

Macromolecules

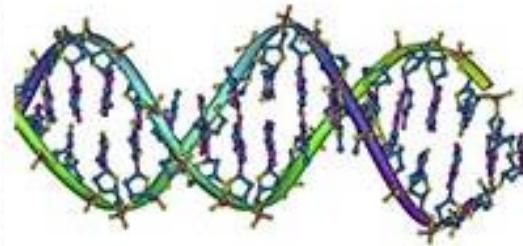
熊栋梁

Macromolecules are large, organic molecules essential for life, primarily composed of carbon, hydrogen, oxygen, nitrogen, and phosphorus. The four main types - **carbohydrates, lipids, proteins, and nucleic acids** - function as structural components, energy sources, and genetic storage in organisms.



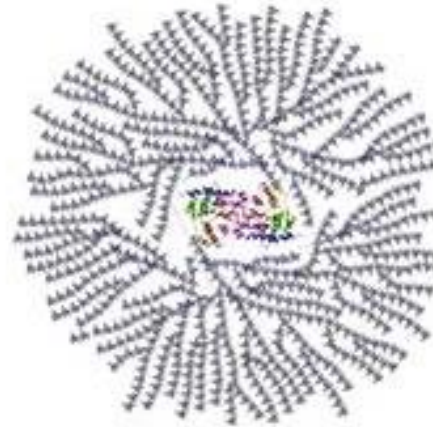
LIPIDS

脂质



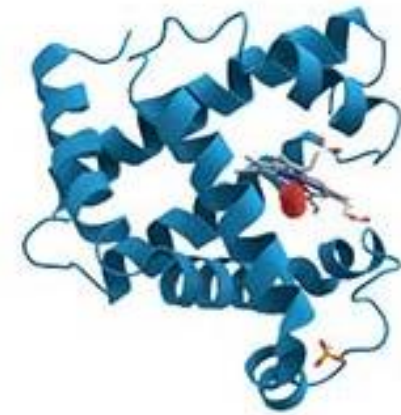
NUCLEIC ACIDS

核酸



CARBOHYDRATES

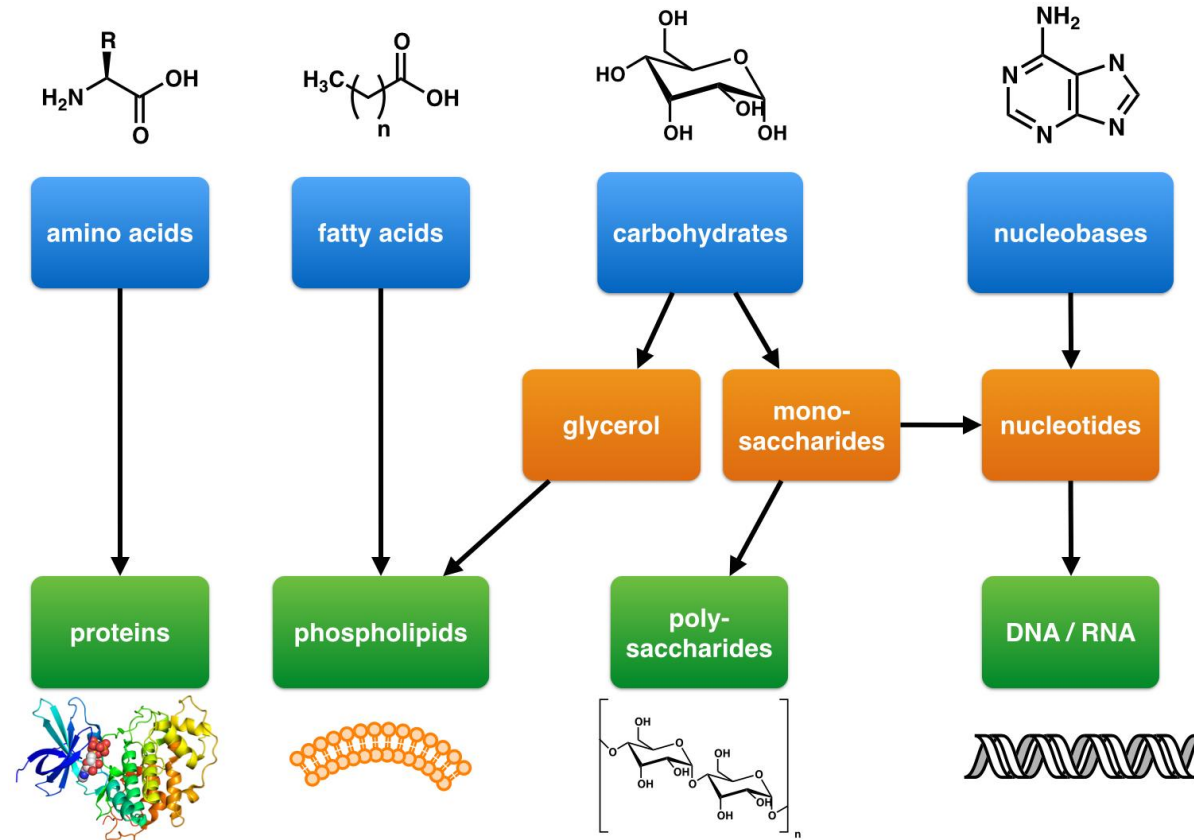
糖



PROTEINS

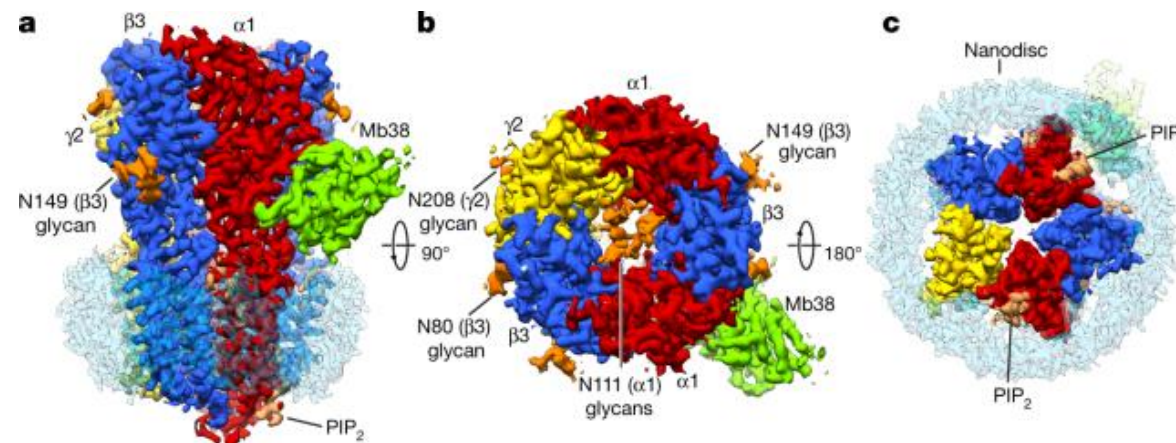
蛋白

Macromolecules are generally formed by linking smaller subunits, called **monomers**, into long chains known as **polymers**.



Monomer
单体

Polymer
聚合物



Tertiary & quaternary
空间结构

Nucleic acids are the carriers of genetic material; the synthesis of **proteins** is determined by nucleic acids. **Carbohydrates** and **lipids** are synthesized through catalysis by enzymes (which are primarily proteins); they can also bind with proteins, increasing the diversity of protein structure and function.

The four categories of biological macromolecules, along with other biological molecules and inorganic molecules (ions), together constitute the various hierarchical structures of the biological organism.

Contents

1. Nucleic Acid

2. Proteins

3. Carbohydrates

4. Lipids

For each group

- **Classification and Types:** Categorization of the specific molecules within the group.
- **Distribution:** Their prevalence and location across different biological organisms and cellular compartments.
- **Structural Composition:** Detailed examination of their molecular architecture.
- **Polymerization States:** The specific makeup of their **monomers**, **oligomers**, and **polymers**.
- **Physicochemical Properties:** Analysis of their physical and chemical characteristics, such as solubility, stability, and reactivity.

1/4 Nucleic Acid



Outline

- **Discovery**

核酸的发现历史

- **Types and Biological Distribution**

核酸的类型及生物分布

- **Chemical Components**

化学组成

- **Structure**

结构

- **Physicochemical Properties**

理化性质

Historical Discovery of Nucleic Acids

1869 — Friedrich Miescher

Discovered a phosphorus-rich substance in the nuclei of white blood cells and named it “nuclein (核素)”

1928 — Frederick Griffith

Bacterial transformation phenomenon in *Streptococcus pneumoniae*.

1944 — Avery, MacLeod & McCarty

DNA is the transforming principle, identifying DNA as the genetic material.

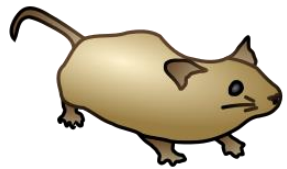
1952 — Hershey & Chase

DNA carries genetic information in bacteriophages using radioactive labeling.

1953 — Watson & Crick

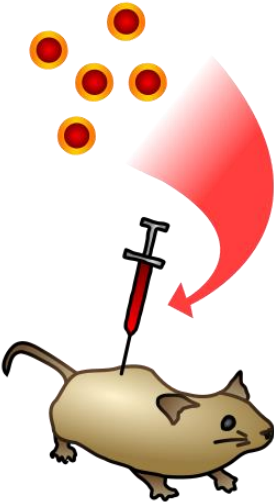
Proposed the **double helix model of DNA**, based on X-ray diffraction data.

粗糙型 (R) 菌株
(无毒性)



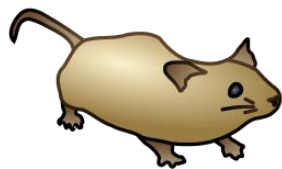
小鼠存活

光滑型 (S) 菌株
(有毒性)



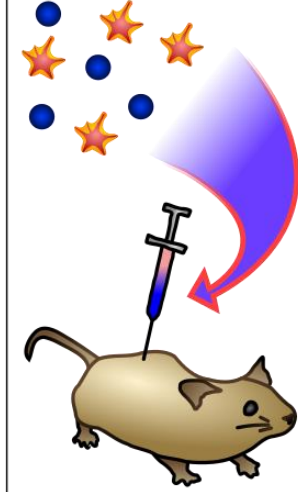
小鼠死亡

高温加热杀死的
光滑型 (S) 菌株



小鼠存活

粗糙型 (R) 菌株和
高温加热杀死的
光滑型 (S) 菌株混合

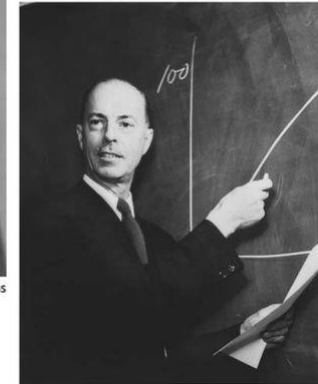


小鼠死亡



Library of Congress

Oswald Avery

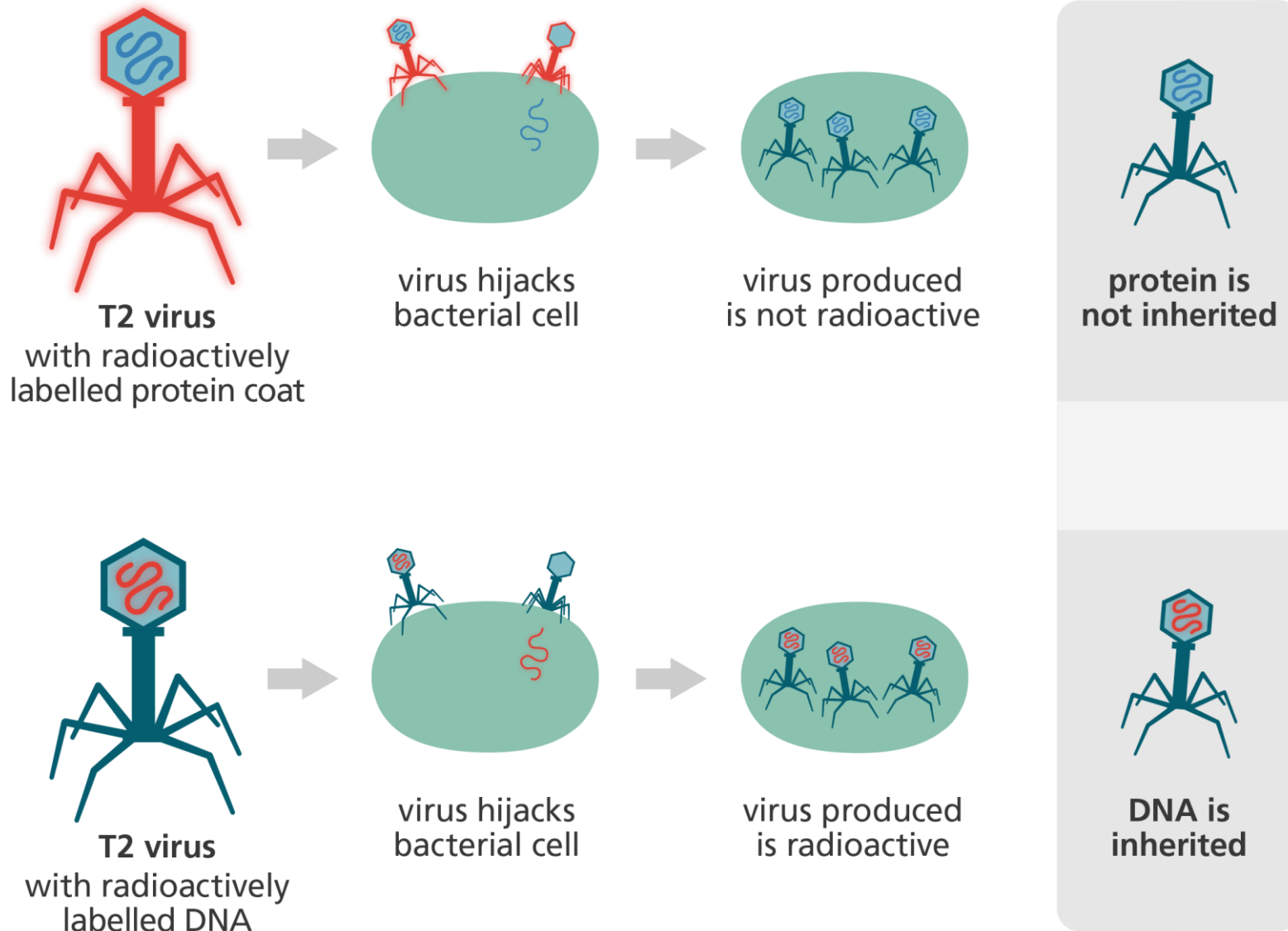


Colin MacLeod

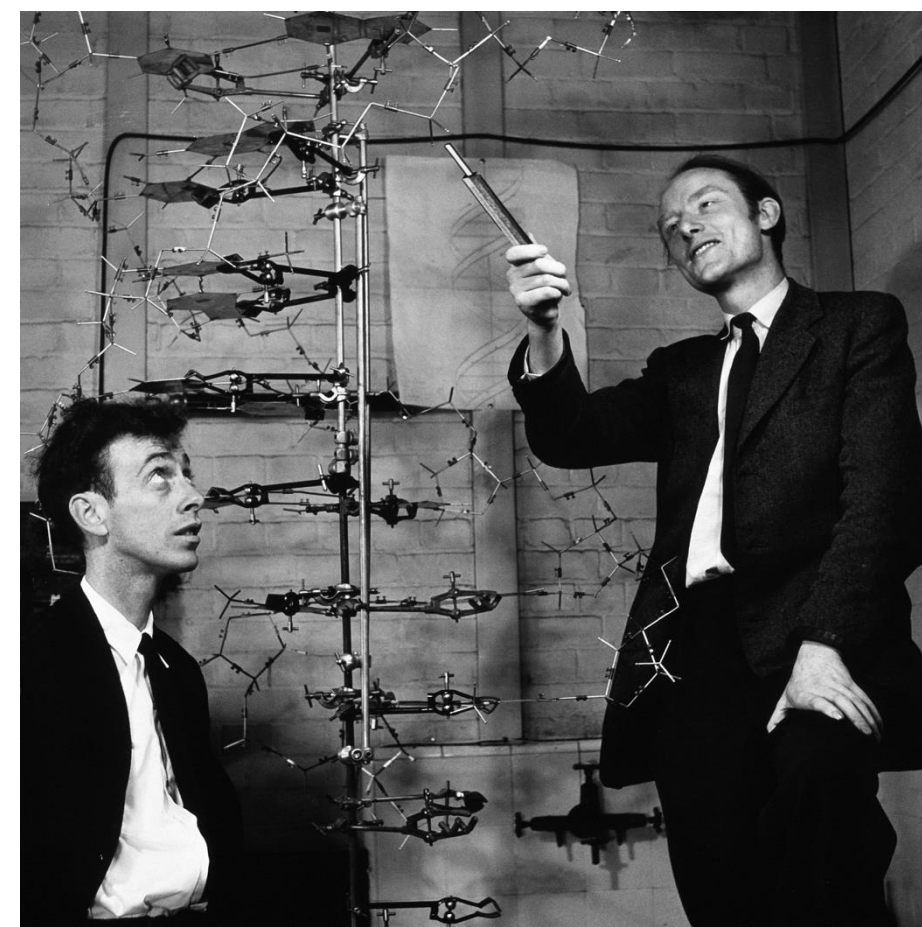
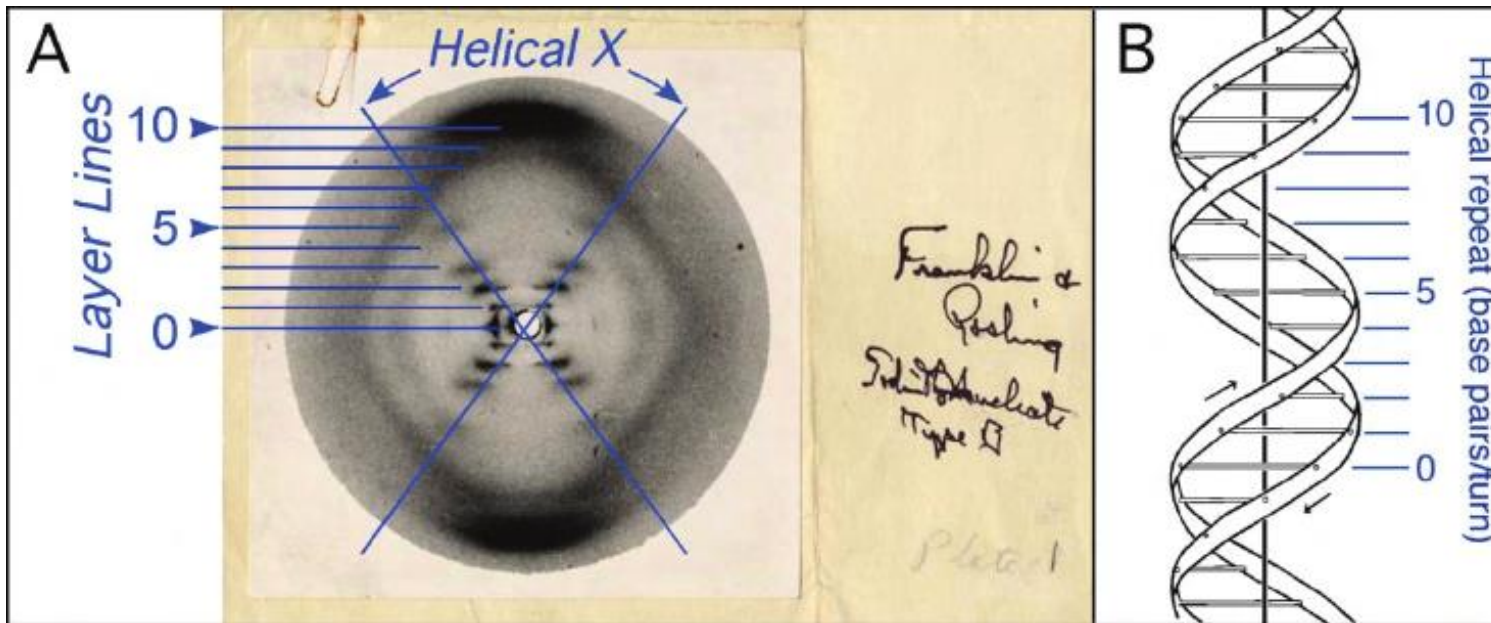


Maclyn McCarty

1944 — Avery, MacLeod & McCarty: DNA is the genetic material



Hershey & Chase (1952) DNA carries genetic information in bacteriophages using radioactive labeling.

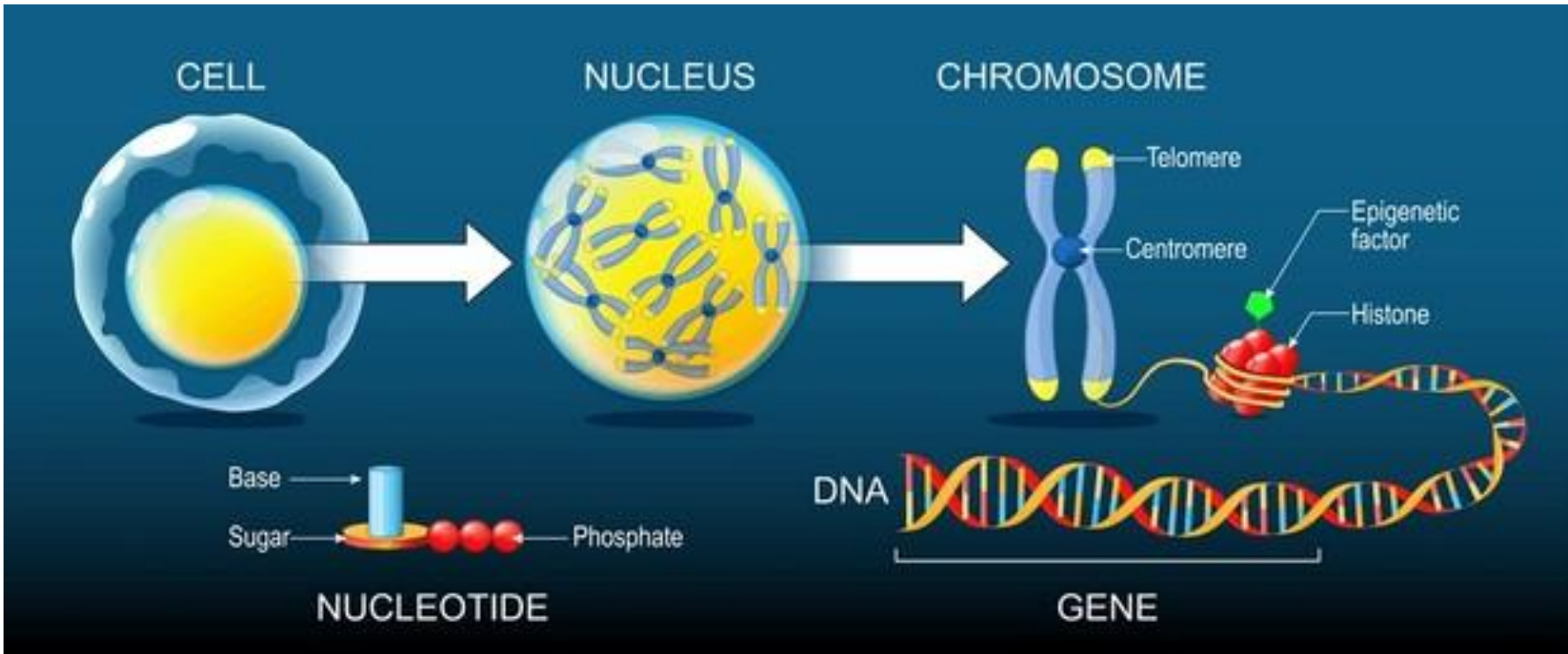
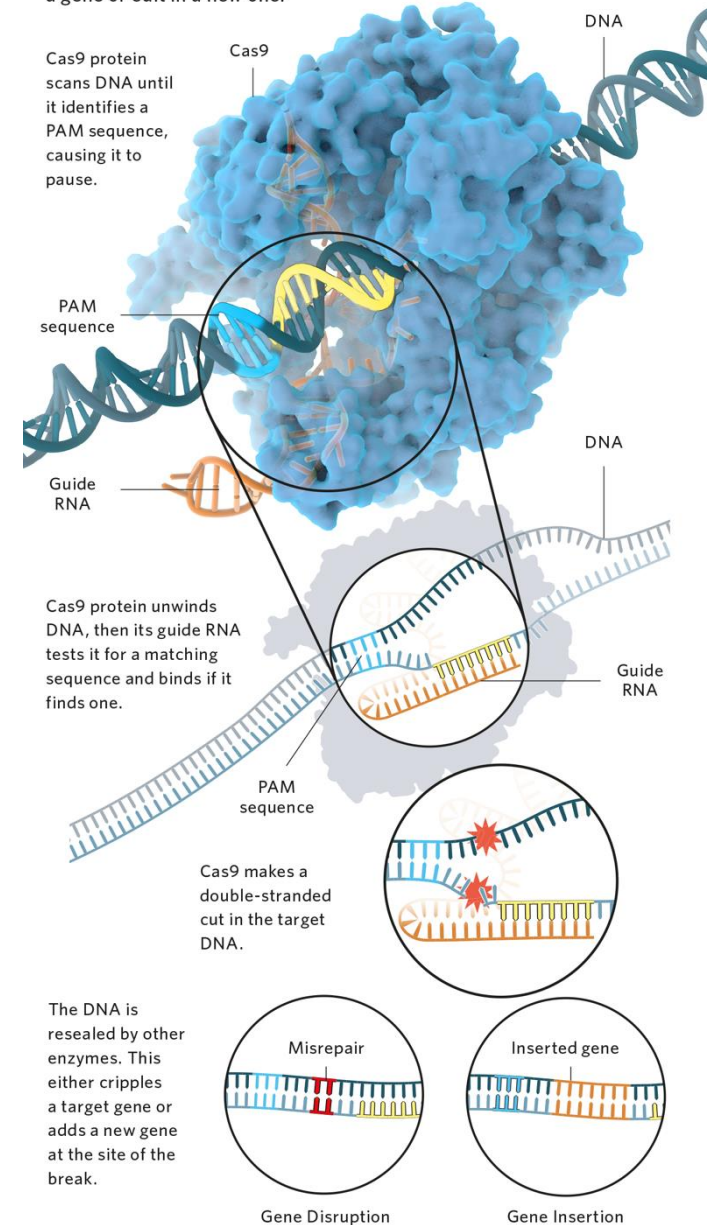


In 1953, James Watson and Francis Crick suggested what is now accepted as the first correct **double-helix model of DNA structure** in the journal Nature. Their double-helix, molecular model of DNA was then based on a single X-ray diffraction image taken by Rosalind Franklin and Raymond Gosling in May 1952, as well as the information that the DNA bases are paired.

The discovery and study of nucleic acids laid the foundation for modern molecular biology and biotechnology.

EDITING THE GENOME

The CRISPR gene-editing system uses an enzyme called Cas9 and a customized guide RNA to help target, cut, alter and stitch up particular stretches of the genome. It can disrupt a gene or edit in a new one.



Outline

- **Discovery**

核酸的发现历史

- **Types and Biological Distribution**

核酸的类型及生物分布

- **Chemical Components**

化学组成

- **Structure**

结构

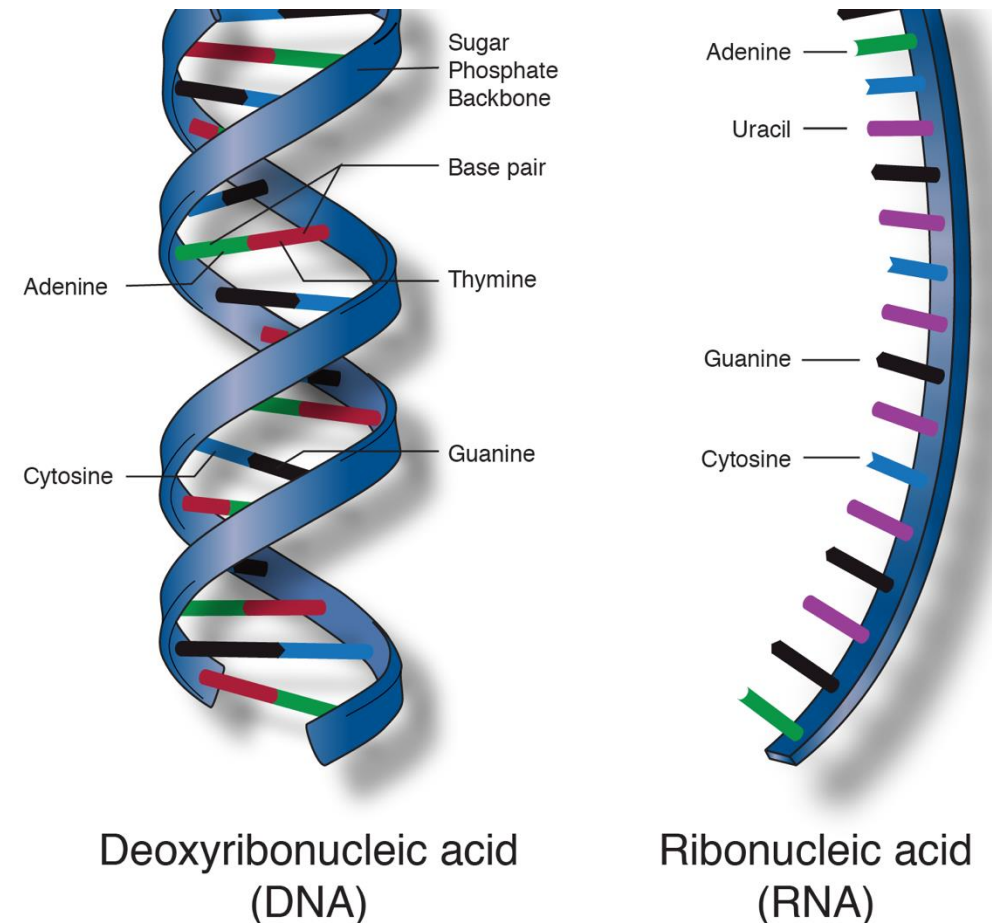
- **Physicochemical Properties**

理化性质

Types of Nucleic Acids

Nucleic acids are classified into two types according to the **pentose sugar** (戊糖) they contain: **Deoxyribonucleic acid (DNA; 脱氧核糖核酸)**, **Ribonucleic acid (RNA; 核糖核酸)**

- ❖ DNA is the primary genetic material and stores hereditary information. It transmits genetic information from one generation to the next through replication.
- ❖ RNA plays essential roles in the expression of genetic information. It functions in processes such as transcription and protein synthesis.



Types of DNA

❖ Prokaryotic cells

- ✓ Chromosomal DNA
- ✓ Plasmid DNA

❖ Eukaryotic cells

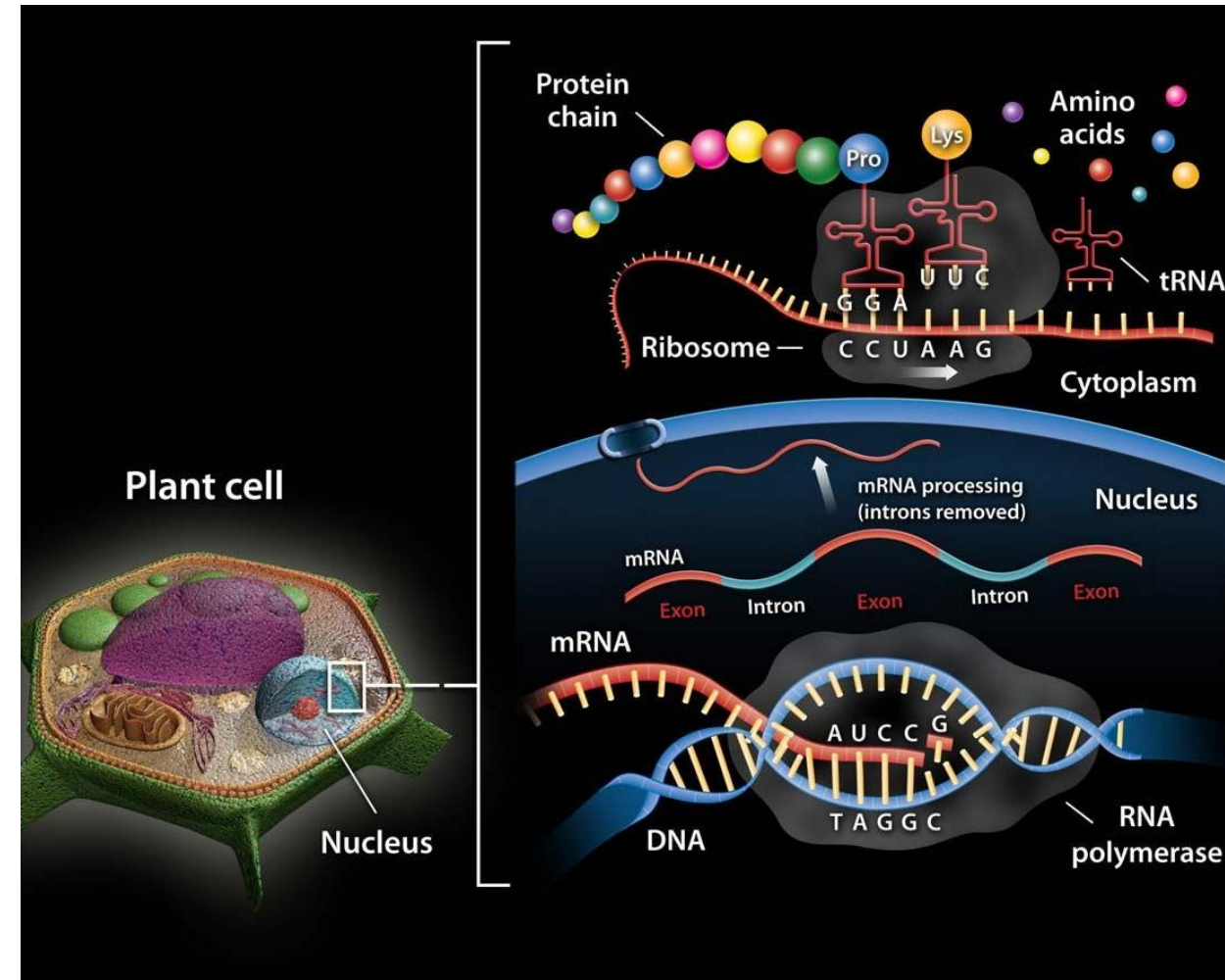
- ✓ Chromosomal DNA (in the nucleus)
- ✓ Organelle(細胞器) DNA (mitochondrial DNA and chloroplast DNA)

Are all DNA molecules double-stranded?

Most cellular DNA exists as a **double-stranded helix**, but some viruses contain **single-stranded DNA (ssDNA)**.

Types of RNA

- ❖ **Ribosomal RNA (rRNA)** – structural and catalytic component of ribosomes
- ❖ **Transfer RNA (tRNA)** – carries amino acids during protein synthesis
- ❖ **Messenger RNA (mRNA)** – carries genetic information from DNA to ribosomes



rRNA \approx 80–85%

tRNA \approx 10–15%

mRNA \approx 1–5%

Types of Nucleic Acids

Cellular compartment	DNA (%)	RNA (%)
Nucleus	~98	<10
Cytoplasm	~2	>90

- ❖ **DNA** content is relatively constant in somatic cells of the same species.
- ❖ **RNA** content varies depending on the cell type and metabolic activity.

Actively growing cells usually contain more RNA because they require more ribosomes for protein synthesis.

Beyond the Classical RNAs

Recent discoveries have revealed that many **non-coding RNAs (ncRNAs)** play important roles in **gene regulation**.

Examples of Regulatory RNAs

❖ Small interfering RNA (siRNA; 小分子干扰RNA)

- ✓ Mediates RNA interference (RNAi)
- ✓ Causes sequence-specific degradation of target mRNA

❖ MicroRNA (miRNA; 微小RNA)

- ✓ Regulates gene expression by base pairing with target mRNA
- ✓ Leads to mRNA degradation or translational repression

❖ Long non-coding RNA (lncRNA; 长链非编码 RNA)

- ✓ Regulates chromatin structure
- ✓ Modulates gene transcription and epigenetic regulation

❖ Piwi-interacting RNA (piRNA; 相互作用 RNA)

- ✓ Functions mainly in germ cells
- ✓ Suppresses transposable elements and protects genome stability

Outline

- **Discovery**

核酸的发现历史

- **Types and Biological Distribution**

核酸的类型及生物分布

- **Chemical Components**

化学组成

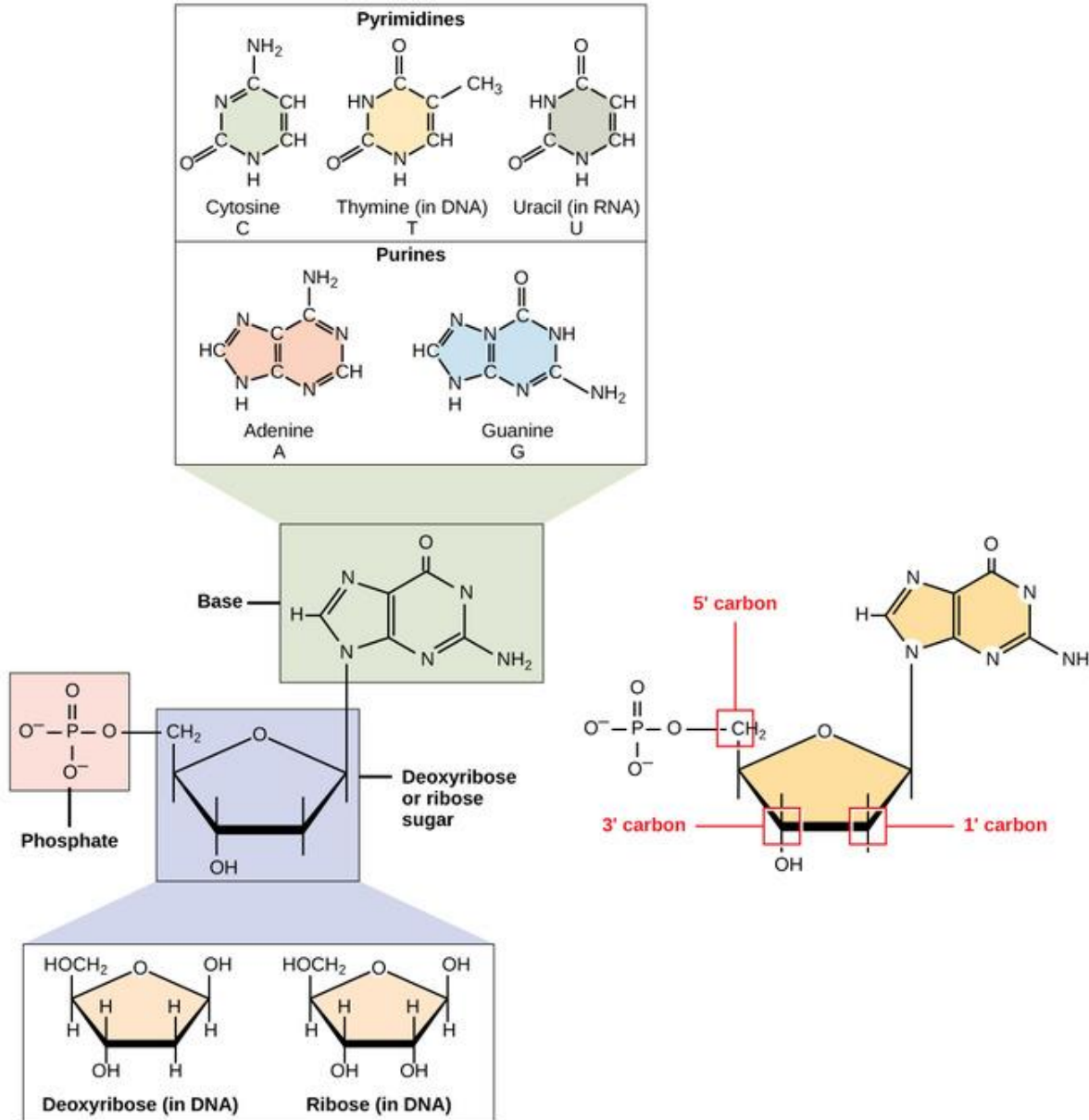
- **Structure**

结构

- **Physicochemical Properties**

理化性质

Chemical Components of Nucleic Acids



Basic Structural Unit: Nucleotide(核苷酸)

- Phosphate group / 磷酸
- Pentose sugar / 戊糖
- Nitrogenous base / 碱基

Nucleoside / 核苷 = Base + Sugar

Pentose Sugars

- ❖ Ribose (R) — found in RNA
- ❖ Deoxyribose (dR) — found in DNA

Bases of Nucleic Acids

sciencenotes.org

Nucleic Acids

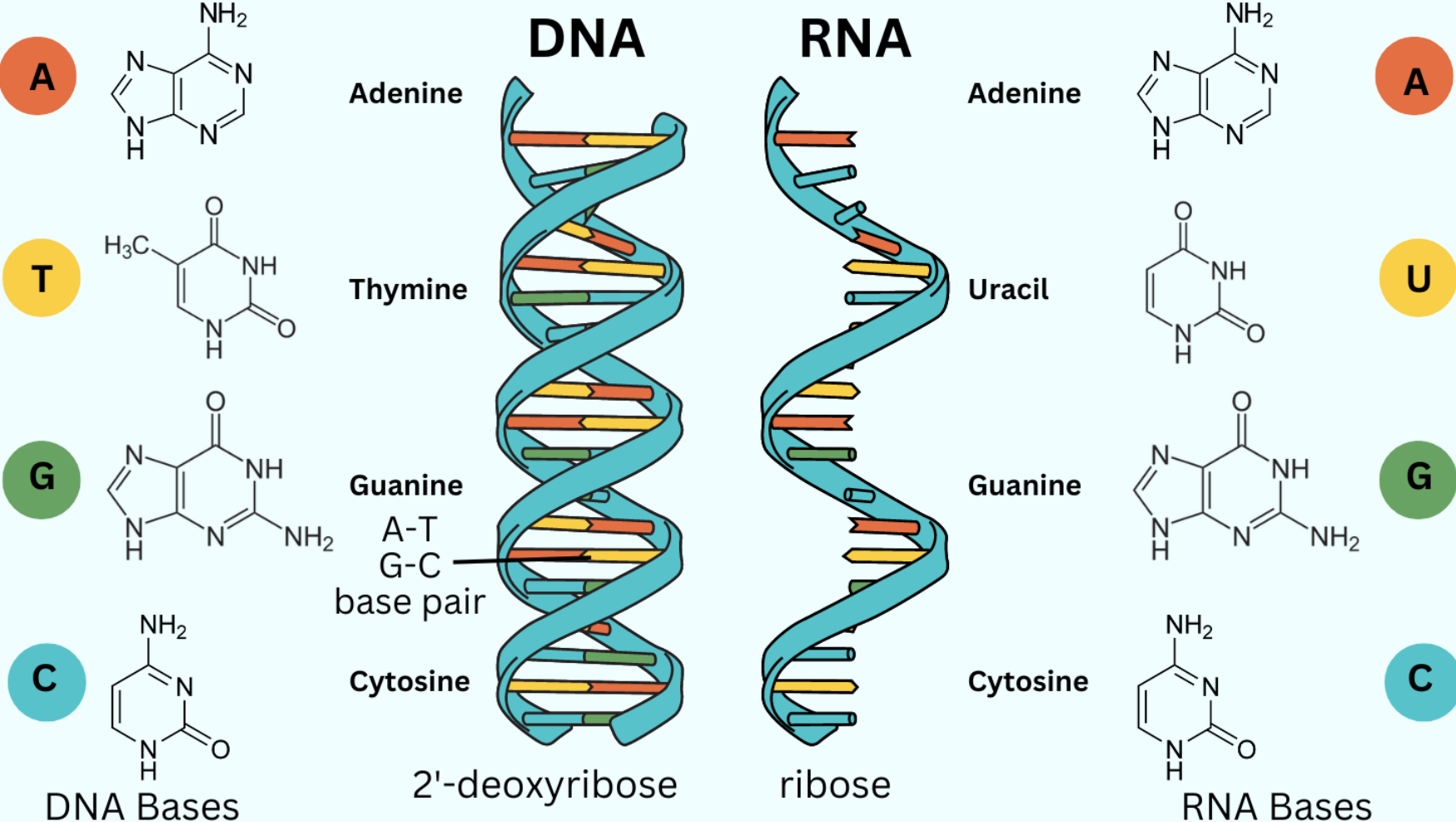
The two classes of nucleic acids are DNA and RNA.

腺嘌呤

胸腺嘧啶

鸟嘌呤

胞嘧啶



腺嘌呤

尿嘧啶

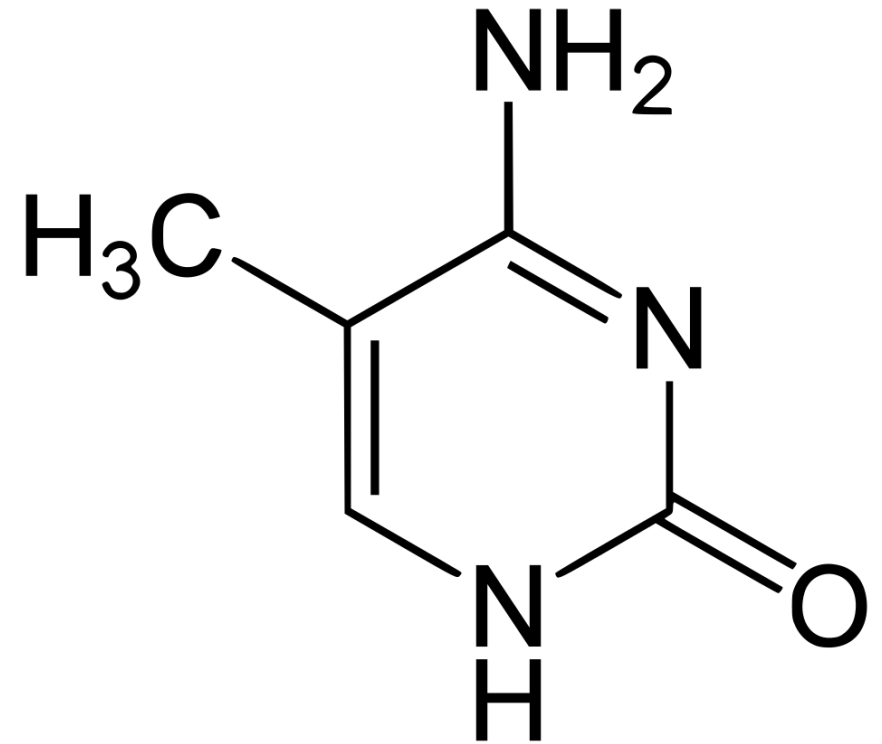
鸟嘌呤

胞嘧啶

Modified (Rare) Bases in Nucleic Acids / 稀有碱基

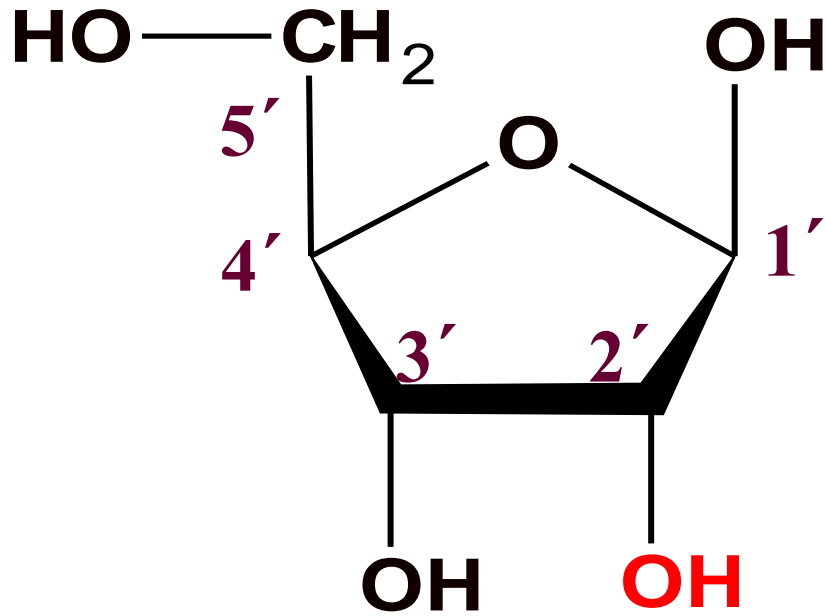
These bases are usually present in small amounts and are often produced by **chemical modification of standard bases**, many are **methylated derivatives**.

- ❖ **5-Methylcytosine (m5C; 5-甲基胞嘧啶)** – important in DNA methylation and epigenetic regulation
- ❖ **Pseudouridine (Ψ ; 假尿苷)** – common modification in tRNA and rRNA
- ❖ **Dihydrouridine (D; 二氢尿苷)** – found mainly in tRNA
- ❖ **Hypoxanthine(次黄嘌呤)** – produced by deamination of adenine

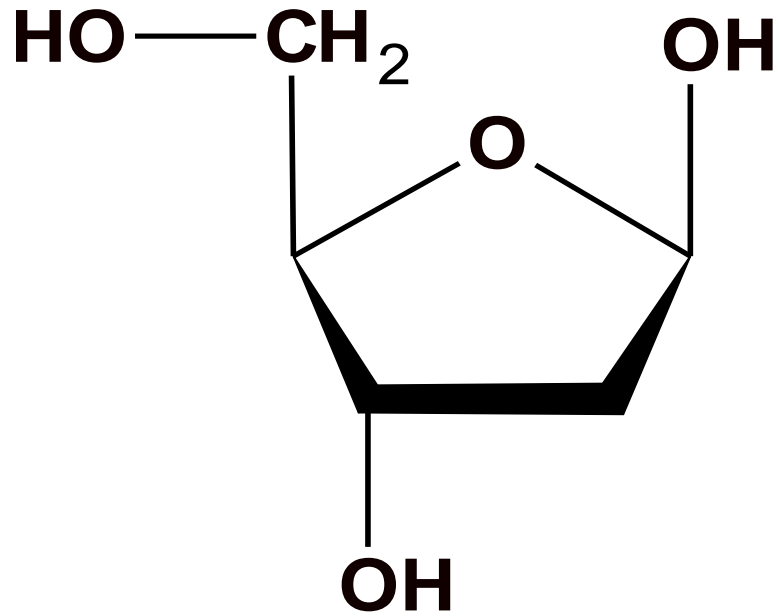


5-Methylcytosine

Pentose sugar / 戊糖



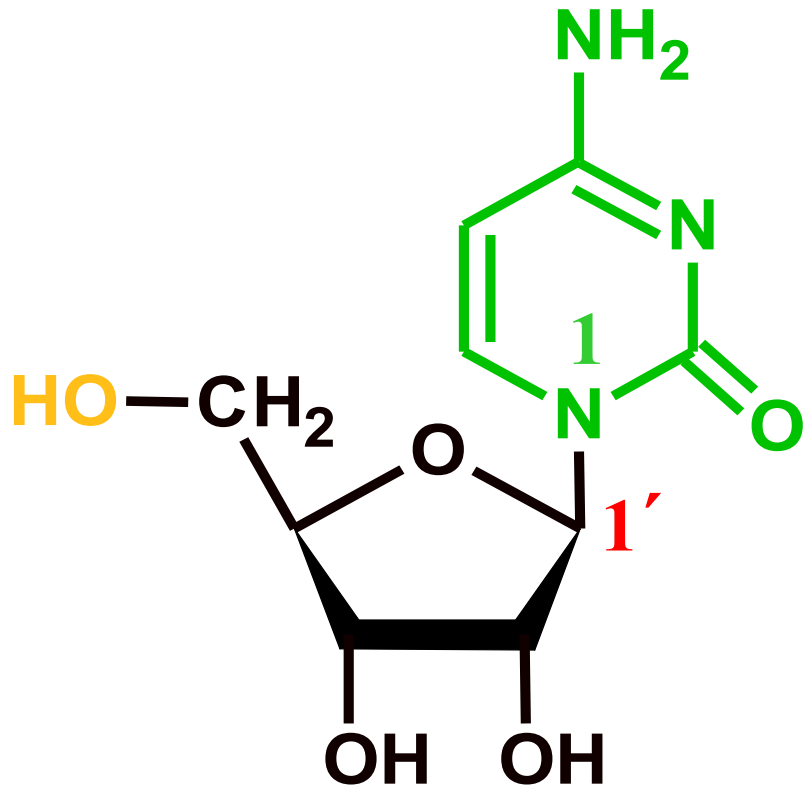
核糖(ribose)
(RNA)



脱氧核糖(deoxyribose)
(DNA)

Formation of Nucleosides (核苷)

A nucleoside is formed by the linkage between a nitrogenous base and a pentose sugar. The base and sugar are connected through a **β -N-glycosidic bond**(糖苷键).

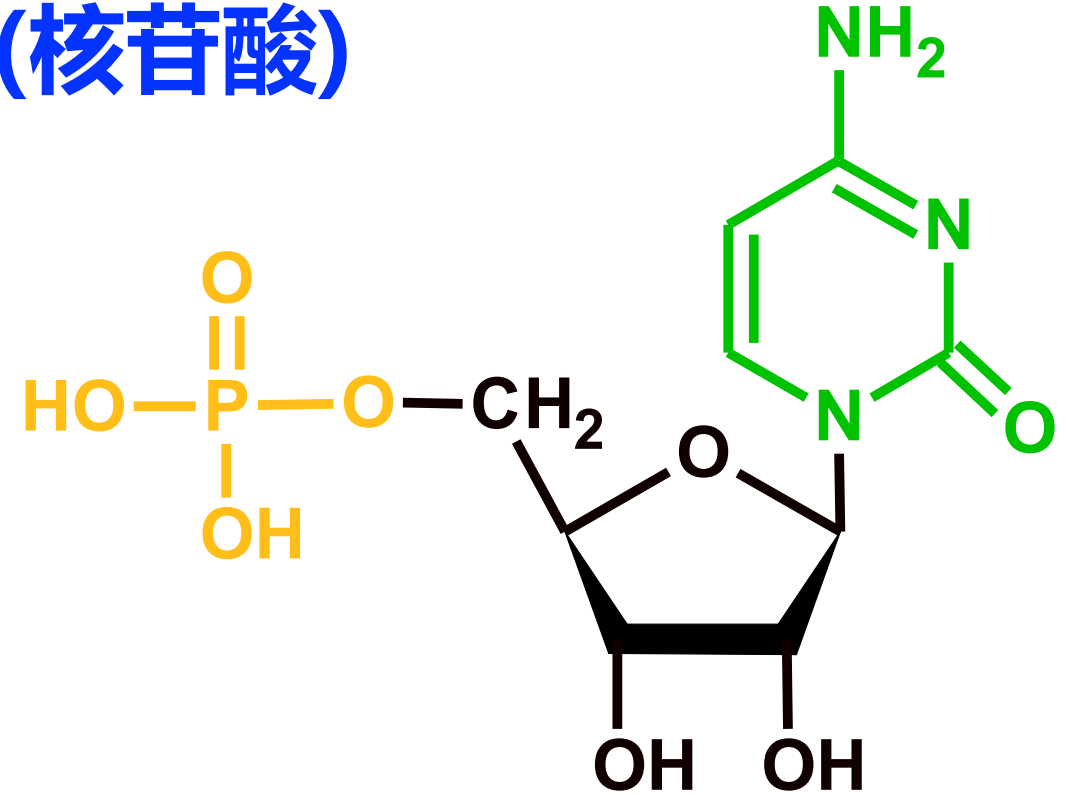


Ribose + Base \rightarrow Ribonucleoside
核苷

Deoxyribose + Base \rightarrow Deoxyribonucleoside
脱氧核苷

Formation of Nucleotides (核苷酸)

A nucleotide is formed when a phosphate group is attached to a nucleoside. The phosphate group is usually linked to the 5' carbon of the pentose sugar via a **phosphoester bond** (磷酸酯键).



Ribonucleotides (RNA building blocks)

AMP – adenosine monophosphate
GMP – guanosine monophosphate
UMP – uridine monophosphate
CMP – cytidine monophosphate

Deoxyribonucleotides (DNA building blocks)

dAMP – deoxyadenosine monophosphate
dGMP – deoxyguanosine monophosphate
dTMP – deoxythymidine monophosphate
dCMP – deoxycytidine monophosphate

Important Free Nucleotides:

Phosphorylated Nucleotides / 核苷酸的磷酸化形式

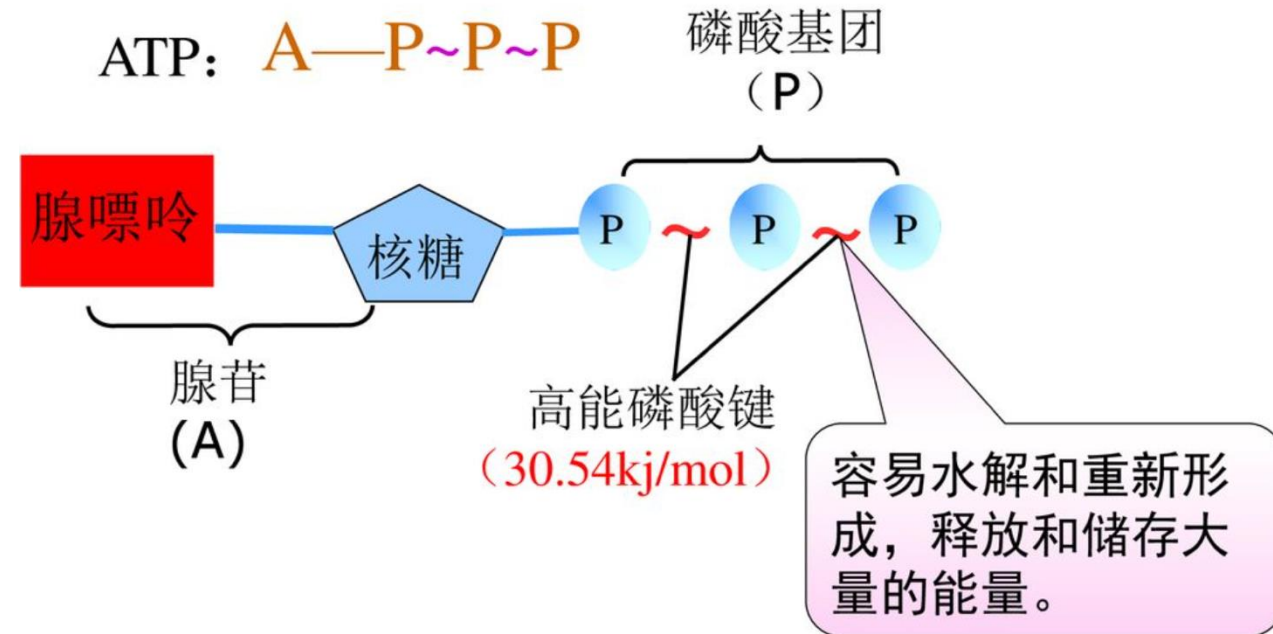
Nucleotides can exist in different **phosphorylation states:**

- ❑ **NMP** – nucleoside monophosphate
- ❑ **NDP** – nucleoside diphosphate
- ❑ **NTP** – nucleoside triphosphate

Examples: AMP, ADP, ATP

Deoxyribonucleotides:

dNMP, dNDP, dNTP



ATP contains three phosphate groups connected by phosphoanhydride bonds.

高能磷酸酐键

Important Free Nucleotides

Cyclic Nucleotides / 环核苷酸

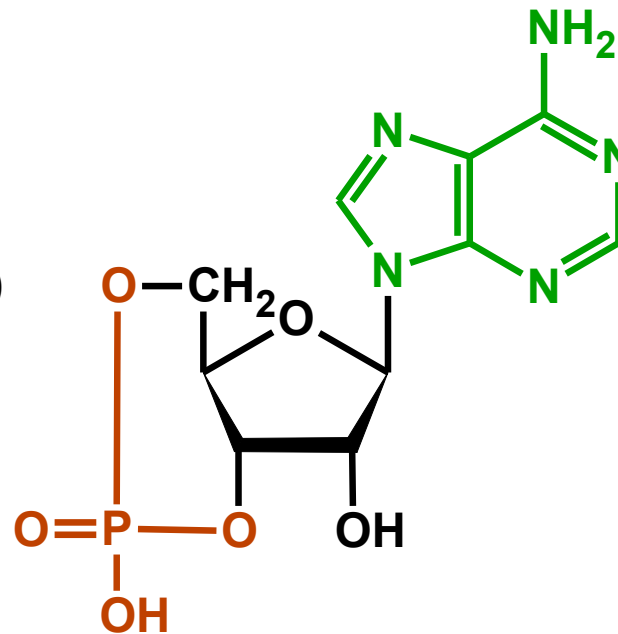
Cyclic nucleotides play key roles in intracellular signal transduction.

The most common cyclic nucleotides are:

- ❖ **cAMP (cyclic adenosine monophosphate)**
- ❖ **cGMP (cyclic guanosine monophosphate)**

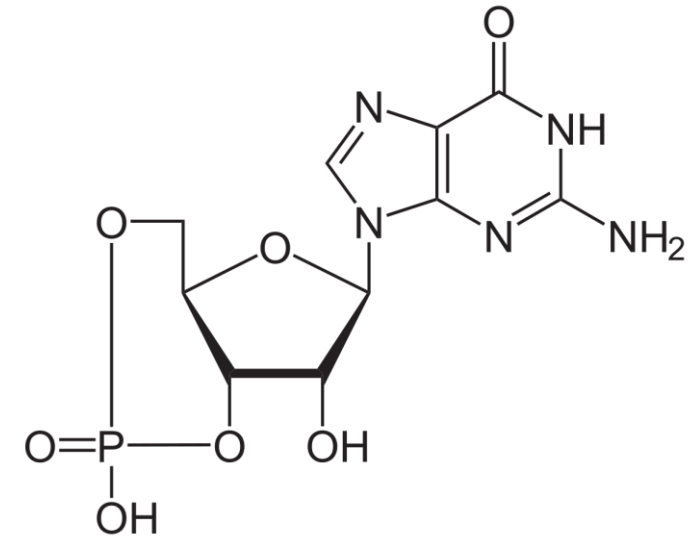
Structural Feature

cAMP and cGMP contain a **3',5'-cyclic phosphate group**, formed by a phosphodiester bond between the **3' and 5' hydroxyl groups** of ribose.



cAMP

环腺苷酸

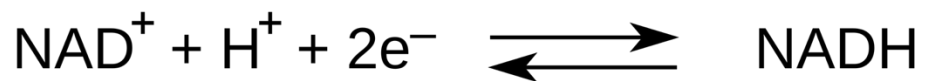
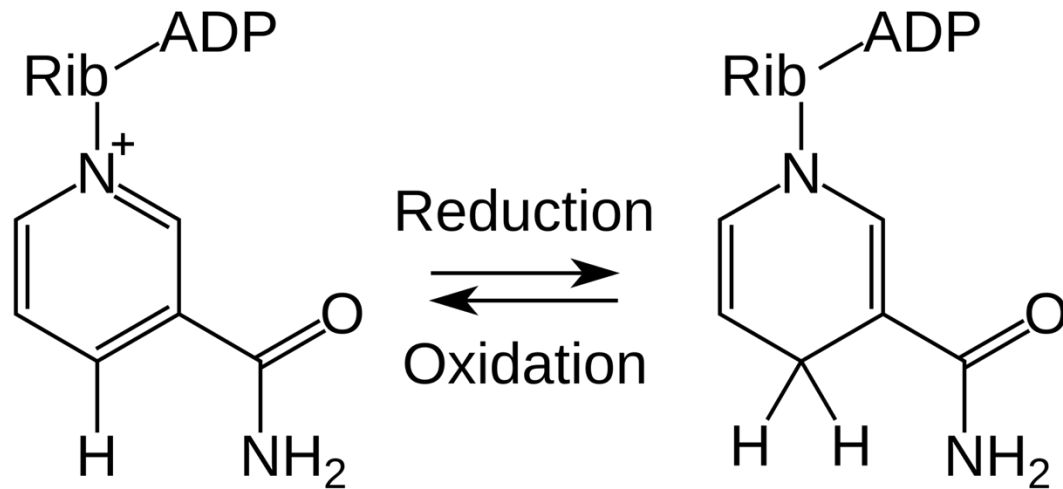


cGMP

环鸟苷酸

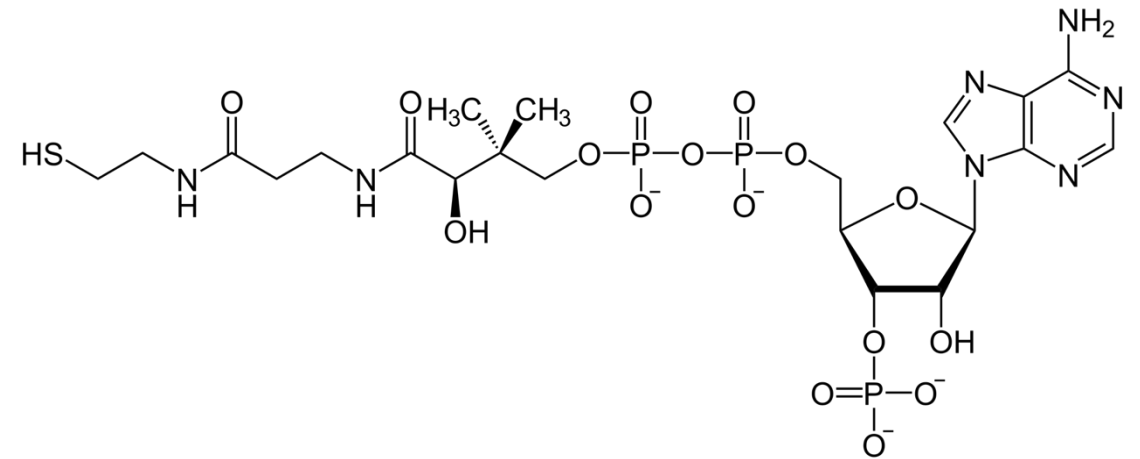
Coenzymes Containing Nucleotide Moieties / 含腺苷酸结构的辅酶

Many important coenzymes contain nucleotide structures, especially an adenosine monophosphate (AMP) moiety.



