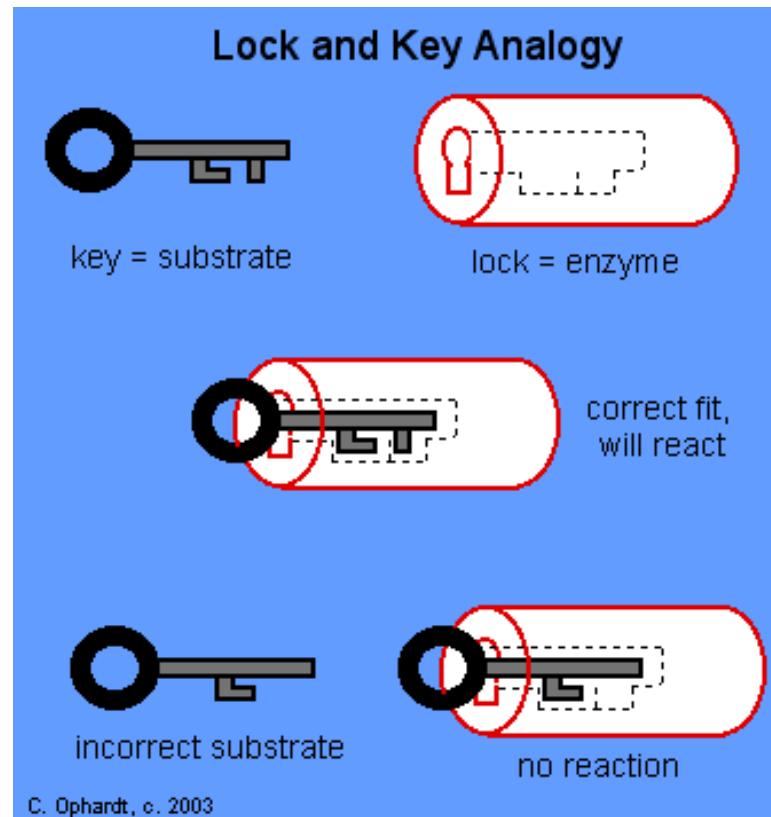
# Cofactor

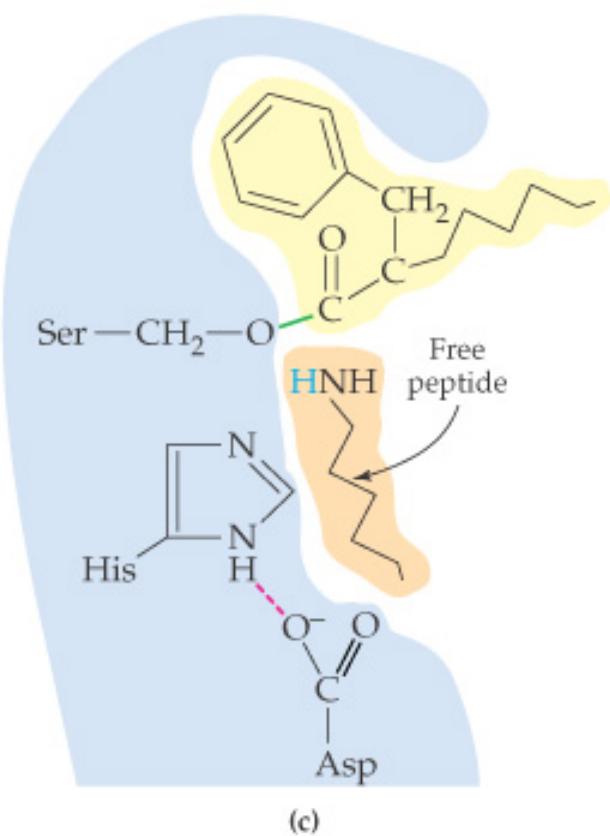
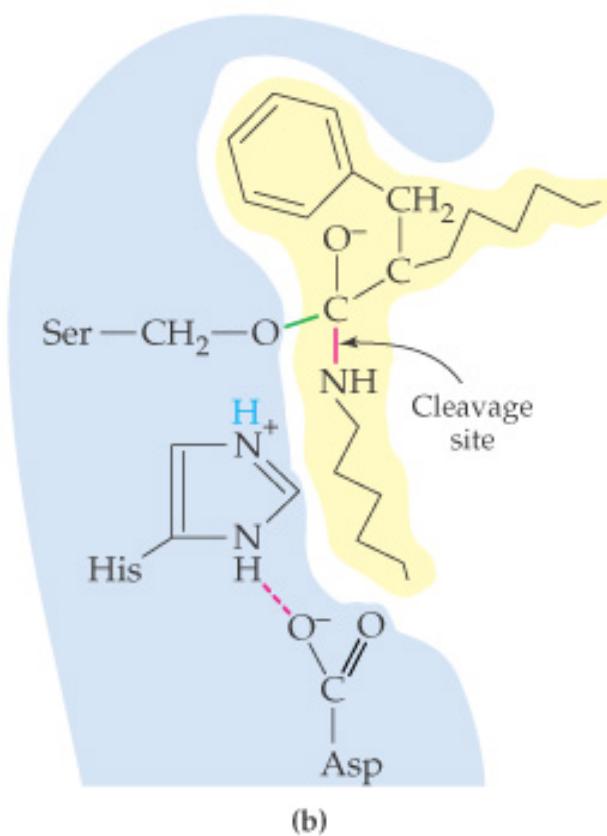
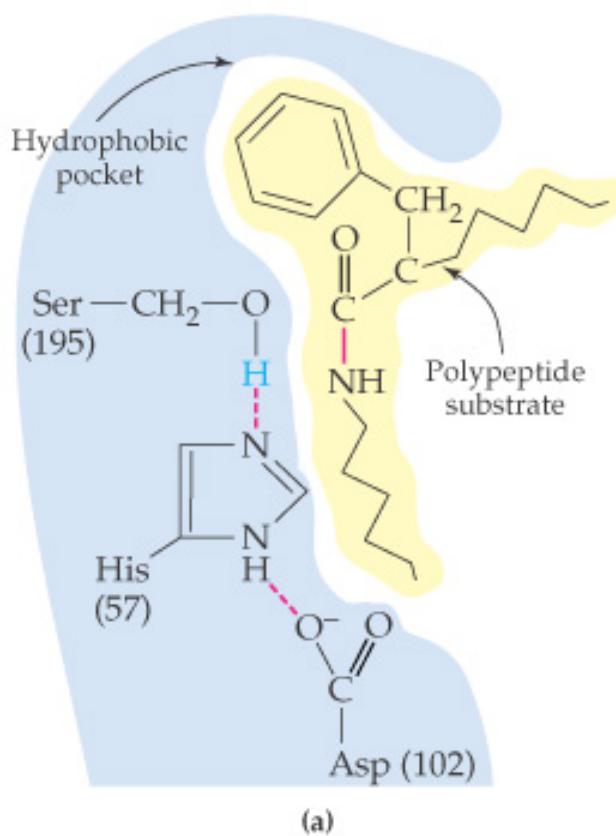


- Cofactors provide additional chemically active functional groups which are not present in the side chains of amino acids that made up the enzyme.
- Metal ions may anchor a substrate in the active site or may participate in the catalyzed reaction.

# How Enzyme Work

- Two modes are invoked to represent the interaction between substrate and enzymes. These are:
- ***Lock-and-key model:*** The substrate is described as fitting into the active site as a key fit into a lock.
- ***Induced-fit-model:*** The enzyme has a flexible active site that changes shape to accommodate the substrate and facilitate the reaction.





# 19.5 Effect of Concentration on Enzyme Activity

- Variation in concentration of enzyme or substrate alters the rate of enzyme catalyzed reactions.
- *Substrate concentration:* At low substrate concentration, the reaction rate is directly proportional to the substrate concentration. With increasing substrate concentration, the rate drops off as more of the active sites are occupied.

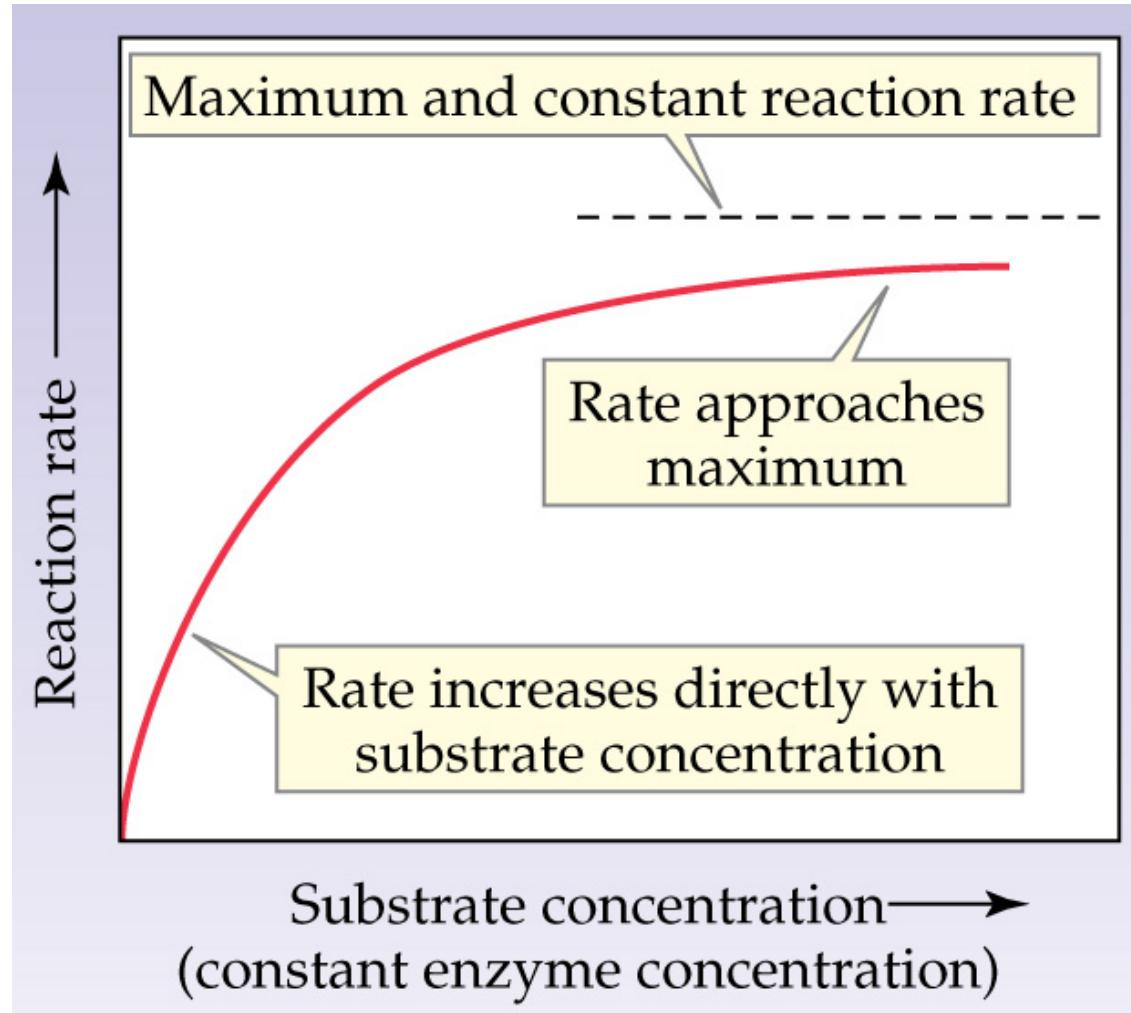
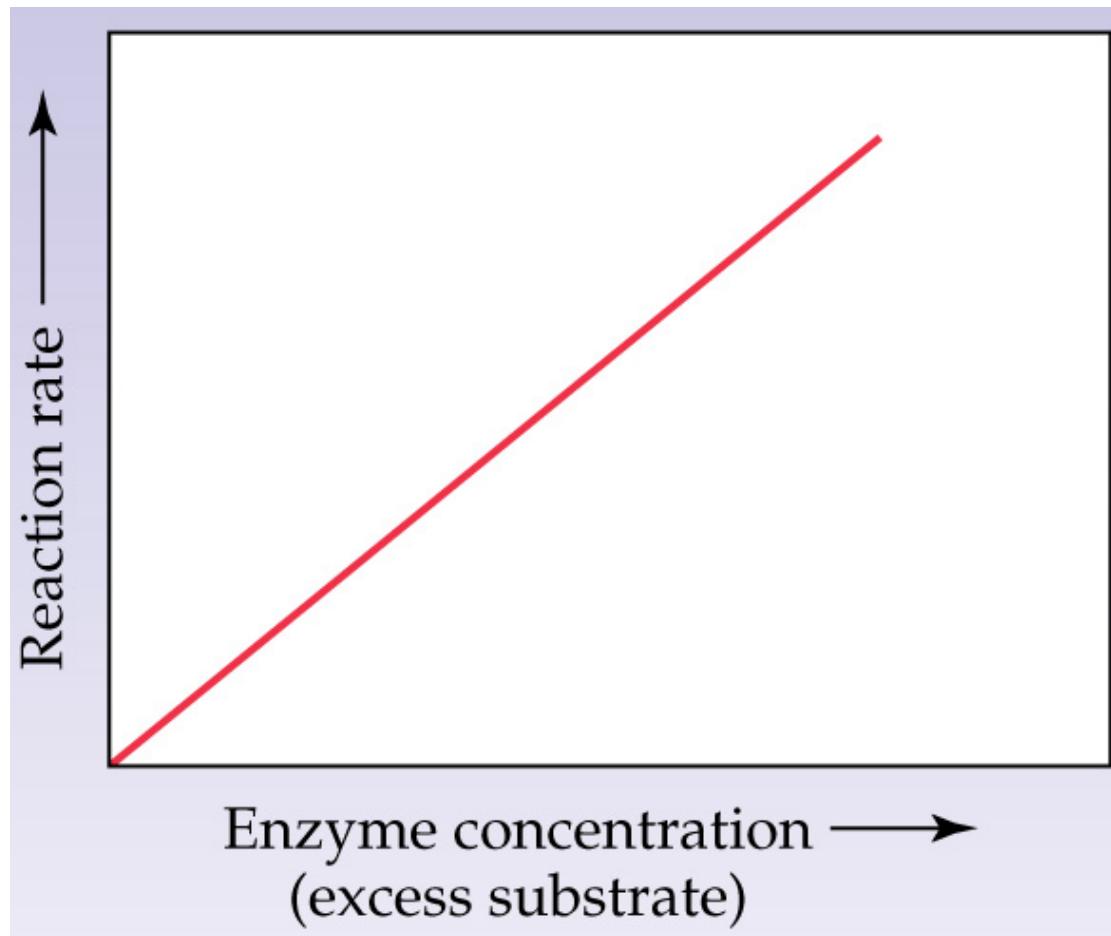


Fig 19.5 Change of reaction rate with substrate concentration when enzyme concentration is constant.

