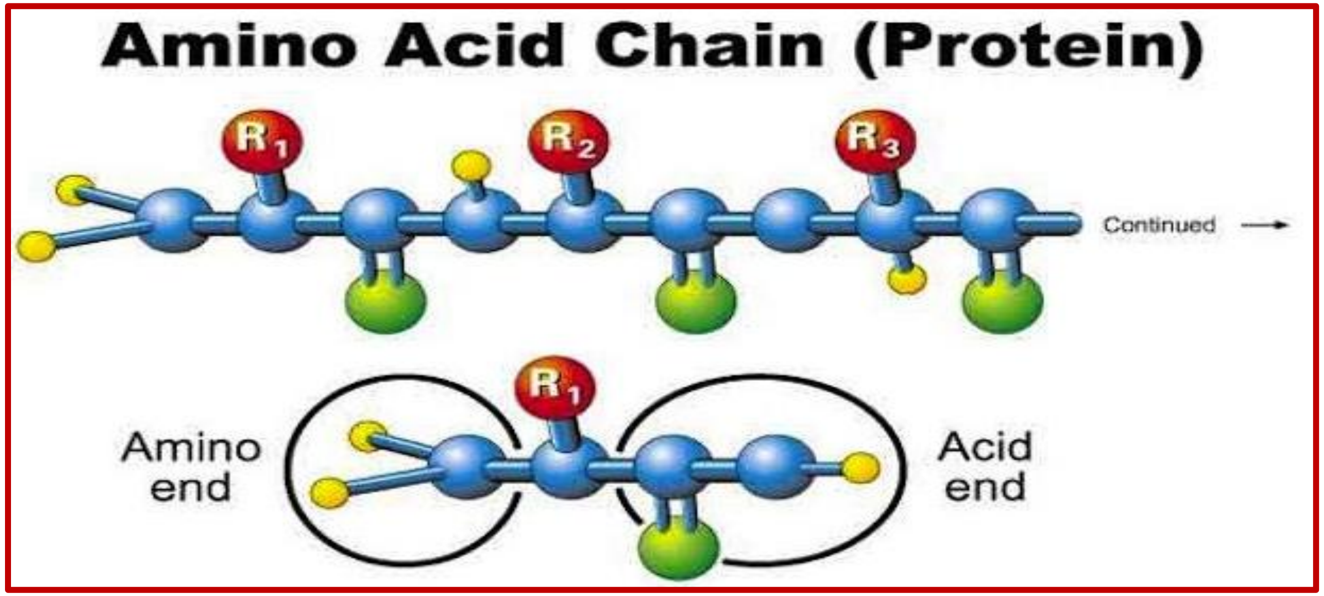
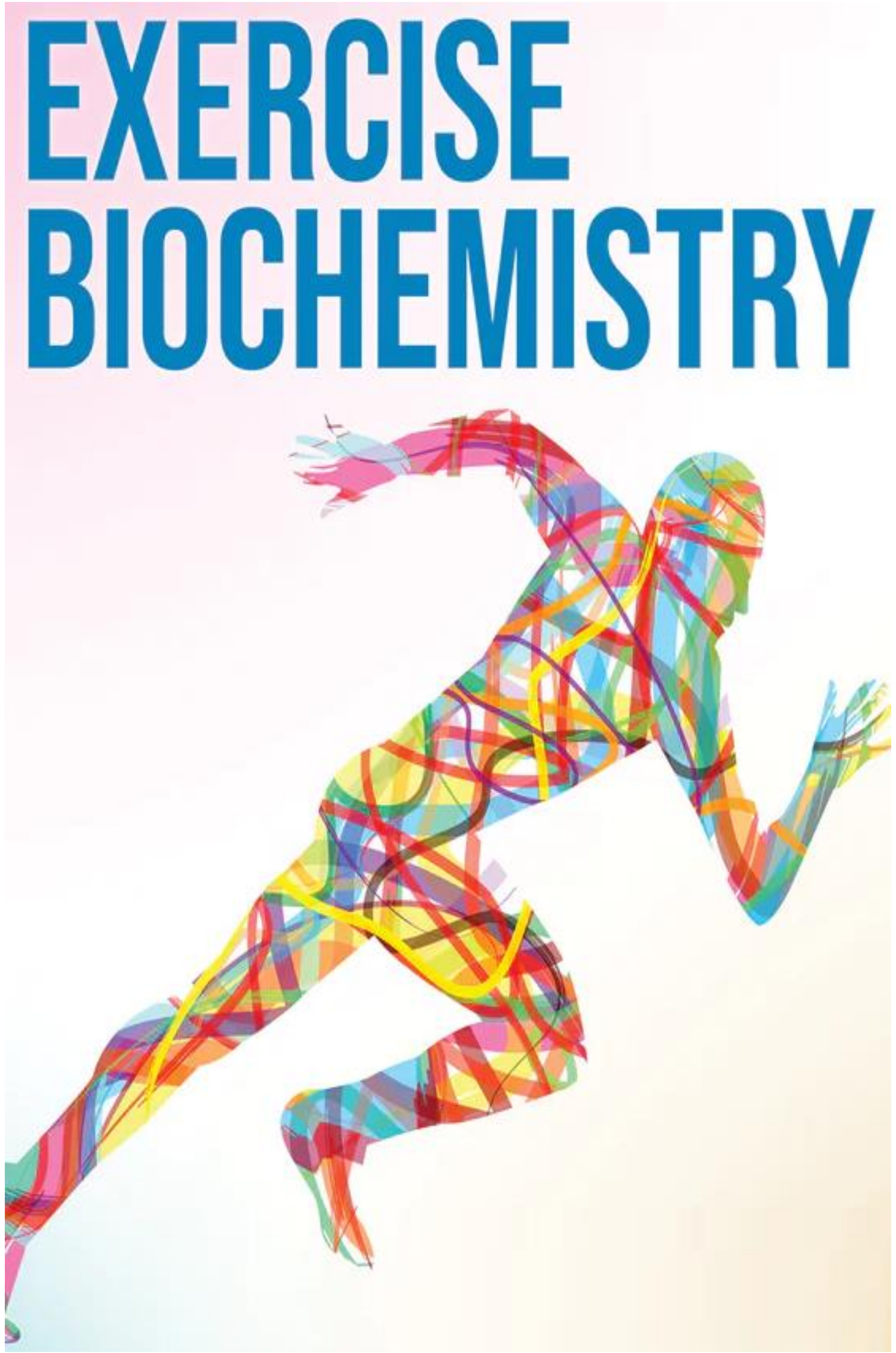
TISHK INTERNATIONAL UNIVERSITY
FACULTY OF APPLIED SCIENCE
Physiotherapy Department

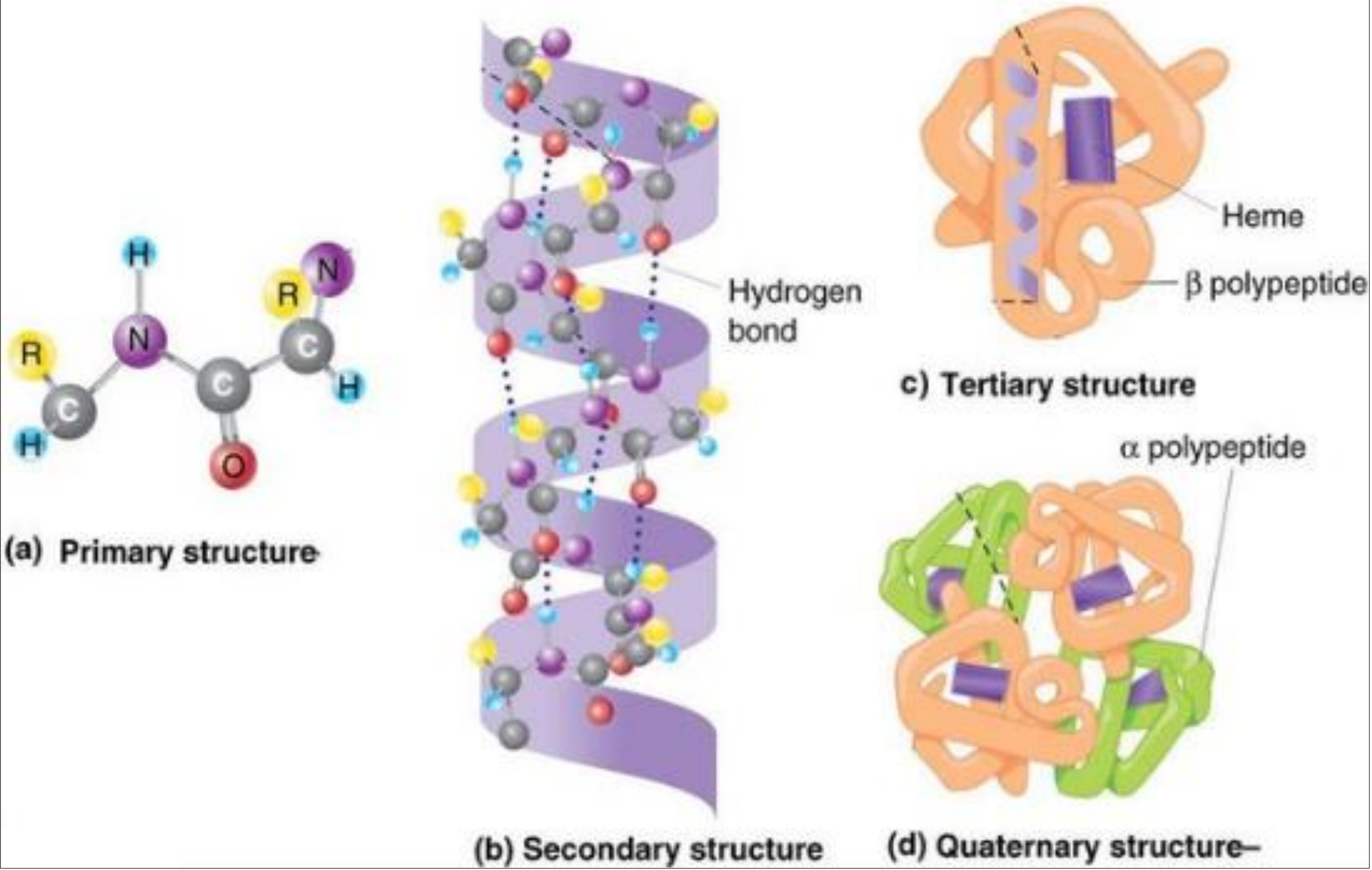


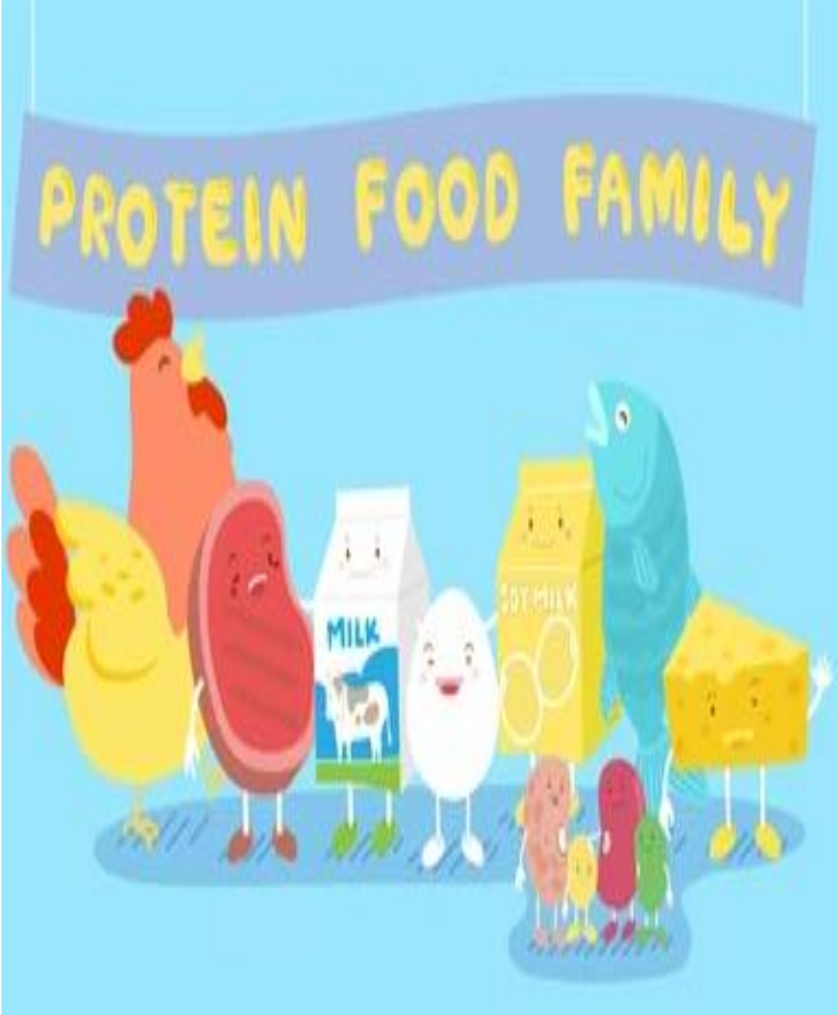
Autumn Semester 2023-2024
Course Name : **Biochemistry (Theory)**
Stage : 2 Lecture-note: 4,5,6
Lecture: Dr. Soma Majedi / Ph.D. in Organic Chemistry



Proteins

- **Proteins** are the most abundant and functionally diverse molecules in living systems.



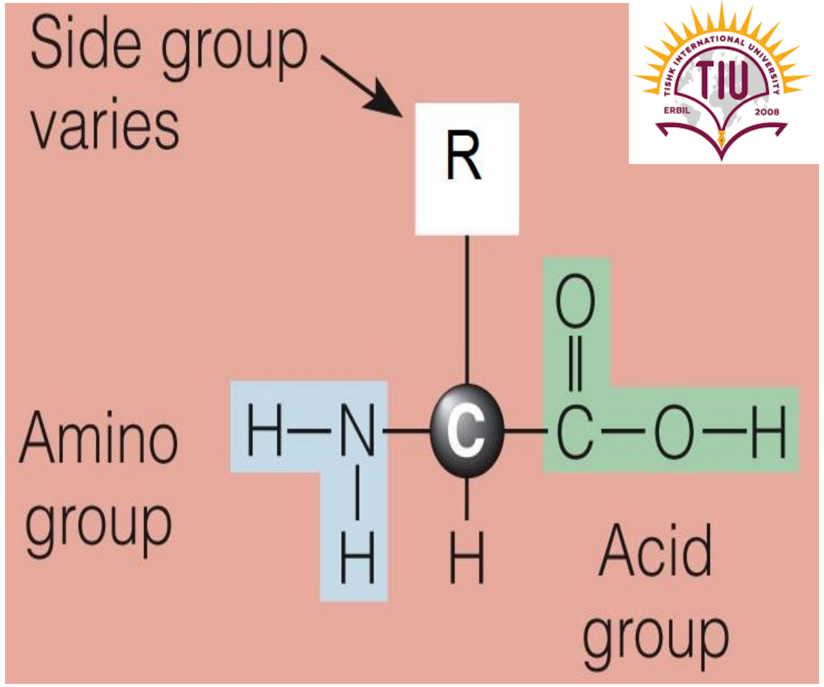


- Proteins are made from **20 different amino acids**, 9 of which are **essential**.

- Each amino acid has an **amino group**, an **acid group**, a **hydrogen** atom, and a **side group**.

- **Side group** makes each amino acid **unique**.

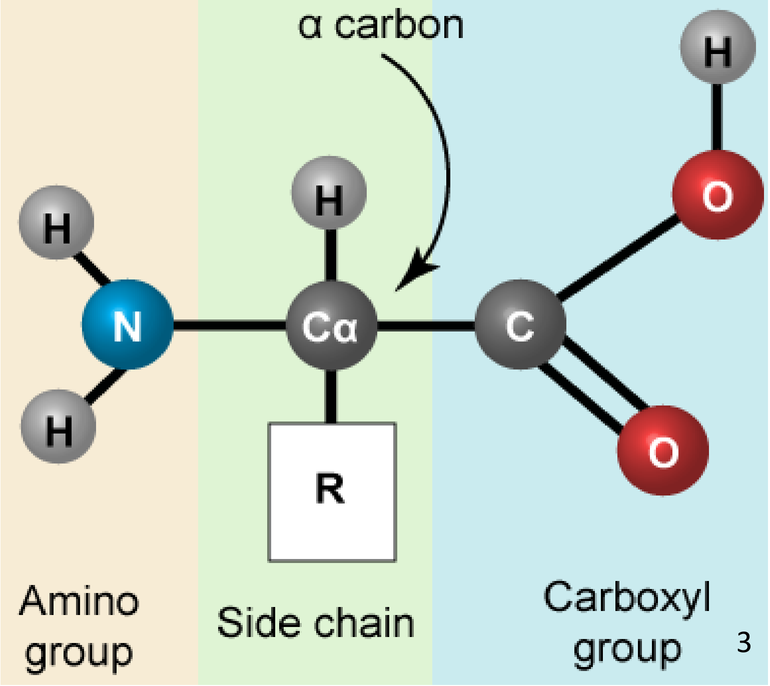
- The sequence of amino acids in each protein **determines** its **unique shape** and **function**.



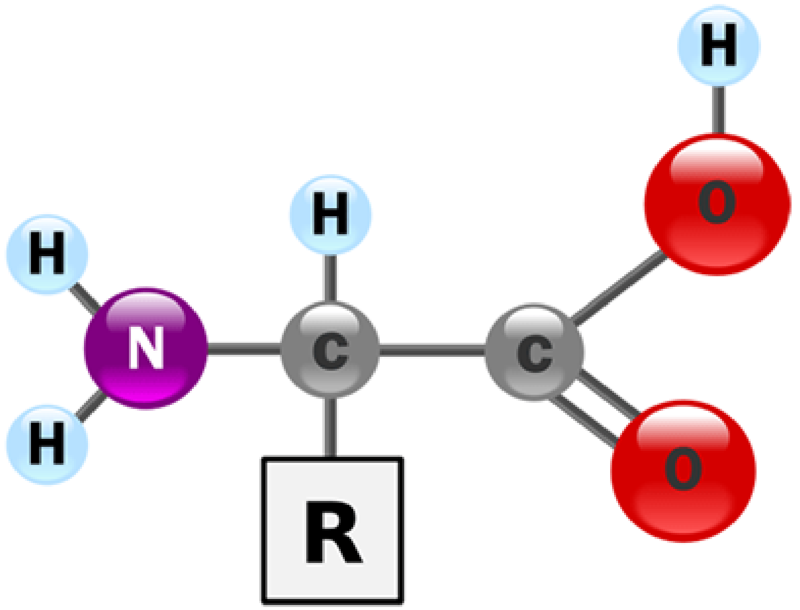
Amino Acids

- Have unique **side groups** that result in differences in the size, shape and electrical charge of an amino acid.
- **Amino acid**, is short for:

α-amino [alpha-amino] carboxylic acid

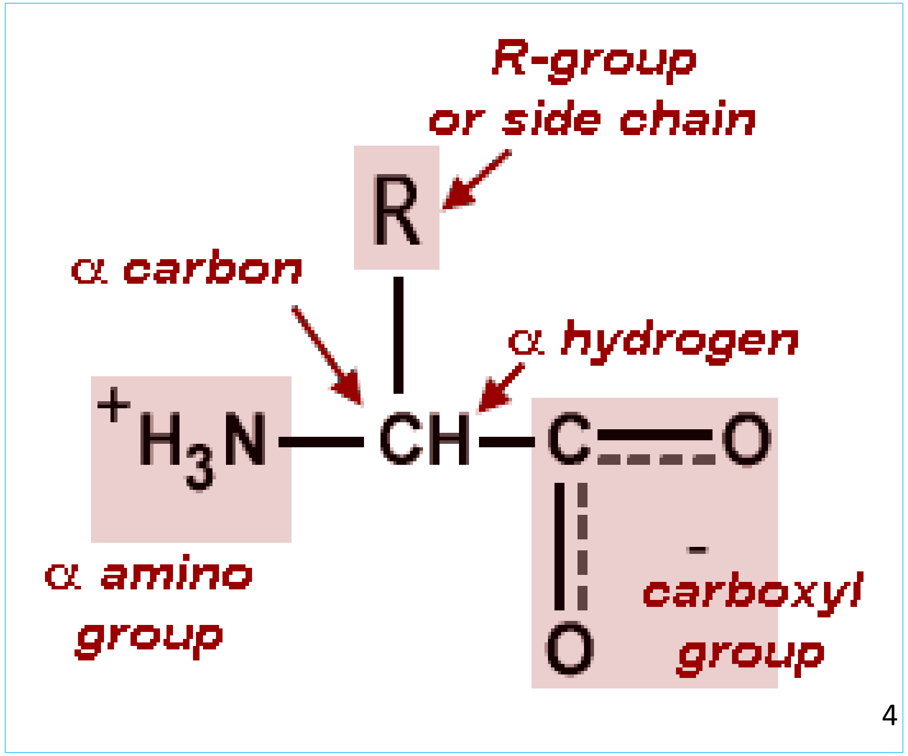


- ✓ **Basic amino group (—NH_2)**
- ✓ Acidic carboxyl group (—COOH)
- ✓ Hydrogen atom (—H)
- ✓ **Organic side chain (—R group)**



Each molecule contains a **central Carbon (C) atom**, called the **α-Carbon**.