NAD⁺ (辅酶I, 烟酰胺腺嘌呤二核苷酸)

NADP⁺ (辅酶II, 烟酰胺腺嘌呤二核苷酸磷酸)



CoA-SH (辅酶A)

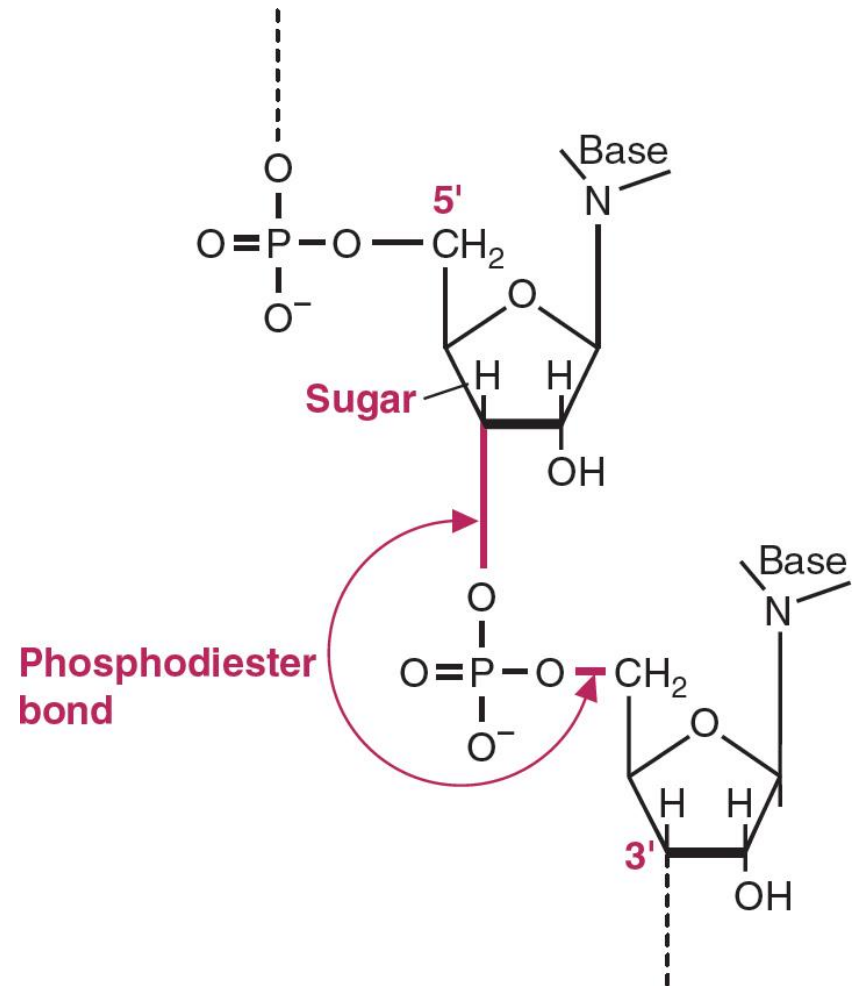
Outline

- **Discovery**
核酸的发现历史
- **Types and Biological Distribution**
核酸的类型及生物分布
- **Chemical Components**
化学组成
- **Structure**
结构
- **Physicochemical Properties**
理化性质

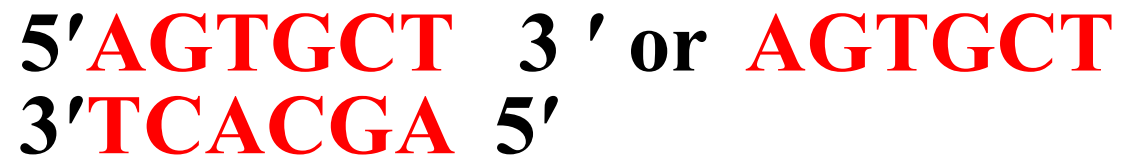
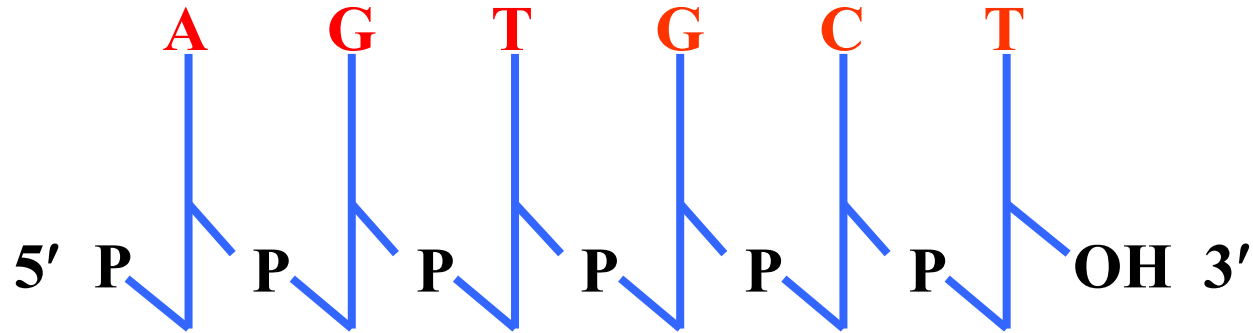
Primary Structure of Nucleic Acids / 一级结构

The primary structure of nucleic acids is the sequence of nucleotides.

Nucleotides are linked together by **3'–5' phosphodiester bonds** (**3'–5' 磷酸二酯键**), forming a **polynucleotide chain**.



Primary Structure of Nucleic Acids / 一级结构

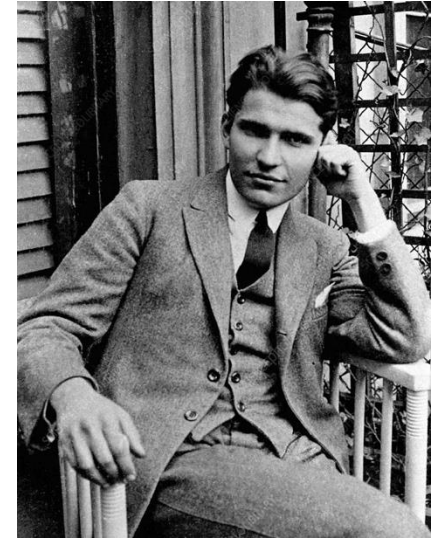


DNA Secondary Structure/ 二级结构

The Discovery of DNA Structure

Chargaff's Rules

- Discovered by **Erwin Chargaff (1940s)**
- Observed base composition in DNA:
 - ✓ $\%A \approx \%T$
 - ✓ $\%G \approx \%C$
- DNA is not random, and Suggests specific pairing between bases



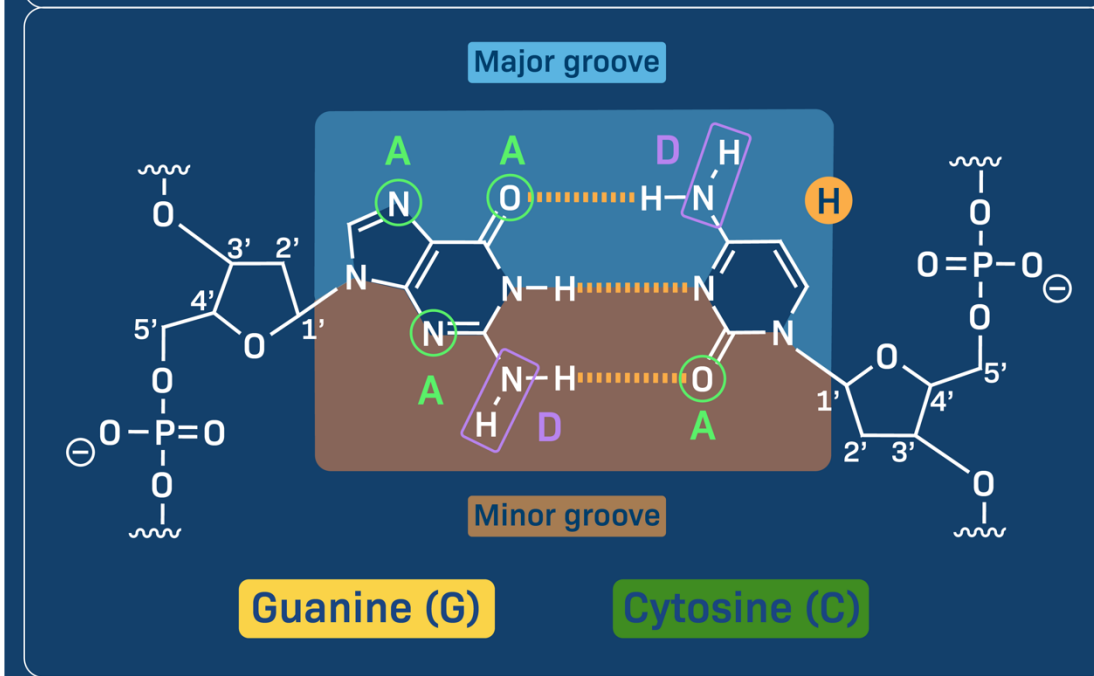
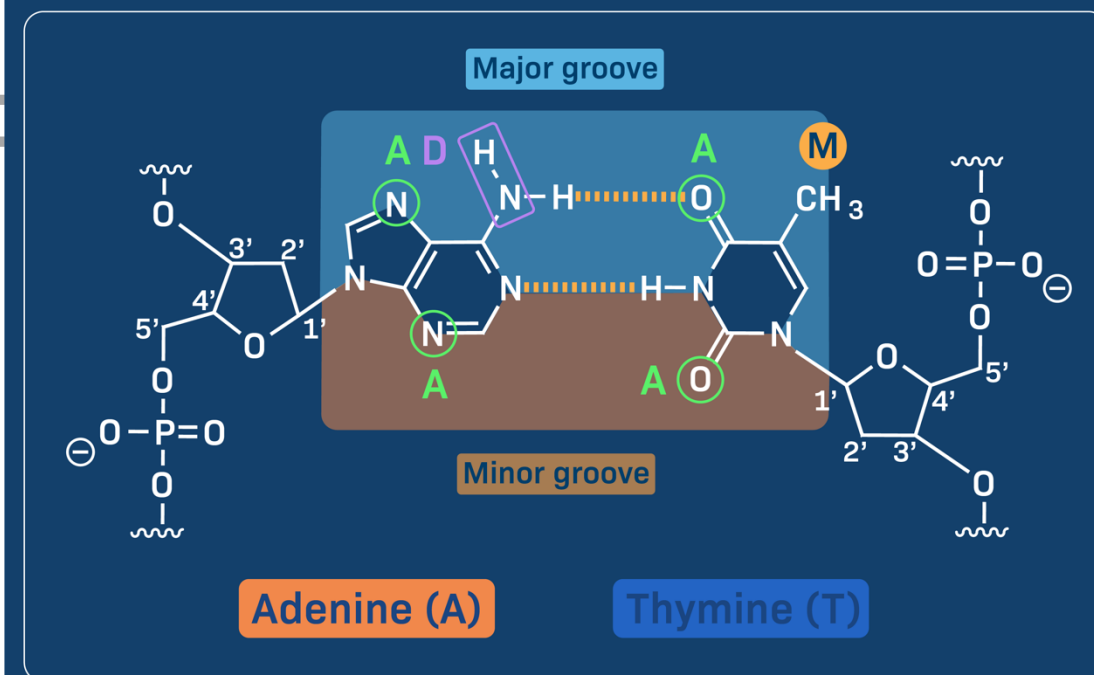
Nucleic Acids

- (A) Adenine
- (T) Thymine
- (G) Guanine
- (C) Cytosine

DNA Secondary Structure/

The Discovery of DNA Structure

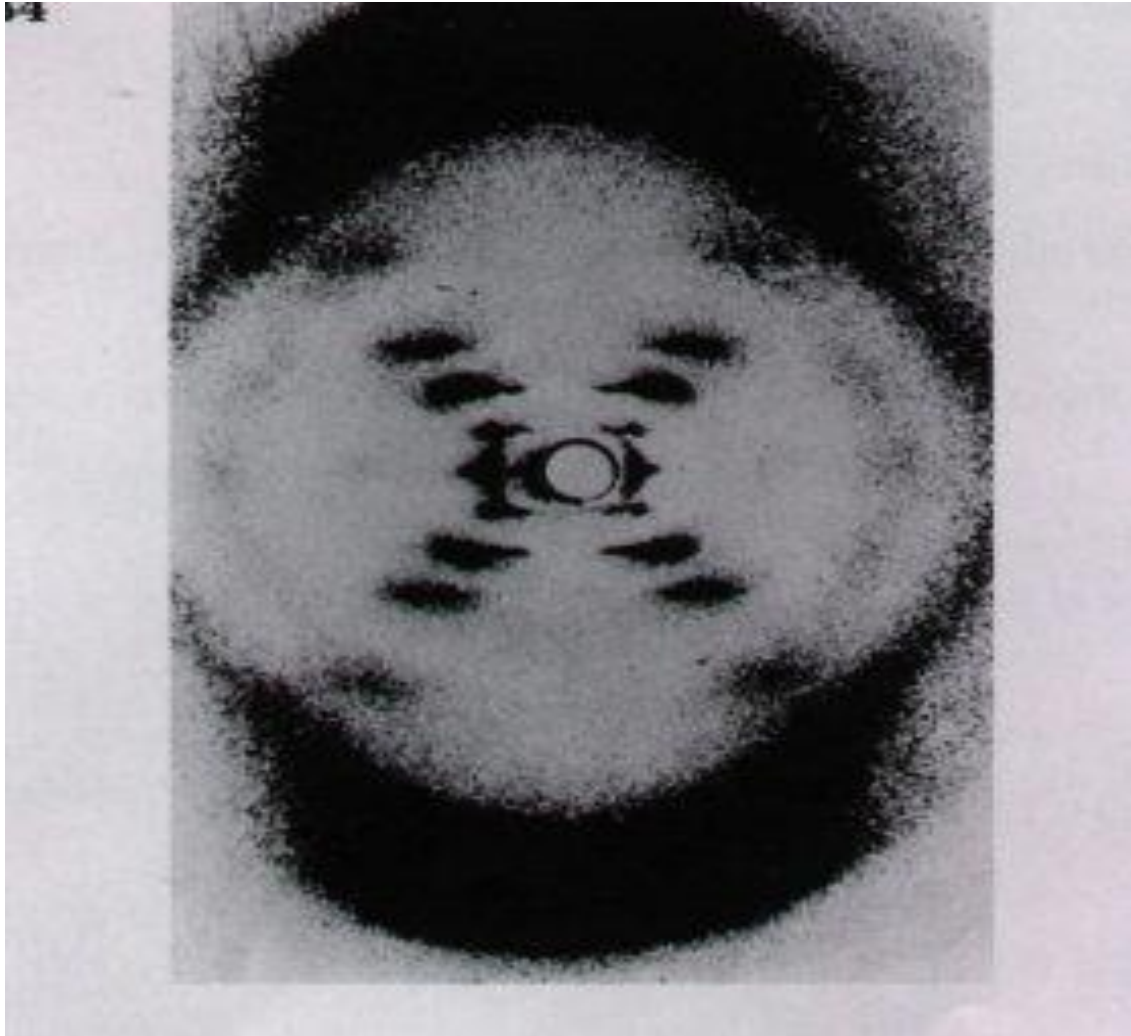
- **A** pairs with **T** (2 hydrogen bonds)
- **G** pairs with **C** (3 hydrogen bonds)
- **Specificity arises from:**
 - ✓ Hydrogen bond donors/acceptors
 - ✓ Geometric compatibility



● Hydrogen bond acceptor ■ Hydrogen bond donor

DNA Secondary Structure/ 二级结构

The Discovery of DNA Structure



X-ray diffraction revealed:

- Helical structure
- Periodic spacing (0.34 nm, 3.4 nm)

Rosalind Franklin, 1952

DNA Secondary Structure/ 二级结构

The Discovery of DNA Structure



DNA Helix / 双螺旋

- ❖ Helix diameter: ~2 nm
- ❖ Distance between adjacent base pairs is about 0.34 nm (层线间距)
- ❖ Helical pitch (one full turn) is about 3.4 nm (螺旋重复周期)
- ❖ ~10 base pairs per turn

DNA Secondary Structure/ 二级结构

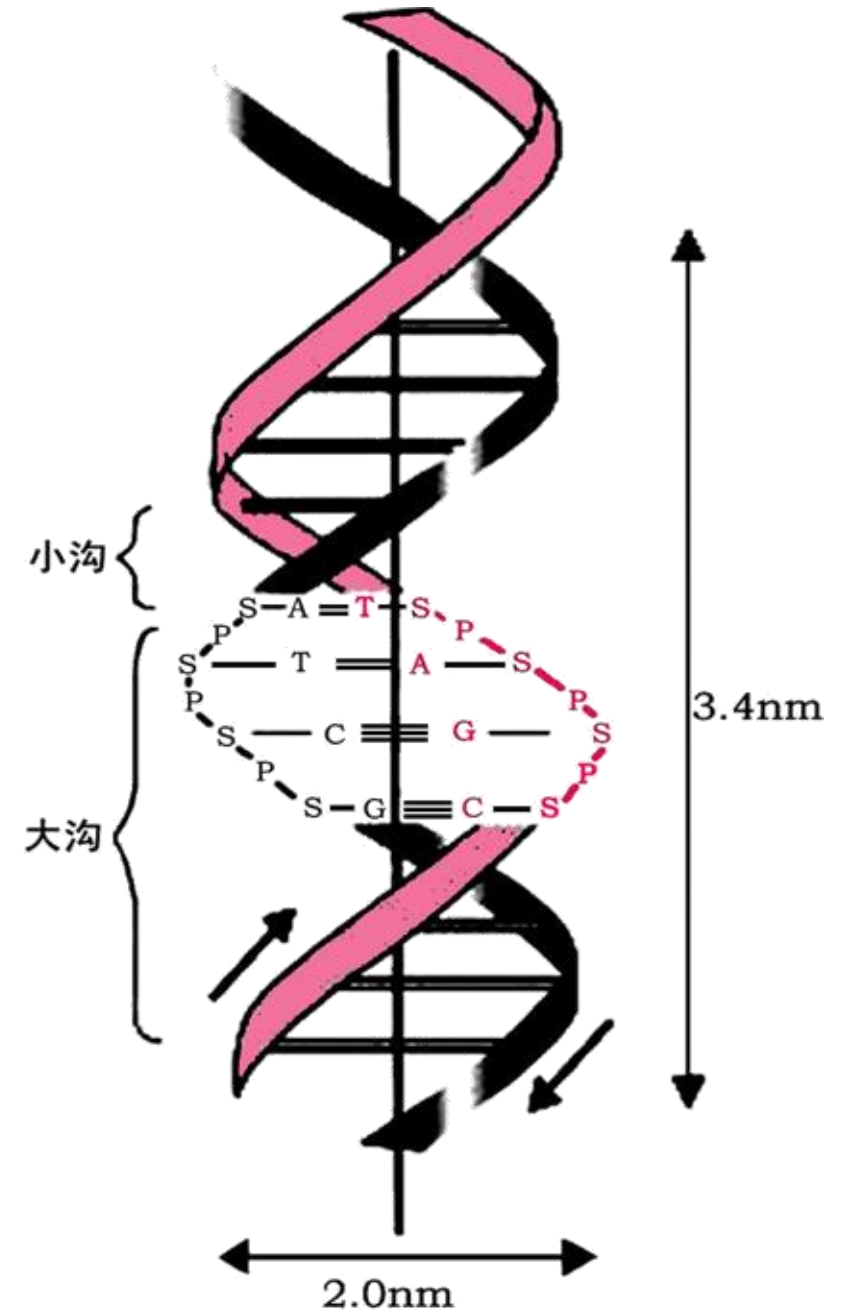
Key Features of DNA Double Helix

❖ Structure

- ✓ Two antiparallel polynucleotide strands
- ✓ Form a right-handed double helix
- ✓ Helix diameter: ~2 nm

❖ Base Pairing

- ✓ Complementary hydrogen bonding:
 - A–T (2 H-bonds)
 - G–C (3 H-bonds)



DNA Secondary Structure/ 二级结构

Key Features of DNA Double Helix

❖ Molecular Organization

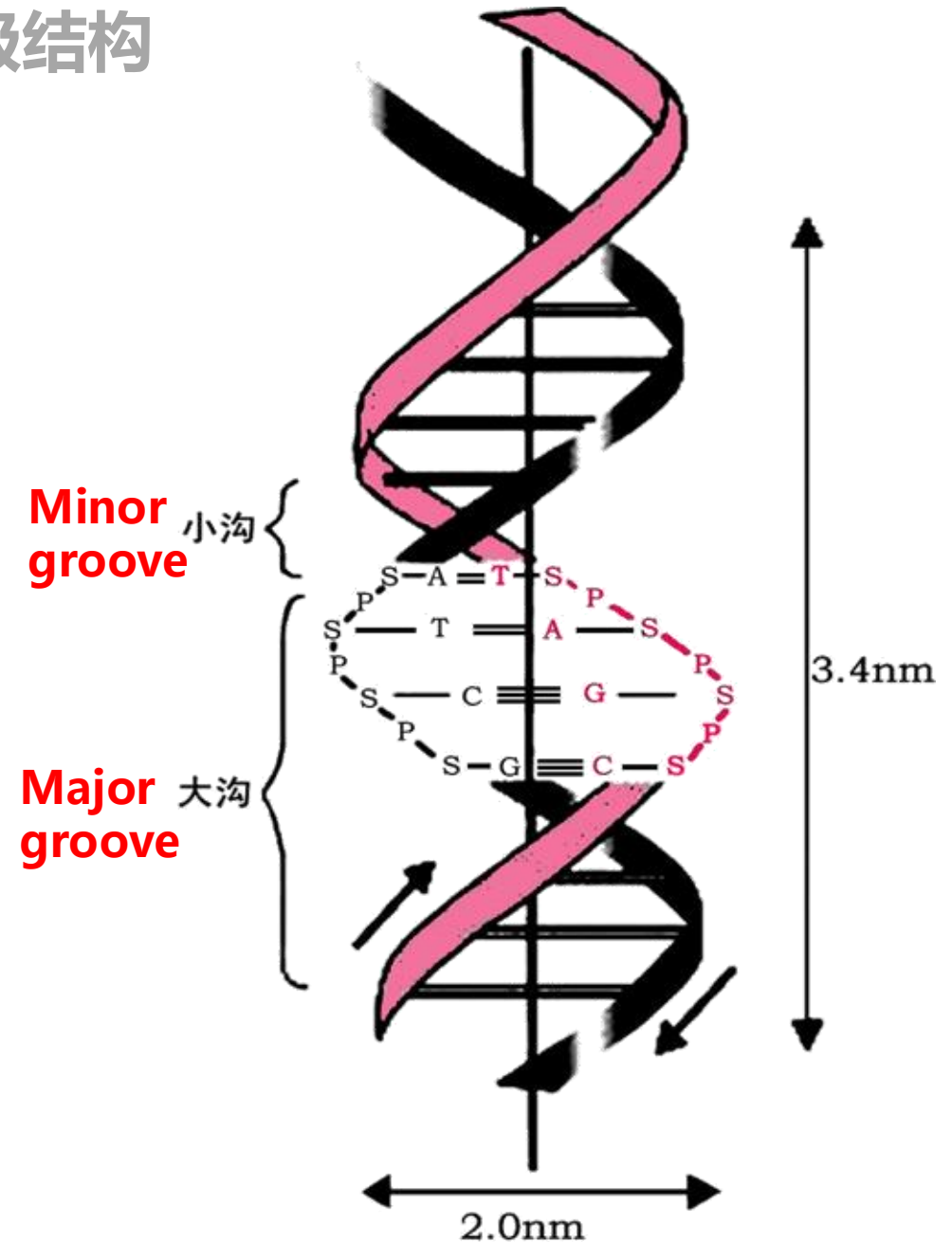
- ✓ Bases lie perpendicular to the helical axis
- ✓ Sugar-phosphate forms the backbone

❖ Helical Parameters

- ✓ Distance between base pairs: 0.34 nm
- ✓ One helical turn: 3.4 nm
- ✓ ~10 base pairs per turn

❖ Groove Structure (protein recognition)

- ✓ Major groove (wide)
- ✓ Minor groove (narrow)



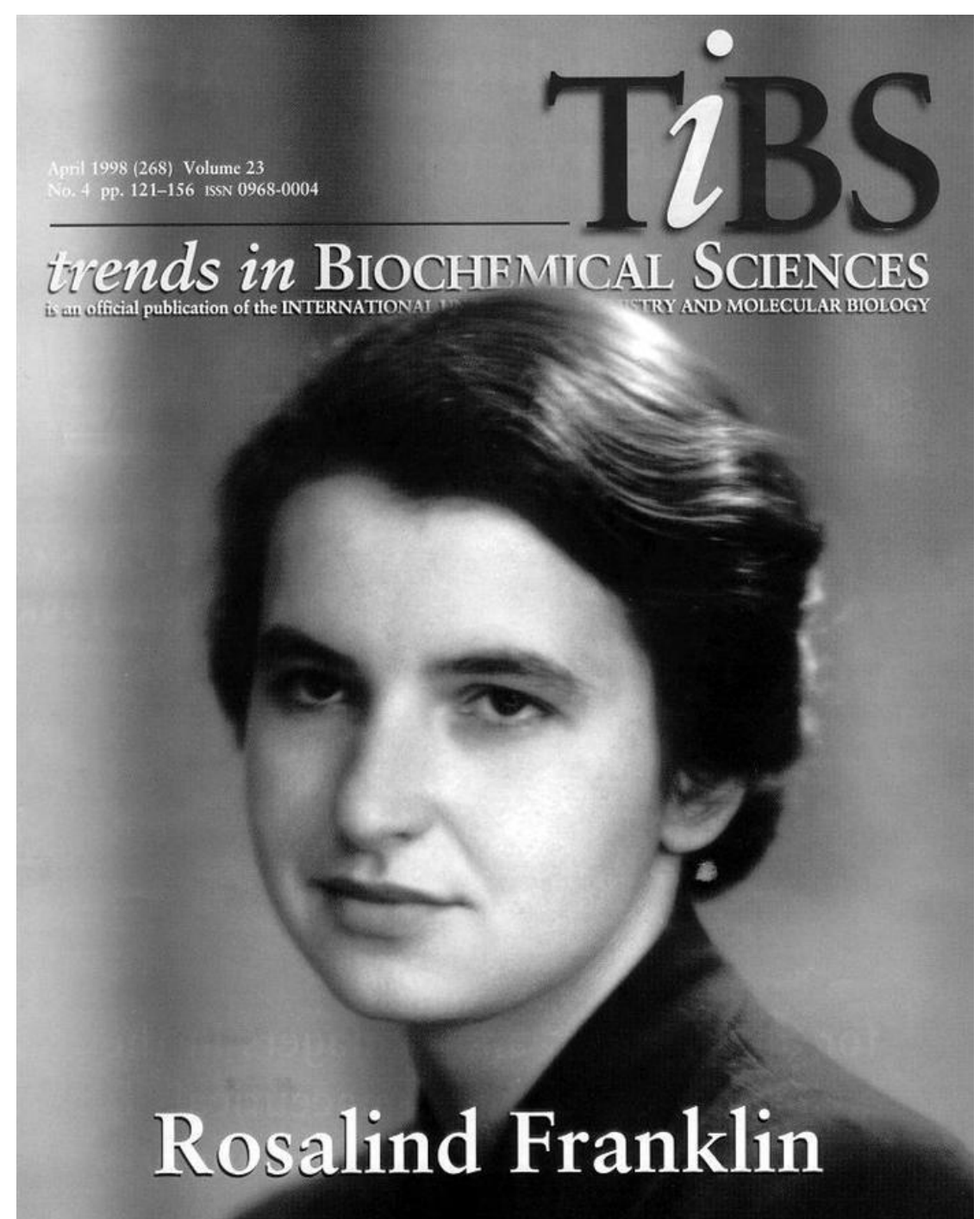
The Story Behind the Double Helix

- ❖ Published in *Nature*, alongside two other crucial papers in the same issue of *Nature* (April 25, 1953).
- ❖ 1962: **Watson, Crick**, and **Wilkins** shared the **Nobel Prize**.

Feature	Watson & Crick (The Model)	Wilkins & Franklin (The Evidence)
Role	Theoretical/Synthetic: They built a physical cardboard and wire model.	Experimental/Analytical: They used X-ray crystallography to photograph DNA.
Contribution	Proposed the double helix, anti-parallel strands, and base pairing (A-T, G-C).	Provided the physical dimensions and symmetry that proved the helix existed.
Nature Paper	<i>Molecular Structure of Nucleic Acids</i>	<i>Molecular Structure of Deoxyribose Nucleic Acids</i>

The Story Behind the Double Helix

Wilkins shown to Watson without Franklin's knowledge, which played a crucial role in model building



The Story Behind the Double Helix

Scientific Reflections

- ❑ **Publish timely and confidently / 研究得及时发表**
- ❑ **Ideas matter as much as experiments / 理论和模型研究与试验研究同等重要**
- ❑ **Integrating knowledge leads to breakthroughs / 理解前人工作是科研突破的根基**
- ❑ **Respect contributions of others / 尊重别人的工作**

DNA Secondary Structure/ 二级结构

Stability of the DNA Double Helix

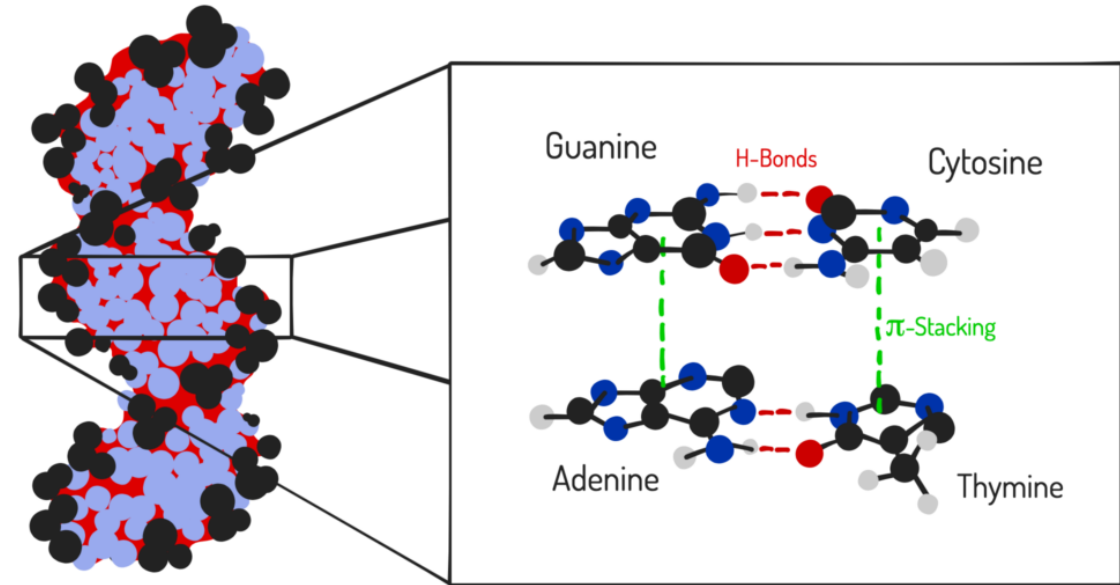
❖ Base Stacking (碱基堆积力)

Most important stabilizing force/最主要的作用力

- π - π interactions between adjacent bases
- Hydrophobic bases stack to minimize water exposure
- Provides primary stabilization energy

❖ Hydrogen Bonding (氢键)

- A-T: 2 hydrogen bonds
- G-C: 3 hydrogen bonds



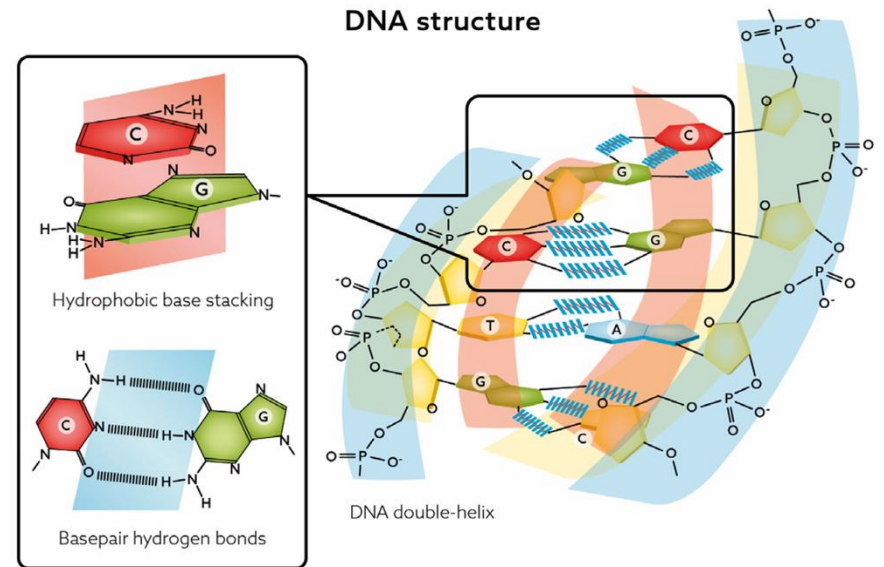
GC content vs stability

DNA Secondary Structure/ 二级

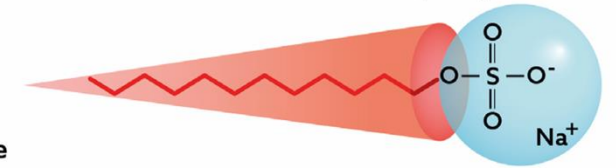
Stability of the DNA Double Helix

❖ Hydrophobic Effect

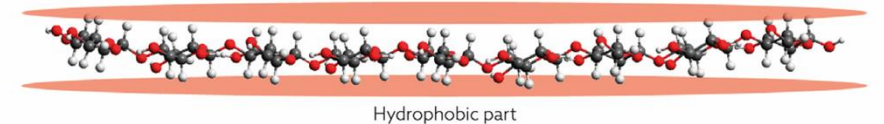
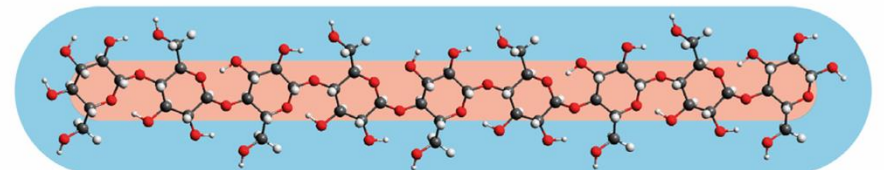
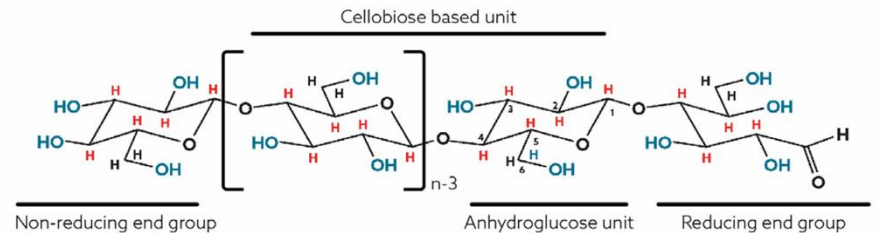
- Bases are hydrophobic → buried inside helix
- Backbone is hydrophilic → exposed to water
- Drives helix formation in aqueous environment



Surfactant structure (SDS)



Cellulose structure

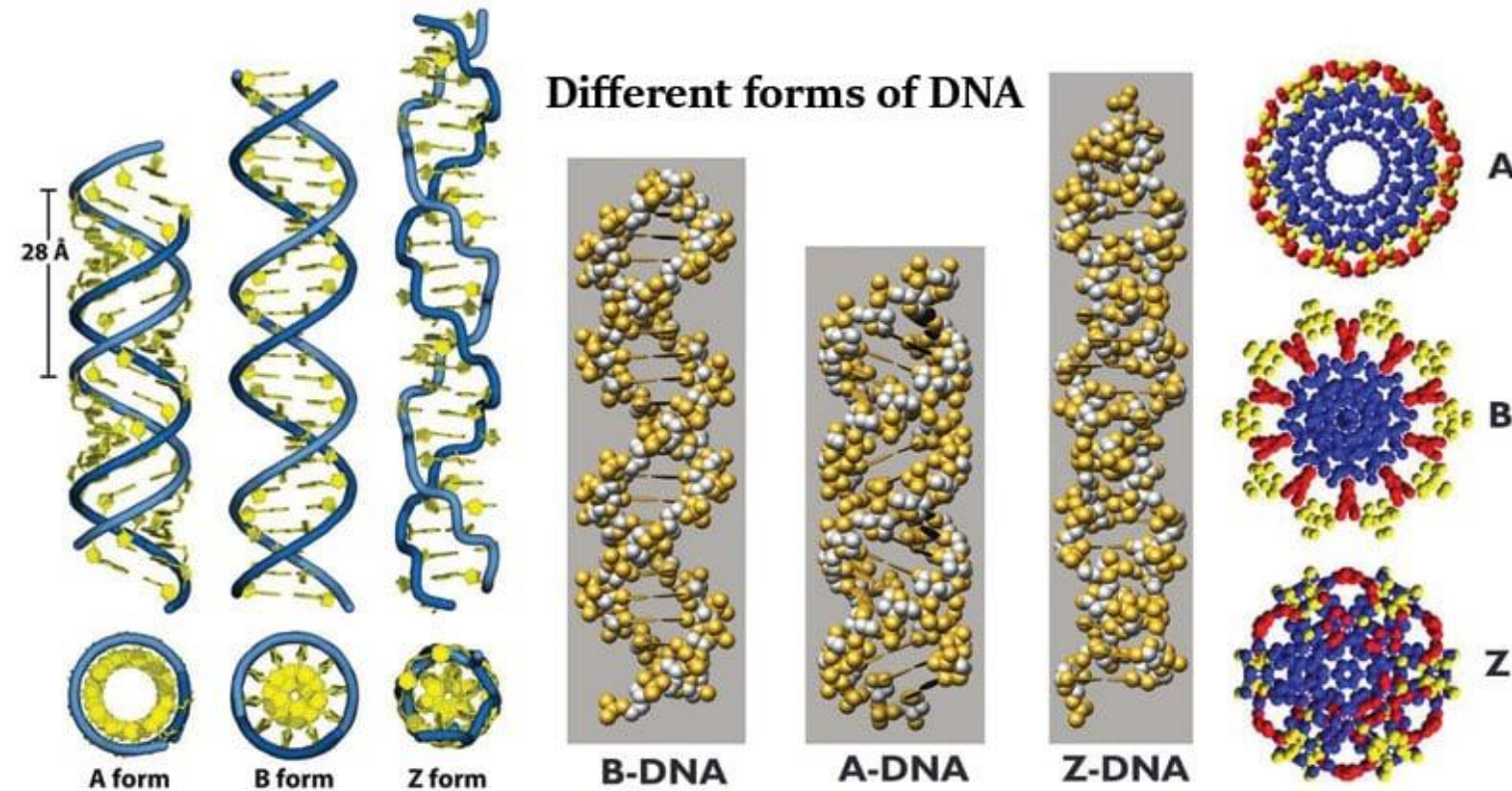


❖ Electrostatic Interactions

- Negative charges on phosphate backbone
- Stabilized by:
 - Metal ions (e.g., Na^+ , Mg^{2+})
 - Cellular environment

DNA Secondary Structure/ 二级结构

Major Forms of DNA Helix



❖ B-DNA (Most Common Form)

- Right-handed helix
- ~10 base pairs per turn
- Standard Watson–Crick model

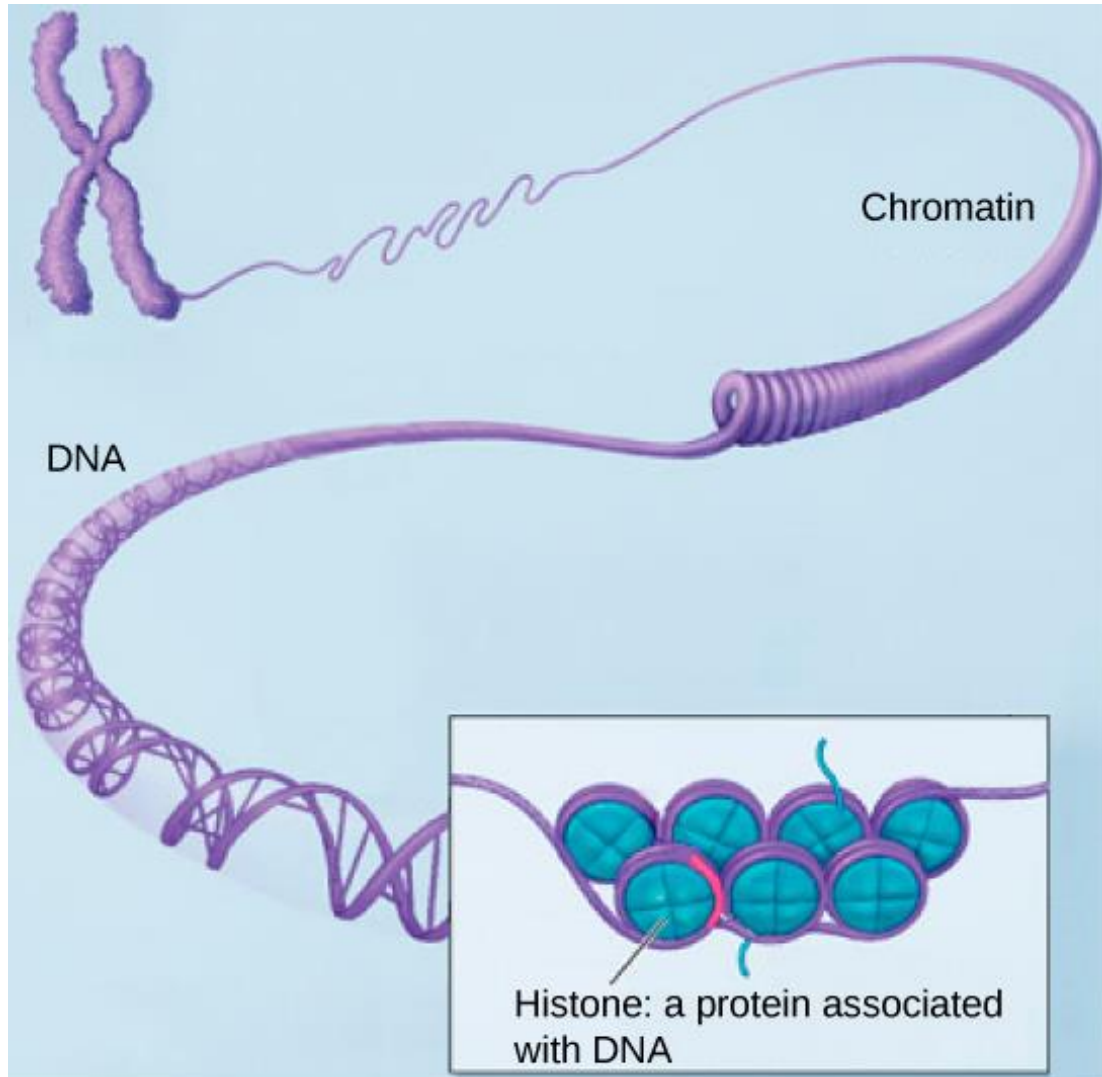
❖ A-DNA

- Right-handed helix
- Shorter and wider than B-DNA
- Forms under dehydrated conditions
- Found in DNA–RNA hybrids

❖ Z-DNA

- Left-handed helix
- Zigzag backbone structure
- Forms in GC-rich sequences
- May play roles in gene regulation

DNA Supercoiling (Superhelix) / 高级结构



A superhelix is a molecular structure in which a helix is itself coiled into a helix.

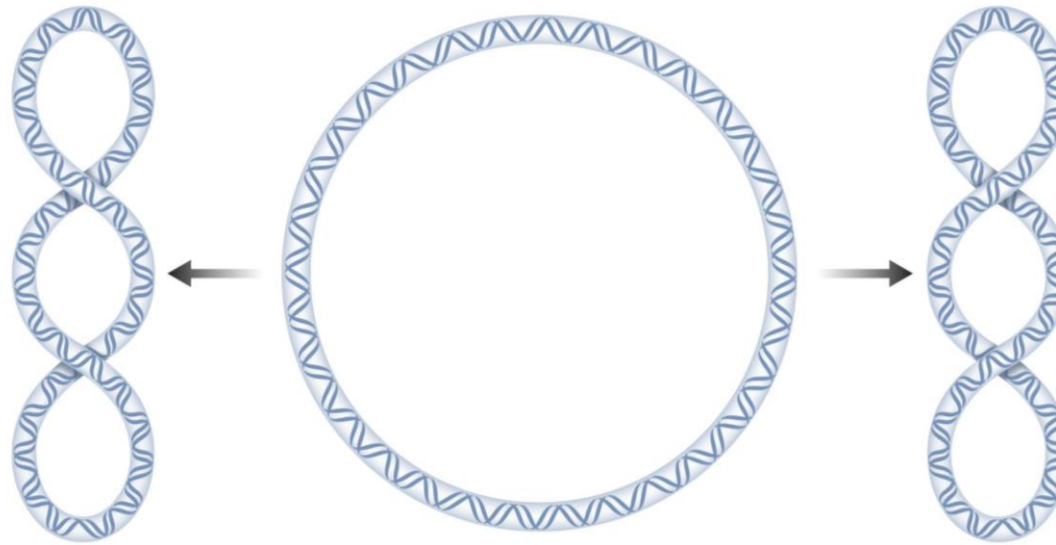


DNA Supercoiling (Superhelix) / 高级结构

Types of Supercoiling

❖ Positive Supercoiling

- ❖ Overwound DNA
- ❖ Occurs ahead of replication/transcription
- ❖ More compact and harder to unwind



盘绕方向与DNA双螺旋方向相同,即**右手超螺旋**(目前仅嗜热菌体内存在).

❖ Negative Supercoiling

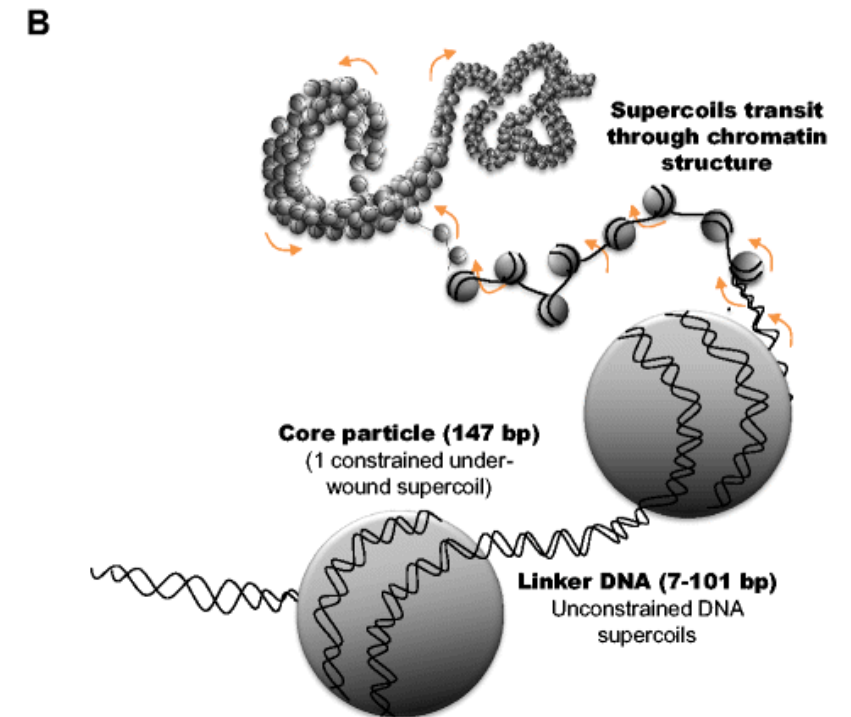
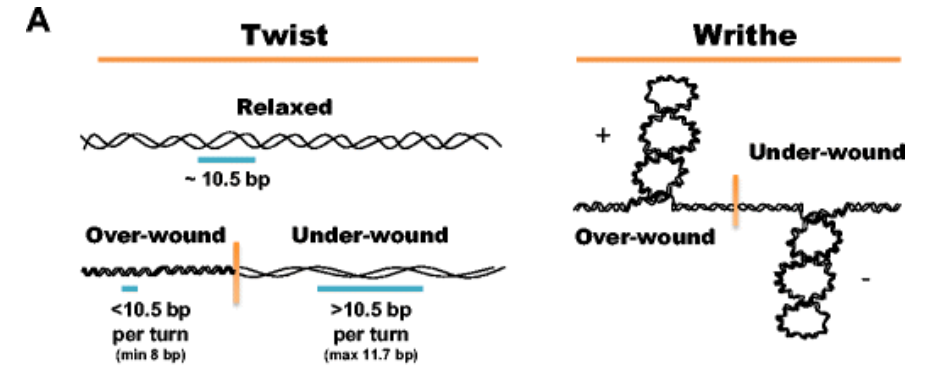
- ❖ Underwound DNA
- ❖ Most common in cells
- ❖ Facilitates strand separation

盘绕方向与DNA双螺旋方向相反,即**左手超螺旋**(常见生物体状态).

DNA Supercoiling (Superhelix) / 高级结构

Biological Significance

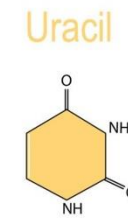
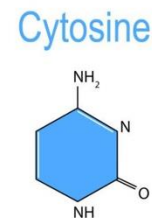
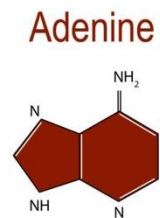
- ❖ Compacts DNA into limited cellular space
- ❖ Regulates DNA accessibility
- ❖ Important for:
 - ❖ Replication
 - ❖ Transcription



RNA

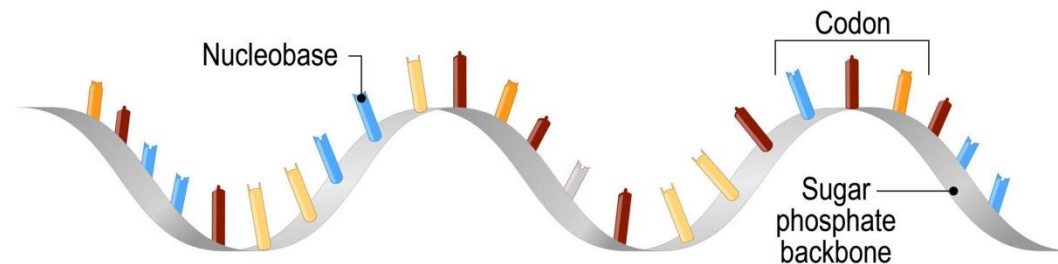
❖ Basic Building Units

- AMP (adenosine monophosphate)
- GMP (guanosine monophosphate)
- CMP (cytidine monophosphate)
- **UMP (uridine monophosphate)**



❖ Backbone Structure

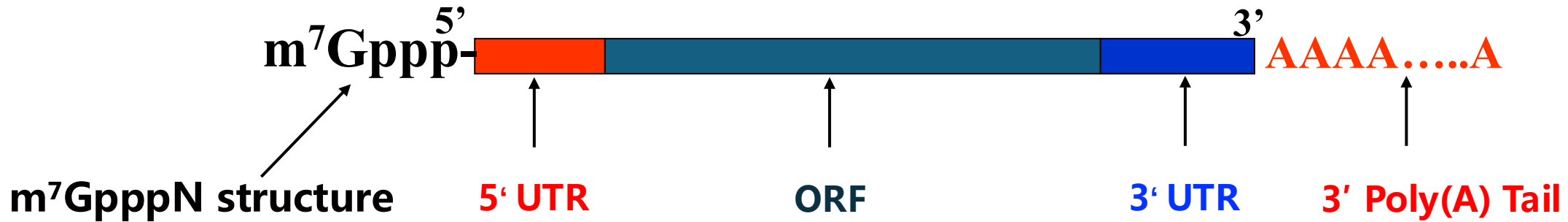
- Nucleotides linked by 3'–5' phosphodiester bonds, similar to DNA
- Forms a linear polynucleotide chain



RNA

Messenger RNA (mRNA): a type of single-stranded RNA involved in protein synthesis.

Eukaryotic mRNA is typically monocistronic / 单顺反子



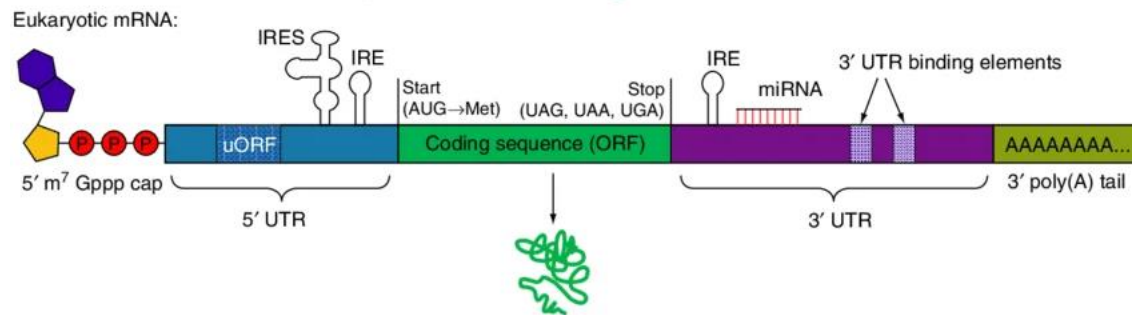
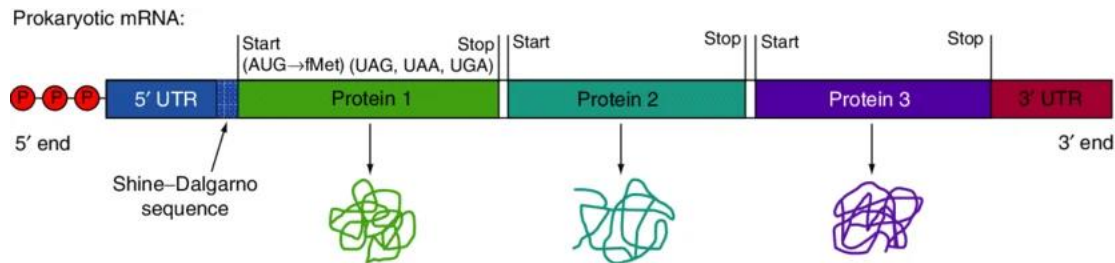
7-甲基鸟苷帽

sUTRs: Untranslated Region

ORF : Open reading frame

RNA

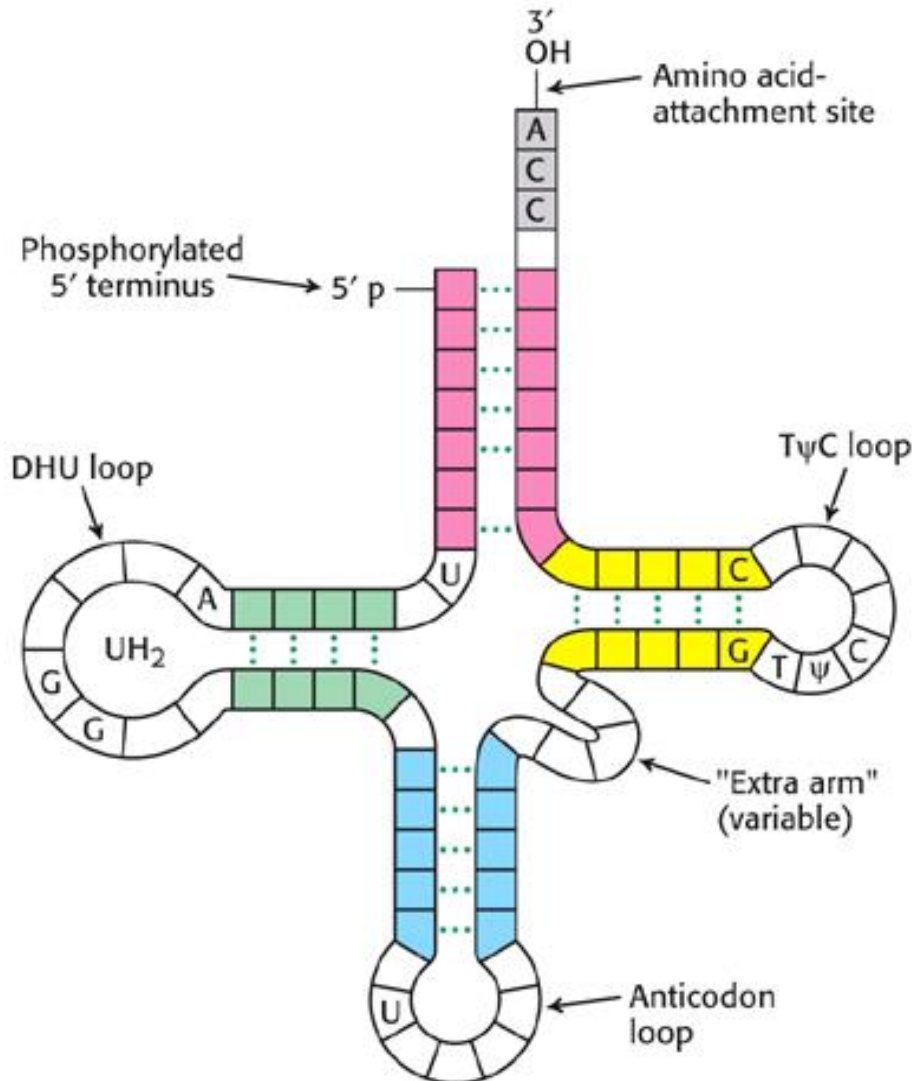
Feature	Prokaryotic mRNA	Eukaryotic mRNA
Structure	Polycistronic	Monocistronic
5' End	No cap	5' cap (m ⁷ G)
3' End	No poly(A) tail (or short)	Poly(A) tail
Processing	Minimal	Extensive processing
Introns	Absent	Present (splicing required)
Translation	Coupled with transcription	Separated (nucleus to cytoplasm)
Stability	Short-lived	More stable



- ❖ Prokaryotic mRNA is efficient and rapid
- ❖ Eukaryotic mRNA is regulated and processed

RNA

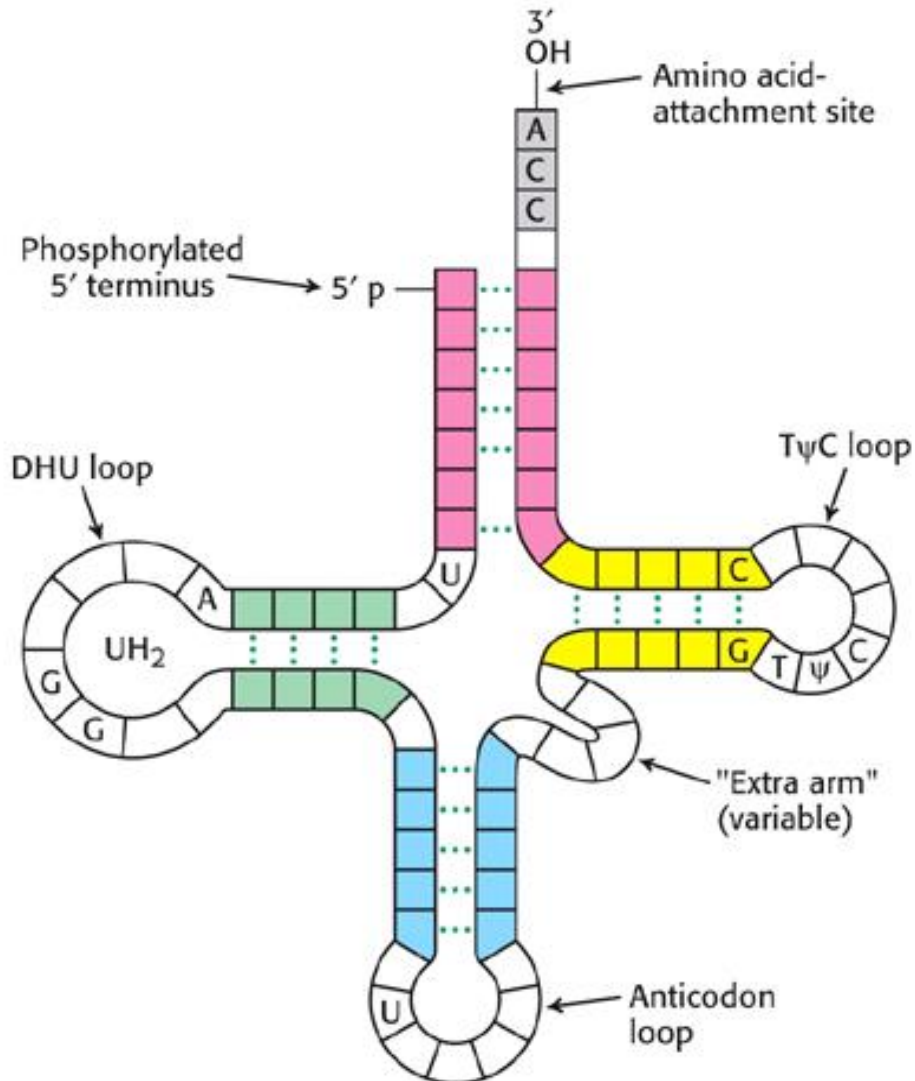
Transfer RNA (tRNA): a small RNA plays a key role in protein synthesis



- ✓ **Small RNA (~70–90 nucleotides)**
 - ✓ **Single-stranded but highly folded**
 - ✓ **Contains unusual/modified bases**
-
- ✓ 由70 - 90个核苷酸组成;
 - ✓ 含10~20%的稀有/修饰核苷 (DHU, 假尿嘧啶, mG, mA)