- *Enzyme concentration:* The reaction rate varies directly with the enzyme concentration as long as the substrate concentration does not become a limitation, Fig 19.6 below.



# 19.6 Effect of Temperature and pH on Enzyme Activity

- Enzymes maximum catalytic activity is highly dependent on temperature and pH.
  - Increase in temperature increases the rate of enzyme catalyzed reactions. The rates reach a maximum and then begins to decrease. The decrease in rate at higher temperature is due to denaturation of enzymes.

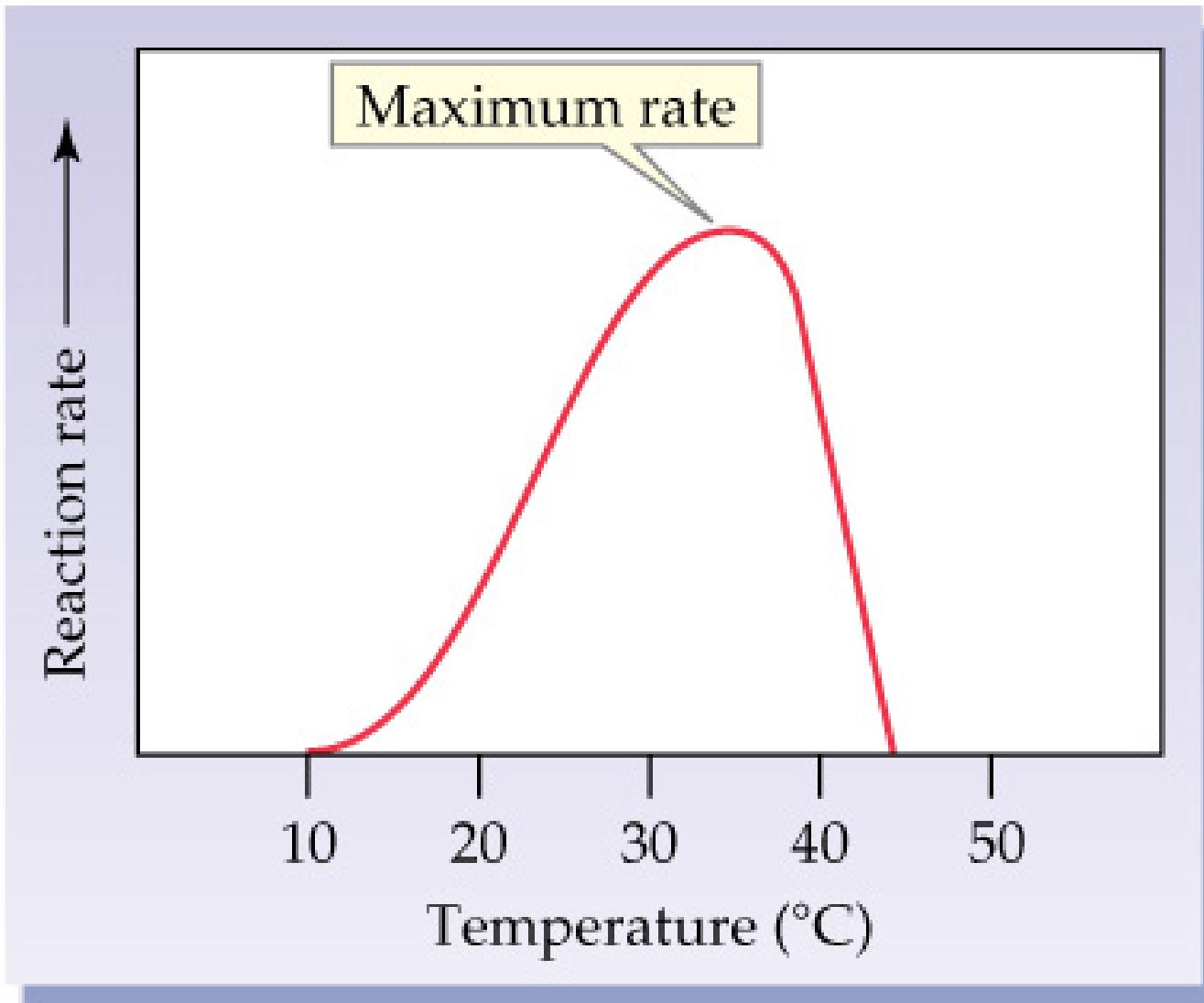
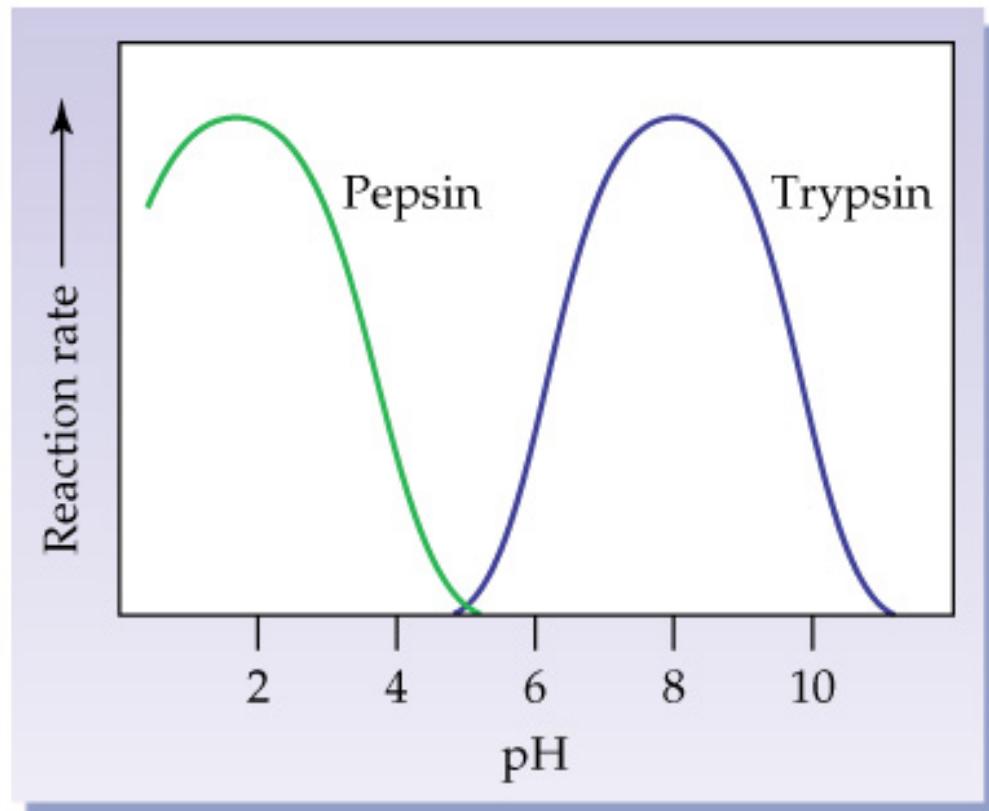


Fig 19.7 (a) Effect of temperature on reaction rate

- Effect of pH on Enzyme activity: The catalytic activity of enzymes depends on pH and usually has a well defined optimum point for maximum catalytic activity Fig 19.7 (b) below.



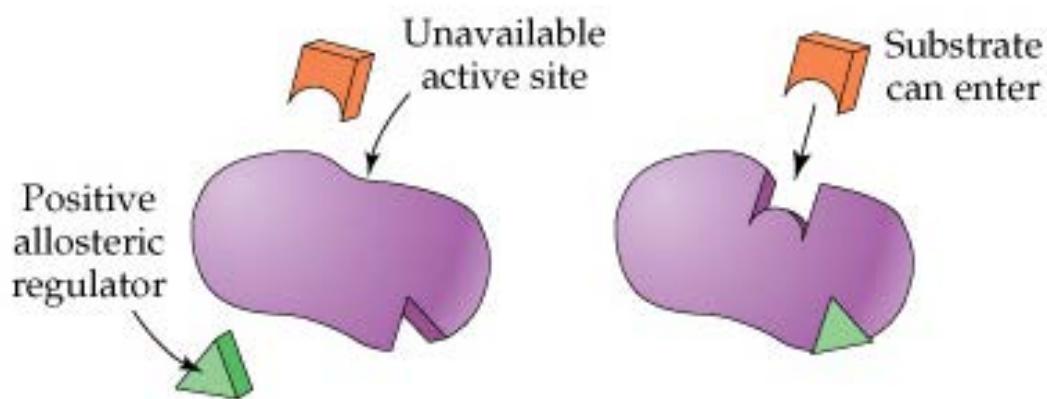
# 19.7 Enzyme Regulation: Feedback and Allosteric Control

- Concentration of thousands of different chemicals vary continuously in living organisms which requires regulation of enzyme activity.
- Any process that starts or increase the activity of an enzyme is ***activation***.
- Any process that stops or slows the activity of an enzyme is ***inhibition***.

# Two of the mechanism

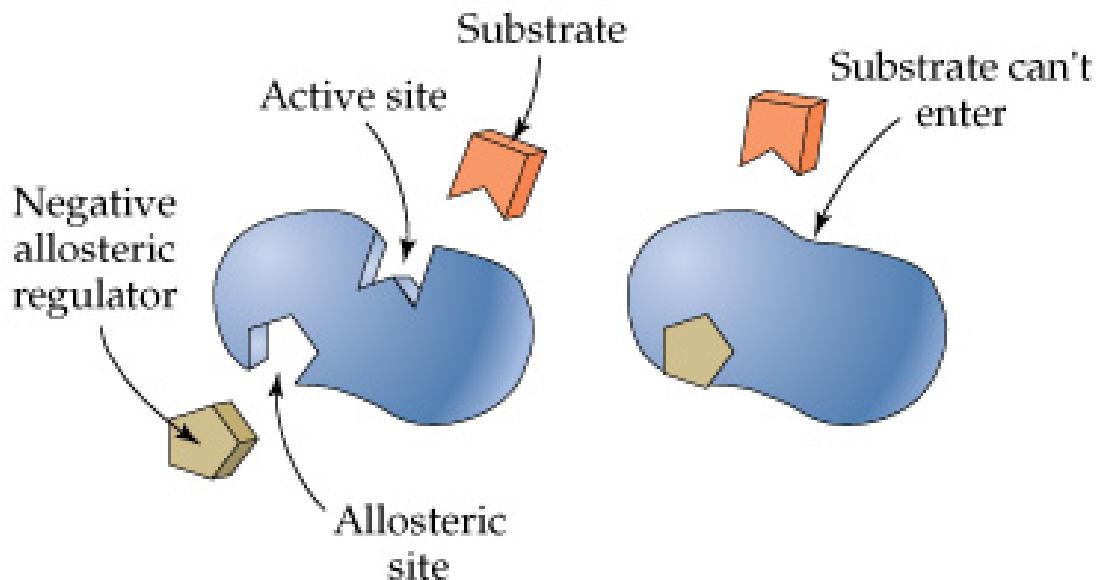
- **Feedback control:** Regulation of an enzyme's activity by the product of a reaction later in a pathway.
- **Allosteric control:** Activity of an enzyme is controlled by the binding of an activator or inhibitor at a location other than the active site. Allosteric controls are further classified as positive or negative.
  - A positive regulator changes the activity site so that the enzyme becomes a better catalyst and rate accelerates.
  - A negative regulator changes the activity site so that the enzyme becomes less effective catalyst and rate slows down.

### *Positive allosteric control*



A positive regulator changes the activity site so that the enzyme becomes a better catalyst and rate accelerates.