Hydrogen atom (H), **R group**, **Amino and Carboxyl groups** are attached to **α-Carbon.**



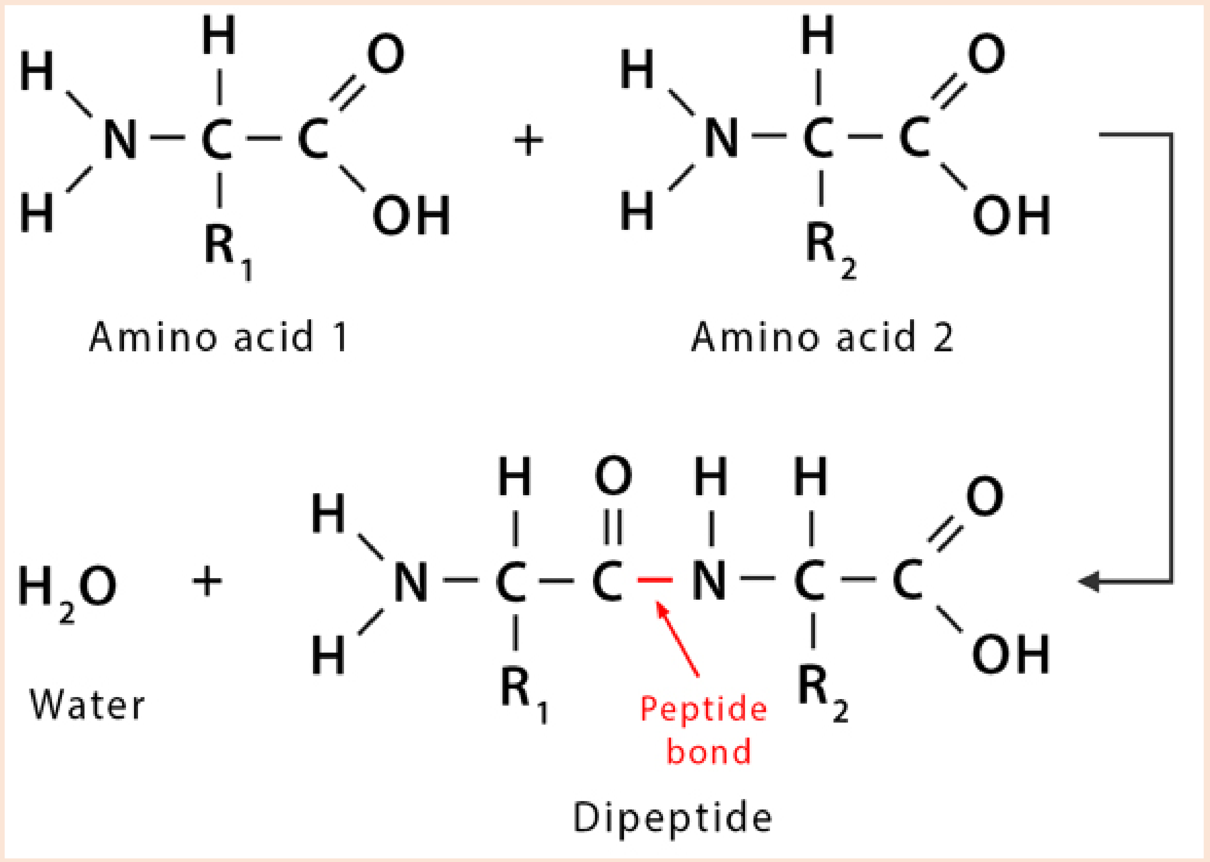
Amino Acids

- Amino acid chains are linked by **peptide bonds** in **condensation reactions**.

- **Dipeptides** have two amino acids bonded together.

- **Tripeptides** have three amino acids bonded together.

- **Polypeptides** are long chains of amino acids linked together by peptide bonds.



Amino Acids

- Amino acid sequences are all different, which allows for a wide variety of possible sequences.

They are different

Arg	Val	Val	Gly	Gly	Glu	Asp	Ala
Val	Arg	Val	Gly	Gly	Glu	Asp	Ala
Arg	Val	Val	Gly	Gly	Glu	Thr	Ala

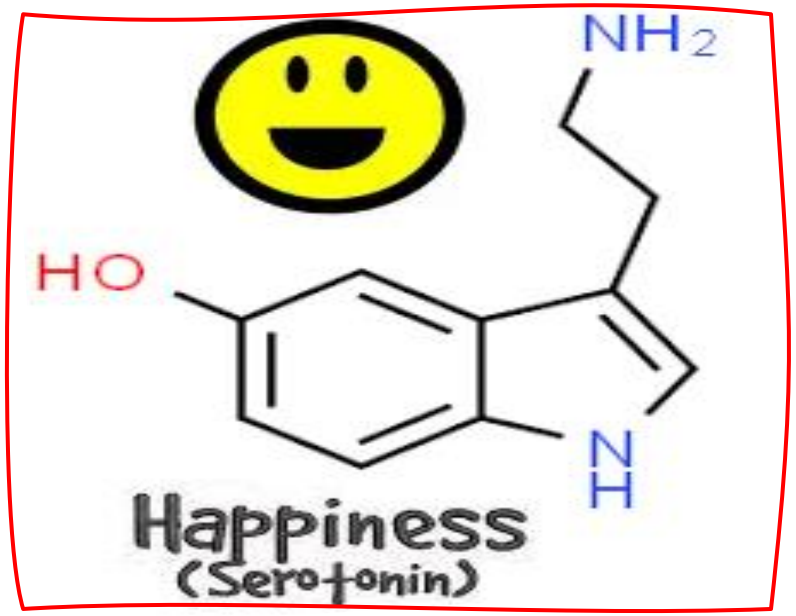
They are different

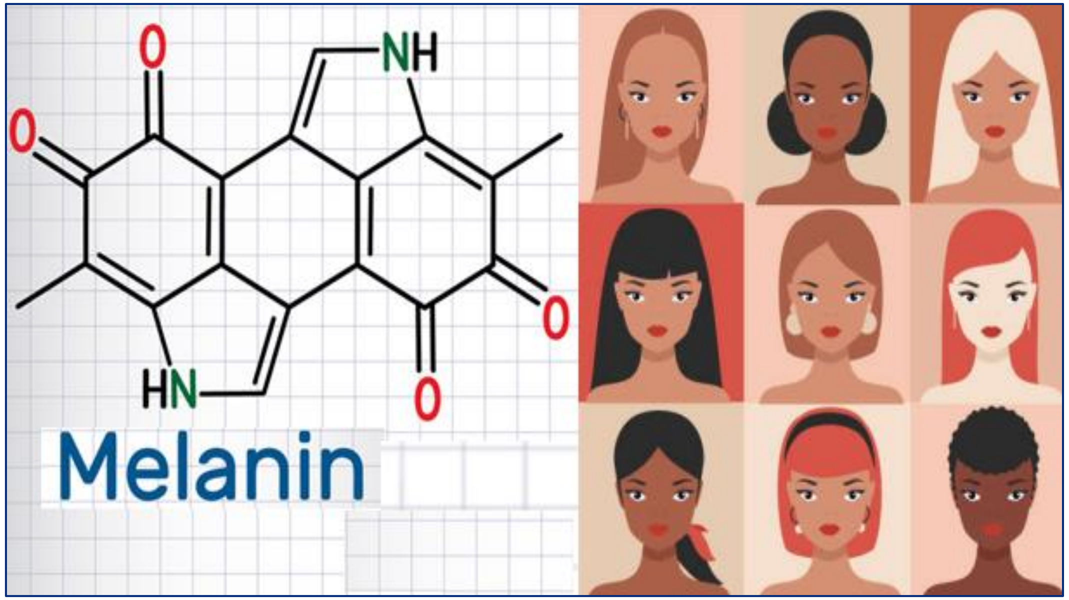
- **Proteins** contain nitrogen and they are **main source of Nitrogen** for the body.

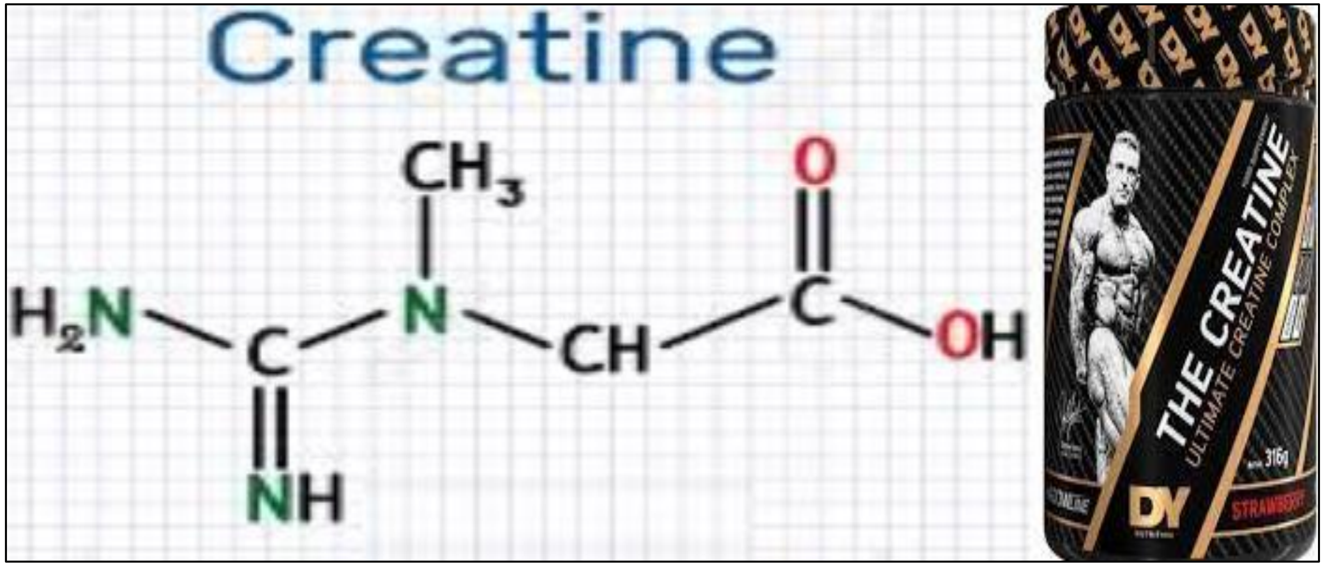
- Dietary Proteins are the sources of **essential** amino acids for the body.

Amino Acids

- **All amino acids** are required for the synthesis of **proteins** and many amino acids serve as **precursors** for the synthesis of biologically important compounds (e.g. Melanin, Serotonin, Creatine etc.)



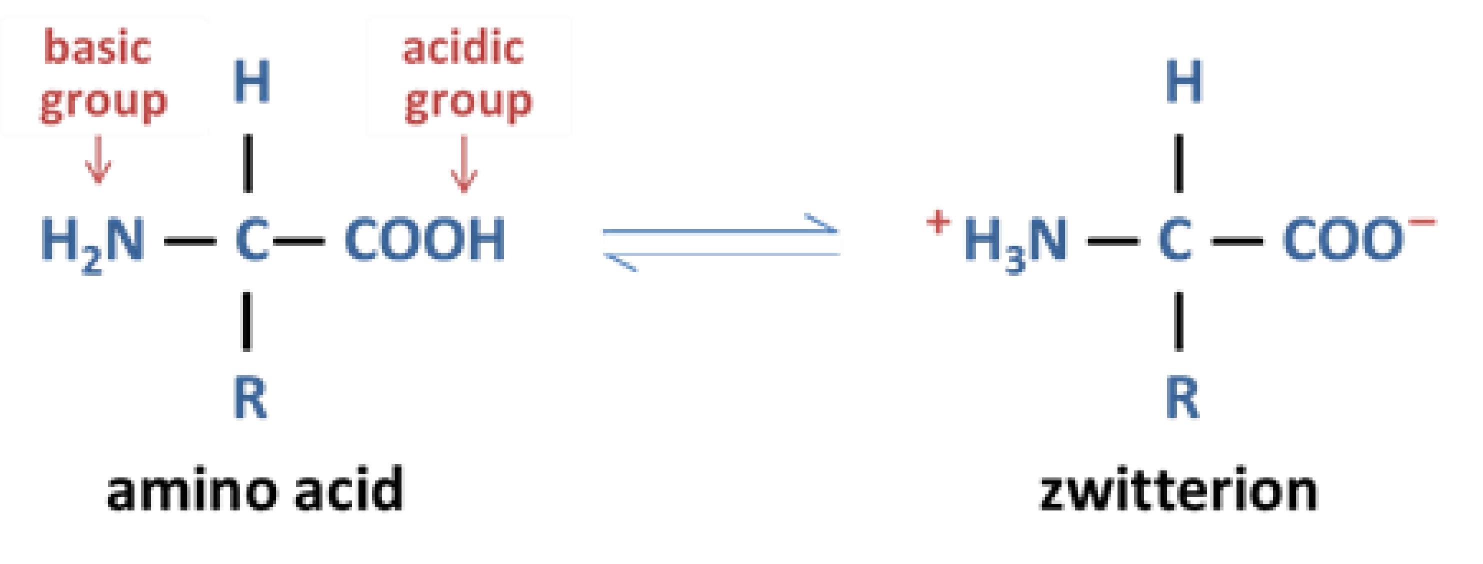




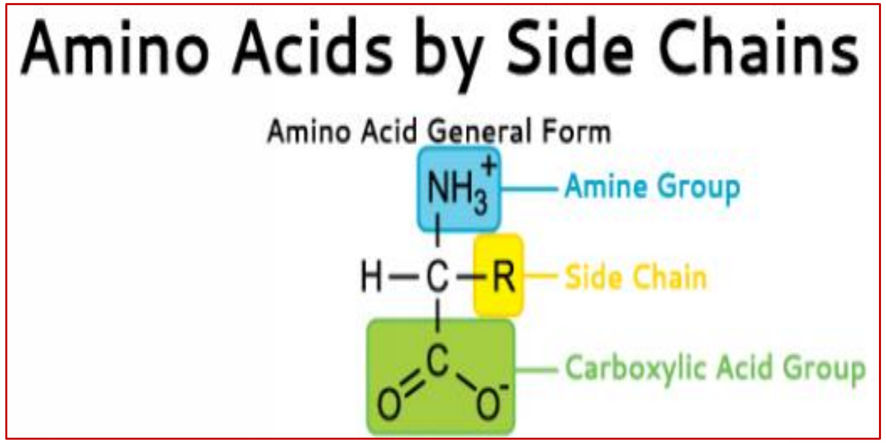
Zwitterions and Amino Acids

- A zwitterion is a compound that has both **positive** and **negative** charges but is **electrically neutral** as a whole.
- Zwitterion typically occur in molecules with both **acidic** and **basic** functional groups.

Amino acids **are the best-known examples** of Zwitterions

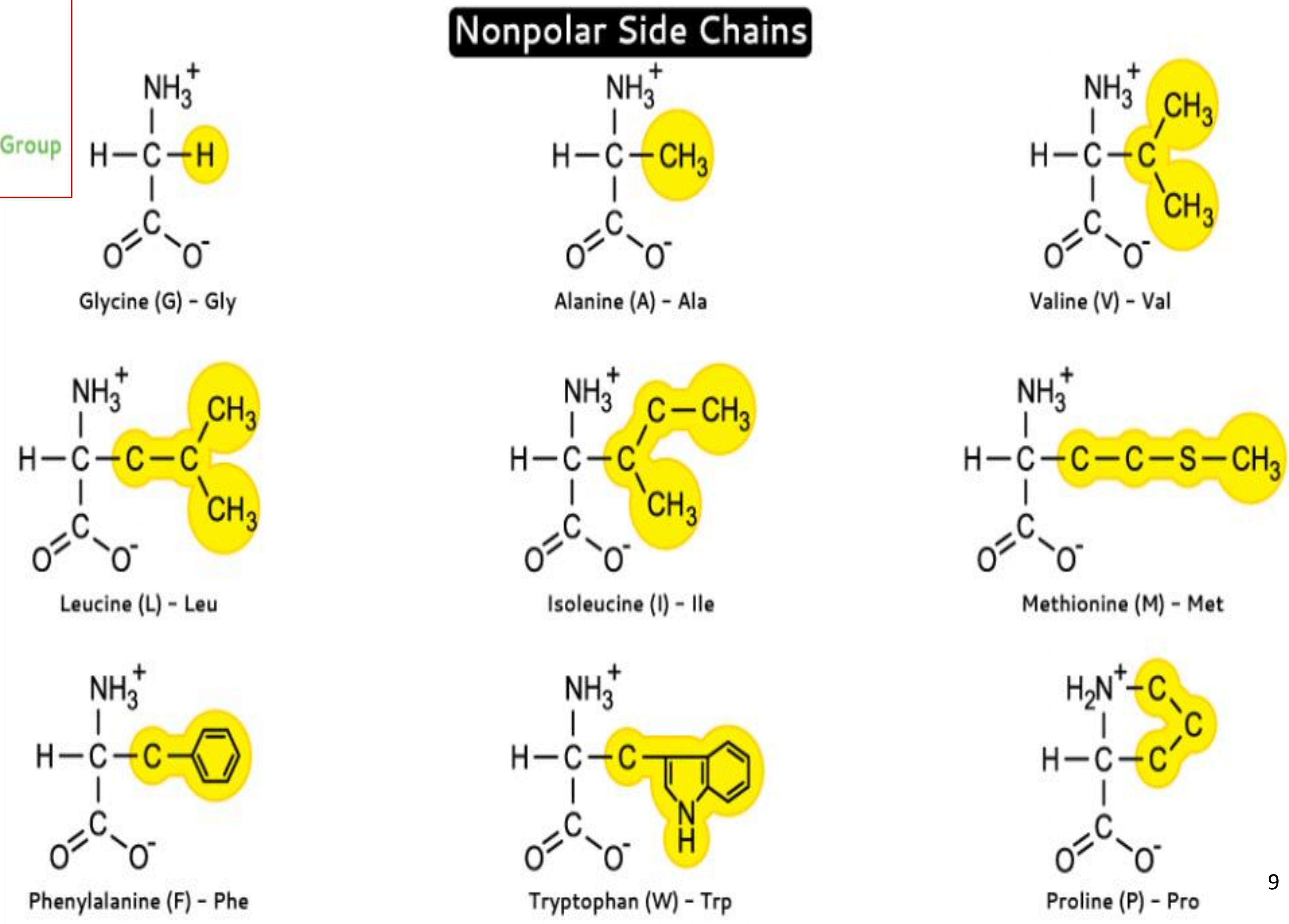


Non-Polar Hydrophobic Amino Acids

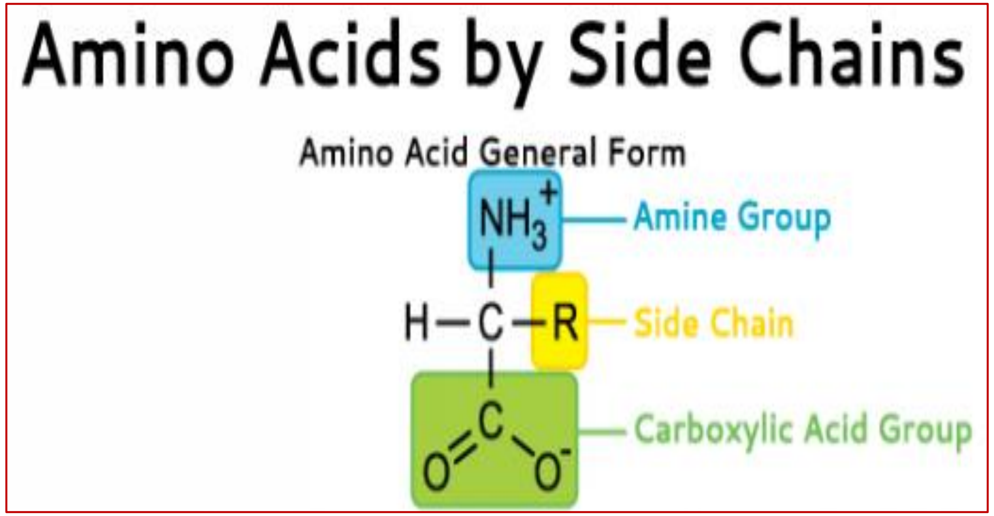


They lack side chain **polarity** and tend not to interact with water molecules.

