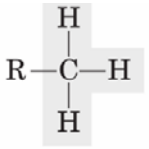
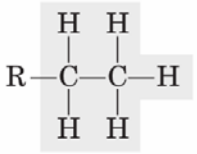
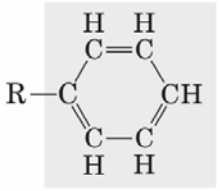
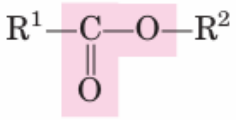
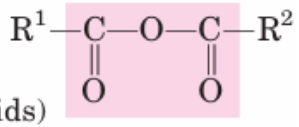
Basic Functional Group in Biomolecules

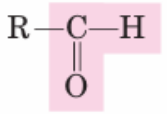
Methyl 

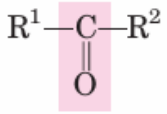
Ethyl 

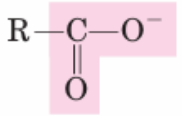
Phenyl 

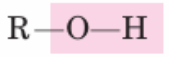
Ester 

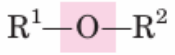
Anhydride (two carboxylic acids) 

Carbonyl (aldehyde) 

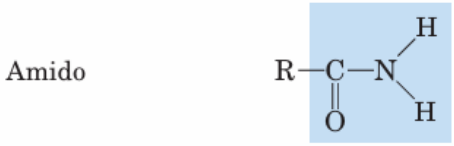
Carbonyl (ketone) 

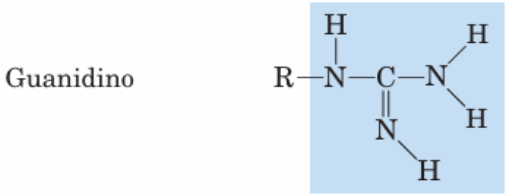
Carboxyl 

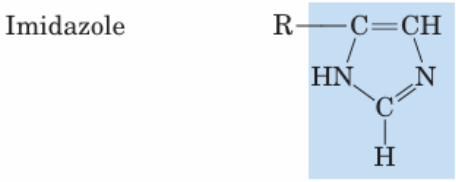
Hydroxyl (alcohol) 

Ether 

Amino

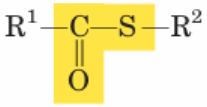
Amido 

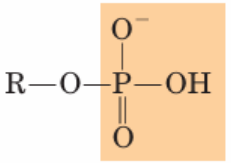
Guanidino 

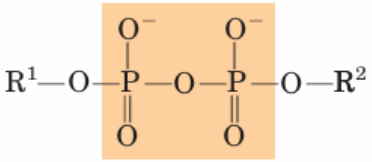
Imidazole 

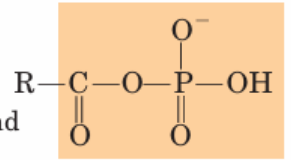
Sulfhydryl

Disulfide

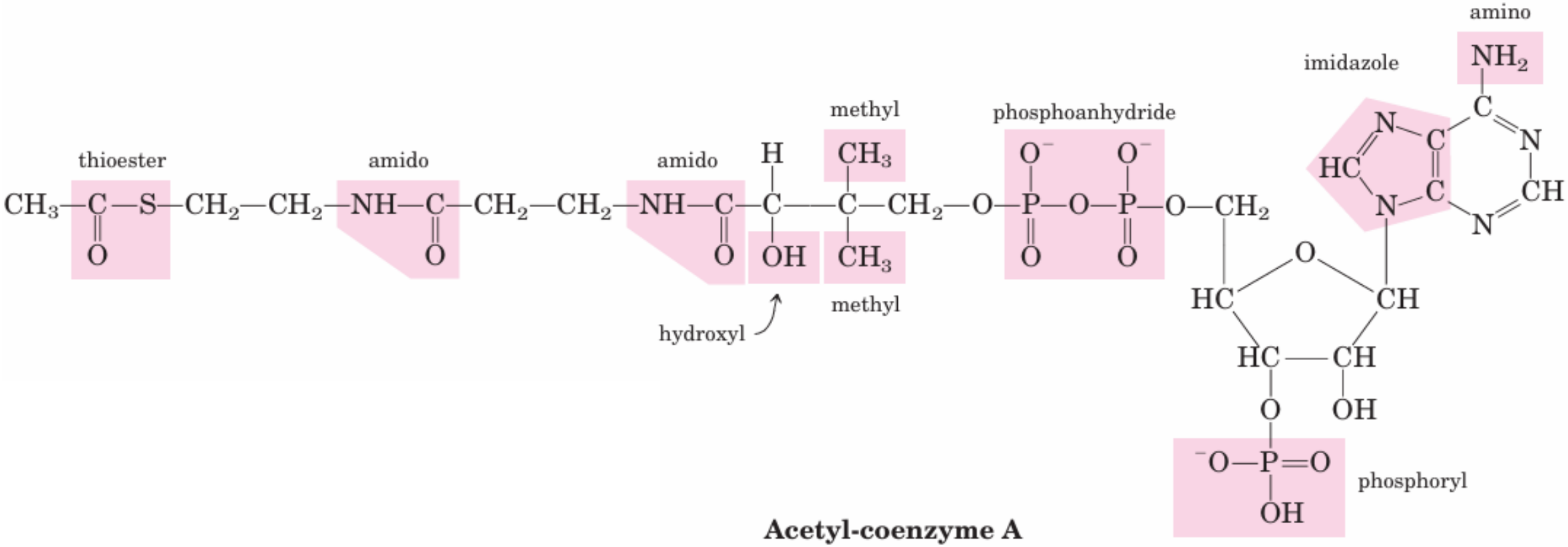
Thioester 

Phosphoryl 

Phosphoanhydride 

Mixed anhydride (carboxylic acid and phosphoric acid; also called acyl phosphate) 

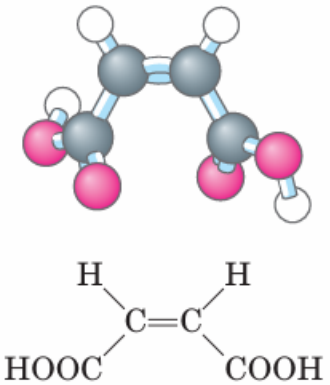
Several common functional groups, in a single biomolecule.



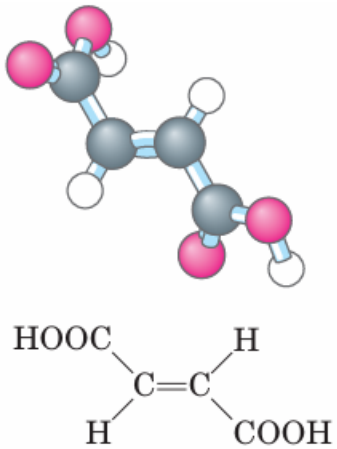
Acetyl-coenzyme A

Three-Dimensional Structure: Configuration and Conformation

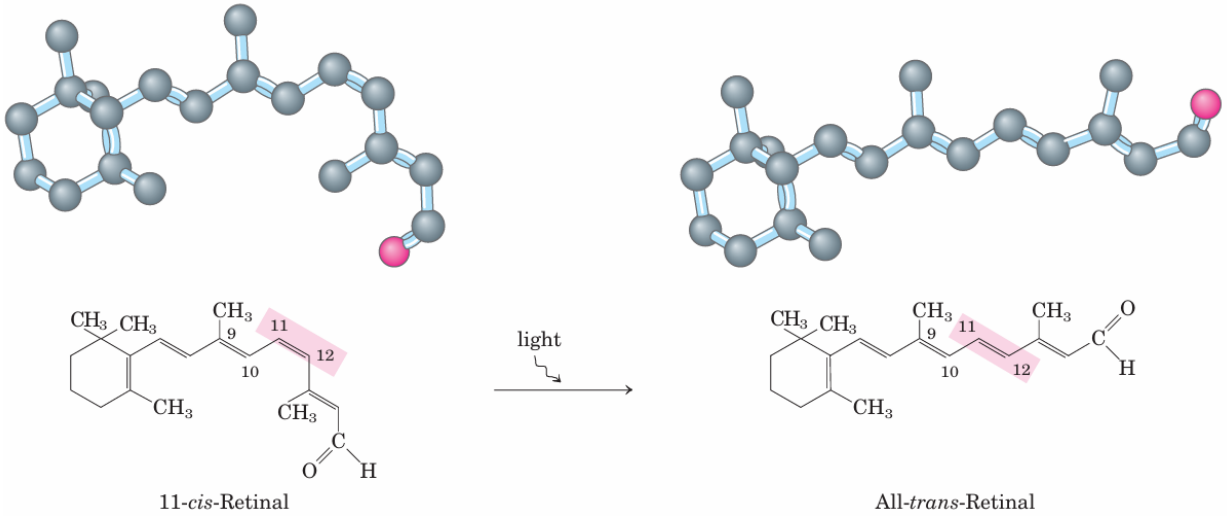
Configurations of geometric isomers:



Maleic acid (cis)



Fumaric acid (trans)