### *Negative allosteric control*



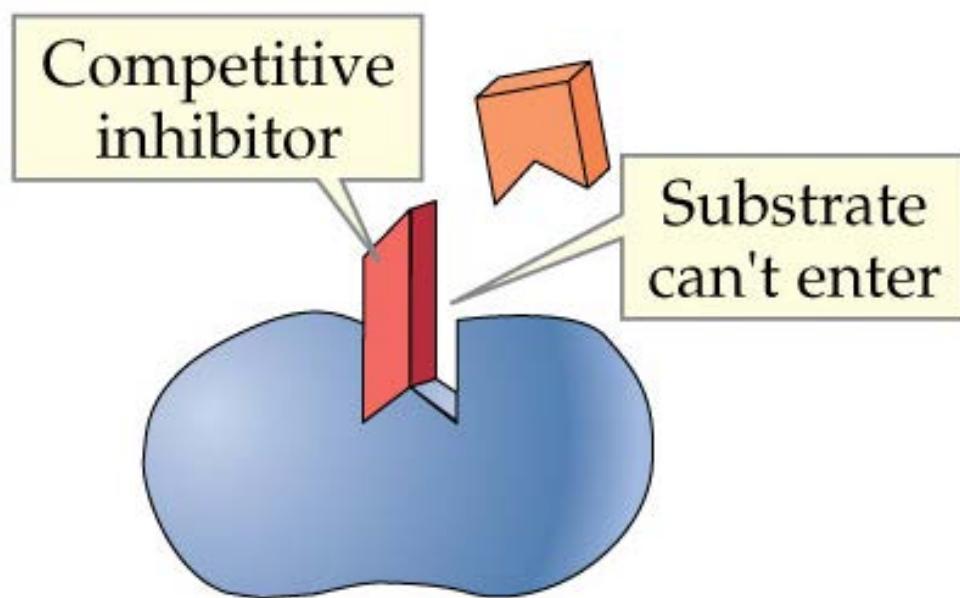
A negative regulator changes the activity site so that the enzyme becomes less effective catalyst and rate slows down.

# 19.8 Enzyme Regulation: Inhibition

- The inhibition of an enzyme can be *reversible* or *irreversible*.
- In *reversible inhibition*, the inhibitor can leave, restoring the enzyme to its uninhibited level of activity.
- In *irreversible inhibition*, the inhibitor remains permanently bound to the enzyme and the enzyme is permanently inhibited.

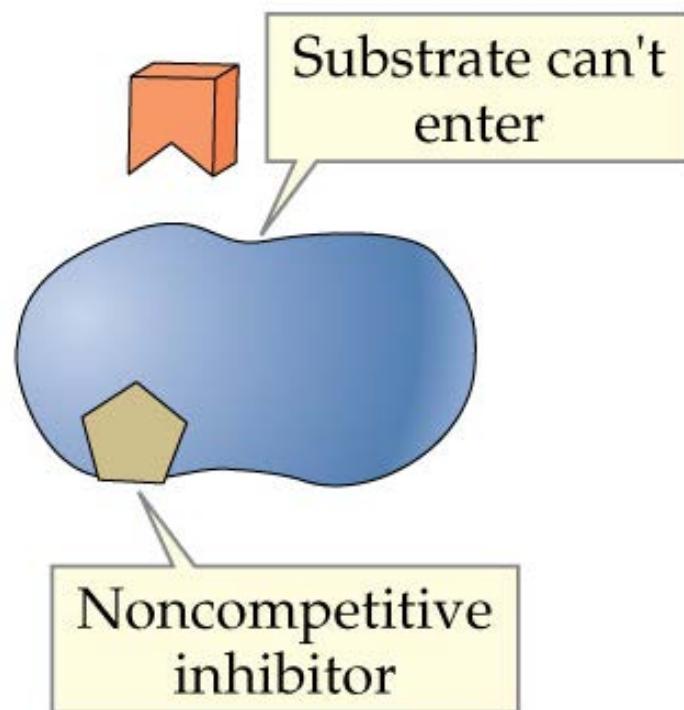
- Inhibitions are further classified as:
- *Competitive inhibition* if the inhibitor binds to the active site.

### *Competitive inhibition*

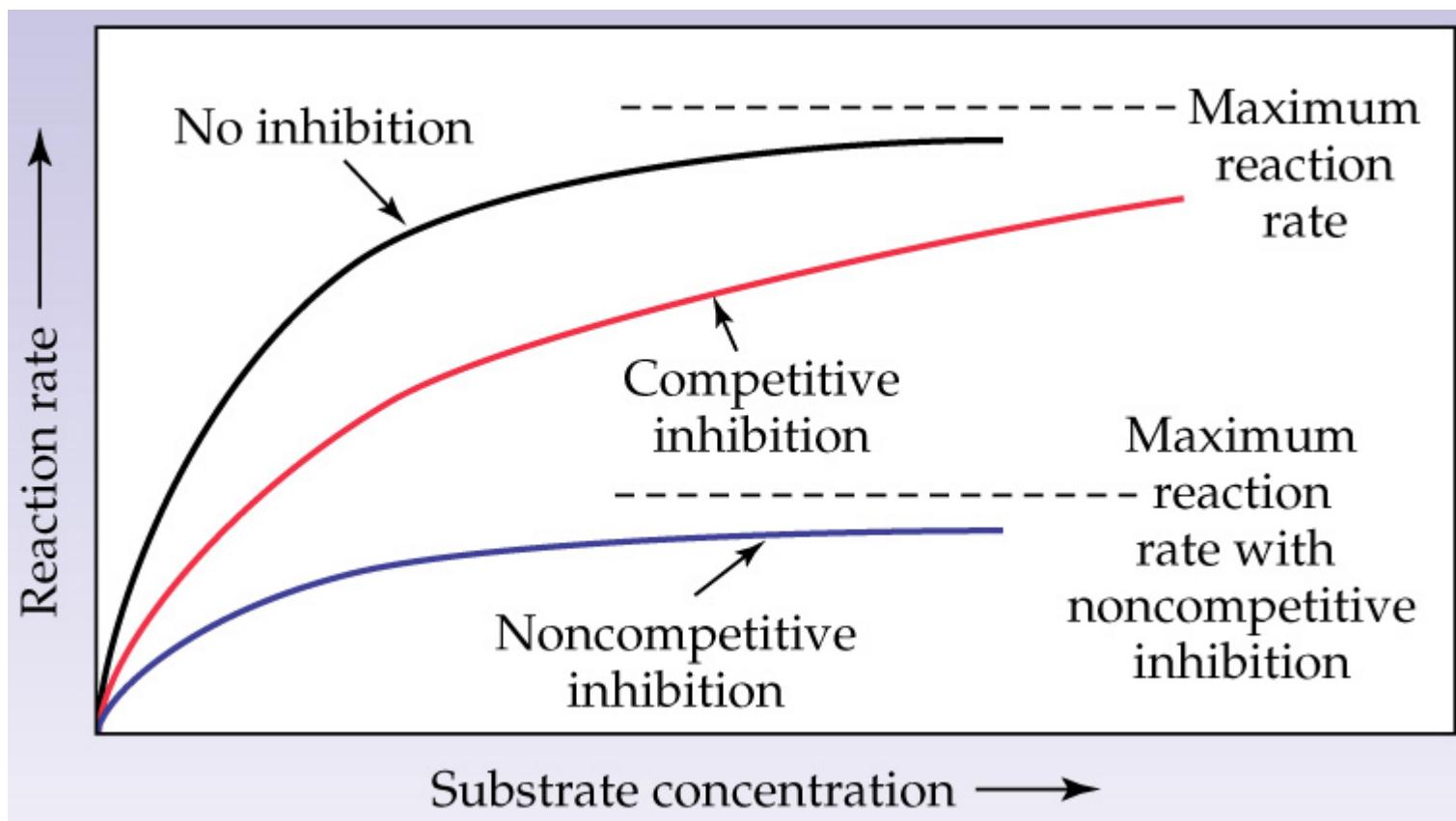


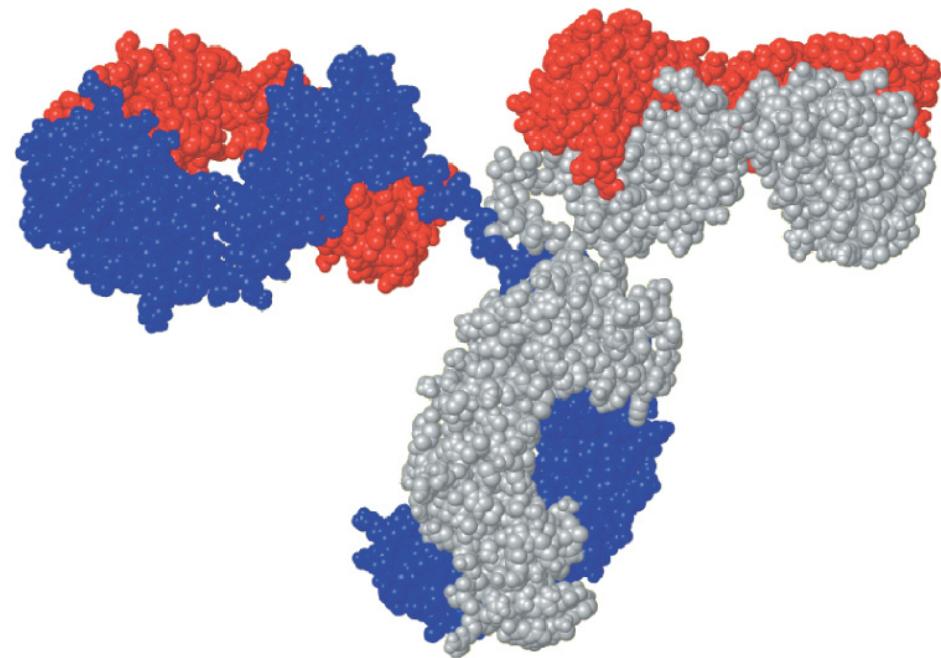
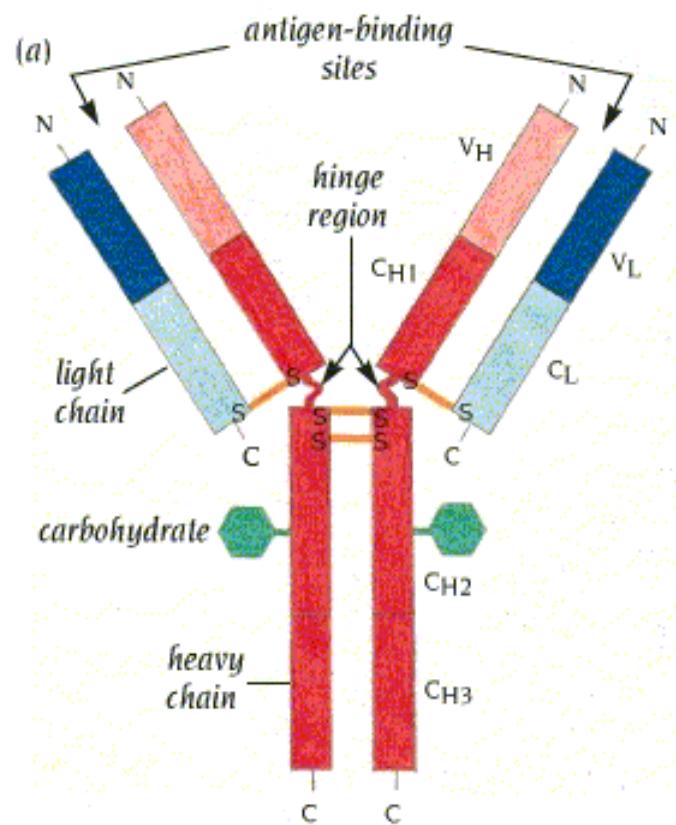
- *Noncompetitive inhibition*, if the inhibitor binds elsewhere and not to the active site.

### *Noncompetitive inhibition*

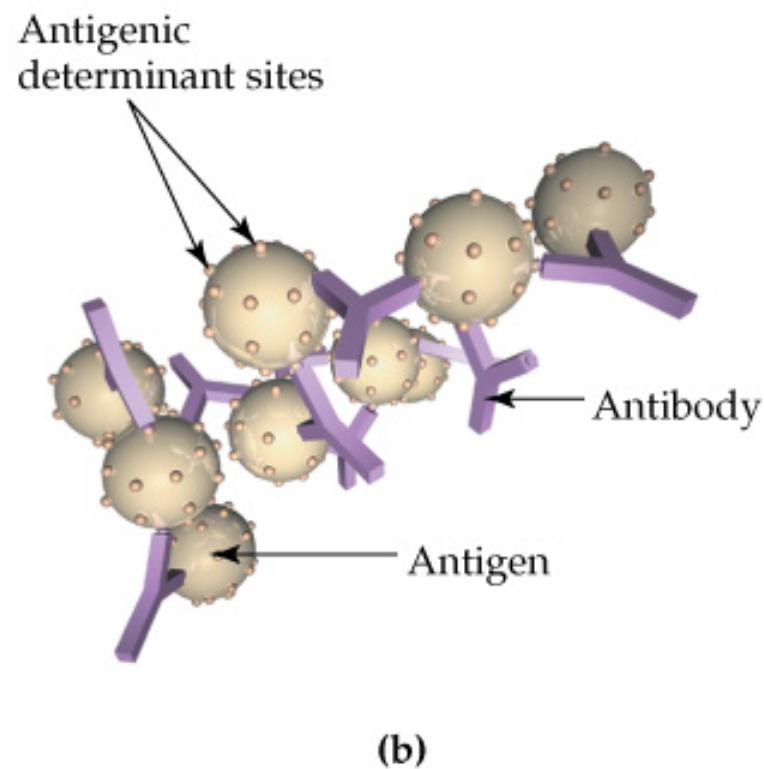
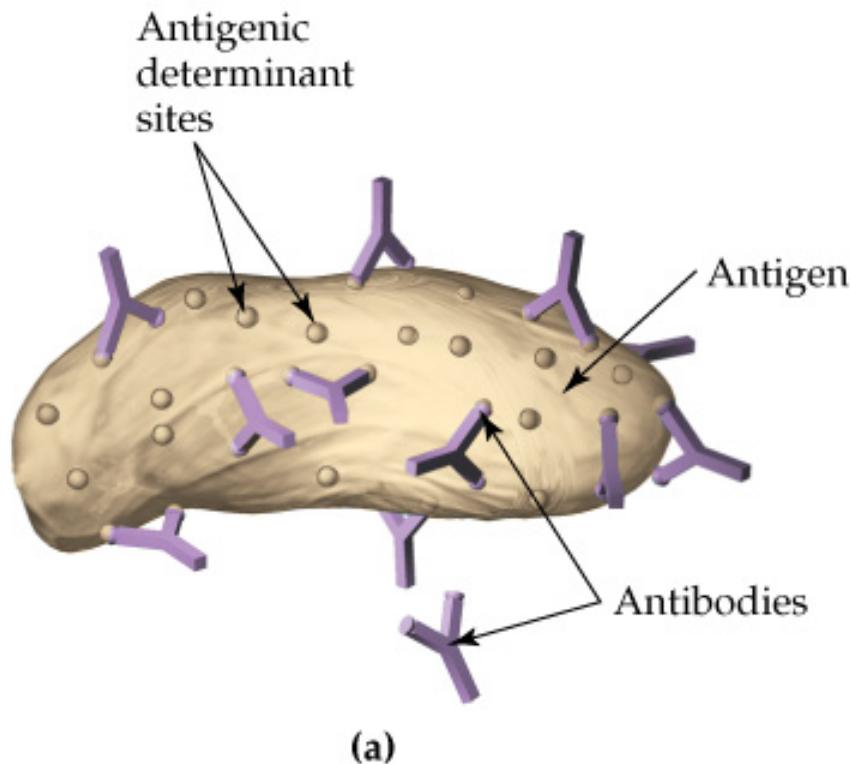


- The rates of enzyme catalyzed reactions with or without a competitive inhibitor are shown in the Fig 19.9 below.