These amino acids are →

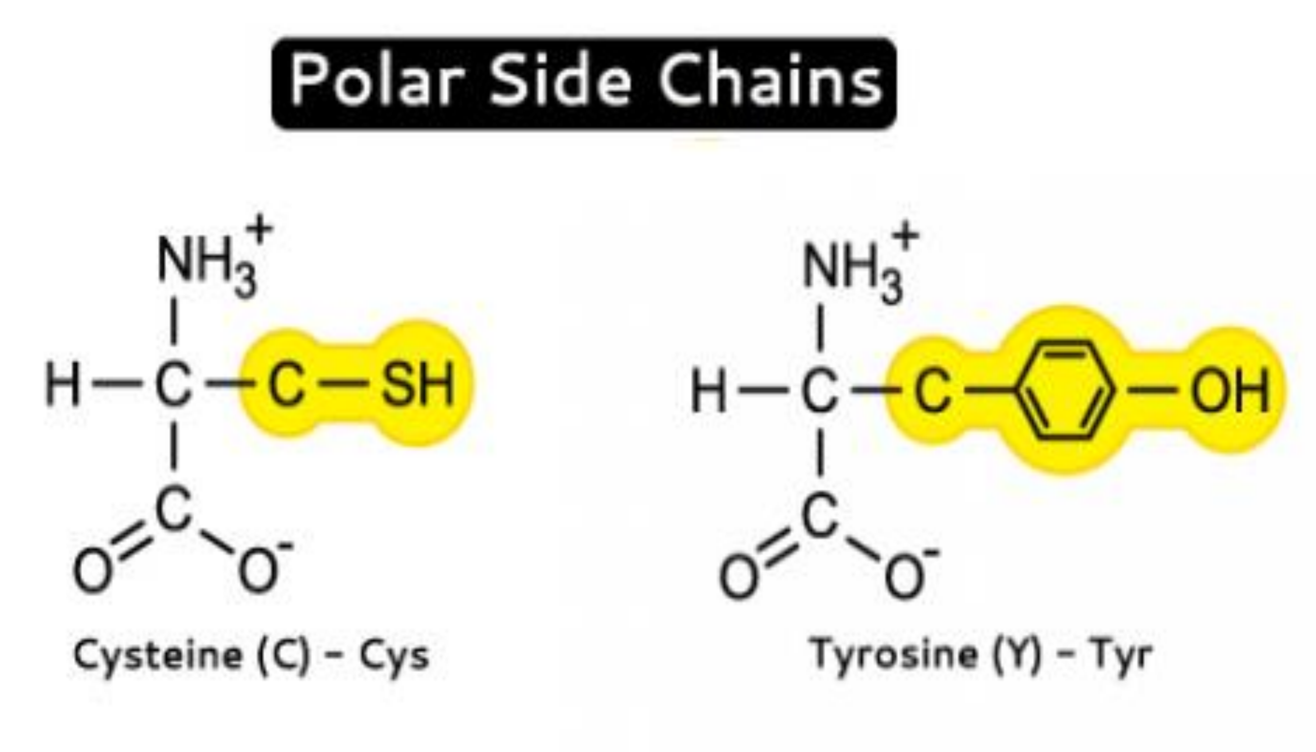


Polar **Hydrophobic** Amino Acids



Even though these amino acids are polar, they only weakly interact with water.

Polar hydrophobic amino acids are either weakly hydrophobic or else the configuration of the side chain prohibits interaction with water.

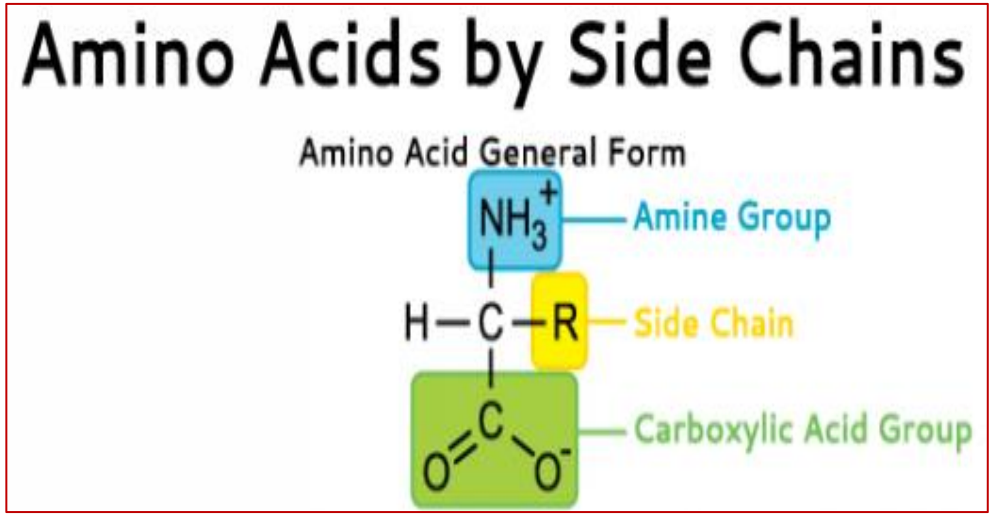


These amino acids are

→

Polar **Hydrophilic** Amino Acids

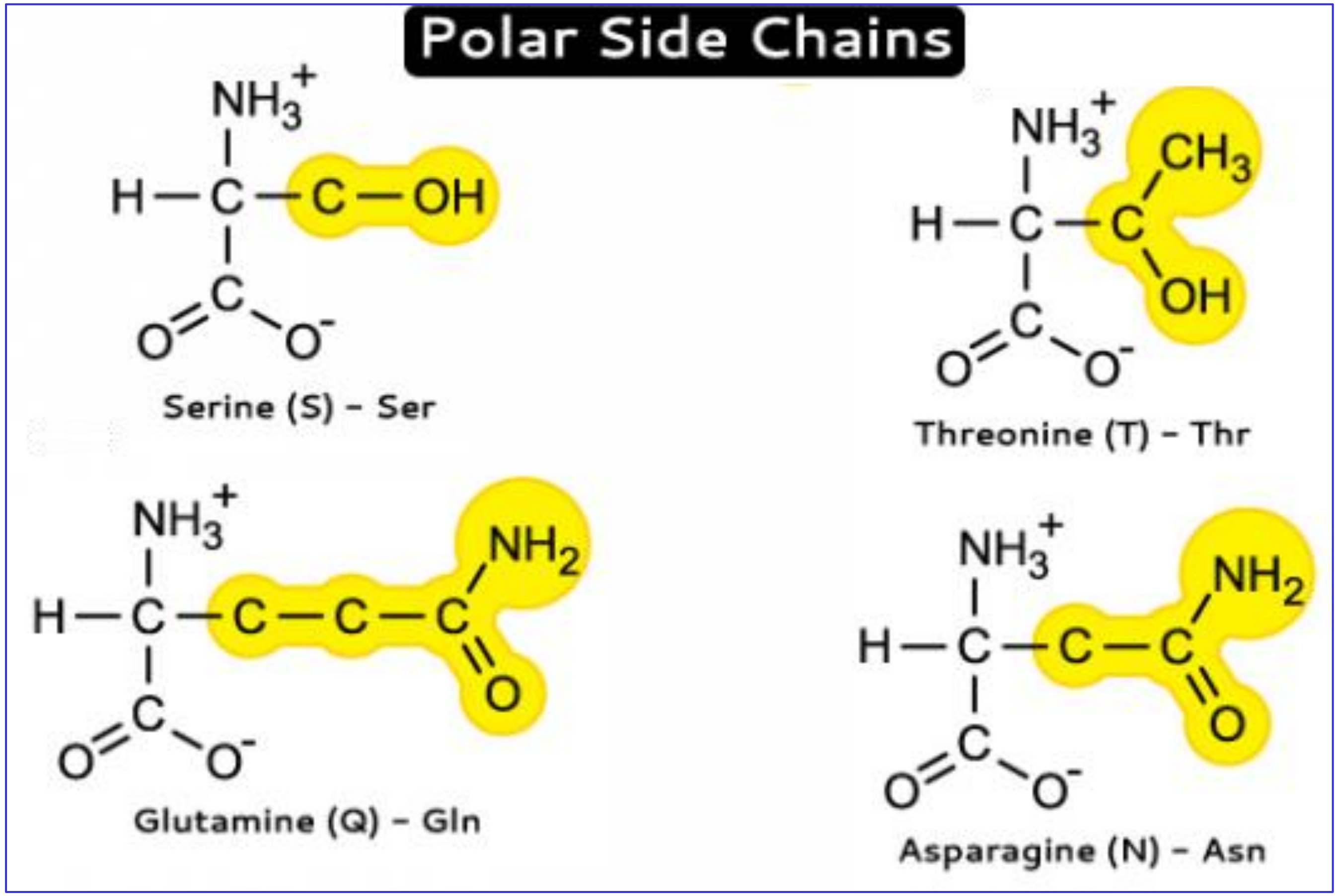
These amino acids are water-loving because of electronegativity differences between atoms in the side chains (e.g., N and O).

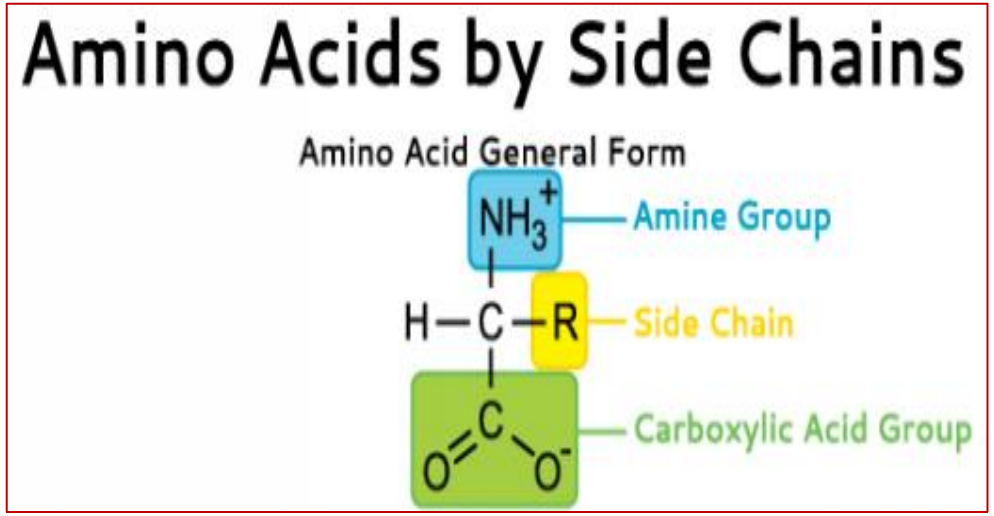


Their presence causes a polypeptide chain to twist toward water, while a hydrophobic chain causes a twist away from water.

These amino acids are

→





Acidic Amino Acids

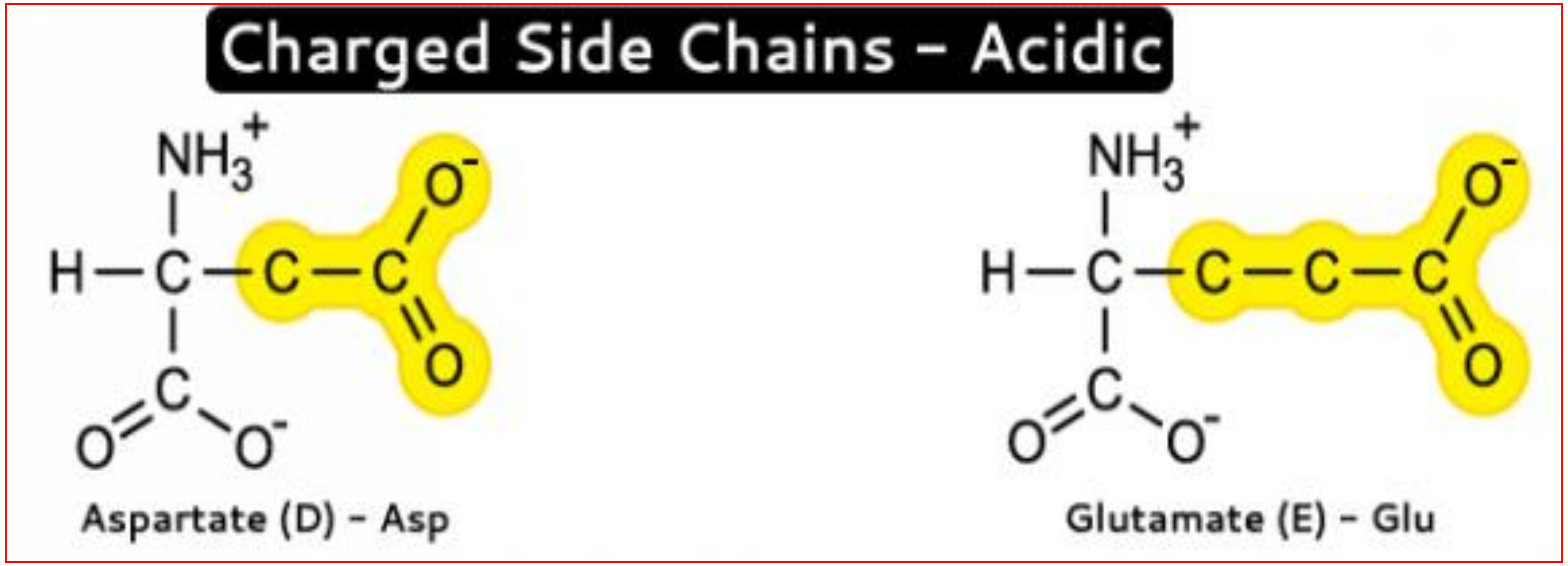
If there is a carboxylic acid in a side chain, you get an acidic side chain.

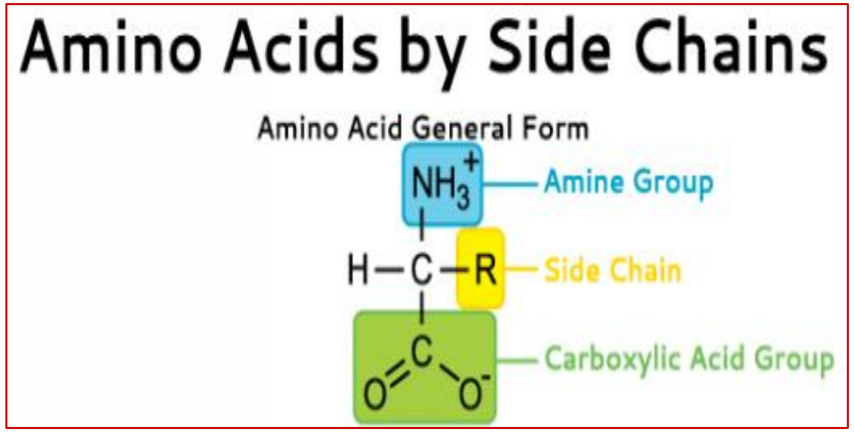
If the NH2 group is swapped for an OH group, you can an acidic carboxyl group.

Aspartic acid / Aspartate
Glutamic acid / Glutamate

Acidic amino acids are

→



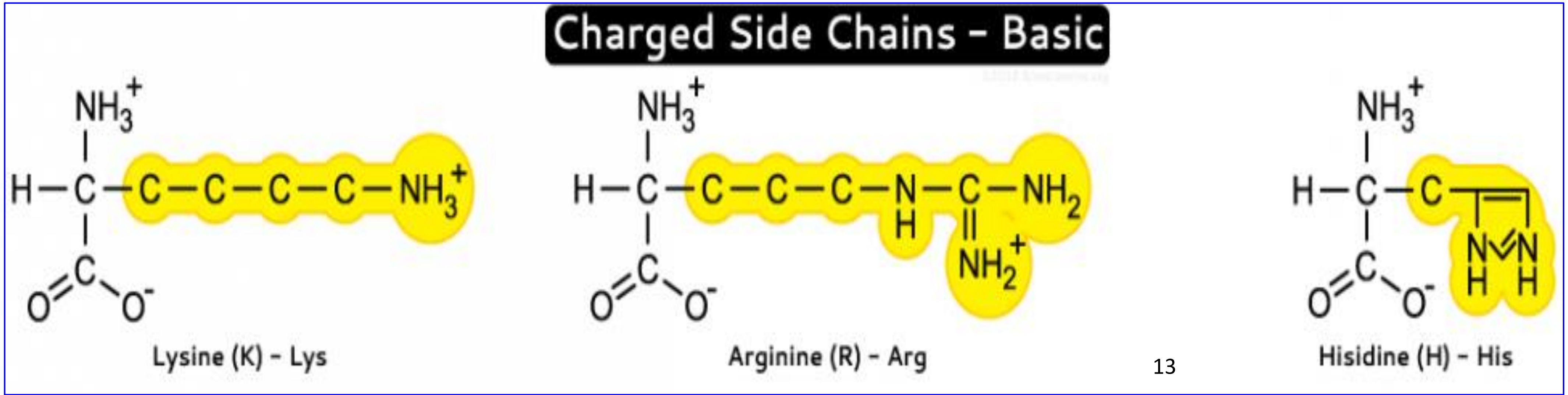


Basic Amino Acids

Basic amino acids have a **Nitrogen** atom that has a **lone electron pair** that can react with a Hydrogen ion (**H^+**).

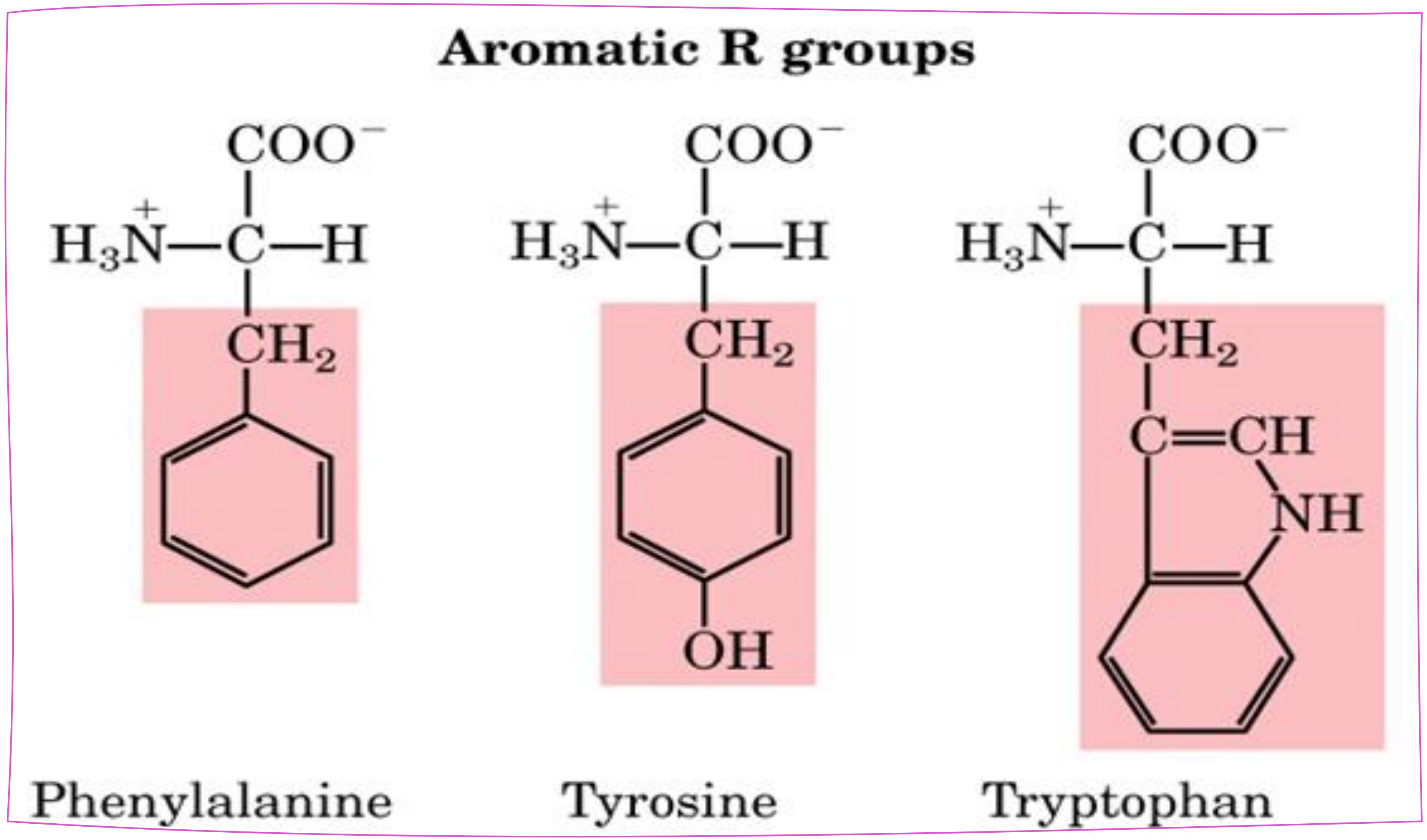
- ✓ At a **low pH** (acidic conditions), the amino acid may **attach** to a **proton** to form a **conjugate acid salt**.
- ✓ Identify a basic amino acid by the presence of a **positive-charged Nitrogen** in its **side chain**.