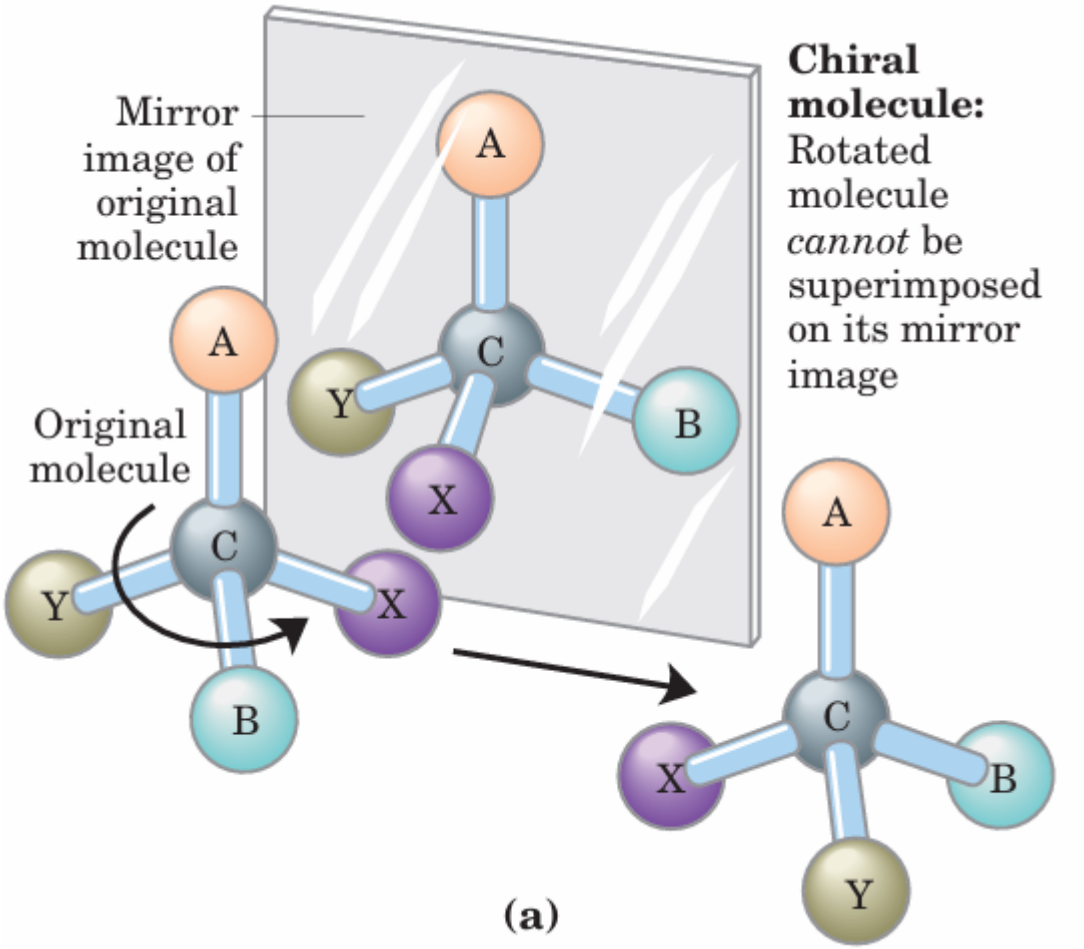


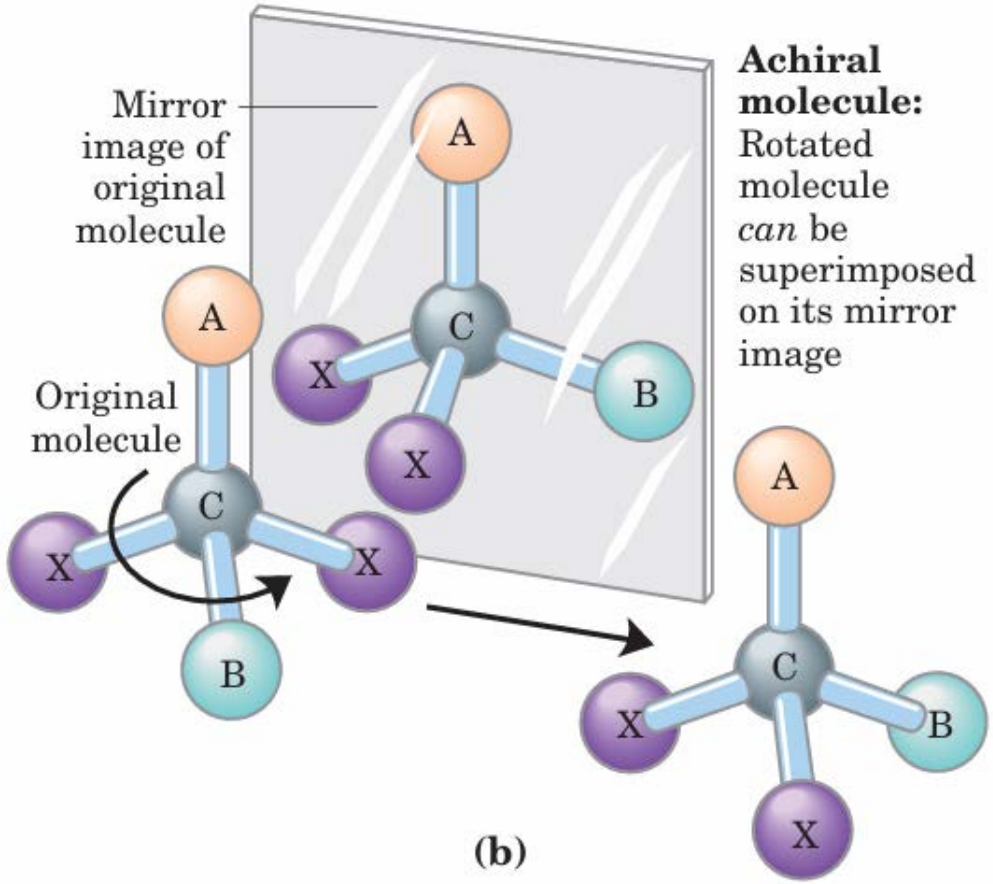
11-*cis*-Retinal

All-*trans*-Retinal

Three-Dimensional Structure: Configuration and Conformation

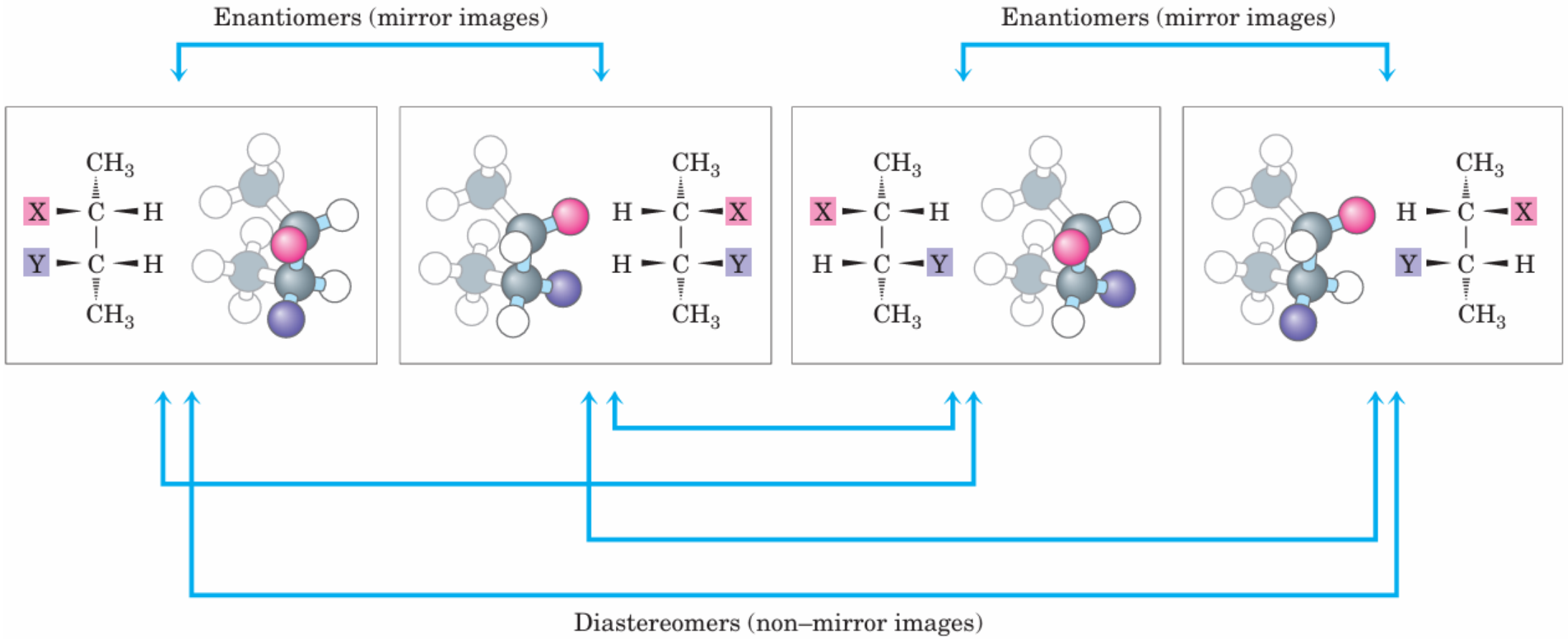
Molecular asymmetry: chiral and achiral molecules





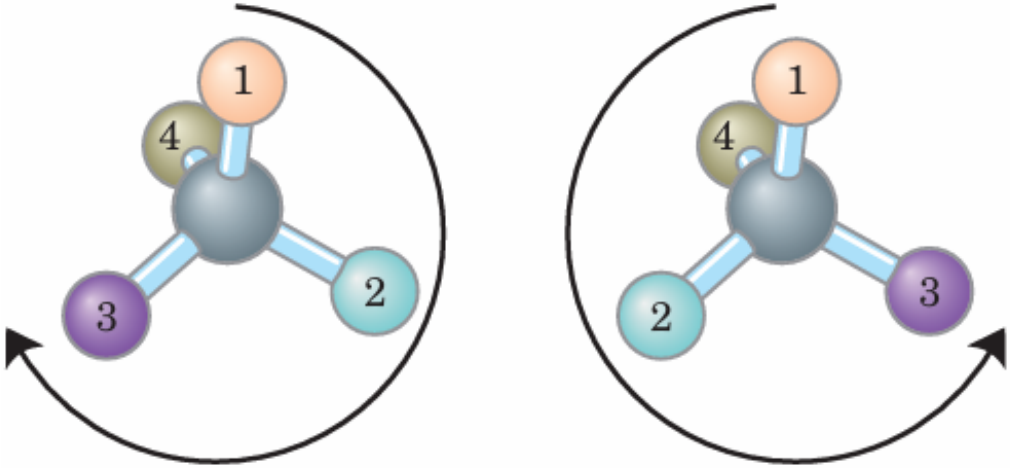
Three-Dimensional Structure: Configuration and Conformation

Molecular asymmetry: chiral and achiral molecules

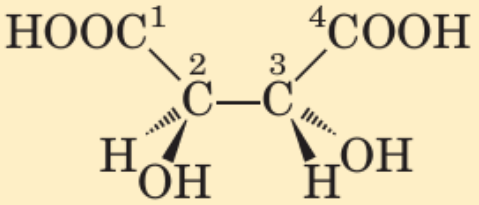


Three-Dimensional Structure: Configuration and Conformation

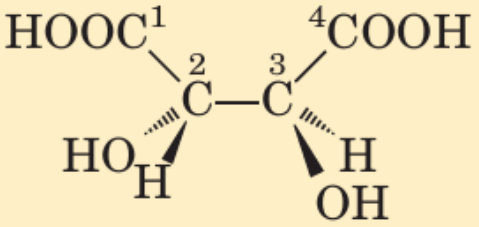
R/S and D/L configuration:



L-Glyceraldehyde (*S*)-Glyceraldehyde

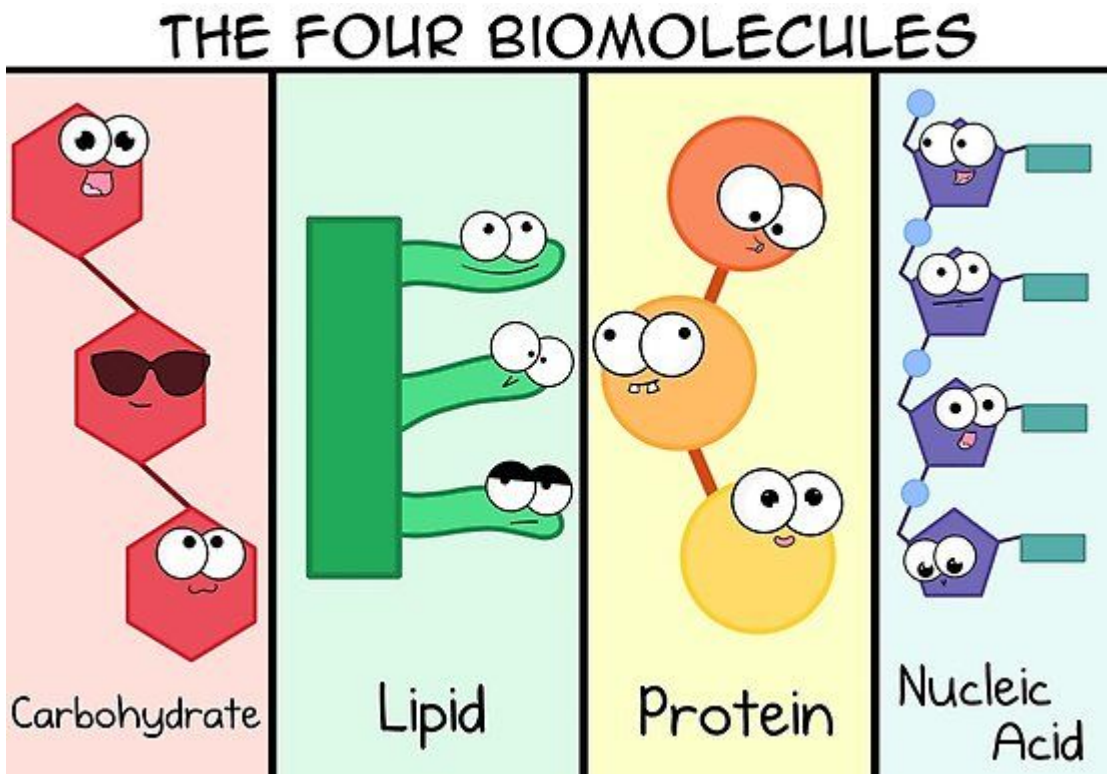


(2*R*,3*R*)-Tartaric acid
(dextrorotatory)



(2*S*,3*S*)-Tartaric acid
(levorotatory)

What is Biomolecules?

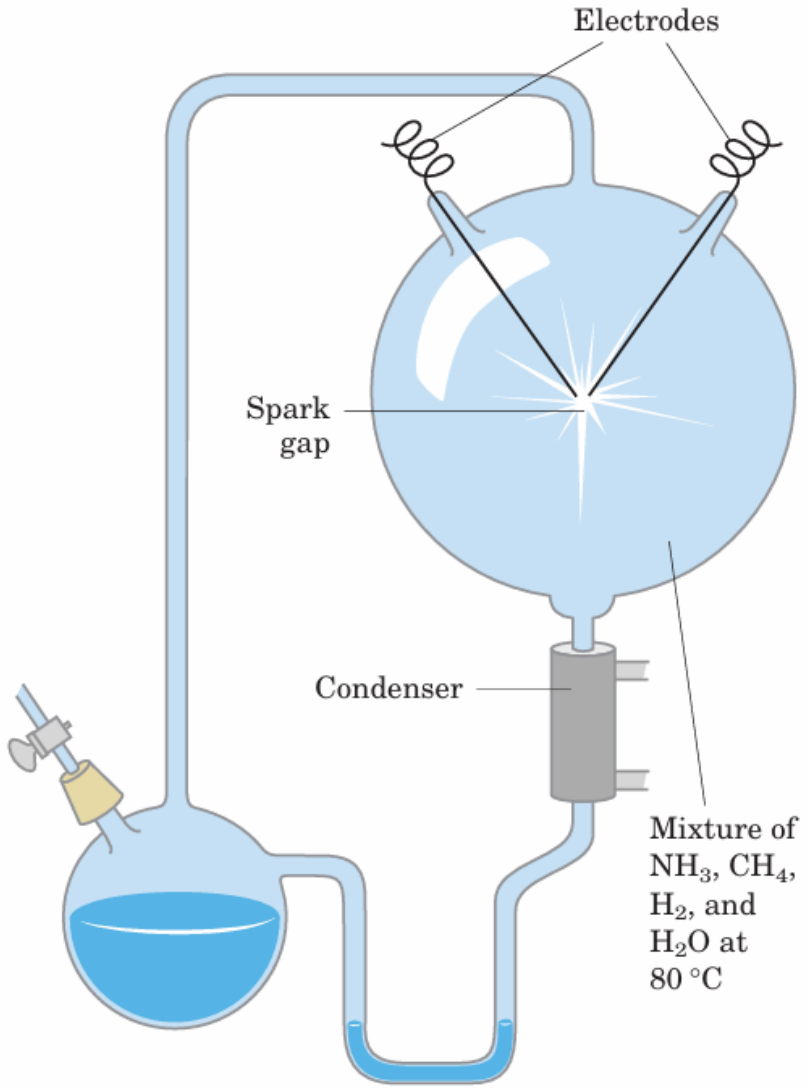


Biomolecules are organic molecules that occur naturally in living organisms. They provide the basic structural and functional constituents to the living cells

- ✓ Found in all living organisms, from bacteria to humans.
- ✓ Composed mainly of C, H, O, N, P, and S atoms.
- ✓ Responsible for structure, function, energy storage, genetic information, and biochemical reactions.
- ✓ Broadly classified into four major types: (Carbohydrates, Proteins, Nucleic Acids, Lipids)

https://in.pinterest.com/pin/four-biomolecules-poster-poster-by-amoebasisters--663366220095611631/

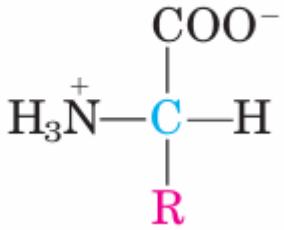
Abiotic production of biomolecules



Spark-discharge apparatus of the type used by ***Miller*** and ***Urey*** in experiments demonstrating abiotic formation of organic compounds under primitive atmospheric conditions. After the subjection of the gaseous contents of the system to electrical sparks, products were collected by condensation. Biomolecules such as **amino acids** were among the products.