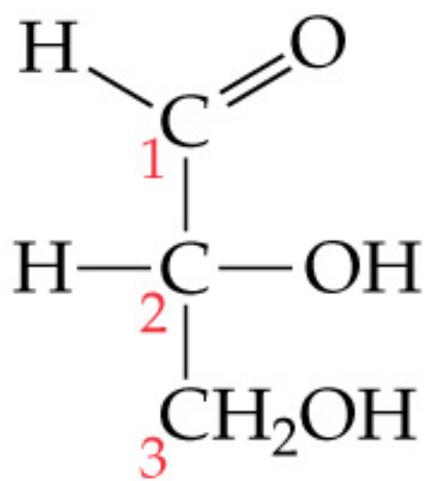
(b)



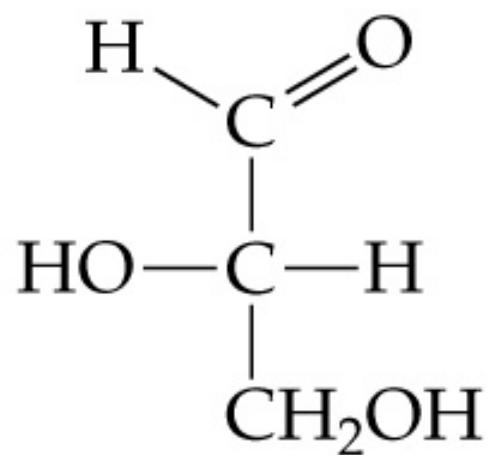
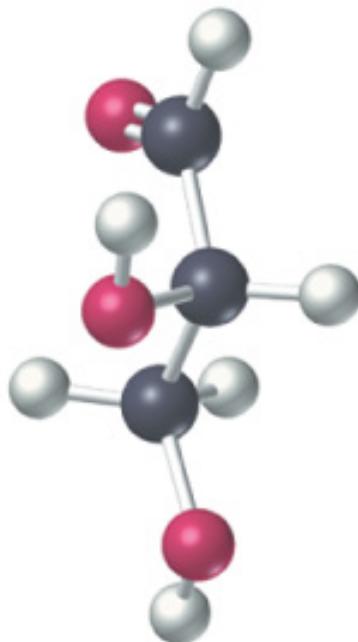
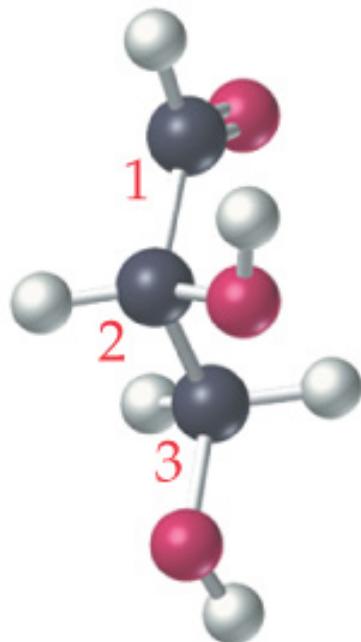
# An Introduction to Carbohydrates

- *Carbohydrates* are a large class of naturally occurring polyhydroxy aldehydes and ketones.
- Monosaccharides also known as simple sugars, are the simplest carbohydrates containing 3-7 carbon atoms.
- sugar containing an aldehydes is known as an aldose.
- sugar containing a ketones is known as a ketose.

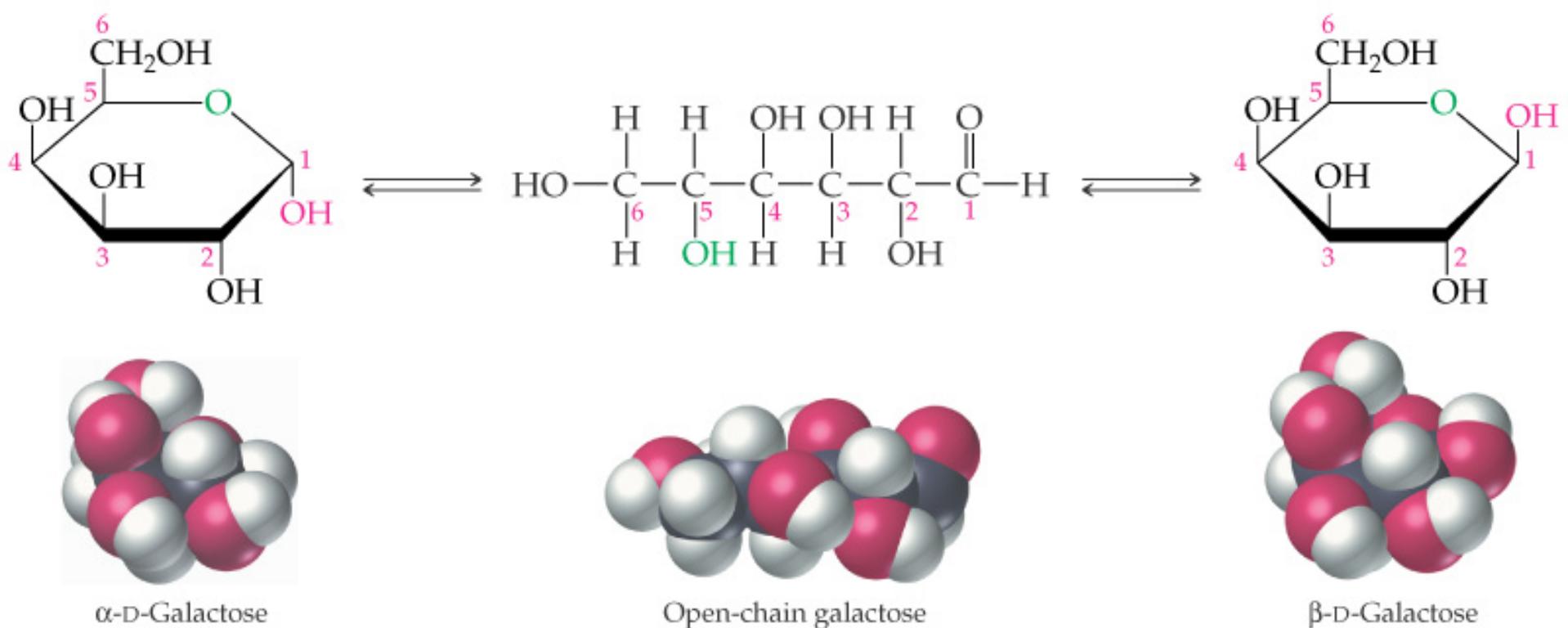
- The number of carbon atoms in an aldose or ketose may be specified as by tri, tetr, pent, hex, or hept. For example, glucose is aldohexose and fructose is ketohexose.
- Monosaccharides react with each other to form disaccharides and polysaccharides.
- Monosaccharides are chiral molecules and exist mainly in cyclic forms rather than the straight chain.



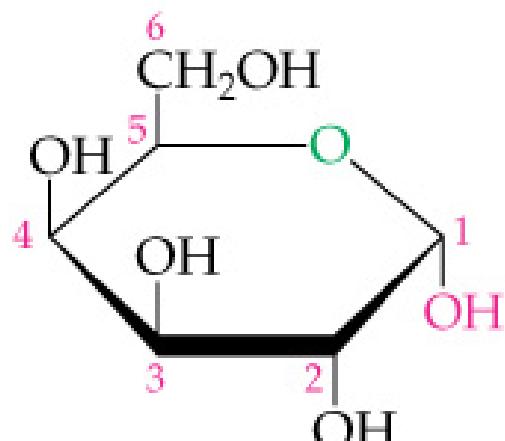
D-Glyceraldehyde  
Right-handed



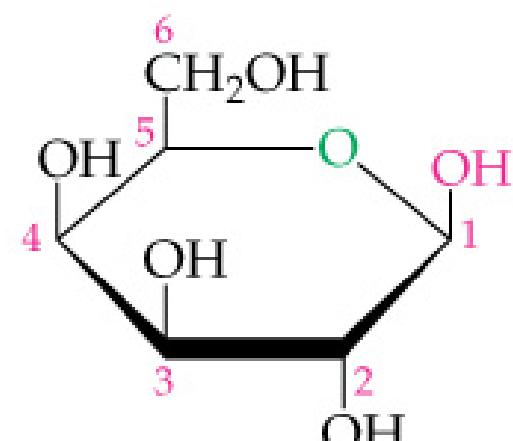
L-Glyceraldehyde  
Left-handed



- *Anomers*: Cyclic sugars that differs only in positions of substituents at the hemiacetal carbon; the  $\alpha$ -form has the  $-\text{OH}$  group on the opposite side from the  $-\text{CH}_2\text{OH}$ ; the  $\beta$ -form the  $-\text{OH}$  group on the same side as the  $-\text{CH}_2\text{OH}$  group.



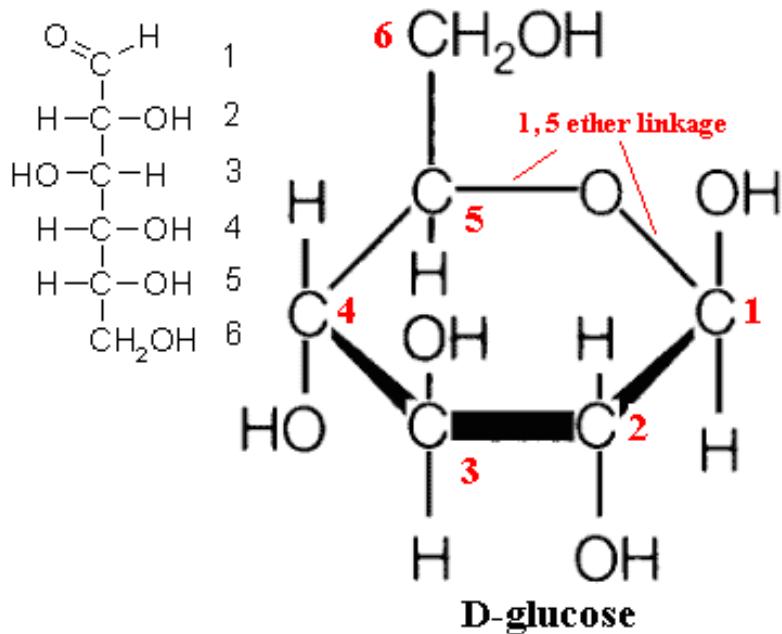
$\alpha$ -D-Galactose

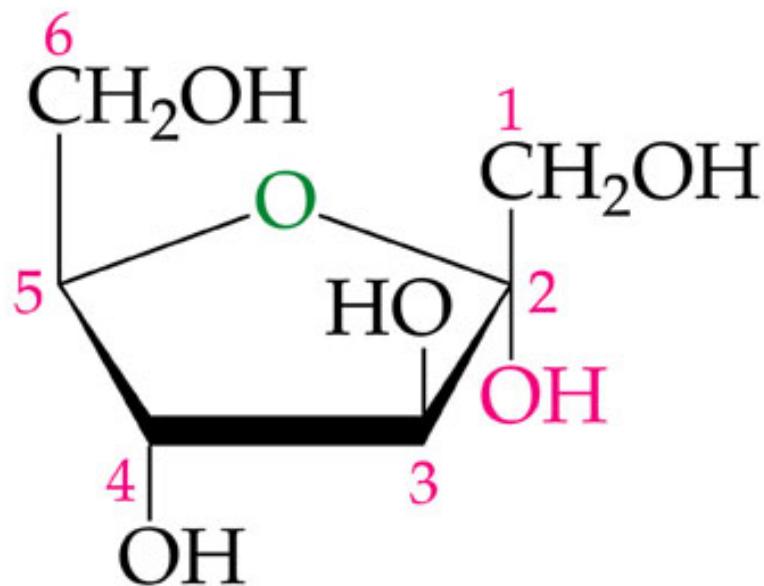


$\beta$ -D-Galactose

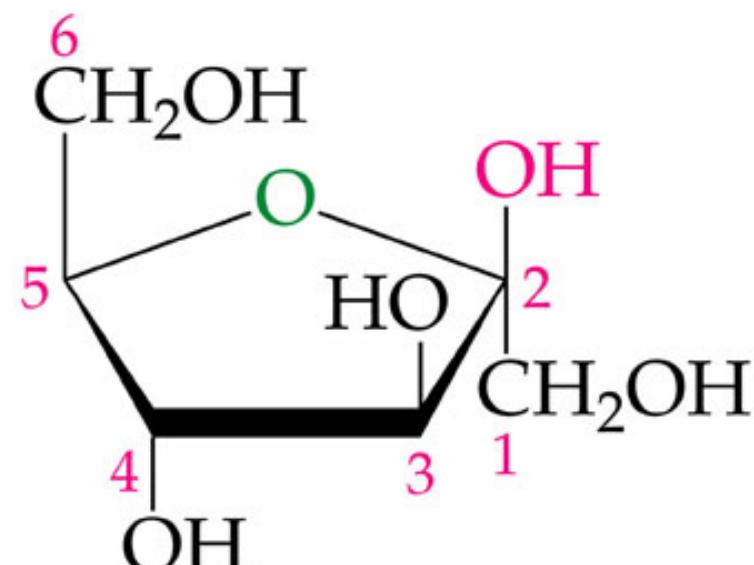
# Some Important Monosaccharides

Monosaccharides are generally high-melting, white, crystalline solids that are soluble in water and insoluble in nonpolar solvents. Most monosaccharides are sweet tasting, digestible, and nontoxic.