Basic amino acids are →



Aromatic Amino Acids

An aromatic amino acid is an amino acid that includes an aromatic ring in their side chain.



Essential amino acids

Nine amino acids that the body needs to obtain these from the diet because **our bodies can not make them**.

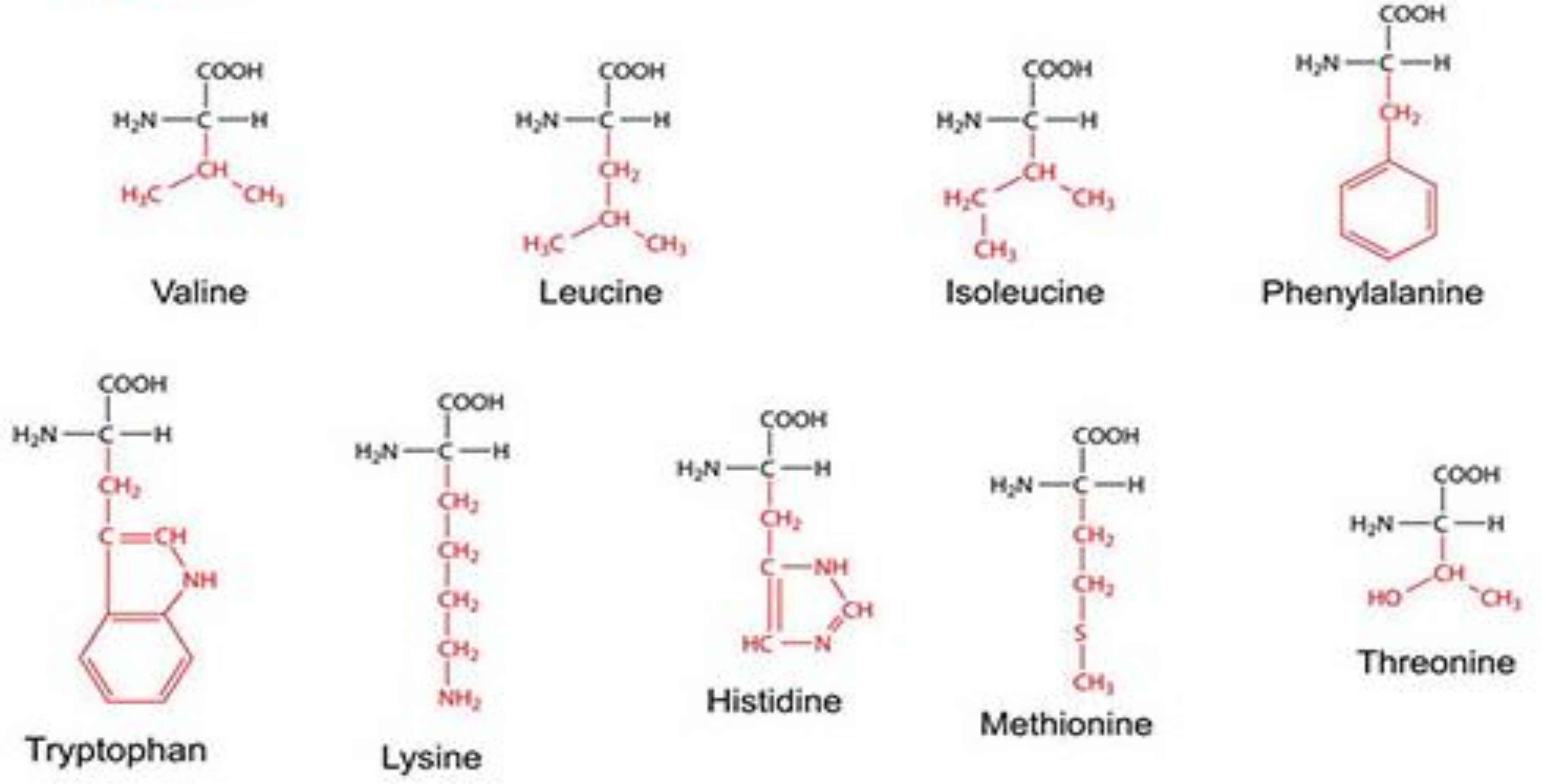
Nonessential amino acids

Eleven amino acids that can be **synthesized in the body itself** and hence not necessarily need to be acquired through diet.

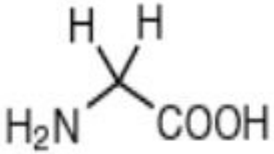
Essential	Non-Essential
Histidine	Alanine
Isoleucine	Arginine
Leucine	Asparagine
Lysine	Aspartic acid
Methionine	Cysteine
Phenylalanine	Glutamic acid
Threonine	Glutamine
Tryptophan	Glycine
Valine	Proline
	Selenocysteine
	Serine
	Tyrosine

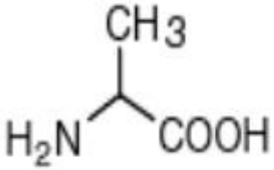
Essential and non-essential amino acids

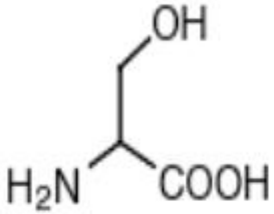
Essential Amino Acids

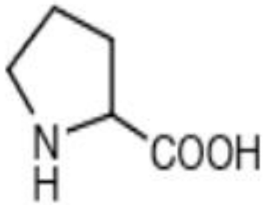


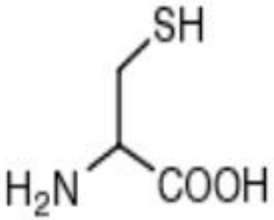
Non-Essential Amino Acids

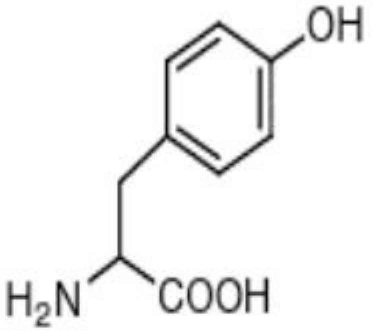

Glycine (Gly, G)

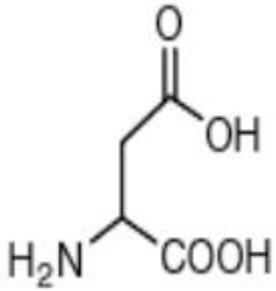

Alanine (Ala, A)

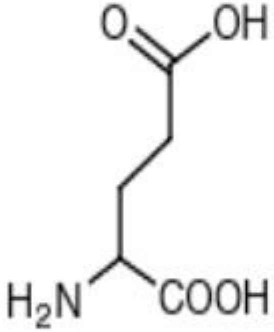

Serine (Ser, S)

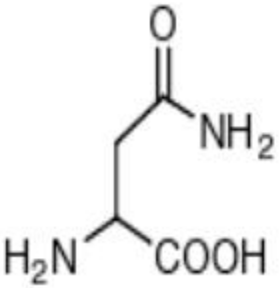

Proline (Pro, P)

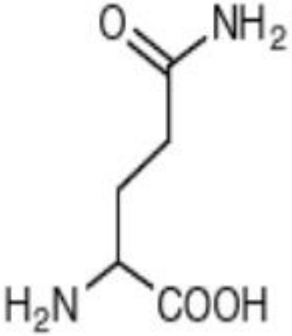

Cysteine (Cys, C)

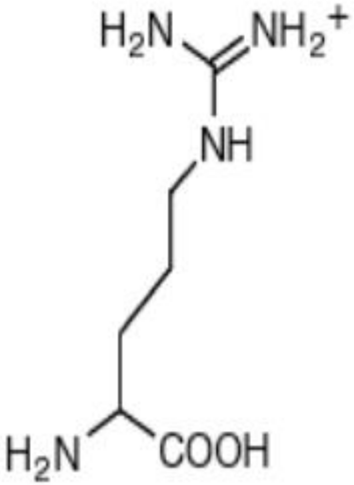

Tyrosine (Tyr, Y)


Aspartic Acid (Asp, D)


Glutamic Acid (Glu, E)


Asparagine (Asn, N)


Glutamine (Gln, Q)


Arginine (Arg, R)

Protein

- Monomer: Amino Acids
- Elements found in it: C, H, N, and O
- Function:

a) Serve as antibodies to protect against diseases

b) Help to transport substances through the body

c) Serve as enzymes

d) Form muscles, skin, hair, bone, ligaments, etc.

Proteins display an incredible diversity of **functions**

1. **Biocatalyst:** Such as **Enzymes**

2. **Hormonal** functions**:** Some Hormones are polypeptides such as **Insulin** or **Glucagon** which direct and regulate metabolism in the body.

3. Contractile proteins in **muscle** permit movement.

4. In **bone**, the protein **collagen** forms a framework for the deposition of calcium phosphate crystals, acting like the steel cables in reinforced concrete.

Proteins display an incredible diversity of **functions**

5. In the **bloodstream**, proteins, such as **hemoglobin** and plasma **albumin**, shuttle molecules essential to life

6. **Immuno globulins** fight infectious bacteria and viruses.

7. **Storage**: Such as **Ferritin**

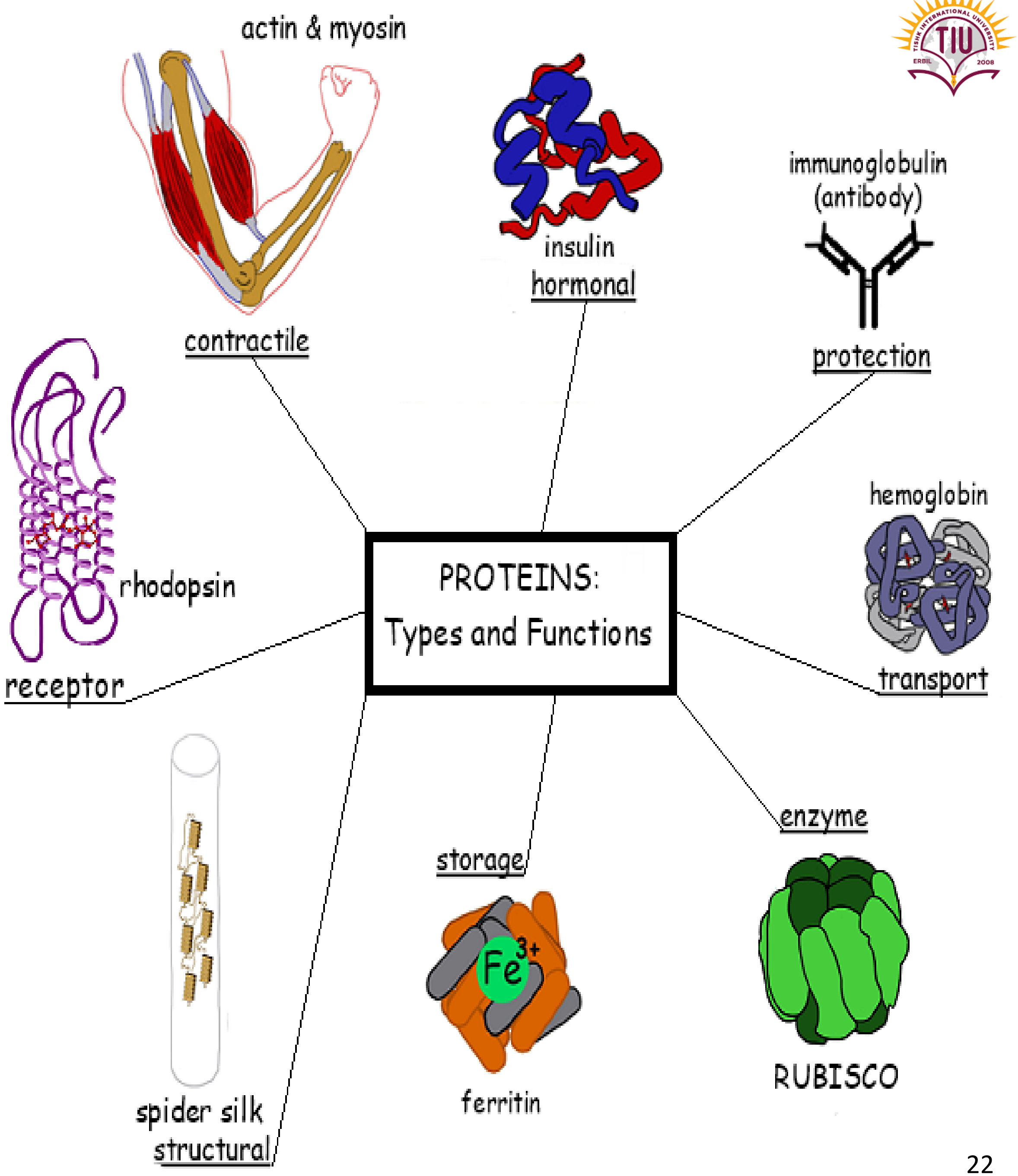
Proteins perform many different functions in the body.

Classification of Some Proteins and their Functions

Class of Protein	Function in the Body	Examples
Structural	Provide structural components	*Collagen* is in tendons and cartilage. *Keratin* is in hair, skin, wool, and nails.
Contractile	Movement of muscles	*Myosin* and *actin* contract muscle fibers.
Transport	Carry essential substances throughout the body	*Hemoglobin* transports oxygen. *Lipoproteins* transport lipids.
Storage	Store nutrients	*Casein* stores protein in milk. *Ferritin* stores iron in the spleen and liver.
Hormone	Regulate body metabolism and nervous system	*Insulin* regulates blood glucose level. *Growth hormone* regulates body growth.
Enzyme	Catalyze biochemical reactions in the cells	*Sucrase* catalyzes the hydrolysis of sucrose. *Trypsin* catalyzes the hydrolysis of proteins.
Protection	Recognize and destroy foreign substances	*Immunoglobulins* stimulate immune responses.

Protein Functions

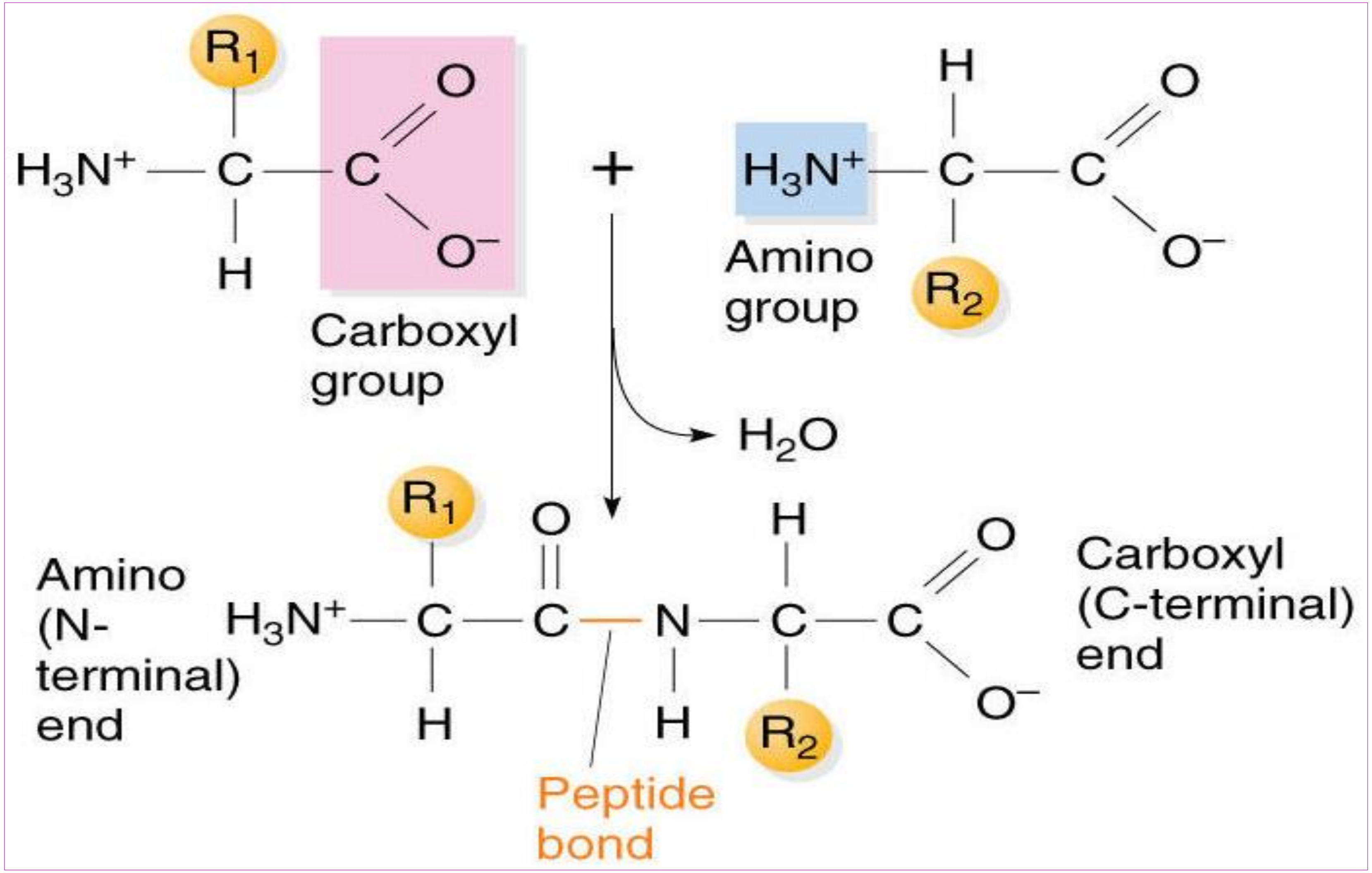
Type of Protein	Function
Structural proteins	Support
Storage proteins	Storage of amino acids
Transport proteins	Transport of other substances
Hormonal proteins	Coordination of an organism's activities
Receptor proteins	Response of cell to chemical stimuli
Contractile proteins	Movement
Defensive proteins	Protection against disease
Enzymatic proteins	Selective acceleration of chemical reactions



Peptides and Proteins

- 20 amino acids are commonly found in protein.
- These 20 amino acids are linked together through "peptide bond forming peptides and proteins.
- The chains containing less than 50 amino acids are called "peptides", while those containing greater than 50 amino acids are called proteins".

Peptide Bond formation between successive amino acids



Peptide Bond Formation

-Amino acids are linked together by condensation reaction between carboxylic and amino groups from two different amino acids (with elimination of water).