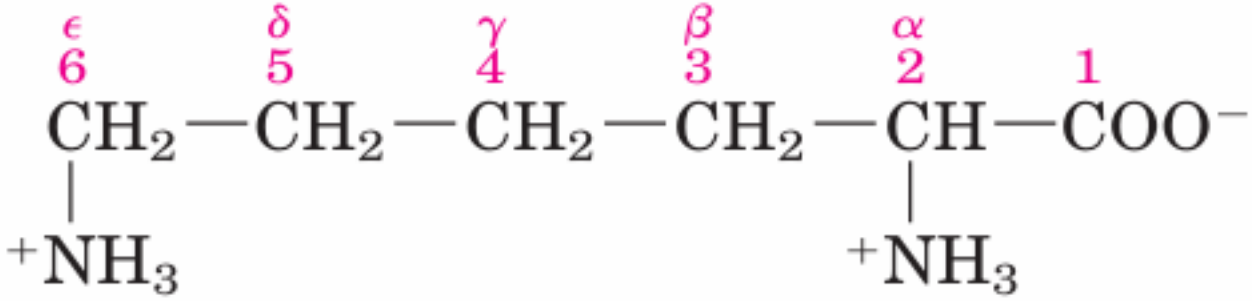
Protein Architecture—Amino Acids

Amino acids are the building blocks of proteins, consisting of an amino group (-NH2), a carboxyl group (-COOH), a hydrogen atom, and a unique side chain (R group), all attached to a central α-carbon.



General structure of an amino acid. This structure is common to all but one of the amino acids. (Proline, a cyclic amino acid, is the exception.) The R group or side chain (red) is attached to the Carbon (blue) and is different in each amino acid.

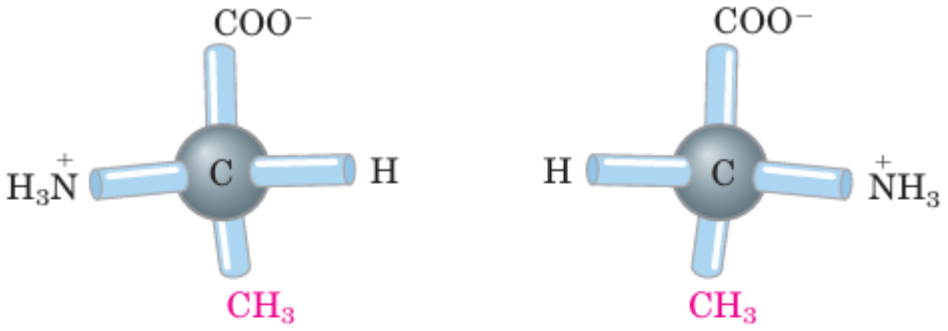
Positions in Amino Acid:



Lysine

For all the common amino acids except glycine, the carbon is bonded to four different groups: a **carboxyl group**, an **amino group**, an **R group**, and a **hydrogen atom**. The α-carbon atom is thus a **chiral center**

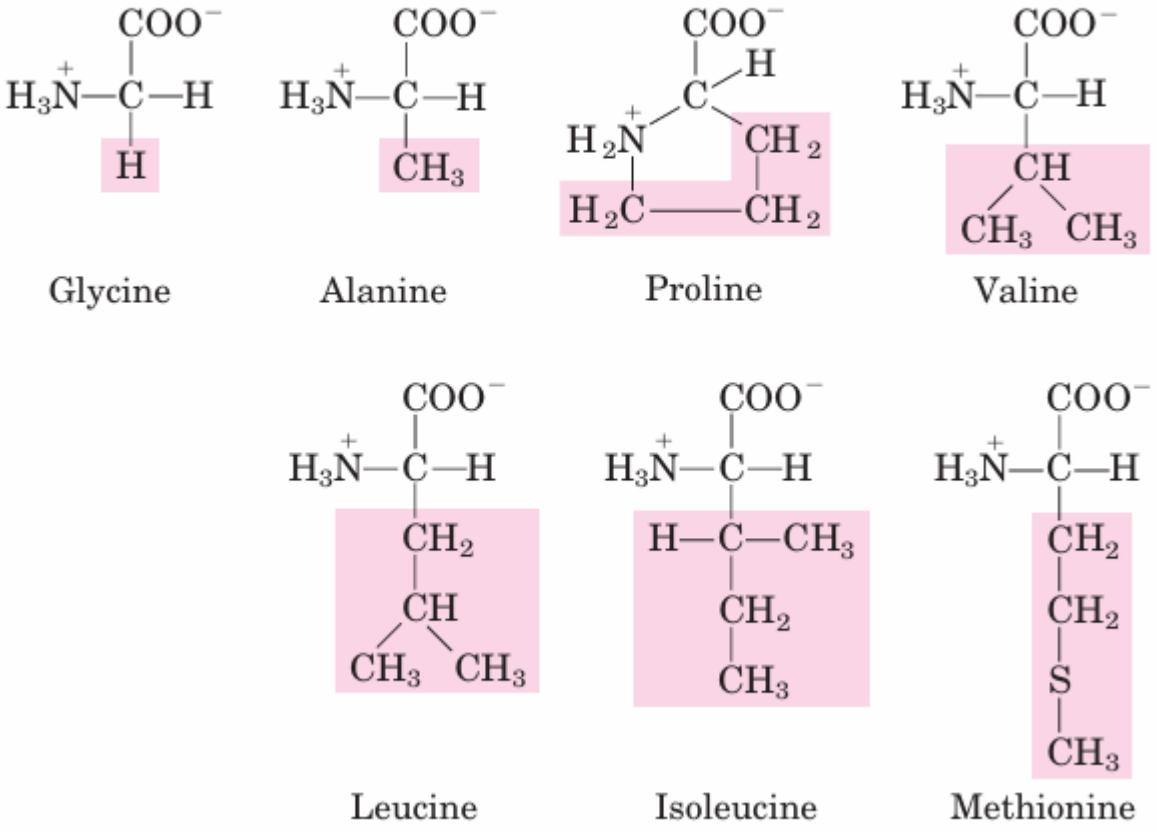
Enantiomers of Amino Acid



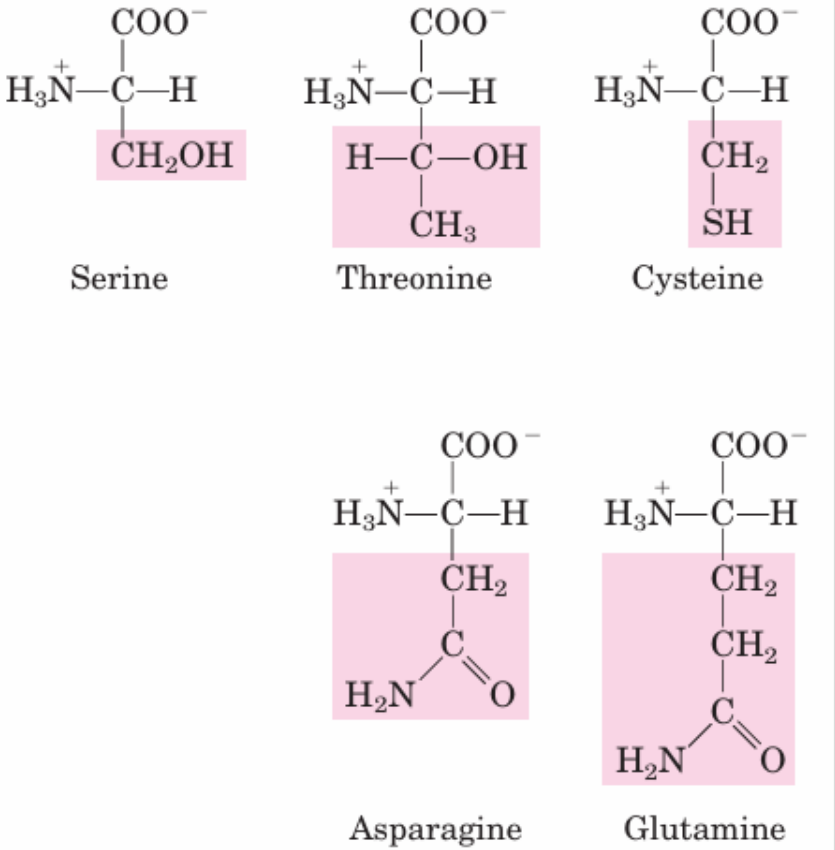
Because of the tetrahedral arrangement of the bonding orbitals around the carbon atom, the four different groups can occupy two unique spatial arrangements, and thus, **amino acids have two possible stereoisomers**. Since they are nonsuperimposable mirror images of each other, the two forms represent a class of stereoisomers called **enantiomers**. *All molecules with a chiral center are also optically active*—that is, they rotate plane-polarized light.

Classification of Amino Acids Based on –R Group

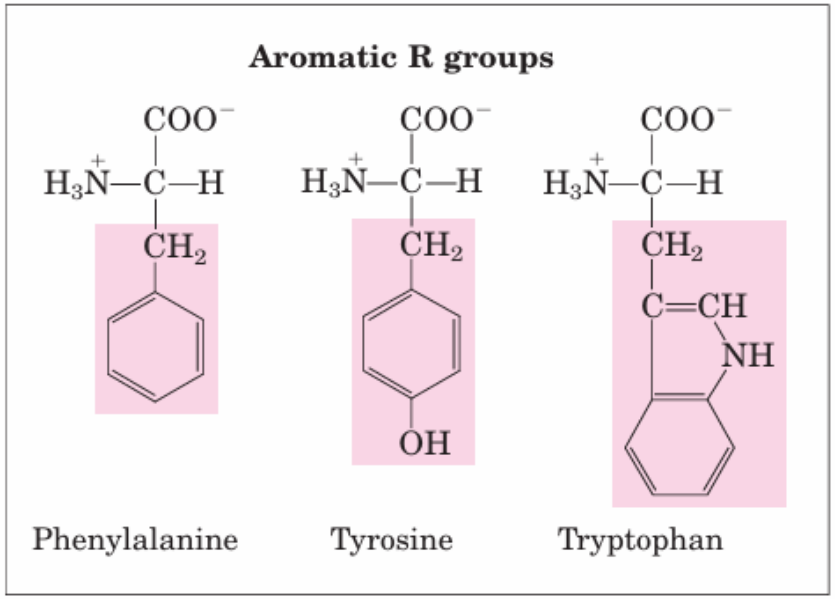
Nonpolar, aliphatic R groups

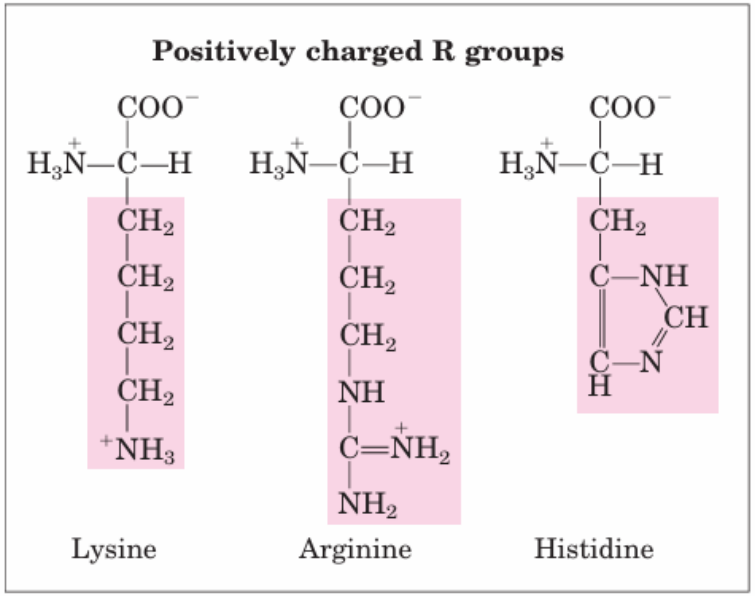


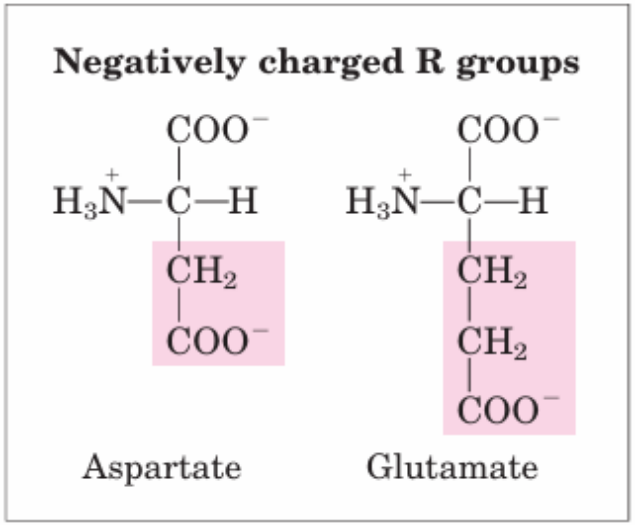
Polar, uncharged R groups



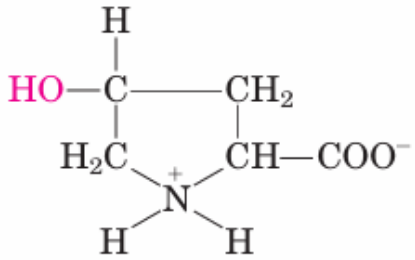
Classification of Amino Acids Based on –R Group