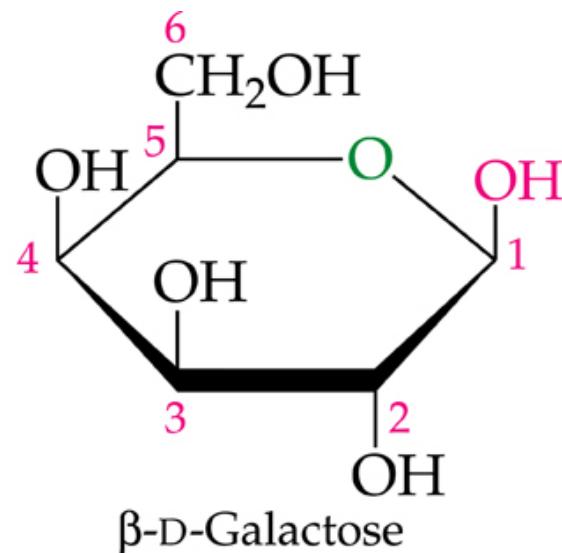
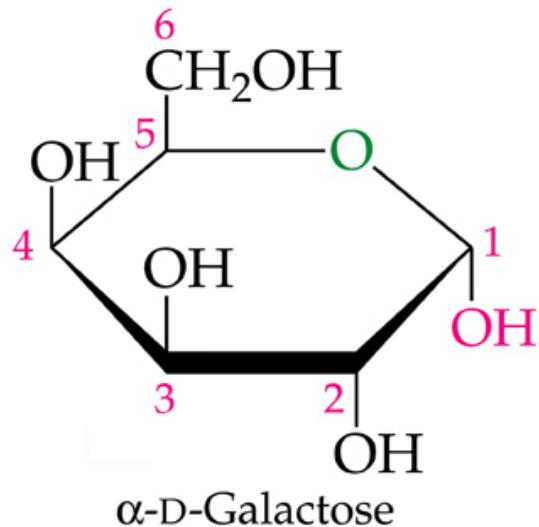