RNA

Transfer RNA (tRNA): a small RNA plays a key role in protein synthesis



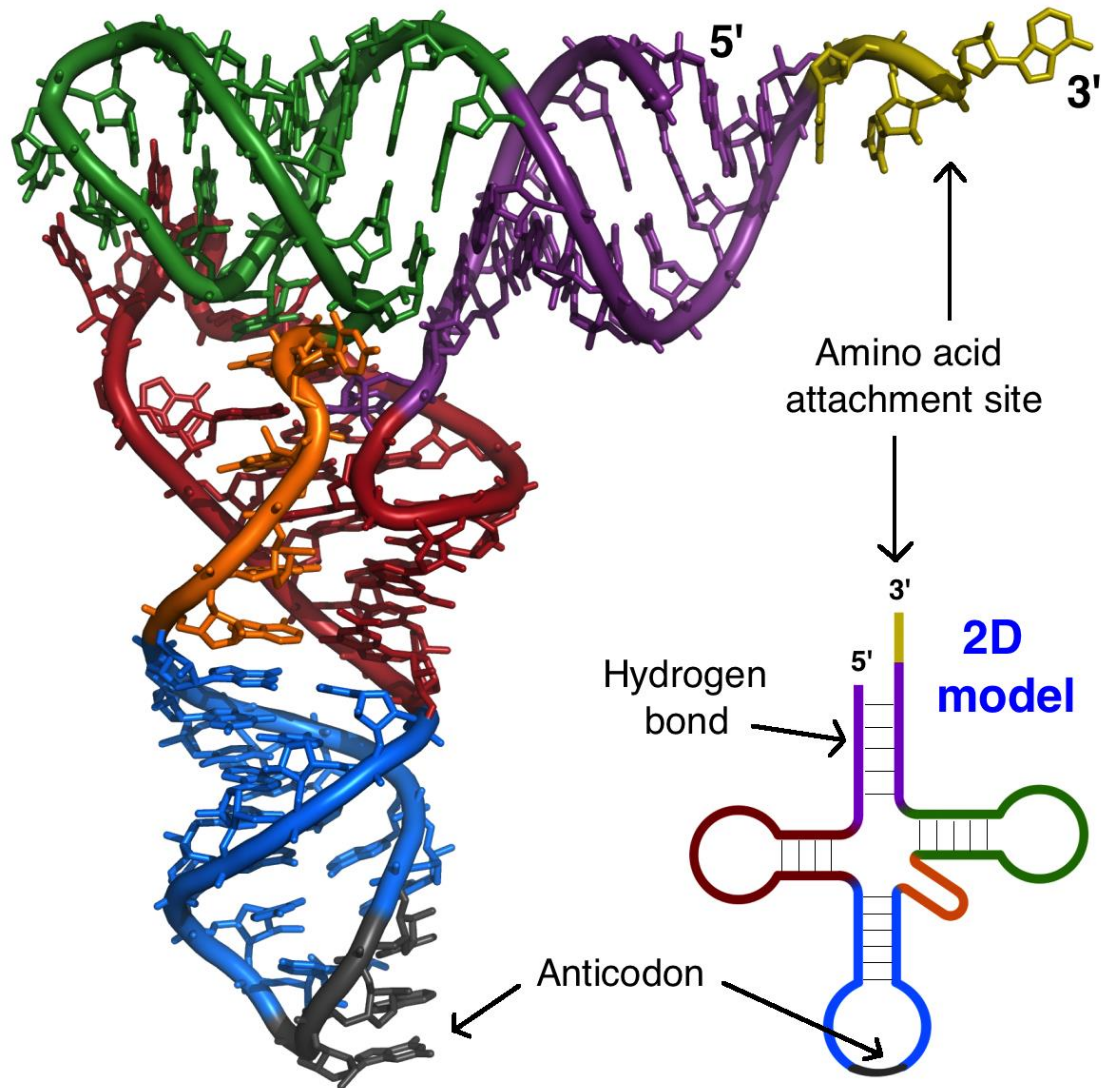
❖ Secondary Structure

- ✓ **Acceptor Stem: CCA sequence**
- ✓ **Anticodon Loop: Contains anticodon triplet**
- ✓ **Dihydrouridine Loop: tRNA recognition**
- ✓ **TΨC Loop: Interacts with ribosome**
- ✓ **Variable Loop: Size varies among tRNAs**

- ✓ 四个臂和四个环;
- ✓ 3' 端为CCA-OH结构, 为接受AA的部位;
- ✓ 反密码子环含有反密码子

RNA

Transfer RNA (tRNA): a small RNA plays a key role in protein synthesis

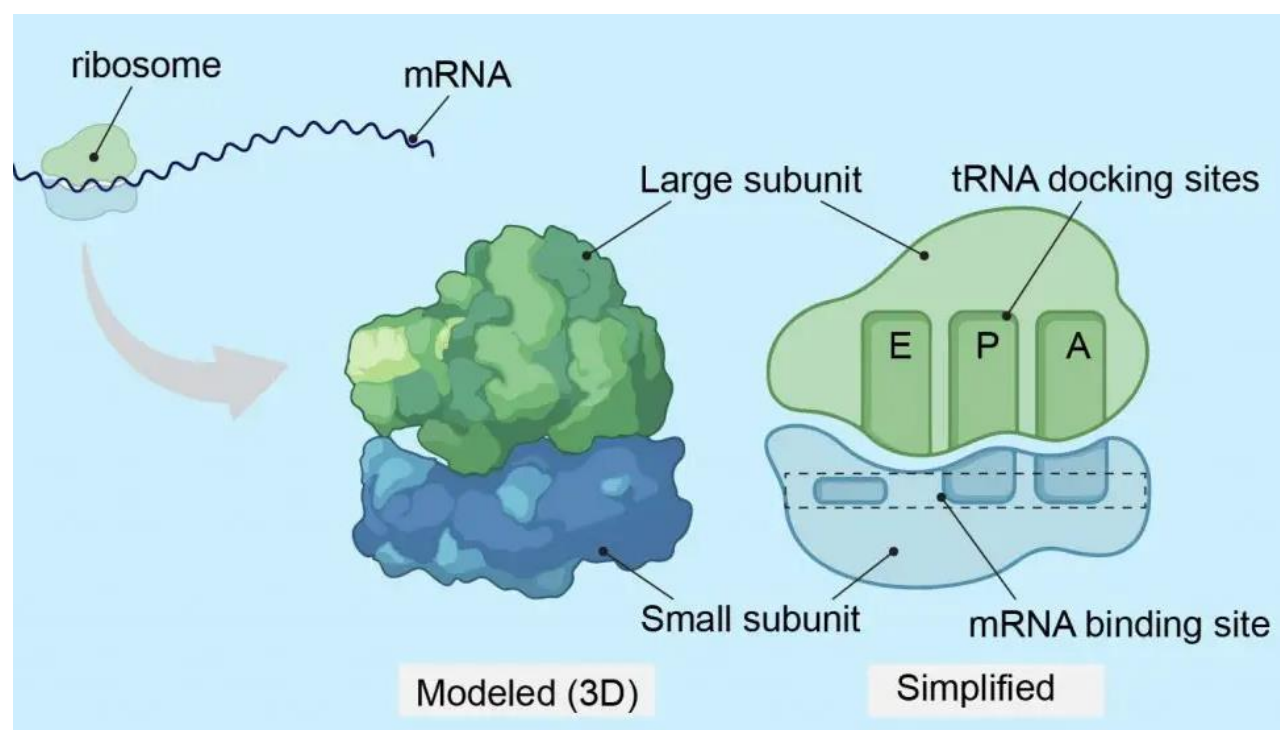


❖ Tertiary Structure

- ✓ **Folds into an L-shaped 3D structure**
- ✓ **Brings:**
 - **Anticodon**
 - **Amino acid attachment site into functional alignment**

RNA

Ribosomal RNA (rRNA) is a major component of the ribosome



❖ Key Functions

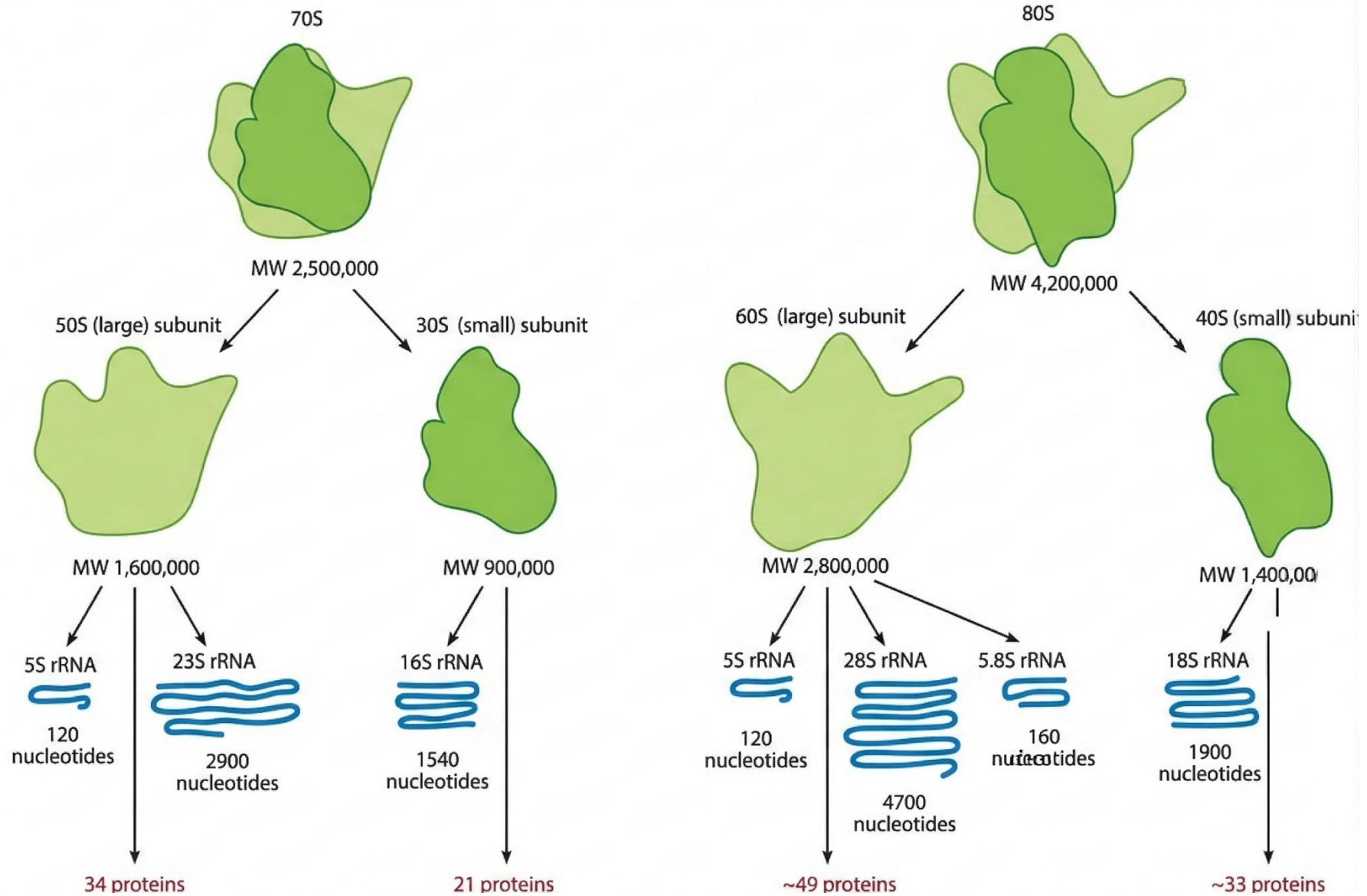
- ✓ **Structural framework of the ribosome**
- ✓ **Catalyzes peptide bond formation**
- ✓ **Positions mRNA and tRNA during translation**

rRNA acts as a ribozyme (RNA with catalytic activity)

RNA

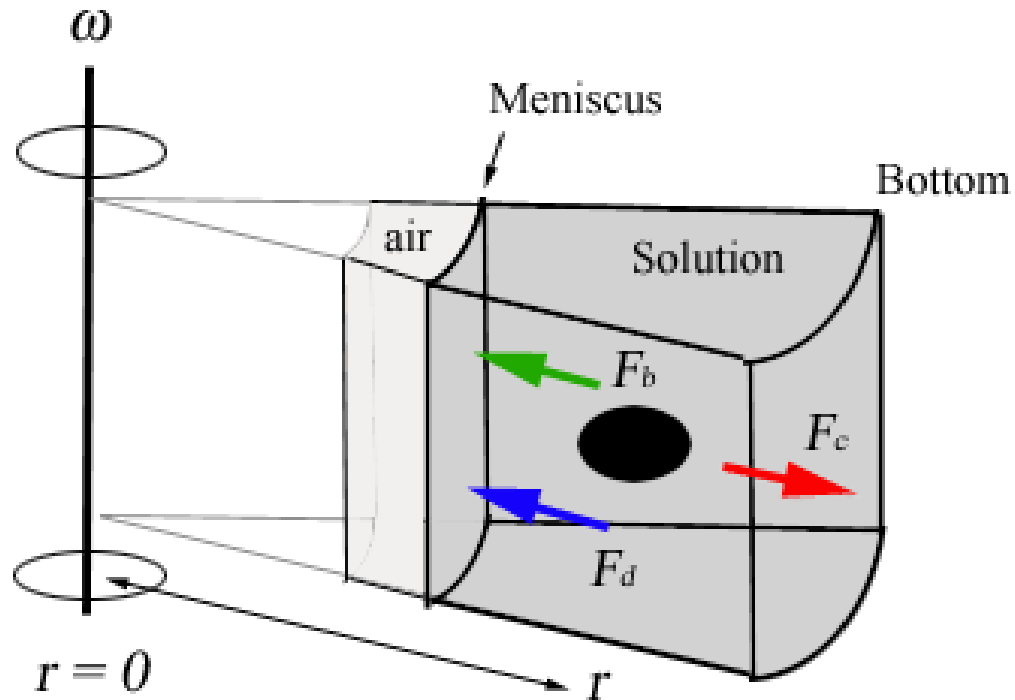
Prokaryotic rRNA

Eukaryotic rRNA



Sedimentation Coefficient (S)/ 沉降系数

The **S** quantifies how fast a particle sediments (moves) in a centrifugal field.

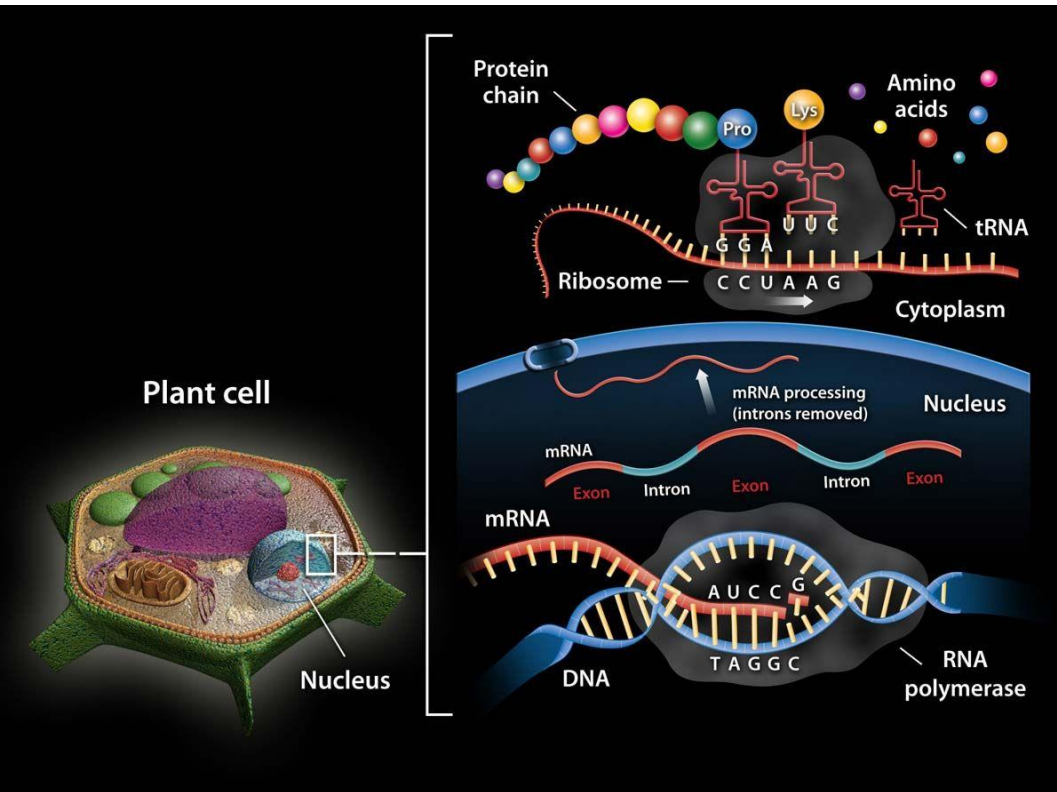


Used in:

- Protein characterization
- Ribosome studies
- Analytical ultracentrifugation

RNA

Functional Comparison of RNA Types



RNA Type	Main Role	Key Feature
mRNA	Template for protein synthesis	Contains codons (genetic code)
tRNA	Adapter molecule	Matches anticodon with codon; carries amino acids
rRNA	Structural & catalytic core	Forms ribosome; catalyzes peptide bonds

mRNA encodes, tRNA decodes, and rRNA catalyzes

Outline

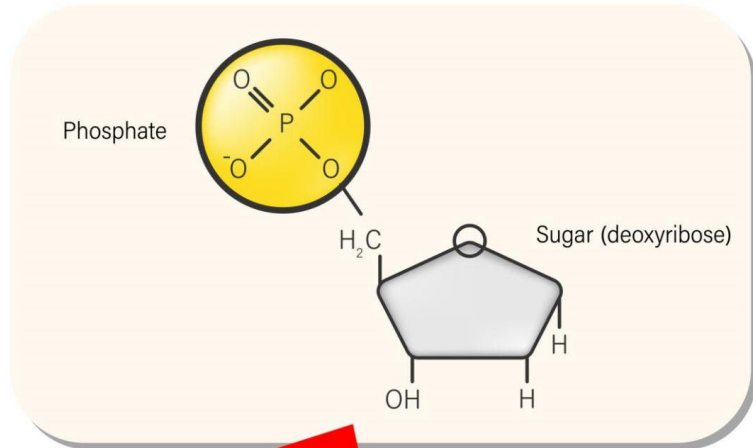
- **Discovery**
核酸的发现历史
- **Types and Biological Distribution**
核酸的类型及生物分布
- **Chemical Components**
化学组成
- **Structure**
结构
- **Physicochemical Properties**
理化性质

Physicochemical Properties

1. Amphoteric and Polyelectrolyte Properties / 两性电解质
2. Macromolecular Properties / 高分子性质
3. UV Absorption / 紫外吸收性质
4. Denaturation and Renaturation / 变性和复性
5. Applications

Physicochemical Properties

Amphoteric and Polyelectrolyte Properties

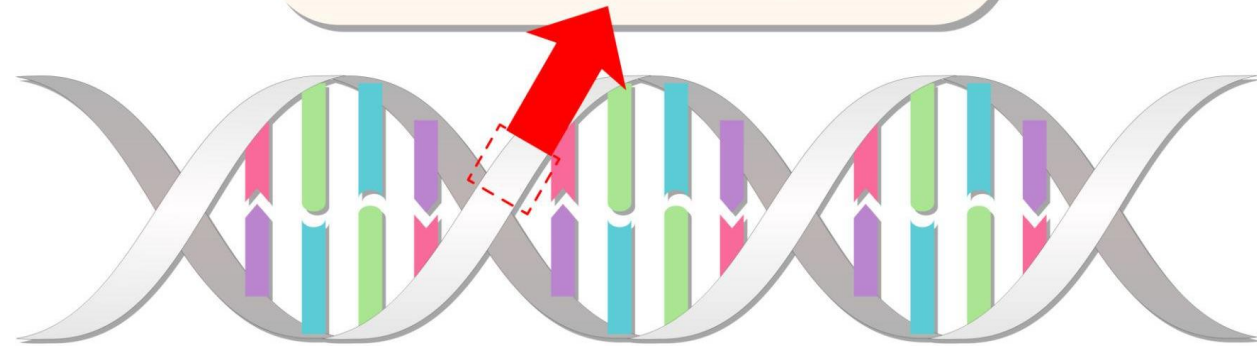


❖ Amphoteric (酸碱两性)

- ✓ **Acidic groups** (phosphate groups)
- ✓ **Basic sites** (nitrogenous bases)

❖ Polyelectrolyte Property (聚电解质)

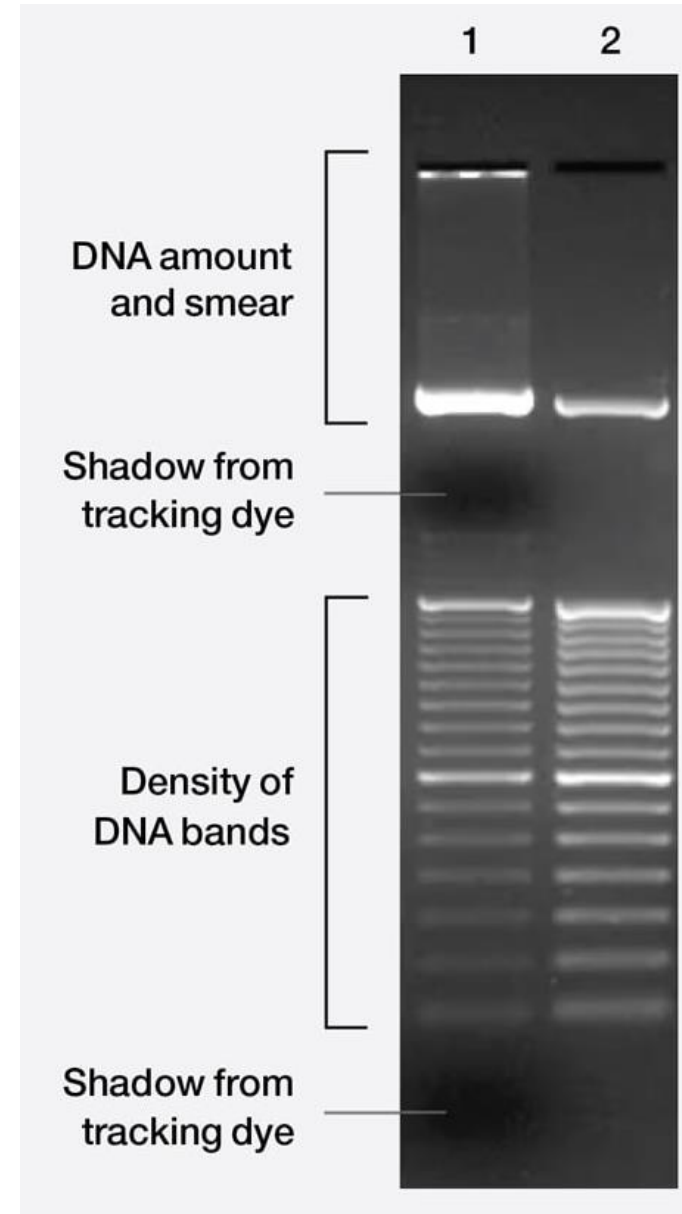
- ✓ **Multiple negatively charged phosphate groups**
- ✓ **DNA/RNA behave as polyanions in solution**



Physicochemical Properties

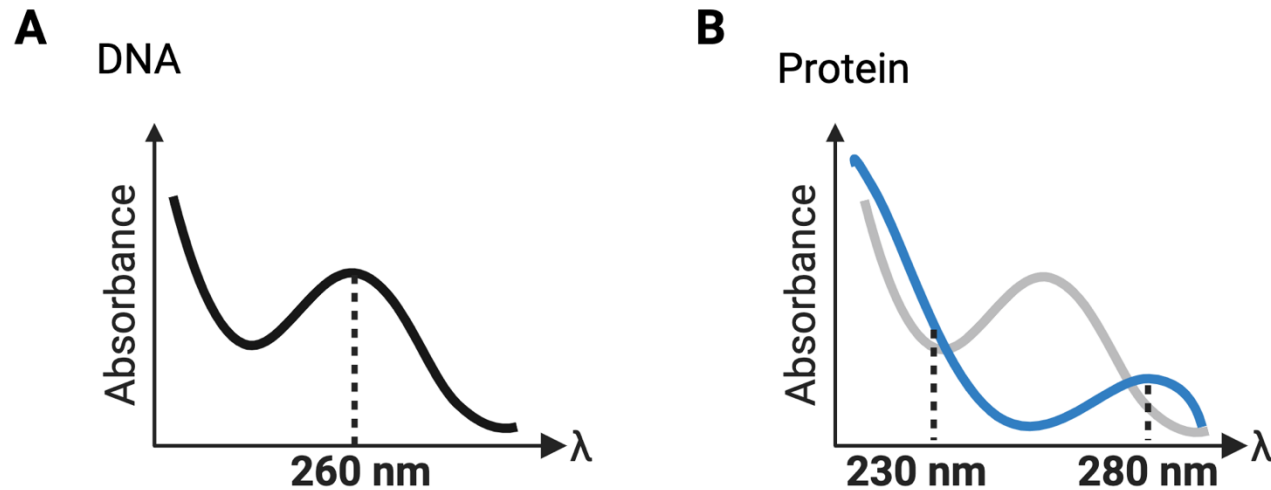
Macromolecular Properties

- ✓ **High molecular weight polymers**
- ✓ **Flexible chain structure (can coil and supercoil)**
- ✓ **High viscosity in solution**
- ✓ **Sensitive to environmental conditions (pH, ions, temperature)**
- ✓ **Can be separated by electrophoresis**



Physicochemical Properties

UV Absorption



- ✓ Maximum absorption at 260 nm, due to aromatic bases (A, G, C, T/U)
- ✓ Absorbance \propto concentration (quantification)
- ✓ Absorbance increases upon denaturation

A260/A280 ratio used to assess purity

DNA: ~ 1.8

RNA: 1.8-2.0

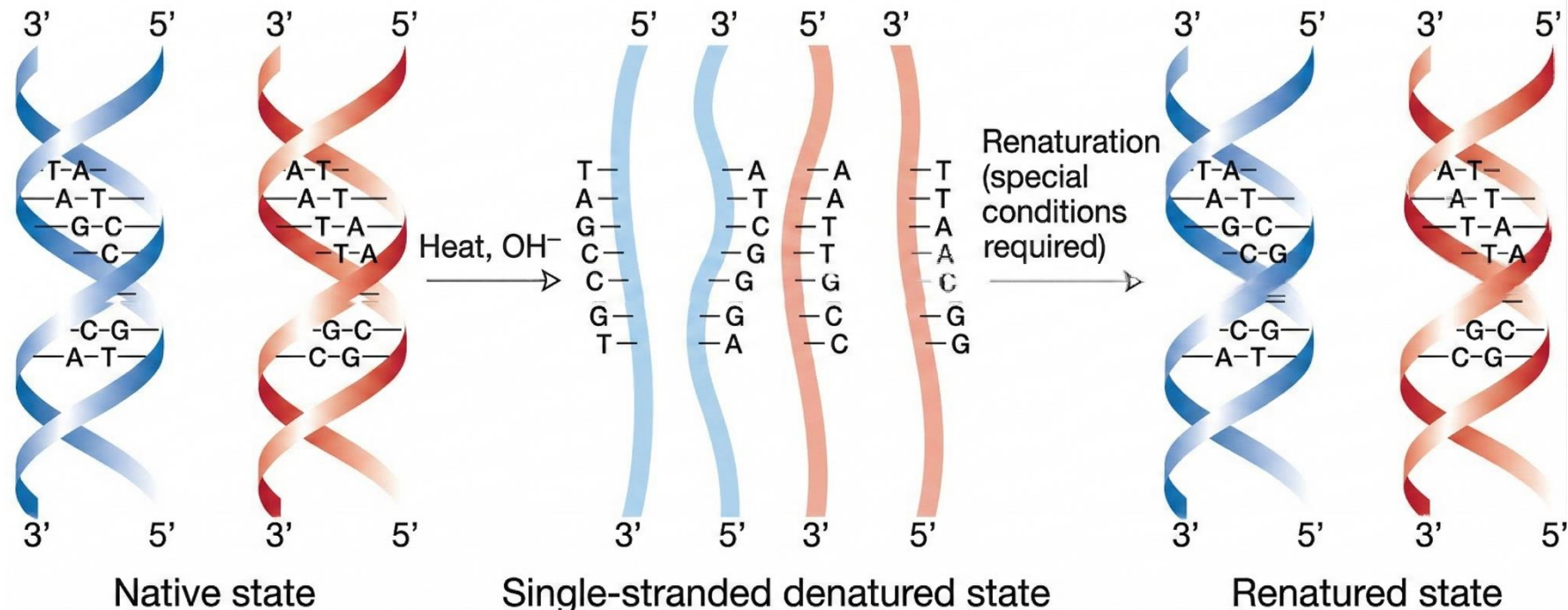
Physicochemical Properties

DNA Denaturation and Renaturation(变性与复性)

Denaturation (melting): Double-stranded DNA separates into two single strands, caused by heat, extreme pH, or chemicals

Renaturation (Annealing): Complementary strands reassociate under proper conditions

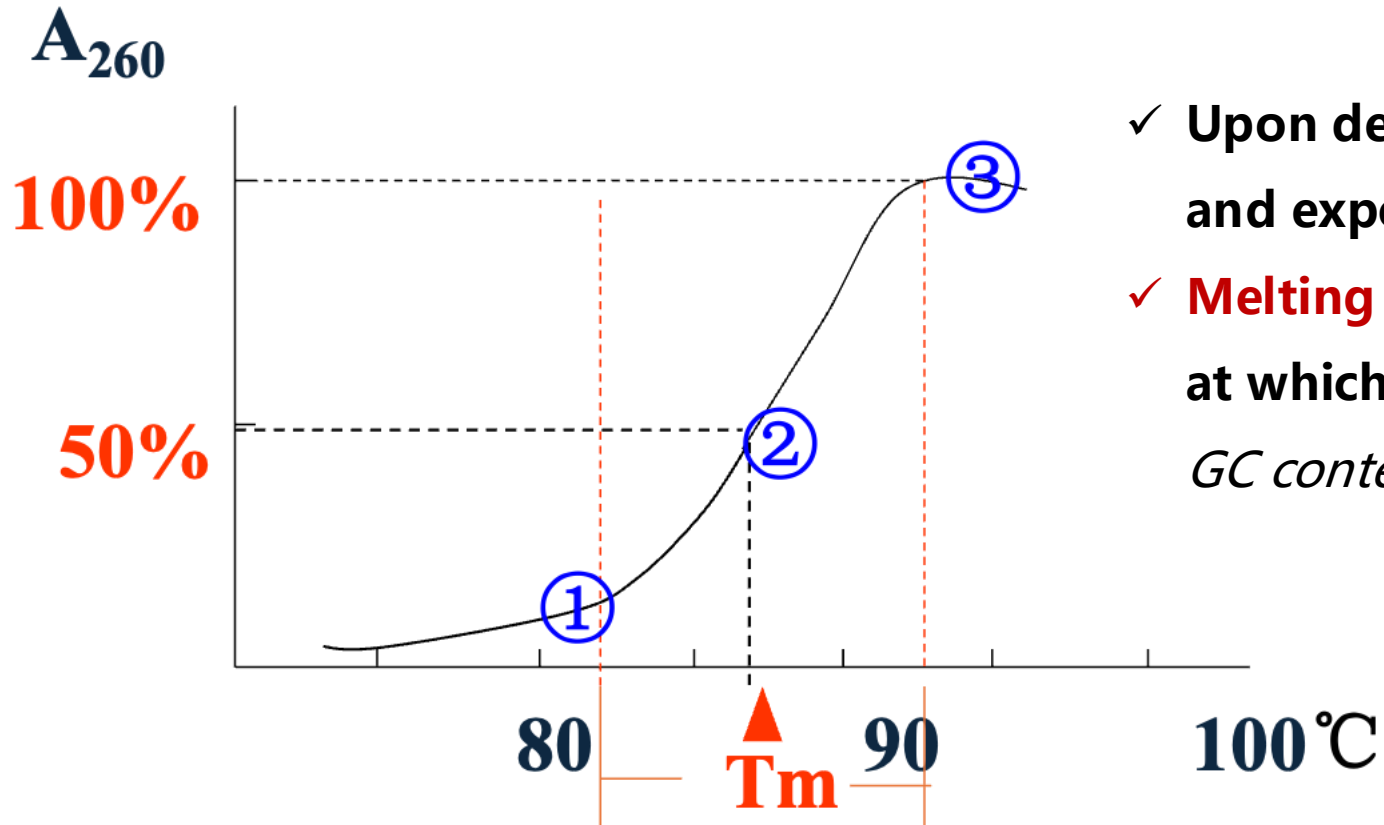
**Disruption of
hydrogen bonds
and base stacking**



Physicochemical Properties

DNA Denaturation

Hyperchromic effect (增色效应): UV absorbance at 260 nm increases, when DNA becomes single-stranded



- ✓ Upon denaturation, bases become unstacked and exposed (reason)
- ✓ **Melting temperature** (T_m ; 熔解温): Temperature at which 50% DNA is denatured (*depends on GC content and ionic strength*)

Physicochemical Properties

DNA Renaturation

Renaturation is specific and reversible, driven by base pairing

❖ **Requires**

- ✓ Complementary sequences
- ✓ Appropriate temperature and ionic strength

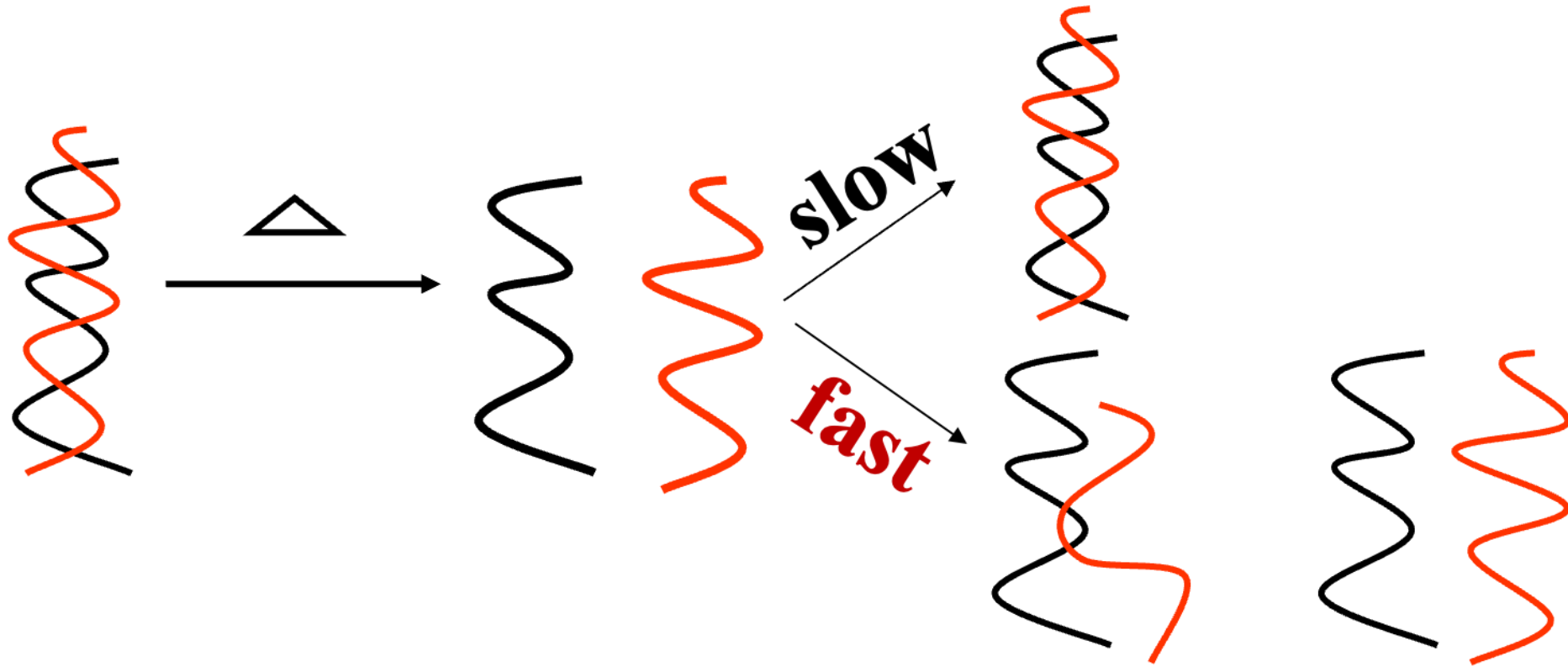
❖ **Process involves**

- ✓ Nucleation (initial base pairing)
- ✓ Zippering (rapid strand pairing)

Hypochromic effect (减色效应): reduced UV absorbance (260 nm) during renaturation

Physicochemical Properties

DNA Renaturation

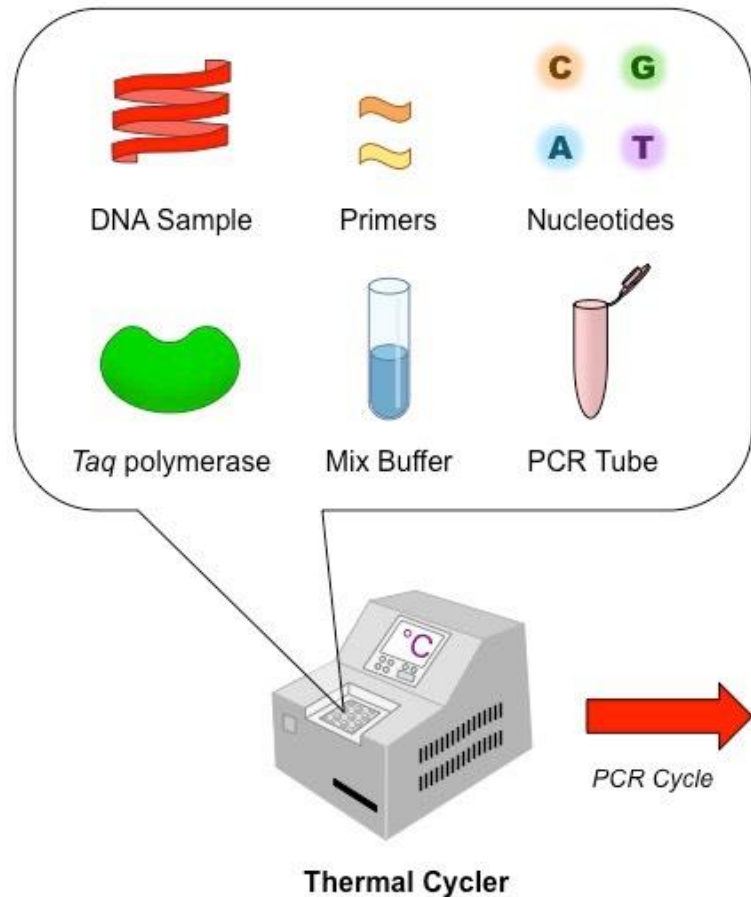


Slow cooling allows complementary strands to find each other, while rapid cooling prevents proper base pairing.

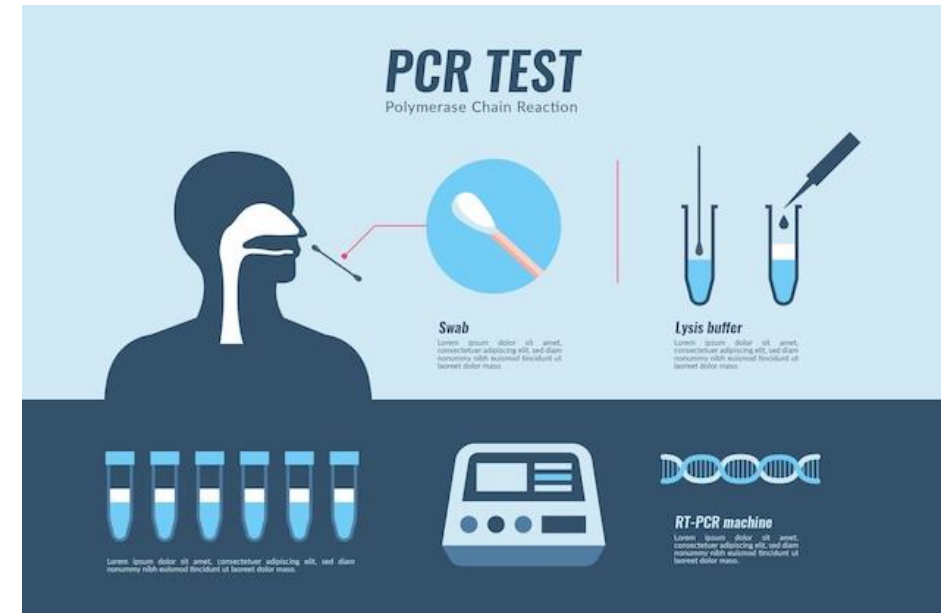
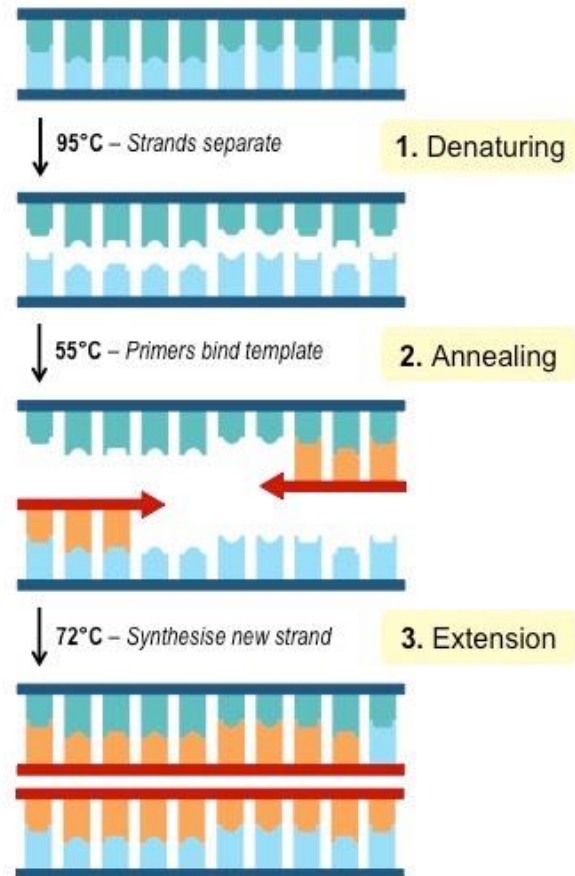
Physicochemical Properties

Application: Polymerase Chain Reaction (PCR)

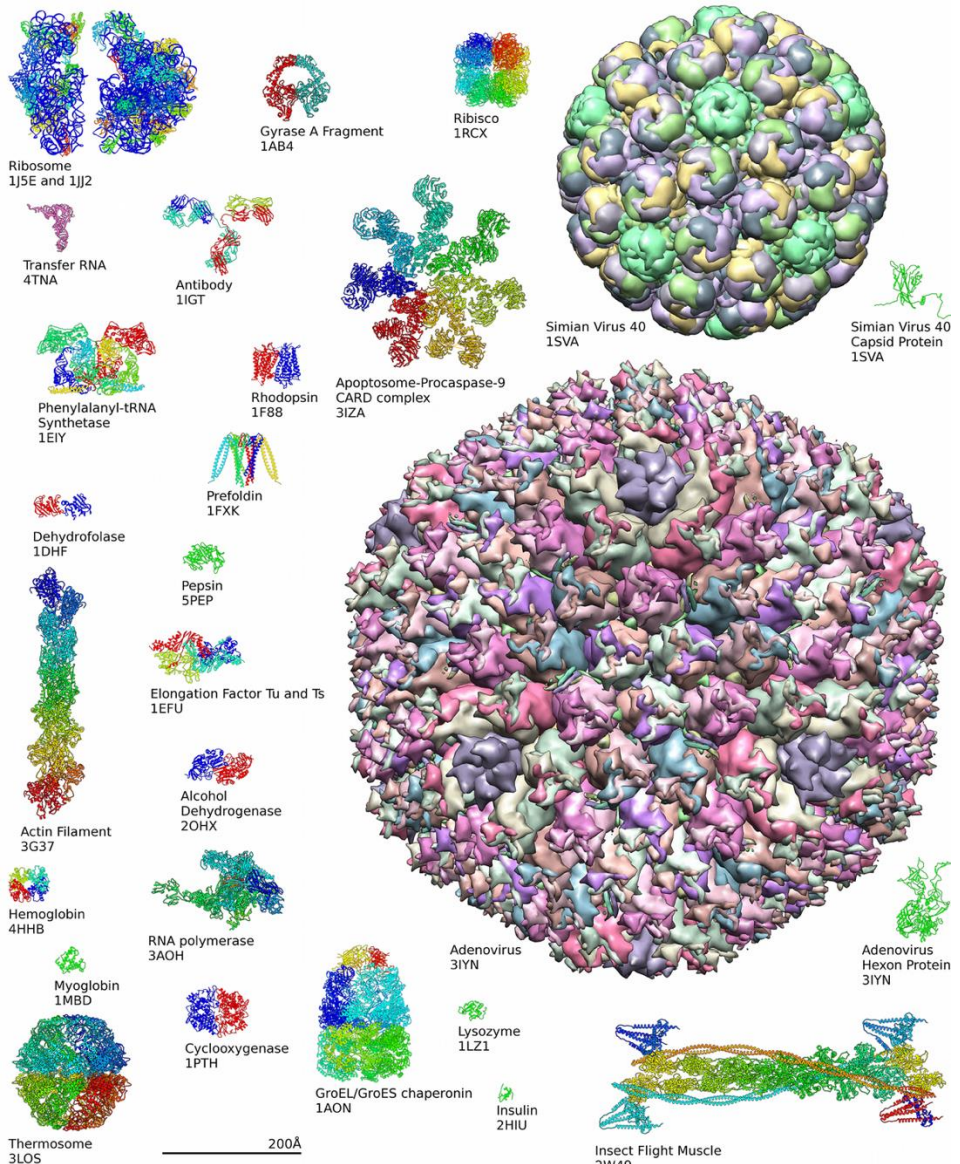
PCR Components



PCR Process (ONE Cycle)



2/4 Protein



Outline

- **About Protein**

- **Amino Acids**
氨基酸

- **Protein Structure**
蛋白质分子结构

- **Structure–Function Relationship**
结构与功能的关系

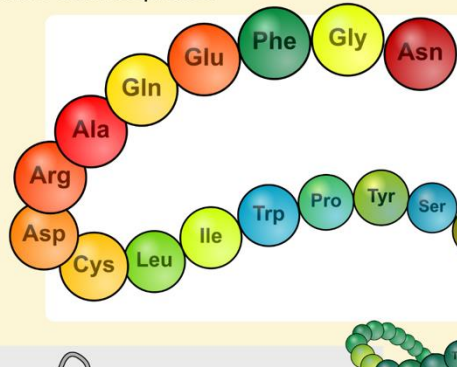
- **Physicochemical Properties of Proteins**
理化性质

- **Protein Separation and Applications**
分离与应用



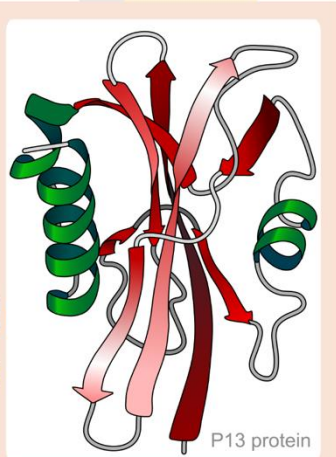
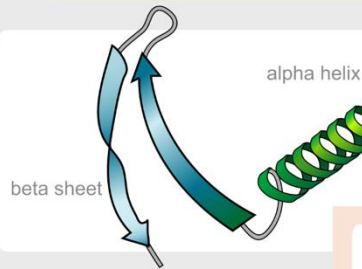
茅膏菜 (Drosera)

Primary structure
amino acid sequence

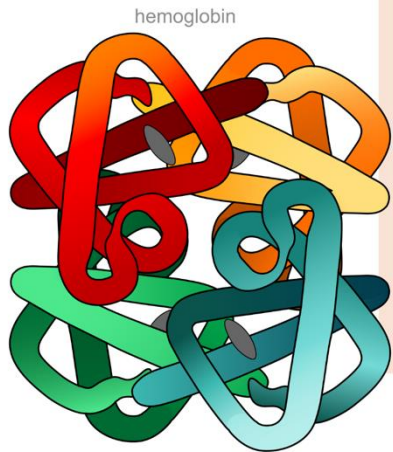


mRNA

Secondary structure
regular sub-structures

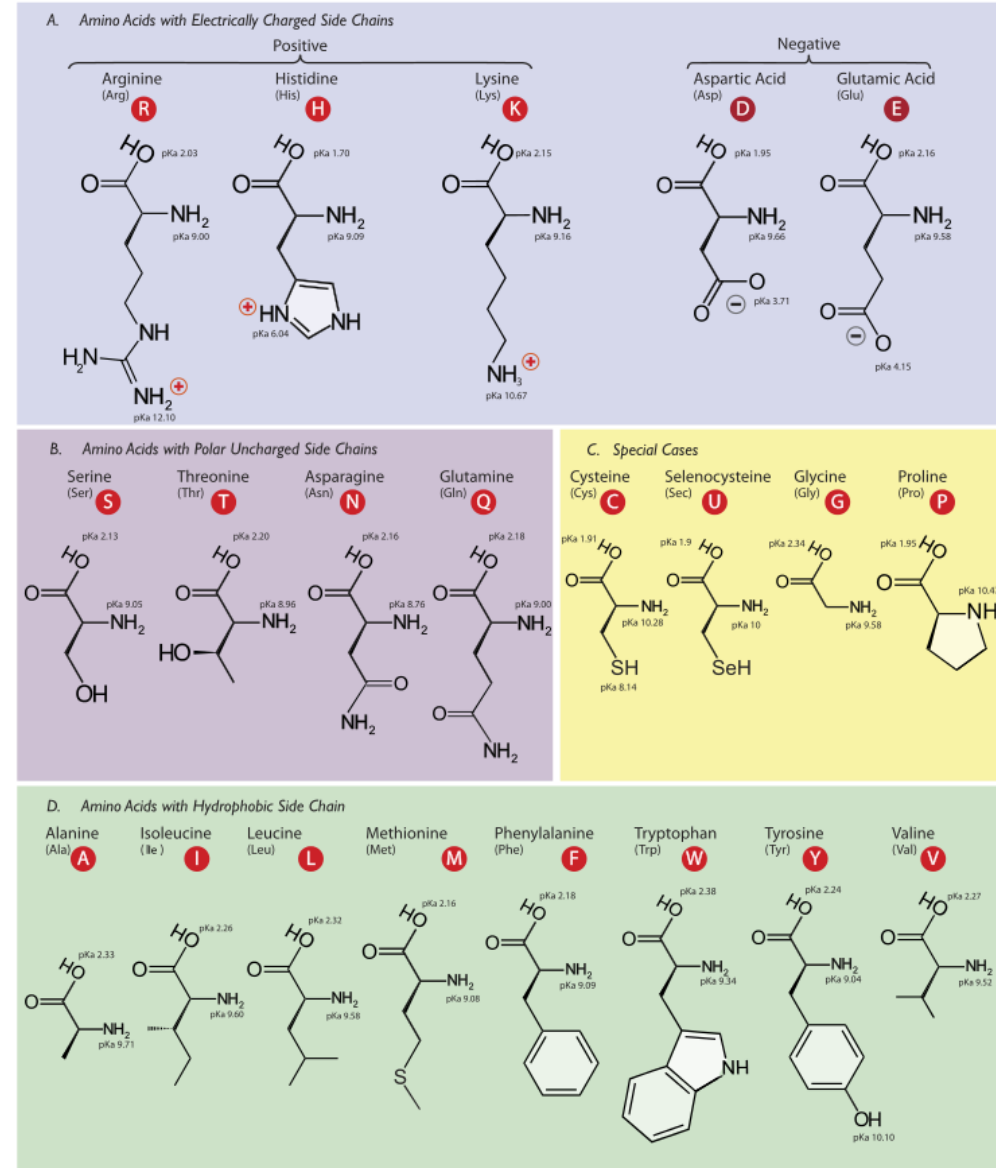


Tertiary structure
three-dimensional structure



Quaternary structure
complex of protein molecules

Monomers: 20 Amino Acids



About Protein

Chemical composition

❖ Elemental Composition

- ✓ Carbon (C): ~50%
- ✓ Hydrogen (H): ~7%
- ✓ Oxygen (O): ~23%
- ✓ Nitrogen (N): ~16%
- ✓ Sulfur (S): 0–3%

❖ Trace elements

- ✓ Phosphorus (P)
- ✓ Iron (Fe)
- ✓ Copper (Cu)
- ✓ Iodine (I)
- ✓ Zinc (Zn)

About Protein

Chemical composition

Kjeldahl N Estimation method:

Proteins contain approximately 16% N on average, therefore, the protein content \approx N content \times 6.25

Explanation:

Since protein is \sim 16% N:

$$\frac{100}{16} = 6.25$$

- ✓ **1 g of nitrogen \approx 6.25 g of protein**
- ✓ The factor is called the **protein conversion factor**

About Protein

Classification

(1) By Molecular Shape

- **Fibrous proteins** (e.g., collagen, keratin)
纤维蛋白
- **Globular proteins** (e.g., enzymes, hemoglobin)
球蛋白

(2) By Chemical Composition

- ❖ **Simple proteins** (e.g., albumin)
- ❖ **Complex proteins** (Protein + non-protein component)
 - ✓ **Lipoproteins / 脂蛋白**
 - ✓ **Glycoproteins / 糖蛋白**
 - ✓ **Nucleoproteins / 核蛋白**

(3) By Biological Function

- ✓ **Enzymes** (catalysis)
- ✓ **Structural proteins**
- ✓ **Motor proteins**
- ✓ **Defense proteins** (immune-related)
- ✓ **Transport proteins**
- ✓ **Signaling and recognition proteins**
- ✓ **Storage proteins**
- ✓ **Hormonal proteins**

About Protein

Proteins are long-chain macromolecules composed of **20 L- α -amino acids**

Molecular weight \approx number of amino acid residues \times 110 Da

- ✓ Average molecular weight of free amino acids \approx 126–128 Da
- ✓ BUT during peptide bond formation H₂O (18 Da) is lost per bond
- ✓ Therefore, Average residue mass \approx 110 Da

Outline

- About Protein

- **Amino Acids**
氨基酸

- **Protein Structure**
蛋白质分子结构

- **Structure–Function Relationship**
结构与功能的关系

- **Physicochemical Properties of Proteins**
理化性质

- **Protein Separation and Applications**
分离与应用

Are you sure?

杭州绿城足球队
唯一指定营养品

力菲氨基酸 为健康加油!

氨基酸
复合氨基酸饮料
不含咖啡因

Force Amino Acid
复合氨基酸饮料

杭州绿城足球队
唯一指定营养品

(中外合资)福建省力菲克药业有限公司

中国天下网: http://china.111.com 电话: 059276048

cherish Now
婵芮时

沐浴露时代

巴西波旁圣多斯咖啡豆 法国科西嘉岛深海叉珊瑚藻
温和净肤的多种氨基酸 诺贝尔化学奖日本富勒烯 欧洲生物精胺
美国二列酵母发酵产物溶胞物 中国白黎芦醇 蓝风铃香梨

cherish Now | 减肥
婵芮时 | 新时代

DELICATE FIRING
by Amino Acid Formula
氨基酸轻盈紧致沐浴露



打造清透水润感

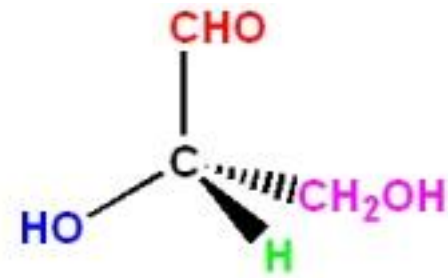
- 1 萃取高浓度精华
洗完即润正
- 2 质地轻盈, 不油不腻,
自然柔爽
- 3 改善粗糙暗沉肌肤,
净透滋养肌肤

DANZHI
氨基酸沐浴露

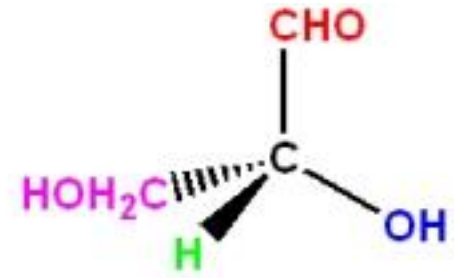
Amino Acids in Proteins

More than 300 amino acids have been identified in nature; However, only 20 (19 AA + 1IA, proline) are commonly used to build proteins

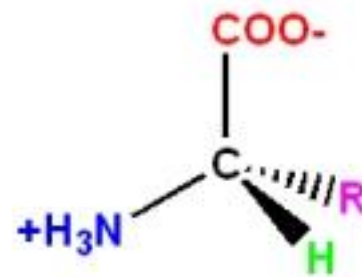
Most of amino acids are formed through post-translational modifications (PTM)



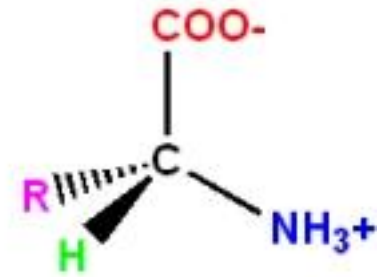
L-Glyceraldehyde



D-Glyceraldehyde

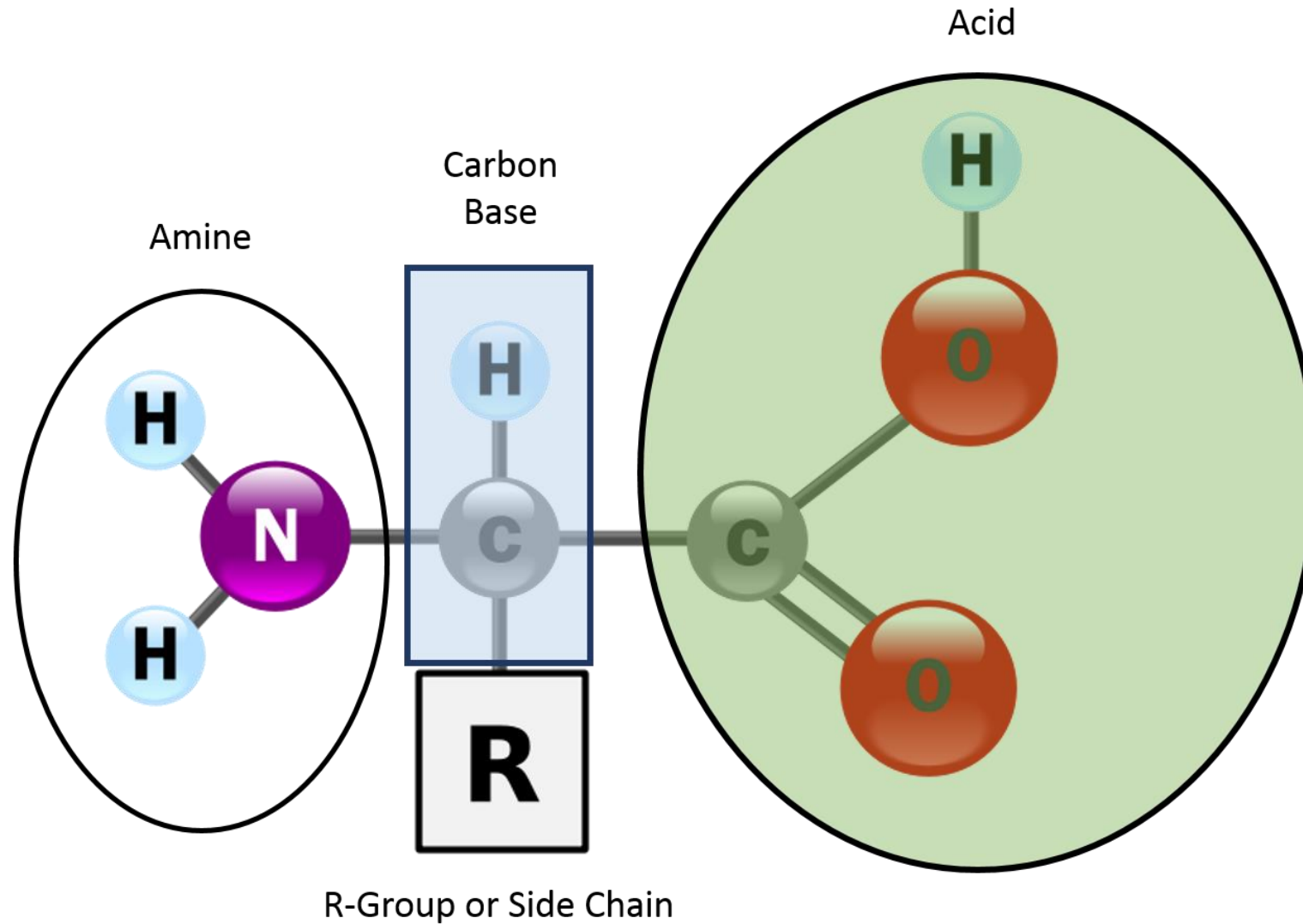


L-Amino acid



D-Amino acid

Amino Acids in Proteins



Amino Acids in Proteins

Amino acids that make up proteins share many common features, but some exhibit distinct structural and chemical properties.