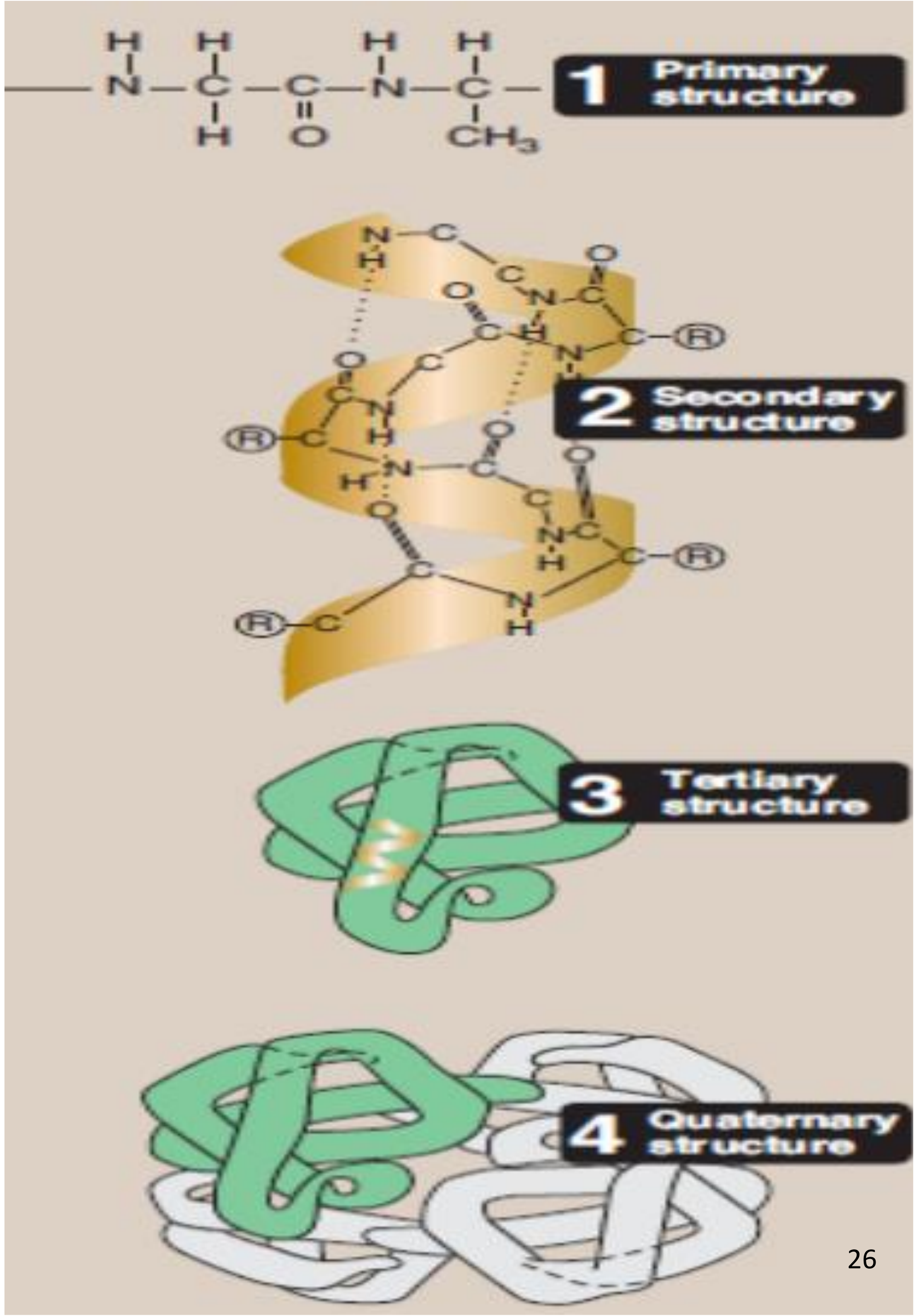
-The amide bond formed is called peptide bond.

Structure of the Proteins

- The **20 amino acids** commonly found in proteins are joined together by **peptide bonds**.

- The **linear sequence** of the linked amino acids contains the **information** necessary to generate a protein molecule with a **unique** three-dimensional shape.

- The **complexity** of **protein structure** is best analyzed by considering the molecule in terms of **four organizational levels:** primary, secondary, tertiary, quaternary



Primary Structure of Protein

The **sequence** of **amino acids** in a **protein** is called the **primary structure** of the protein.

Understanding the **primary structure** of proteins is **important** because many **genetic diseases** result in proteins with abnormal amino acid sequences.

If the **primary structures** of the normal and the mutated proteins are known, this information may be used to **diagnose** or **study** the **disease**.

Primary Structure of Protein

In proteins, amino acids are joined **covalently** by **peptide bonds**.

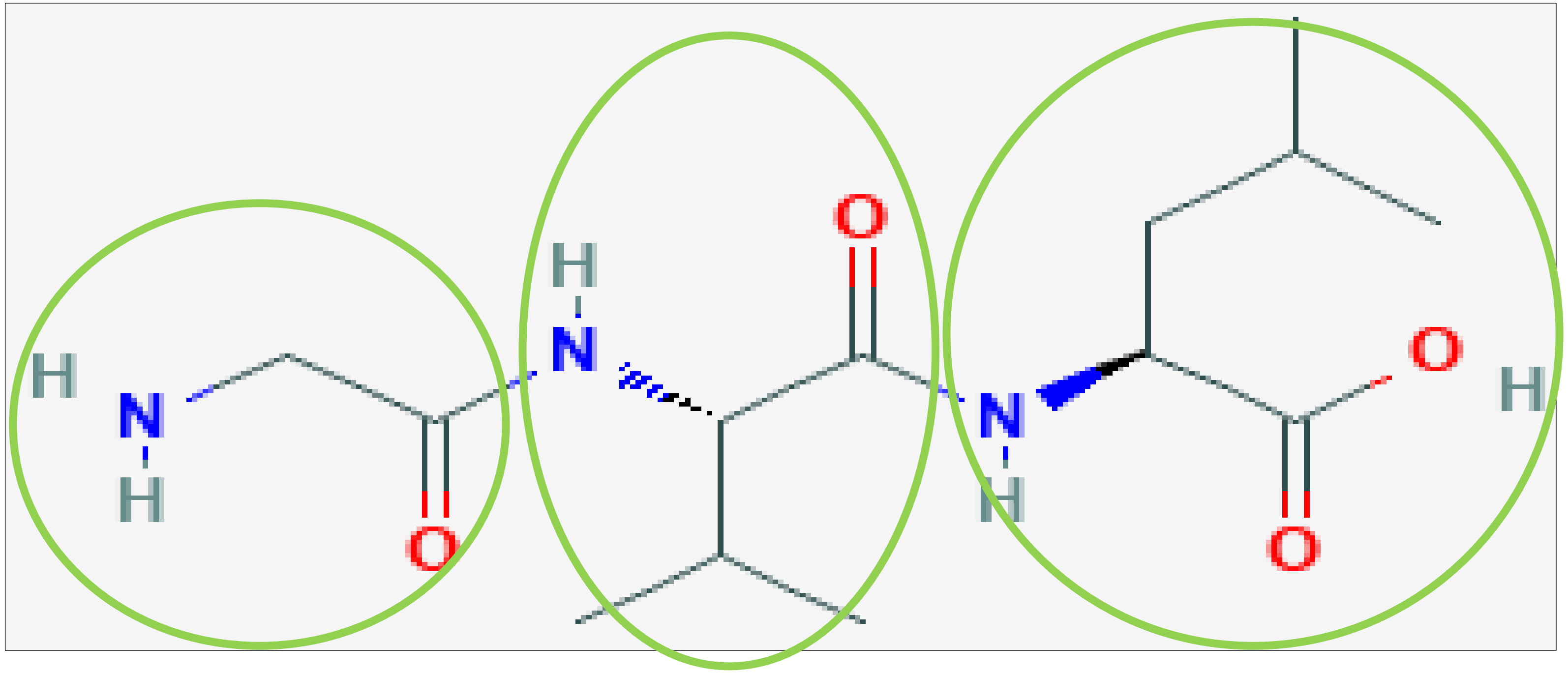
Peptide bonds are not broken by conditions that denature proteins, such as **heating** or **high concentrations** of **urea**.

Prolonged exposure to a **strong acid** or **base** at **elevated temperatures** is required to **hydrolyze** these bonds non enzymically.

Naming the Peptide

When a polypeptide is named, the **suffixes** of **all amino acid** residues **changed** to **-yl**, with the exception of the C-terminal amino acid.

For example: a tripeptide composed of an N-terminal valine, a glycine, and a C-terminal leucine is called **glycyl valyl leucine**.



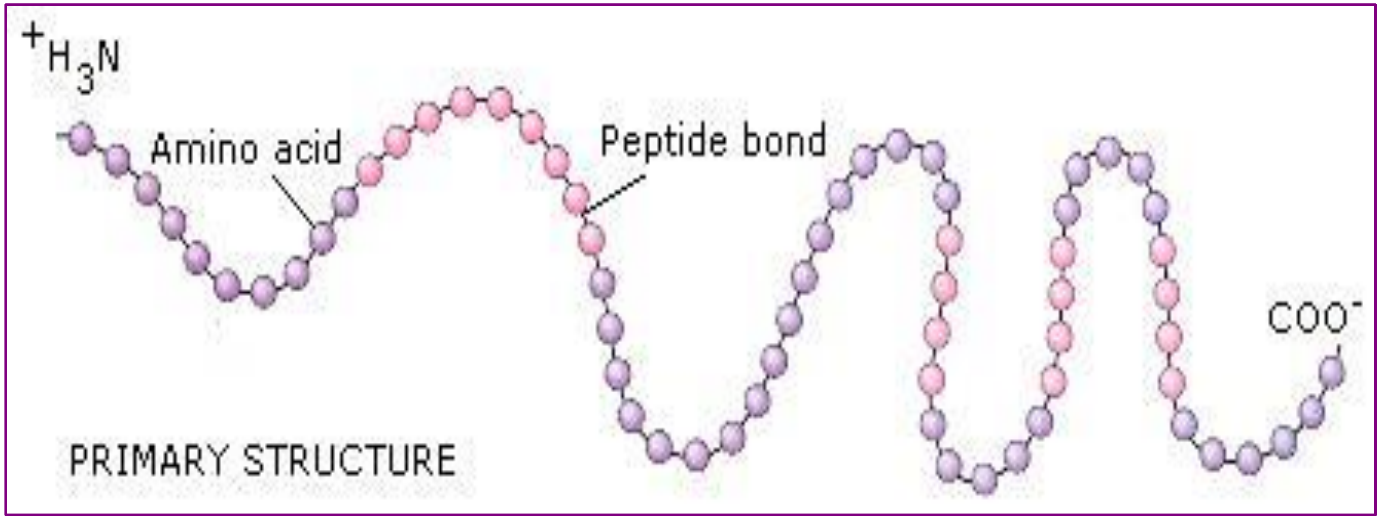
Polarity of the **Peptide bonds**

- The **–C=O** and **–NH** groups of the peptide bond are **polar**.

- **Hydrogen bonding** between **amino groups** and **carboxyl groups** in **neighboring regions** of the **protein chain** sometimes causes certain patterns of folding to occur which are known as **alpha helices** and **beta sheets**. These stable folding patterns make up the **secondary structure** of a **protein**.

- Groups present in the side chains of the constituent amino acids are critical to protein structure because these side chains can bond with one another to hold a length of protein in a certain shape or conformation.

Levels of Protein Organization

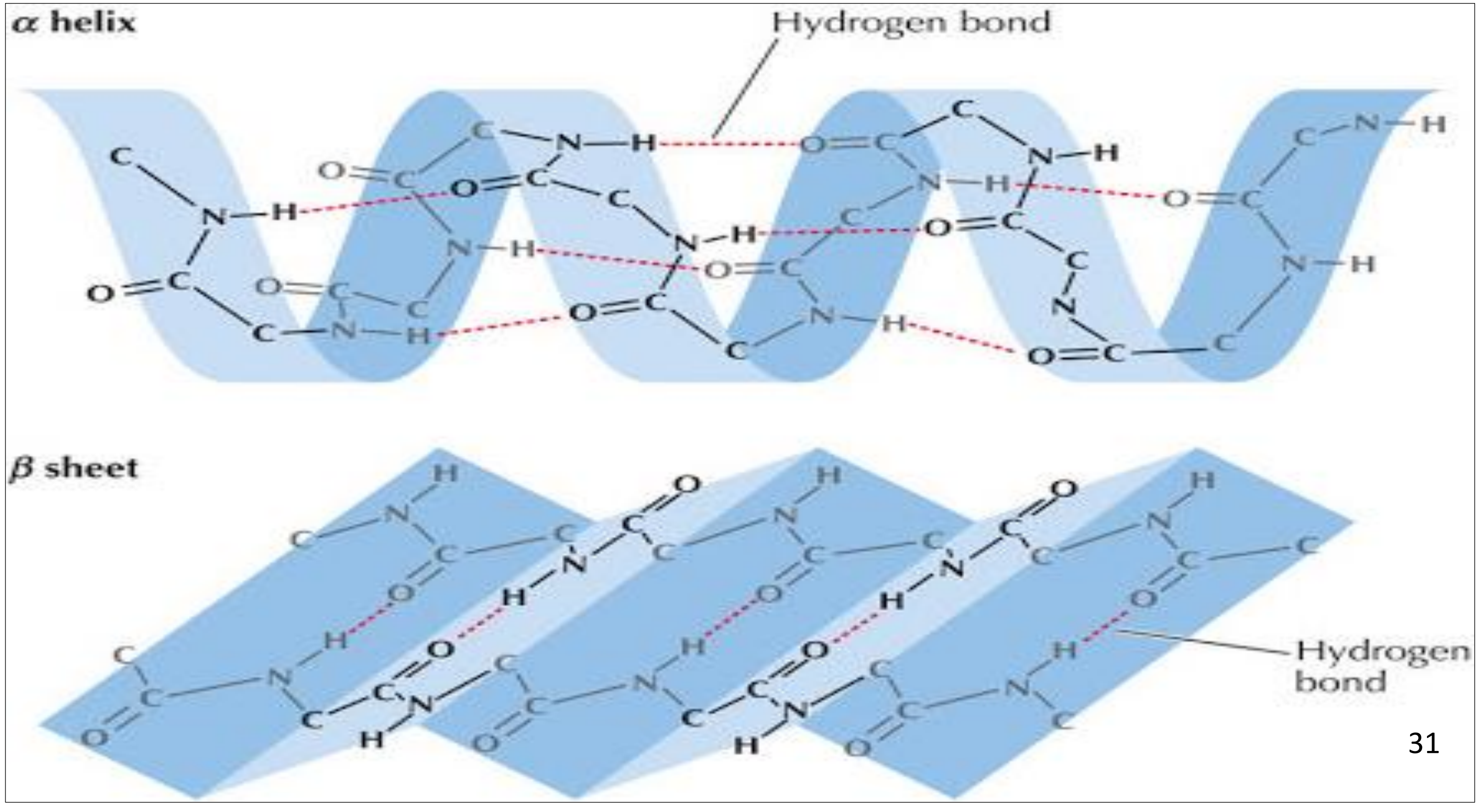


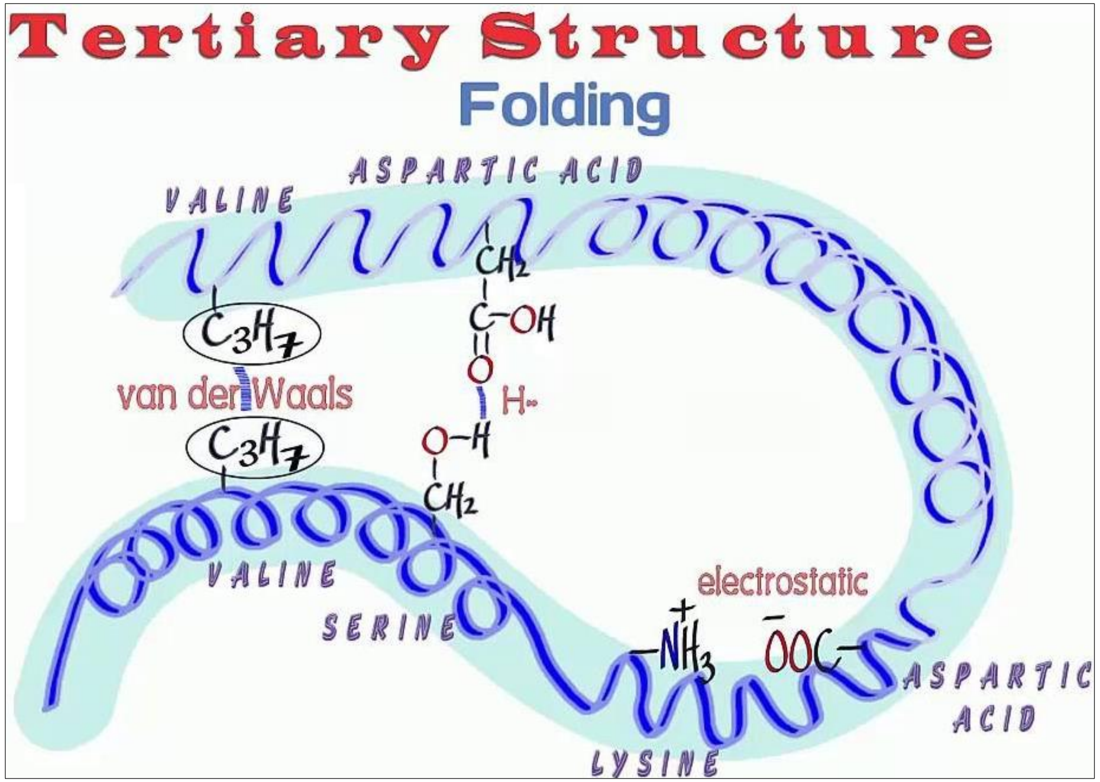
Primary Structure:

The **sequence** of **amino acids** in the polypeptide chain that determines the **folding** of the peptide molecule.

Secondary Structure:

The **formation** of **α-helices** and **β-pleated sheets** due to hydrogen bonding between the peptide backbone.



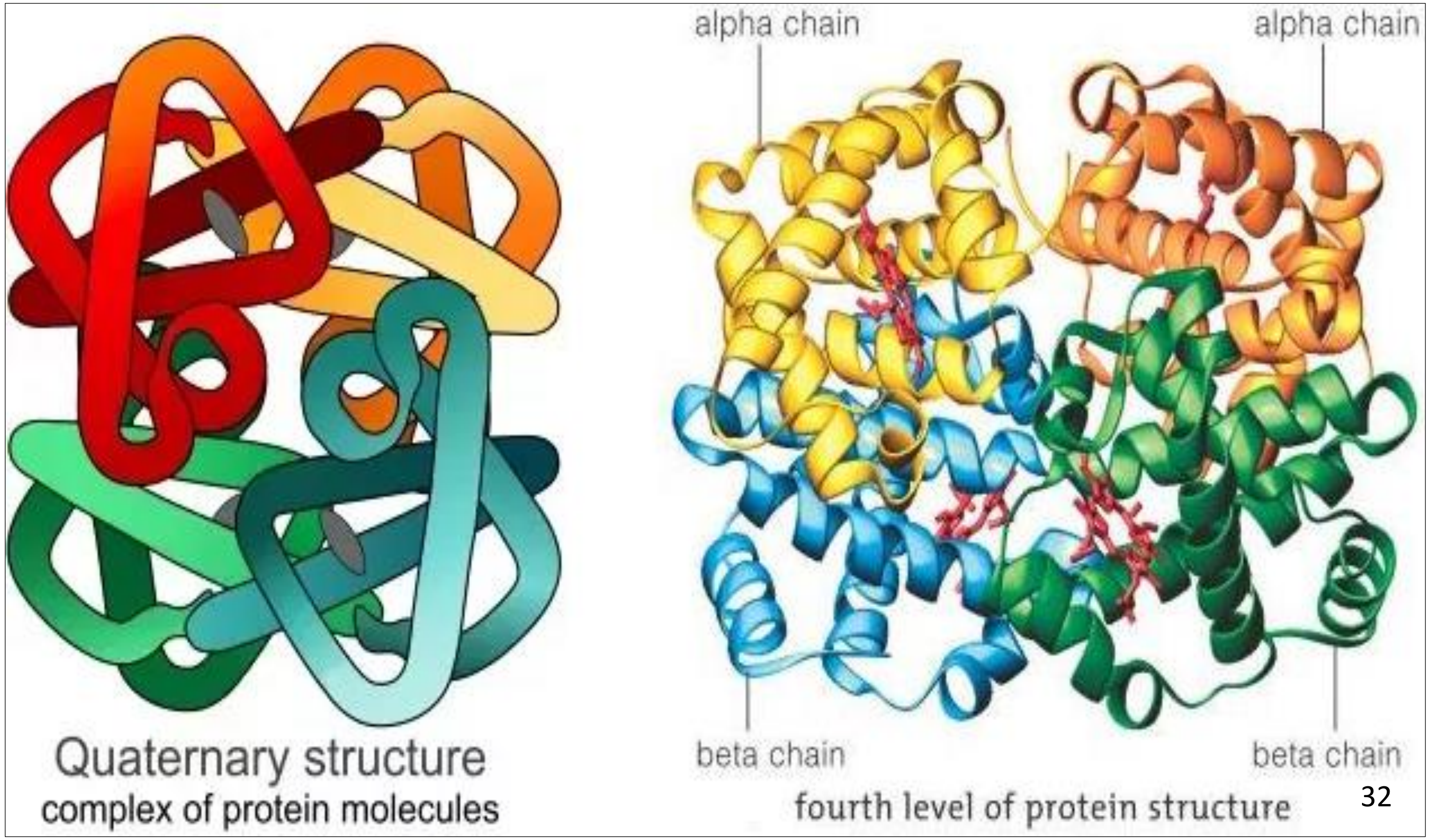


Tertiary Structure:

Folding of helices and sheets **influenced** by R group bonding.