$\alpha$ -D-Fructose

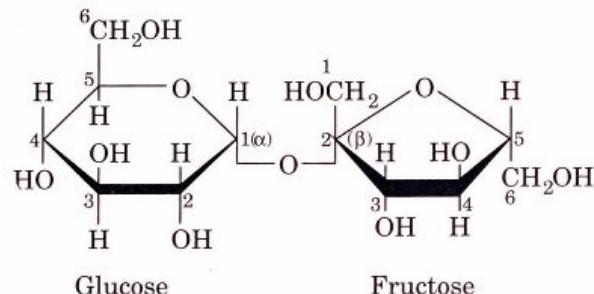


$\beta$ -D-Fructose

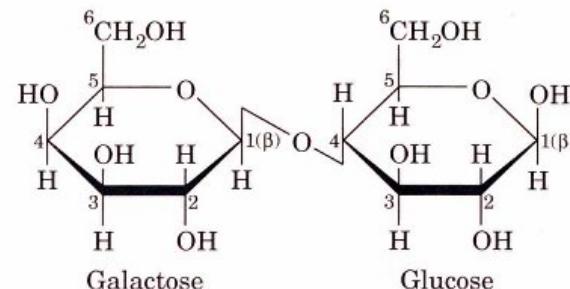


$\beta$ -D-Galactose

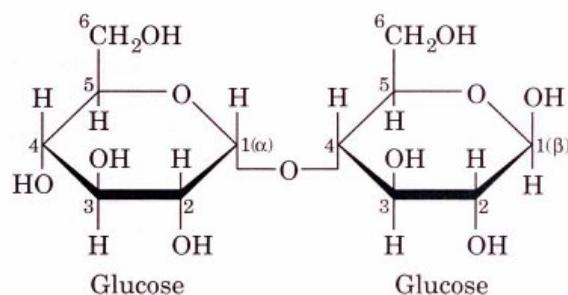
# Some Common Disaccharides



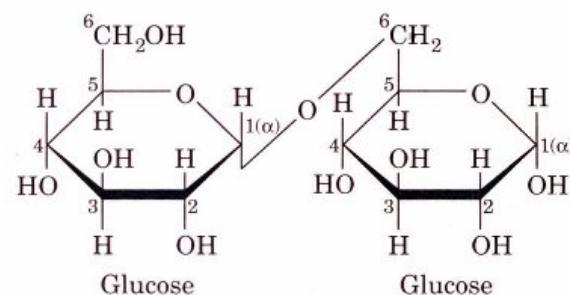
## Sucrose



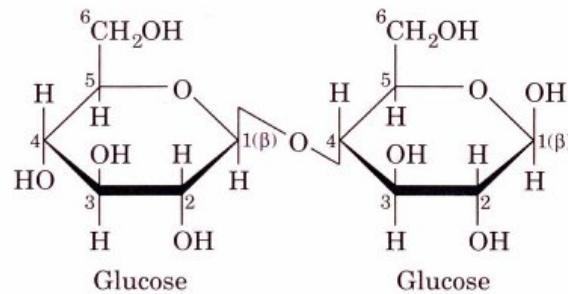
## Lactose



## Maltose

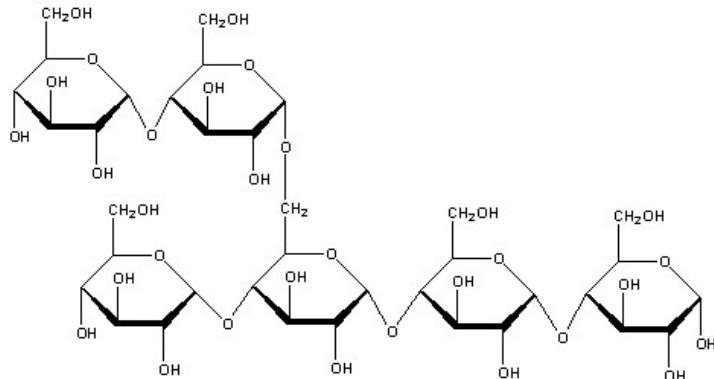


## Isomaltose

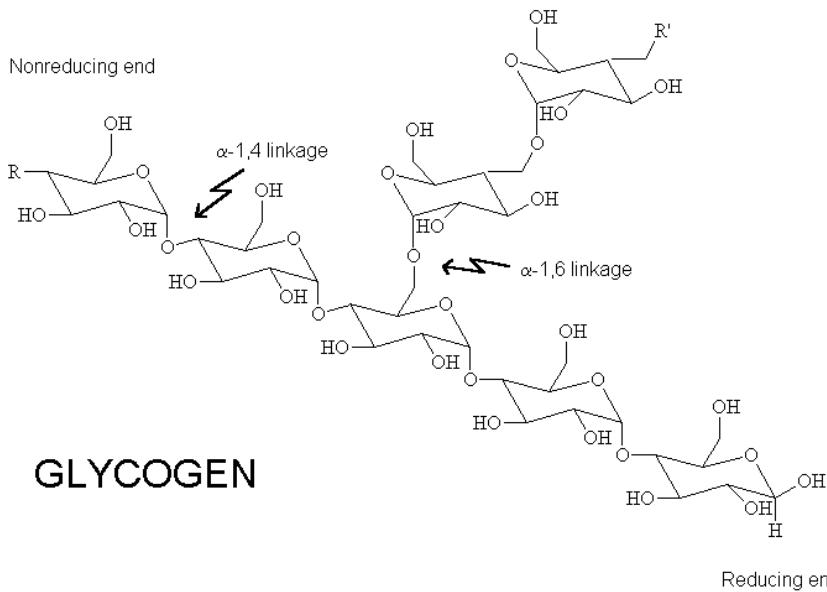


## Cellobiose

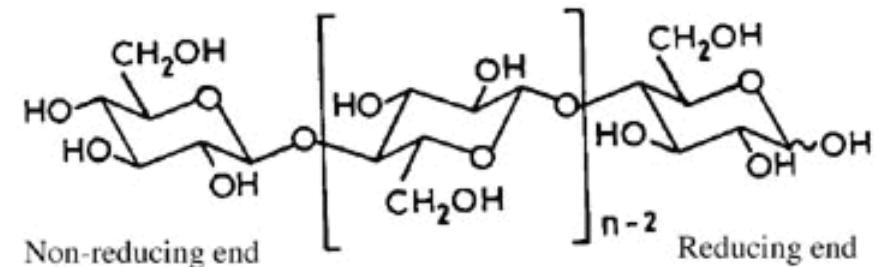
# Polysaccharides



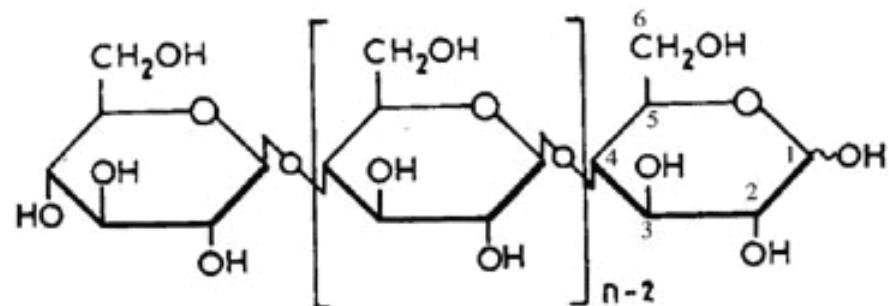
Nonreducing end



GLYCOGEN

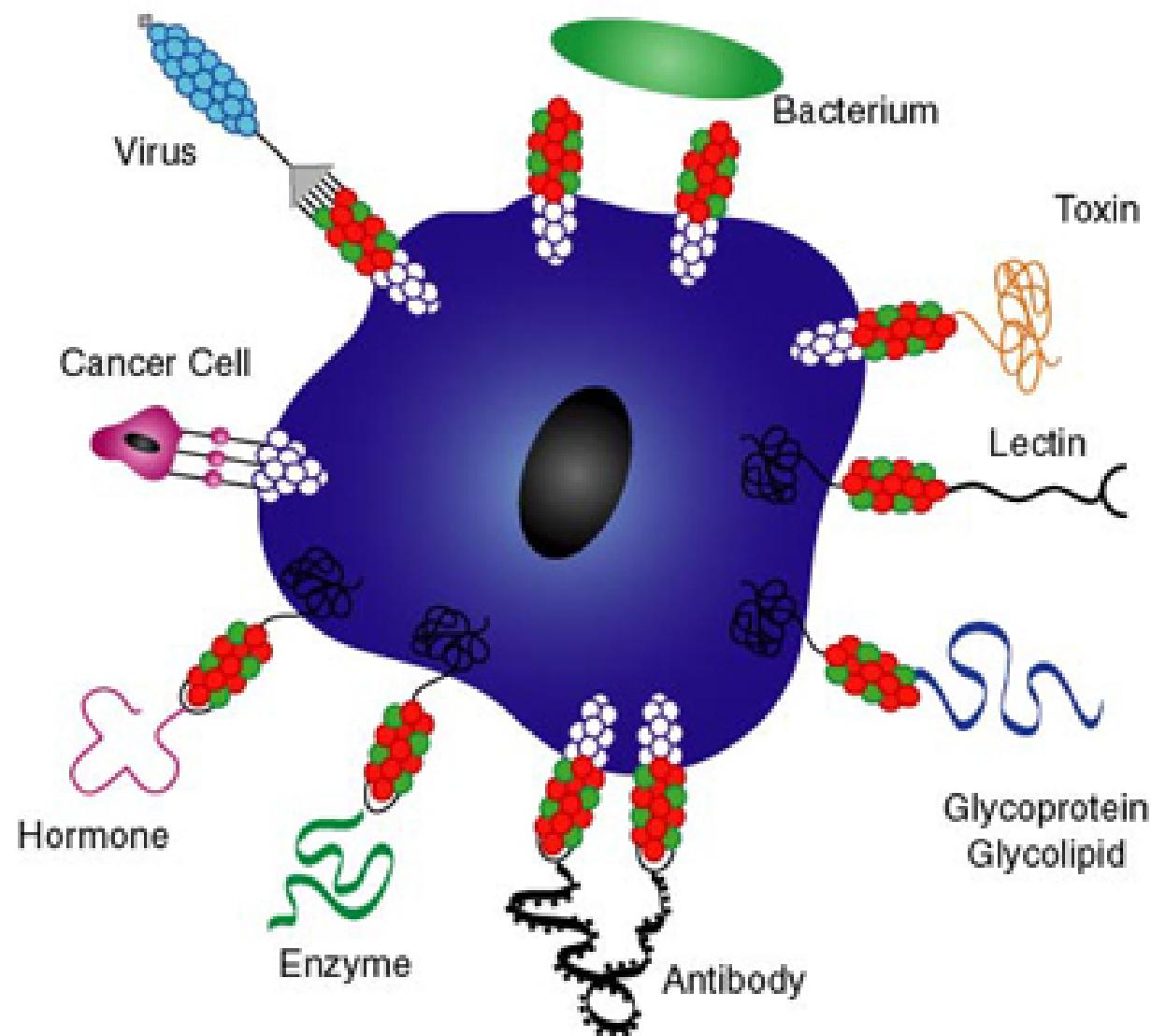


Sometimes shown as



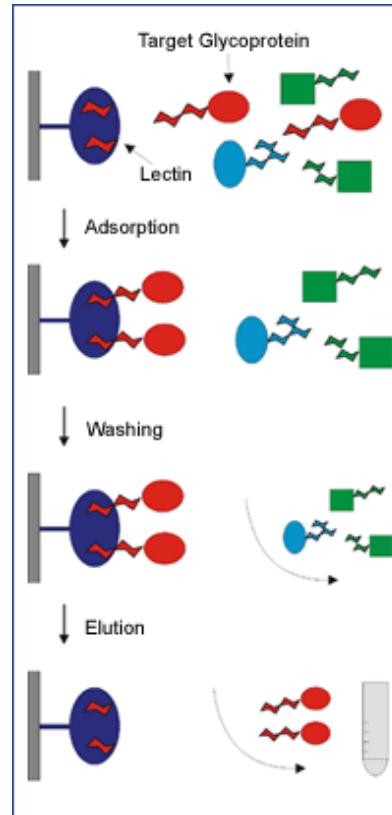
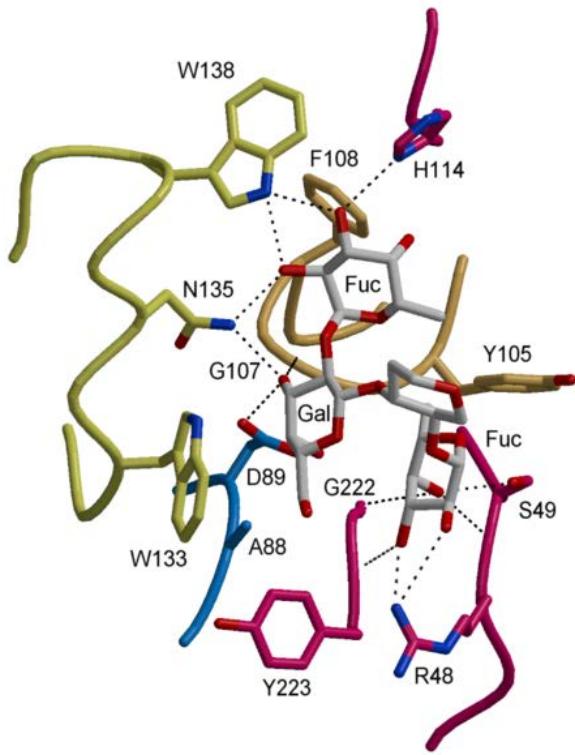
Cellulose

## Cell-Surface Carbohydrates Involved in Molecular Recognition

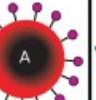
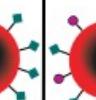


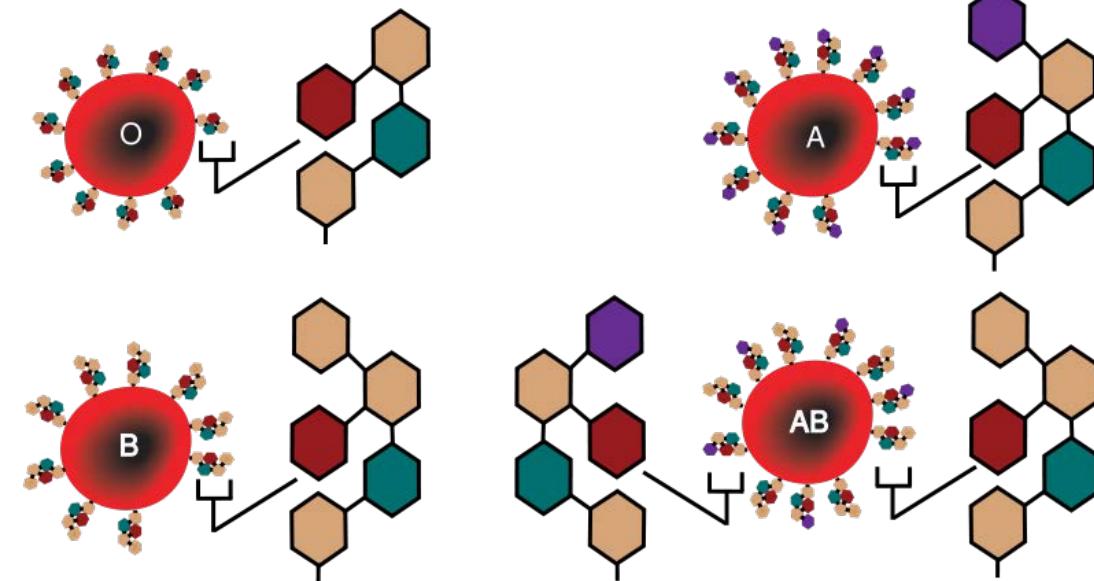
# Lectin

**Lectins** are sugar-binding proteins which are highly specific for their sugar moieties. They typically play a role in biological recognition phenomena involving cells and proteins. For example, some bacteria use lectins to attach themselves to the cells of the host organism during infection.



# Blood Type

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies present			None	
Antigens present	A antigen	B antigen	A and B antigens	No antigens



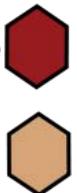
Legend



Red blood cell



N acetyl-galactosamine



Fucose



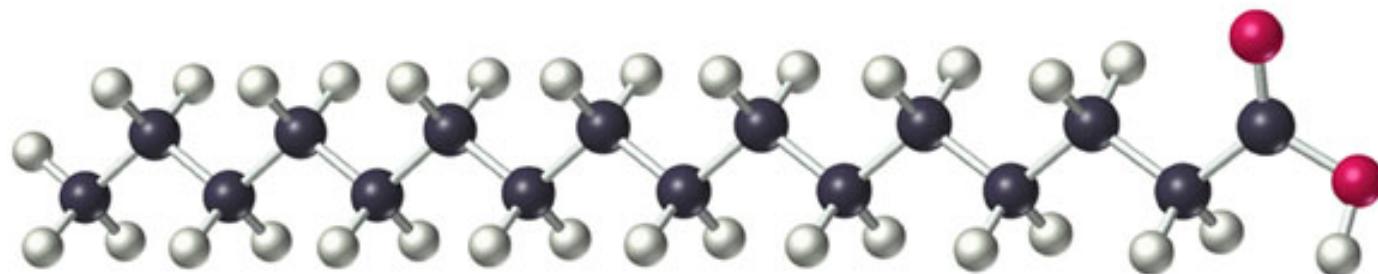
N acetyl-glucosamine



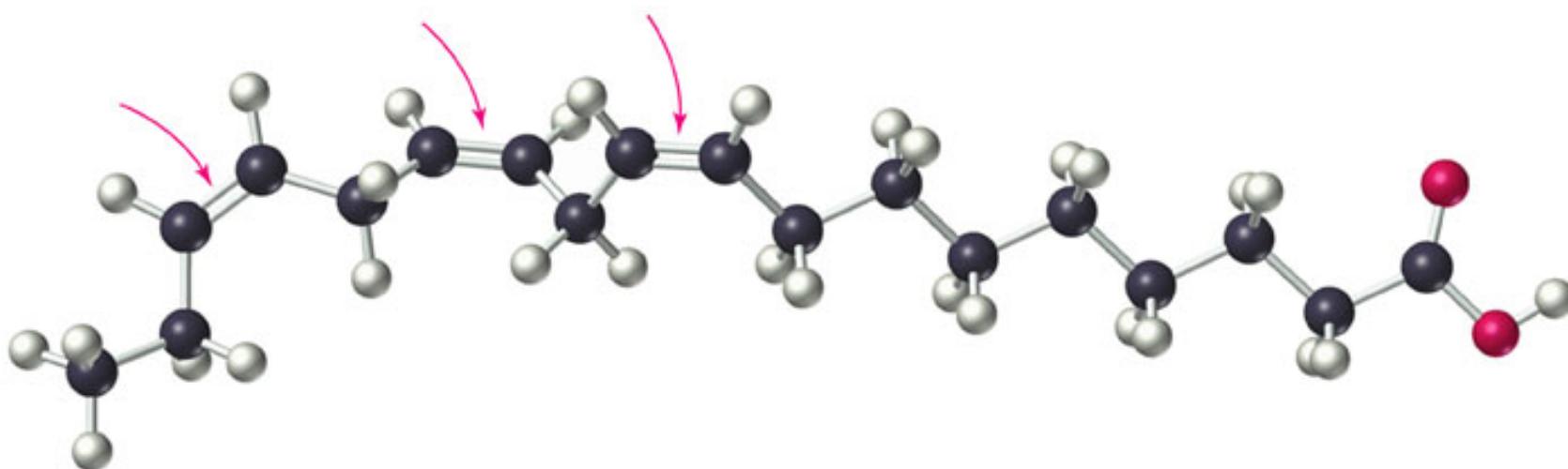
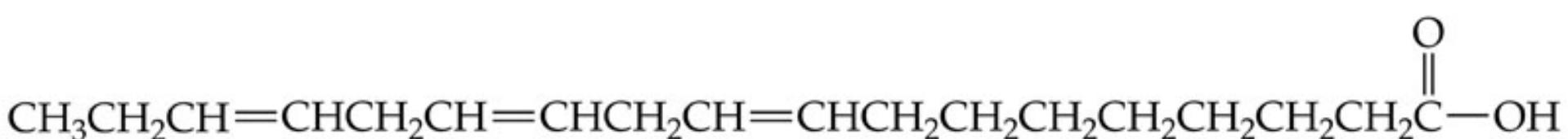
Galactose

# Lipid

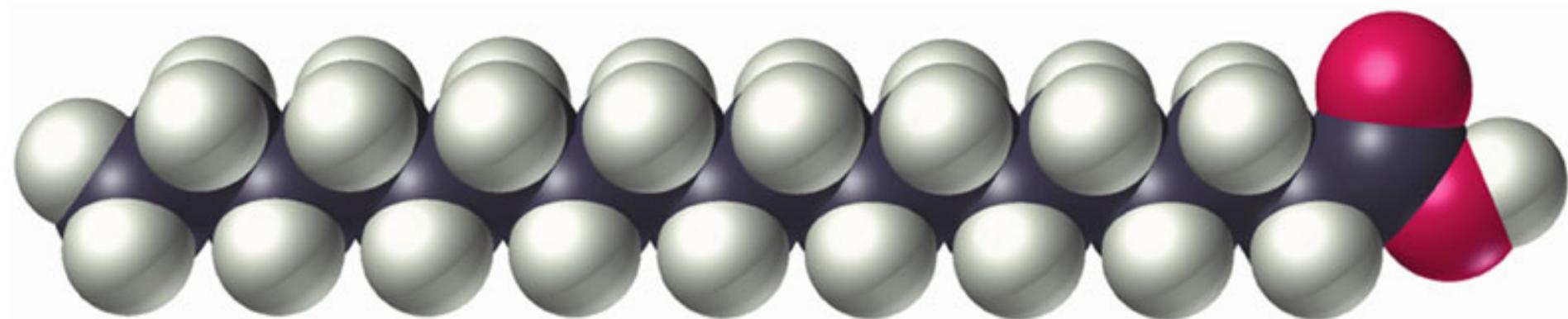
- *Lipids* are naturally occurring molecules from plants or animals that are soluble in nonpolar organic solvents.
- Lipid molecules contain large hydrocarbon portion and not many polar functional group, which accounts for their solubility behavior.