- ❖ **Proline (imino acid, rigid structure)** 脯氨酸
- ❖ **Glycine (smallest, achiral)** 甘氨酸
- ❖ **Cysteine (forms disulfide bonds)** 半胱氨酸

In this course, amino acids are classified into **four major groups based on the properties of their side chains (R groups):**

1. Nonpolar (hydrophobic) amino acids
2. Polar uncharged amino acids
3. **Positively (basic) & negatively (acidic) charged amino acids**
4. Specific cases

**TWENTY-ONE
PROTEINOGENIC
α-AMINO ACIDS**

Side chain charge
at physiological
pH 7.4

pK_a values shown
italicized

⊕ Positive
⊖ Negative

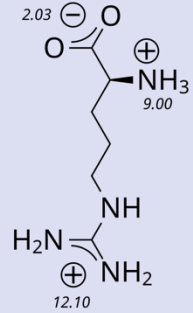
A. Amino Acids with Electrically Charged Side Chains

Positive

Negative

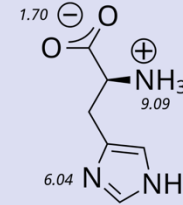
Arginine

Arg R



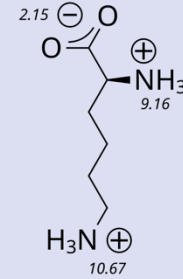
Histidine

His H



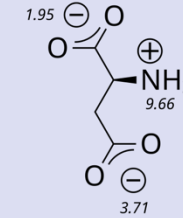
Lysine

Lys K



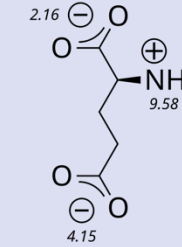
Aspartic Acid

Asp D



Glutamic Acid

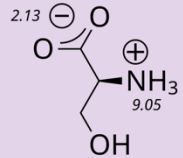
Glu E



B. Amino Acids with Polar Uncharged Side Chains

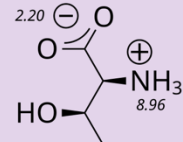
Serine

Ser S



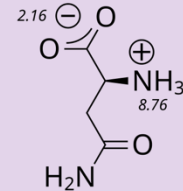
Threonine

Thr T



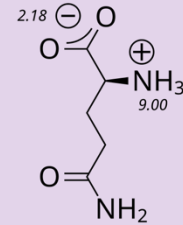
Asparagine

Asn N



Glutamine

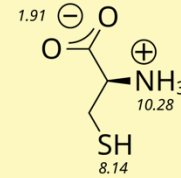
Gln Q



C. Special Cases

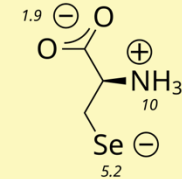
Cysteine

Cys C



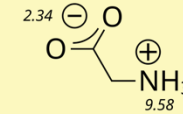
Selenocysteine

Sec U



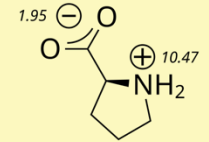
Glycine

Gly G



Proline

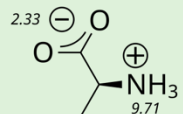
Pro P



D. Amino Acids with Hydrophobic Side Chains

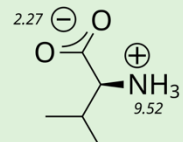
Alanine

Ala A



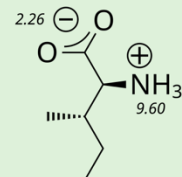
Valine

Val V



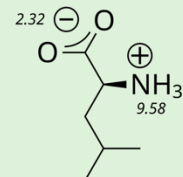
Isoleucine

Ile I



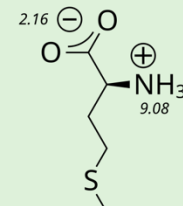
Leucine

Leu L



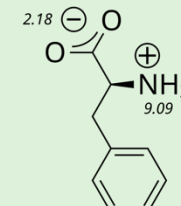
Methionine

Met M



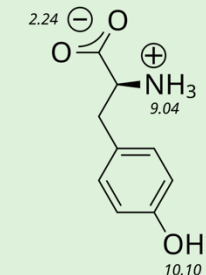
Phenylalanine

Phe F



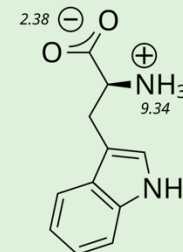
Tyrosine

Tyr Y



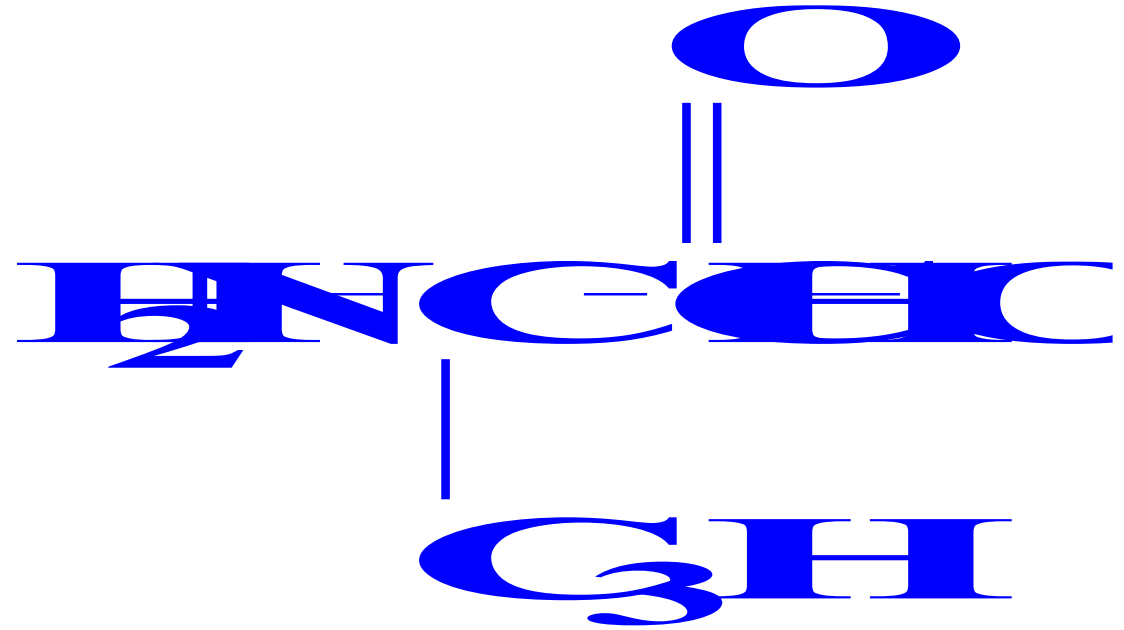
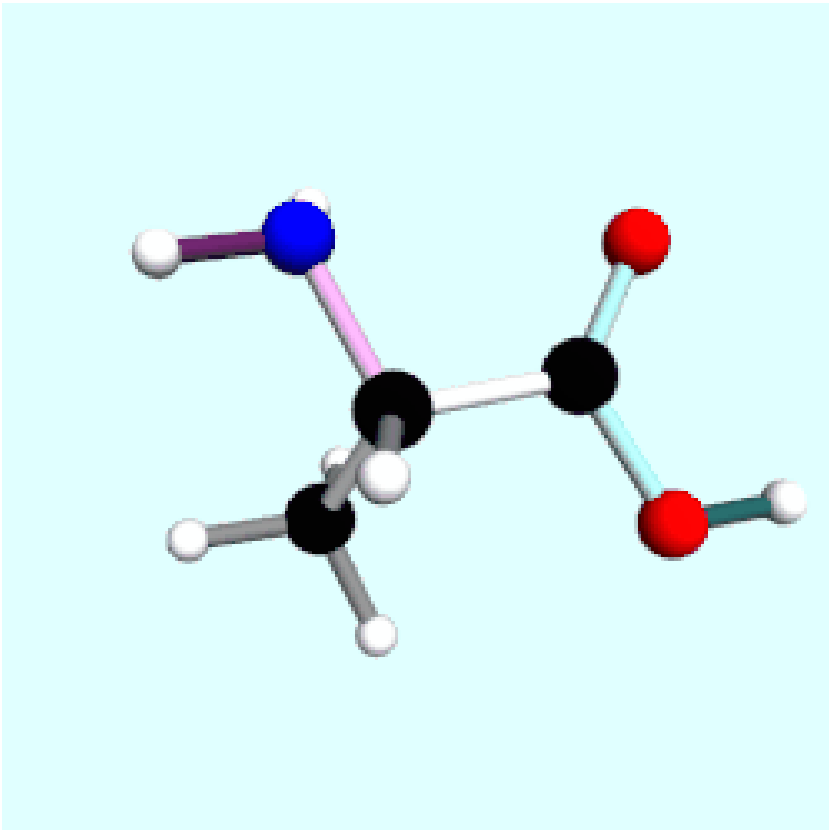
Tryptophan

Trp W



Amino Acids in Proteins

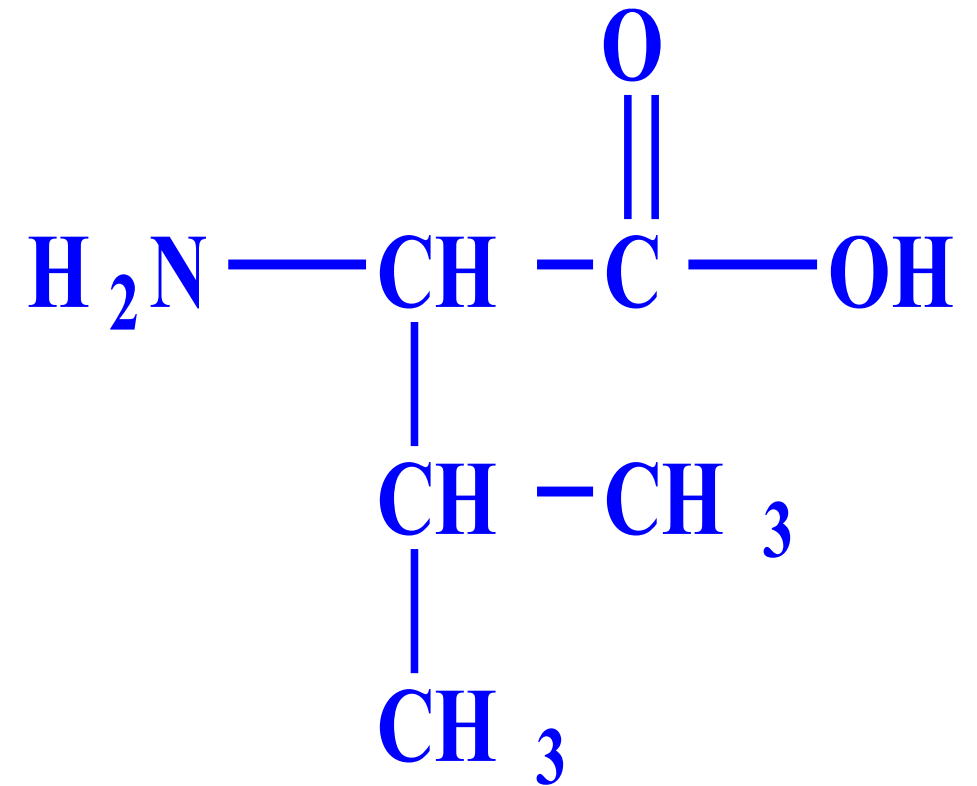
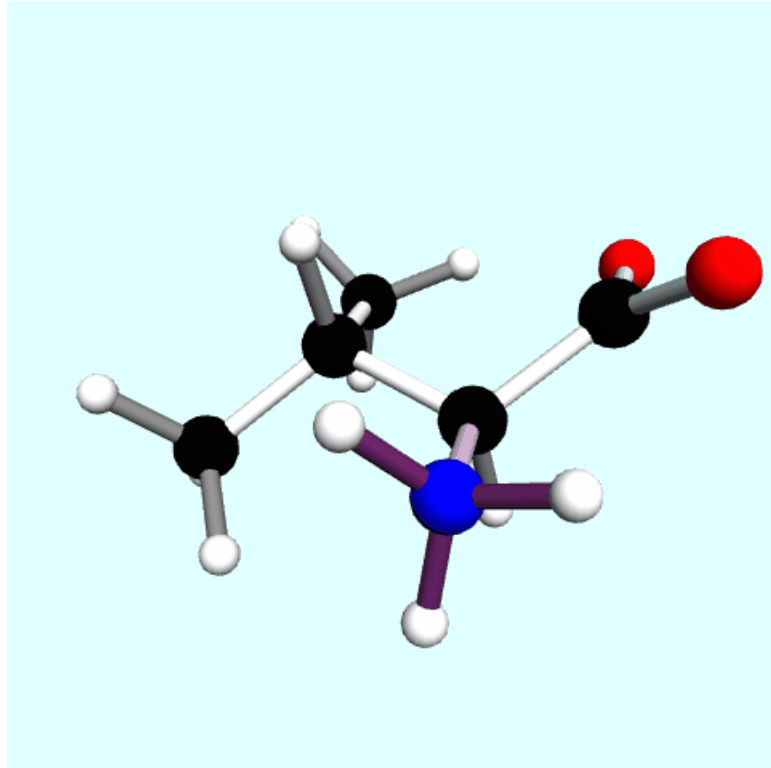
丙氨酸 **Alanine** /'æ.l.ə.ni:n/ **(A)**



α -氨基丙氨酸

Amino Acids in Proteins

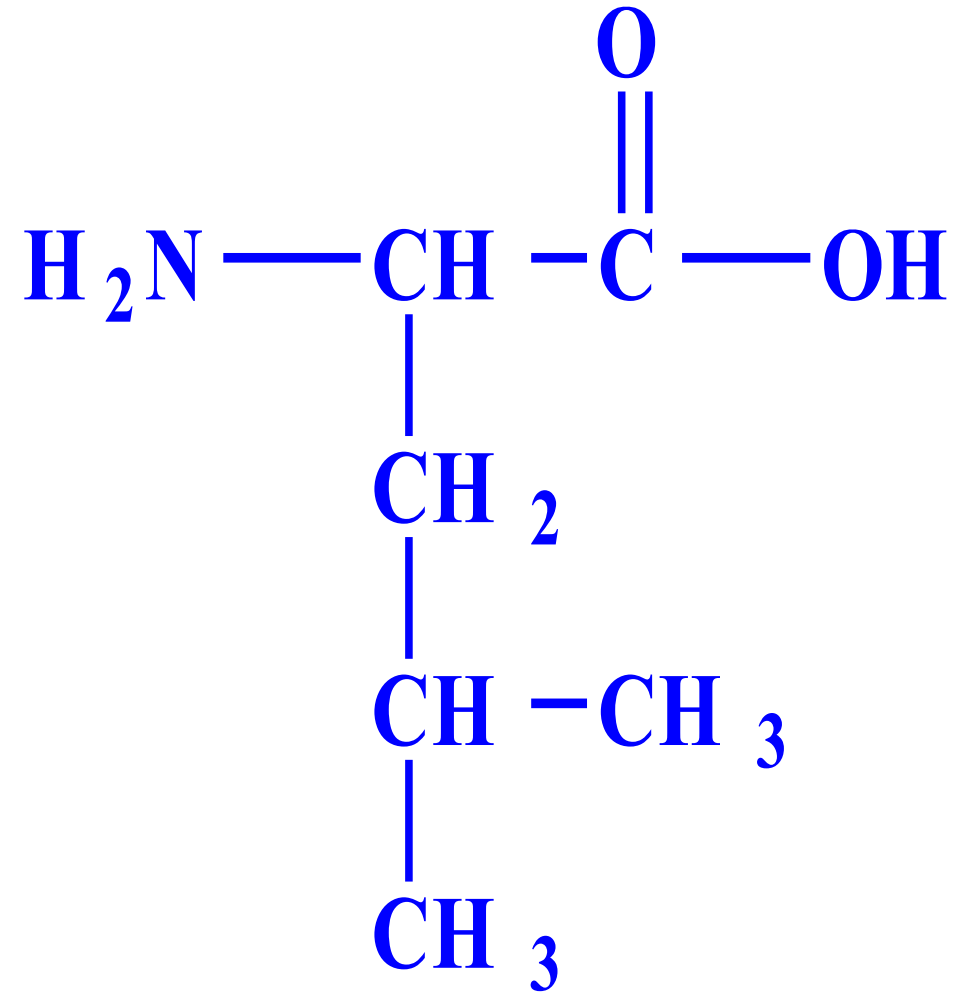
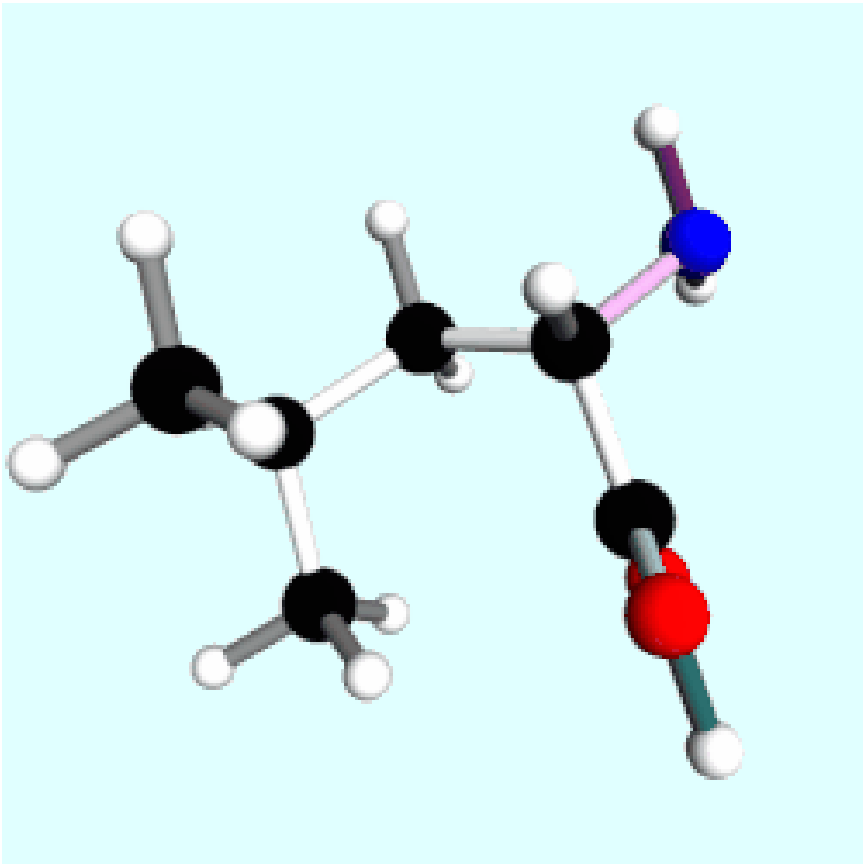
缬氨酸 **Valine** /'veɪ.li:n/ (**V**)



α -氨基异戊酸

Amino Acids in Proteins

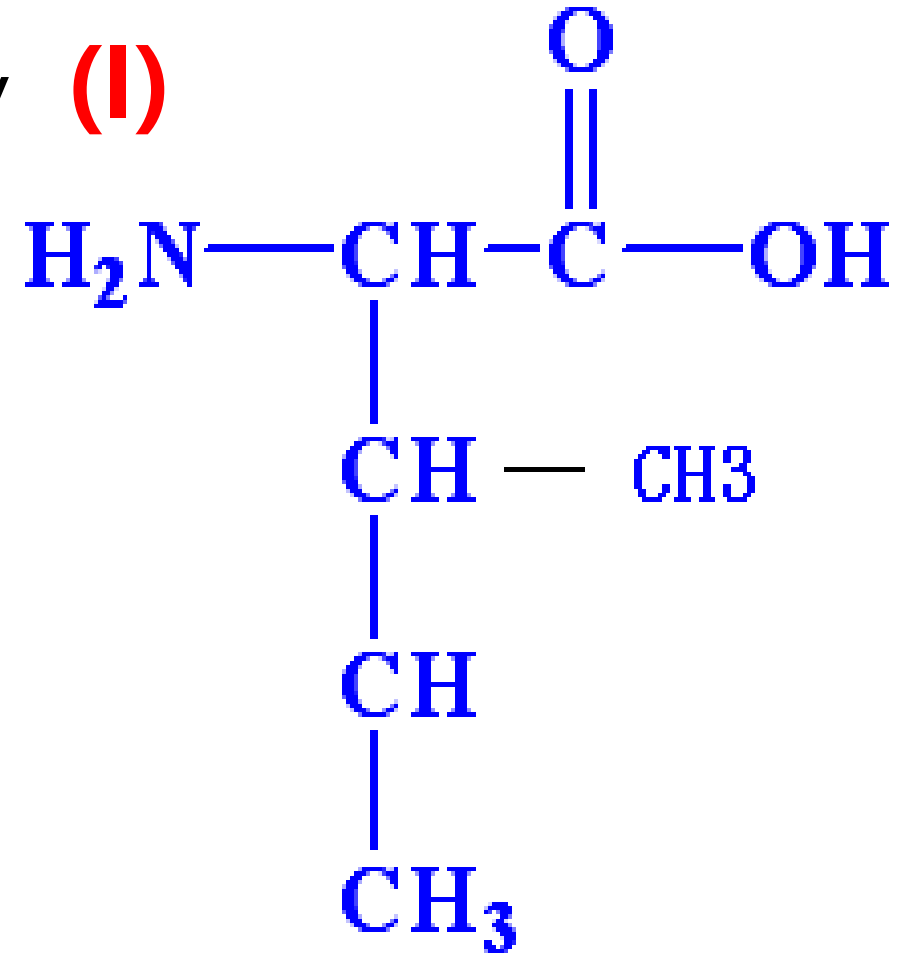
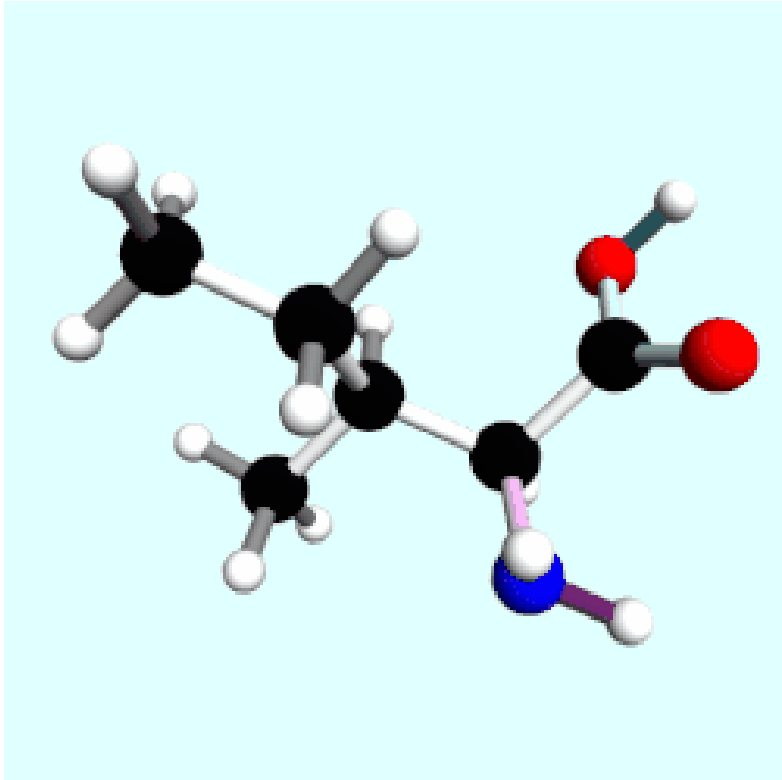
亮氨酸 **Leucine** /'lu:.si:n/ (L)



α -氨基异己酸

Amino Acids in Proteins

异亮氨酸 **Isoleucine** /,aɪ.souˈluː.siːn/ (I)

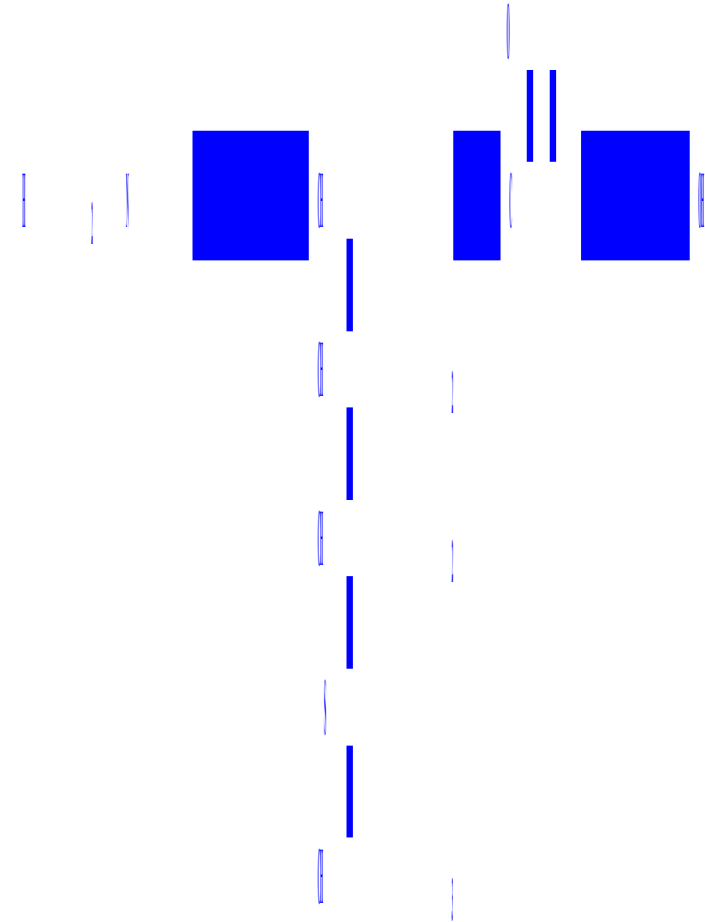
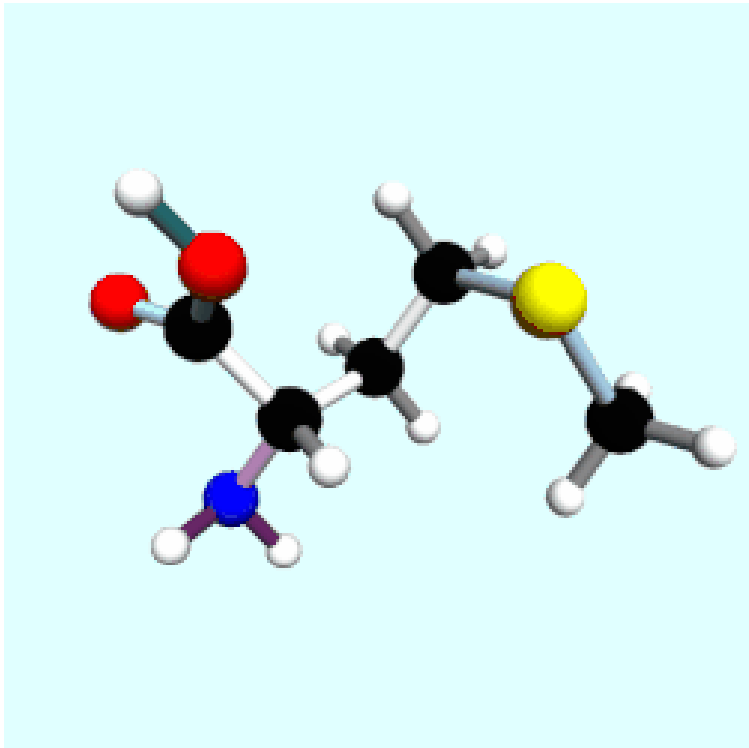


α -氨基- β -甲基戊酸

Amino Acids in Proteins

甲硫氨酸 / 蛋氨酸

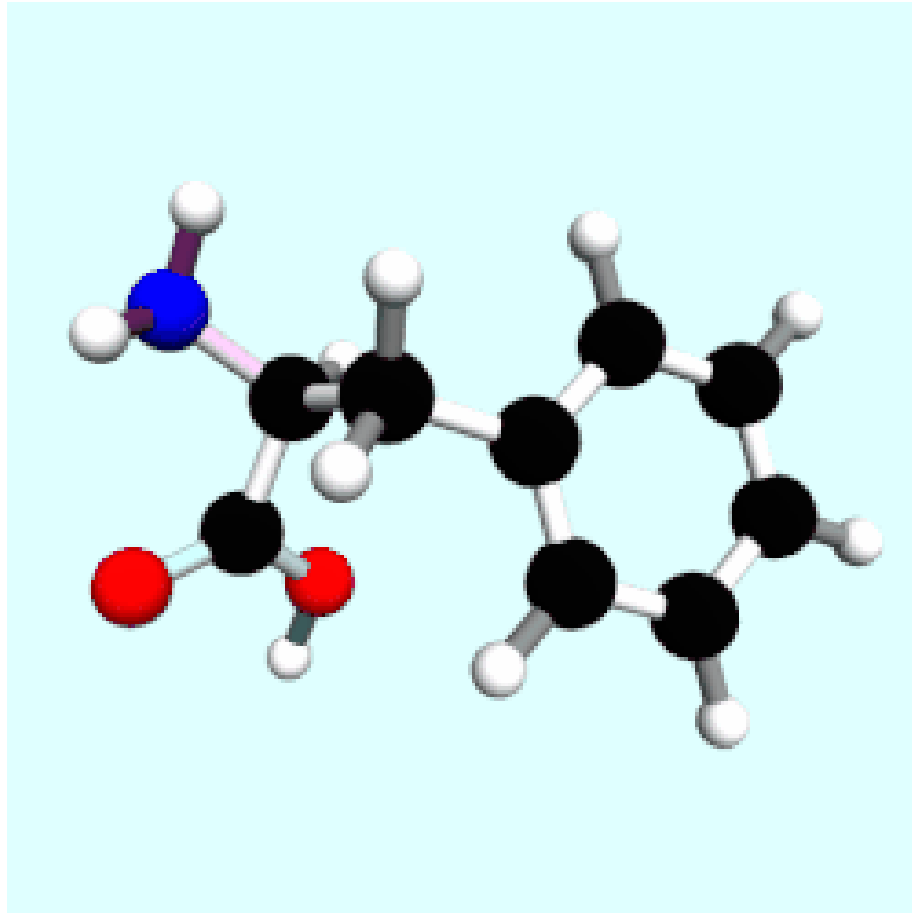
Methionine /mə'tθaɪ.ə.ni:n/ (M)



α -氨基- γ -甲硫基丁酸

Amino Acids in Proteins

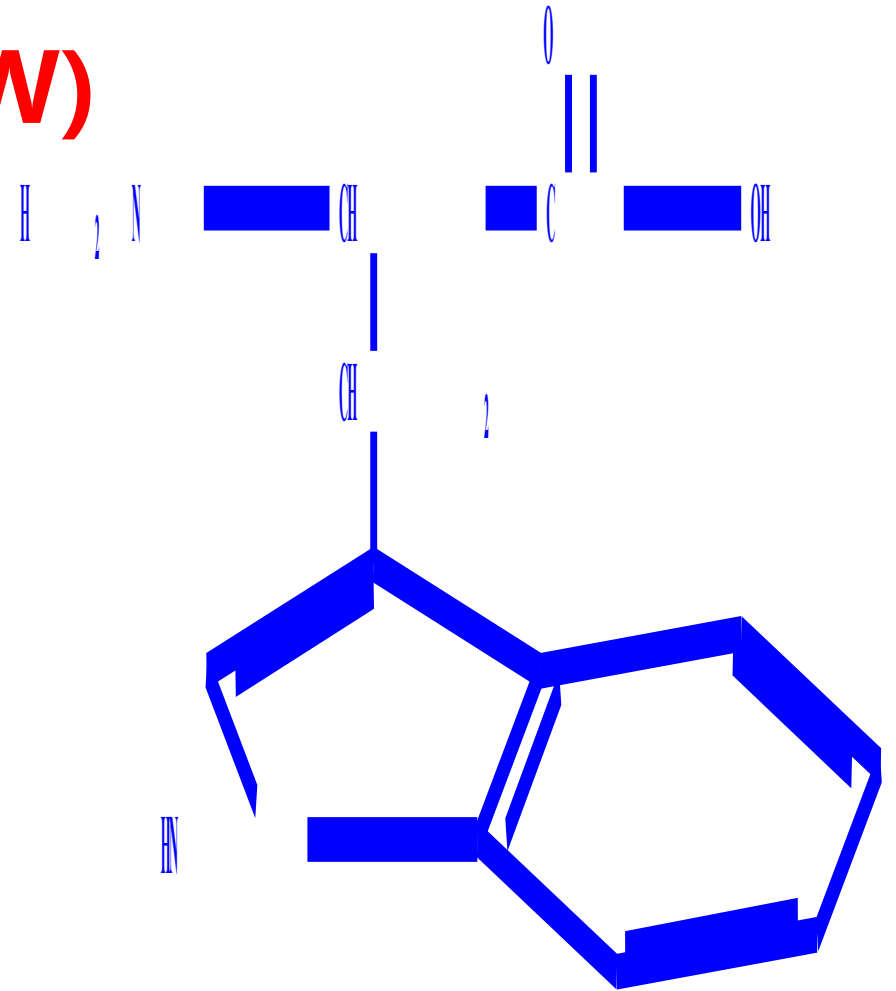
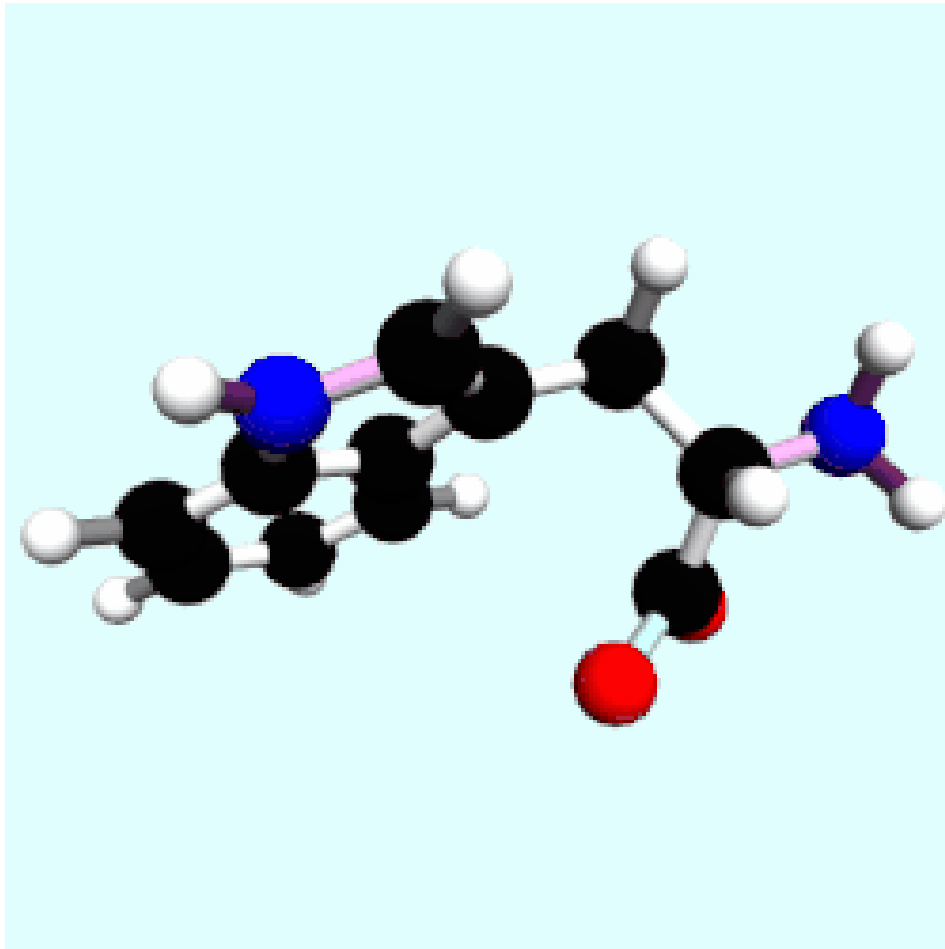
苯丙氨酸 Phenylalanine /ˌfiːnɪlˈæɪ.ləniːn/ (F)



α -氨基- β -苯基丙酸

Amino Acids in Proteins

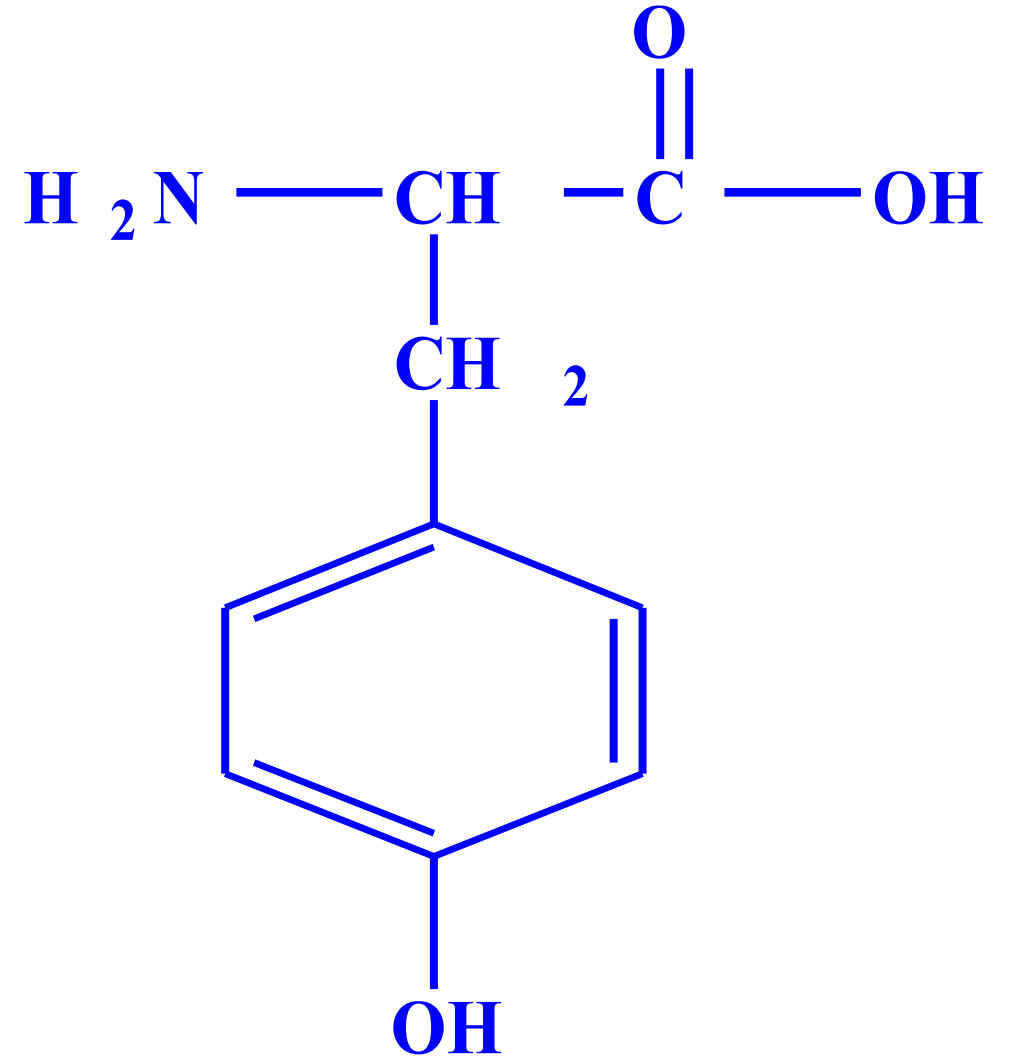
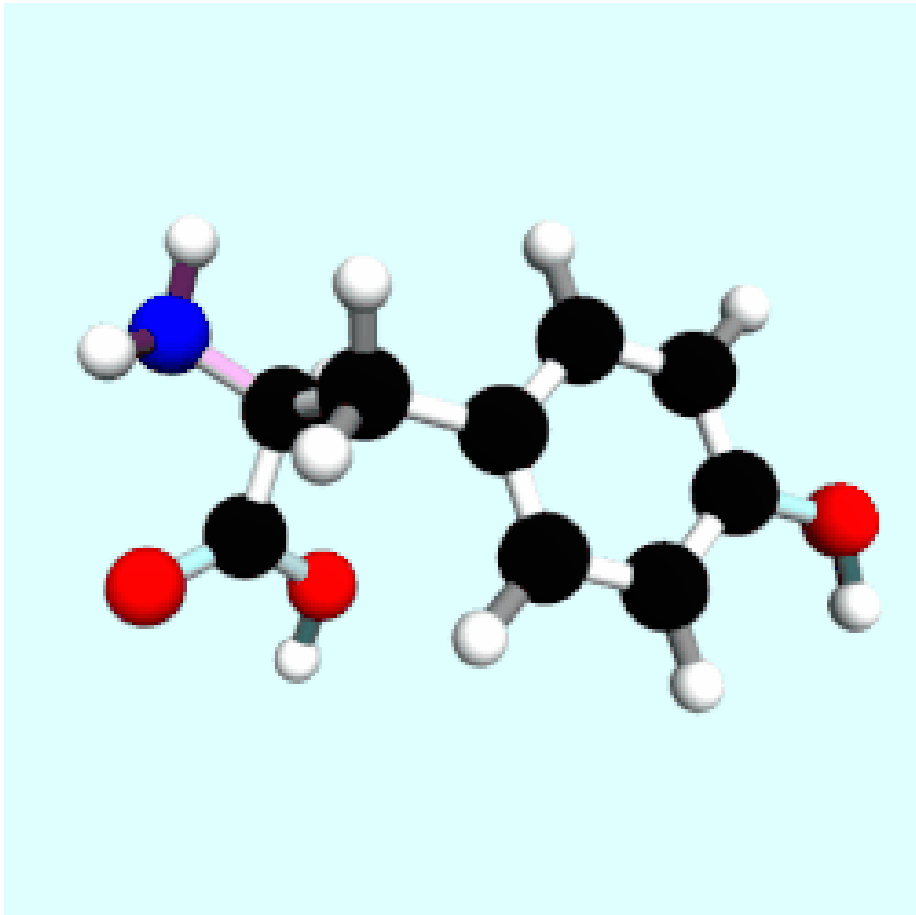
色氨酸 **T**ryptophan /'trɪp.tə.fæn/ **(W)**



α -氨基- β -吲哚基丙酸

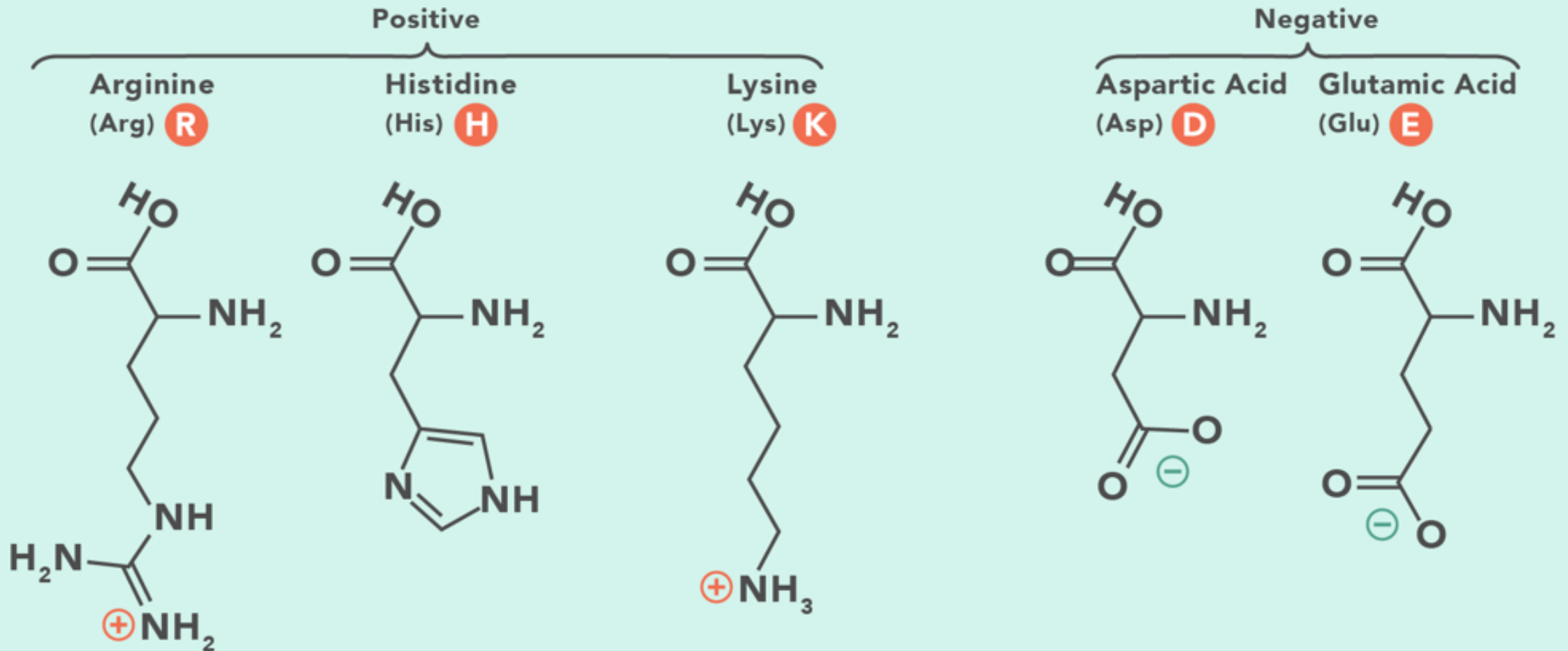
Amino Acids in Proteins

酪氨酸 Tyrosine /'taɪ.rə.si:n/ (Y)



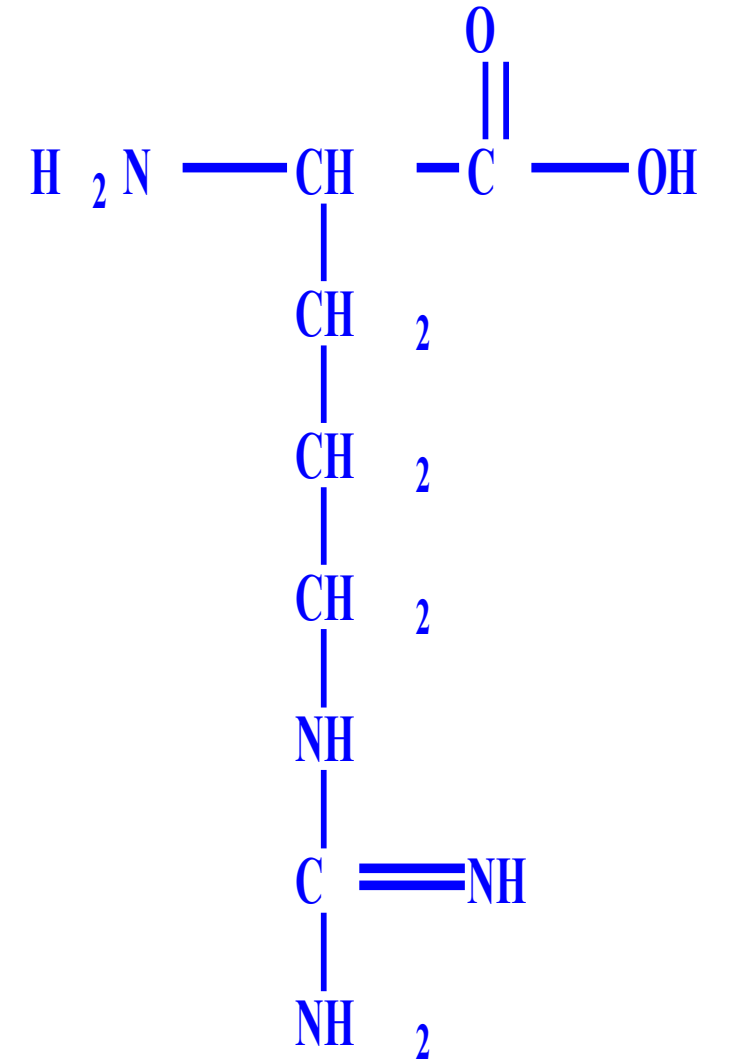
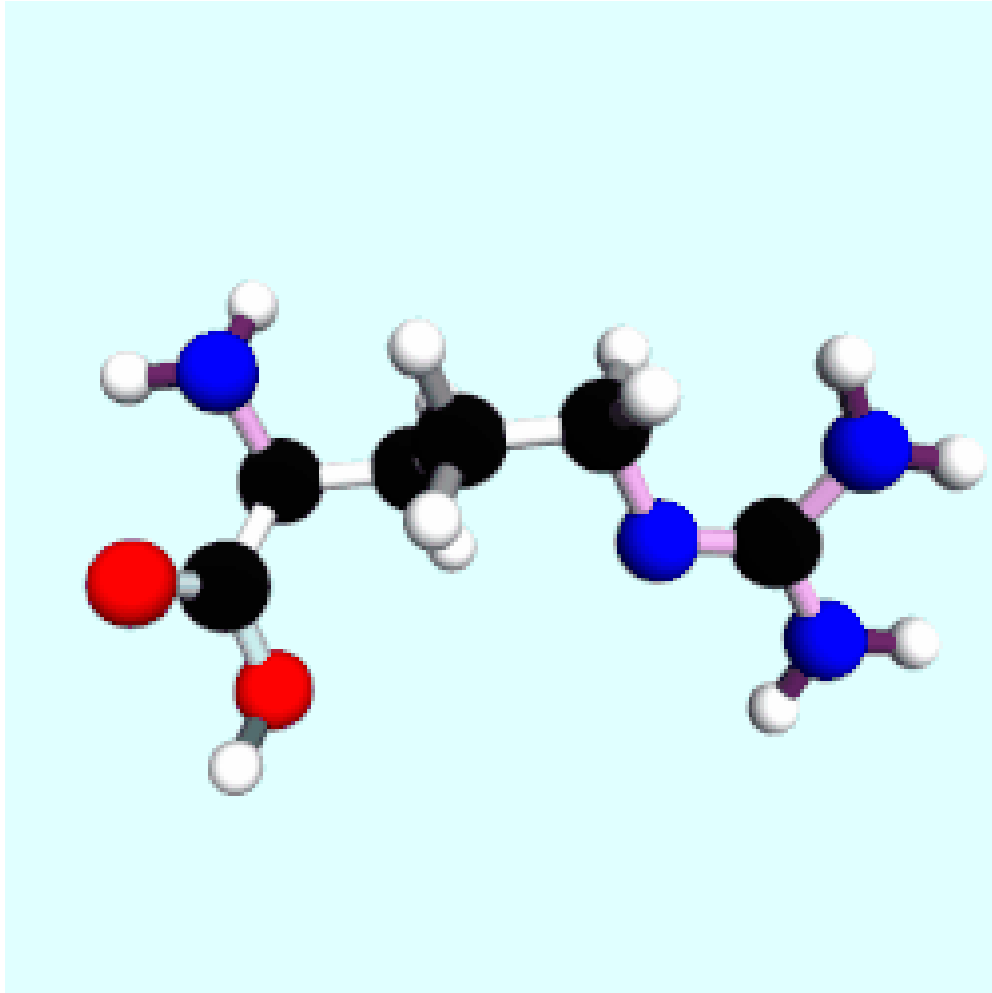
α -氨基- β -对羟基苯基丙酸

Charged amino acids



Amino Acids in Proteins

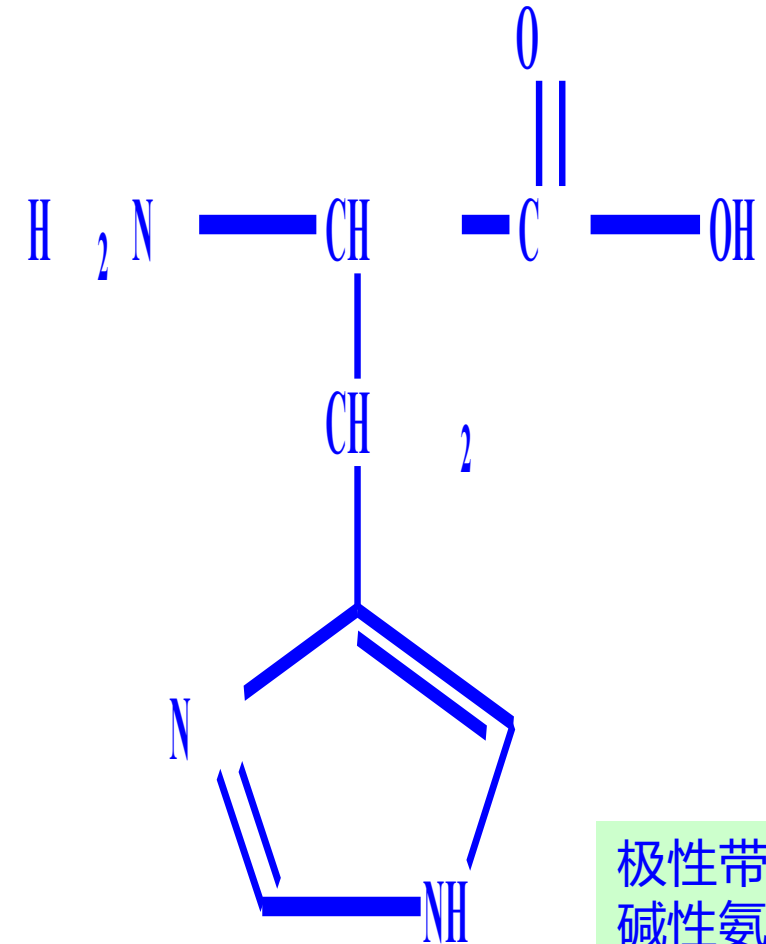
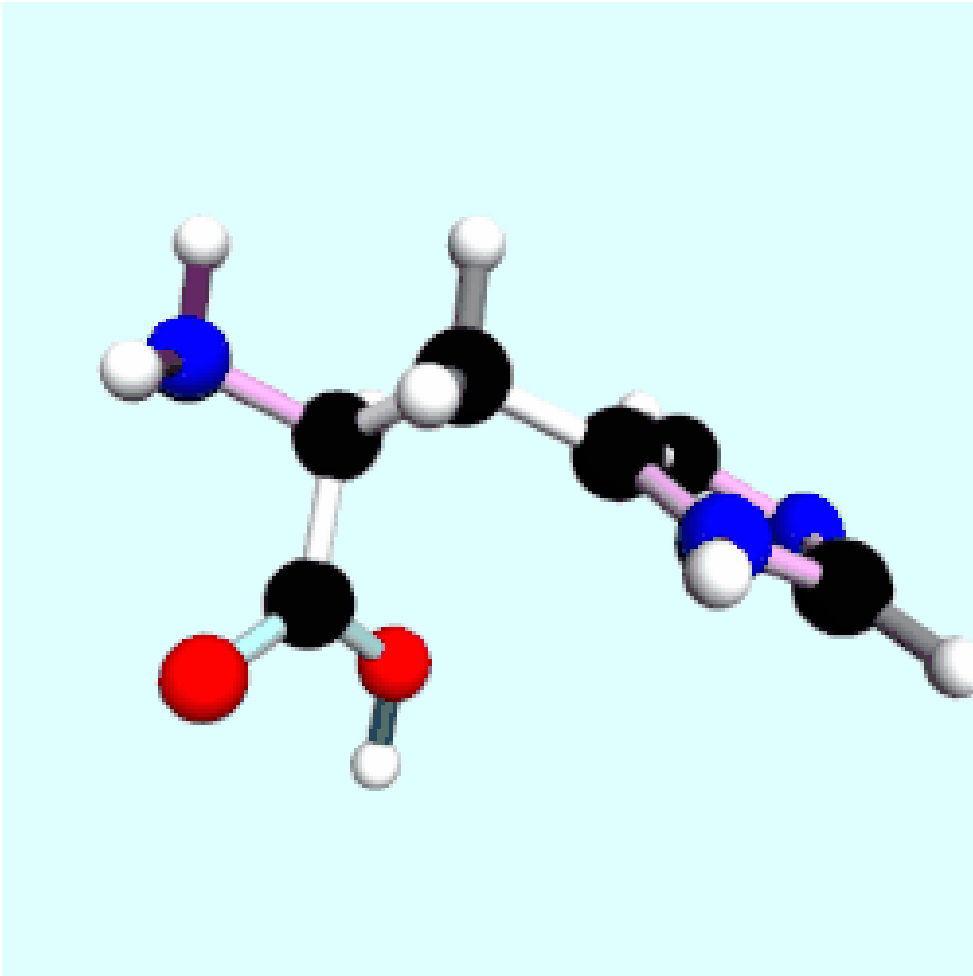
精氨酸 **Arginine** /'ɑ:r.dʒɪ.ni:n/ **(R)**



α -氨基- δ -胍基戊酸

Amino Acids in Proteins

组氨酸 Histidine /'hɪs.tɪ.di:n/ (H)

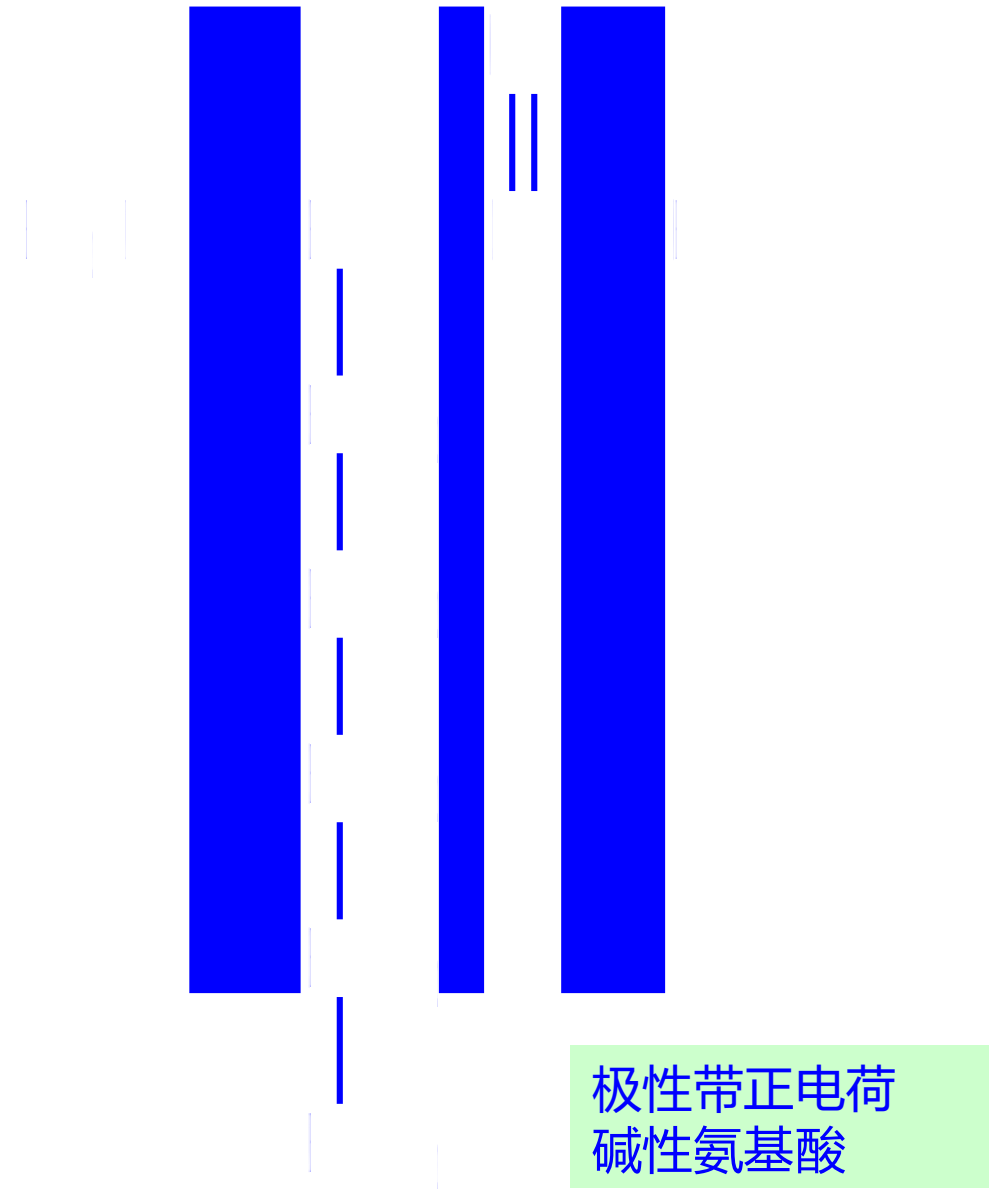
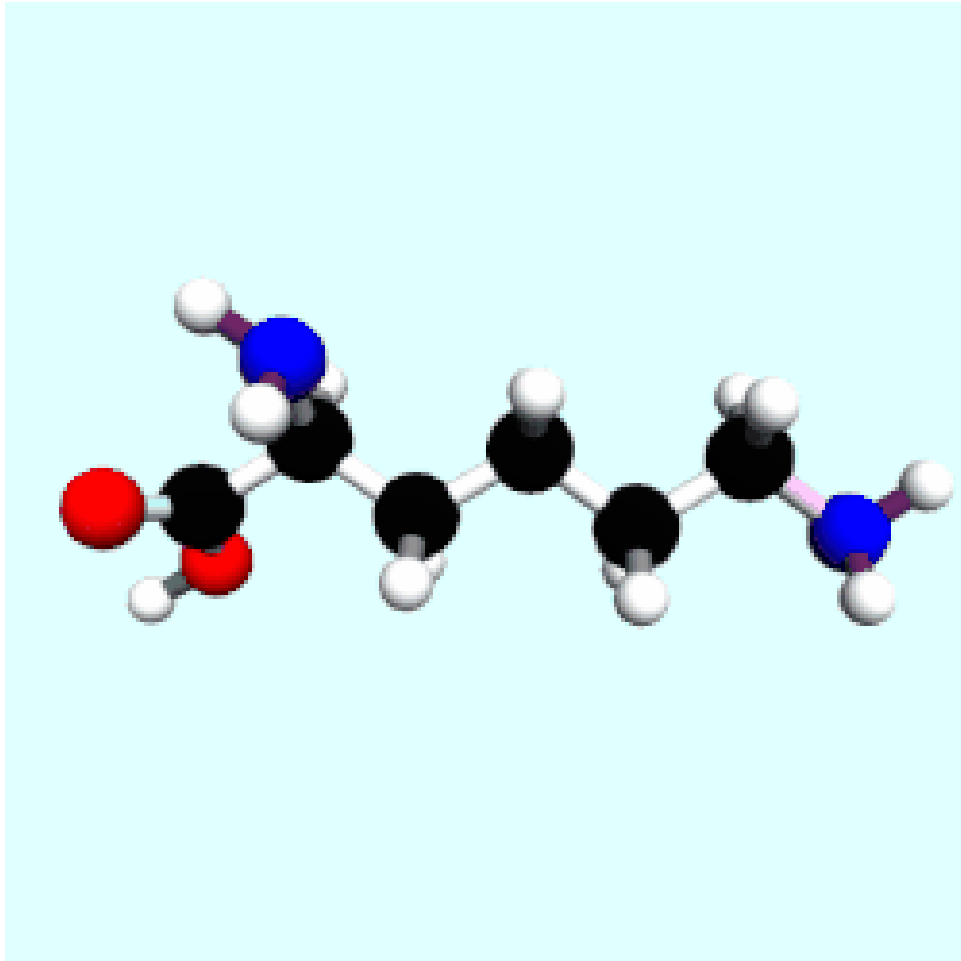


极性带正电荷
碱性氨基酸

α -氨基- β -咪唑基丙酸

Amino Acids in Proteins

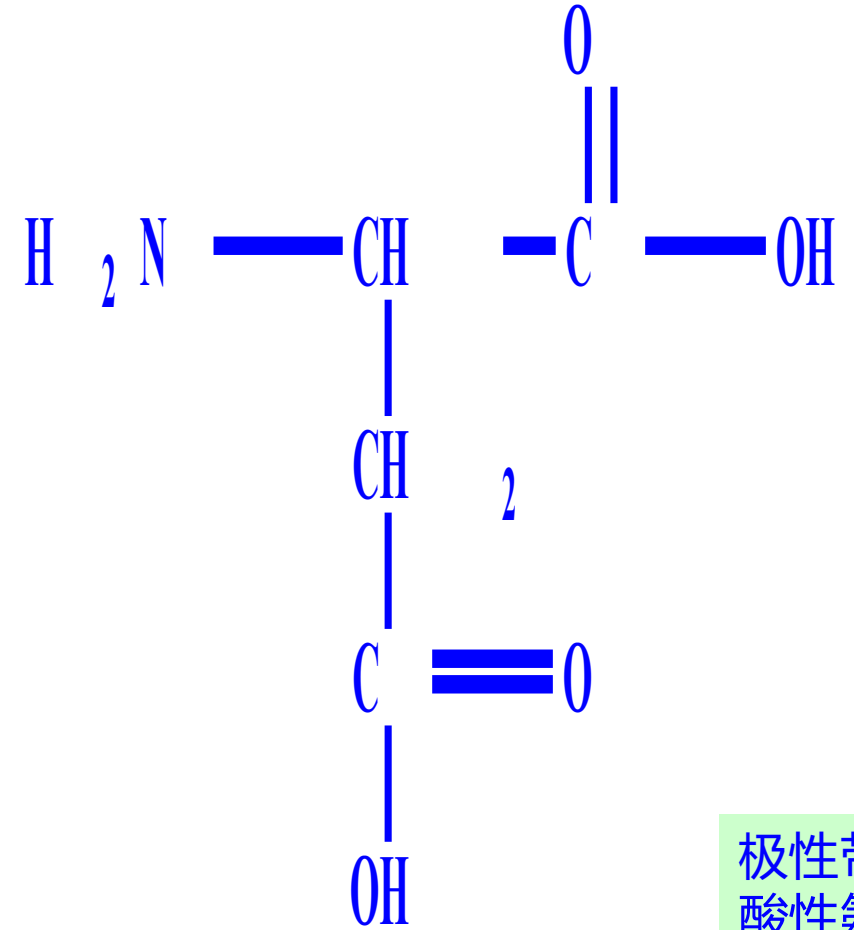
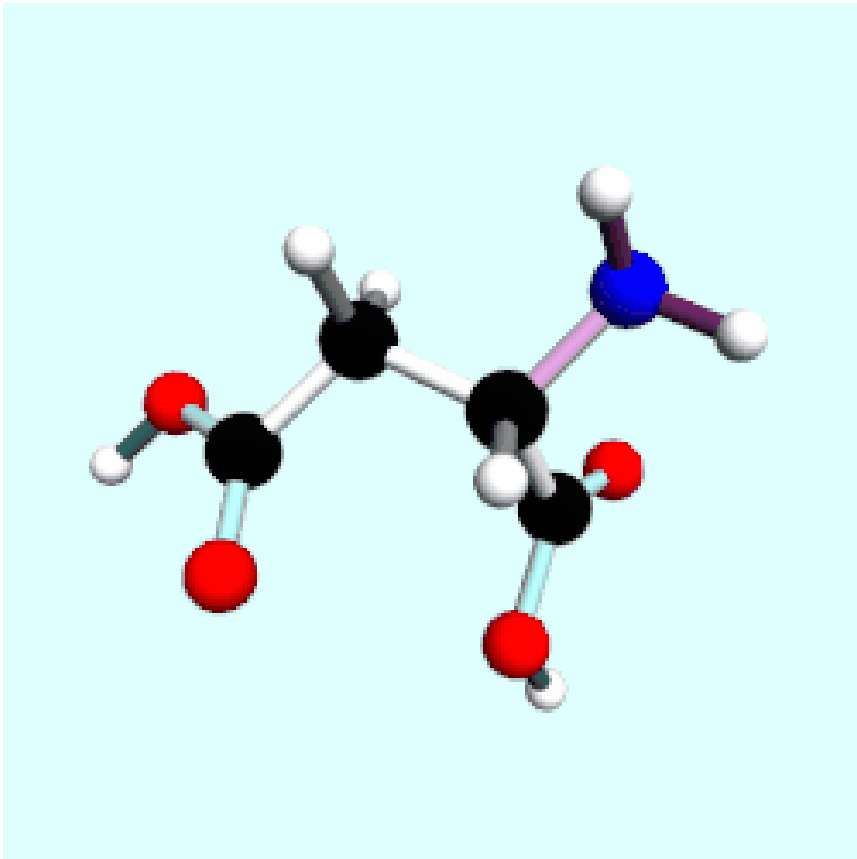
赖氨酸 **Lysine** /'laɪ.sɪ:n/ (K)



α, ϵ -二氨基己酸

Amino Acids in Proteins

天冬氨酸 Aspartic Acid (D)