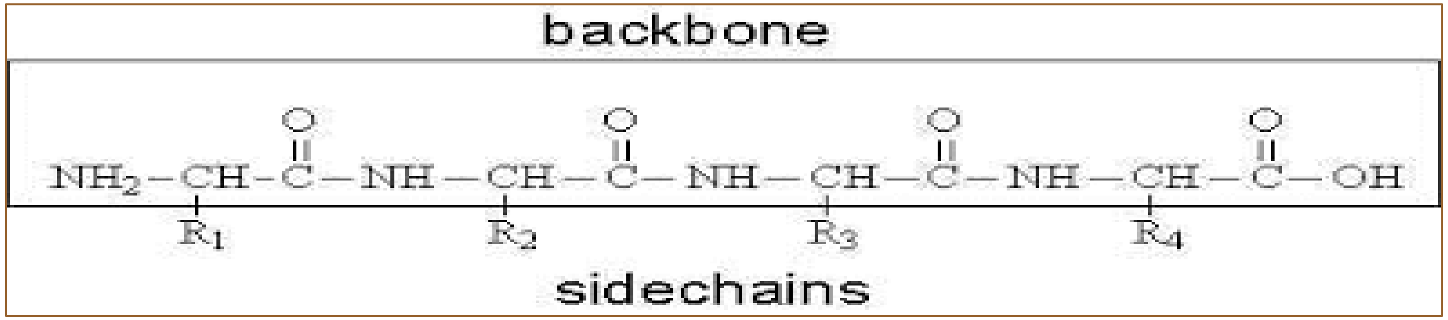
Quaternary Structure:

The **association** of more than one polypeptide into a protein complex **influenced** by R group bonding.



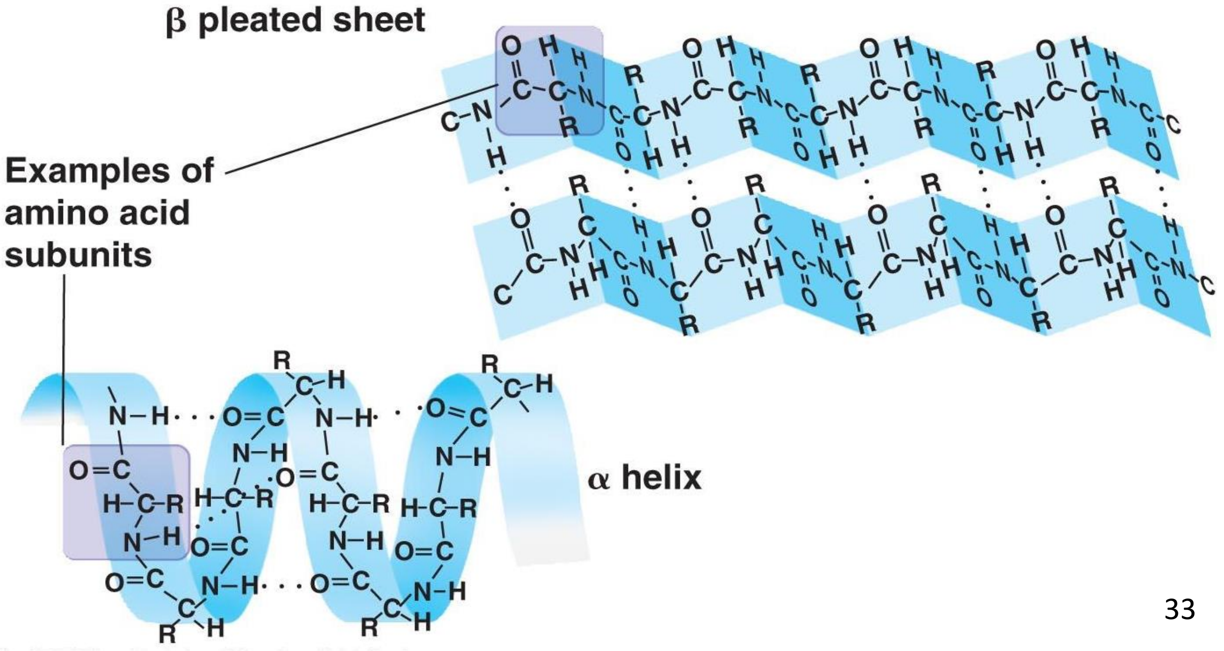
Protein Secondary Structure

✓ The **peptide backbone** has areas of **positive charge** and **negative charge**.



✓ These areas can <u>interact with one another</u> to **form <u>hydrogen bonds</u>**.

➢ The result of these hydrogen bonds are two types of structures: **α-helices & β-pleated sheets**



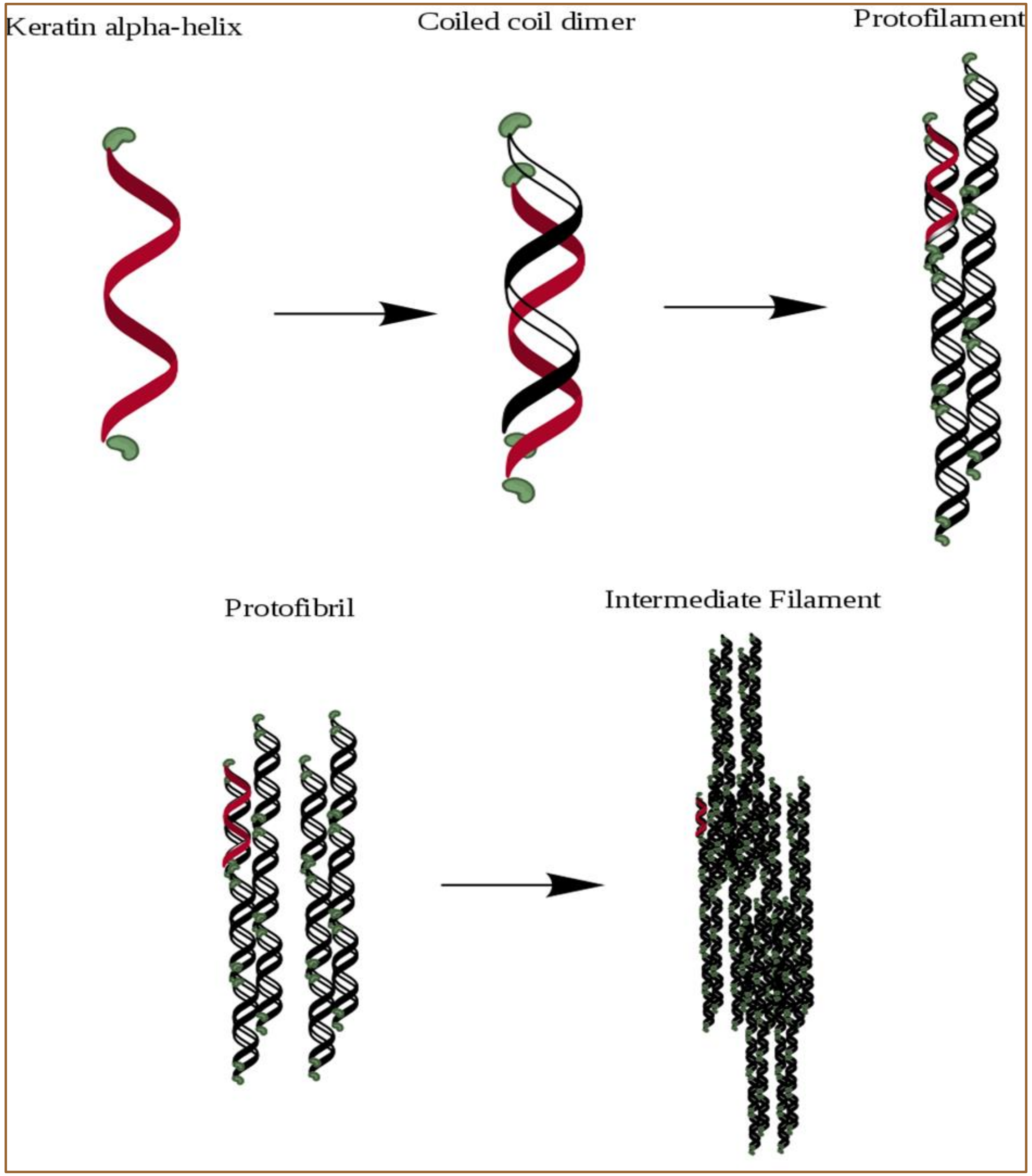
Protein Secondary Structure

- **α-Helices:**

A **spiral structure**, consisting of **coiled polypeptide** backbone core to **avoid interfering sterically** with each other.

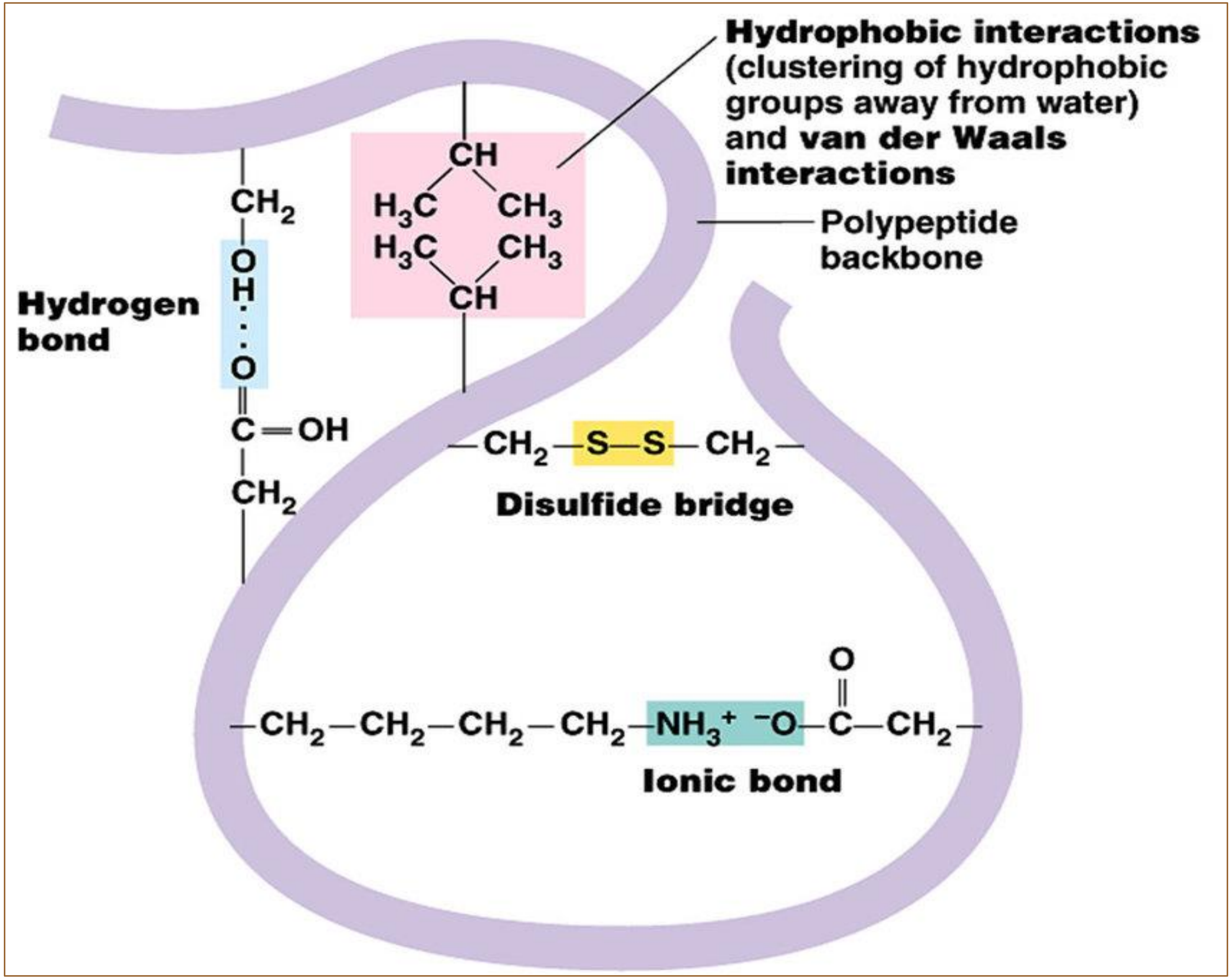
✓ **For example:**

- **Keratins** are a major component of tissues such as Hair, Skin glands, and Nails.

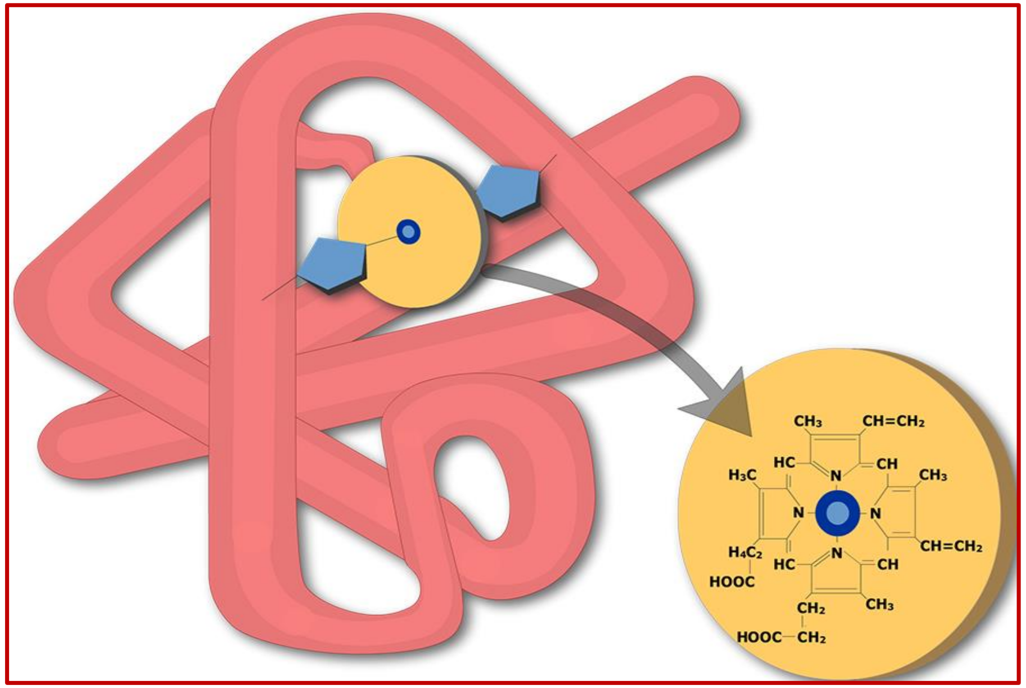


Keratin molecule with intra-molecular bonds

- Their rigidity is determined by the number of **disulfide bonds** between the constituent polypeptide chains.



- In contrast to keratin, **Myoglobin**, whose structure is also highly α-helical, is a globular, flexible molecule.

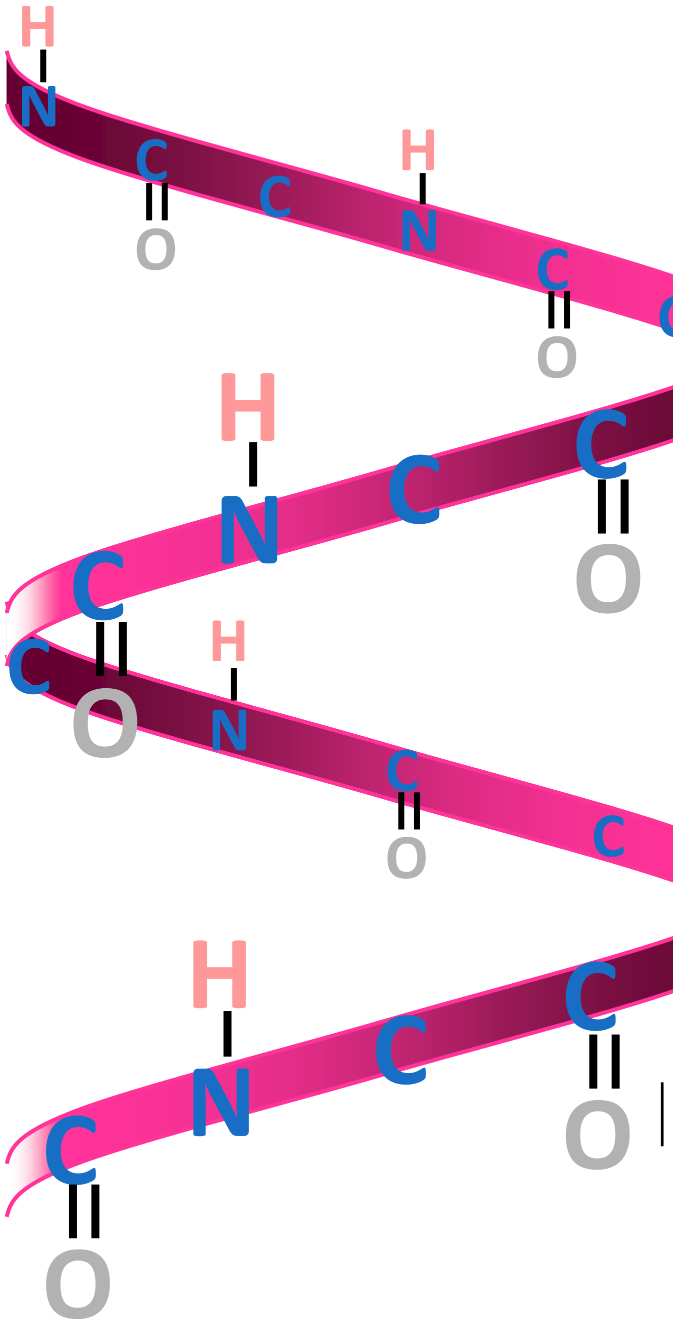


Myoglobin (Mb)

Myoglobin function is to store molecular oxygen in muscles.

(myo = muscles)

- It has two main components: a single polypeptide chain, and heme ligand inside the protein.