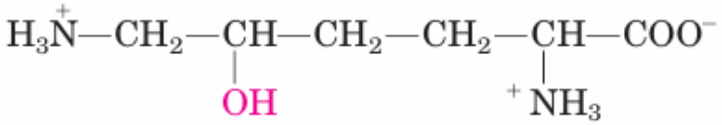




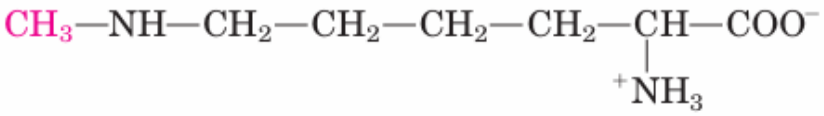
Uncommon Amino Acids



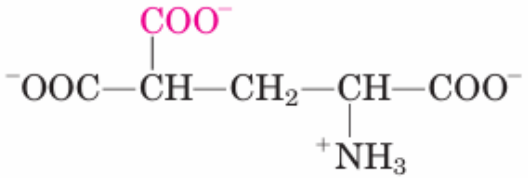
4-Hydroxyproline



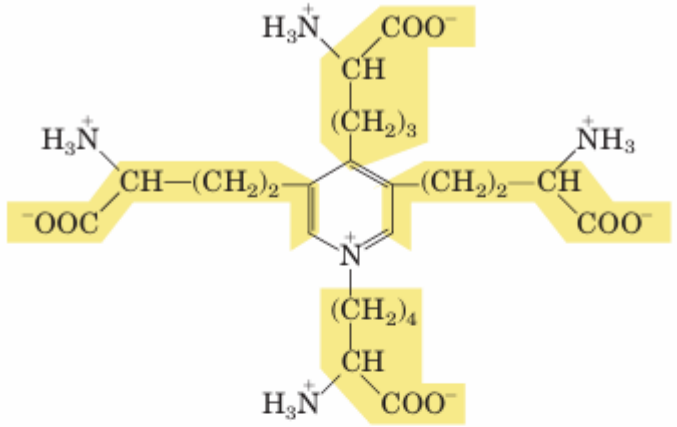
5-Hydroxylysine



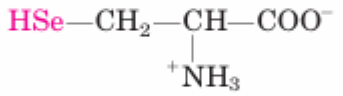
6-*N*-Methyllysine



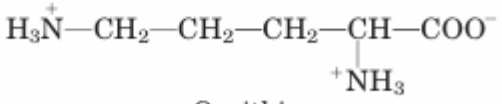
γ-Carboxyglutamate



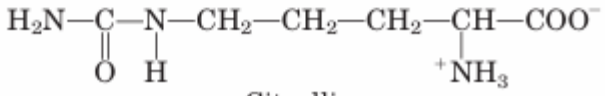
Desmosine



Selenocysteine



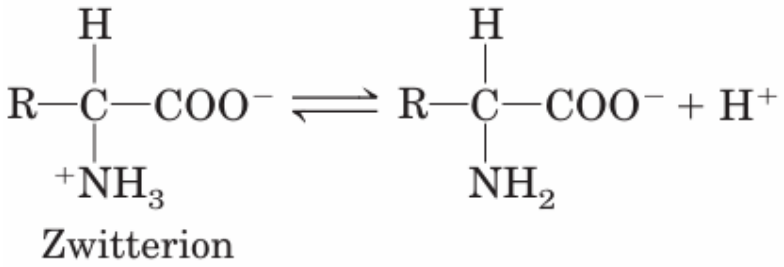
Ornithine



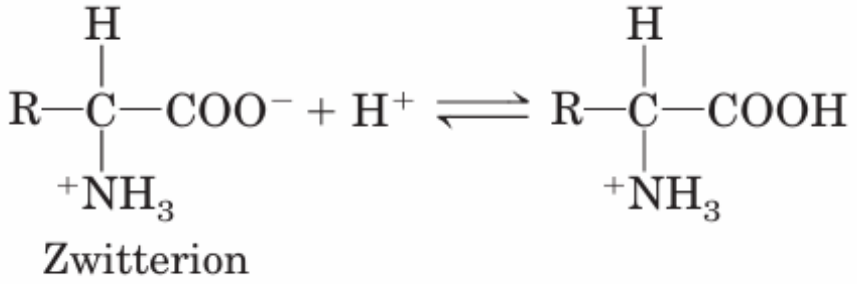
Citrulline

Amino Acids Can Act as Acids and Bases

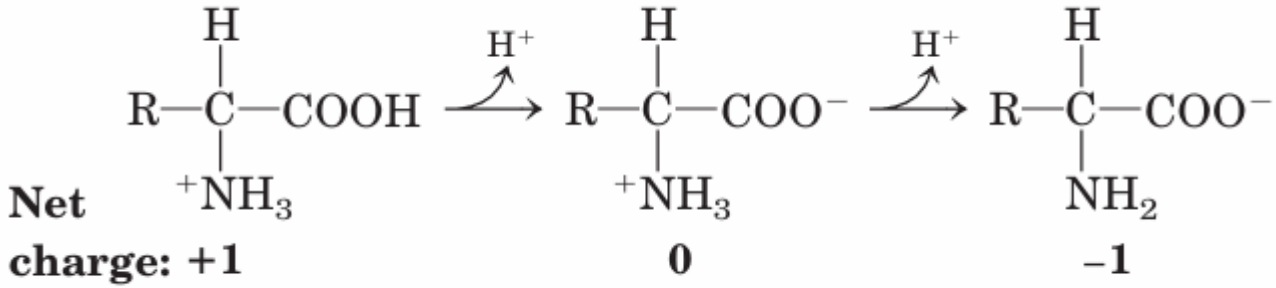
acid (proton donor):



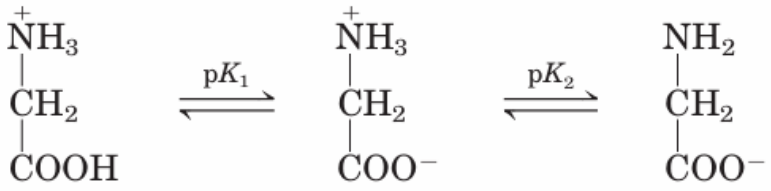
base (proton acceptor):

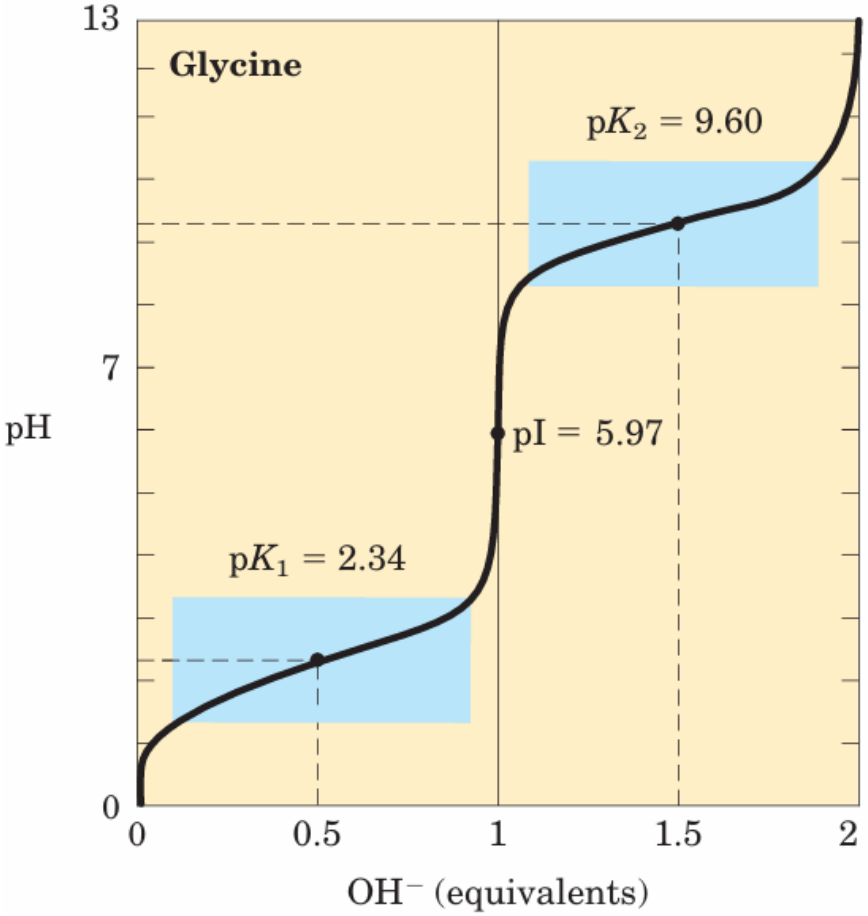


Substances having this dual nature are **amphoteric** and are often called **ampholytes** (from "*amphoteric electrolytes*").