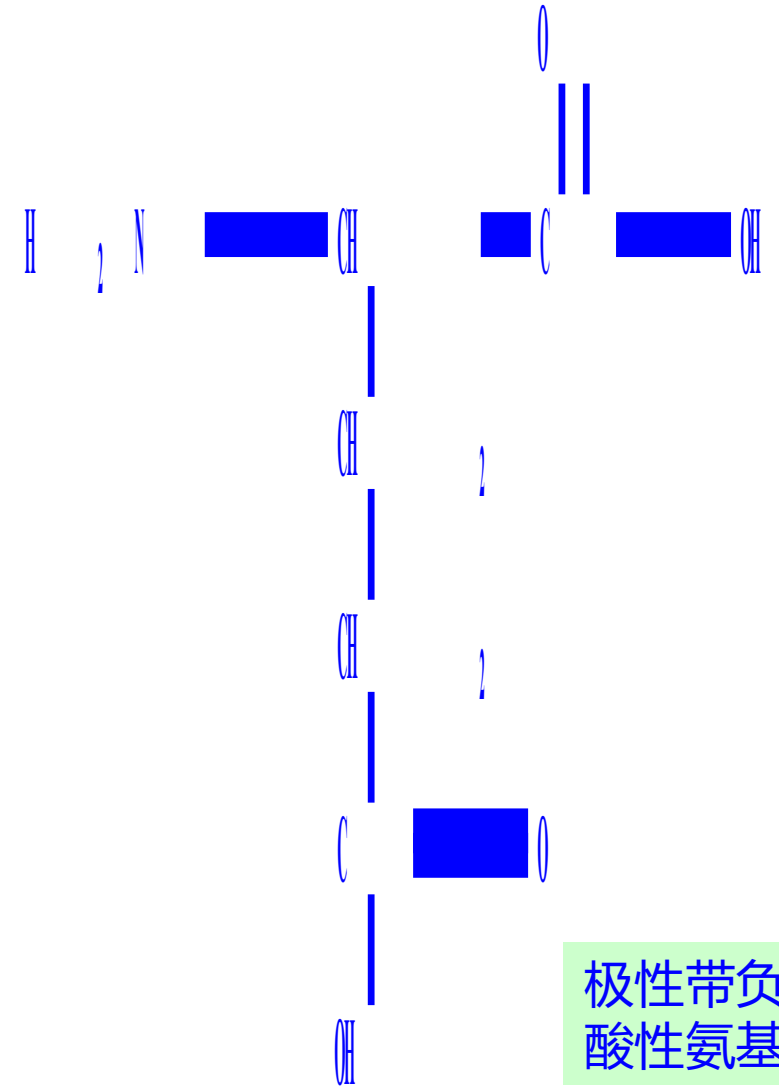
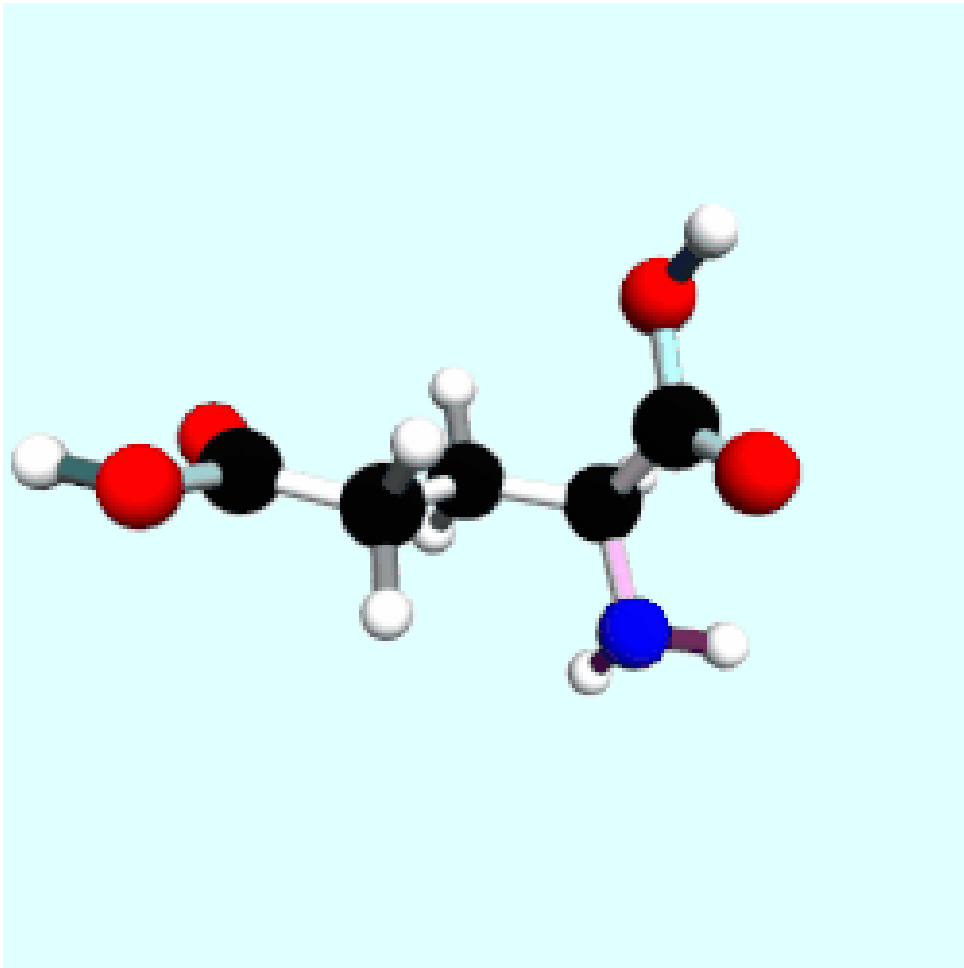


极性带负电
酸性氨基酸

α -氨基丁二酸

Amino Acids in Proteins

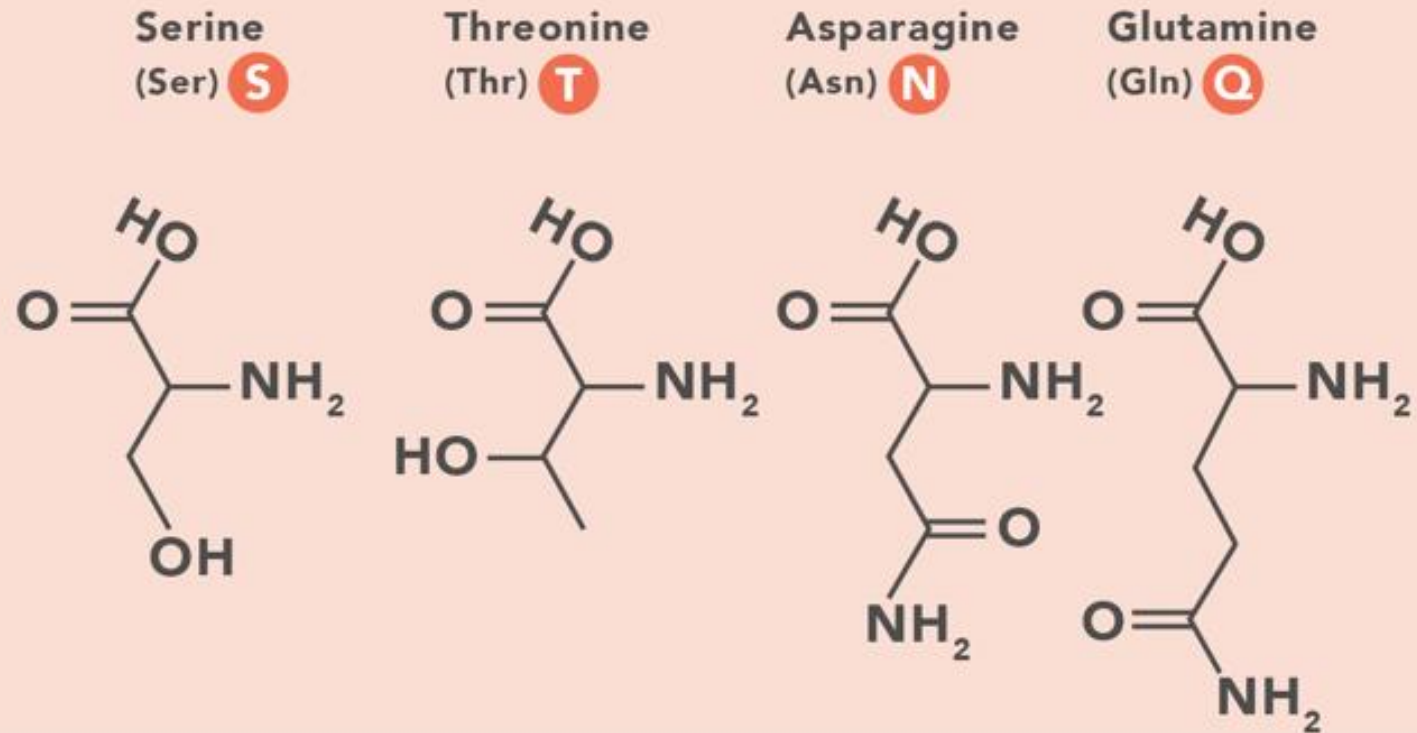
谷氨酸 **Glutamic** /'glu:.tə.mi:k/ **Acid (E)**



极性带负电
酸性氨基酸

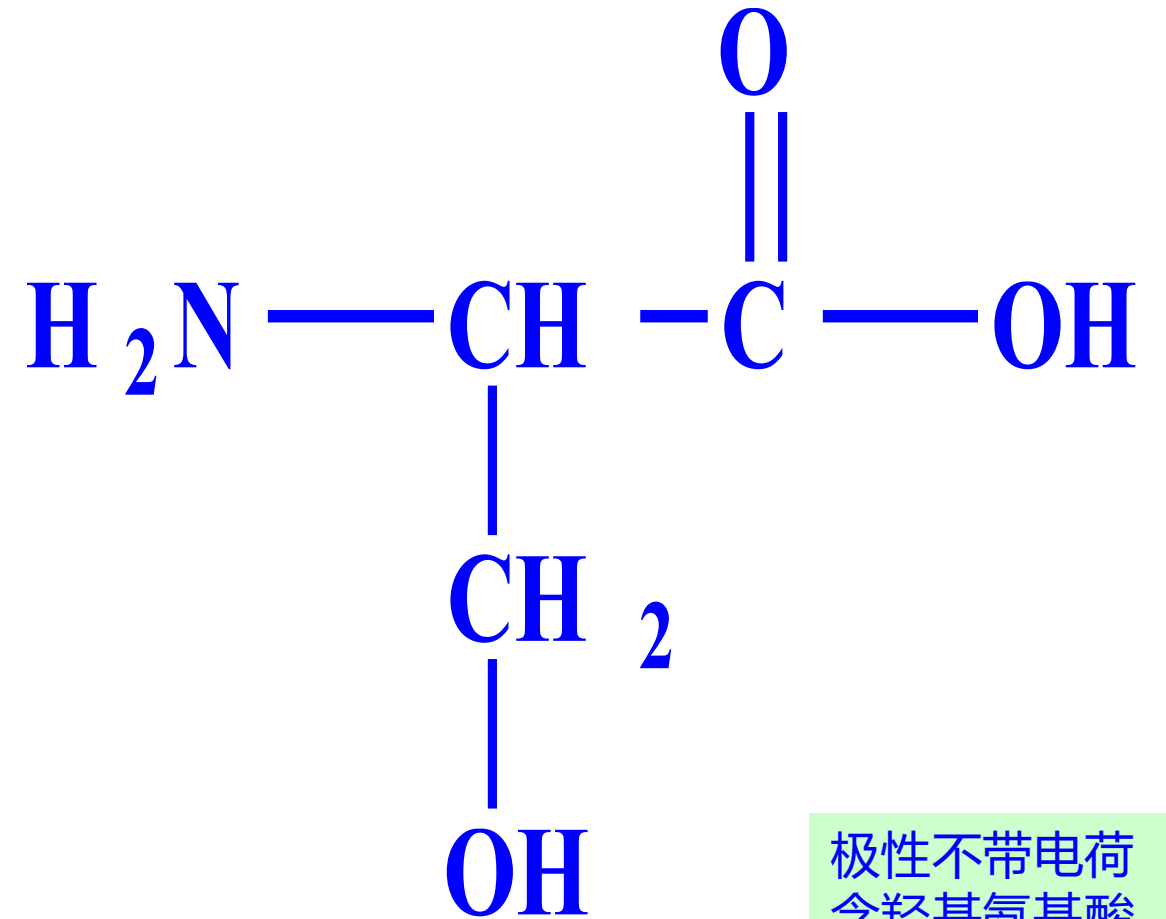
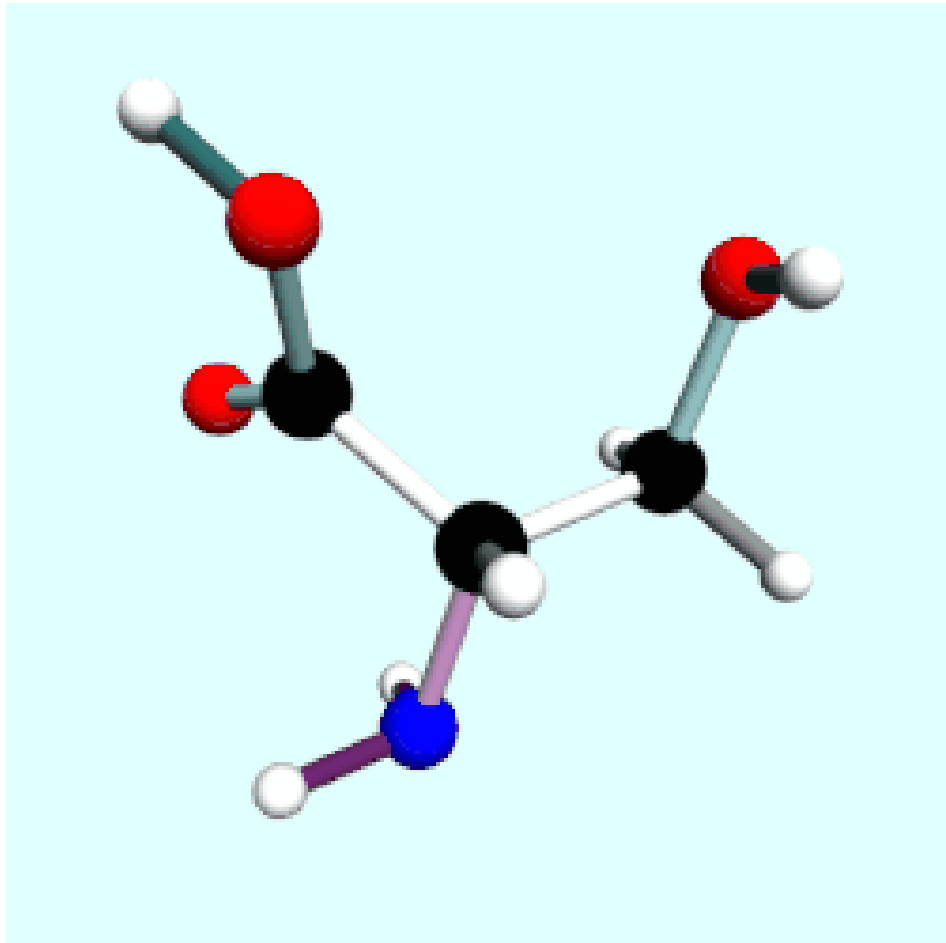
α -氨基戊二酸

Unchanged amino acids



Amino Acids in Proteins

丝氨酸 Serine /'siə.rɪ:n/ (S)

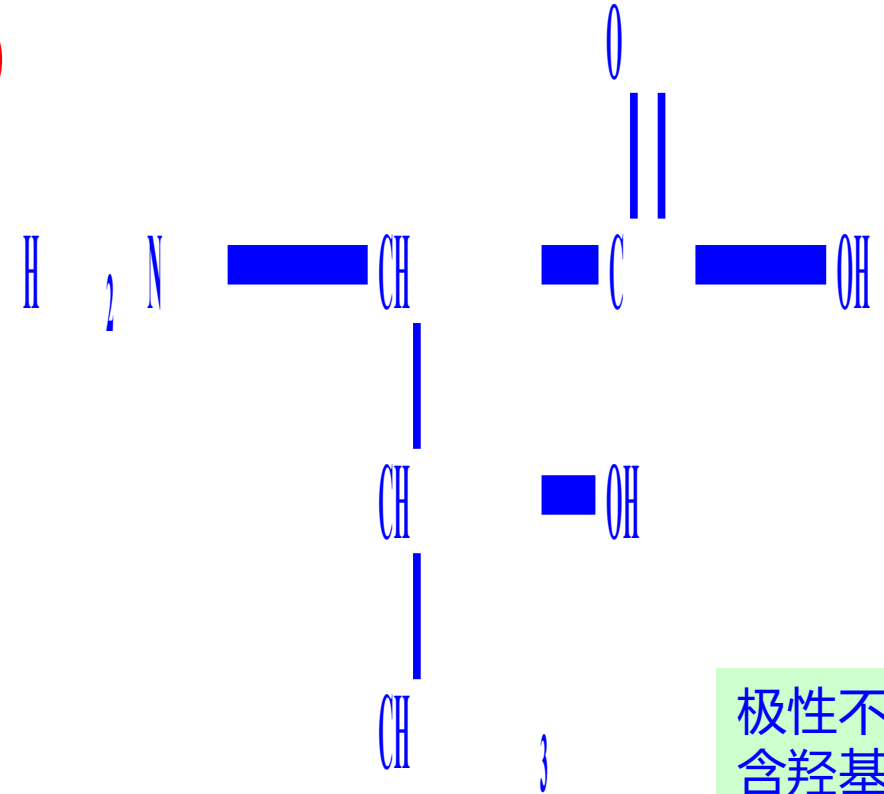
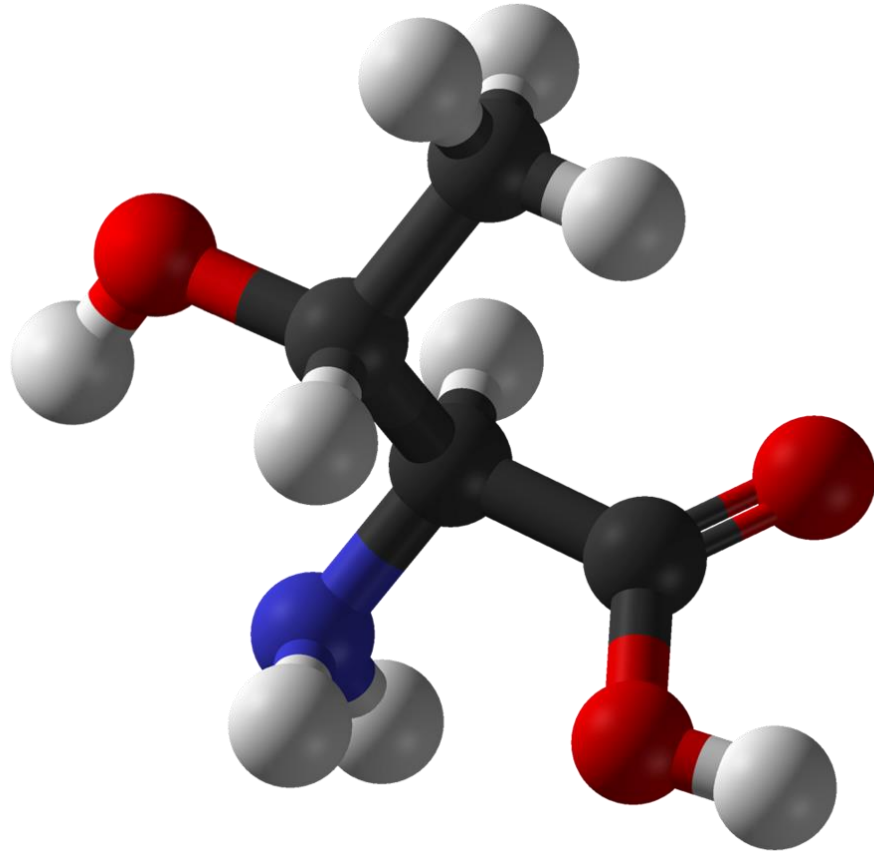


极性不带电荷
含羟基氨基酸

α -氨基- β -羟基丙酸

Amino Acids in Proteins

苏氨酸 Threonine /'θri:ə.ni:n/ (T)

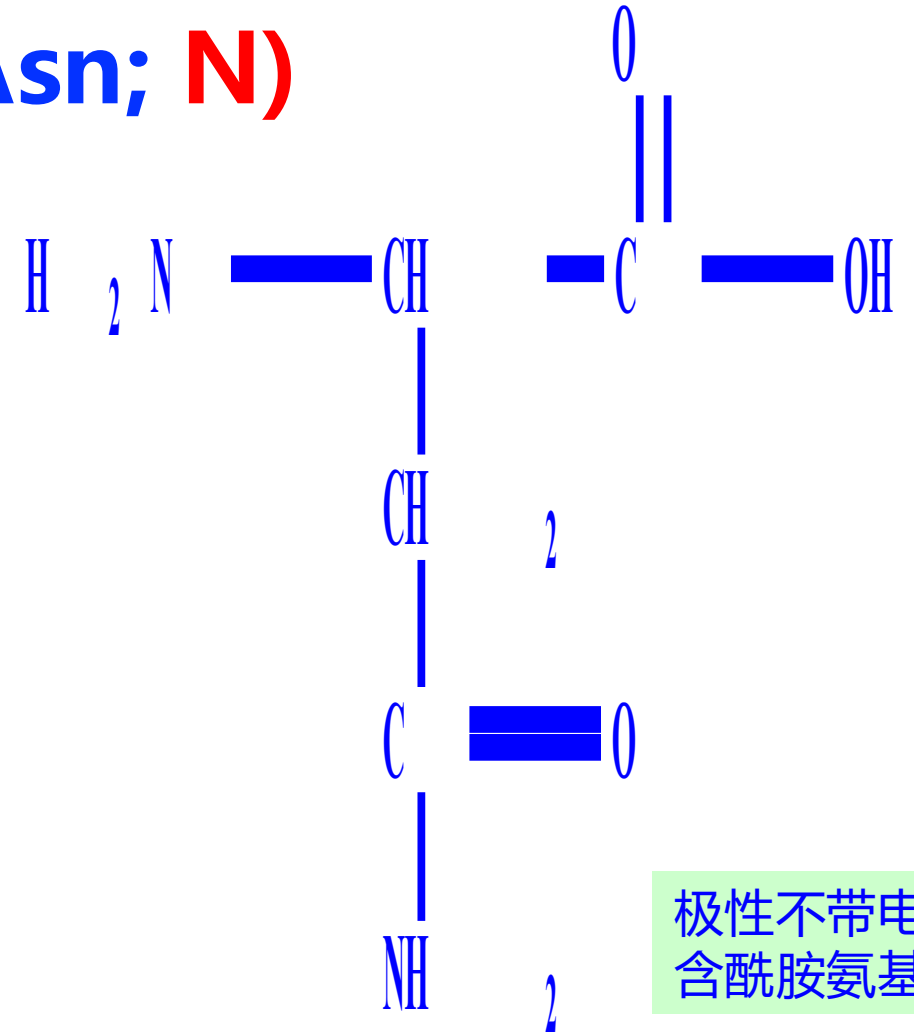
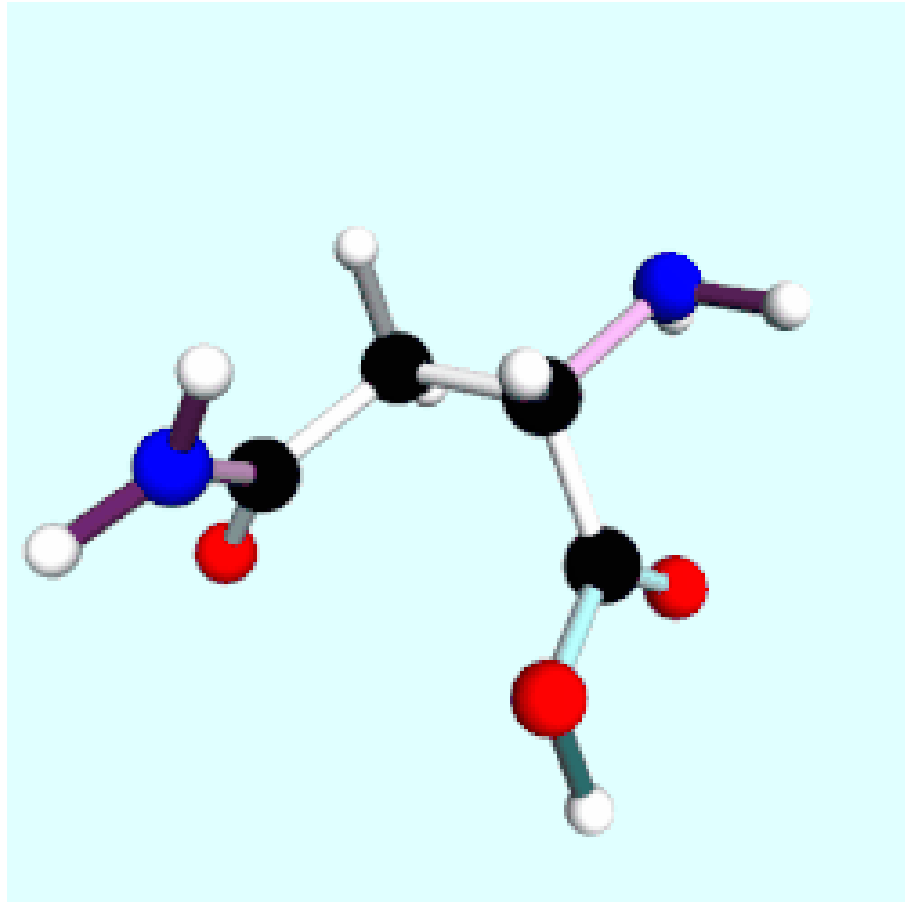


极性不带电荷
含羟基氨基酸

α -氨基- β -羟基丁酸

Amino Acids in Proteins

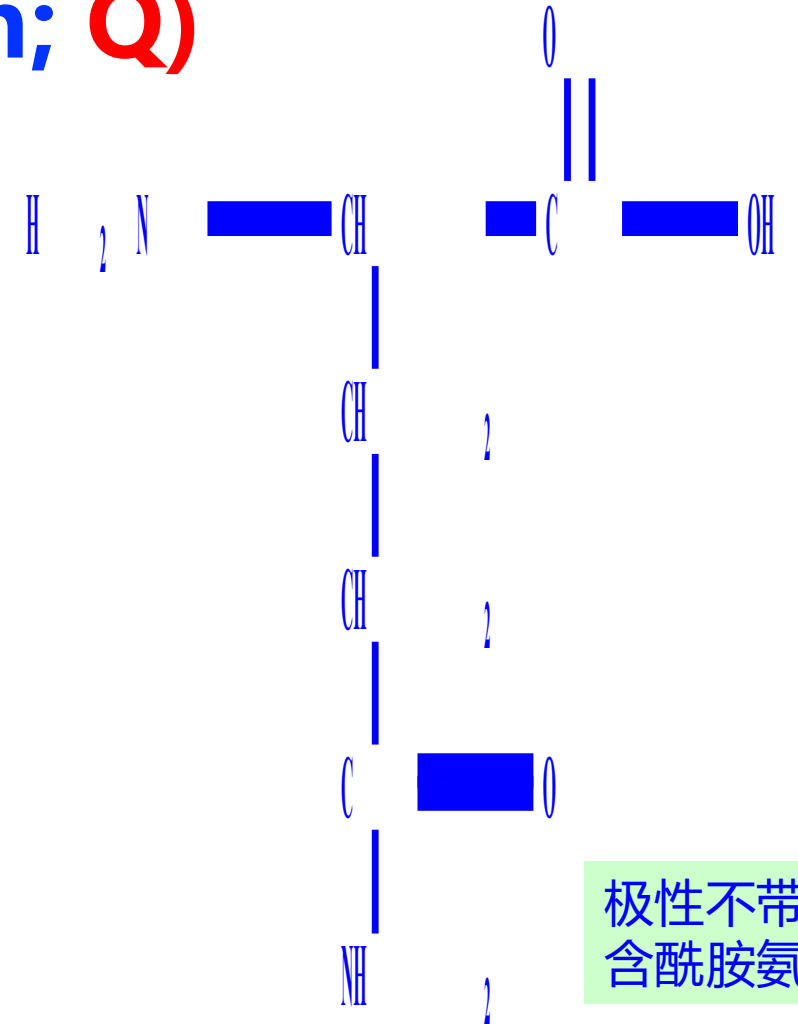
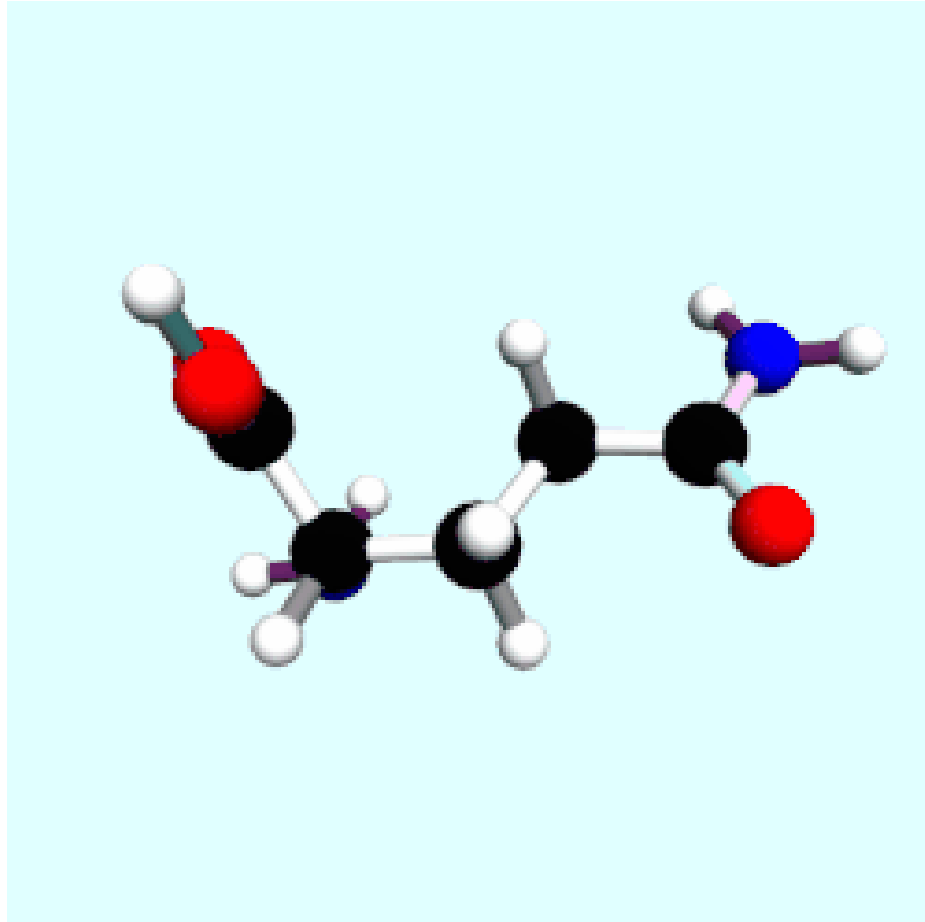
天冬酰胺 **Asparagine** /ə'spær.ə.dʒi:n/ (**Asn; N**)



极性不带电荷
含酰胺氨基酸

Amino Acids in Proteins

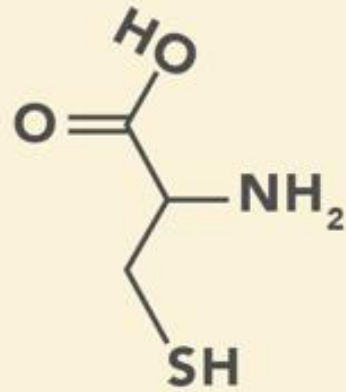
谷氨酰胺 **Glutamine** /'glu:.tə.mi:n/ (**Gln**; **Q**)



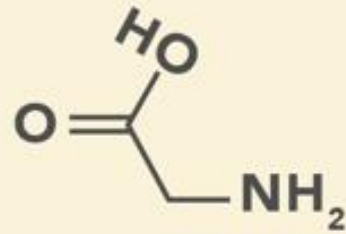
极性不带电荷
含酰胺氨基酸

Special cases

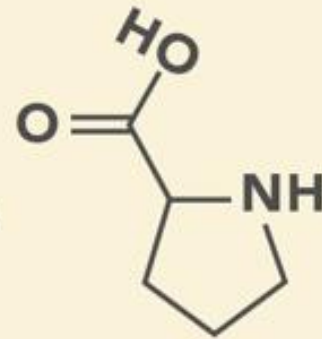
Cysteine
(Cys) **C**



Glycine
(Gly) **G**

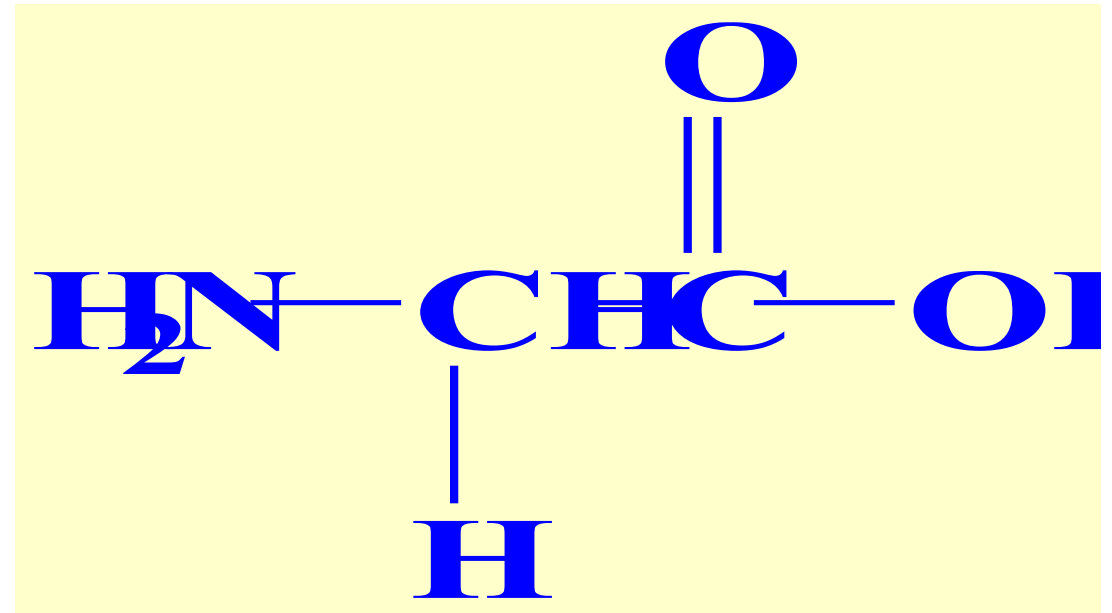
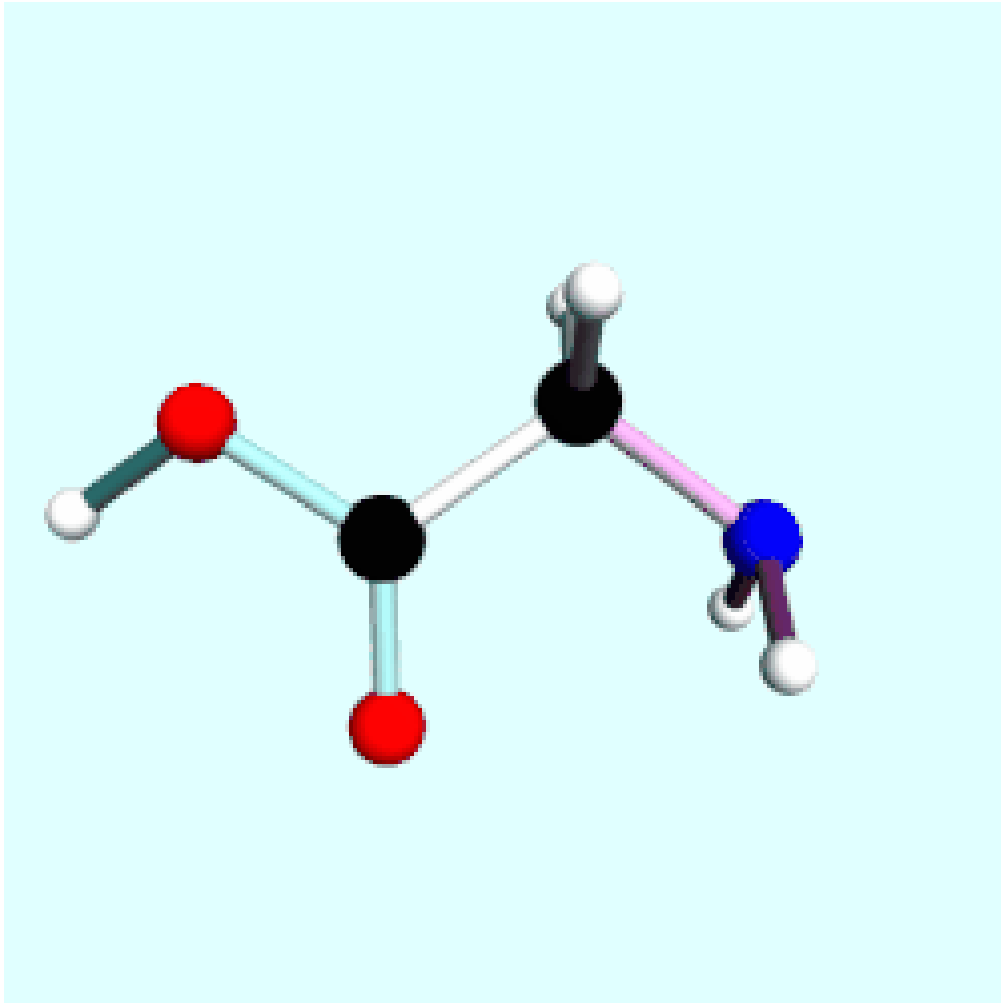


Proline
(Pro) **P**



Amino Acids in Proteins

甘氨酸 **Glycine** /'glai.si:n/ **(G)**

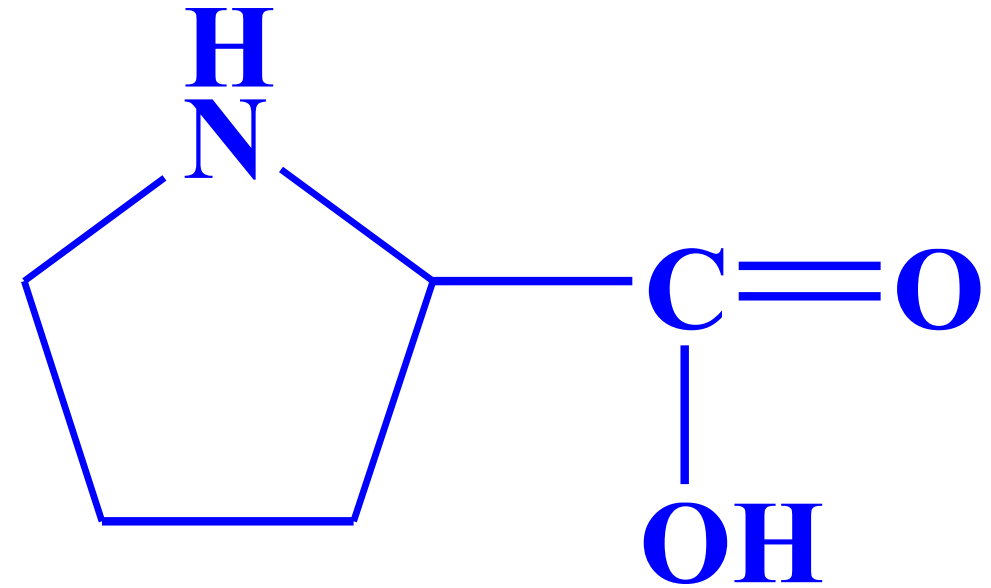
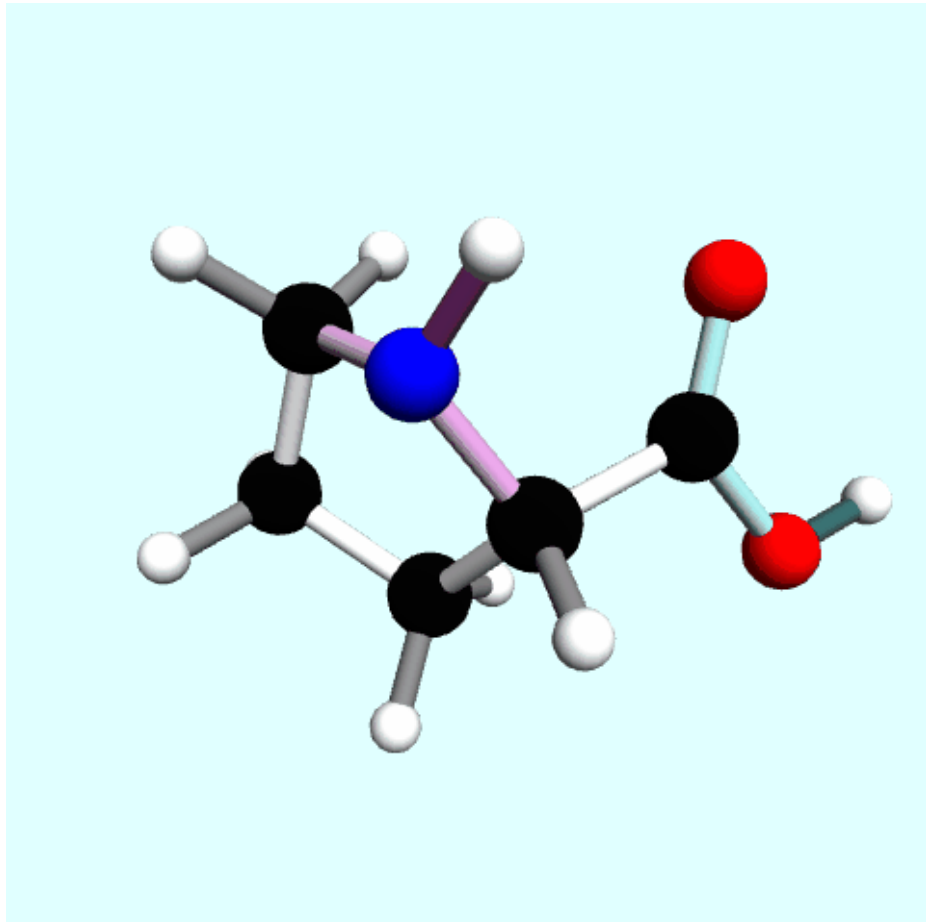


氨基乙酸

极性不带电荷
脂肪族氨基酸

Amino Acids in Proteins

脯氨酸 **Proline** /'prɒʊ.li:n/ **(P)**

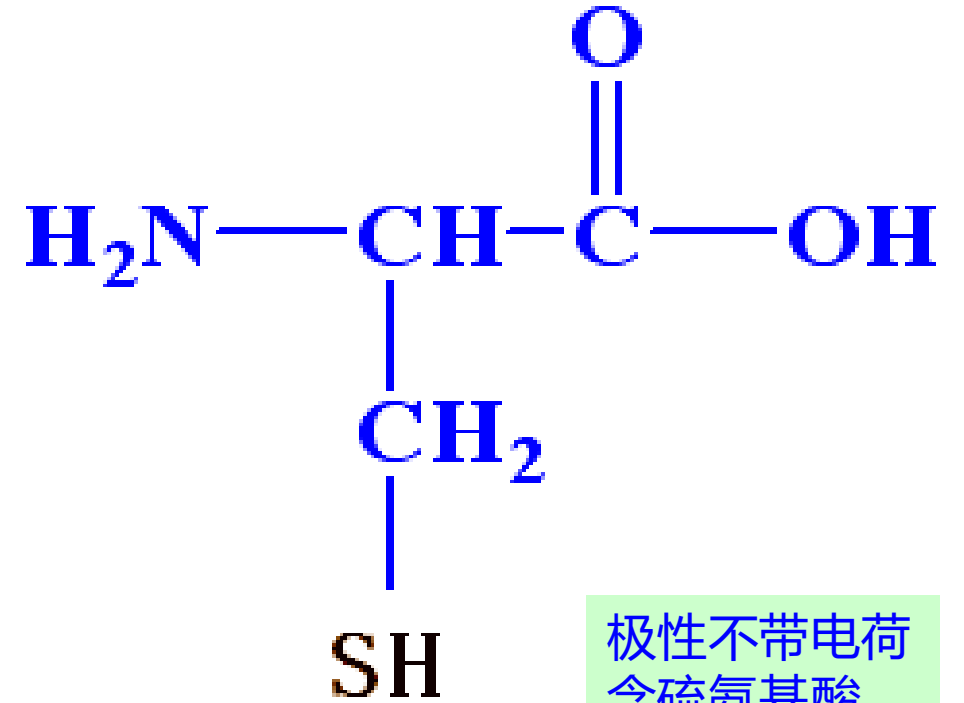
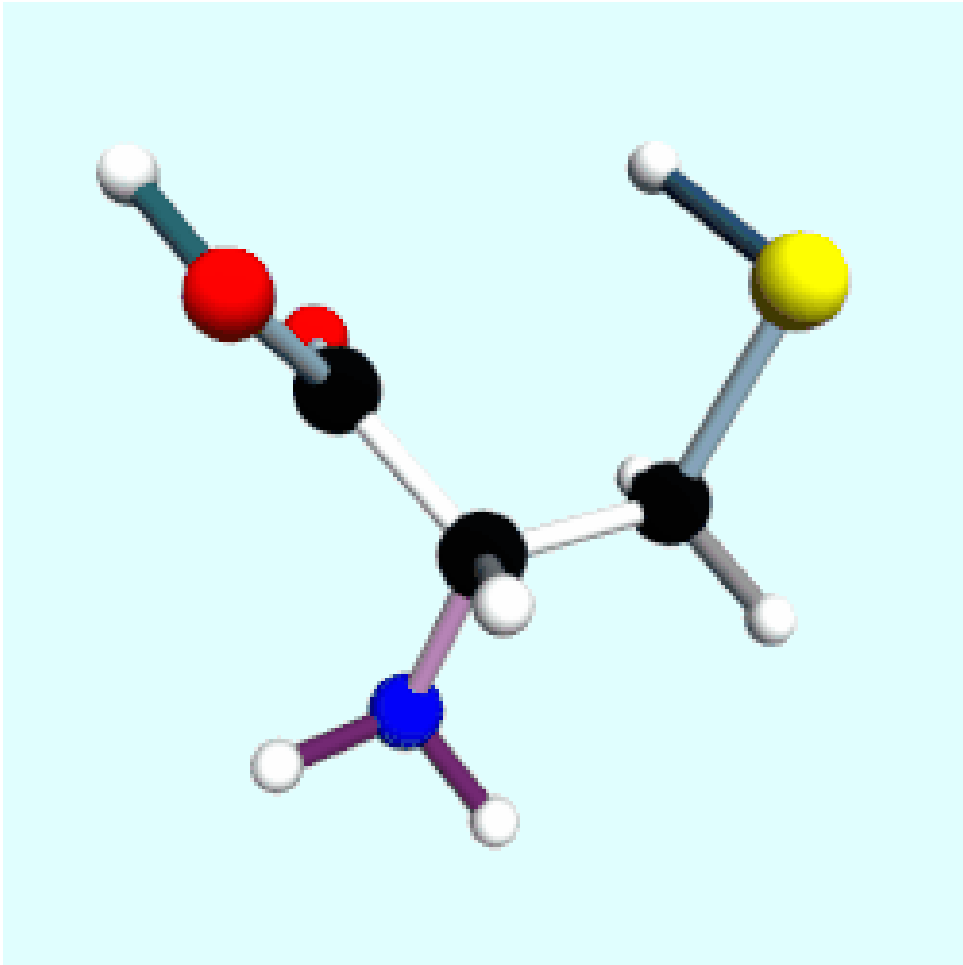


亚氨基酸

β -吡咯烷基- α -羧酸

Amino Acids in Proteins

半胱氨酸 **Cysteine** /'sɪs.ti:n/ (C)

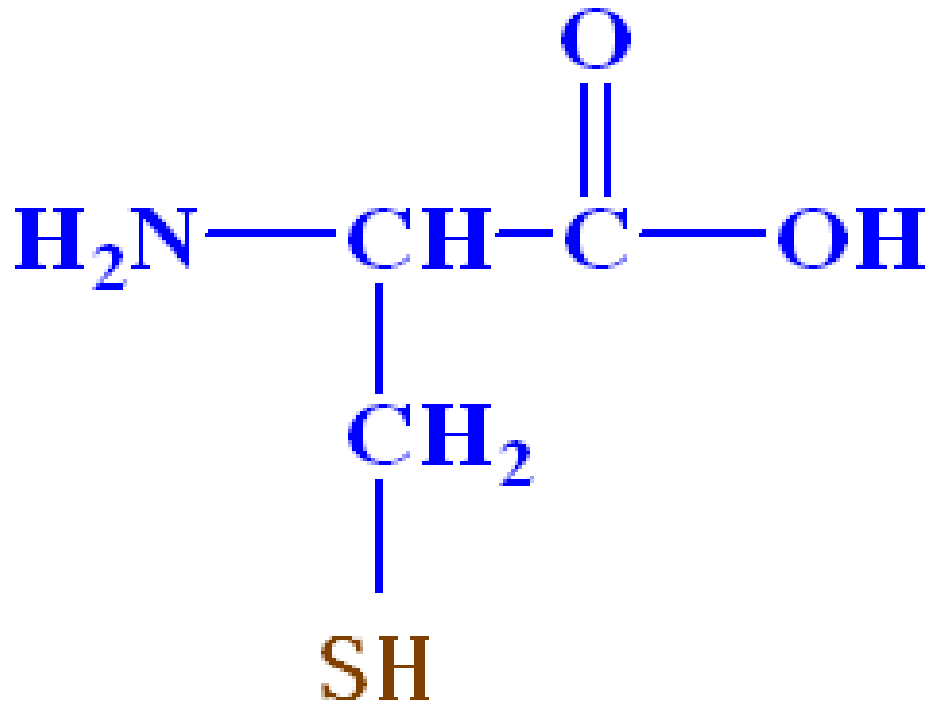


极性不带电荷
含硫氨基酸

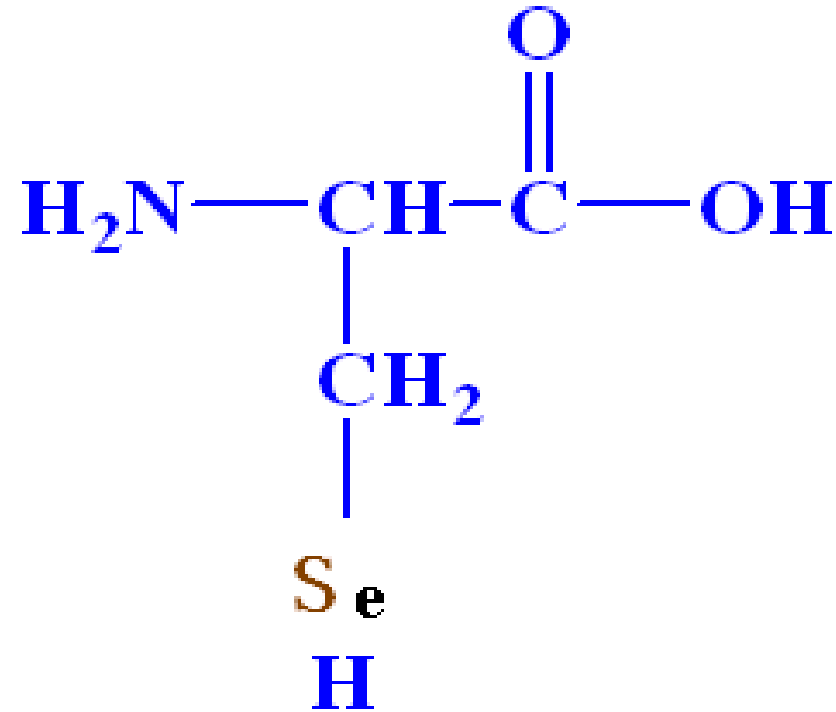
α -氨基- β -巯基丙酸

The 21st Amino Acid: Selenocysteine (U)

In 1996, the 21st naturally occurring amino acid was recognized: Selenocysteine (Sec, U)



半胱氨酸



硒半胱氨酸

Amino acid	3-letter	1-letter	Chemical polarity	Molecular mass	Abundance in proteins (%)
Alanine	Ala	A	Nonpolar	89.094	8.76
Arginine	Arg	R	Basic polar	174.203	5.78
Asparagine	Asn	N	Polar	132.119	3.93
Aspartate	Asp	D	Brønsted base	133.104	5.49
Cysteine	Cys	C	Brønsted acid	121.154	1.38
Glutamate	Glu	E	Brønsted base	147.131	6.32
Glutamine	Gln	Q	Polar	146.146	3.9
Glycine	Gly	G	Nonpolar	75.067	7.03
Histidine	His	H	Brønsted acid and base	155.156	2.26
Isoleucine	Ile	I	Nonpolar	131.175	5.49
Leucine	Leu	L	Nonpolar	131.175	9.68
Lysine	Lys	K	Brønsted acid	146.189	5.19
Methionine	Met	M	Nonpolar	149.208	2.32
Phenylalanine	Phe	F	Nonpolar	165.192	3.87
Proline	Pro	P	Nonpolar	115.132	5.02
Serine	Ser	S	Polar	105.093	7.14
Threonine	Thr	T	Polar	119.119	5.53
Tryptophan	Trp	W	Nonpolar	204.228	1.25
Tyrosine	Tyr	Y	Brønsted acid	181.191	2.91
Valine	Val	V	Nonpolar	117.148	6.73

Structural Features of Amino Acids in Proteins

- ❖ With the exception of proline, all protein AA are α -amino acids;
- ❖ The α -carbon is bonded to:
 - ✓ One amino group ($-\text{NH}_2$)
 - ✓ One carboxyl group ($-\text{COOH}$)
 - ✓ One hydrogen atom ($-\text{H}$)
 - ✓ One side chain (R group)
- ❖ Except for glycine, all AA have a chiral (asymmetric) α -carbon; therefore, they exhibit optical activity (旋光性)
- ❖ Protein AA are almost exclusively in the L-configuration Glycine is achiral (no stereoisomers, 手性)

Classification from a Nutritional Perspective

(1) Nonessential Amino Acids

Can be **synthesized by the human body**; therefore, **not required from the diet**

(2) Essential Amino Acids (Humans)

Cannot be synthesized (or not in sufficient amounts) by the body, and must be obtained from **dietary sources**

9 Essential Amino Acids in Humans

- ❖ Valine (Val)
- ❖ Isoleucine (Ile)
- ❖ Leucine (Leu)
- ❖ Phenylalanine (Phe)
- ❖ Methionine (Met)
- ❖ Tryptophan (Trp)
- ❖ Threonine (Thr)
- ❖ Lysine (Lys)
- ❖ Histidine (His)

Physical Properties of Amino acids

Solubility

Most of the amino acids are usually soluble in water and insoluble in organic solvents.

Melting Point

Amino acids are generally melted at a higher temperature of ten above 200 °C.

Taste

Amino acids may be sweet (Gly, Ala & Val), tasteless (Leu) or Bitter (Arg & Ile).

Optical Properties

All amino acids possess optical isomers due to the presence of asymmetric α -carbon atoms.

Zwitter ion and Isoelectric point

Zwitter ion (or) (dipolar ion) is a hybrid molecule containing positive and negatively ionic groups.

两性离子(Zwitterion)与等电点 (Isoelectric point, pI)

Titration Curve of Glycine

Glycine is optically inactive and the simplest amino acid. Acid-base titration involves the gradual addition (or) removal of protons

甘氨酸的滴定曲线是理解氨基酸酸碱性质的经典模型

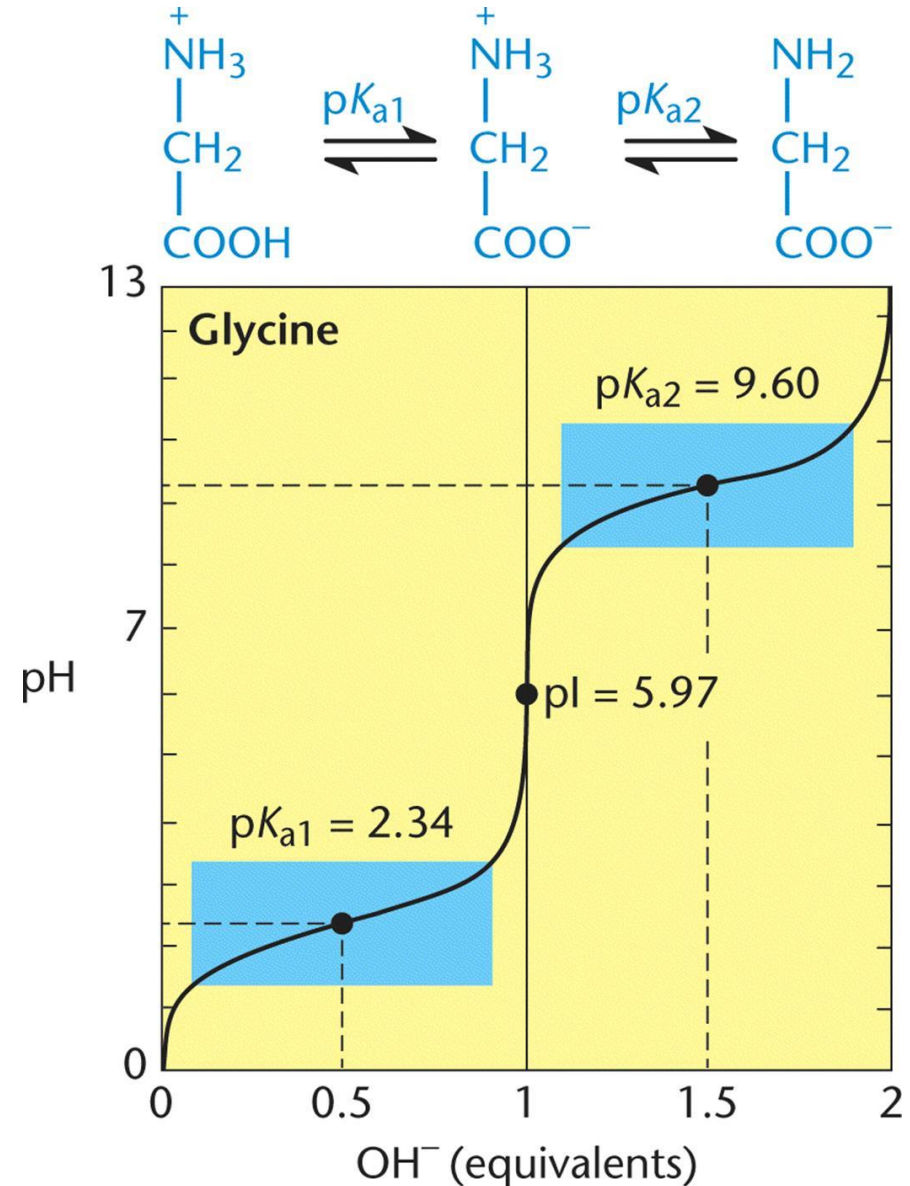
Physical Properties of Amino acids

Titration Curve

Definition of Isoelectric Point (pI): the pH at which an amino acid carries no net charge

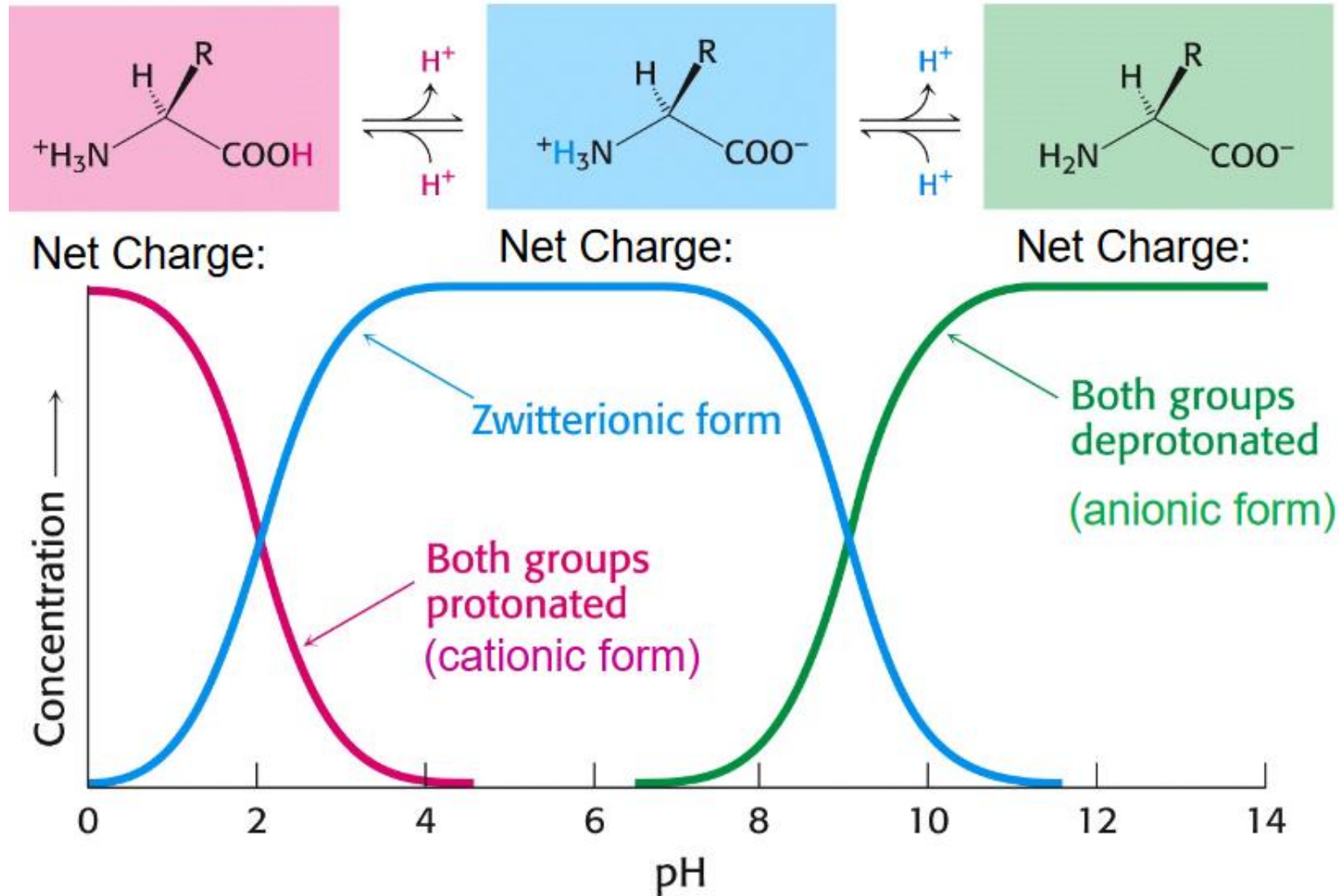
$$pI = \frac{pK_1 + pK_2}{2}$$

$$pI = \frac{2.34 + 9.60}{2} \approx 5.97$$



Physical Properties of Amino acids

Titration Curve / 滴定曲线



Physical Properties of Amino acids

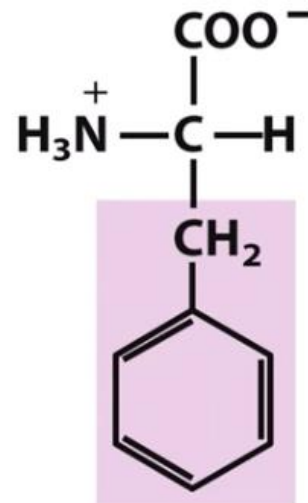
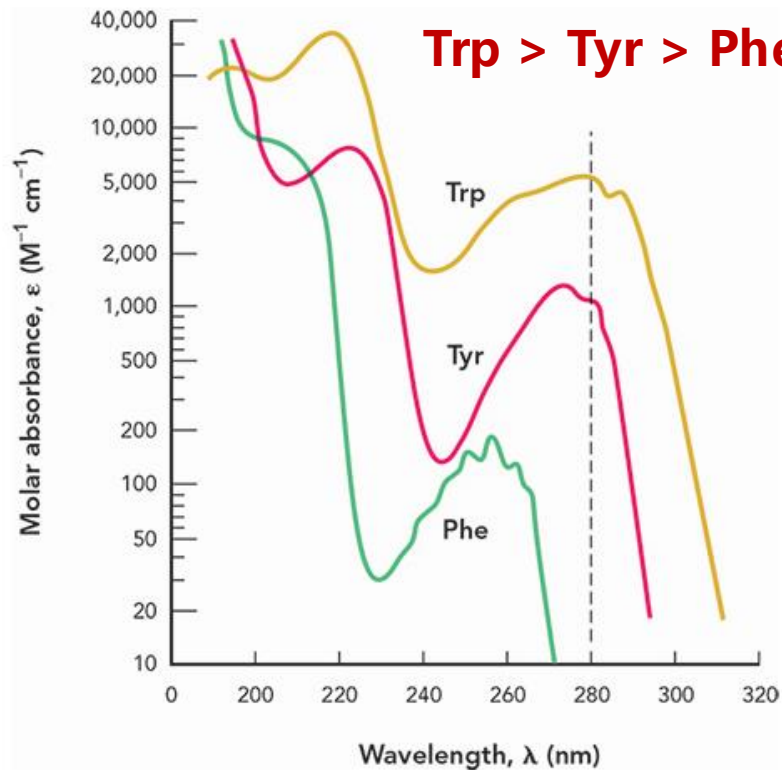
Titration Curve

Relationship Between pH and pI

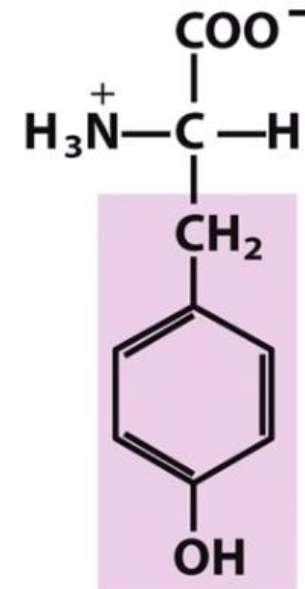
- ❖ **pH > pI** : amino acid carries **net negative charge, and** migrates toward the **anode (+)**
- ❖ **pH = pI** : **net charge = 0**; no migration in electric field
- ❖ **pH < pI** : amino acid carries **net positive charge, and** migrates toward the **cathode (-)**

Physical Properties of Amino acids

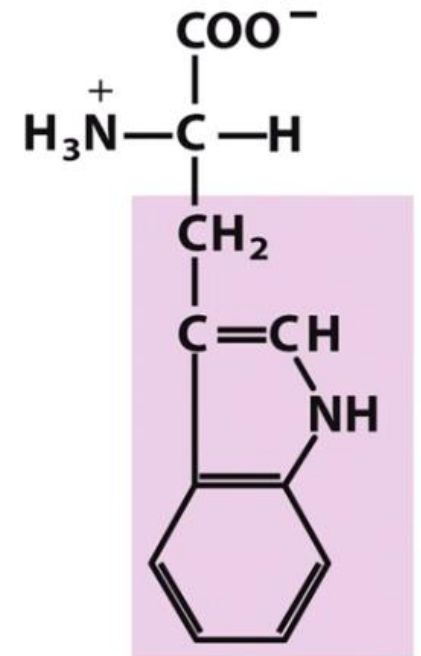
Tyrosine (Tyr), Phenylalanine (Phe), and Tryptophan (Trp) have aromatic side chains with conjugated π systems and they absorb ultraviolet (UV) light in the range: $\sim 220\text{--}300$ nm (**280nm**)



Phenylalanine



Tyrosine



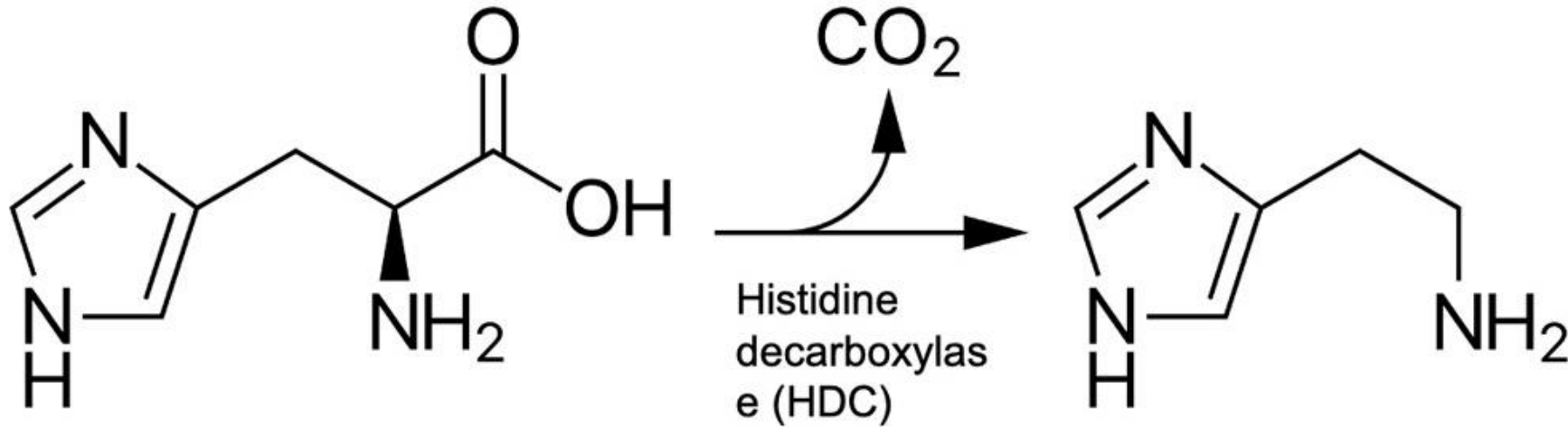
Tryptophan

Chemical Properties of Amino acids

Due to the Carboxyl group

Decarboxylation (脱羧)

The amino acids will undergo alpha decarboxylation to form the corresponding “amines.”
Thus, important amines are produced from amino acids.