H
N
C
C
O
H
N
C
C
O
H
N
H
N
C
C
O
C
C
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H
N
C
C
O
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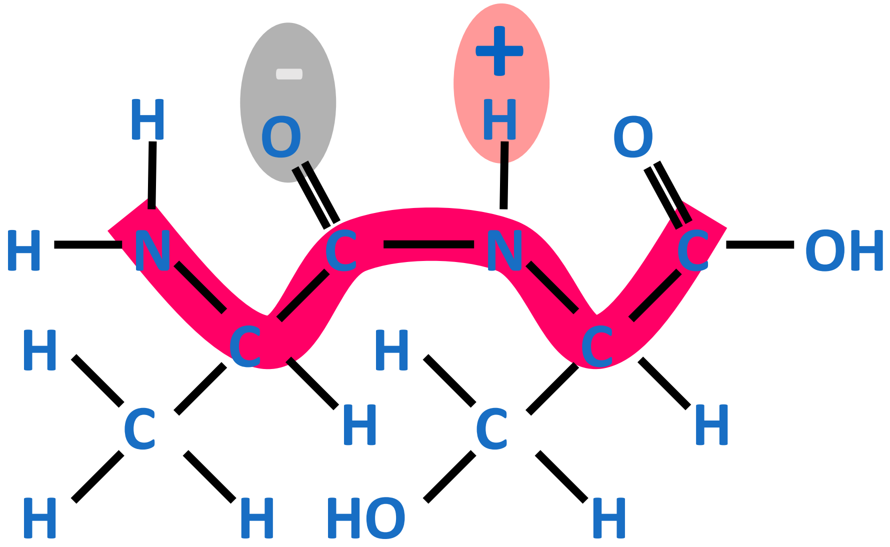
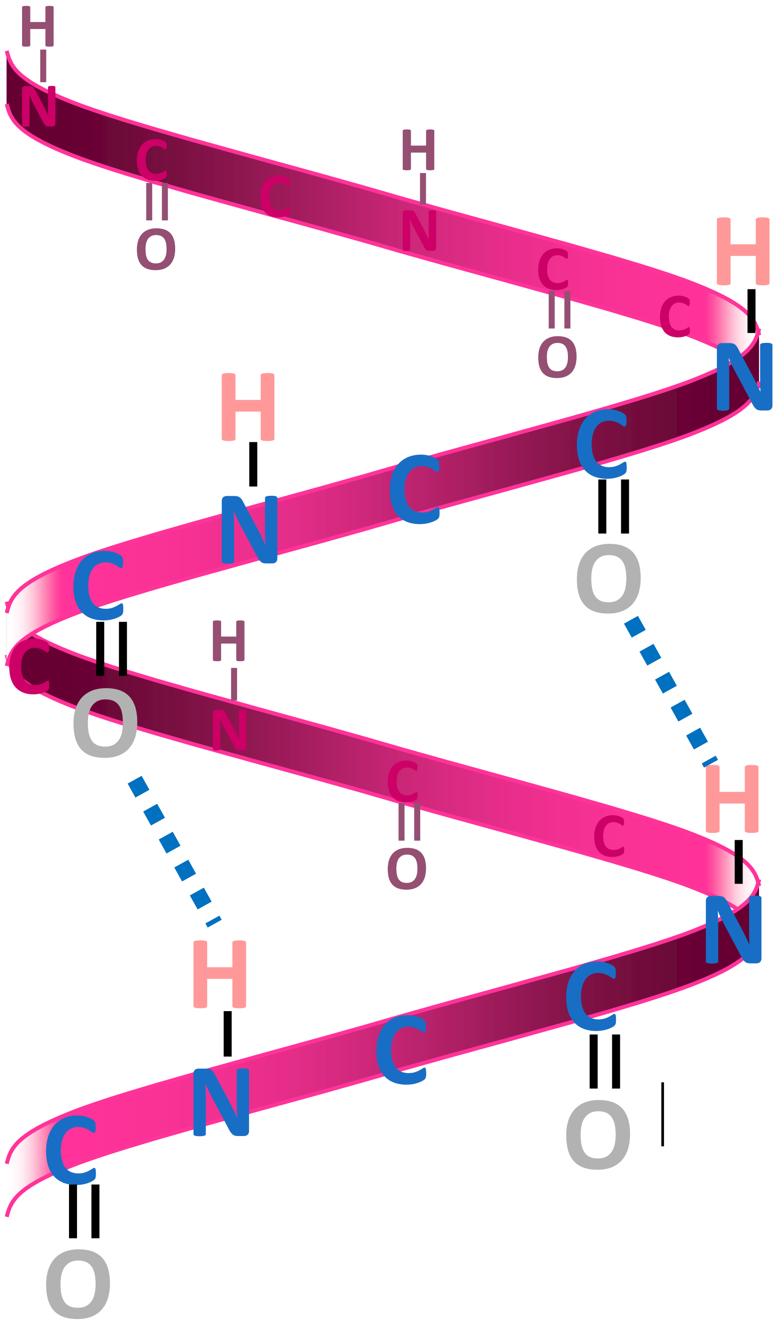
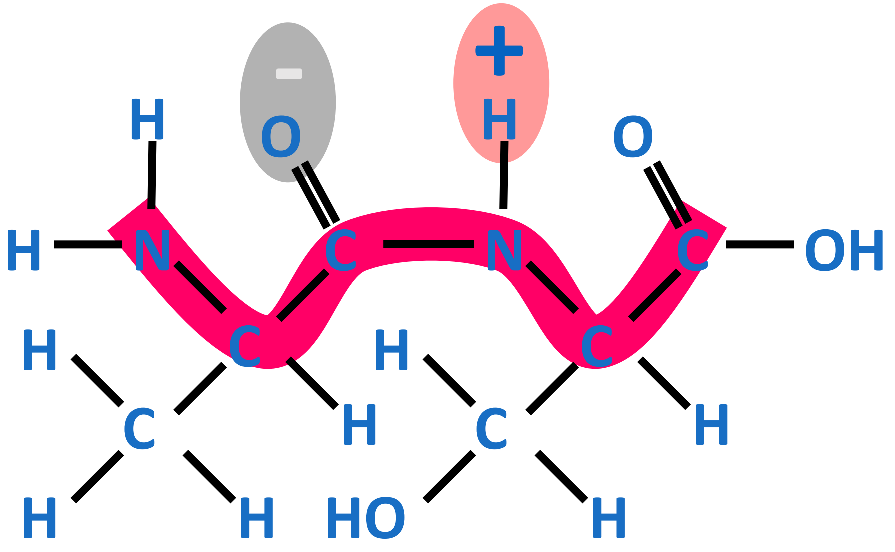
O
H
N
C
C
O
C
O

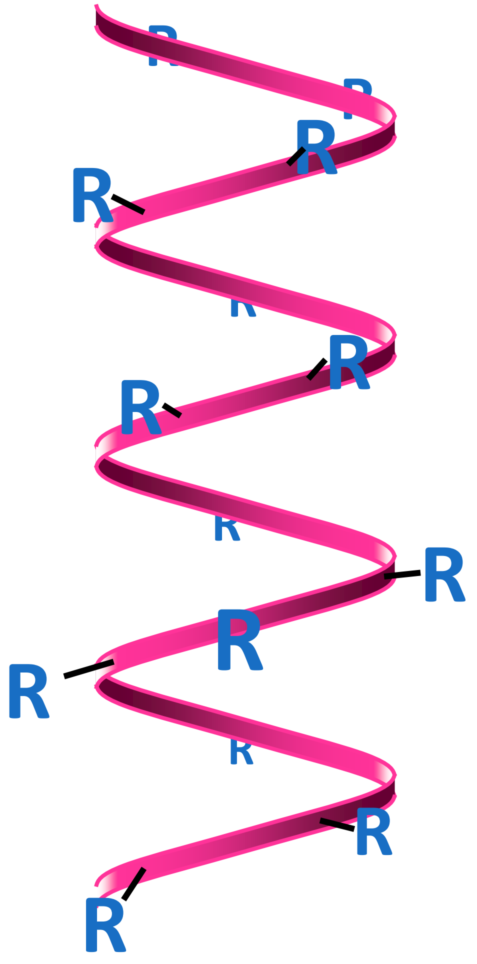

-
+
H
O
H
O
H
N
C
N
C
OH
H
C
H
C
H
H
H
C
H
C
H
H
HO
H



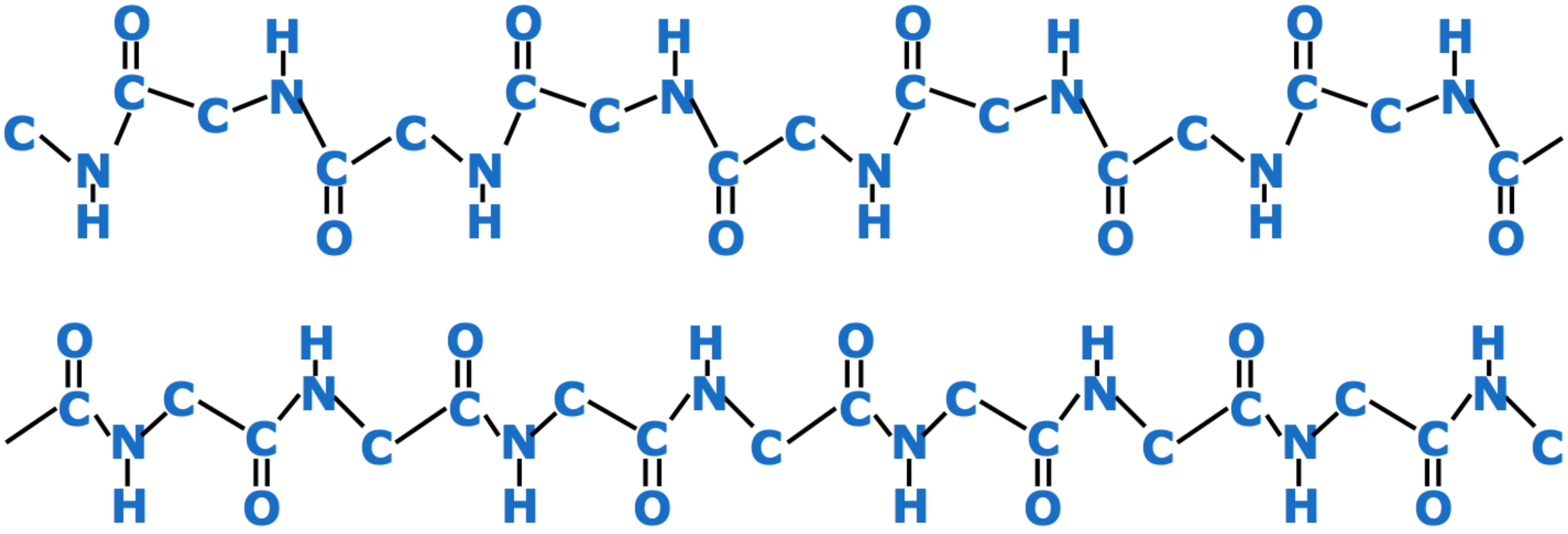


Amino acids per turn:
Each turn of an α-helix contains 3.6 amino acids.

➢ **R groups** stick out from the α-helix influencing higher levels of protein organization



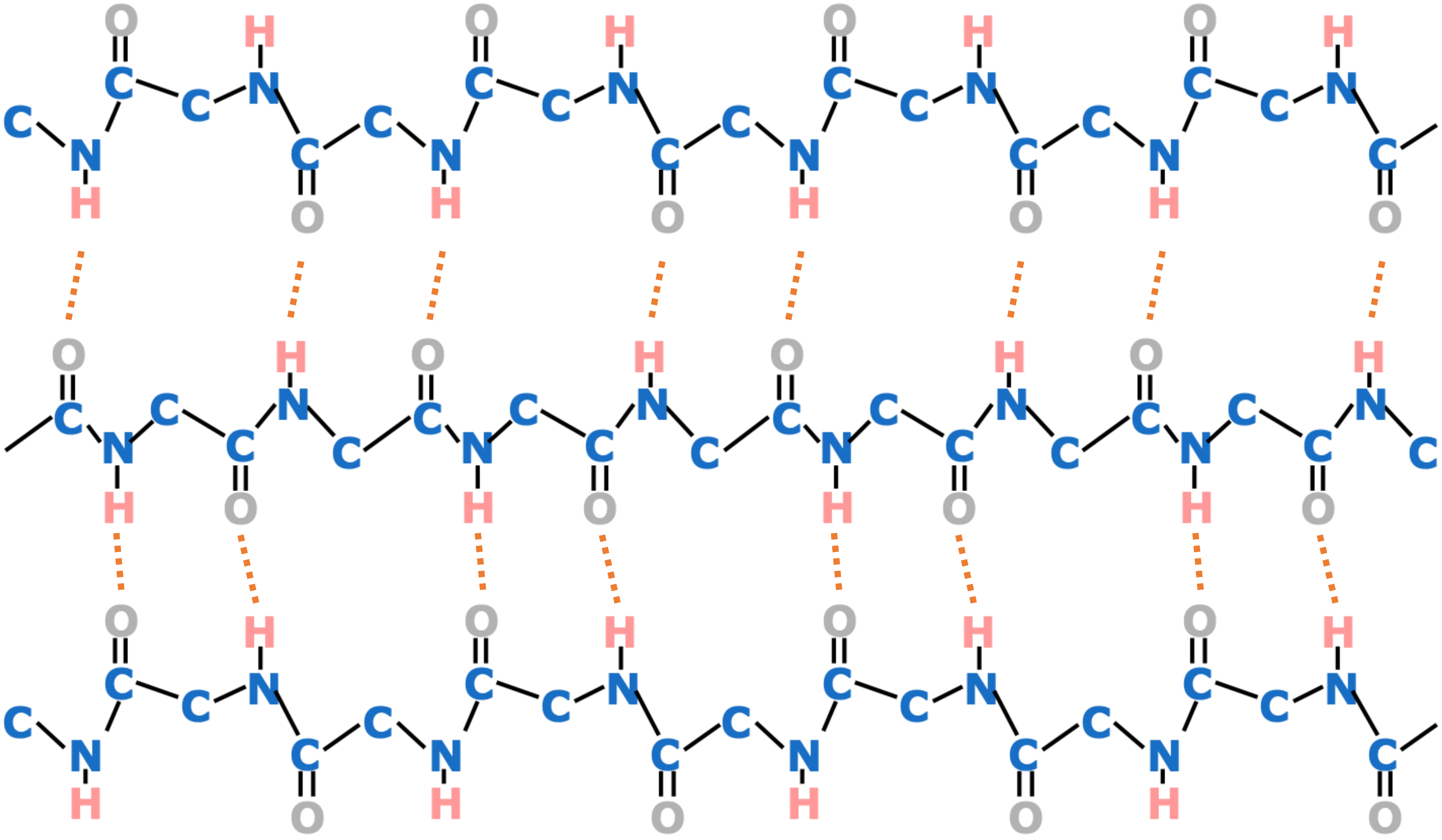
Protein Secondary Structure:
β-Pleated sheets

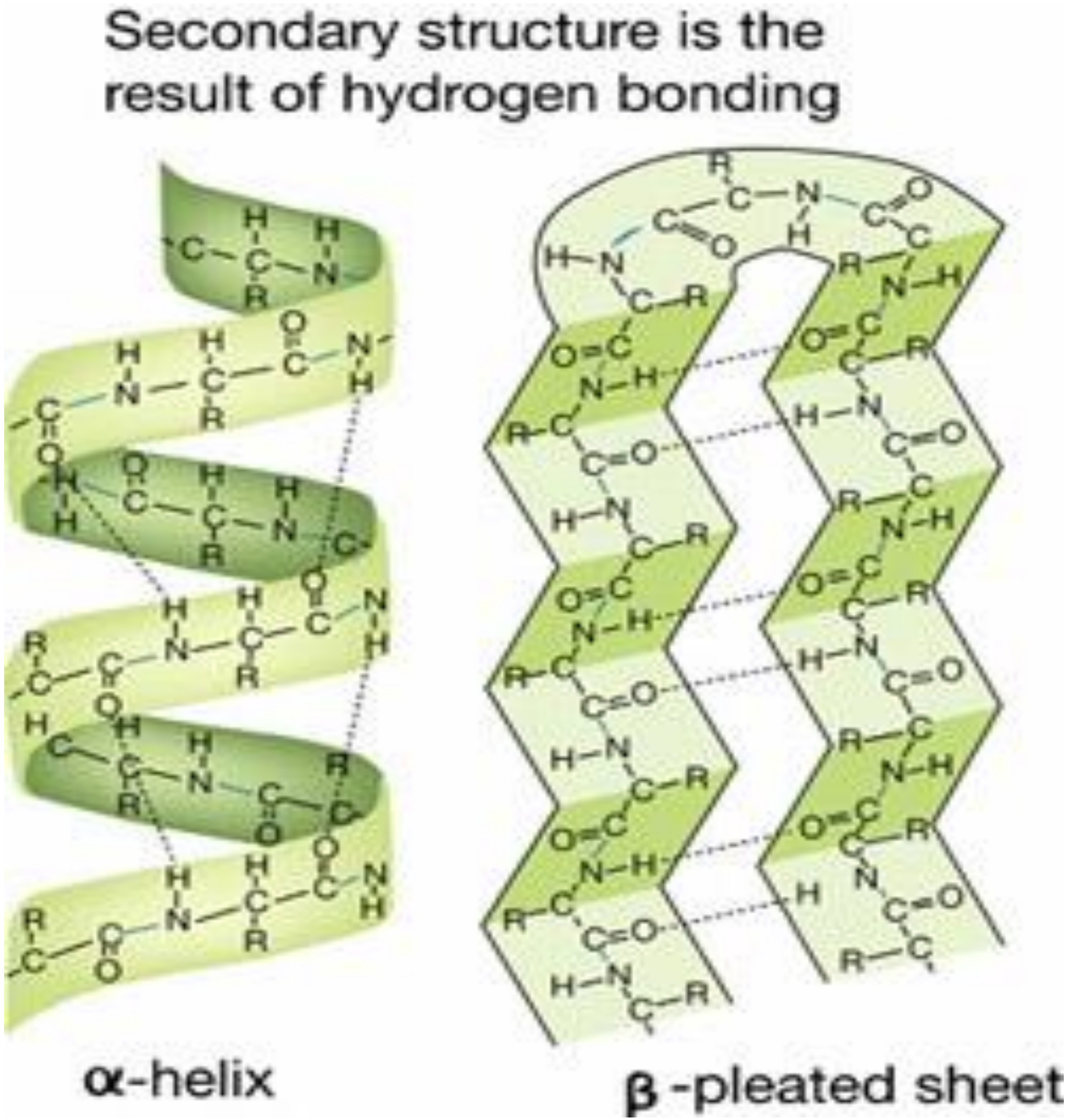


β-Sheet

The β-sheet is another form of **secondary structure** in which all of the peptide bond components are involved in **hydrogen bonding**.

Protein Secondary Structure:
β-Pleated sheets





Comparison of β-sheet & α-helix:

Unlike the α-helix, **β-sheets** are composed of **two or more** peptide chains (β-strands) or segments of polypeptide chains.

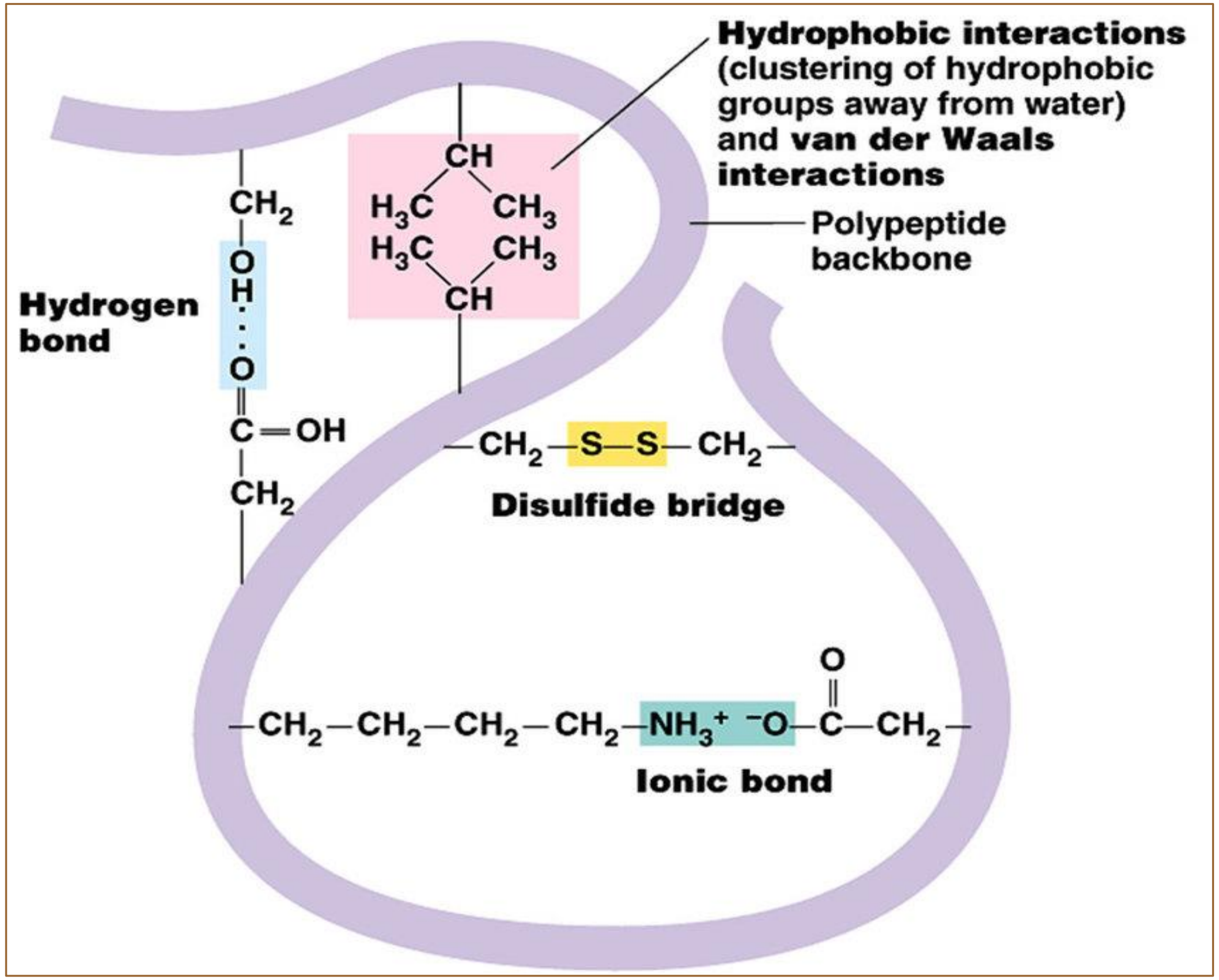
✓ Note also that in β-sheets the **hydrogen bonds** are **perpendicular** to the **polypeptide backbone**.