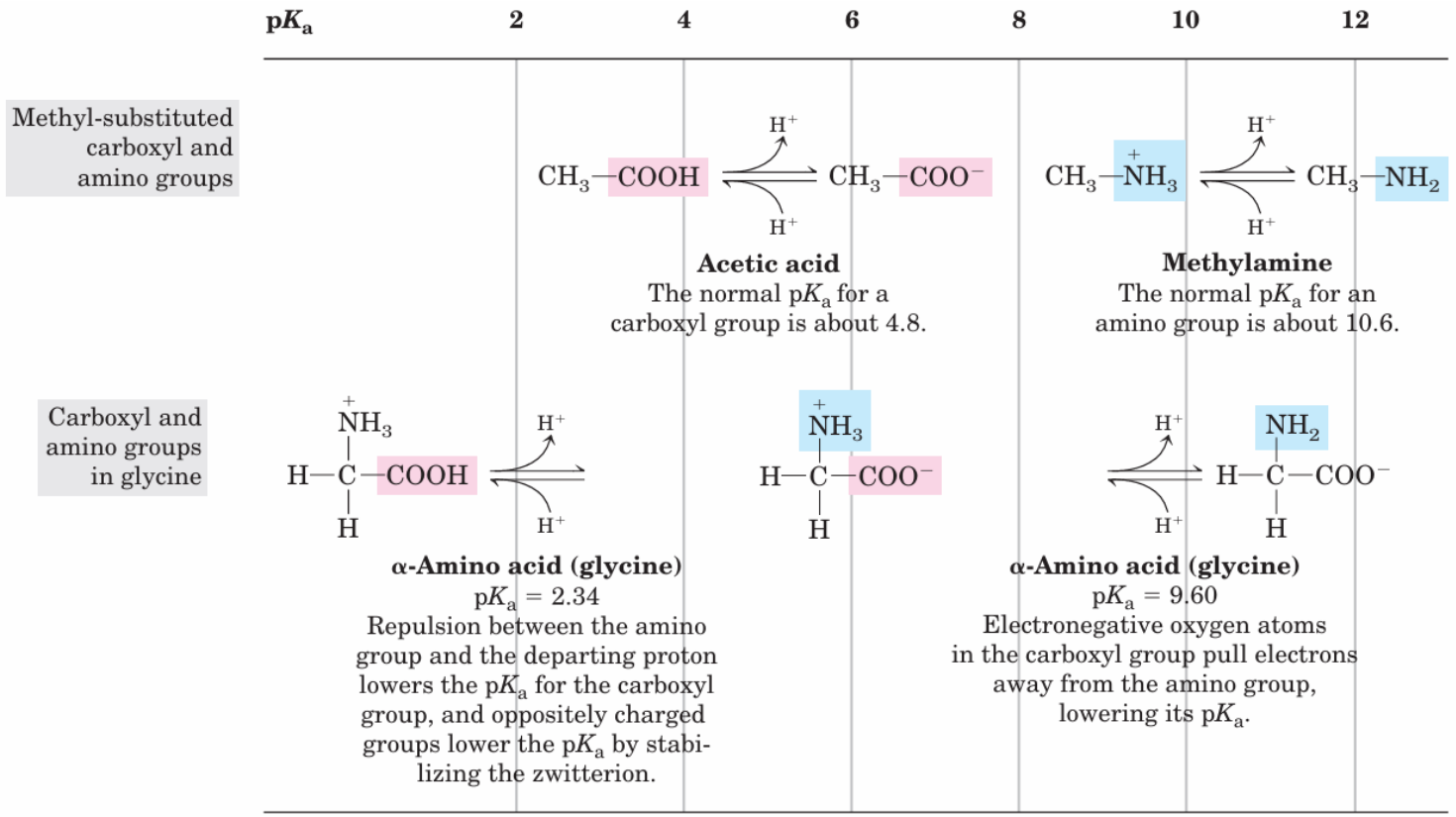


pH Titration of an Amino Acid

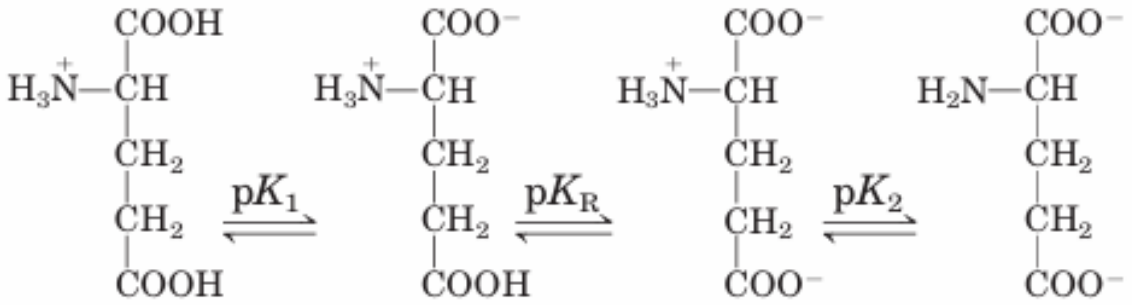


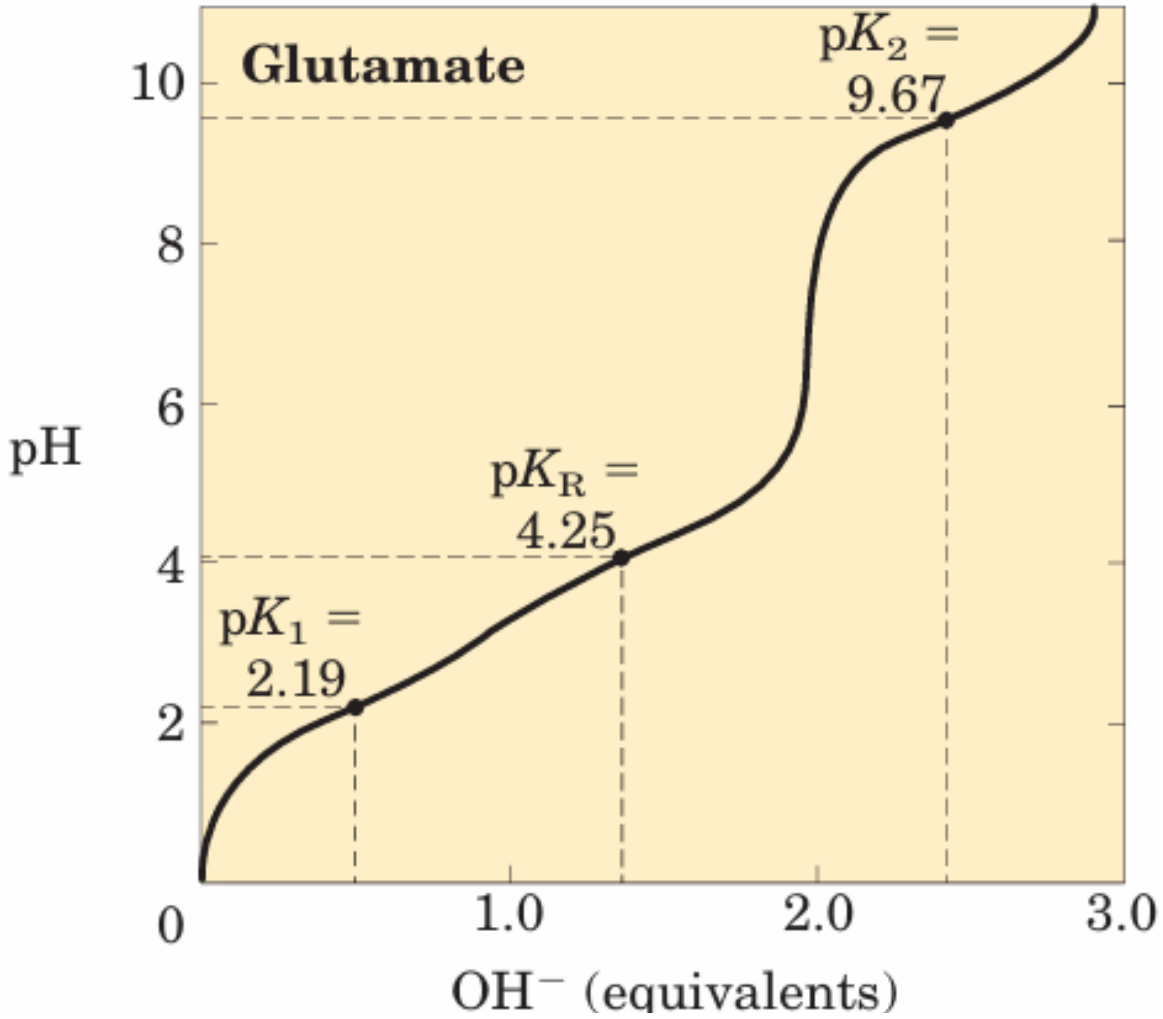


Effect of the chemical environment on *pKa*



pH Titration of an Amino Acid





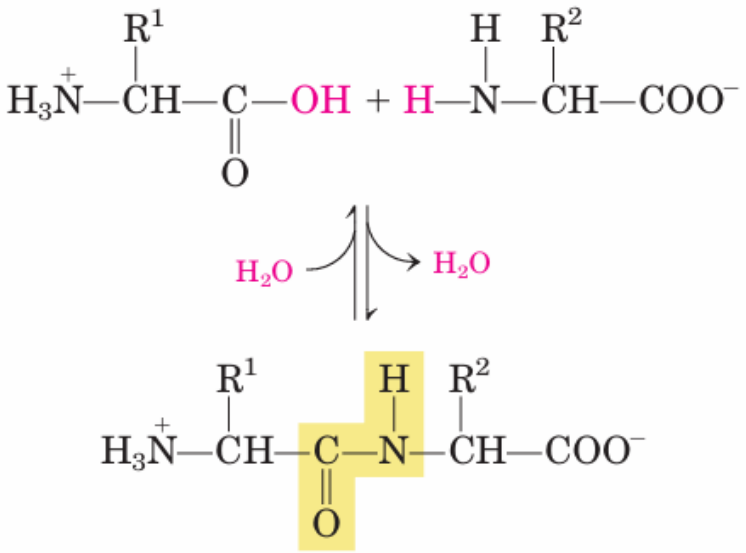
Summary

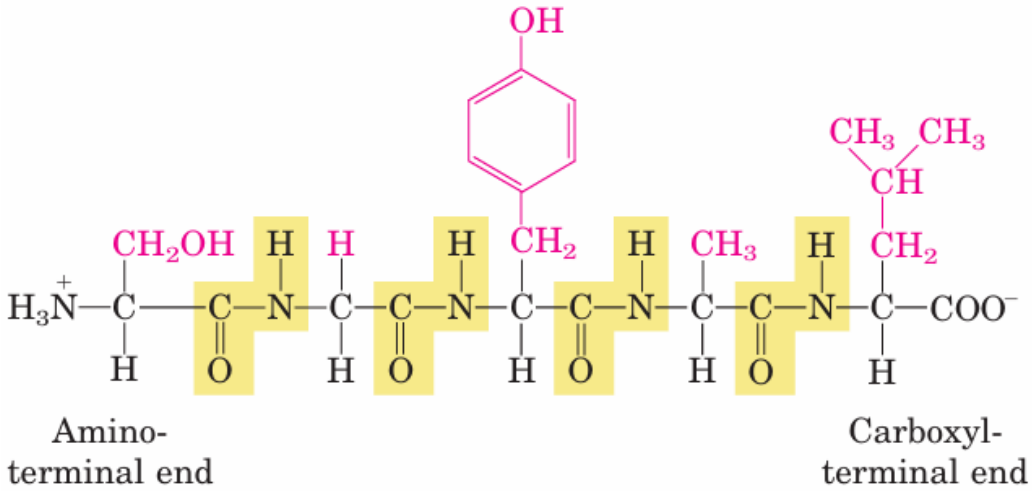
- The 20 amino acids commonly found as residues in proteins contain a carboxyl group, an amino group, and a distinctive R group substituted on the carbon atom.

- The α-carbon atom of all amino acids except glycine is asymmetric, and thus amino acids can exist in at least two stereoisomeric forms. Only the *L*-stereoisomers, with a configuration related to the absolute configuration of the reference molecule *L*-glyceraldehyde, are found in proteins.

- Amino acids are classified into **five types** on the basis of the polarity and charge (at pH 7) of their R groups.

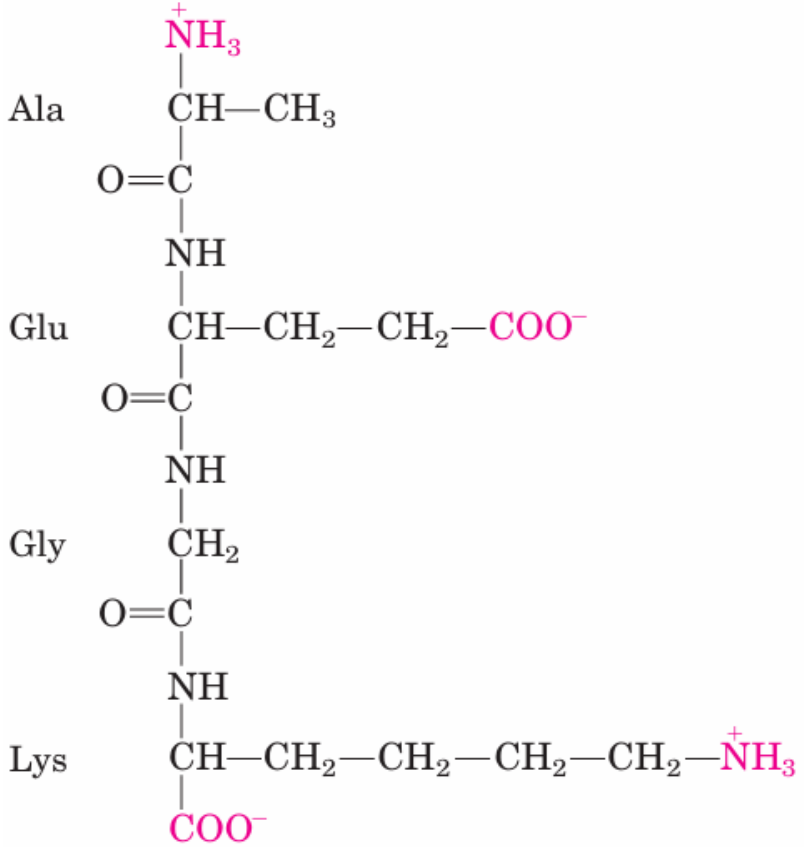
Peptides Are Chains of Amino Acids





Two amino acid molecules can be covalently joined through a substituted amide linkage, termed a **peptide bond**, to yield a dipeptide. Such a linkage is formed by the removal of the elements of water (dehydration) from the carboxyl group of one amino acid and the amino group of another

Peptides and Proteins

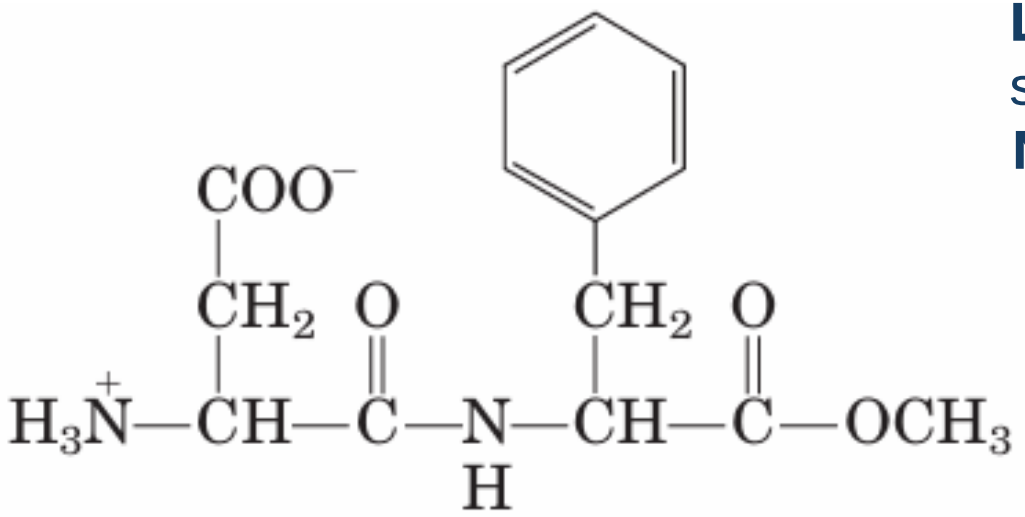


Tetrapeptide
Alanylglutamylglycyllysine

When **a few amino acids** are joined, the structure is called an **oligopeptide**. When many amino acids are joined, the product is called a **polypeptide**. Proteins may have thousands of amino acid residues. Although the terms "**protein**" and "**polypeptide**" are sometimes used interchangeably, molecules referred to as polypeptides generally have molecular weights below 10,000, and those called proteins have higher molecular weights.

In a peptide, the amino acid residue at the end with a **free amino group is the amino-terminal** (or **N-terminal**) residue; the residue at the other end, which has a free **carboxyl group**, is the **carboxyl-terminal** (**C-terminal**) residue.

Commercially Synthesized Dipeptide



L-Aspartyl-L-phenylalanine methyl ester
(aspartame)

commercially synthesized dipeptide **L-aspartyl-L-phenylalanine methyl ester**, the artificial sweetener better known as **aspartame** or **NutraSweet**.

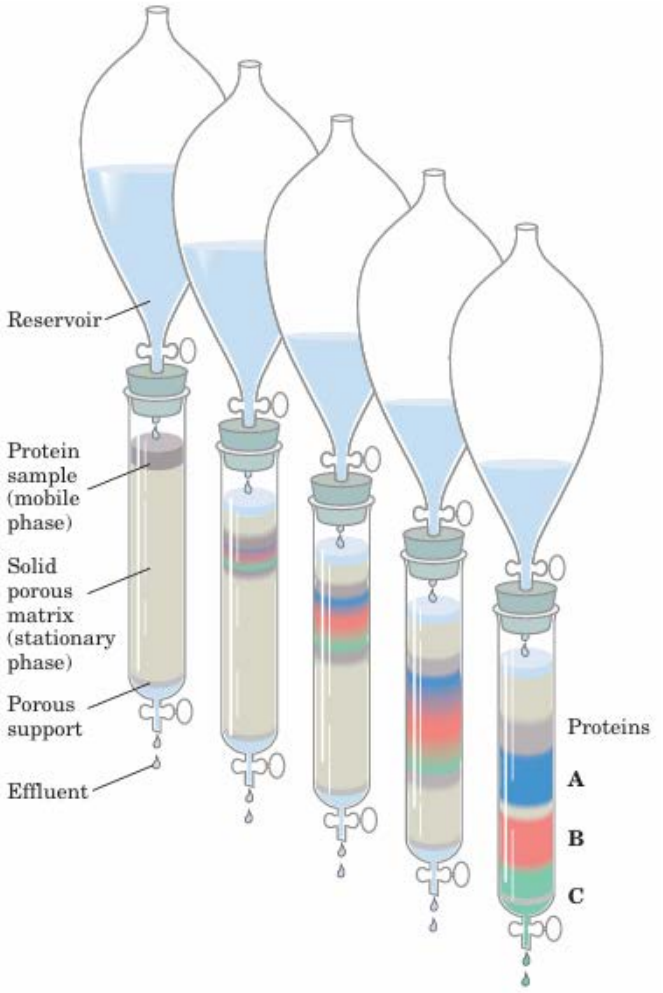
Molecular Data on Some Proteins

	Molecular weight	Number of residues	Number of polypeptide chains
Cytochrome *c* (human)	13,000	104	1
Ribonuclease A (bovine pancreas)	13,700	124	1
Lysozyme (chicken egg white)	13,930	129	1
Myoglobin (equine heart)	16,890	153	1
Chymotrypsin (bovine pancreas)	21,600	241	3
Chymotrypsinogen (bovine)	22,000	245	1
Hemoglobin (human)	64,500	574	4
Serum albumin (human)	68,500	609	1
Hexokinase (yeast)	102,000	972	2
RNA polymerase (*E. coli*)	450,000	4,158	5
Apolipoprotein B (human)	513,000	4,536	1
Glutamine synthetase (*E. coli*)	619,000	5,628	12
Titin (human)	2,993,000	26,926	1