组氨酸 (Histidine)

组胺 (Histamine)

Chemical Properties of Amino acids

Due to the Carboxyl group

Reaction with Alkalies (Salt formation)

The carboxyl group of amino acids can release an H⁺ ion with the formation of carboxylate (COO⁻) ions. These may be neutralized by cations like Na⁺ and Ca²⁺ to form salts. Thus, amino acids react with alkalies to form "salts."

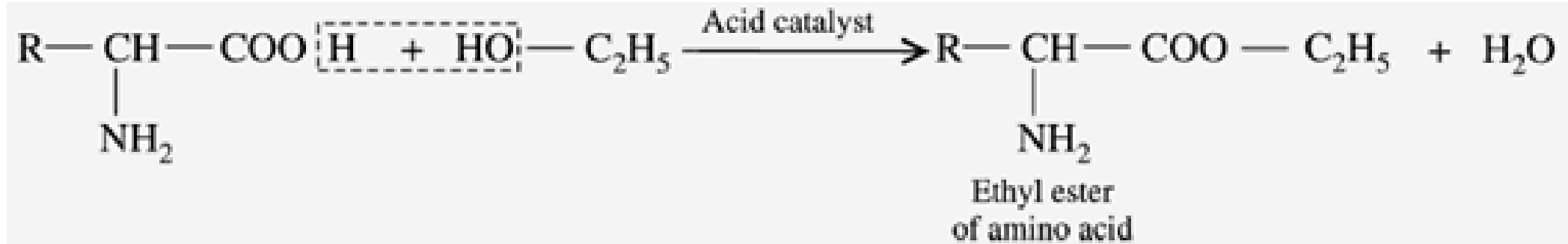


Chemical Properties of Amino acids

Due to the Carboxyl group

Reaction with Alcohols (Esterification)

When the amino acids are reacted with alcohol to form “ester” . The esters are volatile, in contrast to the form of amino acids.

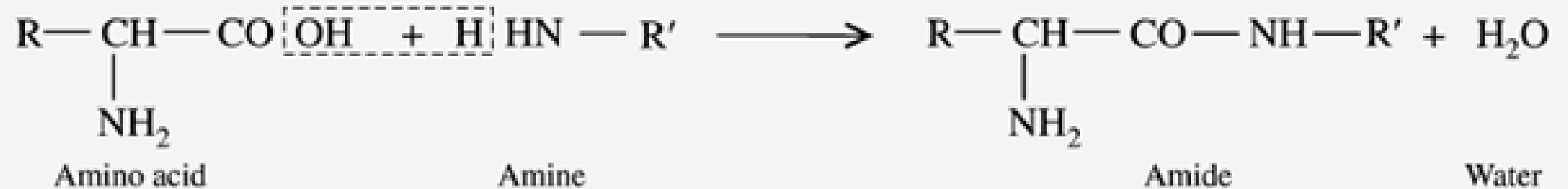


Chemical Properties of Amino acids

Due to the Carboxyl group

Reaction with Amines

An amino acid reacts with amines to form "amides" .



Chemical Properties of Amino acids

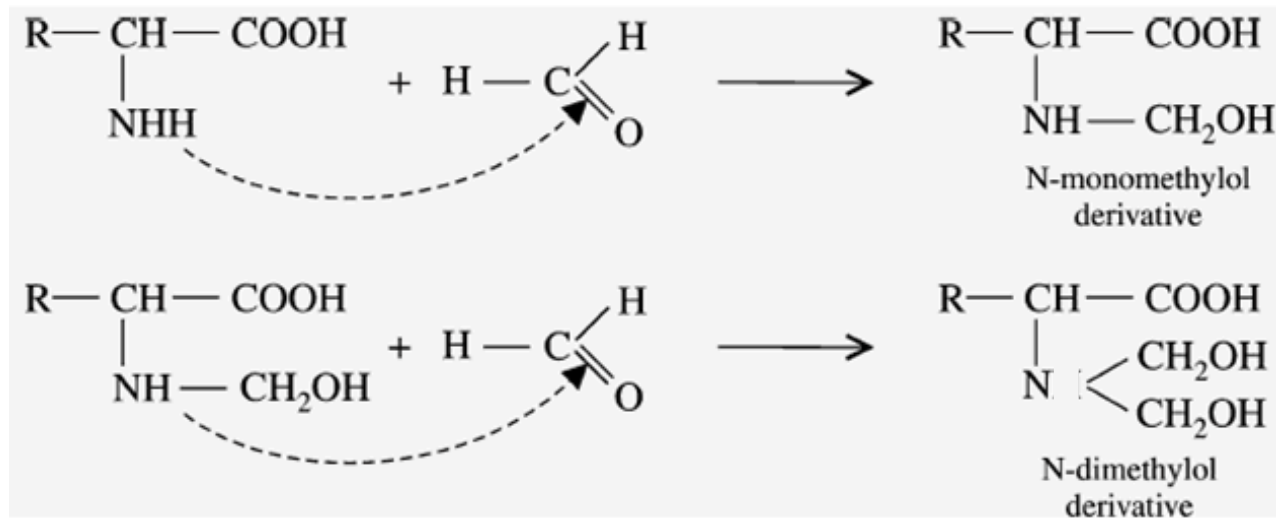
Due to Amino group

Reaction with Mineral acids (Salt formation)

When the amino acids are treated with mineral acids (like HCl), they form “acid salts” .

Reaction with Formaldehyde/羟甲基化反应

When the amino acid reacts with two molecules of formaldehyde, it forms an “N-dimethylol derivative” (hydroxy-methyl derivative). This reaction is done in two steps. These derivatives are insoluble in water and resistant to attack by microorganisms.



单羟甲基化生成N-单羟甲基衍生物

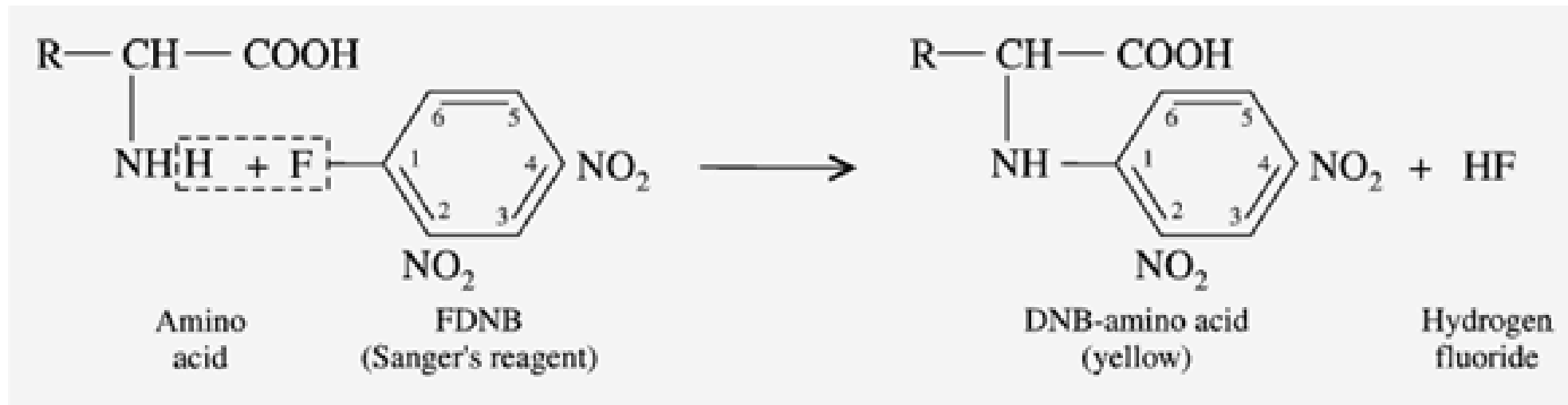
双羟甲基化生成N-二羟甲基衍生物

Chemical Properties of Amino acids

Due to Amino group

Reaction with Sanger's reagent/ 桑格反应

"1-fluoro-2,4-dinitrobenzene" is called Sanger reagent (FDNB). In a mildly alkaline solution, the Sanger reagent reacts with α -amino acid to produce a yellow-colored derivative, DNB-amino acid.



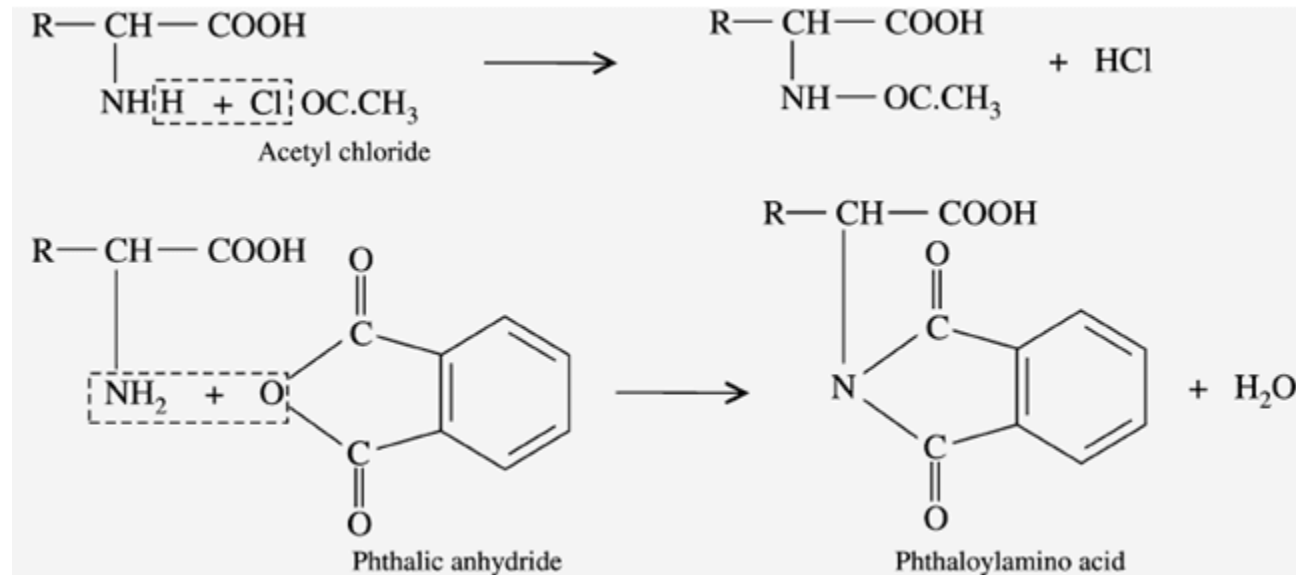
重要的蛋白质测序方法

Chemical Properties of Amino acids

Due to Amino group

Reaction with acylating agents (Acylation)/酰化反应

When the amino acids react with “acid chloride” and acid anhydride (phenic anhydride) in an alkaline medium, it gives “phthaloyl amino acid” .

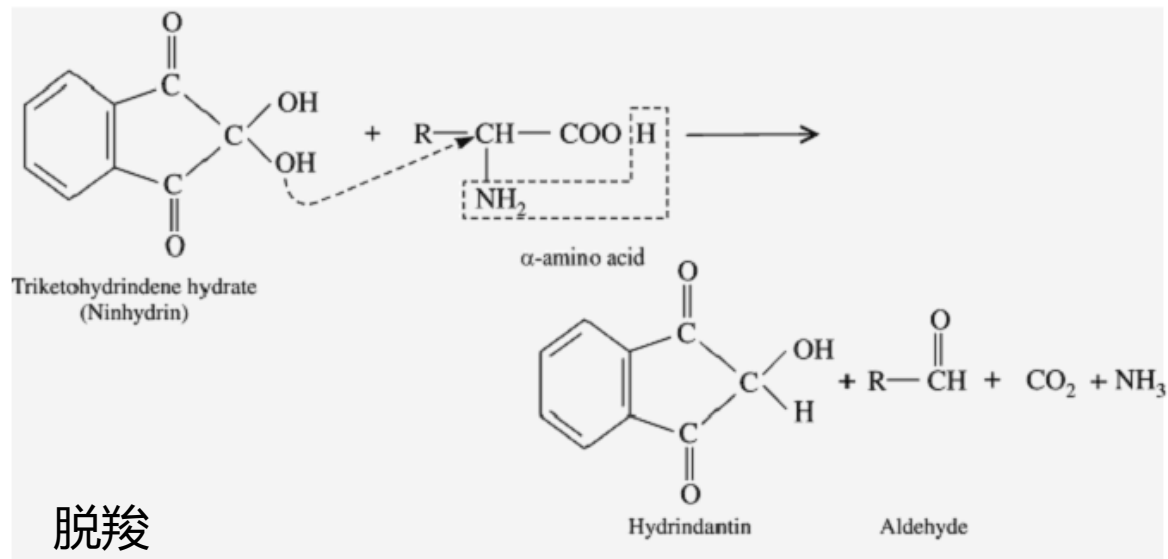


Chemical Properties of Amino acids

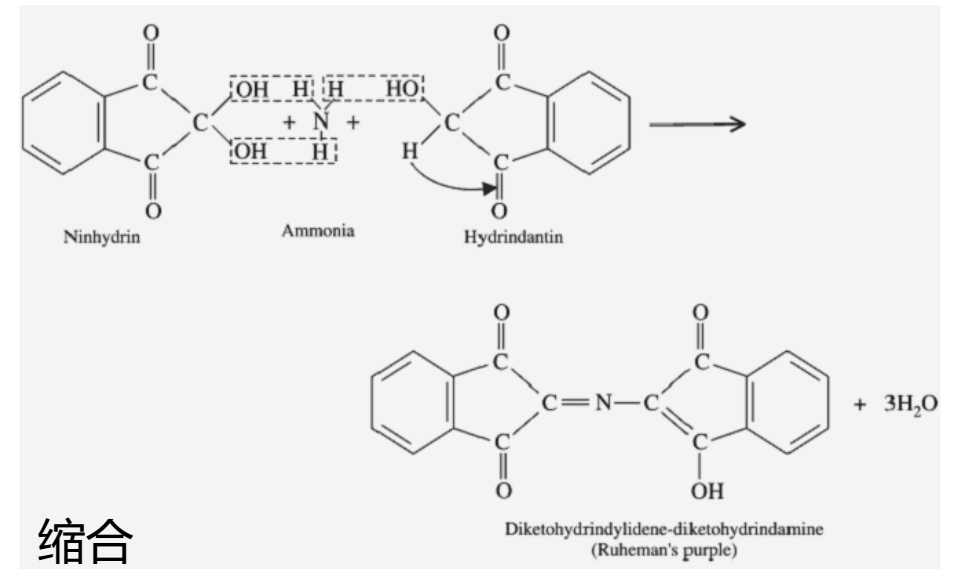
Due to amino & carboxyl group

Ninhydrin reaction / 茚三酮反应

Step1: Ninhydrin is a powerful oxidizing agent and causes oxidative decarboxylation of α -amino acids, producing CO_2 , NH_3 , and an aldehyde with one fewer carbon atom than the parent amino acid.



Step2: The reduced ninhydrin then reacts with the liberated NH_3 and a mole of ninhydrin, forming a blue-colored Ruhmann complex.



Outline

- About Protein

- Amino Acids
氨基酸

- Protein Structure
蛋白质分子结构

- Structure–Function Relationship
结构与功能的关系

- Physicochemical Properties of Proteins
理化性质

- Protein Separation and Applications
分离与应用

Primary Structure of Proteins

Definition: The primary structure refers to the linear sequence of amino acids in a polypeptide chain and the covalent connections between them.

Key Features (Covalent Structure)

- ✓ **Number of polypeptide chains (肽链的数目)**
- ✓ **Amino acid (AA) sequence (AA 序列)**
- ✓ **Positions of disulfide bonds (–S–S–)**

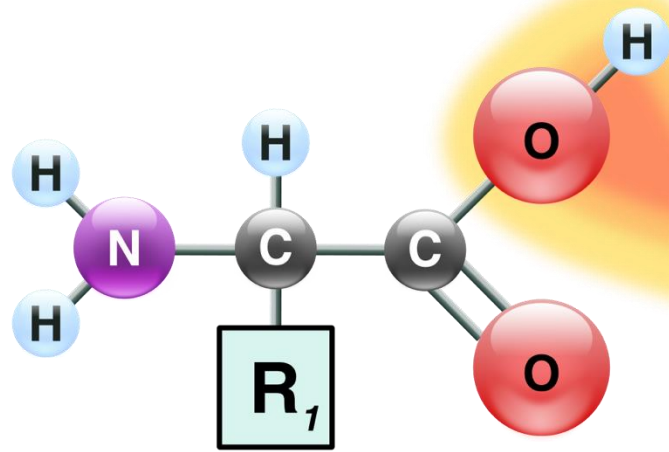
Peptide (肽)

A peptide is a compound formed by condensation (dehydration reaction) between the carboxyl group (–COOH) of one amino acid and the amino group (–NH₂) of another amino acid

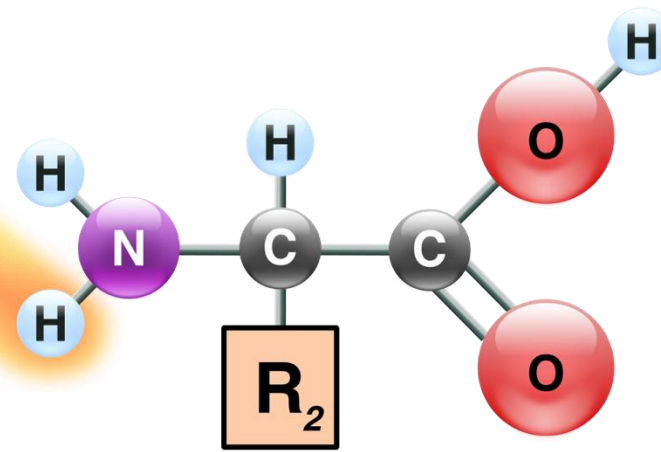
Peptide Bond (肽键)

A peptide bond is a covalent amide bond (–CO–NH–) formed after removal of one molecule of water (H₂O) between two amino acids.

Amino acid (1)



Amino acid (2)

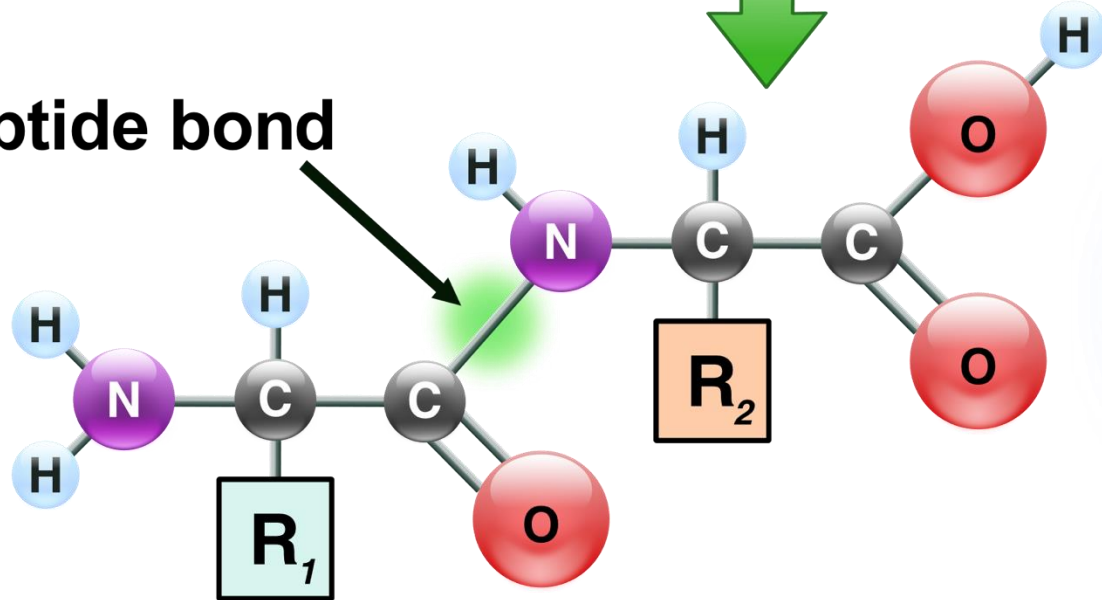


N-terminus

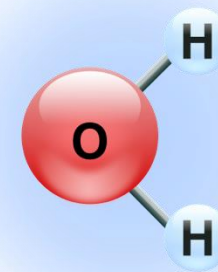
C-terminus



Peptide bond



Dipeptide



Water

Primary Structure of Proteins

Amino Acid Residue(氨基酸残基): refers to an amino acid unit within a polypeptide chain, after loss of elements of water during peptide bond formation.

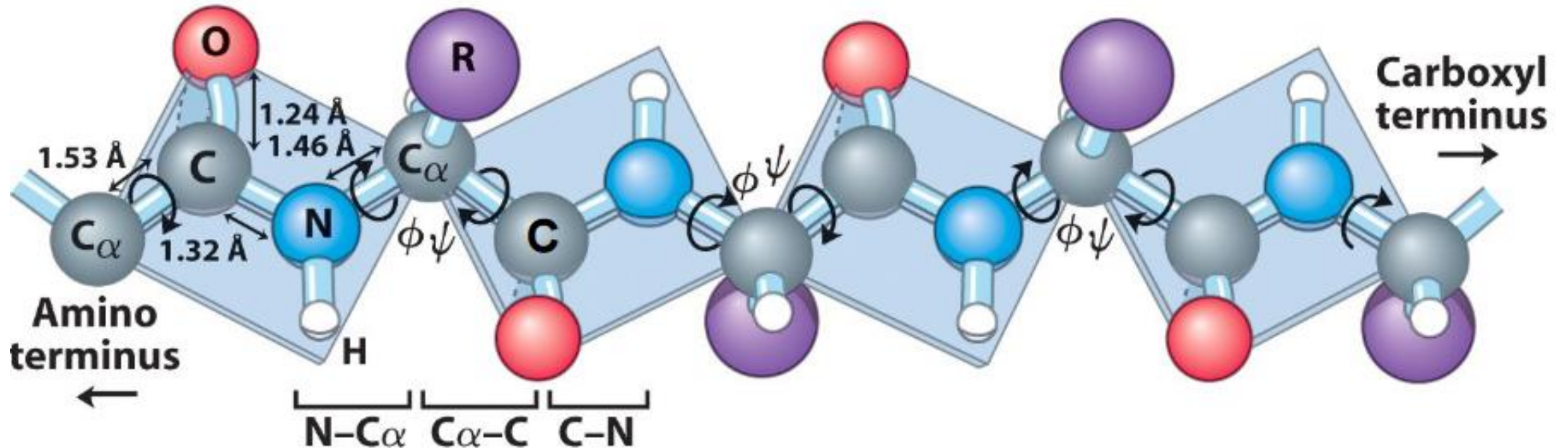
Peptide Classification (by Length)

- ❖ **Oligopeptide (寡肽):** typically 2–10 amino acid residues
- ❖ **Polypeptide (多肽):** a chain of more than ~10 amino acid residues
- ❖ **Protein:** usually one or more polypeptides folded into a functional 3D structure

Primary Structure of Proteins

Amide Plane 肽平面

The peptide bond ($-\text{CO}-\text{NH}-$) forms a rigid, planar structure due to: resonance (partial double-bond character)

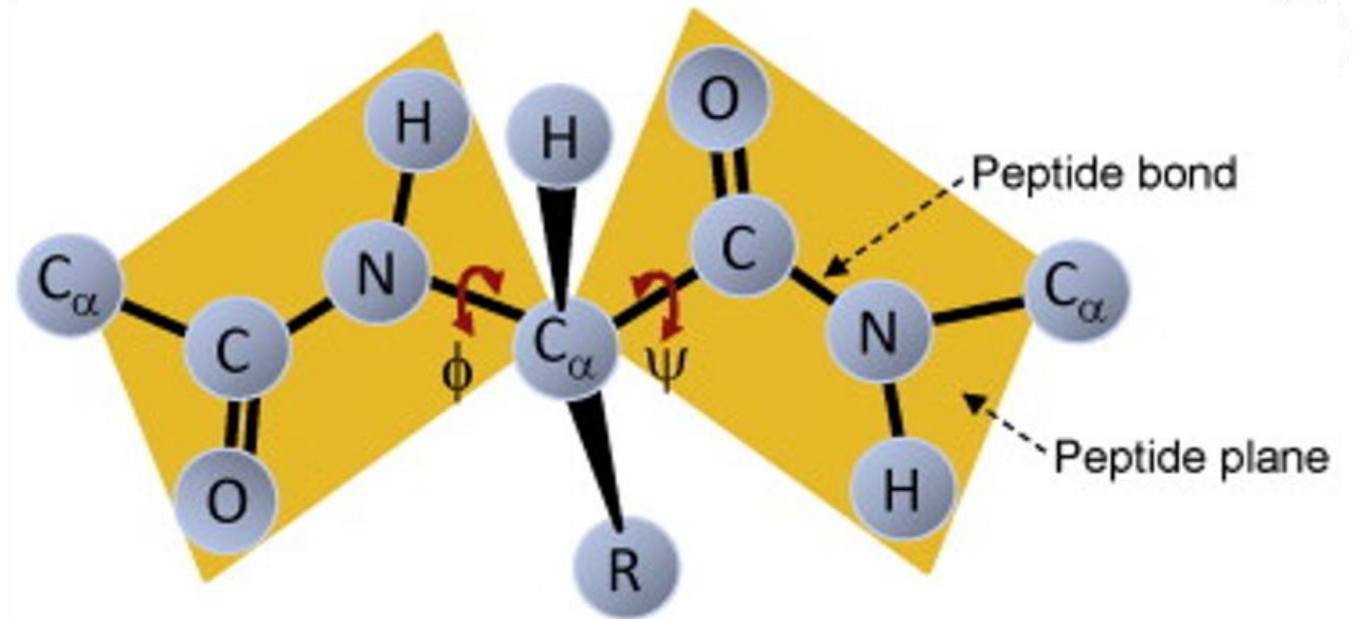


Primary Structure of Proteins

Amide Plane 肽平面

The peptide plane includes

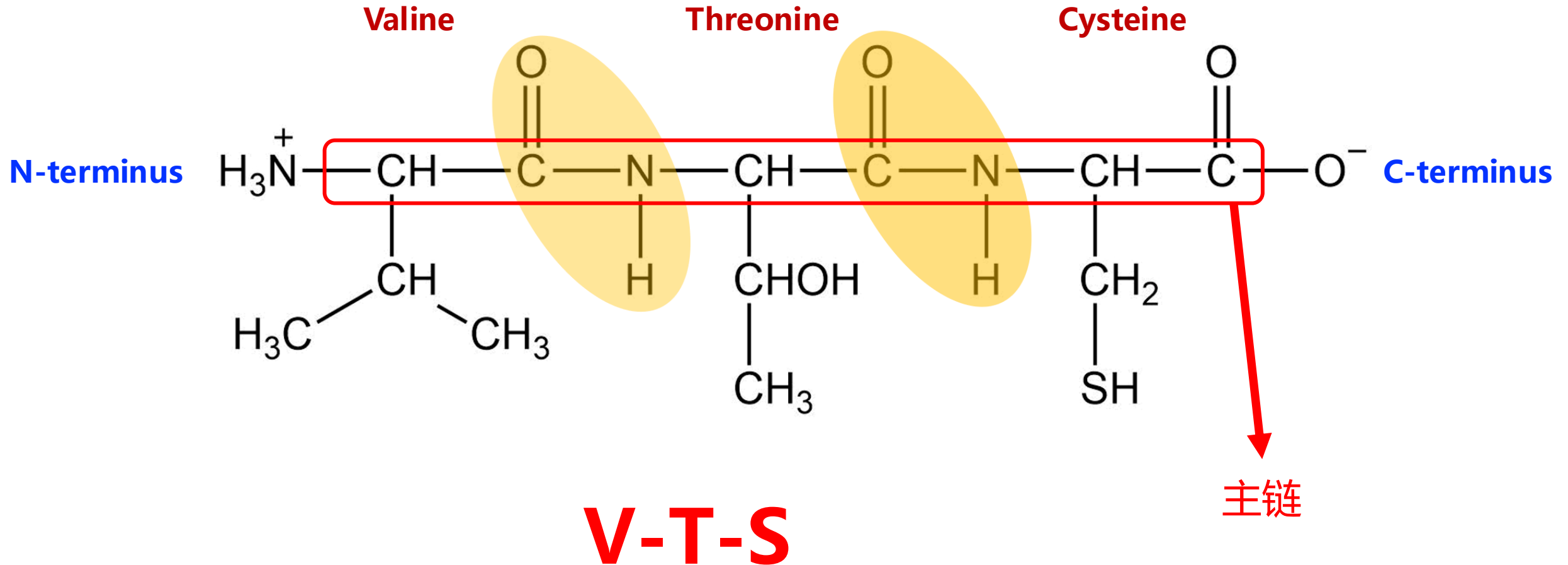
- ✓ C=O group
- ✓ N-H group
- ✓ Two adjacent α -carbons (C_α)



This plane is often called the "peptide plane" or "amide plane"

Primary Structure of Proteins

Amino Acid Sequences



Secondary Structure of Proteins

The secondary structure refers to the local spatial arrangement of the polypeptide backbone, stabilized primarily by hydrogen bonds. It arises from regular folding patterns of the backbone, not side chains.

Common Types of Secondary Structure

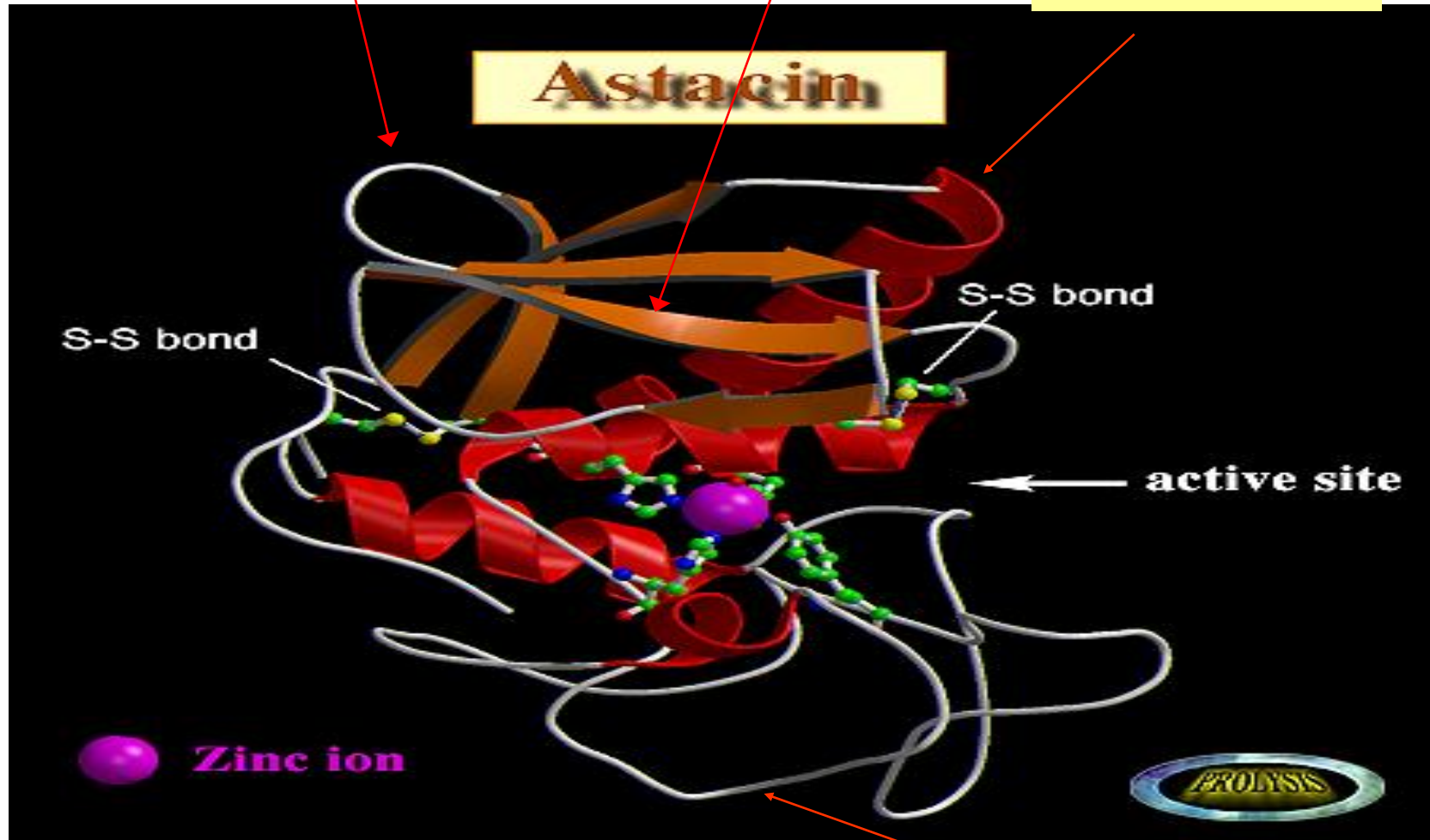
- ✓ **α -Helix** / α 螺旋
- ✓ **β -Pleated Sheet** / β 折叠片
- ✓ **β -Turns / Loops** / β 转角
- ✓ **Random Coil** / 无规则卷曲

Secondary Structure of Proteins

β 转角

β 折叠片

α 螺旋



无规卷曲

Secondary Structure of Proteins

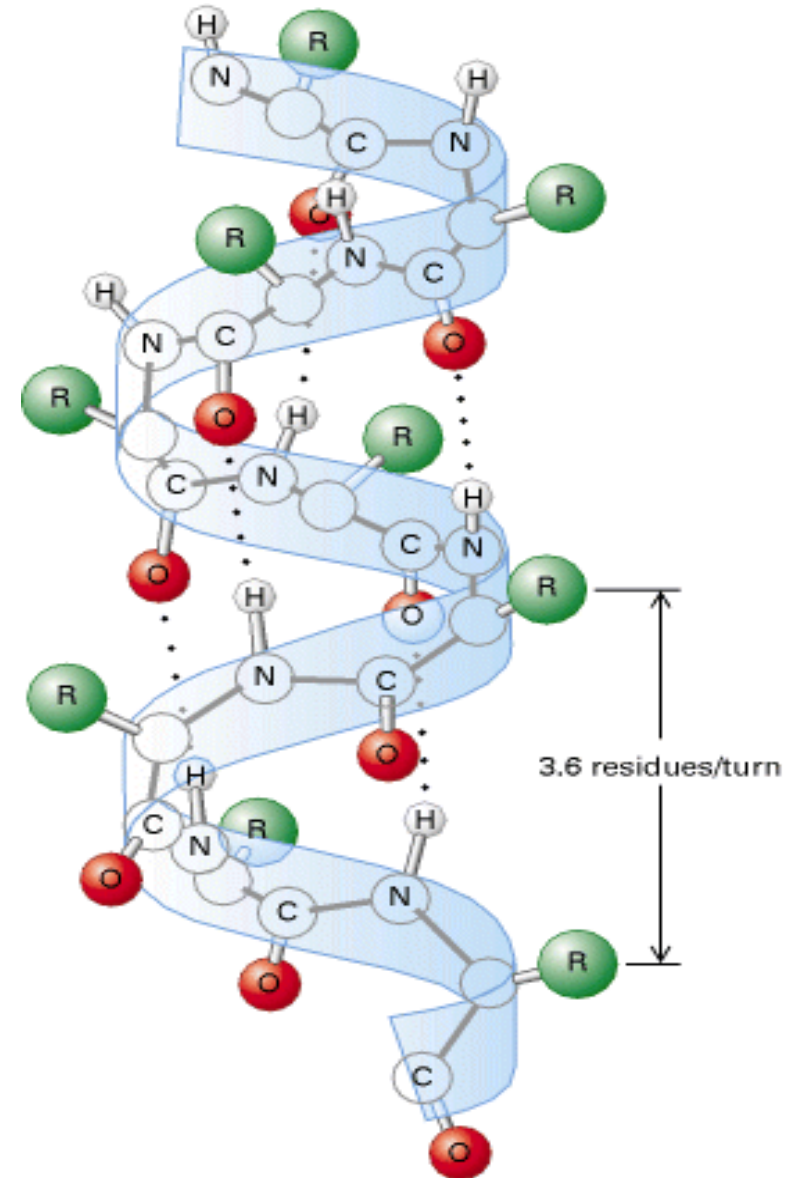
α -Helix

General feature

- ✓ The α -helix is a right-handed helical structure formed by the polypeptide backbone.
- ✓ The backbone coils in a regular, repeating pattern, while side chains (R groups) project outward.

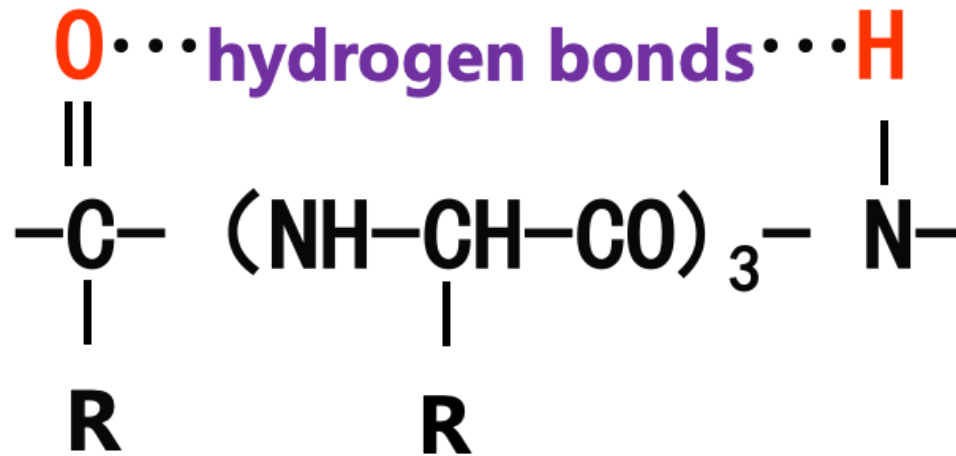
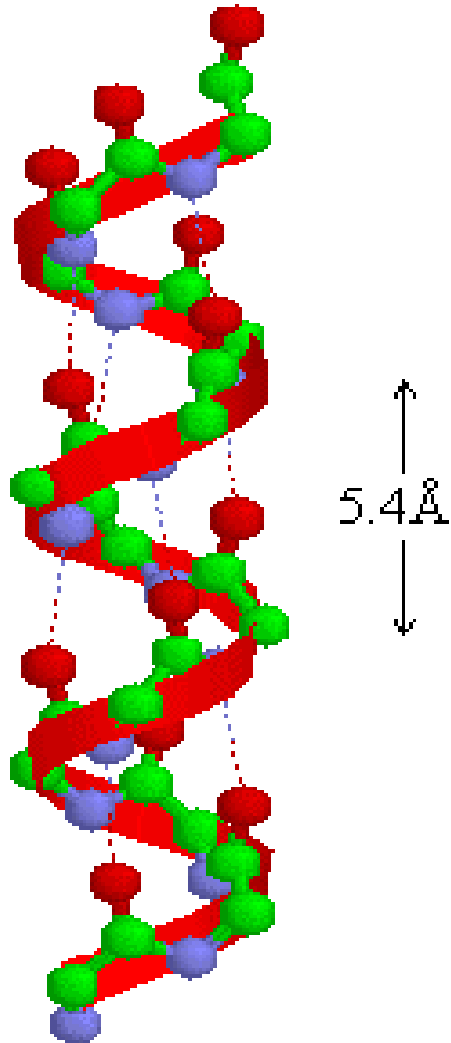
Geometric Parameters

- ✓ 3.6 amino acid residues per turn
- ✓ Pitch (rise per turn): 0.54 nm (5.4 Å)
- ✓ Rise per residue: 0.15 nm (1.5 Å)



Secondary Structure of Proteins

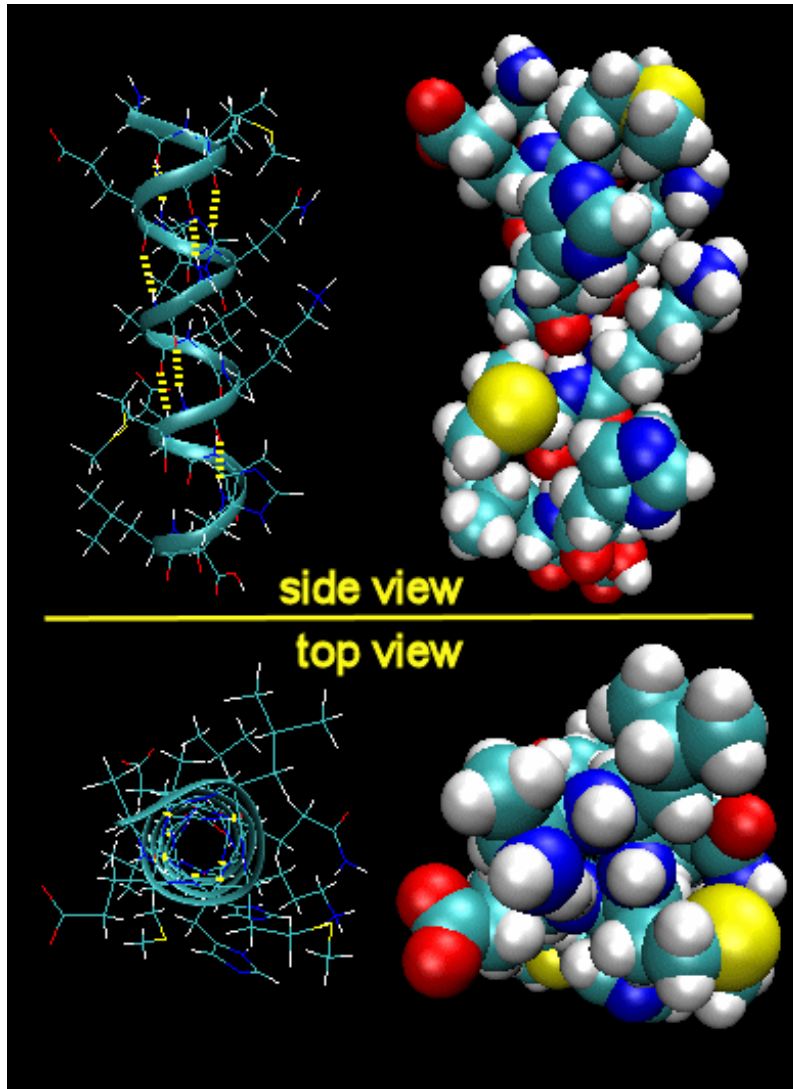
α -Helix



- Stabilized by intrachain hydrogen bonds; Between C=O of residue i and N-H of residue $i+4$
- These hydrogen bonds run parallel to the helix axis

Secondary Structure of Proteins

α -Helix

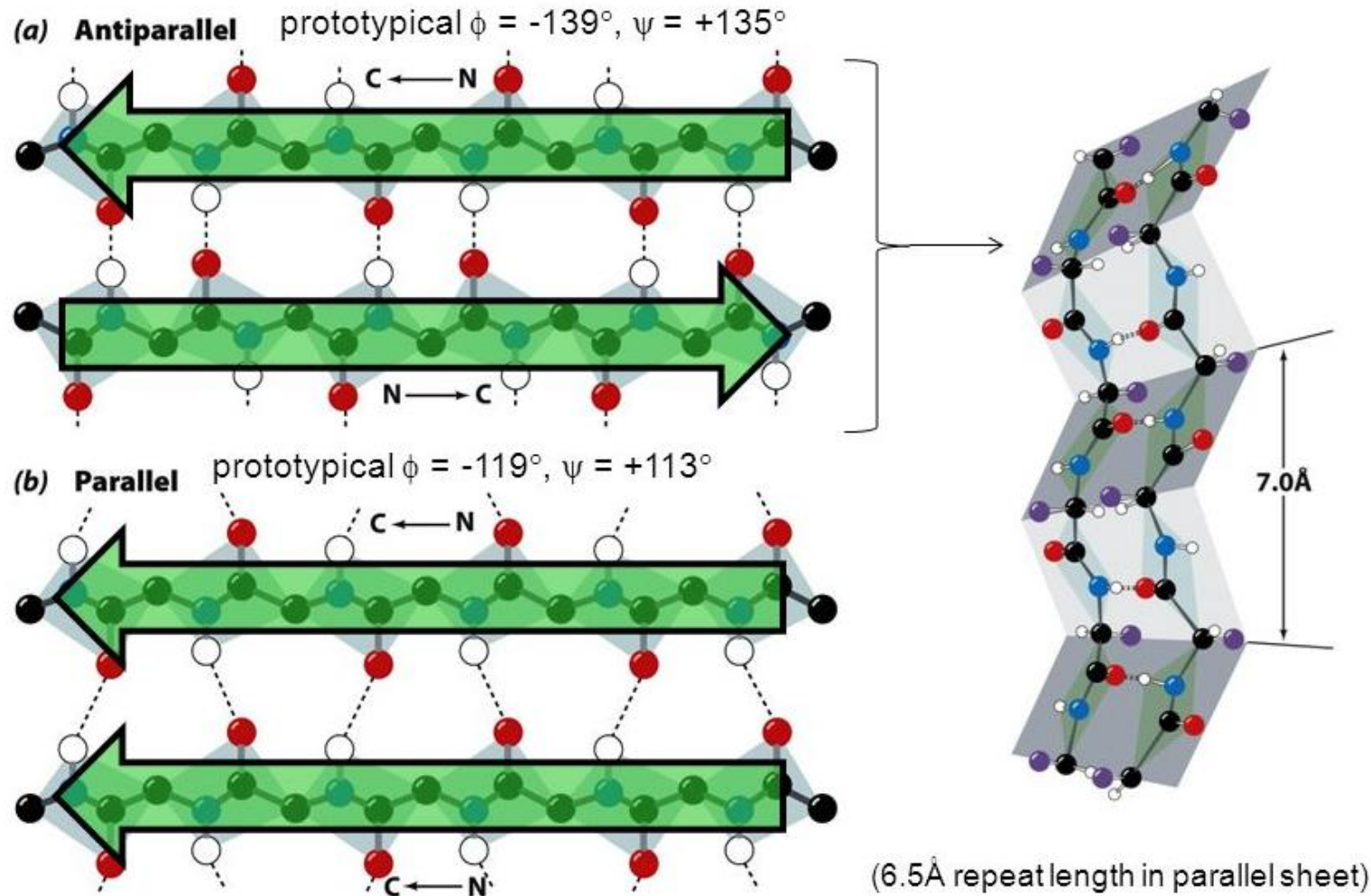


Effect of R Groups (Side Chains) on α -Helix Formation

- ❖ **Electrostatic effects:** Clusters of like-charged residues (e.g., Lys⁺, Glu⁻) **destabilize** the α -helix due to electrostatic repulsion.
- ❖ **Proline (Pro):** Rigid structure and lack of amide hydrogen **disrupt** α -helix hydrogen bonding.
- ❖ **Side chain size:** Small residues favor helix formation; bulky/branched residues hinder it.
- ❖ **Charge:** Uncharged residues are generally more favorable than clustered charged residues.

Secondary Structure of Proteins

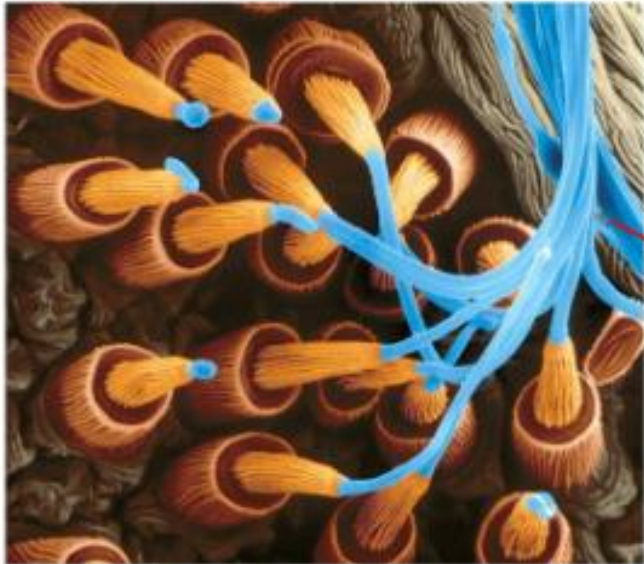
β -Pleated Sheet



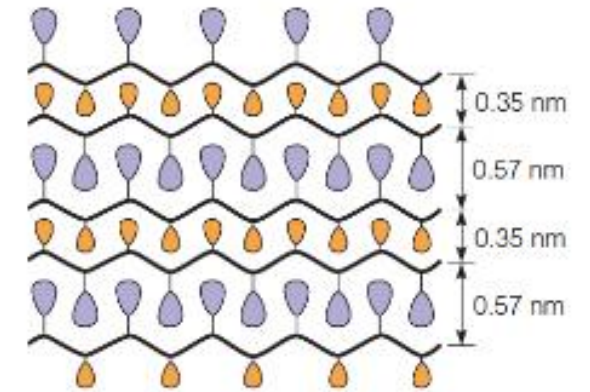
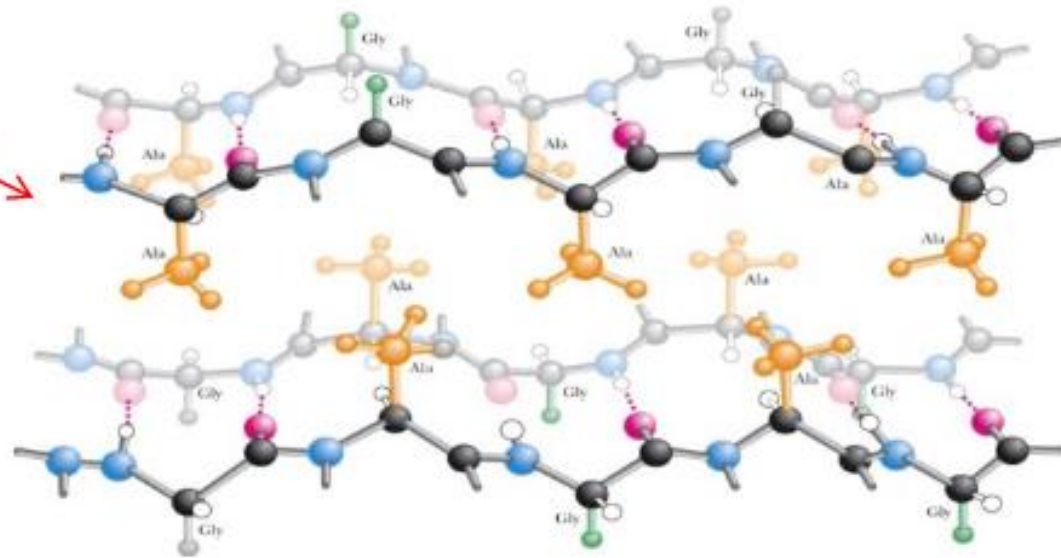
- ❖ Extended strands form **sheet via H-bonds**
- ❖ **Parallel vs antiparallel** arrangements
- ❖ R groups **alternate above/below**
- ❖ **Pleated (zigzag) backbone**
- ❖ Stabilized by **H-bonds + side-chain packing**

Secondary Structure of Proteins

β -Keratin/角蛋白



Fibroin strands (blue) emerge from the spinnerets of a spider



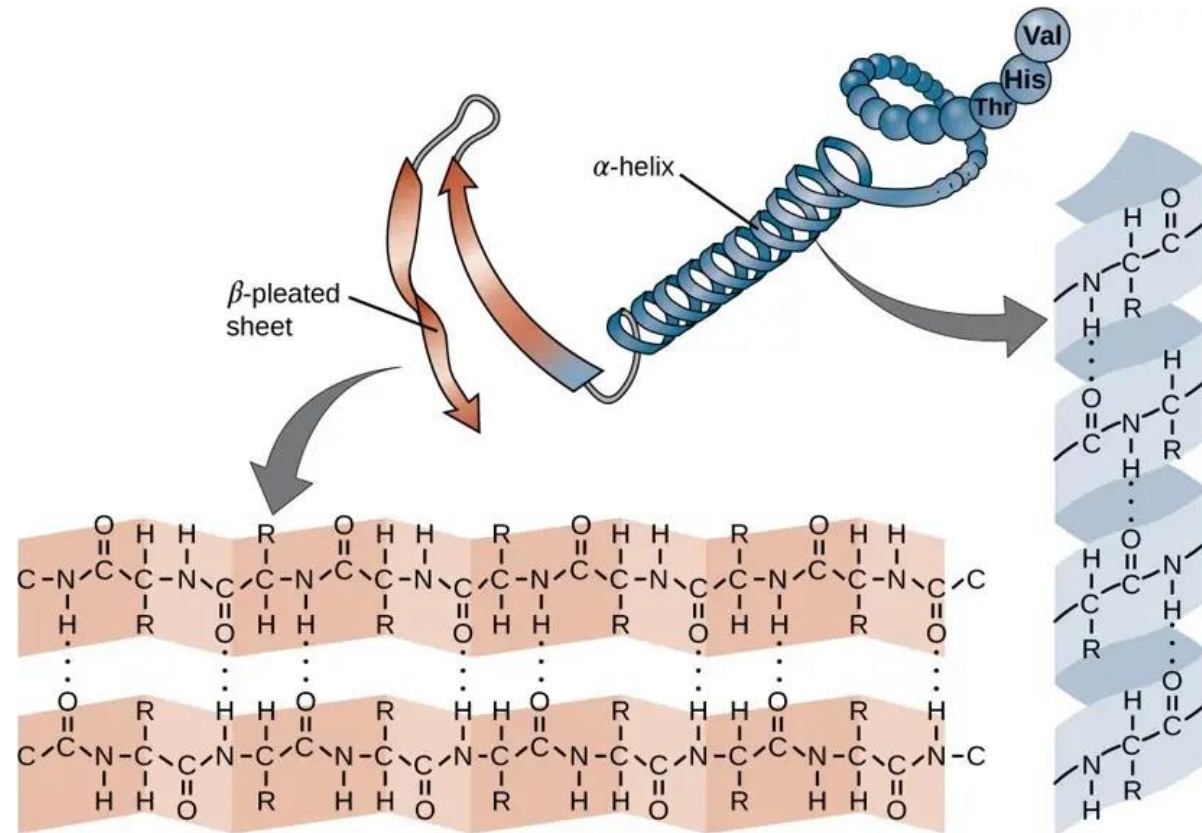
Side chains of
■ Gly
■ Ala or Ser

Secondary Structure of Proteins

α -Helix VS β -Pleated Sheet

β -Pleated Sheet

- ❖ Structure: Nearly fully extended strands forming a sheet-like structure
- ❖ Hydrogen bonding: Interstrand (between chains or segments) hydrogen bonds
- ❖ Arrangement: Can be parallel or antiparallel
- ❖ Backbone shape: Zigzag (pleated) conformation
- ❖ Side chains: Alternate above and below the sheet



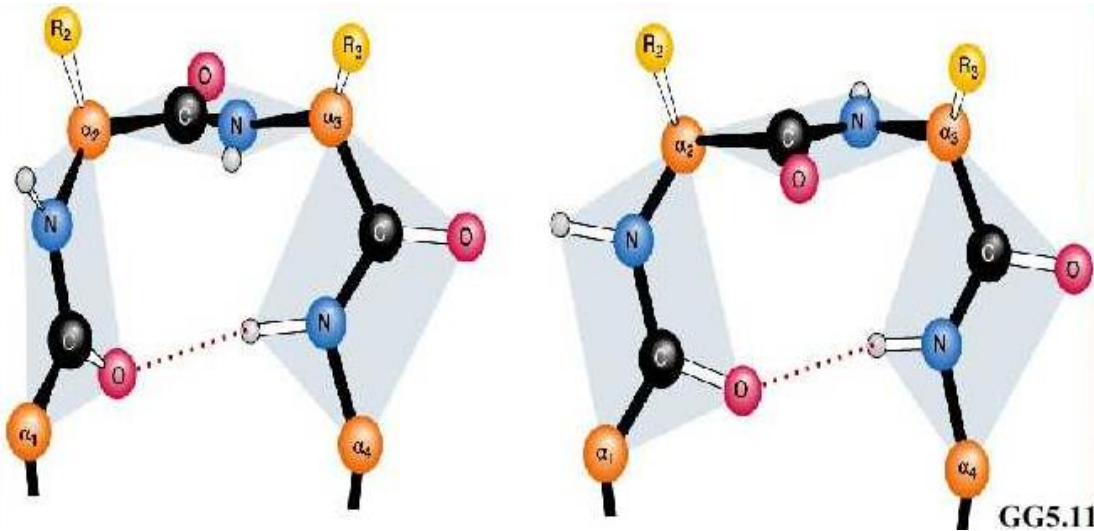
α -Helix

- ✓ Structure: Coiled, rod-like (helical) structure
- ✓ Hydrogen bonding: Intrachain (within the same chain) hydrogen bonds ($i \rightarrow i+4$)
- ✓ Helix type: Mostly right-handed
- ✓ Side chains: Project outward from the helix axis

Secondary Structure of Proteins

β -Turns / Loops

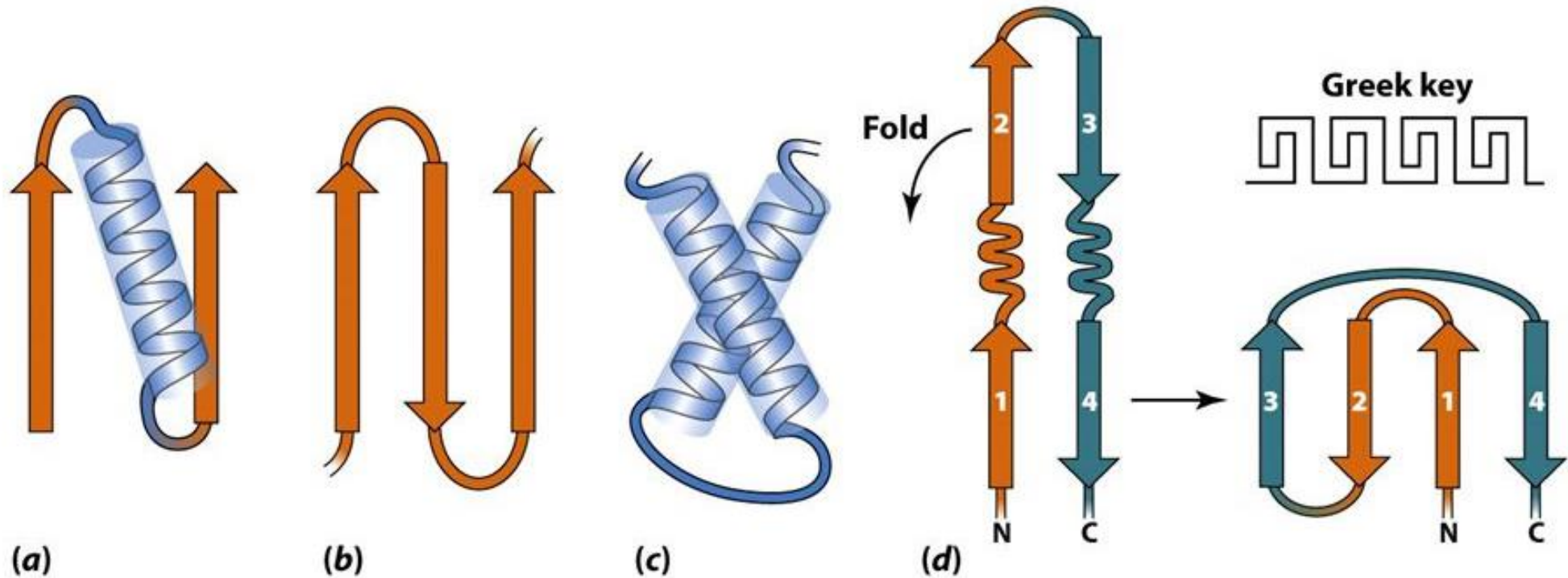
A β -turn is a sharp reversal ($\sim 180^\circ$) in the direction of the polypeptide chain. It allows the chain to fold back on itself, contributing to compact protein structure.



Stabilized by an **intrachain hydrogen bond** between. The **carbonyl (C=O)** of residue **i** and the **amide (N-H)** of residue **i+3**

Supersecondary Structure(Motif)/ 超二级结构

A supersecondary structure (motif) is a specific combination of adjacent secondary structure elements (e.g., α -helices, β -sheets, β -turns) that form a recognizable and recurring structural pattern. These motifs are spatially organized and often have functional significance.