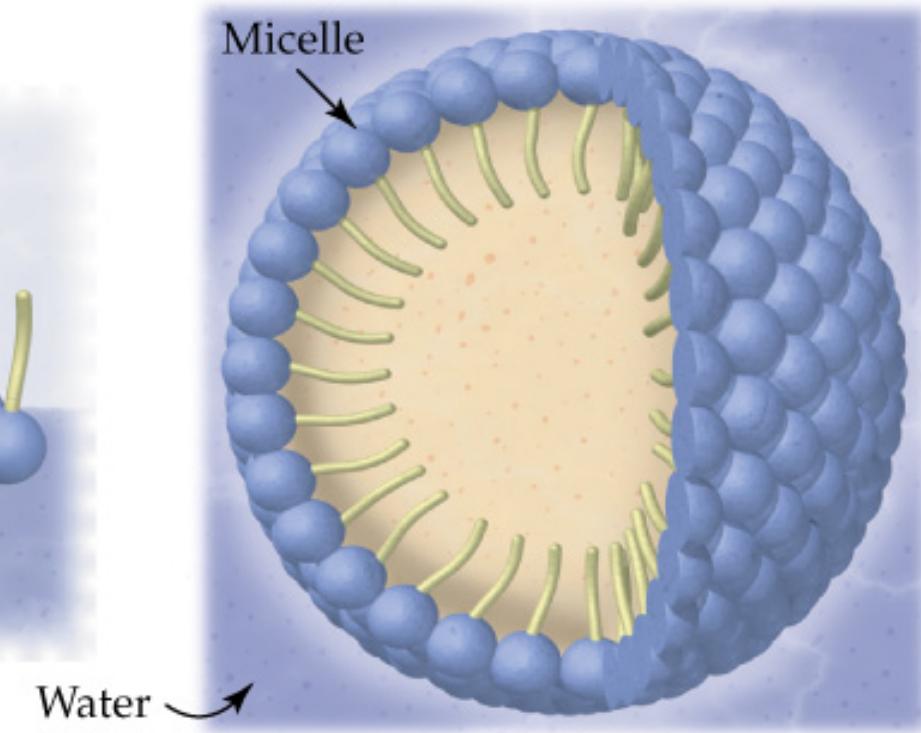
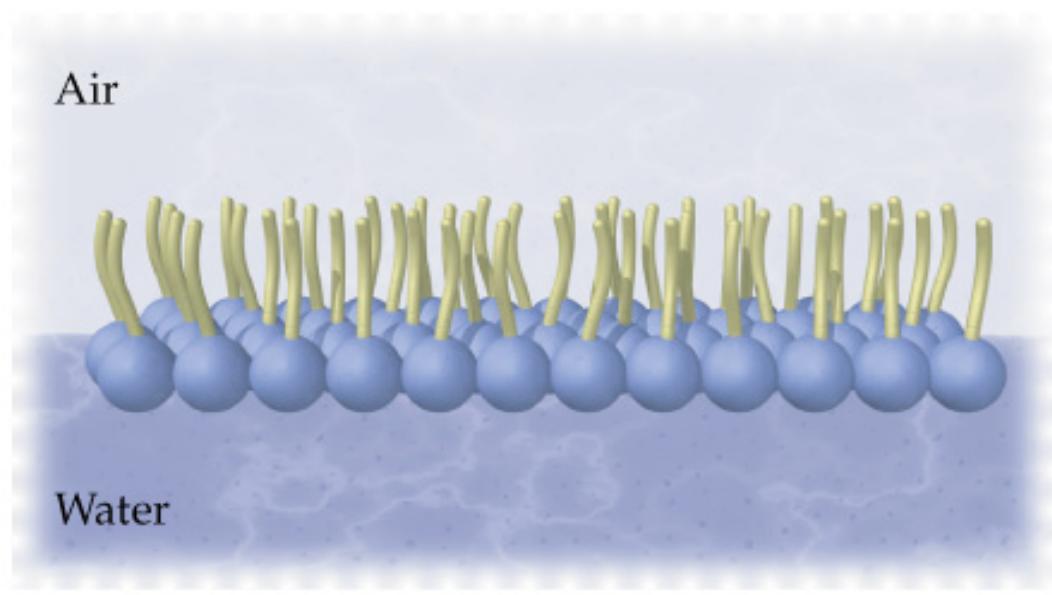
A saturated fatty acid  
(palmitic acid)

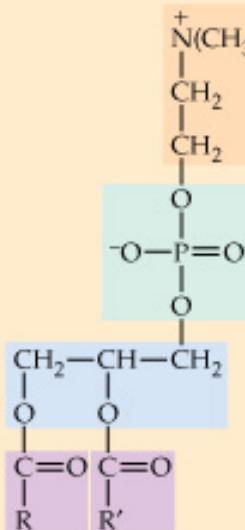
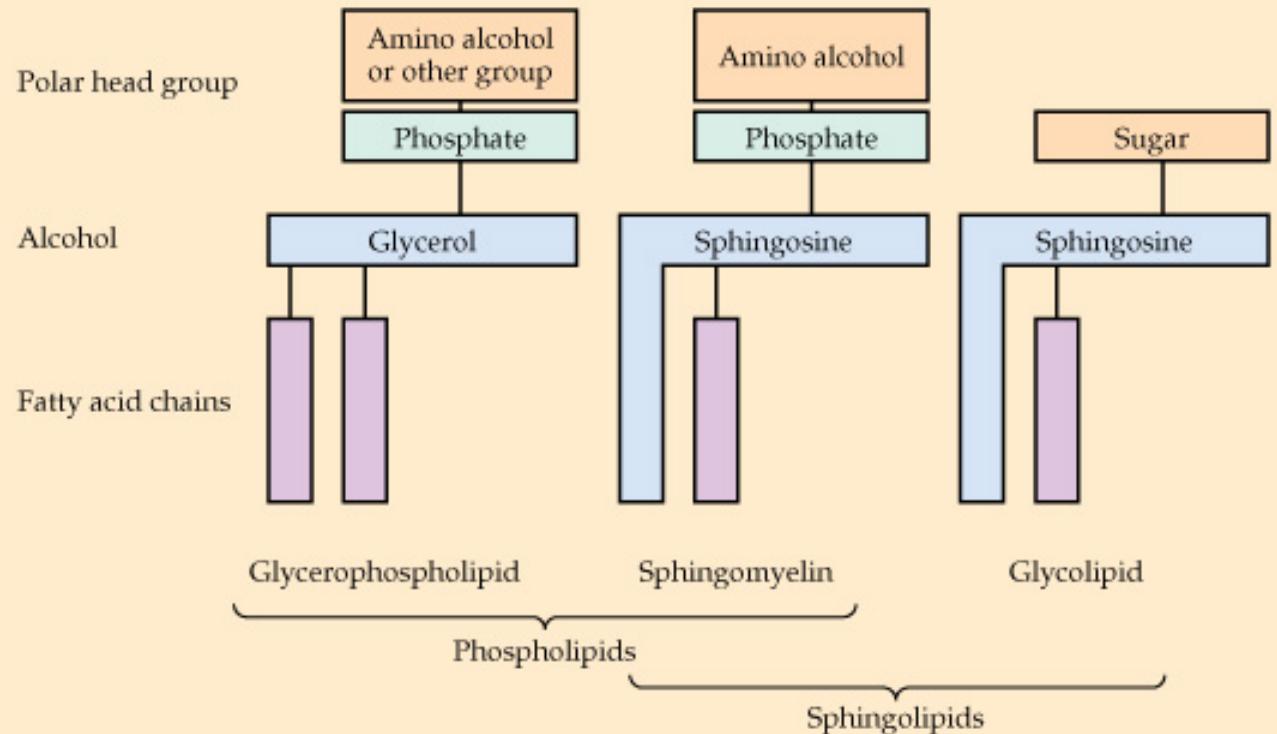


A *cis* unsaturated fatty acid  
(linolenic acid)

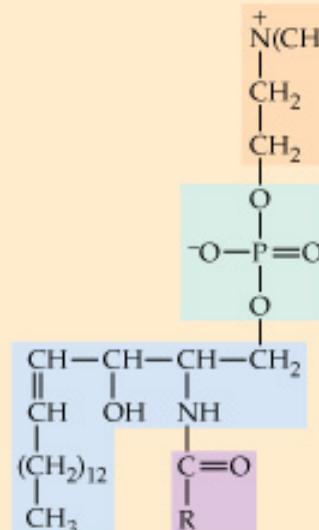


Stearic acid, an 18-carbon saturated fatty acid

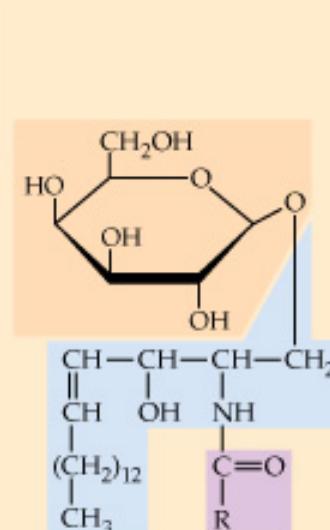




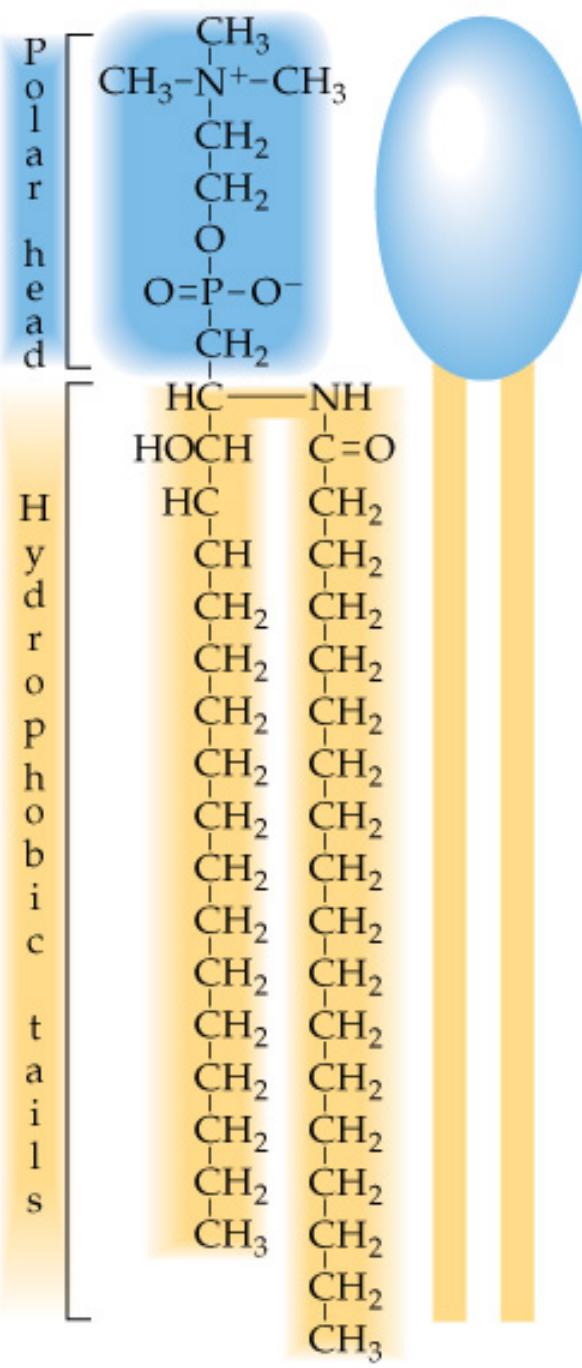
A glycerophospholipid  
(a phosphatidylcholine)



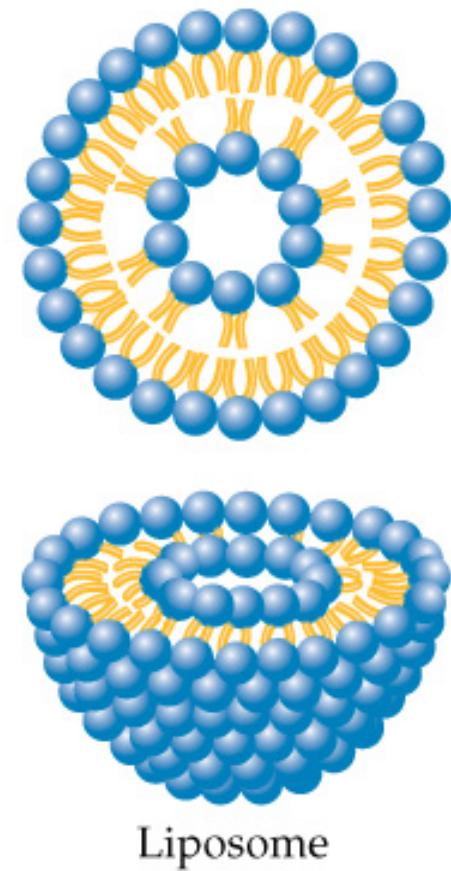
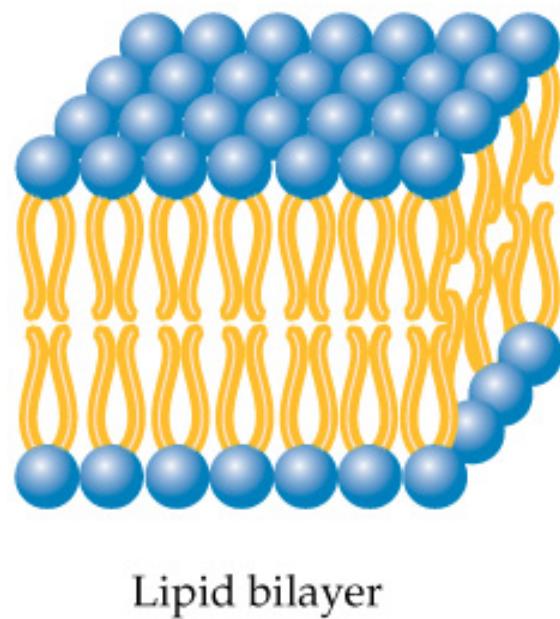
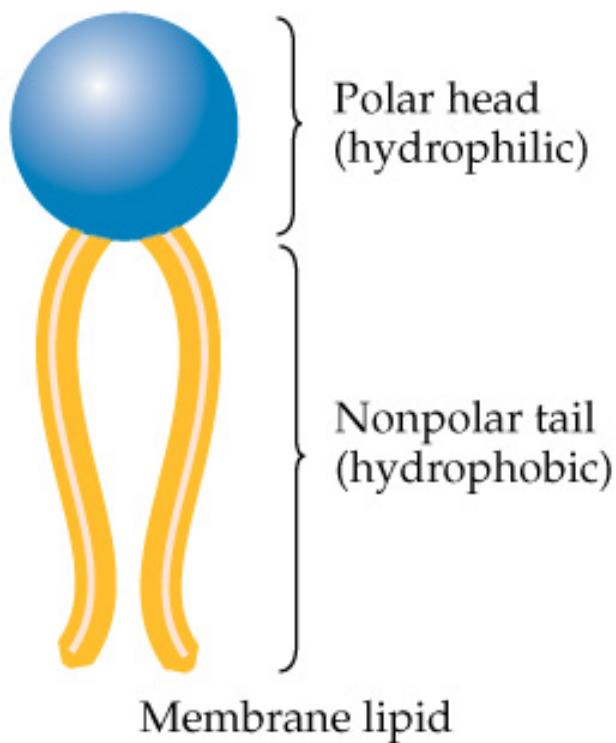
A sphingomyelin