Amino Acid Composition of Two Proteins

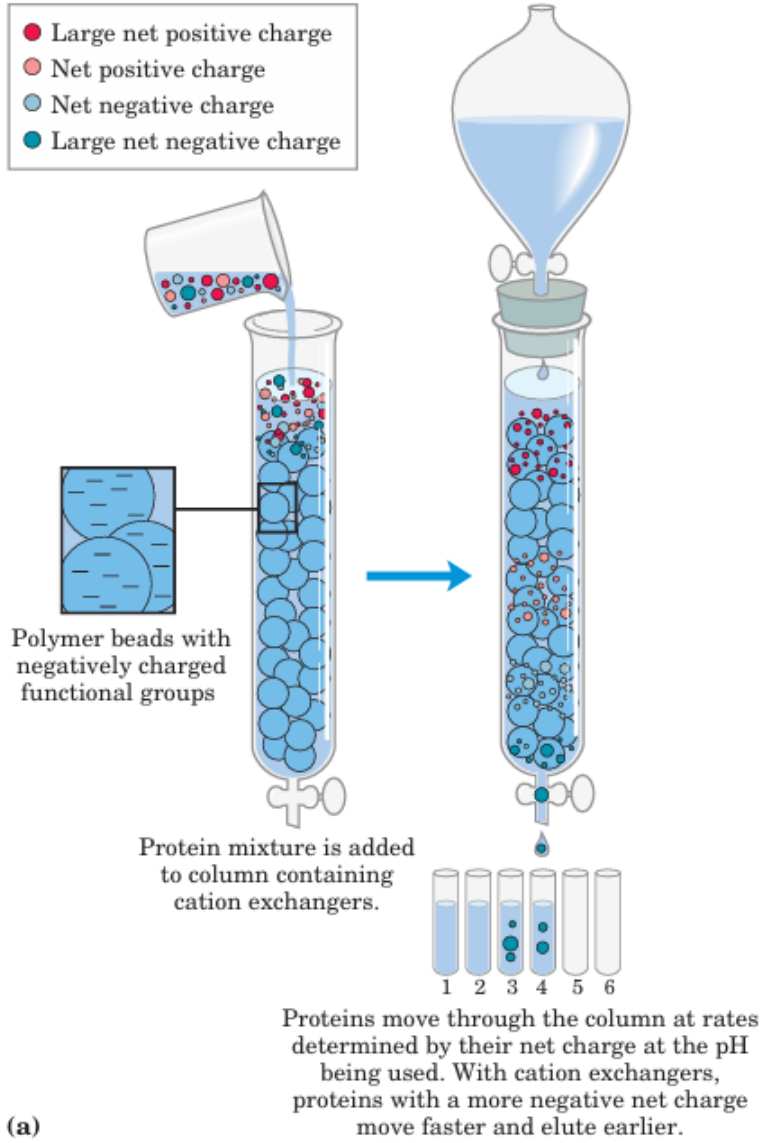
Amino acid	Number of residues per molecule of protein*	
	Bovine cytochrome c	Bovine chymotrypsinogen
Ala	6	22
Arg	2	4
Asn	5	15
Asp	3	8
Cys	2	10
Gln	3	10
Glu	9	5
Gly	14	23
His	3	2
Ile	6	10
Leu	6	19
Lys	18	14
Met	2	2
Phe	4	6
Pro	4	9
Ser	1	28
Thr	8	23
Trp	1	8
Tyr	4	4
Val	3	23
Total	104	245

Purification of Proteins: Column chromatography



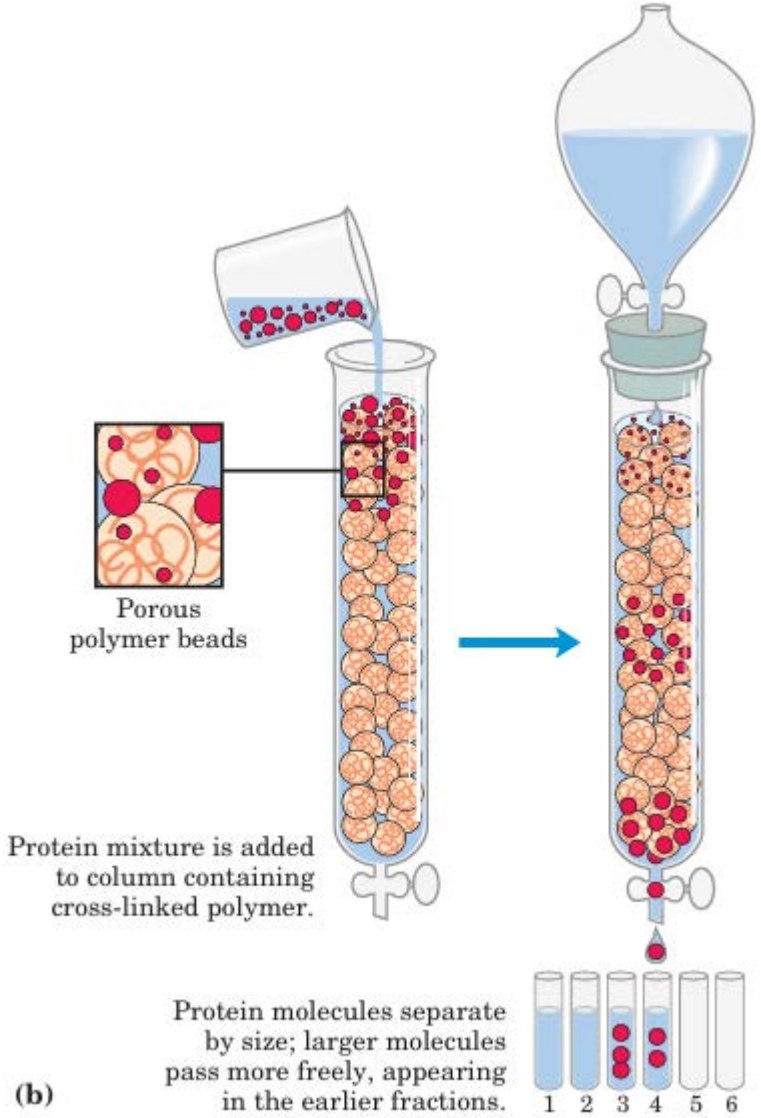
A **chromatographic column** consists of a solid, porous matrix (**stationary phase**) inside a plastic or glass column through which a liquid (**mobile phase**) flows. A protein solution is applied to the top of the column and moves downward, interacting with the matrix. Different proteins migrate at different rates due to varying interactions with the matrix, leading to separation into distinct bands. Longer columns improve separation (resolution), but diffusion causes band spreading over time, which can reduce resolution. In the given example, protein **A** is well separated, while proteins **B** and **C** show partial overlap due to diffusional spreading.

Purification of Proteins: Column chromatography



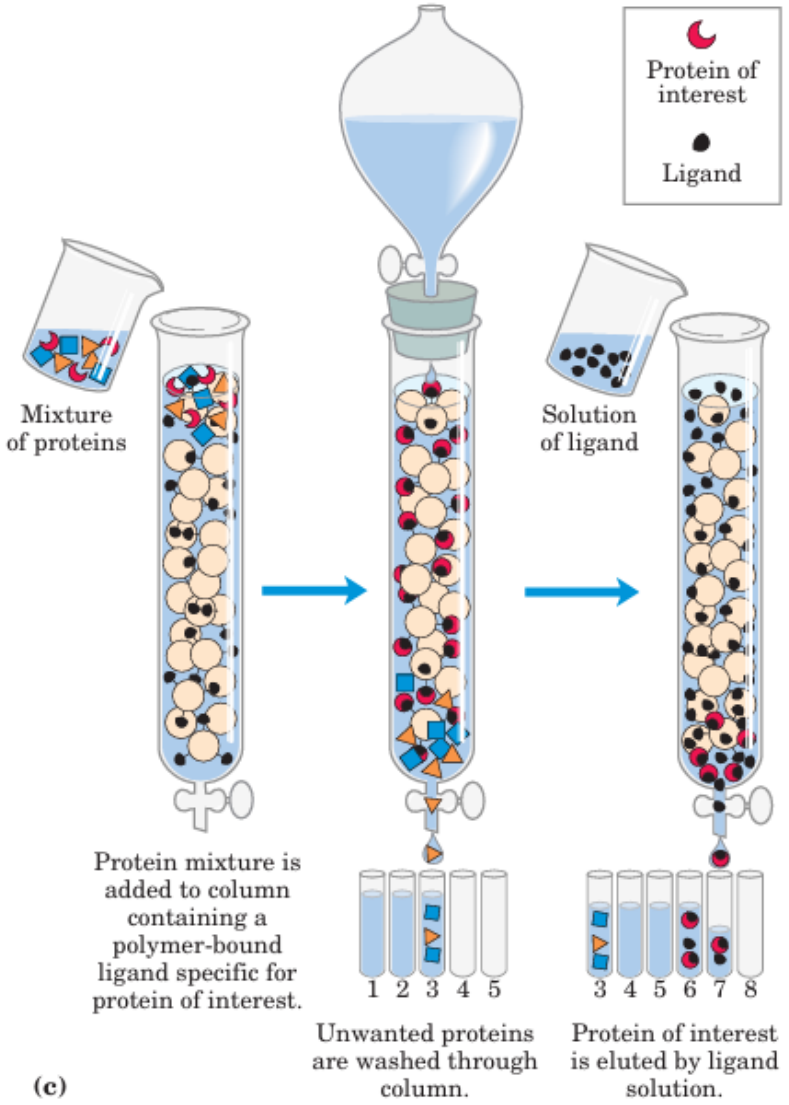
Ion exchange column chromatography:
Ion-exchange chromatography separates proteins based on differences in their net charge at a given pH. The column contains a **charged polymer matrix:** cation exchangers have negatively charged groups, while anion exchangers have positively charged ones. Proteins bind to the matrix depending on their charge, which is influenced by the pH and salt concentration. Separation is optimized by gradually changing the pH or salt concentration to create a gradient, affecting protein binding and elution.

Purification of Proteins: Column chromatography



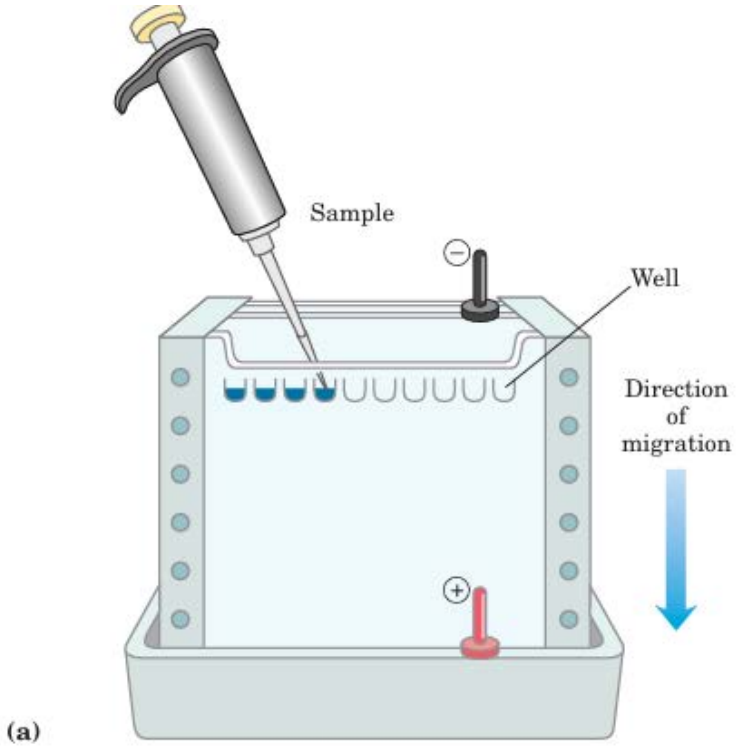
Size-exclusion chromatography, also called gel filtration, separates proteins according to size. The column matrix is a cross-linked polymer with pores of a selected size. Larger proteins migrate faster than smaller ones, because they are too large to enter the pores in the beads and hence take a more direct route through the column. The smaller proteins enter the pores and are slowed by their more labyrinthine path through the column.

Purification of Proteins: Column chromatography



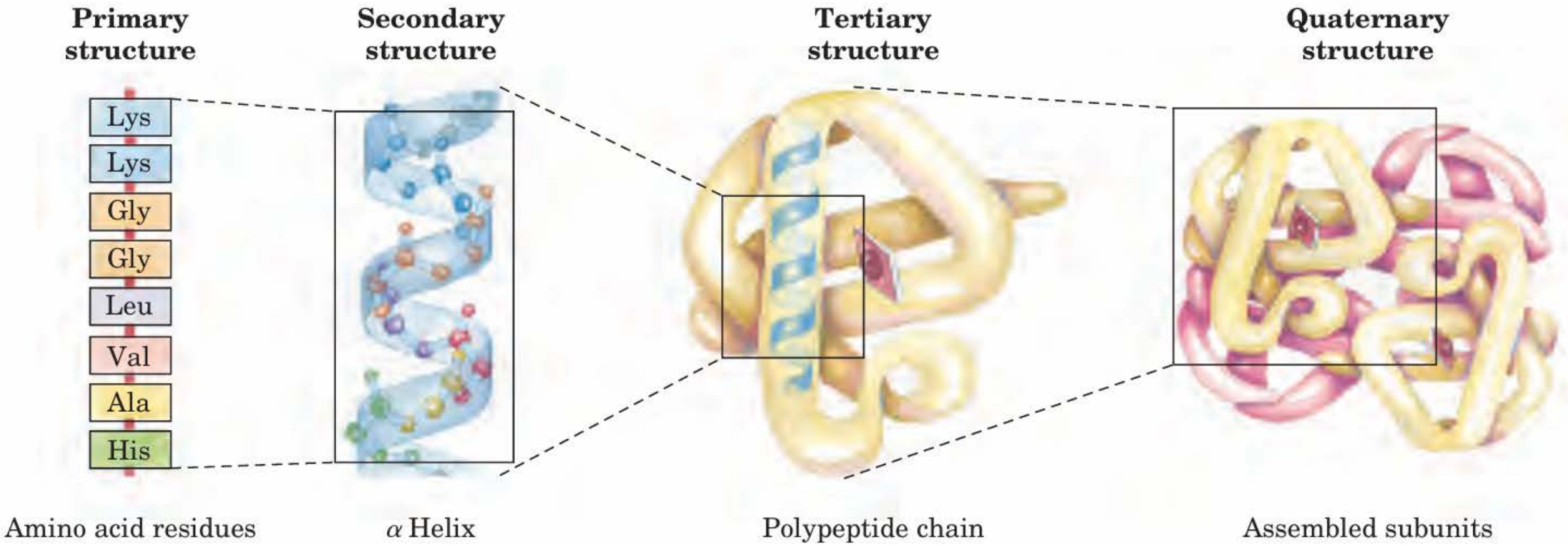
Affinity chromatography separates proteins by their binding specificities. The proteins retained on the column are those that bind specifically to a ligand cross-linked to the beads. (In biochemistry, the term "ligand" is used to refer to a group or molecule that binds to a macromolecule such as a protein.) After proteins that do not bind to the ligand are washed through the column, the bound protein of particular interest is eluted (washed out of the column) by a solution containing free ligand.