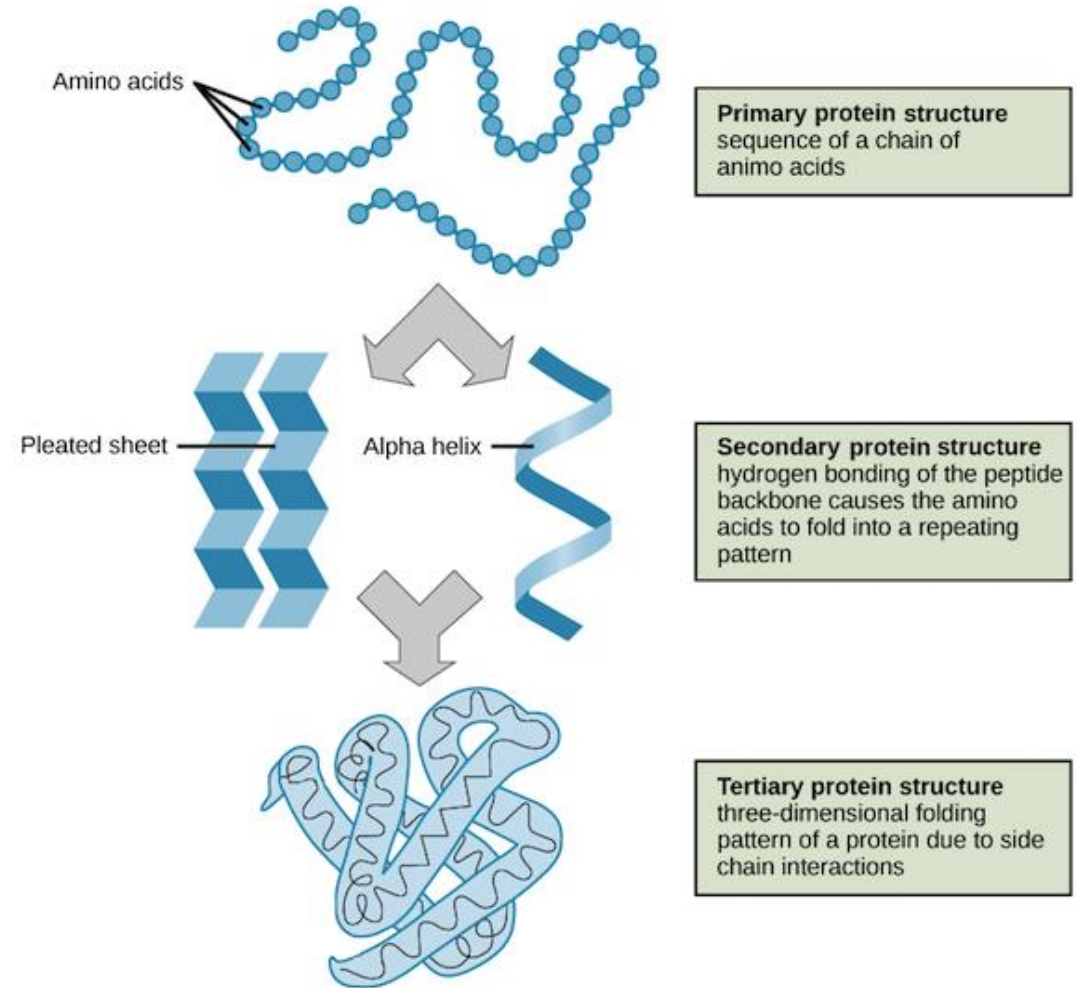
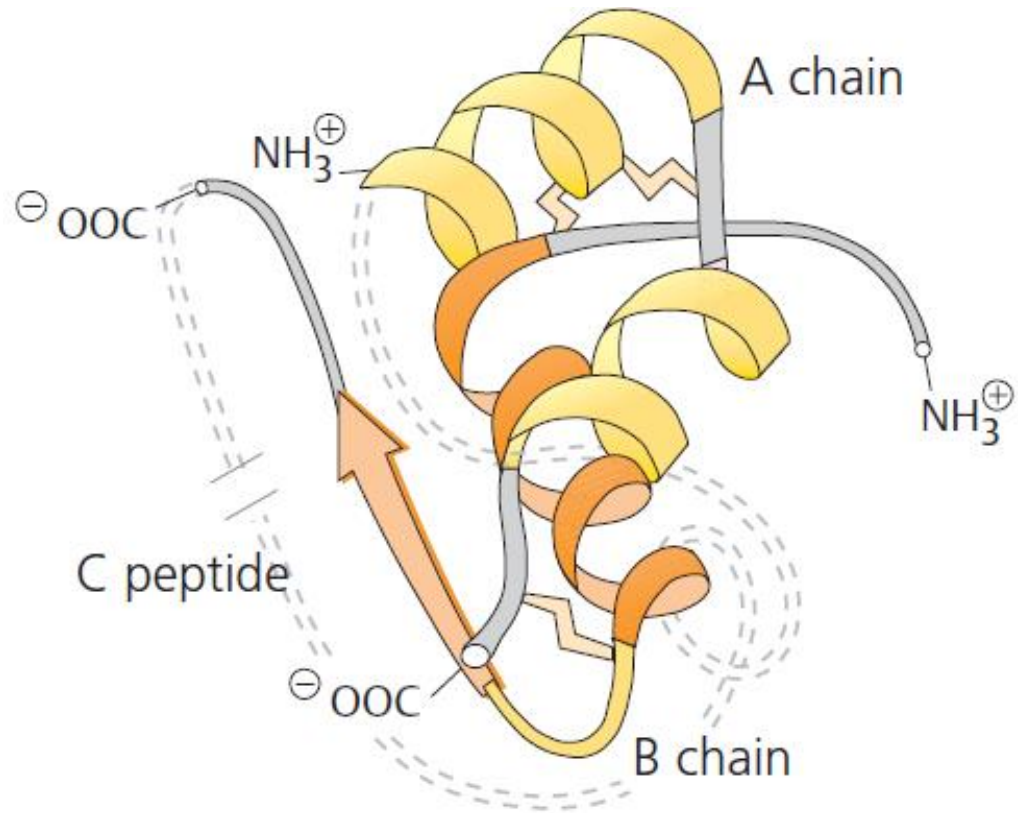


Tertiary Structure of Proteins / 三级结构

Refers to the overall three-dimensional conformation of a polypeptide chain. It is formed by further folding of secondary structures into a specific spatial arrangement.

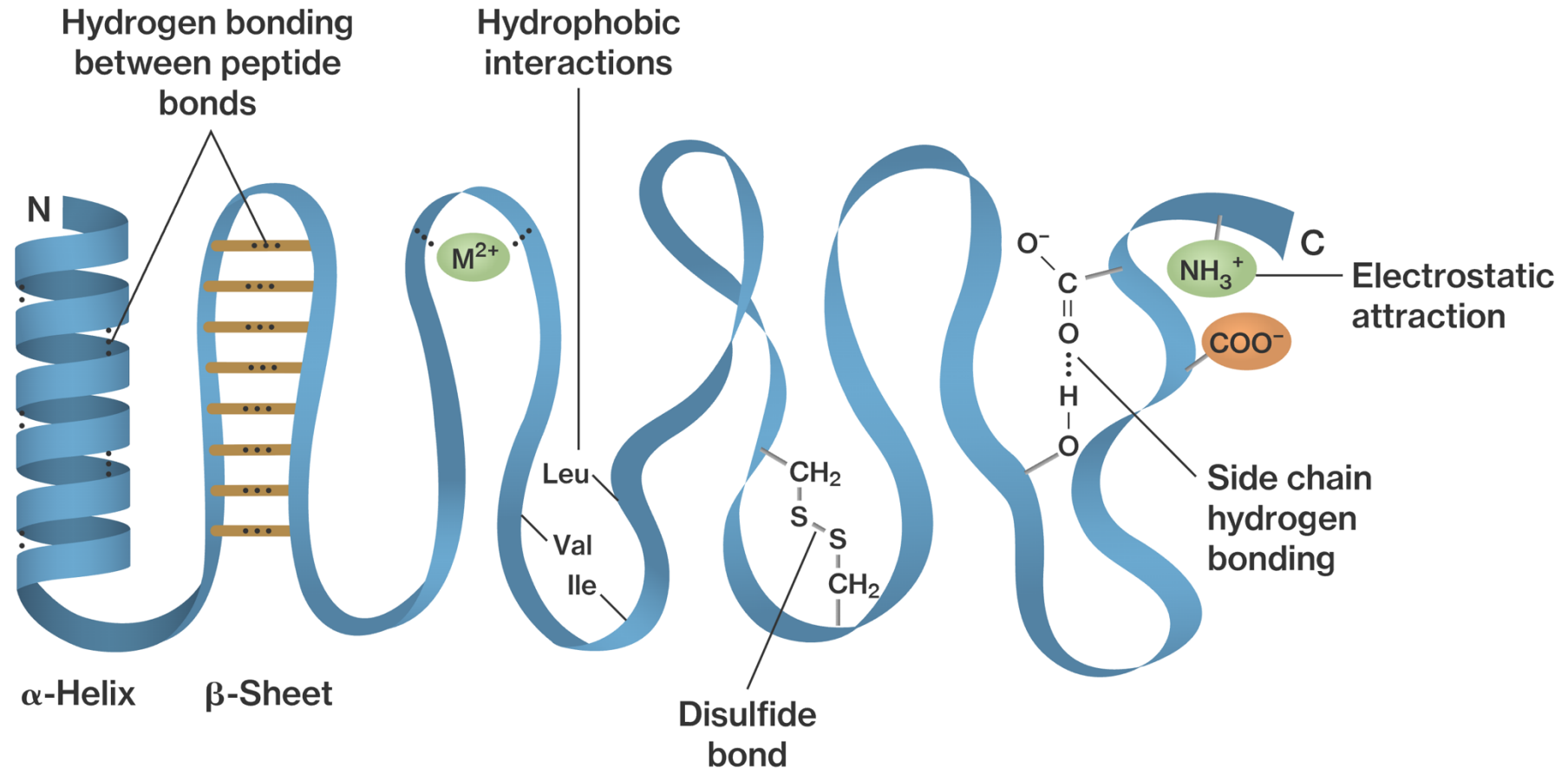
- ❖ **The polypeptide chain folds through interactions involving:**
 - ✓ Backbone conformation
 - ✓ Side chain (R group) interactions
- ❖ The folding results in a **compact, functional 3D structure.**

Tertiary Structure of Proteins / 三级结构



Tertiary Structure of Proteins / 三级结构

- ❖ **Disulfide bonds:**
covalent stabilization
- ❖ **Hydrogen bonds:** polar interactions
- ❖ **Salt bridges:** charge-charge attraction
- ❖ **Hydrophobic effect:** drives folding
- ❖ **Van der Waals:** fine-tunes packing



Tertiary Structure of Proteins / 三级结构

Covalent Bonds

Peptide bond

Disulfide bond

90kcal/mol

Ionic interactions



3kcal/mol

Hydrogen bonds



1kcal/mol

Hydrophobic interactions



1kcal/mol

Van der Waals forces



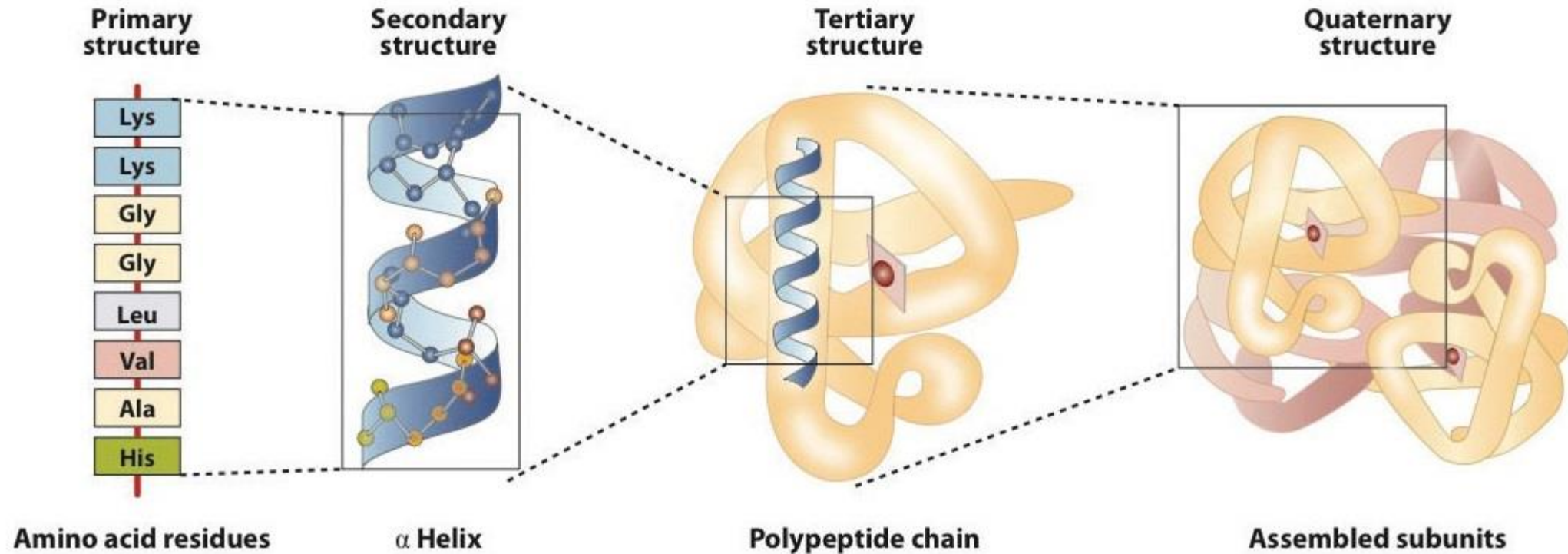
0.1kcal/mol

Noncovalent Interactions

**Individually weak,
but collectively strong**

Noncovalent interactions are much weaker than covalent bonds, but they are the primary forces stabilizing tertiary structure.

Protein quaternary structure / 四级结构



Protein quaternary structure refers to the structure of proteins which are themselves composed of two or more protein chains (also referred to as **subunits**).

Outline

- About Protein

- Amino Acids
氨基酸

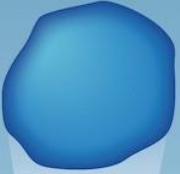
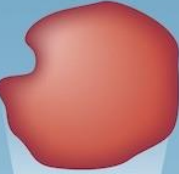
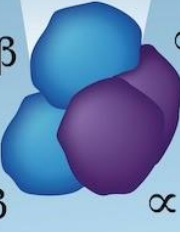
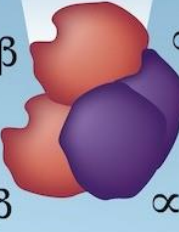
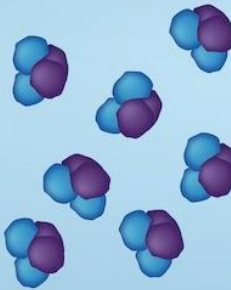
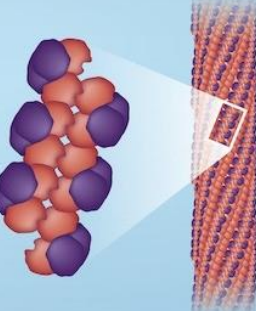
- Protein Structure
蛋白质分子结构

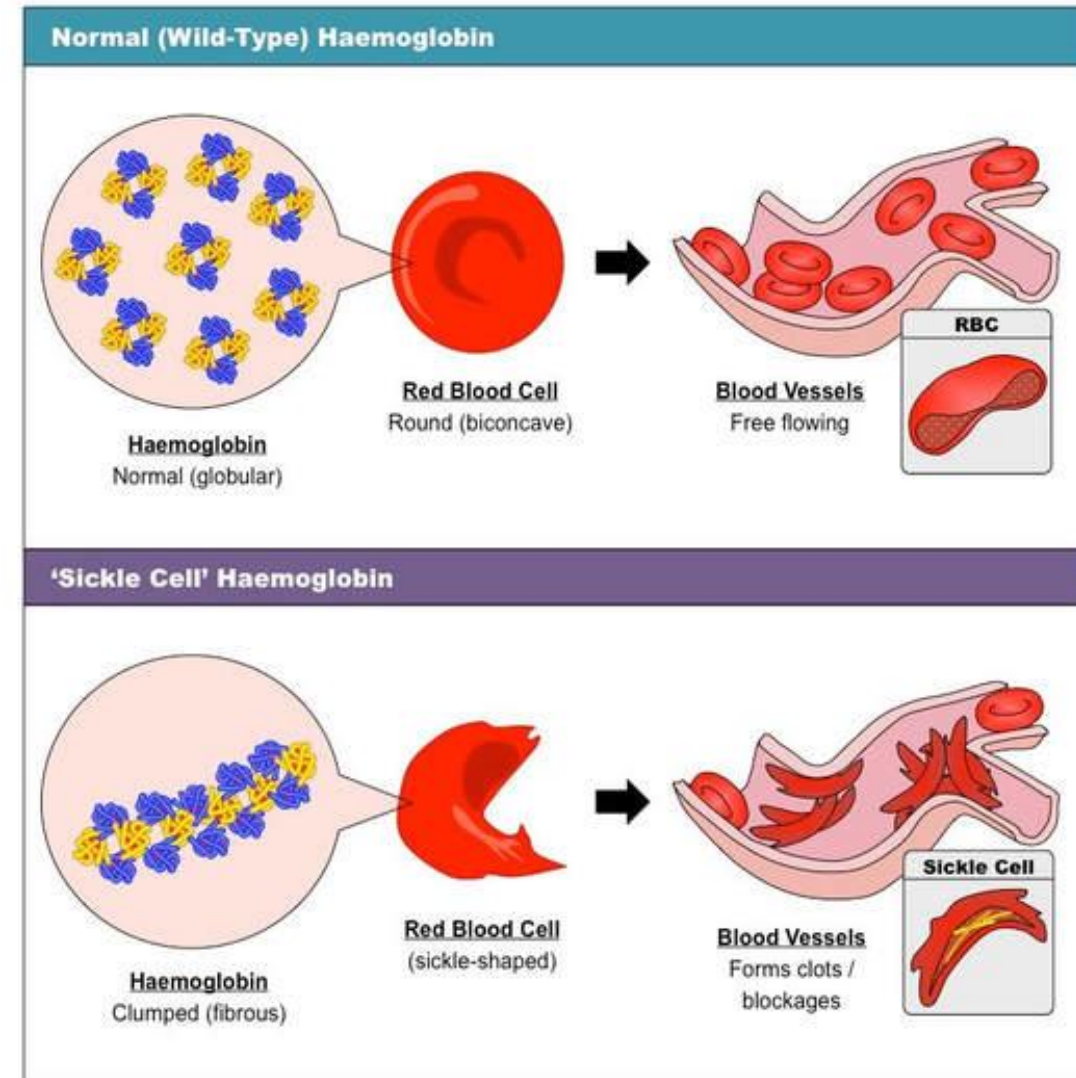
- **Structure–Function Relationship**
结构与功能的关系

- **Physicochemical Properties of Proteins**
理化性质

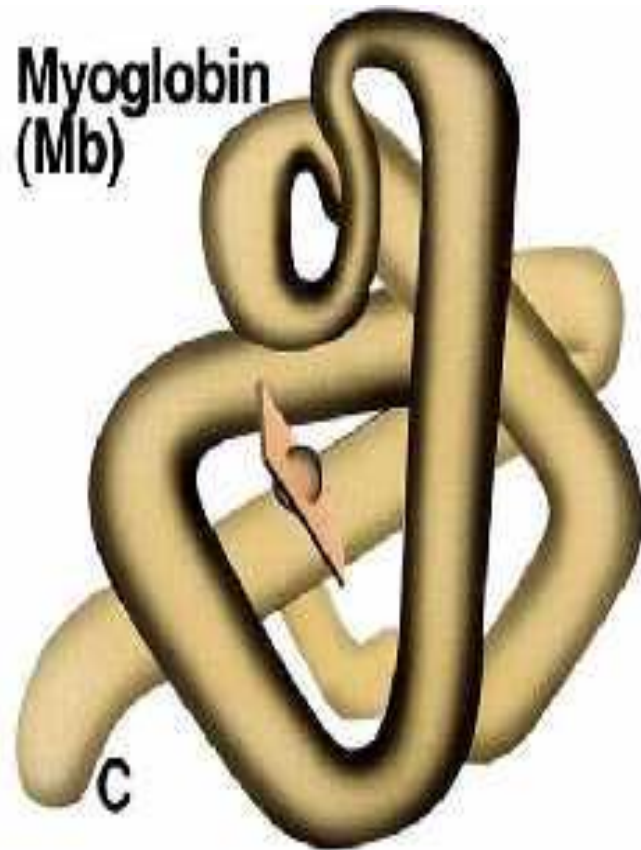
- **Protein Separation and Applications**
分离与应用

Structure determines function

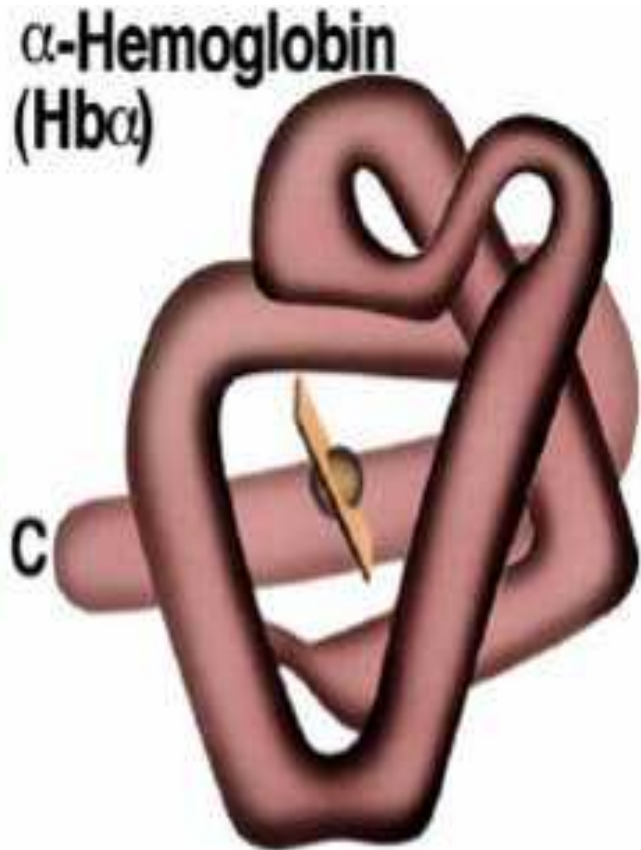
	Normal	Sickle-Cell
Primary Structure	1 2 3 4 5 6 7 Val His Leu Thr Pro Glu Glu	1 2 3 4 5 6 7 Val His Leu Thr Pro Val Glu
Secondary and Tertiary Structures	 Normal β Subunit	 Sickle-Cell β Subunit
Quaternary Structure	 Normal Hemoglobin	 Sickle-Cell Hemoglobin
Function	 Proteins Do Not Associate with One Another; Each Carries Oxygen	 Proteins Aggregate Into a Fiber; Capacity to Carry Oxygen is Reduced



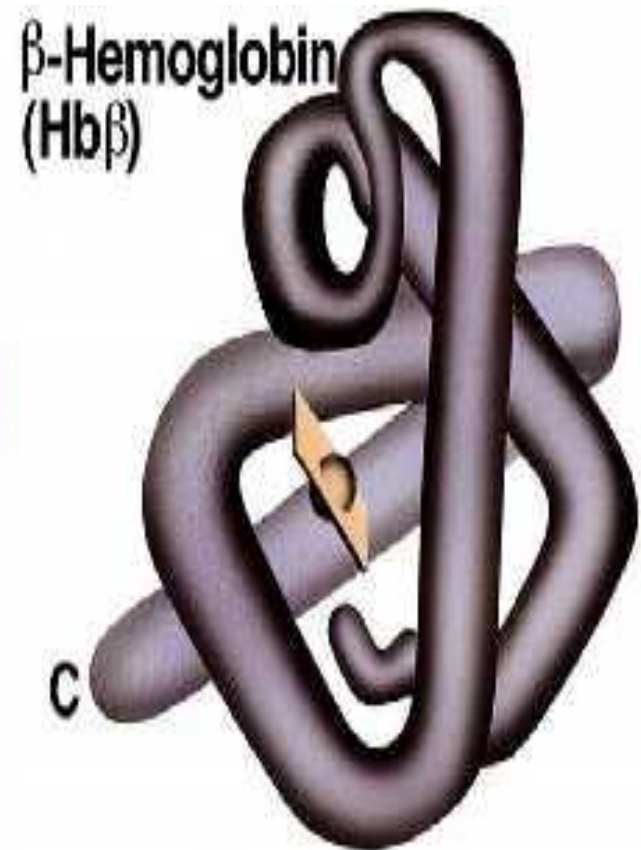
Amino acid sequences differ significantly, but similar biological functions



肌红蛋白



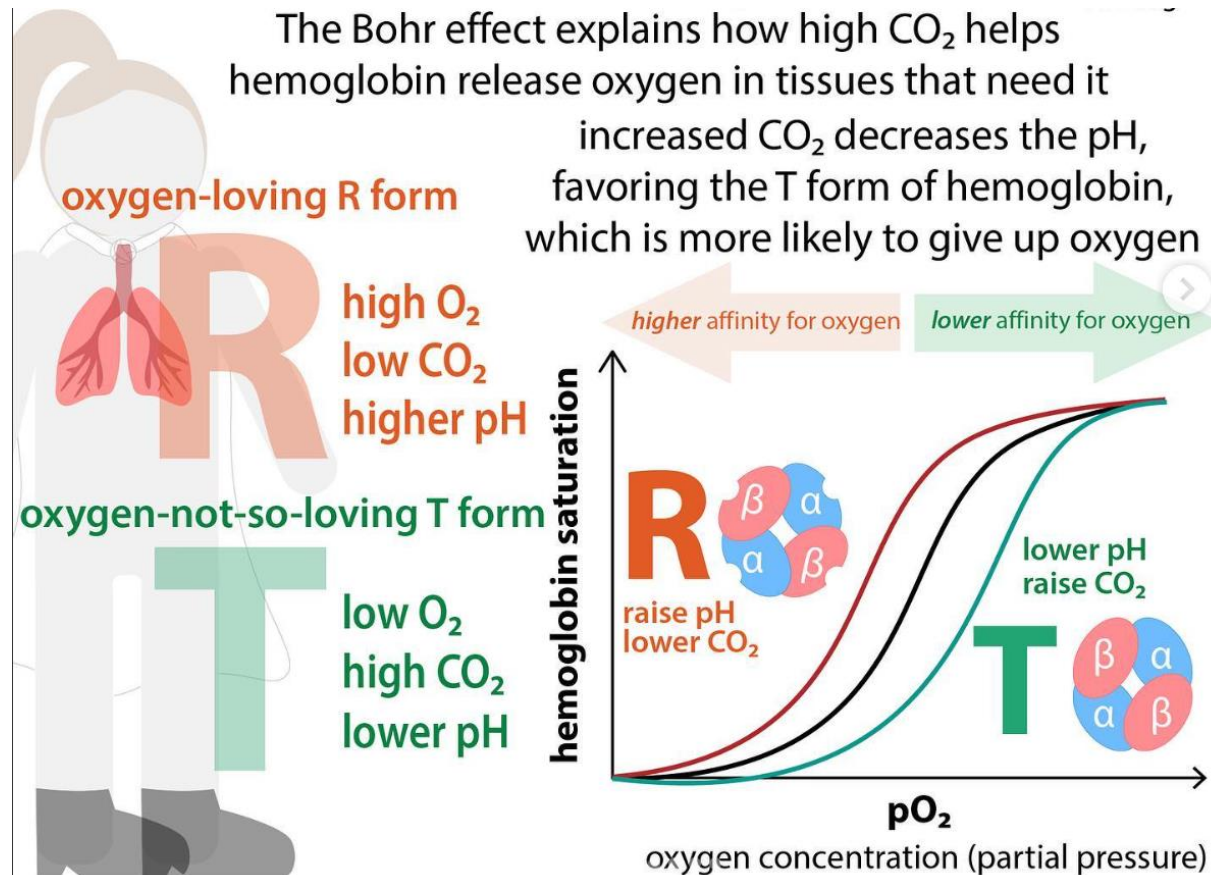
血红蛋白 α



血红蛋白 β

Allosteric Change / 变构现象

External factors (e.g., ligand binding, pH, temperature) induce changes in protein conformation, leading to altered function.



Outline

- About Protein

- Amino Acids
氨基酸

- Protein Structure
蛋白质分子结构

- Structure–Function Relationship
结构与功能的关系

- Physicochemical Properties of Proteins
理化性质

- Protein Separation and Applications
分离与应用

Physical Properties

- ❖ **Colloidal nature / 胶体性质**
- ❖ **Amphoteric behavior, can act as acids or bases**
- ❖ **Solubility (depends on pH, ionic strength, temperature)**
- ❖ **Optical properties (~280 nm)**
- ❖ **High viscosity due to large molecular size**

Physical Properties

1. Isoelectric Point (pI)

- ❖ Proteins contain **ionizable groups** and behave as **ampholytes**
- ❖ **Isoelectric point (pI):**
 - ✓ pH at which **net charge = 0**
 - ✓ Protein exists as a **zwitterion**
 - ✓ **No migration in an electric field**

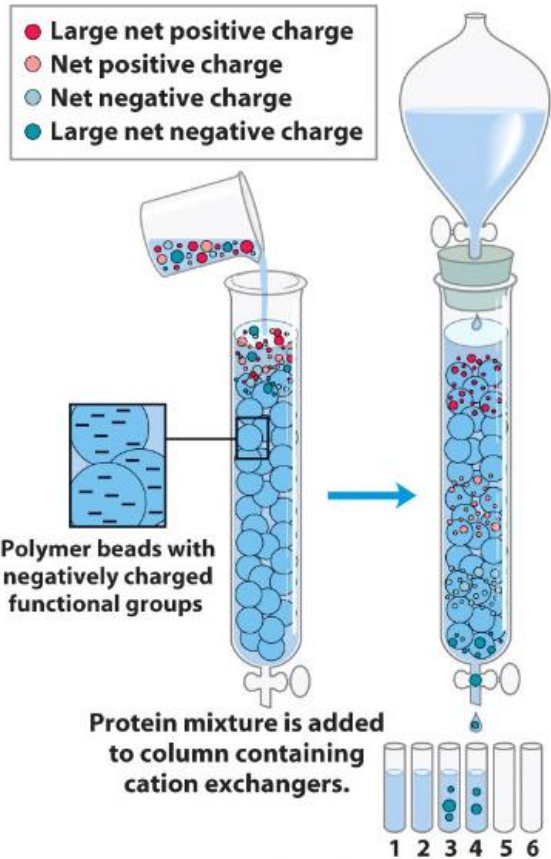
pI is widely used in protein purification

2. Electrophoretic Behavior

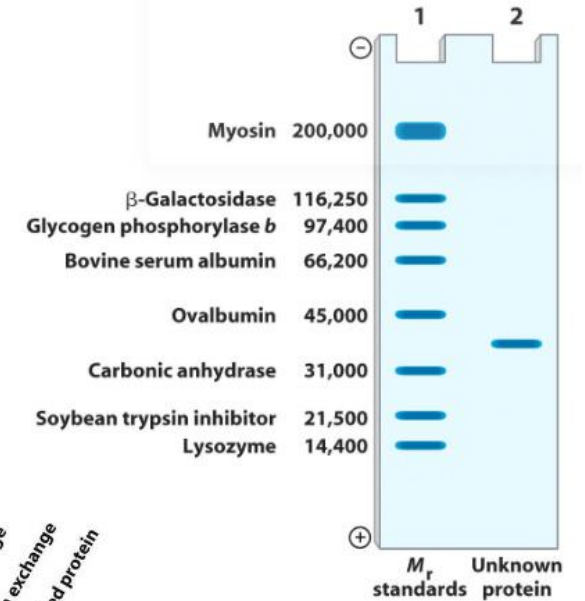
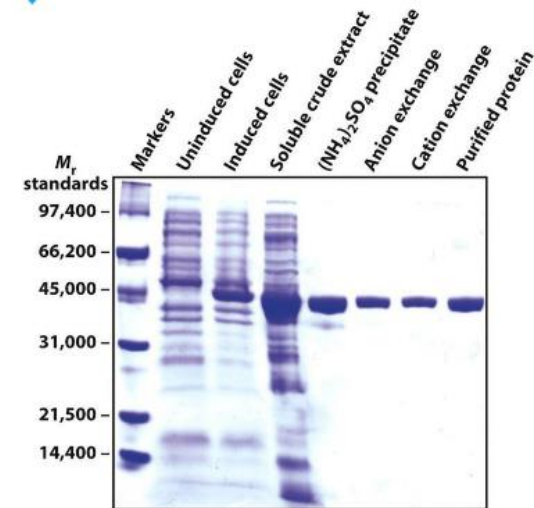
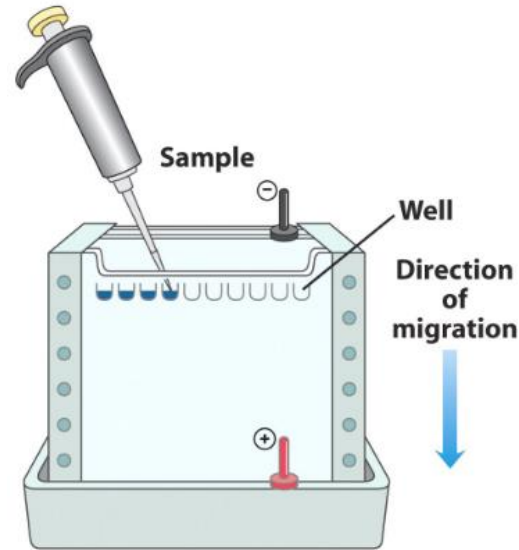
- ❖ **In solution, proteins carry net charge depending on pH:**
 - ✓ $\text{pH} > \text{pI} \rightarrow$ net negative
 - ✓ $\text{pH} < \text{pI} \rightarrow$ net positive
- ❖ **Migration depends on:**
 - ✓ Net charge
 - ✓ Molecular size
 - ✓ Shape

Protein separation purification

Physical Properties

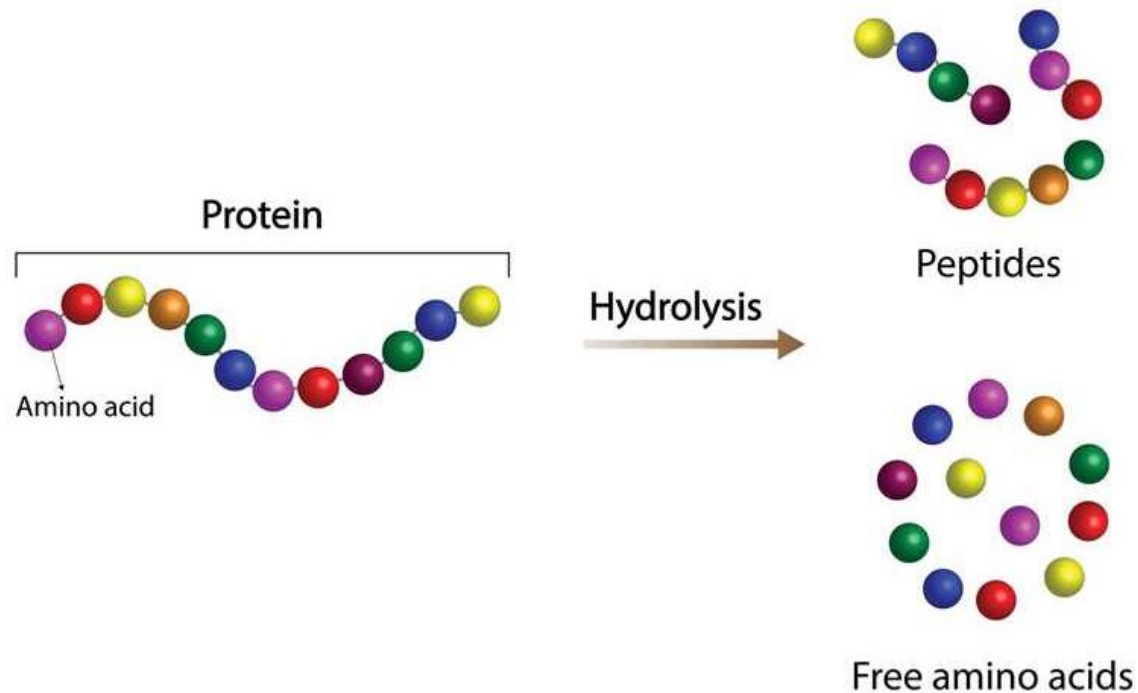


Proteins move through the column at rates determined by their net charge at the pH being used. With cation exchangers, proteins with a more negative net charge move faster and elute earlier.



Chemical Properties

- ❖ **Acid–base properties** (detailed in amino acid section)
- ❖ **Hydrolysis:** proteins can be hydrolyzed into peptides and amino acids
Occurs via acid, base, or enzymatic digestion



Chemical Properties

❖ Denaturation / 变性

- ✓ Loss of **native structure** (secondary, tertiary, quaternary)
- ✓ Caused by:
 - ✓ Heat
 - ✓ pH changes
 - ✓ organic solvents
 - ✓ heavy metals
 - ✓ X-ray
- ✓ Leads to **loss of function**

Renaturation?

Chemical Properties

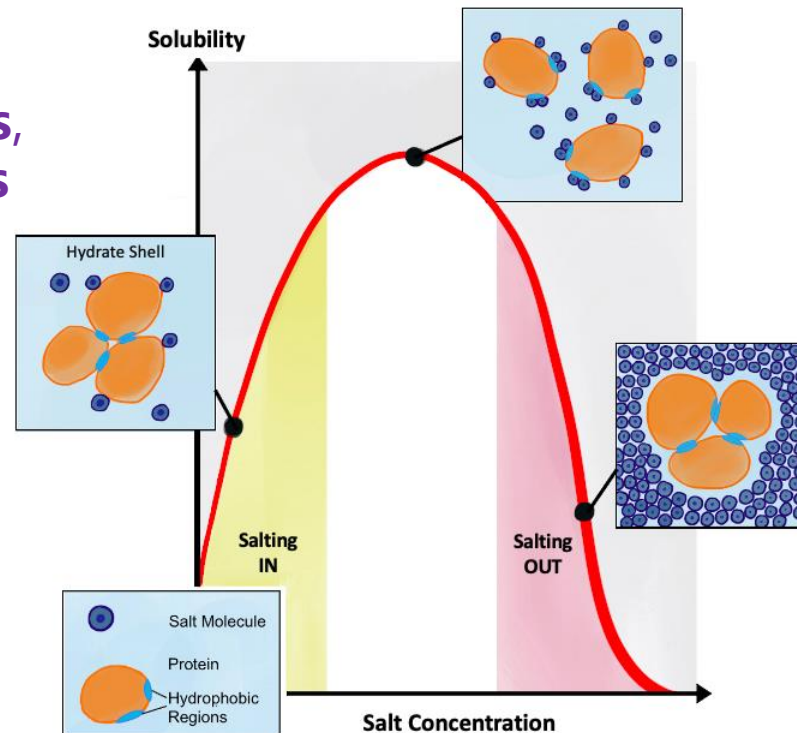
Precipitation / 沉淀

1. Salting Out and In / 盐析与盐溶

Addition of **high concentrations of neutral salts** (e.g., $(\text{NH}_4)_2\text{SO}_4$, Na_2SO_4 , NaCl) leads to **protein precipitation from solution**

At **low salt concentrations**, protein solubility **increases**

- ❖ Ions **shield surface charges**
- ❖ Reduce protein–protein interactions



- ❖ Salt ions **compete with proteins for water molecules**
- ❖ Reduce the **hydration shell** around proteins
- ❖ Decrease protein solubility: **aggregation and precipitation**

Chemical Properties

Precipitation / 沉淀

2. Organic solvents

Examples: Ethanol, methanol, acetone

Mechanism:

- ❖ **Lower the dielectric constant** of the solution
- ❖ **Disrupt the hydration shell** around proteins
- ❖ Increase **protein–protein interactions**

Chemical Properties

Precipitation / 沉淀

3. Metal Ion

Examples: Hg^{2+} , Pb^{2+} , Cu^{2+} , Ag^{+}

Mechanism:

- ❖ Bind to **negatively charged groups** (e.g., $-\text{COO}^{-}$, $-\text{SH}$) in proteins
- ❖ Form **insoluble complexes (metal-protein salts)**

Toxicology note (application)

Proteins in **milk or egg white** can bind heavy metals; therefore, help **reduce absorption in poisoning cases**

Chemical Properties

Precipitation / 沉淀

3. Acids / Alkaloid Reagents

Mechanism

- ❖ Form **insoluble complexes with charged groups** in proteins
- ❖ Often cause **denaturation + precipitation**

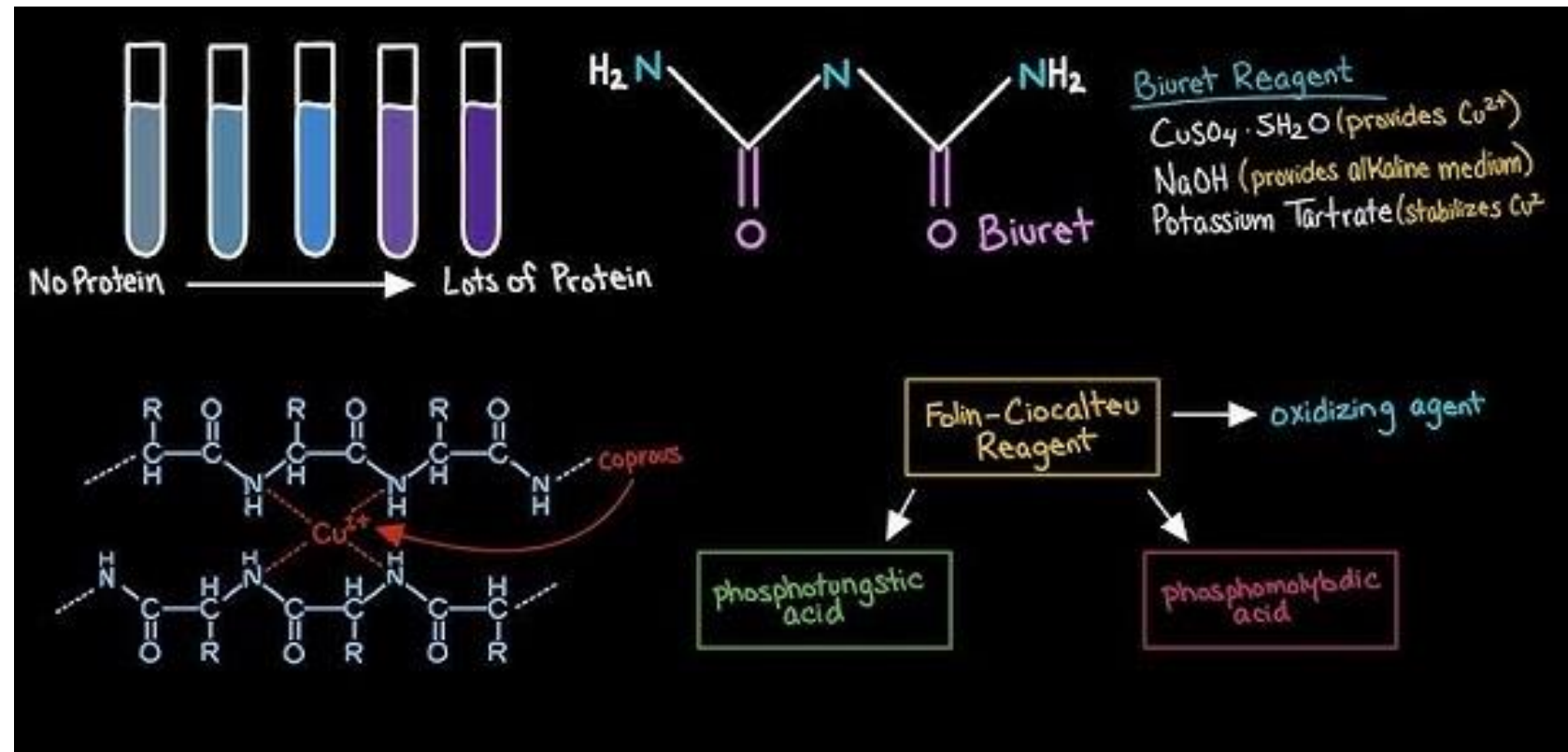


Chemical Properties

Chemical reactions

1. Biuret reaction / 双缩脲反应

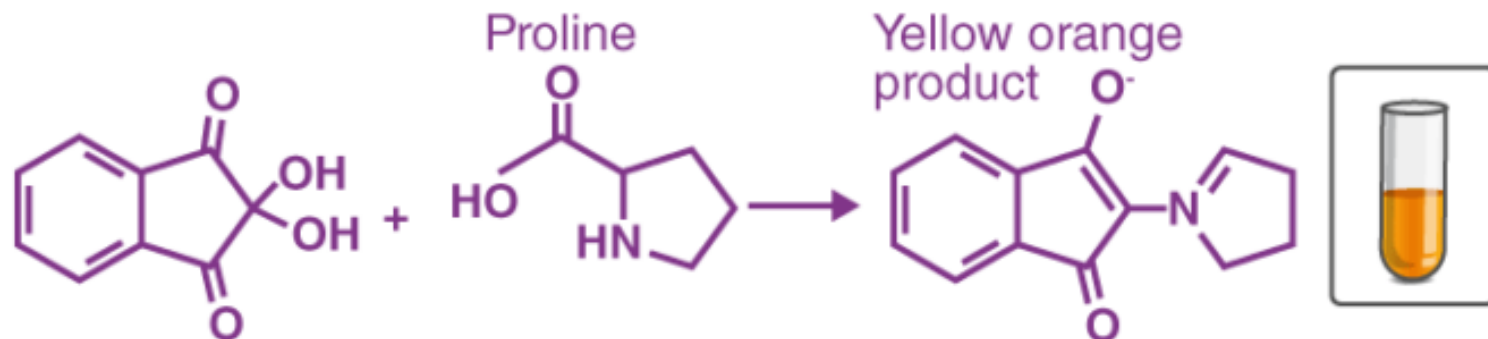
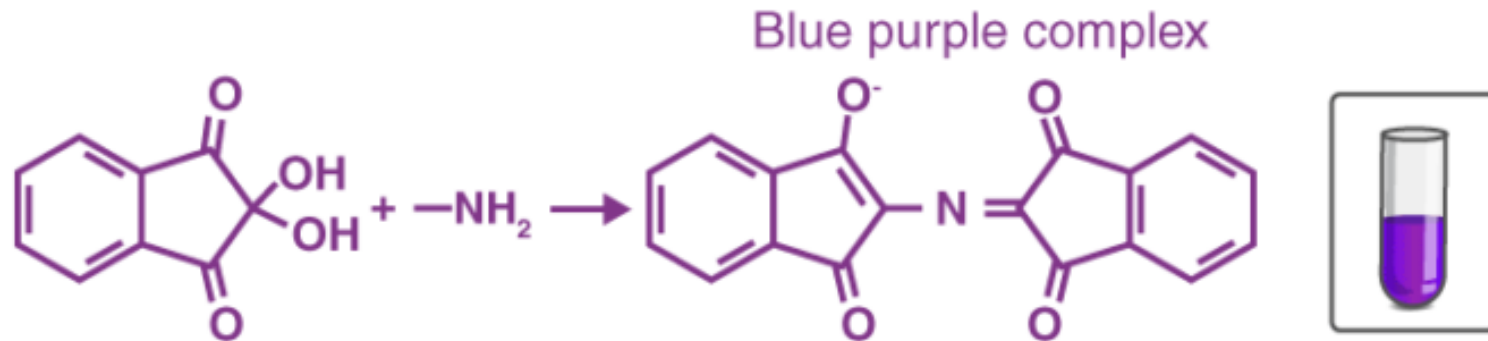
In a strongly alkaline environment, Cu^{2+} from the Biuret reagent form a coordination complex with the N atoms of the peptide bonds, resulting in a color shift from **blue** to **violet or purple**.



Chemical Properties

Chemical reactions

2. Ninhydrin reaction / 茚三酮

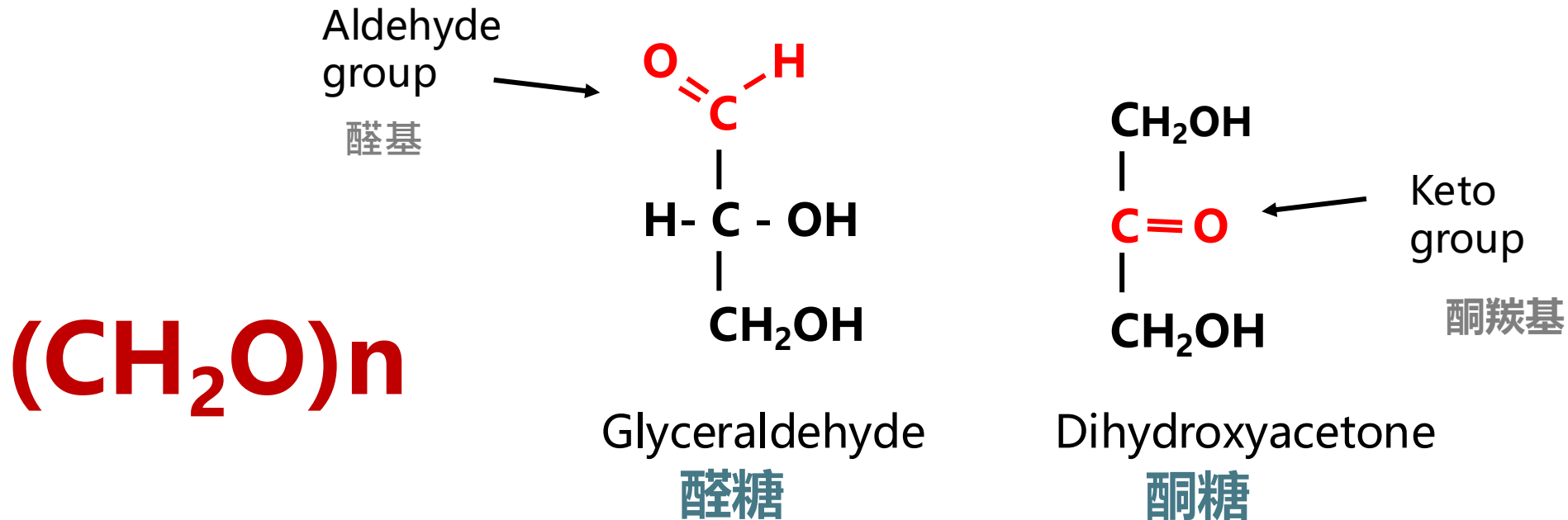


A top-down view of a variety of carbohydrate-rich foods arranged on a wooden surface. The items include several types of pasta (farfalle, shells, and long ribbons), round and braided breads, a cornucopia of corn (two ears), red and yellow potatoes, three ripe yellow bananas, a jar of honey with a wooden dipper, dates, walnuts, and pretzels. The background is filled with grains and seeds.

3/4 Carbohydrates

What is Carbohydrates

Polyhydroxy aldehydes or ketones, or substances that yield these compounds on hydrolysis



Due to asymmetric carbon atoms, monosaccharides exhibit optical isomerism, (+) and (-), as well as D- and L-enantiomers.

What is Carbohydrates

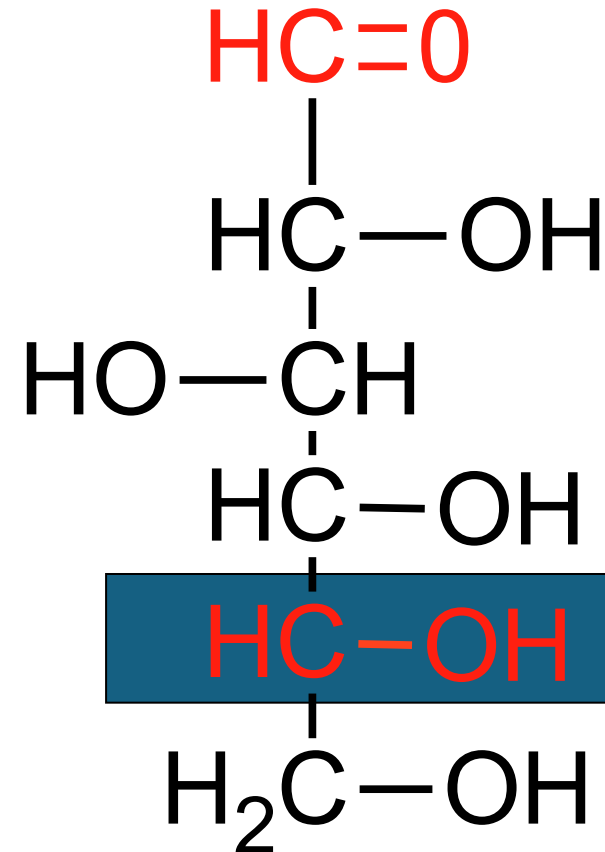
Overall D/L configuration



Classification (aldose/ketose)

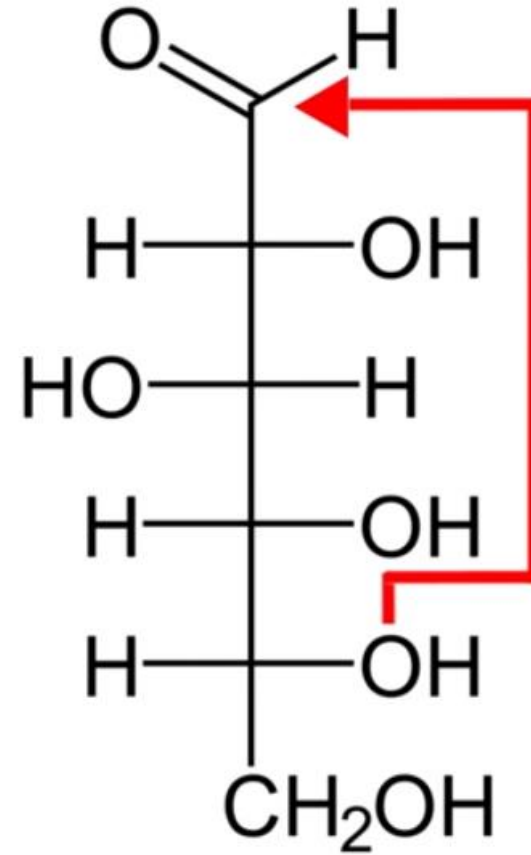
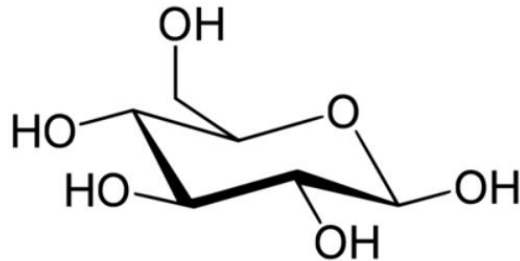
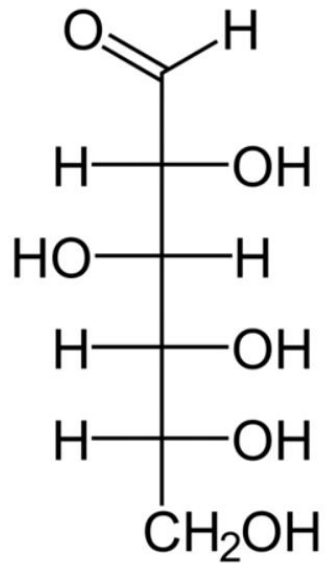


Determine specific name

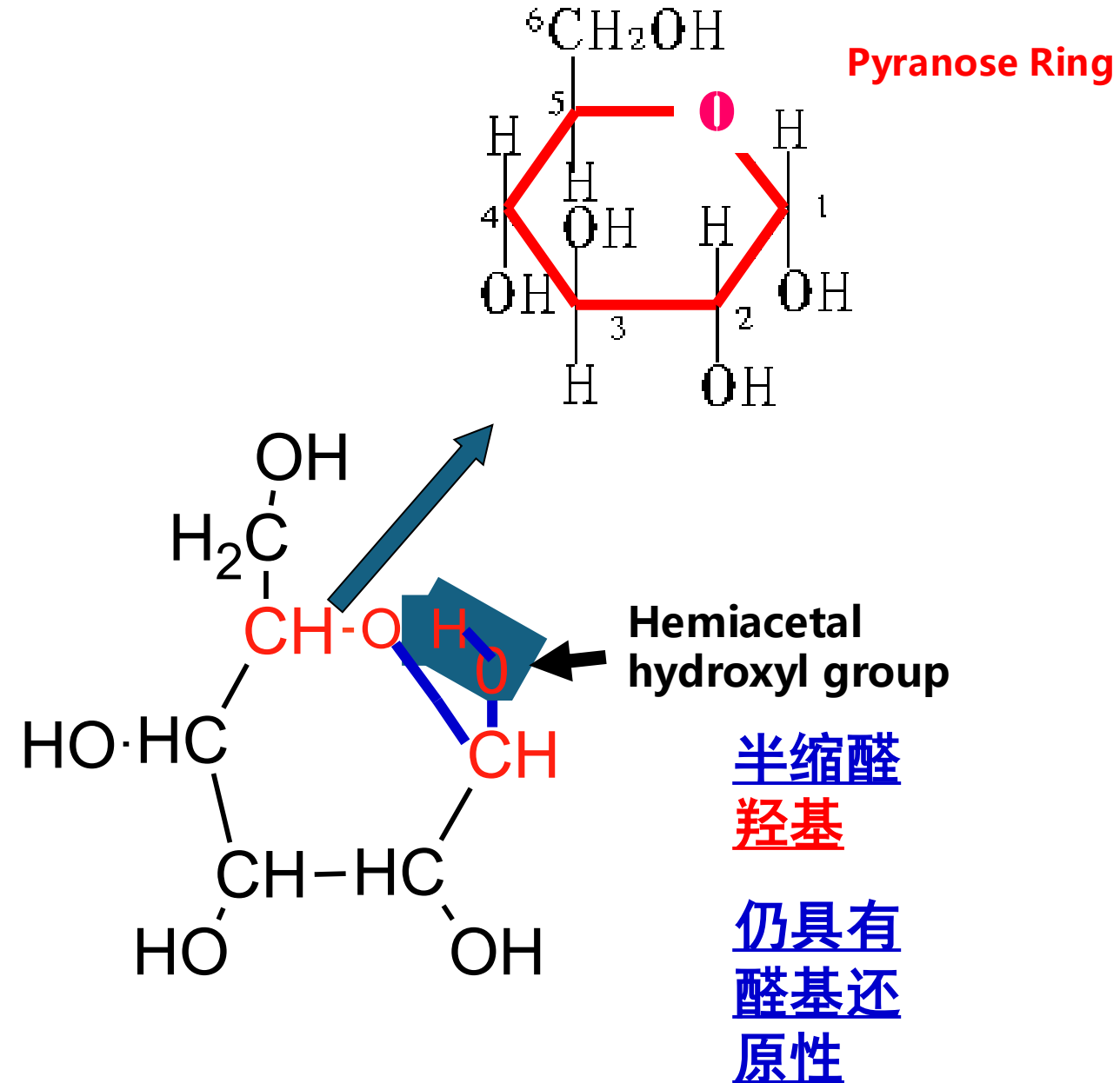
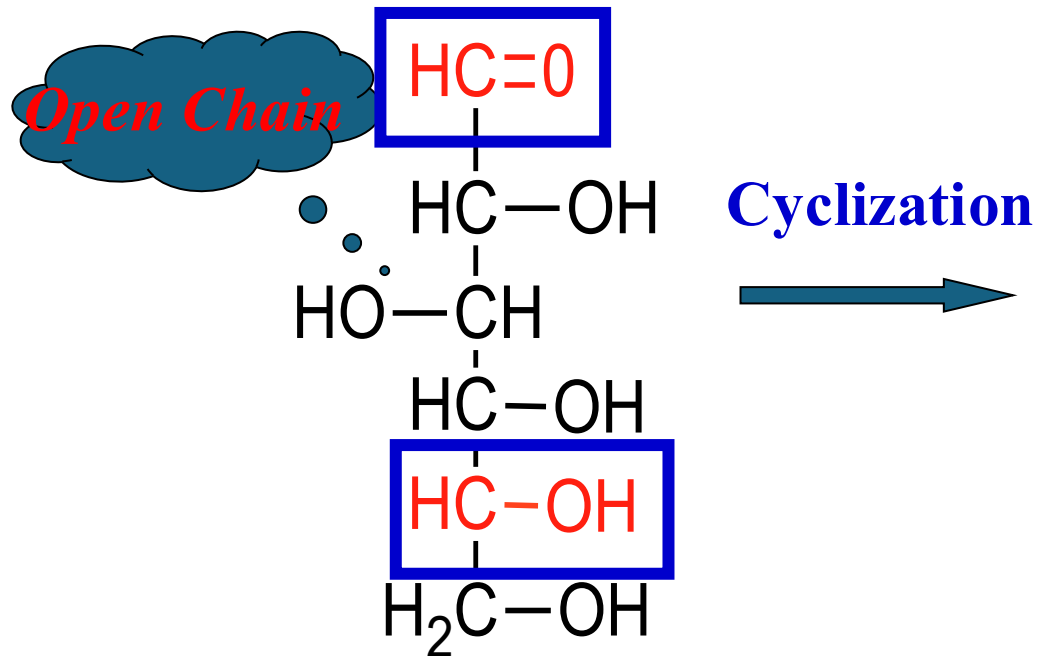


D-Glucose

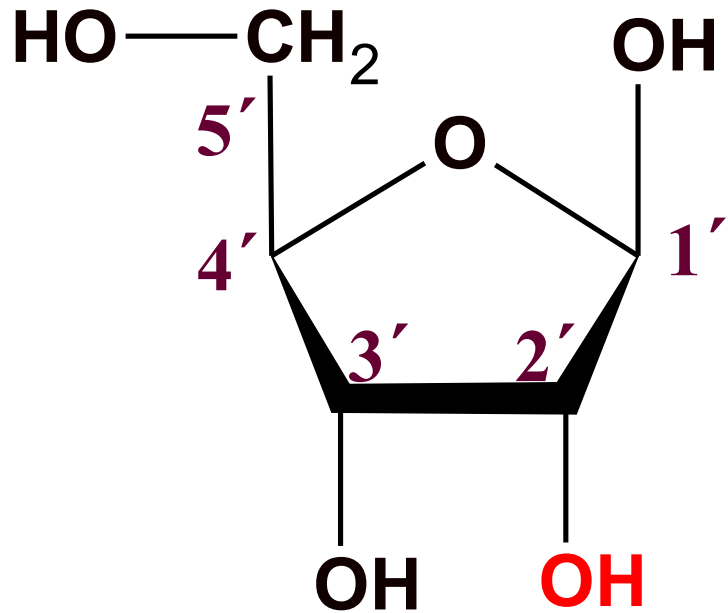
What is Carbohydrates



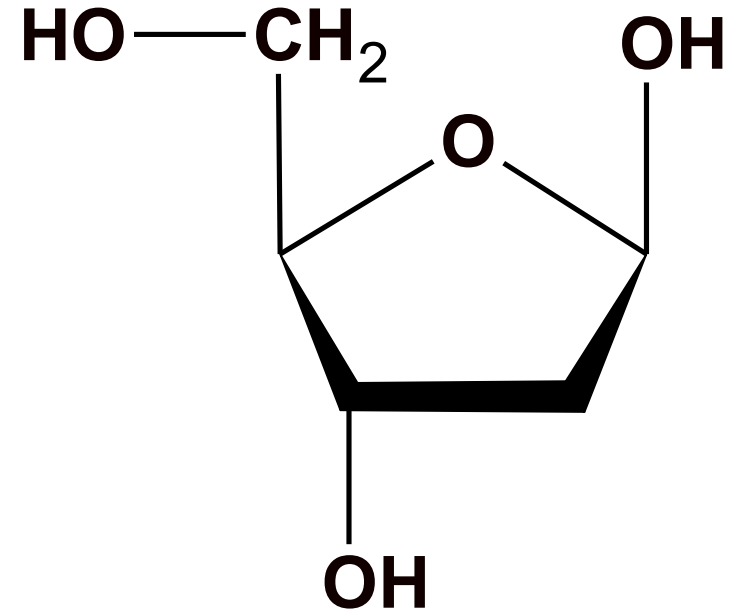
What is Carbohydrates



What is Carbohydrates



核糖(ribose)
(RNA)



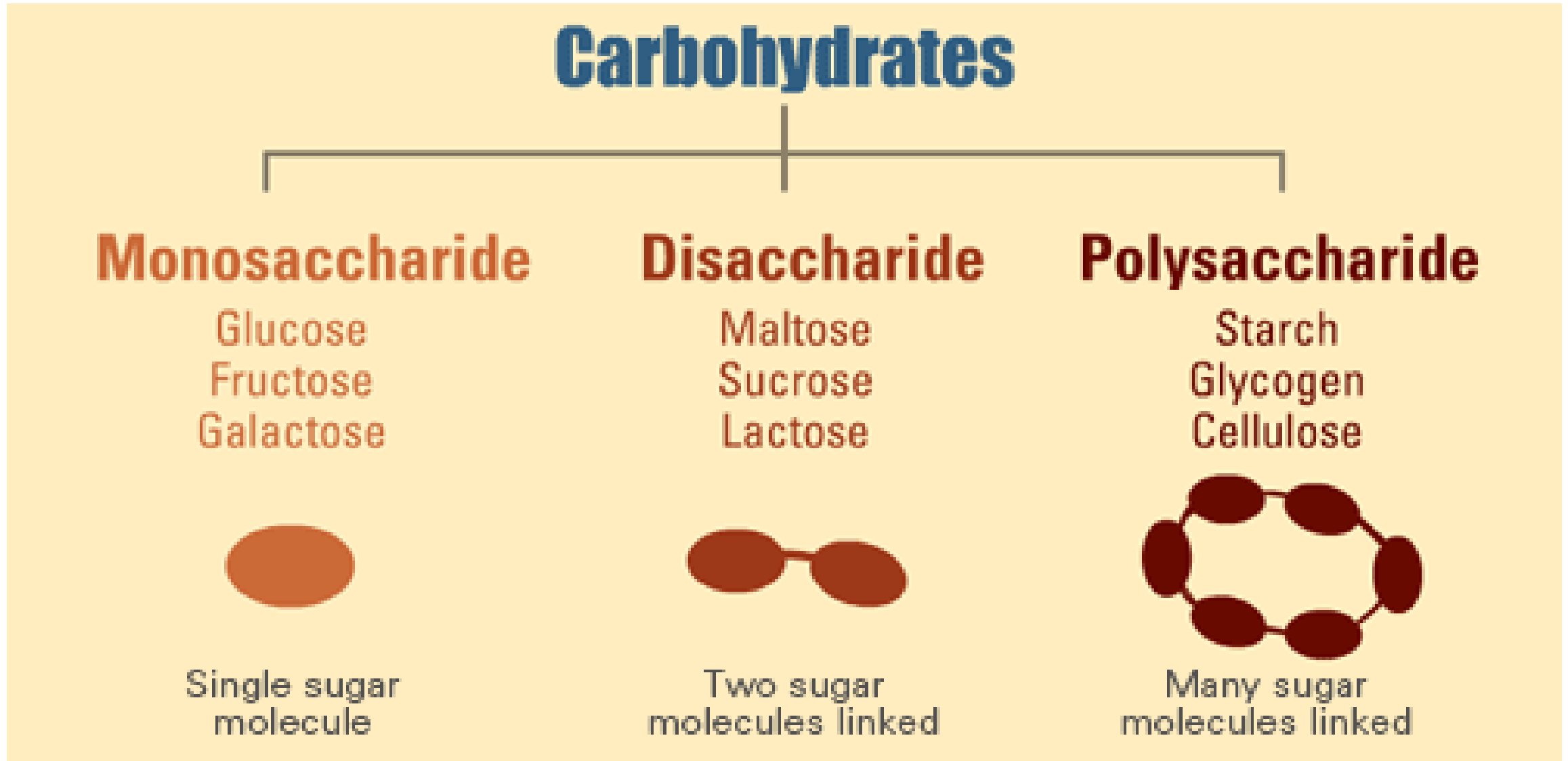
脱氧核糖(deoxyribose)
(DNA)

What is Carbohydrates

Based on the sugar units they contain, carbohydrates are classified into three (four) groups, as

- ❖ **Monosaccharides / 单糖**
- ❖ **Disaccharides / 二糖**
- ❖ **Polysaccharides / 多糖**
- ❖ **Oligosaccharides (a small polymer of sugar)**

Carbohydrate Classification Scheme



Monosaccharides / 单糖

- ❖ Monosaccharides are simple sugars, consisting of single polyhydroxy aldehyde or ketone unit.
- ❖ They cannot be hydrolyzed to yield simpler forms of sugar.