A glycolipid



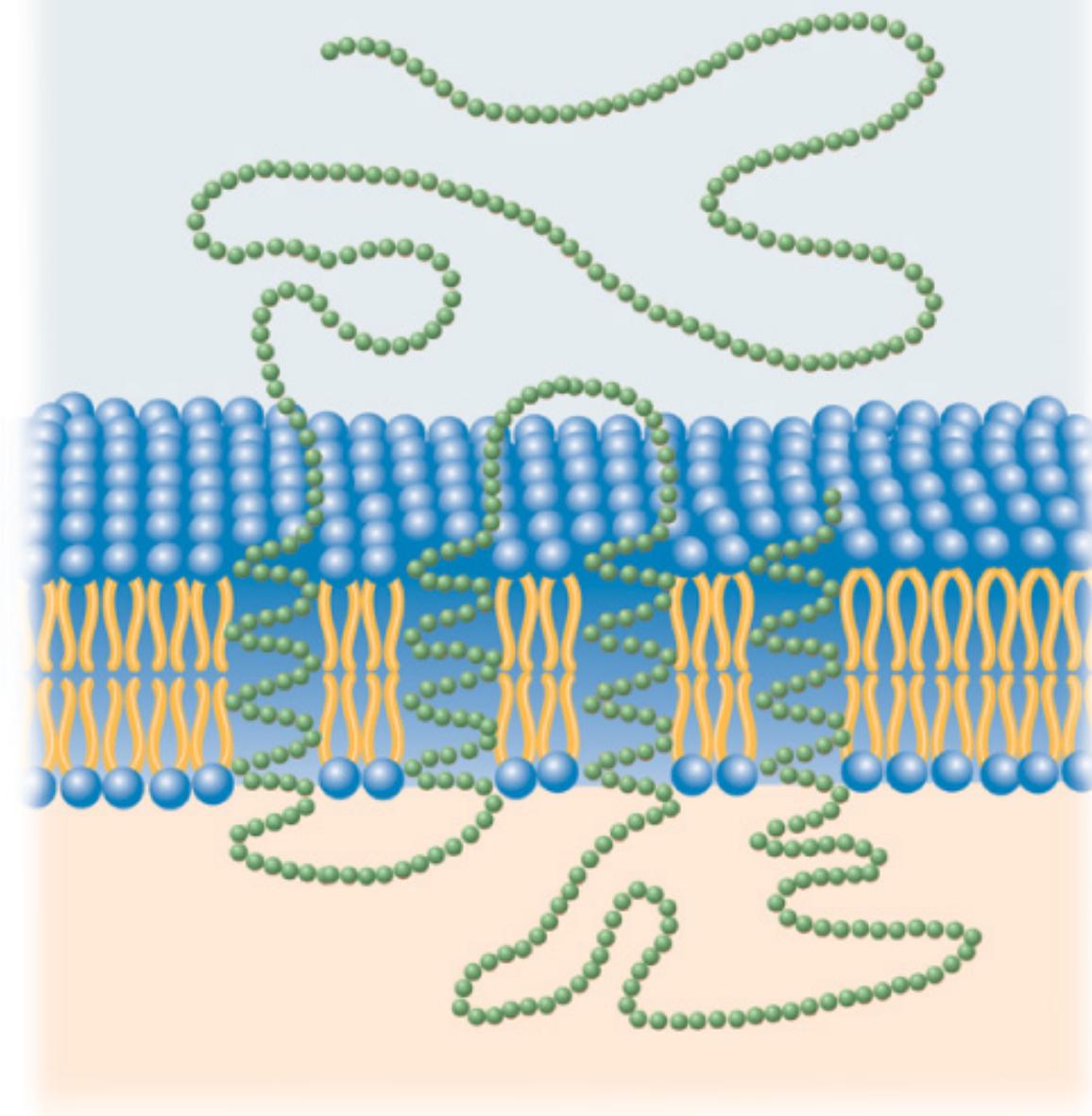
A sphingomyelin



# Properties of cell membranes:

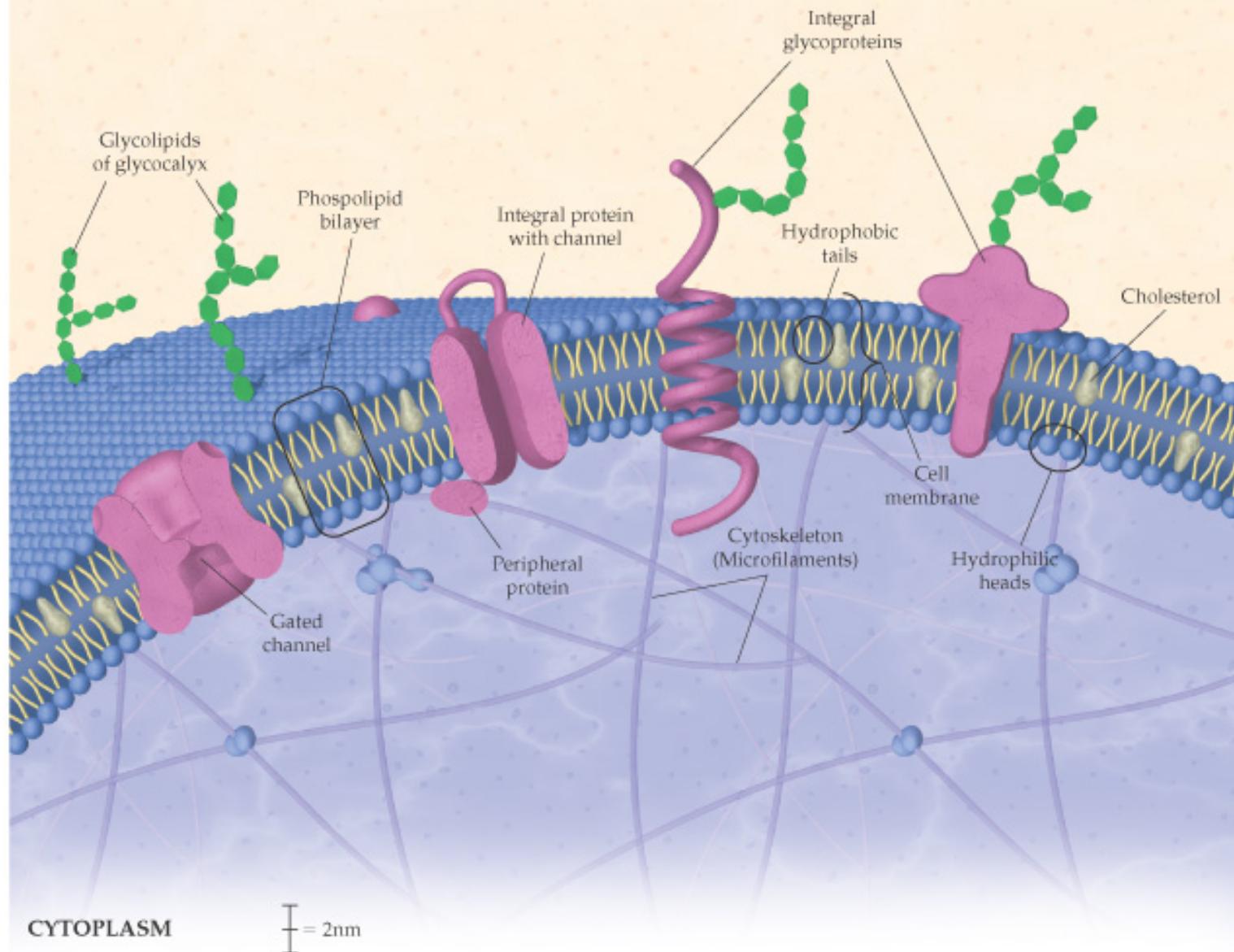
- Cell membranes are composed of a fluid like phospholipid bilayer.
- The bilayer incorporates cholesterol, proteins, and glycolipids.
- Small nonpolar molecules cross by diffusion through the lipid bilayer.
- Small ions and polar molecules diffuse through the aqueous media in protein pores.
- Glucose and certain other substances cross with the aid of proteins without energy input.
- $\text{Na}^+$ ,  $\text{K}^+$ , and other substances that maintain concentration gradients inside and outside the cell cross with expenditure of energy and the aid of proteins.

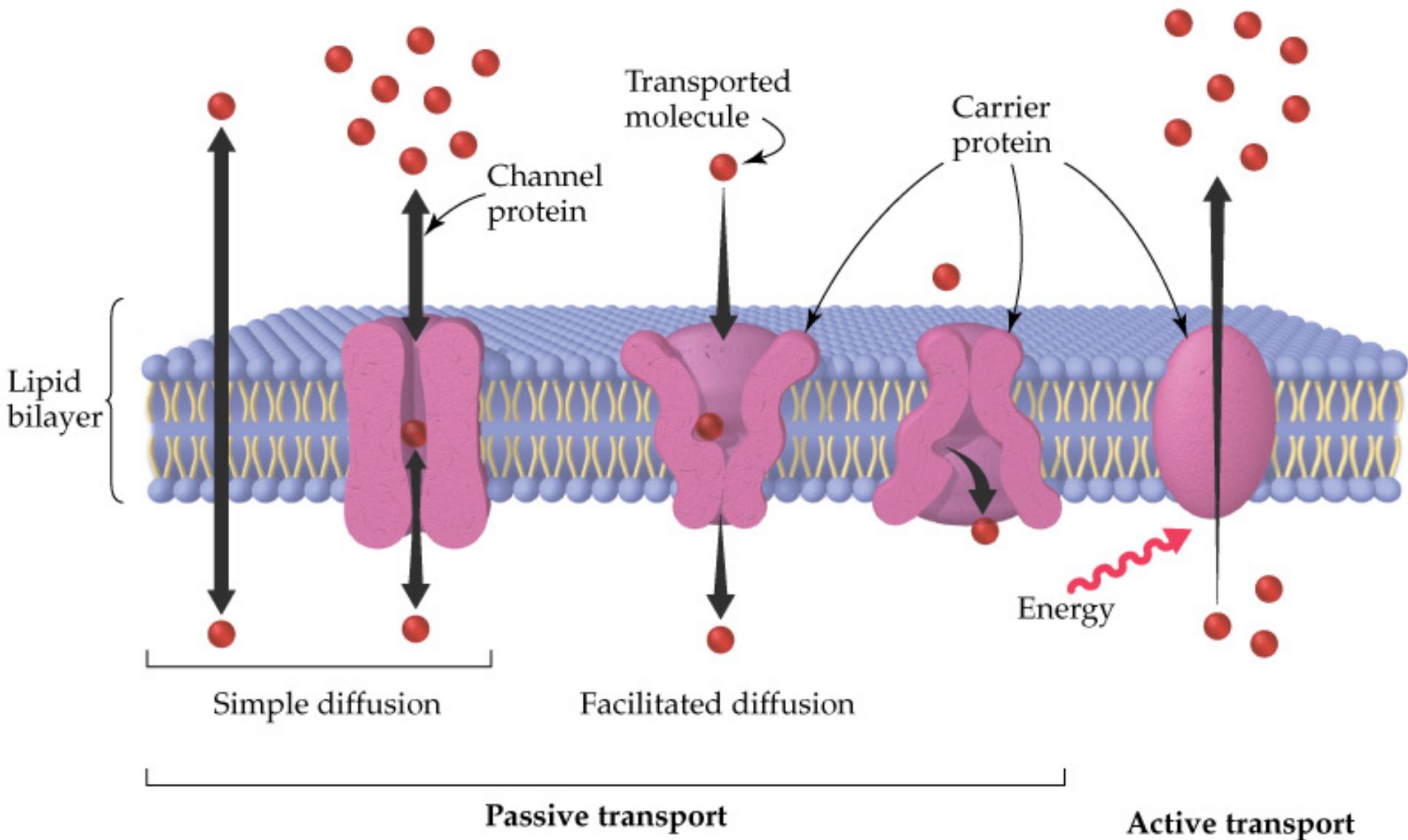
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## EXTRACELLULAR FLUID





Extracellular fluid

Sodium-potassium ATPase

2 K<sup>+</sup>

ATP

ADP

3 Na<sup>+</sup>

Cytoplasm