Purification of Proteins: Electrophoresis

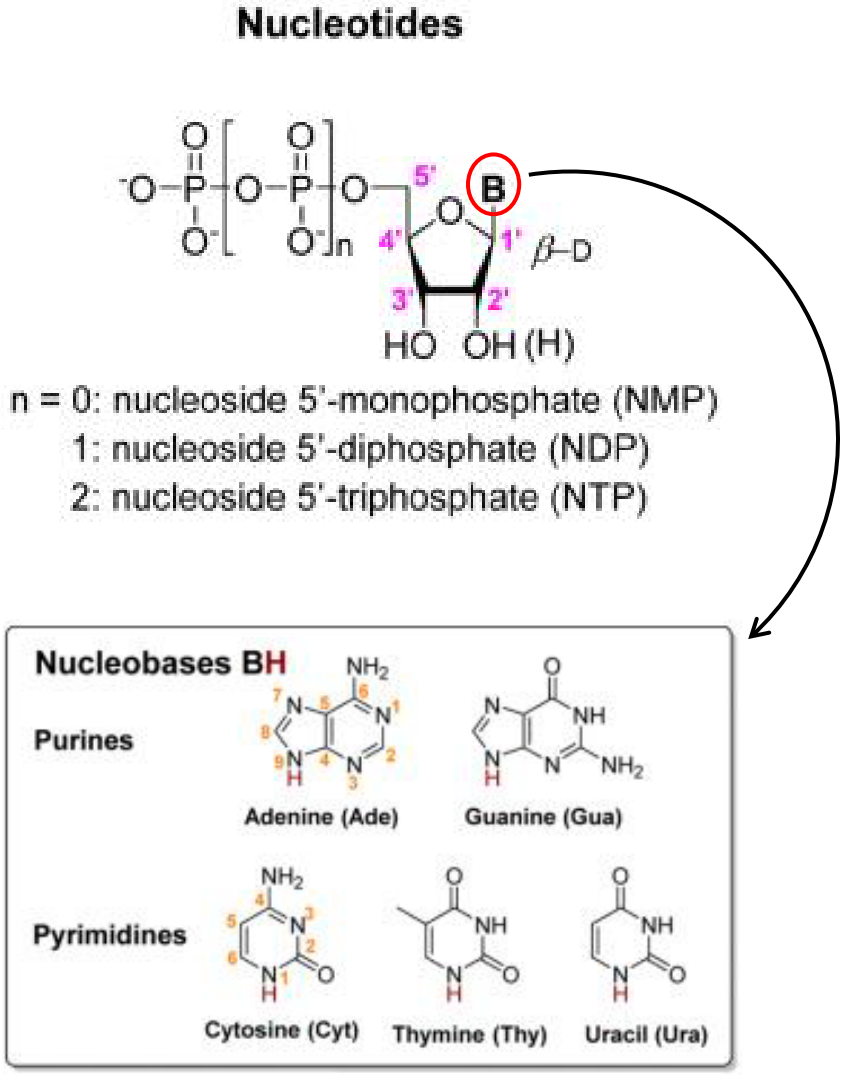


Electrophoresis is a technique used to separate proteins based on size using a polyacrylamide gel and an electric field. Samples are loaded into wells at the top of the gel, and proteins migrate through the gel when voltage is applied. Smaller proteins move faster and appear lower in the gel. After separation, proteins are visualized by staining (e.g., with Coomassie blue). Each band represents a distinct protein or subunit. The gel can track purification progress, as shown in the example of E. coli RNA polymerase, where successive lanes reveal increasing purity, with the final lane displaying its four subunits.

Structures of Protein



Nucleotides, Building Blocks of Nucleic Acids

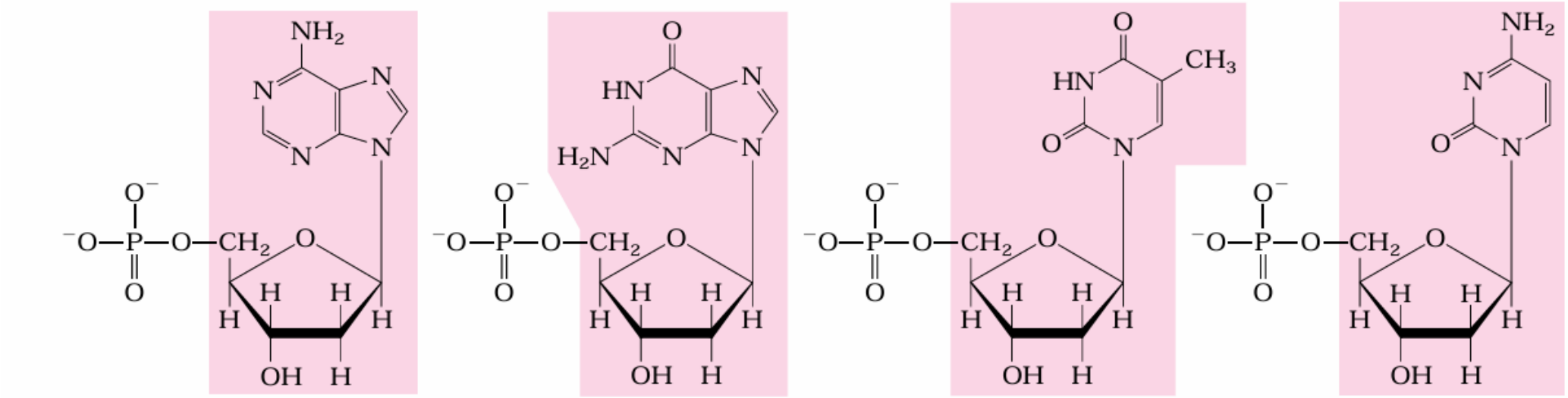


Nucleotide is the basic unit of DNA and RNA, made up of a **nitrogenous base**, a **sugar** (**ribose or deoxyribose**), and a **phosphate group**. It links with other nucleotides to form long chains, creating the structure of genetic material. Nucleotides also play key roles in energy transfer and cellular signaling, such as in **ATP** and **cAMP**.

Nucleic acid is a large biomolecule made up of long chains of nucleotides. The two main types are **DNA (deoxyribonucleic acid)** and **RNA (ribonucleic acid)**, which store and transmit **genetic information**. Nucleic acids are essential for protein synthesis and the regulation of cellular activities.

Deoxyribonucleotides

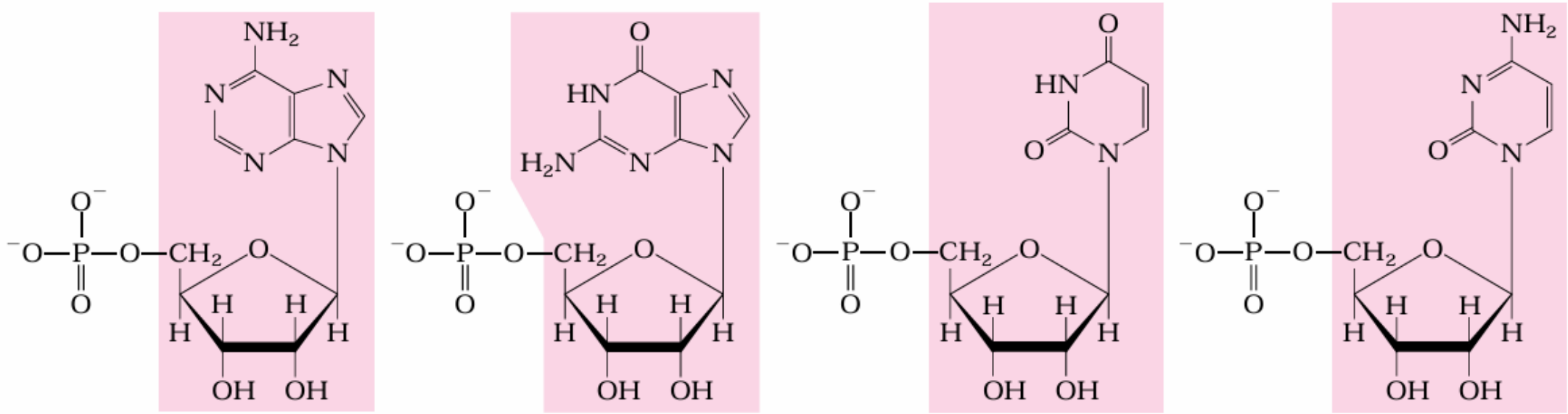
Deoxyribonucleotides are the building blocks of **DNA (deoxyribonucleic acid)**. Each deoxyribonucleotide consists of a nitrogenous base, a deoxyribose sugar, and one or more phosphate groups. They link together to form the DNA strand, carrying genetic information in cells.



Nucleotide:	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

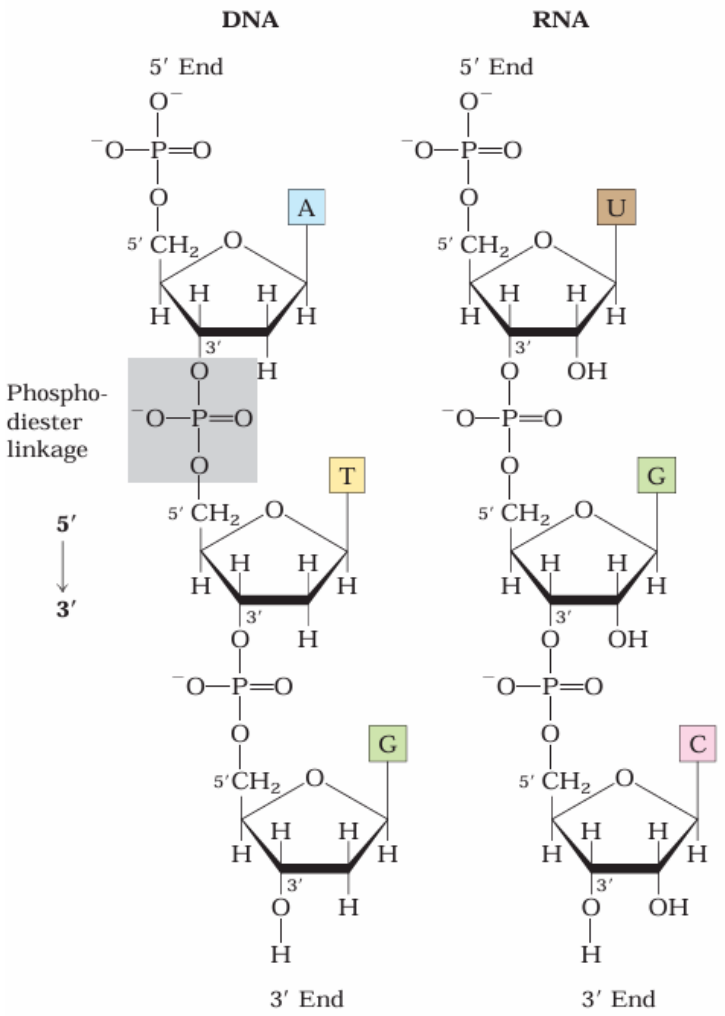
Ribonucleotides

Ribonucleotides are the building blocks of **RNA (ribonucleic acid)**. Each ribonucleotide is made up of a nitrogenous base, a ribose sugar, and a phosphate group. They form RNA strands, which play key roles in protein synthesis and gene regulation.



Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

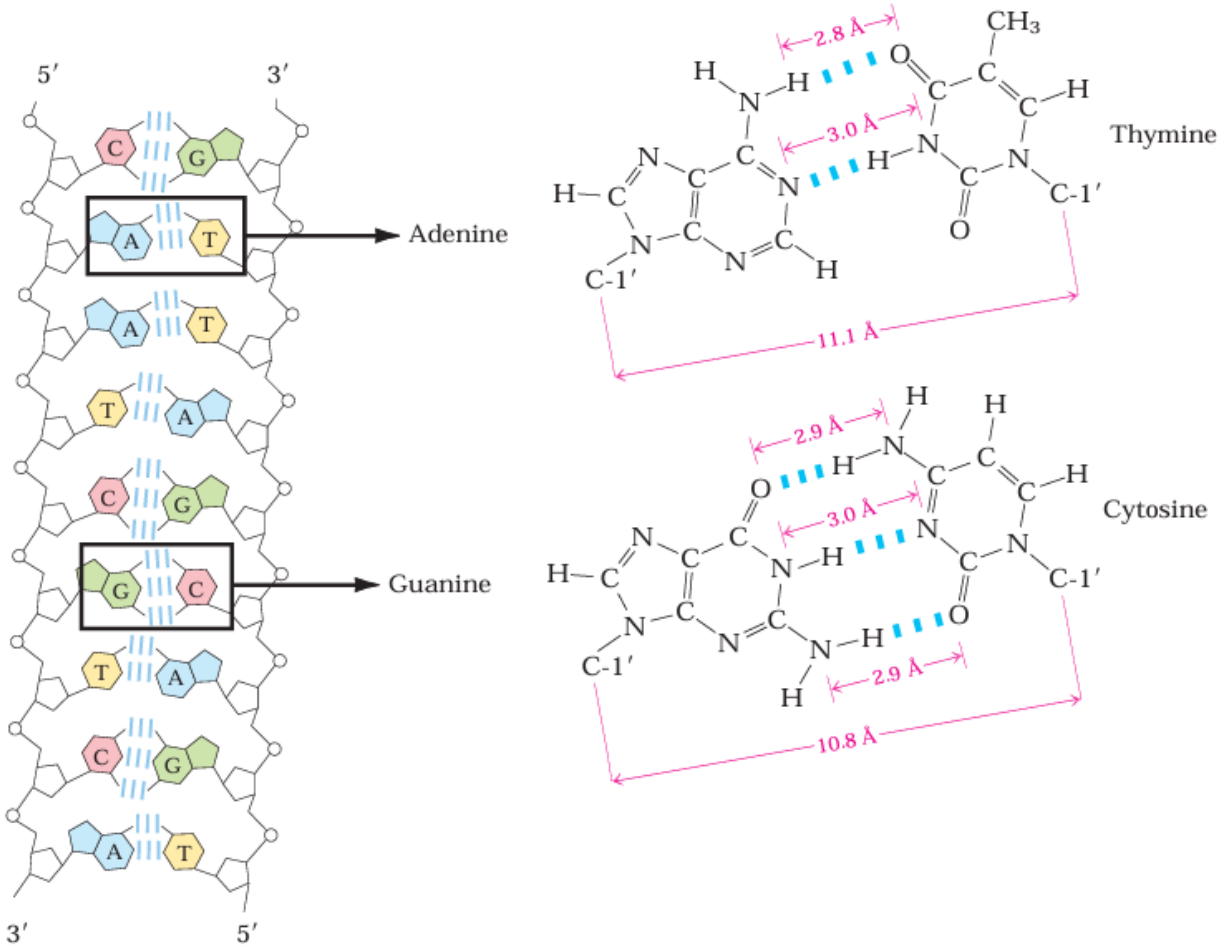
Phosphodiester Linkages in the Covalent Backbone of DNA and RNA



Phosphodiester linkages are the covalent bonds that connect nucleotides in the backbone of DNA and RNA. They form between the phosphate group of one nucleotide and the sugar of the next, creating a strong sugar-phosphate chain. These linkages provide structural stability and directionality (5' to 3') to nucleic acid strands.