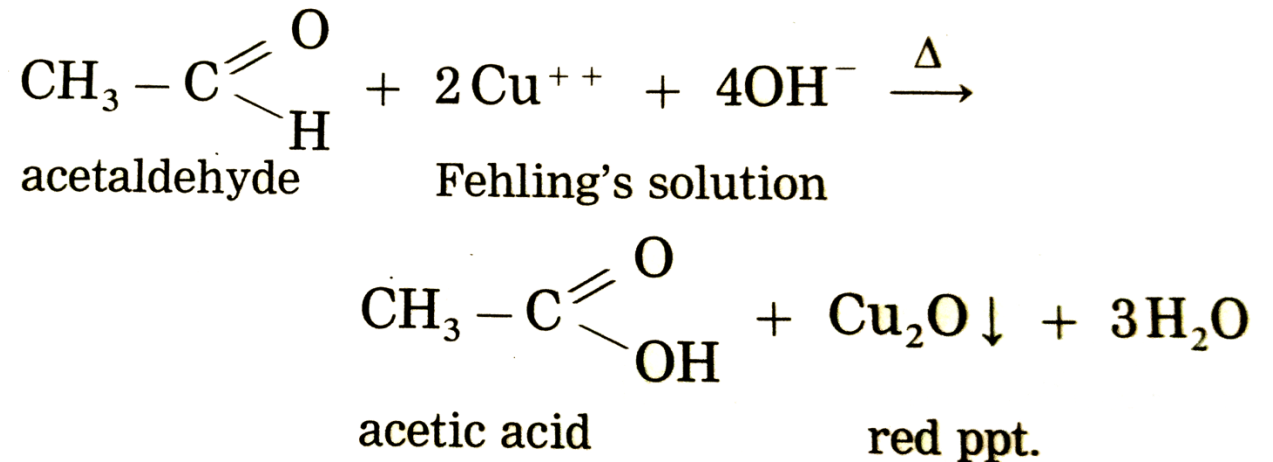
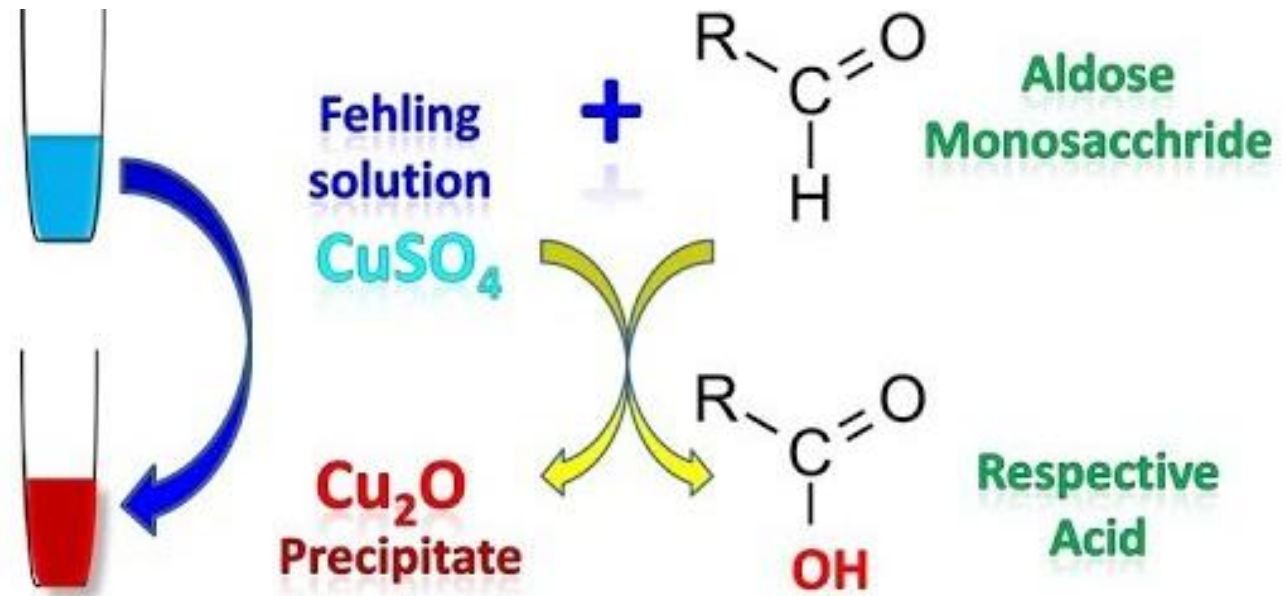
# carbons	Name	Example
3	Trioses/ 三碳糖	Glyceraldehyde/ 甘油醛
4	Tetroses / 四碳糖	Erythrose/ 赤藓糖
5	Pentoses/ 五碳糖	Ribose/ 核糖
6	Hexoses/ 六碳糖	Glucose, Fructose/ 葡萄糖、果糖
7	Heptoses/ 七碳糖	Sedoheptulose/ 景天庚酮糖
9	Nonoses/ 九碳糖	Neuraminic acid/ 神经氨酸

Physical and Chemical Properties of Monosaccharides

- ❖ **Optical Activity/ 旋光性**
- ❖ **Solubility/ 溶解度**
- ❖ **Sweetness/ 甜度** (technically a sensory perception rather than a strict physicochemical property)
- ❖ **Reducing/ 还原性**

Reducing sugars

Sugars capable of reducing Fehling's reagent are called reducing sugars

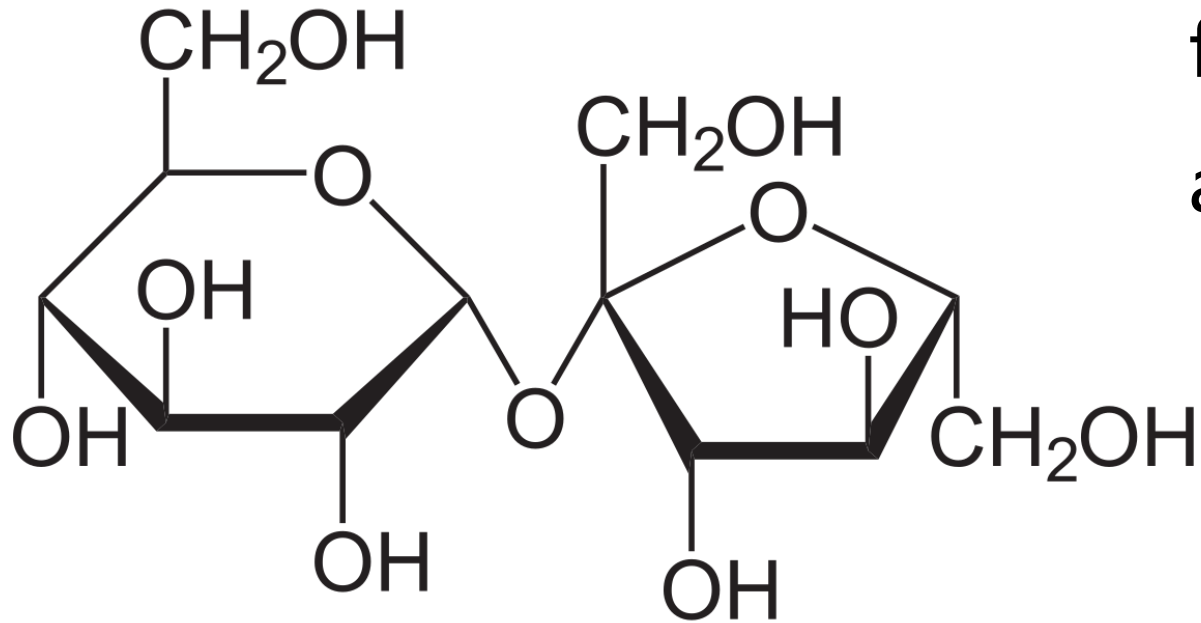


Disaccharides / 二糖

- ❖ Formed by the condensation of two identical or different monosaccharide molecules; can be considered a type of glycoside.
- ❖ Common naturally occurring disaccharides include **Sucrose (蔗糖)**, **Maltose (麦芽糖)**, **Lactose (乳糖)** and **Trehalose (海藻糖)**, and among them, sucrose, maltose, and lactose are the three most commonly discussed in textbooks.
- ❖ Other disaccharides exist in bound forms (e.g., cellobiose).

Disaccharides / 二糖

Sucrose



Sucrose [α -D-glucosyl-(1,2)- β -D-fructoside]

蔗糖[α -D-葡萄糖(1,2) β -D-果糖苷]

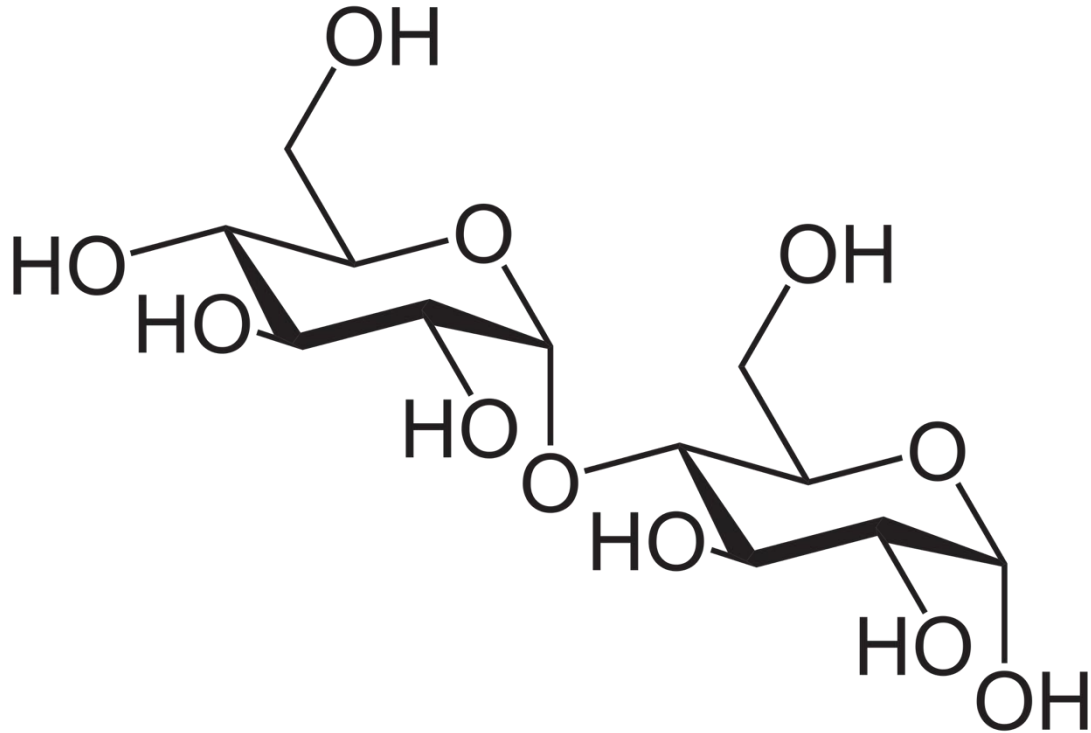
Is the main product of **photosynthesis**, and a primary form of sugar storage and accumulation.

- ❖ In plants, sugar is transported in the form of sucrose.
- ❖ **Non-reducing sugar**

Disaccharides / 二糖

Maltose

A constituent component of starch



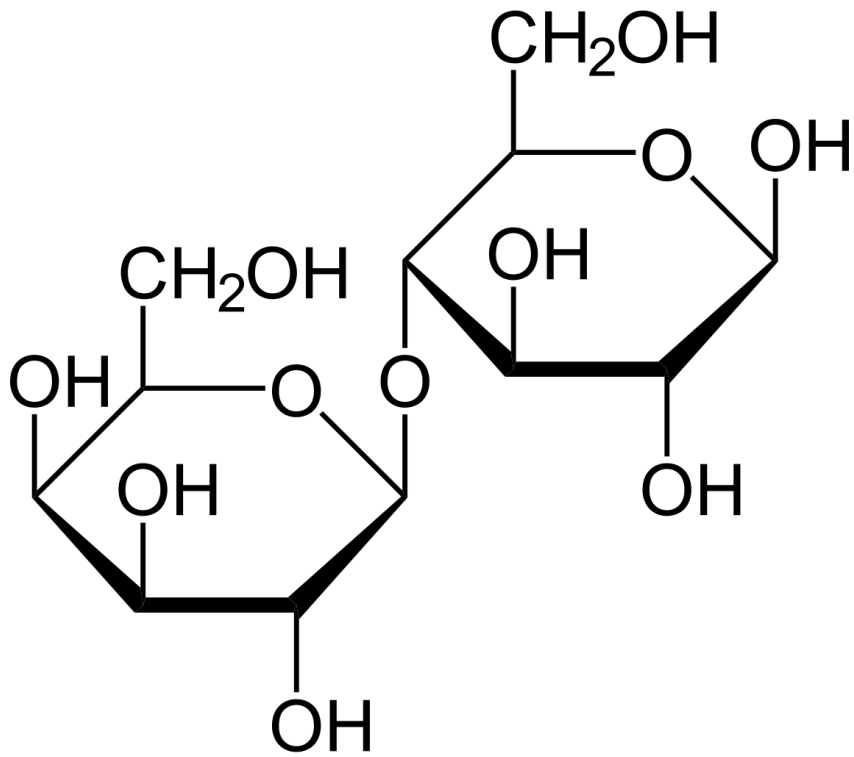
Maltose [α -D-glucosyl-(1,4)- β -D-glucopyranose]

麦芽糖 [α -D-葡萄糖(1,4)D-葡萄糖苷]

- ❖ Like glucose, maltose is a **reducing sugar**
- ❖ It has a sweet taste, but is only about 30–60% as sweet as sugar

Disaccharides / 二糖

Lactose



β -D-galactosyl-(1,4)-D-glucopyranose

乳糖 [β -D-半乳糖(1,4)D-葡萄糖苷]

- ❖ The second most abundant natural disaccharide in nature
- ❖ It is a **reducing sugar**

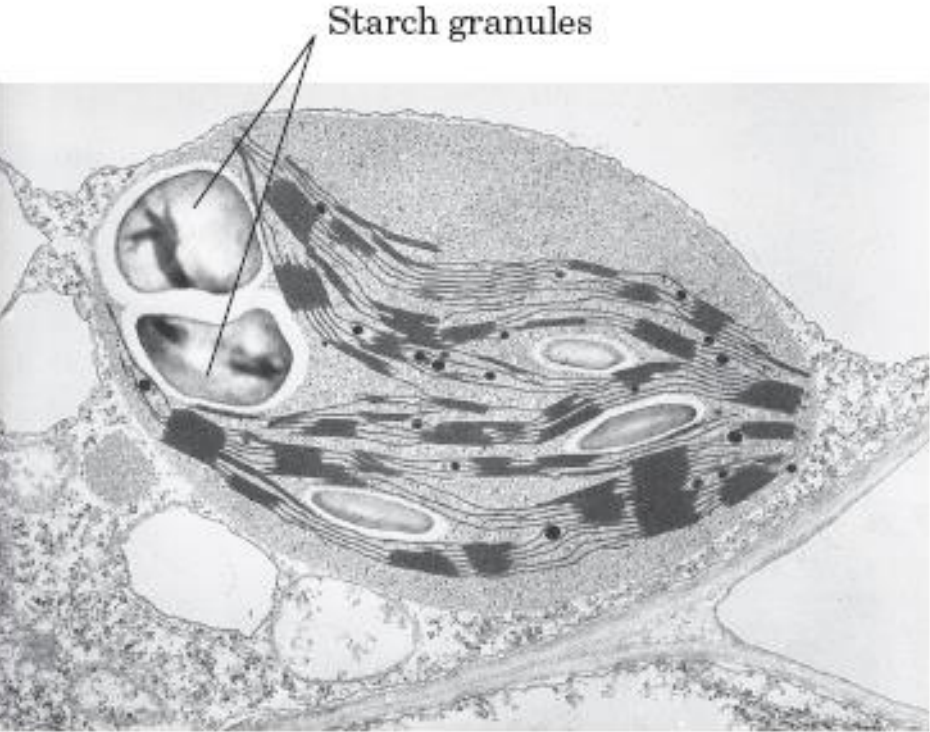
Polysaccharides / 多糖

- ❖ Homopolysaccharides (Homoglycans)/ 同聚多糖: Starch (淀粉), Cellulose (纤维素) , Glycogen (糖原), Pectin (果胶), Agar (琼脂).
- ❖ Heteropolysaccharides (Heteroglycans) /杂聚多糖. e.g.
Hemicellulose: Composed of D-Xylose, Glucose, Mannose, D-Galactose, Hexuronic acids, etc.半纤维素由D-木糖、葡萄糖、甘露糖、D-半乳糖、己糖醛酸等聚合

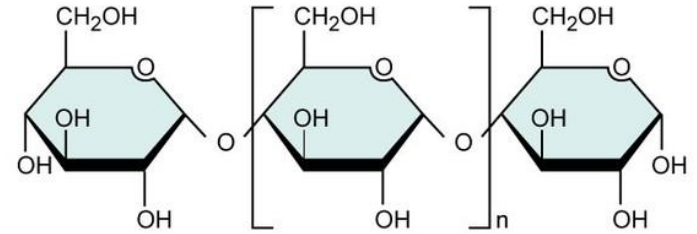
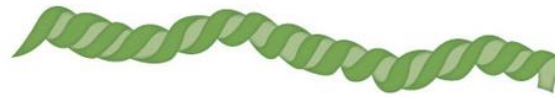
Polysaccharides / 多糖

Starch

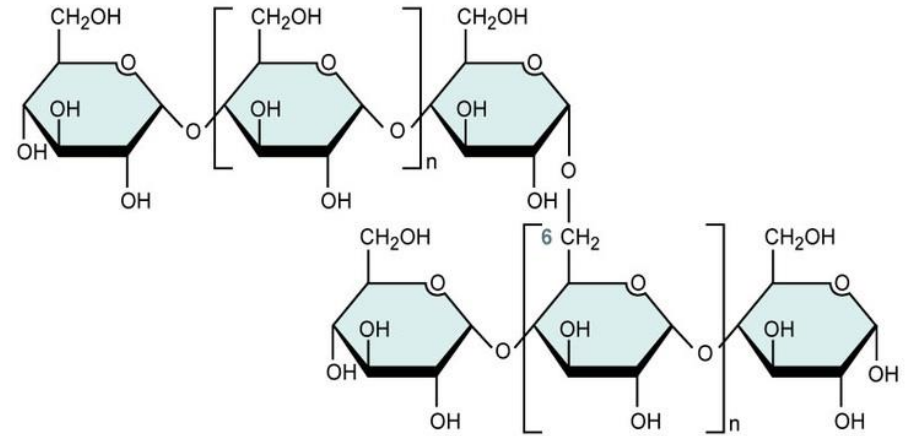
Natural starch contains two components: amylose and amylopectin.



直链淀粉
Amylose



支链淀粉
Amylopectin



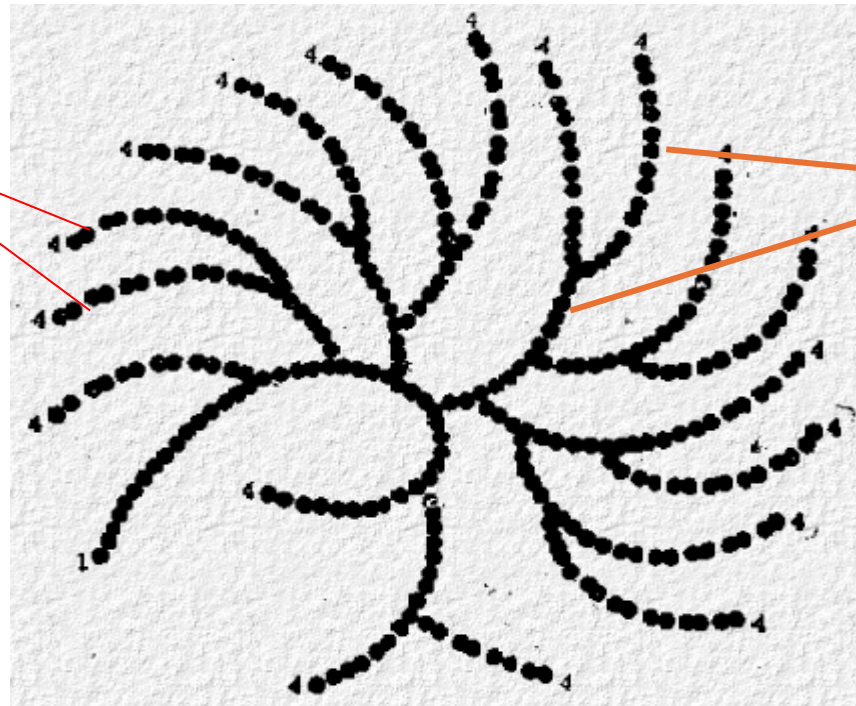
优质大米 ≈ 低直链淀粉大米

Polysaccharides / 多糖

Starch

- ❖ α -Amylase **randomly cleaves internal α -1,4-glycosidic linkages in starch**. It acts within the polysaccharide chain, as an **endoglycosidase**. The main products are **maltose, maltotriose, and branched dextrans**.
- ❖ β -Amylase removes **maltose units sequentially from the non-reducing ends** of starch by cleaving **α -1,4-glycosidic linkages**. It acts from the chain end, as an **exoglycosidase**.

β -淀粉酶
 β -Amylase

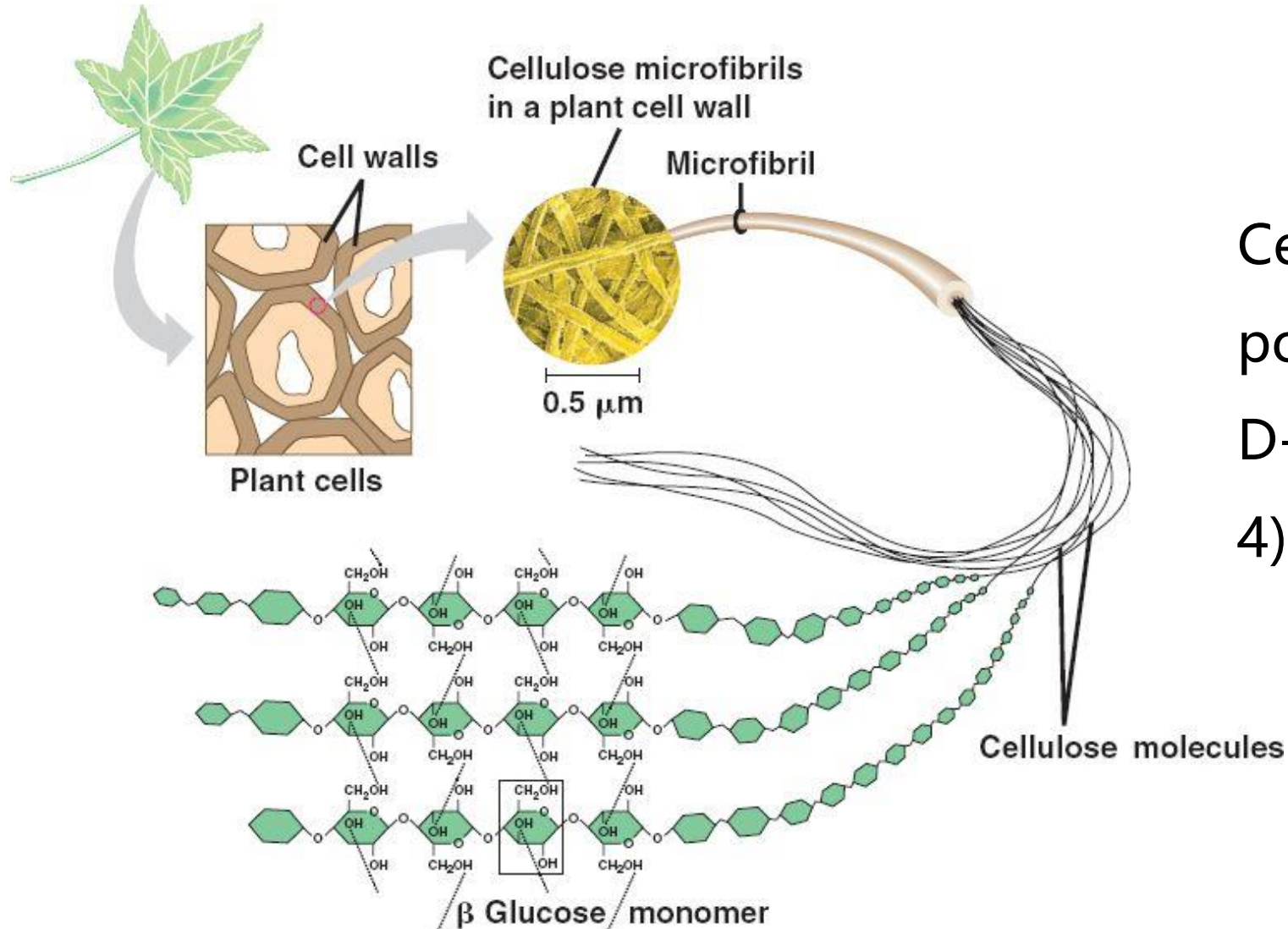


α -淀粉酶
 α -Amylase

Polysaccharides / 多糖

Cellulose

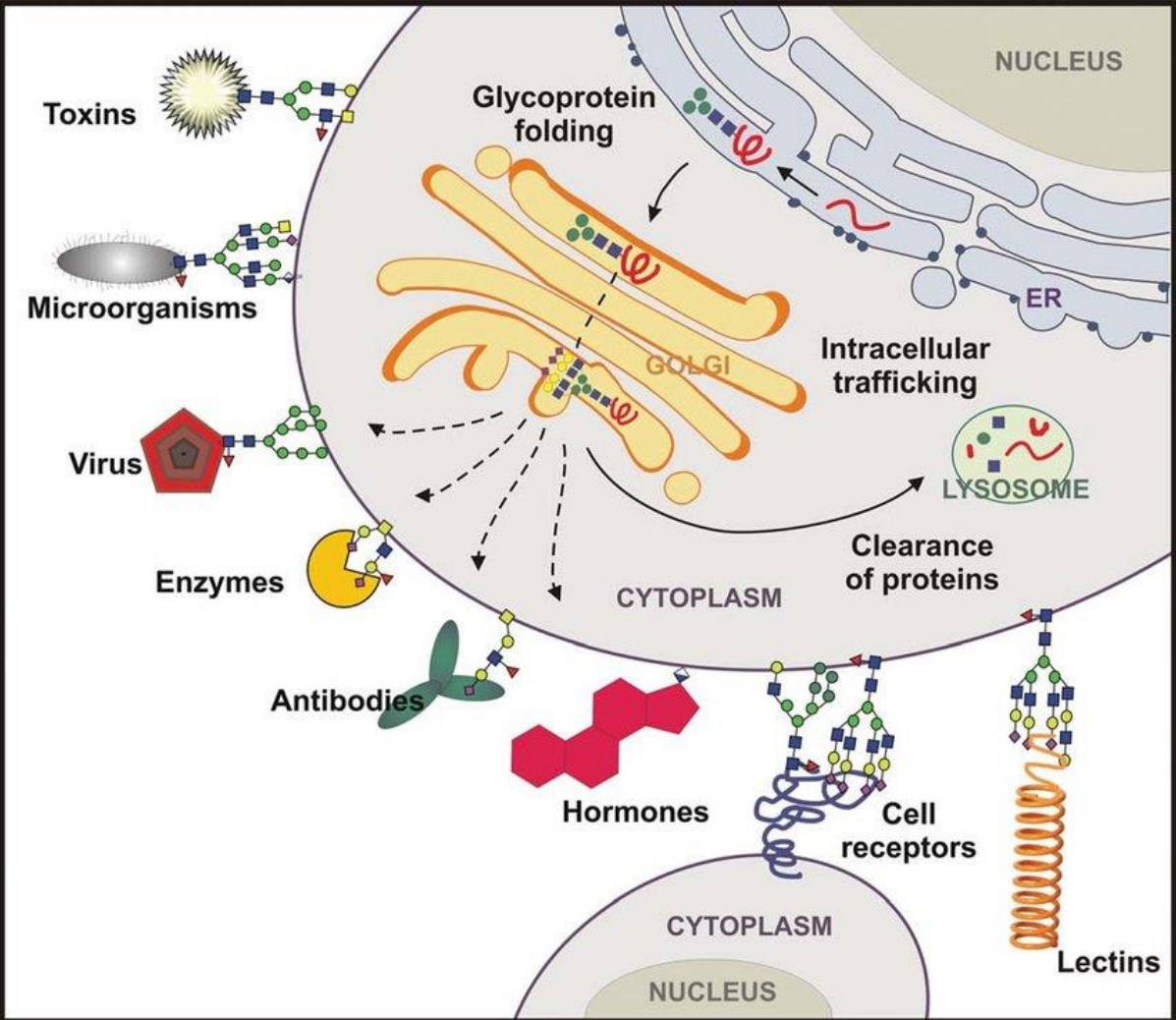
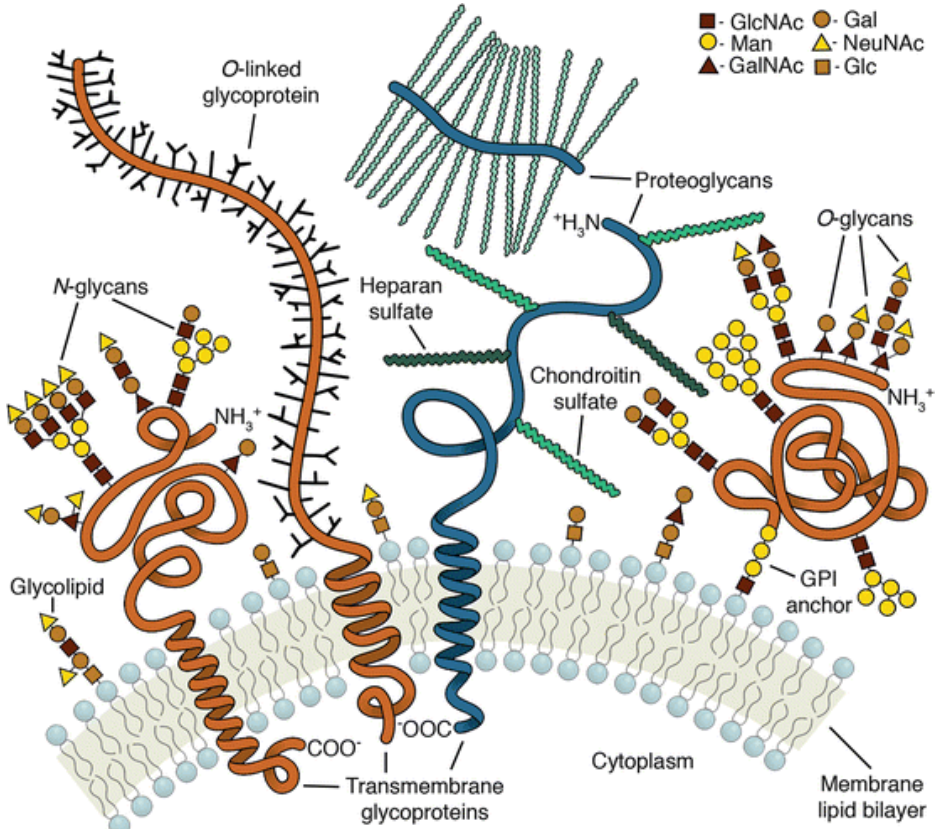
纤维素



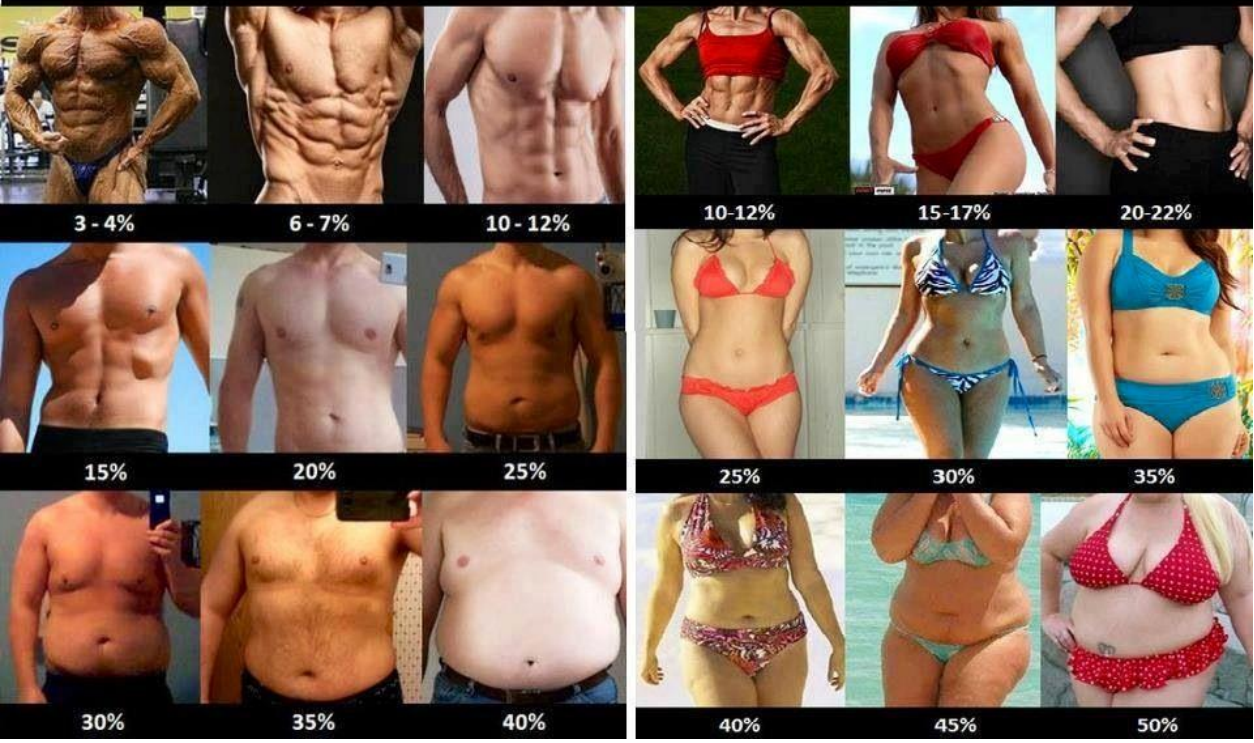
Cellulose is a structural polysaccharide made up of β -D-glucose units joined by $\beta(1-4)$ glycosidic linkages.

Glycoconjugates/: Self-study Topic

糖綴合物

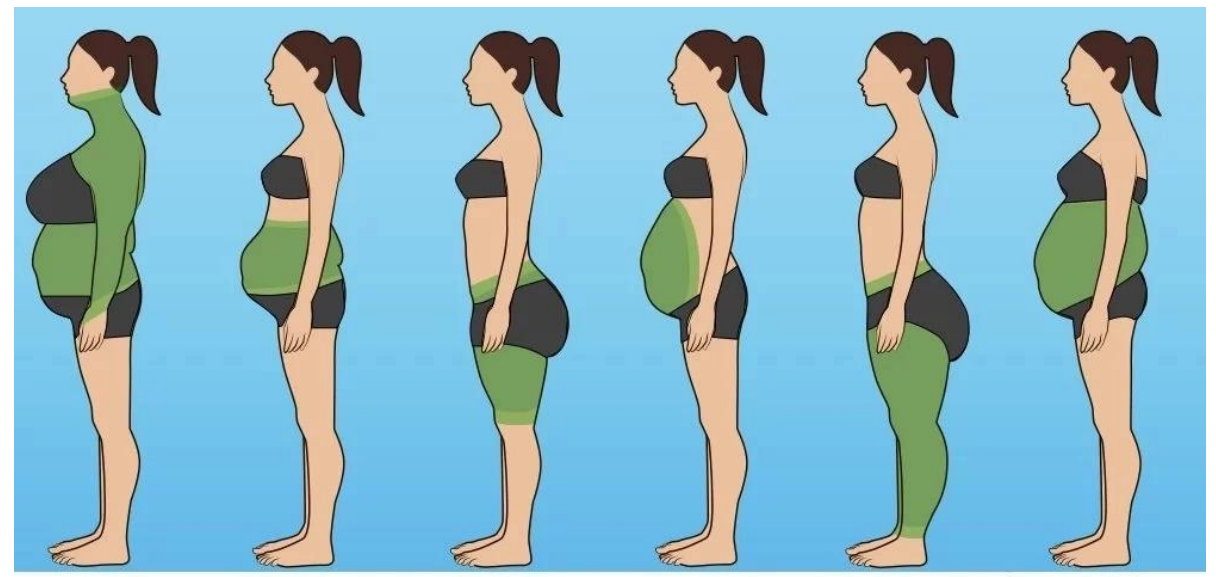


Men & Women Fat Percentage



4/4 Lipid

Fat?



6 types of body fat and ways to get rid of it © iStockphoto.com

What is Lipids

- ❖ **Lipids** are a broad class of biomolecules that includes **fats, oils, waxes, phospholipids, steroids, and related compounds**. Their common property is that they are **insoluble in water** but **soluble in nonpolar organic solvents**, such as **ether and chloroform**. 脂质是一大类生物分子，包括脂肪、油脂、蜡、磷脂、类固醇及相关化合物。它们的共同特征是不溶于水，但溶于非极性有机溶剂，如乙醚和氯仿。

Key features

- ❖ **Hydrophobic or amphipathic** / 疏水性
- ❖ **Relatively reduced** molecules / 还原分子
- ❖ Rich in **hydrocarbon chains or rings** / 富含烃

What is Lipids

Biological Functions of Lipids

- ❖ **Energy storage:** Lipids are a major form of long-term energy storage and yield a large amount of energy upon oxidation.
- ❖ **Membrane structure:** Phospholipids, glycolipids, and cholesterol are essential components of biological membranes.
- ❖ **Regulation and nutrition:** Lipids facilitate the utilization of fat-soluble vitamins and function as precursors of steroid hormones and other regulatory molecules.
- ❖ **Protection and insulation:** Adipose tissue cushions organs against mechanical damage and provides thermal insulation.
- ❖ **Cell recognition:** Membrane lipids and glycolipids contribute to cell–cell recognition, antigenicity, and immune function.

What is Lipids

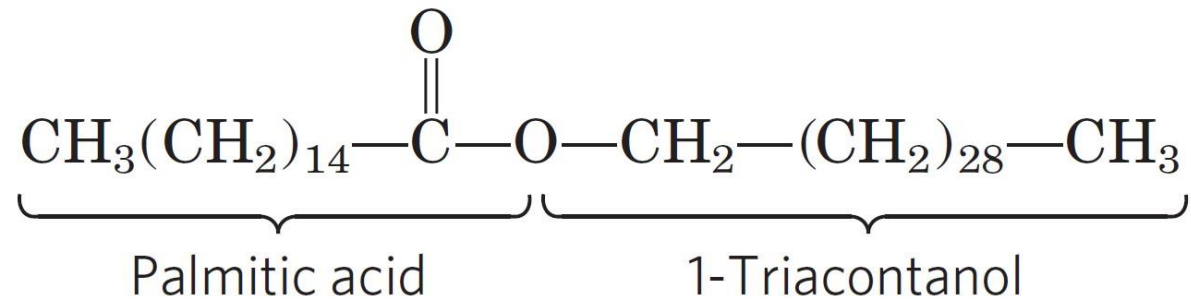
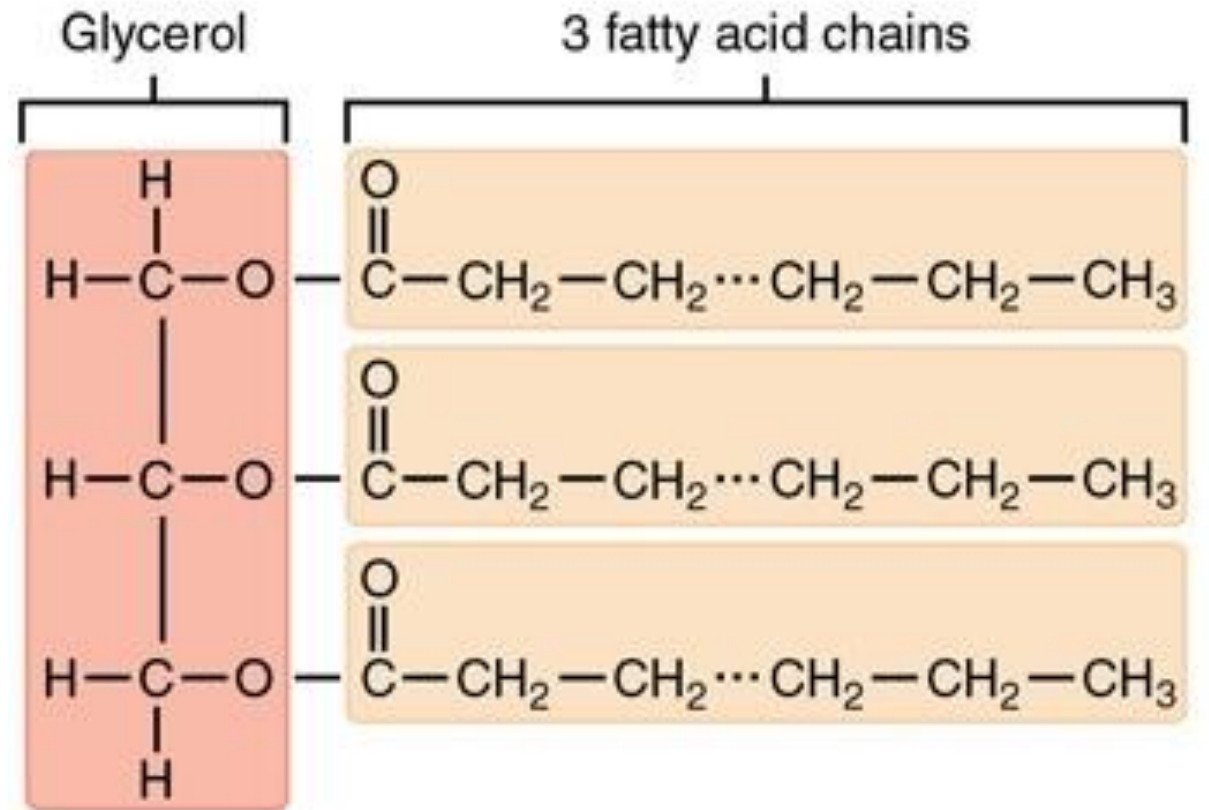
Lipids are commonly divided into three major classes on the basis of their **chemical structure and composition**:

- ❖ **Simple lipids (单纯脂类)**, include **triacylglycerols(甘油三酯)** and **waxes(蜡)**
- ❖ **Complex lipids (复合脂类)**, which include **phospholipids (磷脂)** and **glycolipids (糖脂)**
- ❖ **Derived lipids (衍生脂质; often overlapping with non-saponifiable lipids)**, which include **sterols, terpenes, and other lipid-related compounds**

Simple lipids

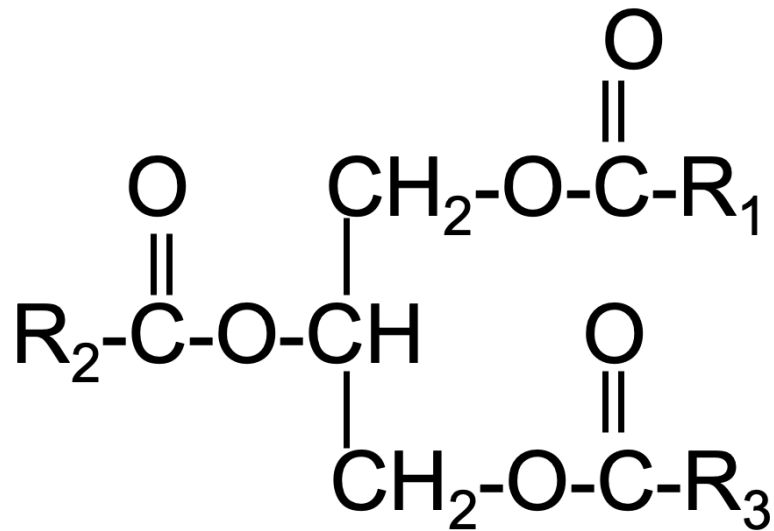
Triacylglycerols 甘油三酯/三酰甘油

Animal and plant fats and oils are composed mainly of acylglycerols(酰基甘油), especially triacylglycerols, with minor amounts of diacylglycerols and monoacylglycerols (二酰甘油和单酰甘油).



Simple lipids

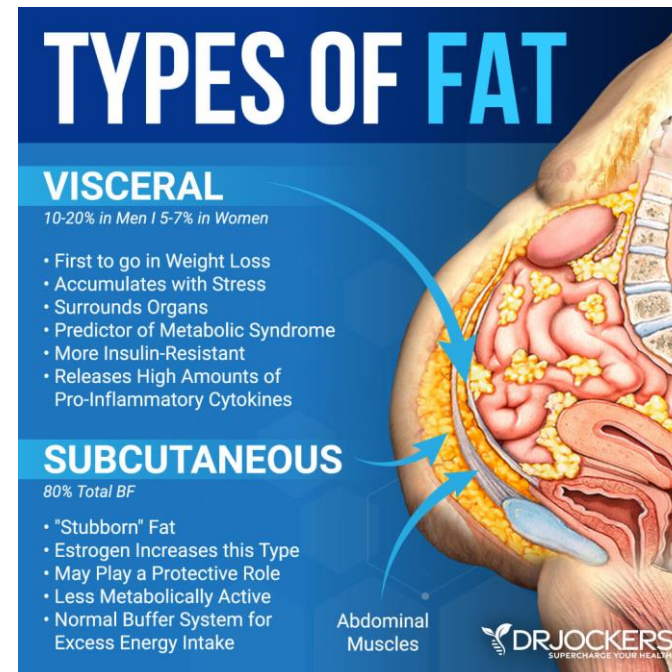
Triacylglycerols 甘油三酯/三酰甘油



$\text{R}_1 = \text{R}_2 = \text{R}_3$: Simple triacylglycerol 甘油三单酯

$\text{R}_1 \neq \text{R}_2 \neq \text{R}_3$: Mixed triacylglycerol 甘油三杂酯

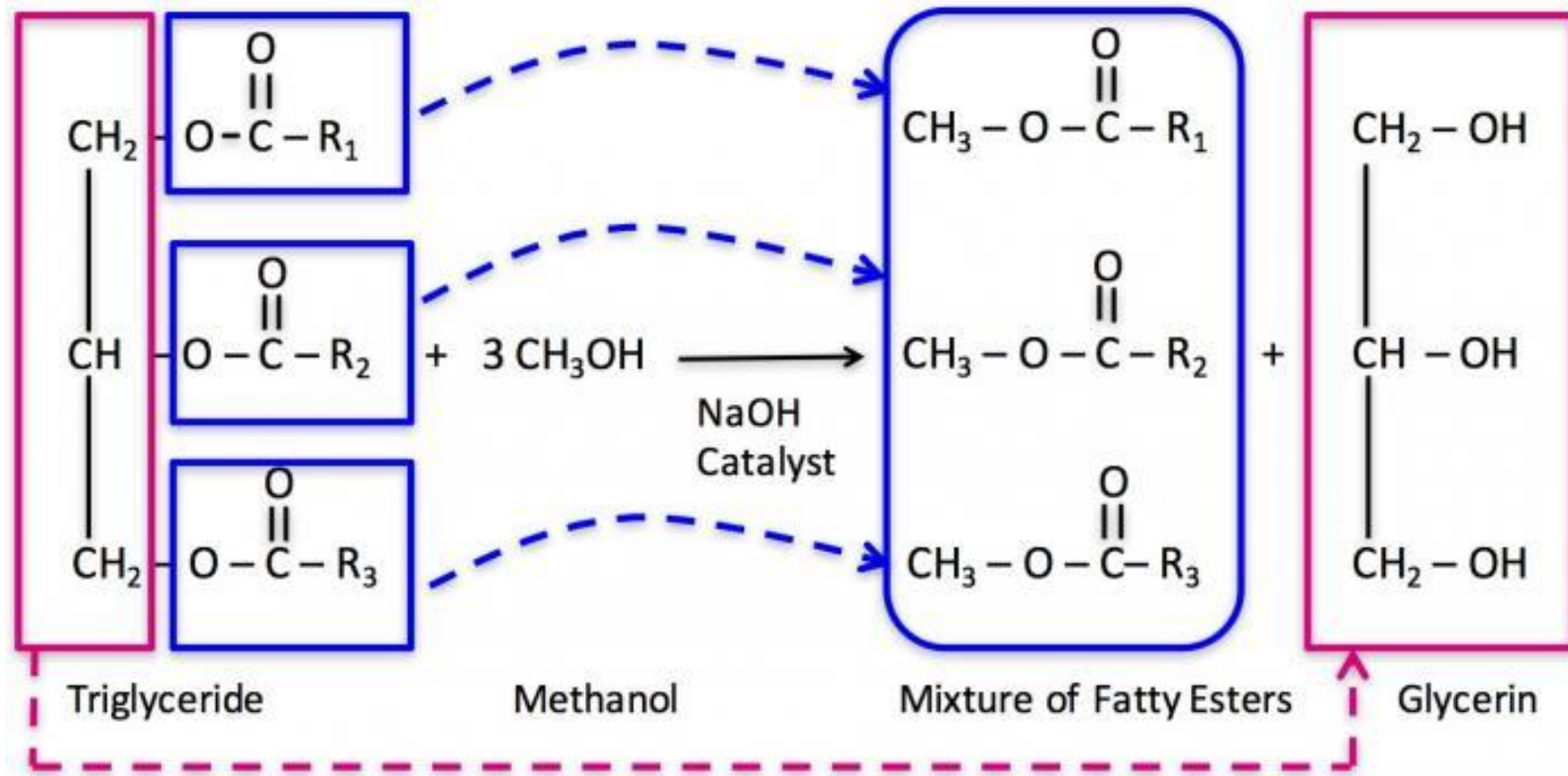
At room temperature, triacylglycerols that are predominantly liquid are referred to as **oils**, whereas those that are predominantly solid are referred to as **fats**.



Simple lipids

Triacylglycerols
甘油三酯/三酰甘油

Hydrolysis and Saponification /水解与皂化



Simple lipids

Triacylglycerols
甘油三酯/三酰甘油

Saturated fatty acids
 $\text{CH}_3(\text{CH}_2)_n\text{COOH}$

- ❖ **Lauric acid** 月桂酸 — **C12:0**
- ❖ **Myristic acid** 豆蔻酸 — **C14:0**
- ❖ **Palmitic acid** 棕榈酸 — **C16:0**
- ❖ **Stearic acid** 硬脂酸 — **C18:0**

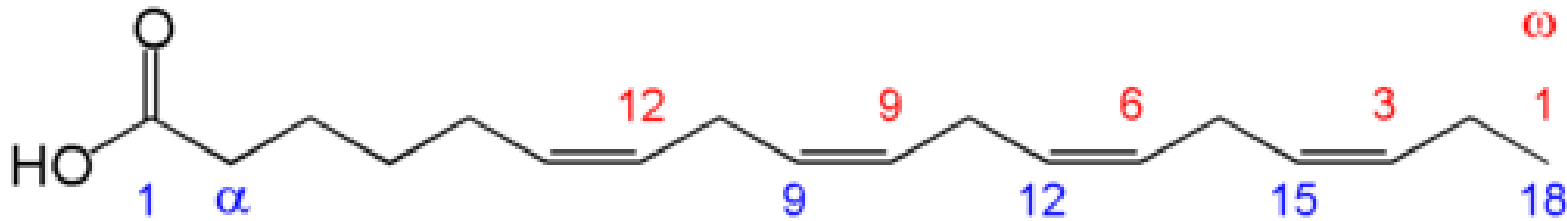
Common Fatty Acids

Unsaturated fatty acids

- ❖ **Monounsaturated fatty acid**
 - ✓ **Oleic acid** 油酸 — **C18:1** Δ^9
- ❖ **Polyunsaturated fatty acids**
 - ✓ **Linoleic acid** 亚油酸 — **C18:2** $\Delta^{9,12}$
 - ✓ **α -Linolenic acid** 亚麻酸 — **C18:3** $\Delta^{9,12,15}$

Essential Fatty Acids

Essential fatty acids (EFAs) are **polyunsaturated fatty acids** that cannot be synthesized de novo by humans and must therefore be supplied through food.

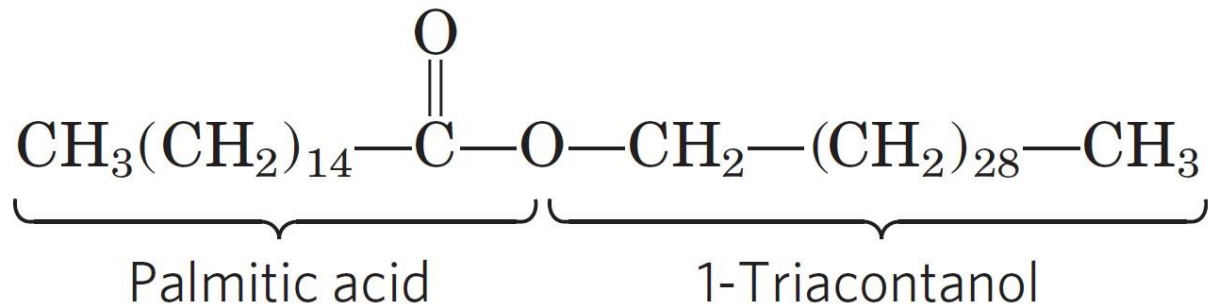


Docosahexaenoic acid/二十二碳六烯酸(DHA; 22:6, n-3) is an important ω -3 polyunsaturated fatty acid, particularly important in the brain and retina.

Simple lipids

Waxes / 蜡

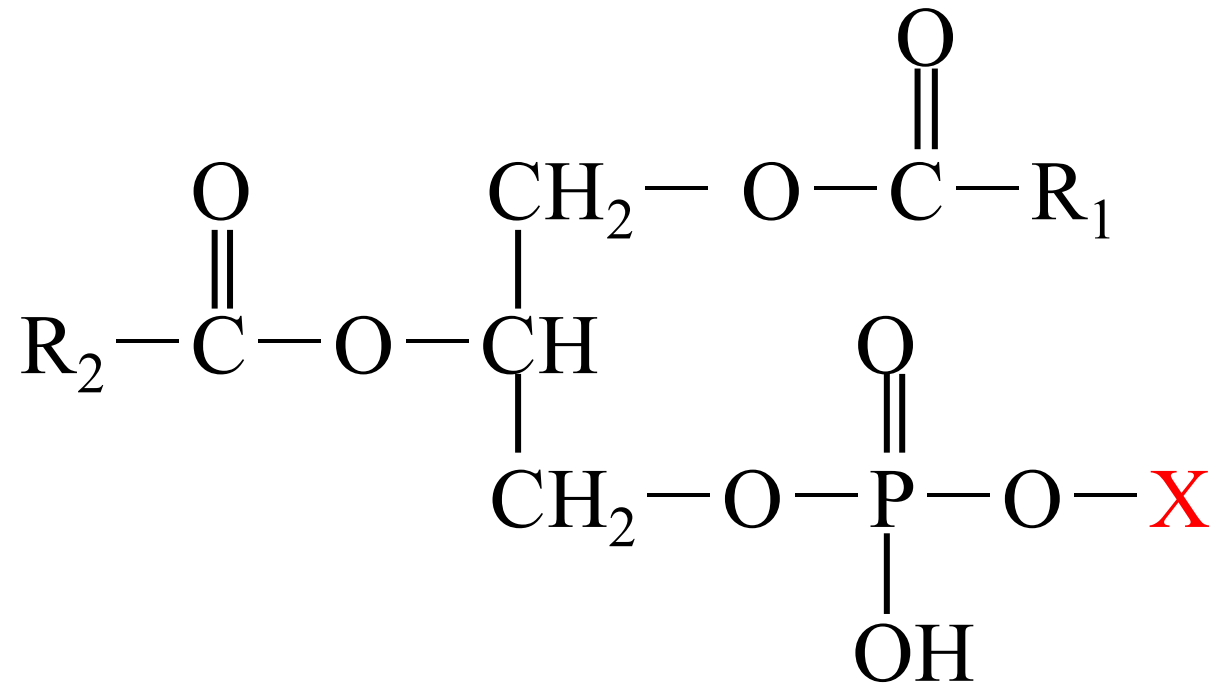
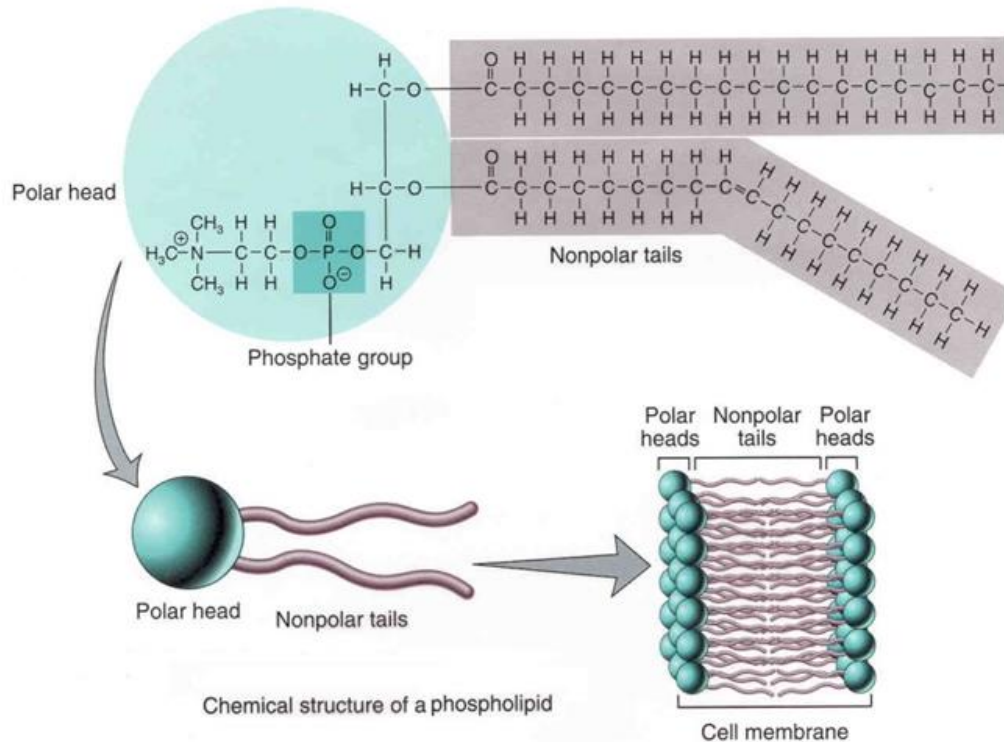
Waxes are simple lipids composed of esters of long-chain fatty acids (高级脂肪酸) and long-chain alcohols (高级元醇). Because of their hydrophobic nature and chemical stability, they are usually water-insoluble solids at room temperature. In nature, waxes function mainly as protective coatings on plant surfaces and on the bodies of insects.



Complex lipids

Phospholipids / 磷脂

Phospholipids: phosphate-containing lipids that serve as major structural components of biological membranes.



Complex lipids

Phospholipids / 磷脂

$X = \text{CH}_2\text{CH}_2\text{N}^+(\text{CH}_3)_3$ Phosphatidylcholine/磷脂酰胆碱 (卵磷脂)

$X = \text{CH}_2\text{CH}_2\text{NH}_2$ Phosphatidylethanolamine/ 磷脂酰乙醇胺 (脑磷脂)

$X = \text{inositol}$ / 肌醇, phosphatidylinositol/ 磷脂酰肌醇

$X = \text{CH}_2 - \underset{\text{COOH}}{\text{CH}} - \text{NH}_2$ phosphatidylserine/ 磷脂酰丝氨酸

Homework Assignments

Scenario: A cell biologist engineers two artificial cells. Both contain nucleic acids, proteins, carbohydrates, and lipids, but they are organized differently. In Model 1, the membrane is unstable but enzyme activity is high. In Model 2, the membrane is stable and selective, but replication and metabolic responses are slow. The researcher wants to determine which macromolecular organization better supports life-like behavior.

- ✓ **Task 1:** Analyze the distinct roles of **lipids, proteins, nucleic acids, and carbohydrates** in determining membrane stability, information storage, catalytic activity, and cellular recognition in the two models.
- ✓ **Task 2:** Discuss whether a system with better **compartmentalization** but weaker metabolic flexibility should be considered more “life-like” than one with high catalytic activity but poor structural stability.
- ✓ **Task 3:** Suggest how changing the relative abundance or arrangement of one or more macromolecule classes could improve the performance of each artificial cell, and explain what new limitations might appear.