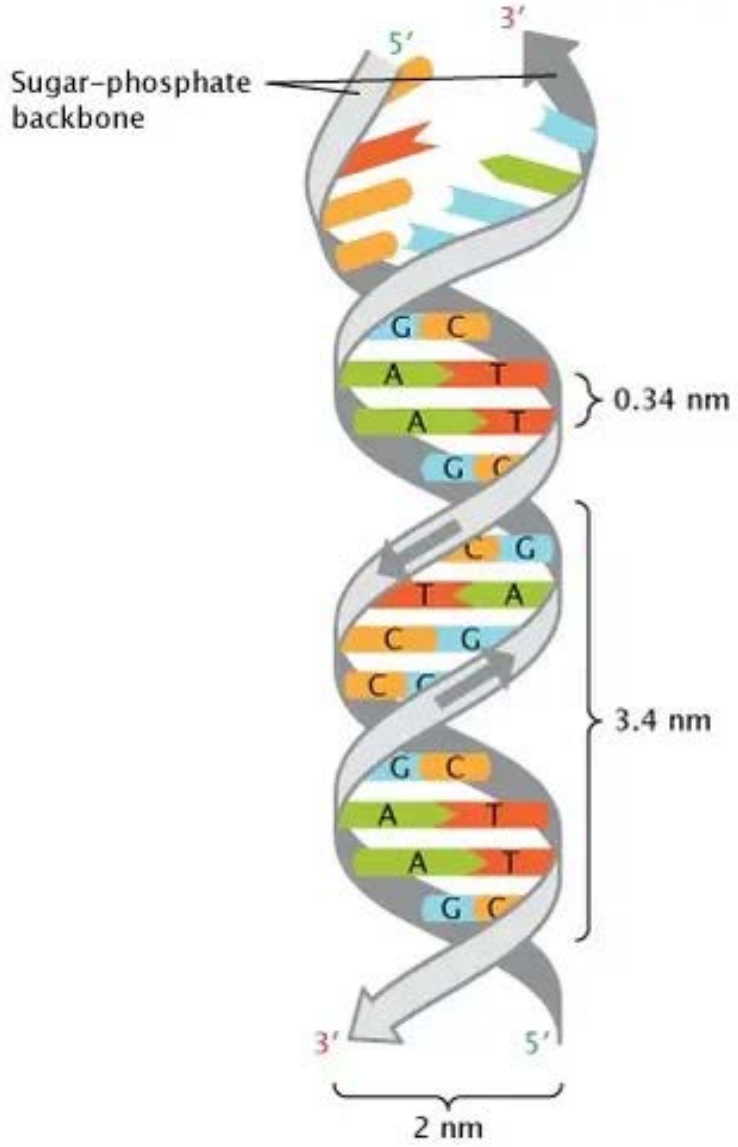
Watson and Crick Model

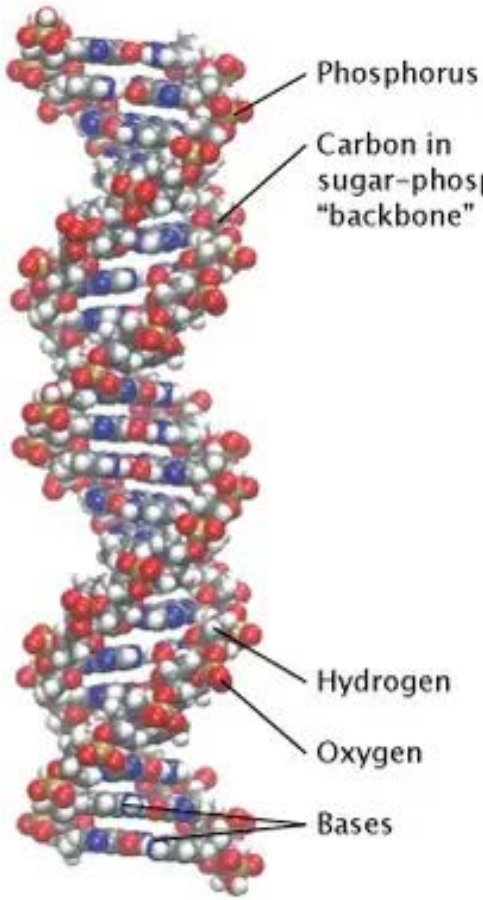
Hydrogen-bonding patterns in the base pairs defined by Watson and Crick.



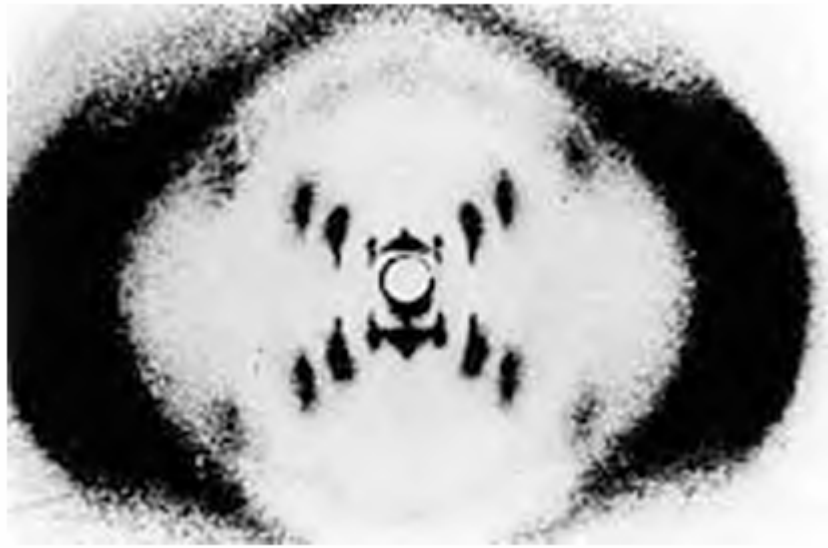
Watson and Crick, James Watson and Francis Crick, were scientists who **discovered the double-helix structure of DNA** in 1953. Their model showed how DNA stores genetic information and how it can be copied during cell division. This discovery was a major breakthrough in molecular biology and earned them the ***Nobel Prize*** in 1962 (shared with Maurice Wilkins).

Watson and Crick Model





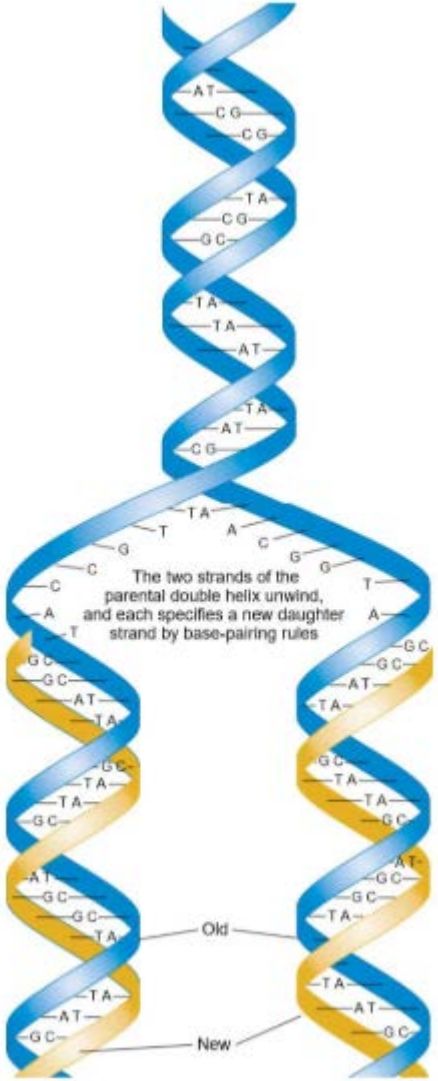
The original model proposed by Watson and Crick had **10 base pairs**, or **34 Å (3.4 nm)**, **per turn of the helix**; subsequent measurements revealed **10.5 base pairs, or 36 Å (3.6 nm), per turn**.



X-ray diffraction pattern of DNA.

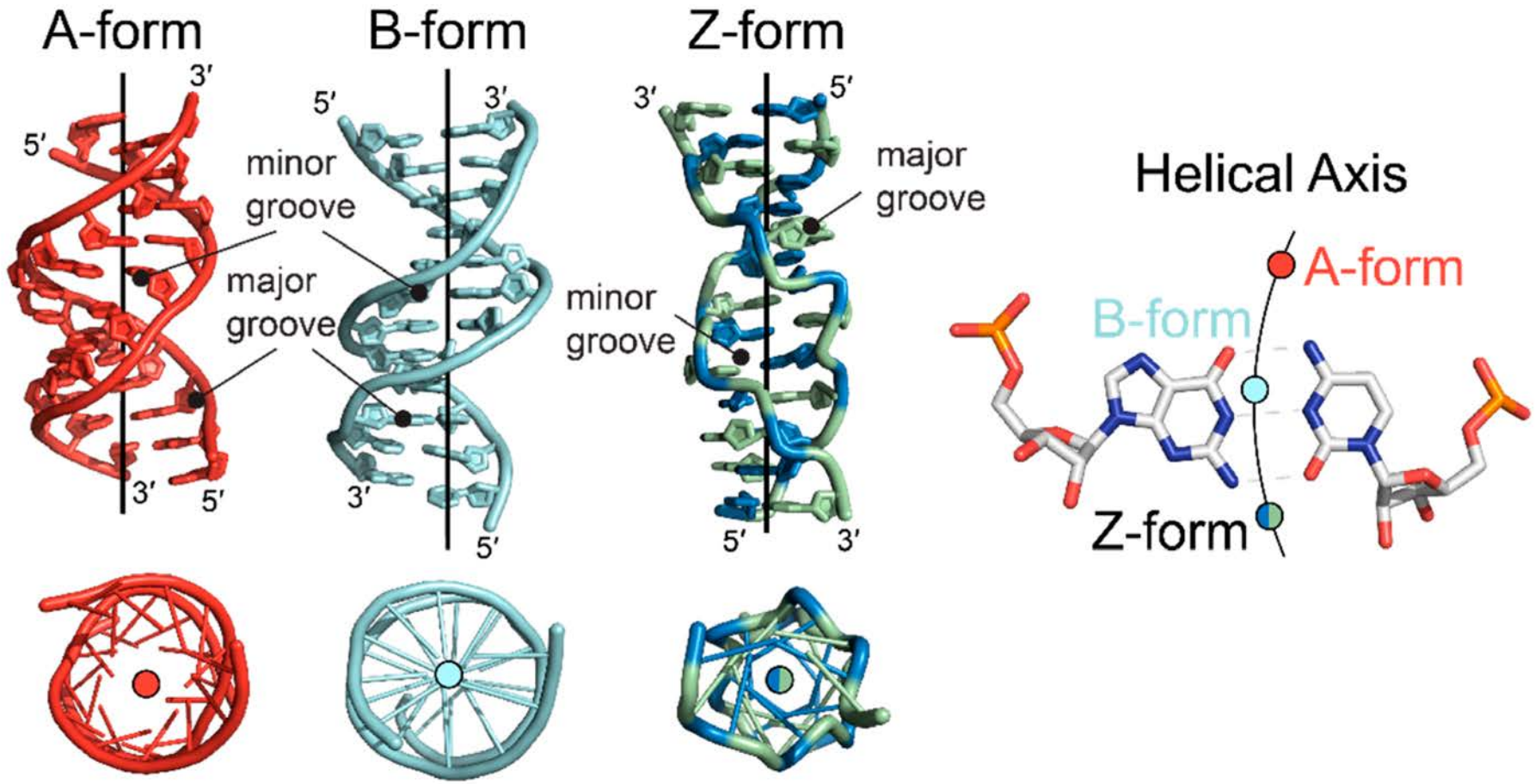
https://microbeonline.com/structure-of-dna/

Replication of DNA as suggested by Watson and Crick



Watson and Crick proposed that **DNA replication is semi-conservative**. This means each new DNA molecule consists of one original (parental) strand and one newly synthesized strand. The complementary base-pairing allows each strand to serve as a template for the formation of its matching strand, ensuring accurate genetic copying.

Comparison of A, B, and Z forms of DNA



Molecules **2023**, *28(2)*, 843; https://doi.org/10.3390/molecules28020843