Tertiary Structure

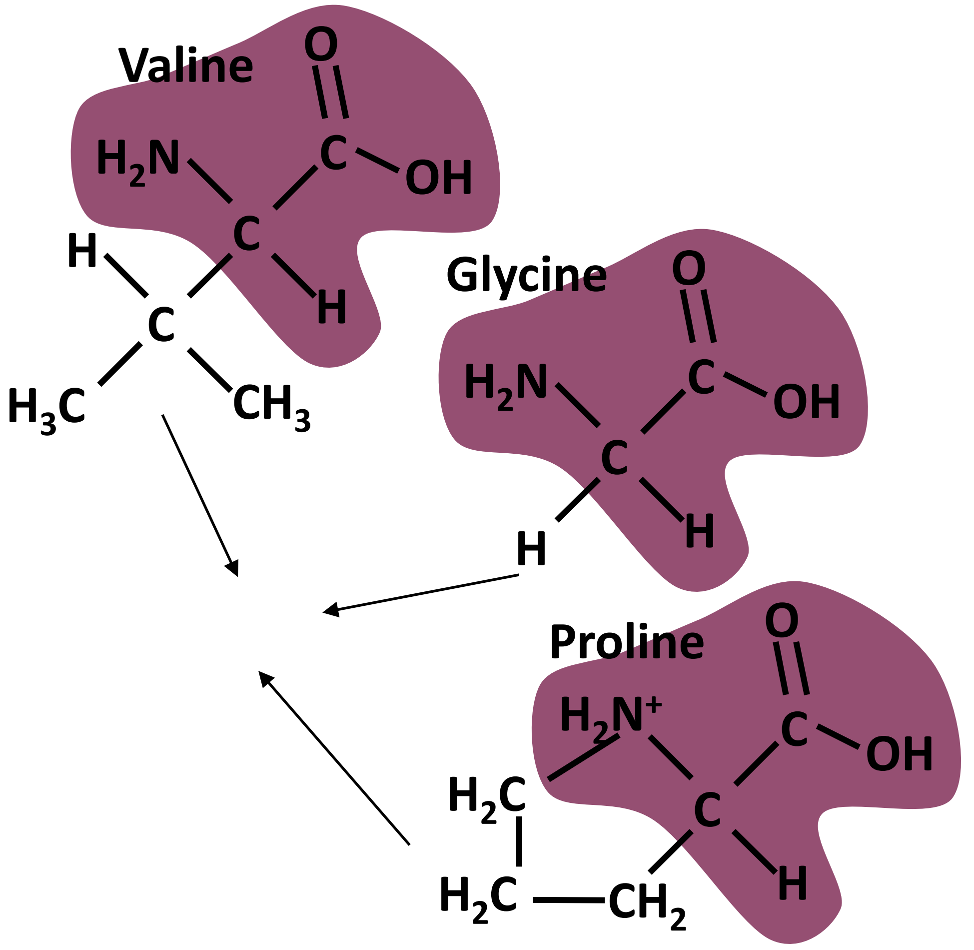
❖ Tertiary structure results from the **folding** of α-helices & β-pleated sheets.

Factors influencing tertiary structure include:

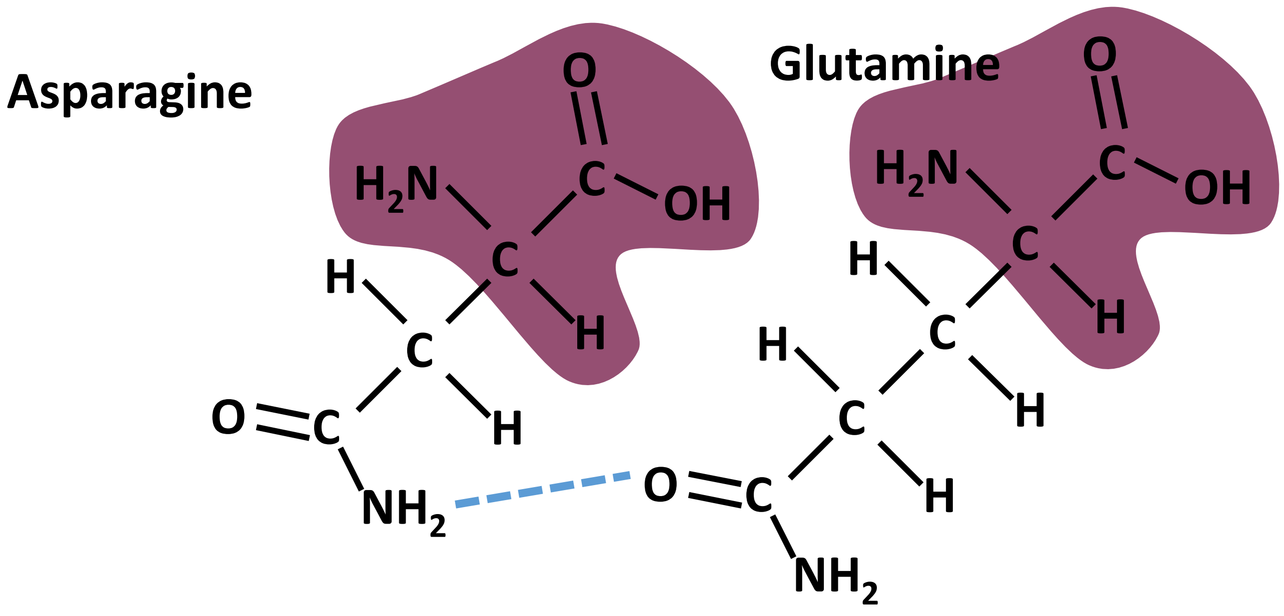
✓ **Hydrophobic interactions**
✓ **Hydrogen bonding**
✓ **Disulphide bridges**
✓ **Ionic bonds**



Hydrophobic interactions



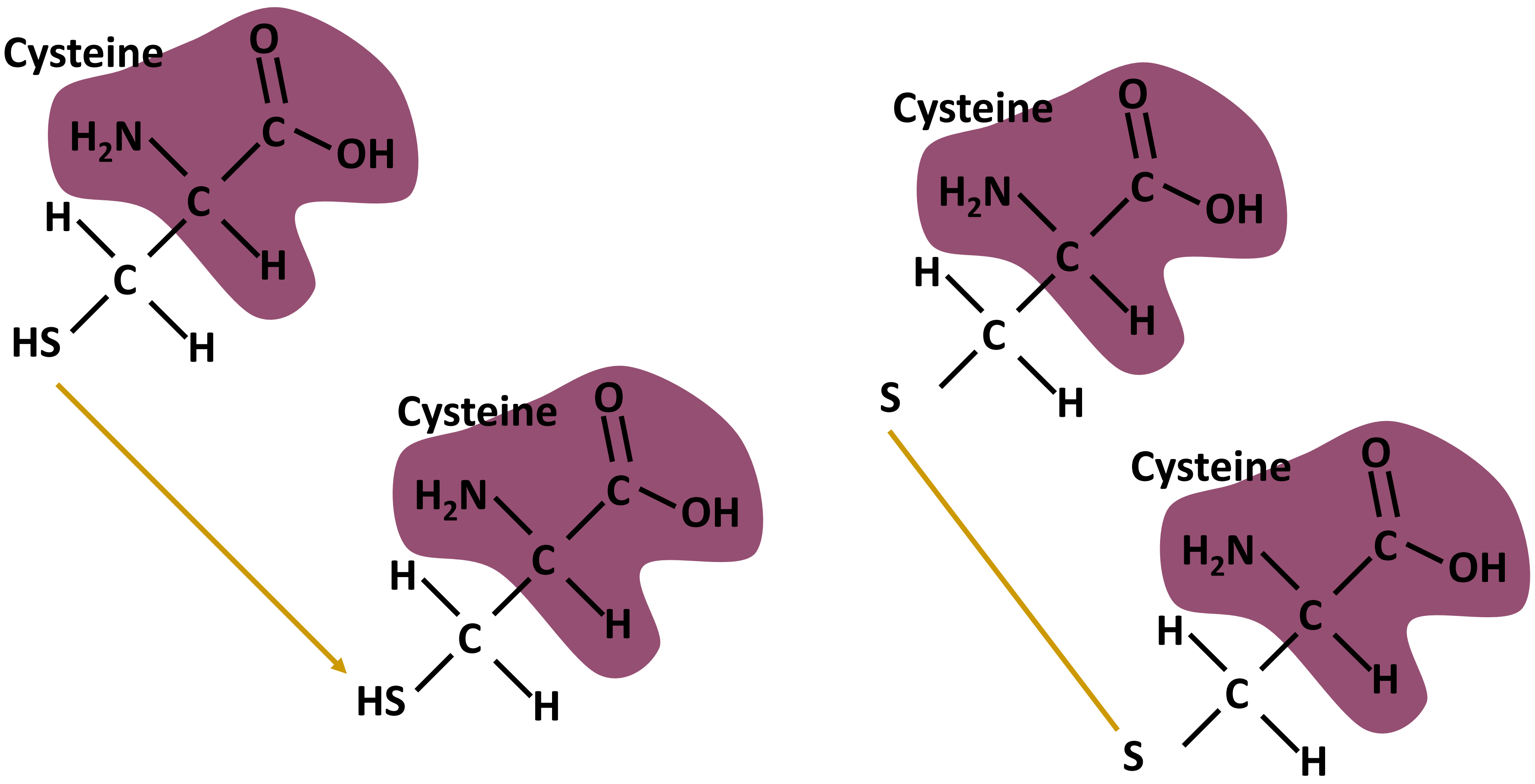
Hydrogen Bonding



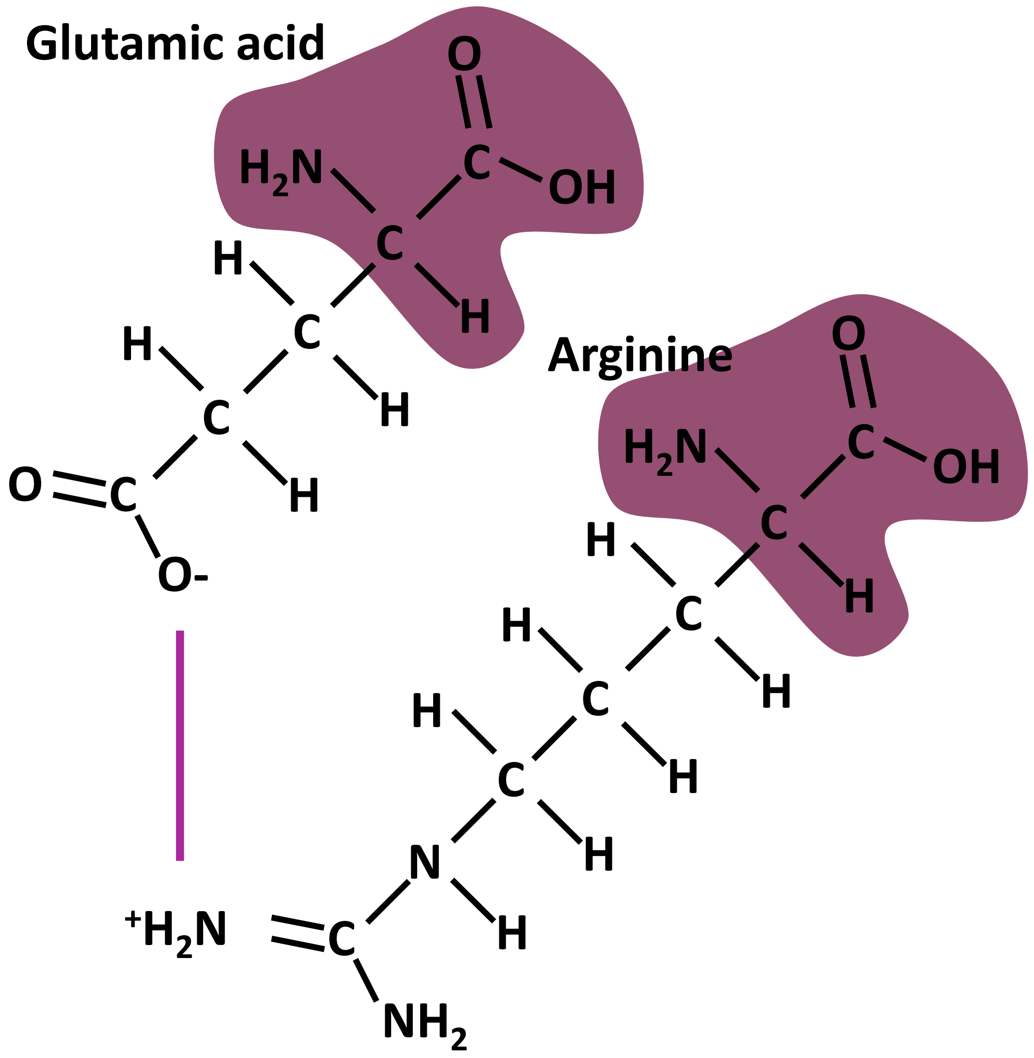
N--------H (+) (-) O --------C

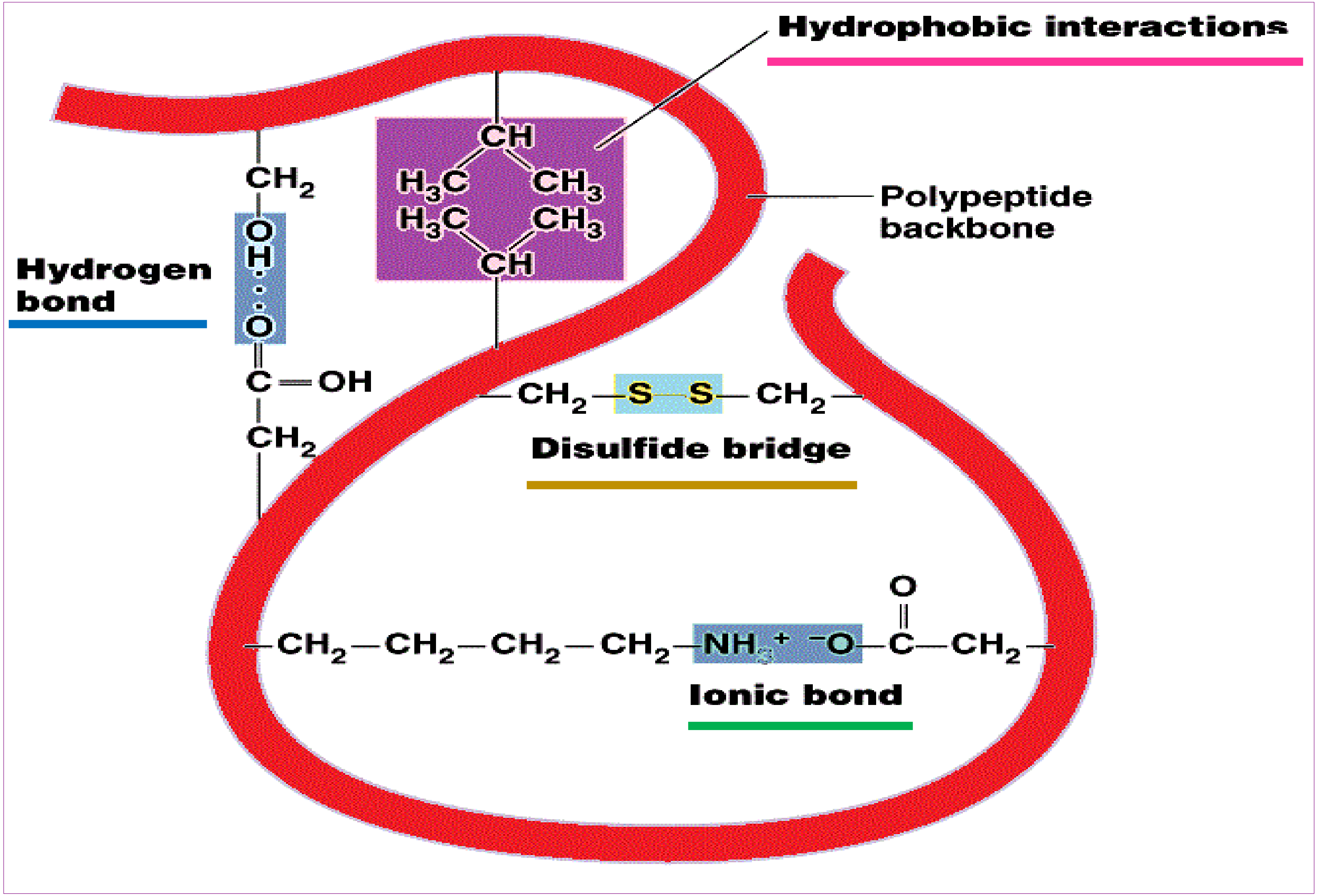
slightly slightly

Disulphide bridges



Ionic Bonds

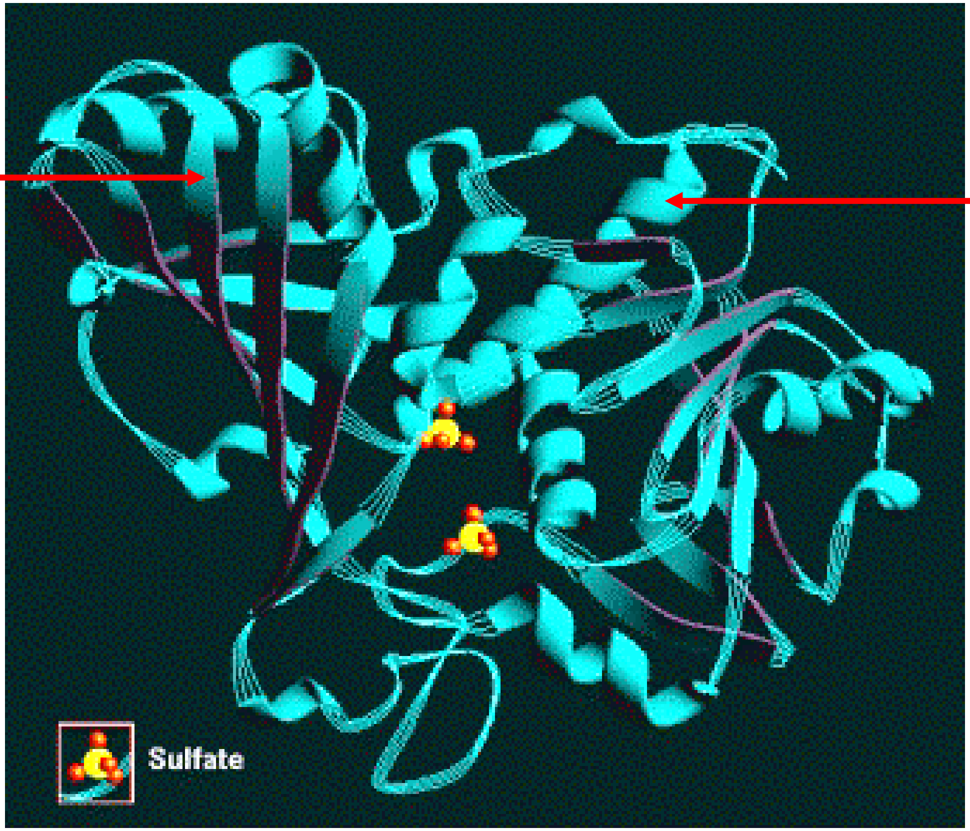

Glutamic acid
O
H_2N
C
OH
C
H
H
C
H
H
C
H
O
C
H
O-
Arginine
O
H_2N
C
OH
C
H
H
C
H
H
C
H
H
C
H
N
H
^+H_2N
C
NH_2


Hydrophobic interactions
Polypeptide backbone
Hydrogen bond
Disulfide bridge
Ionic bond
CH
H3C
CH3
H3C
CH3
CH
CH2
O
H
O
C
OH
CH2
CH2
S
S
CH2
CH2
CH2
CH2
CH2
NH3+
-O
O
C
CH2

G-3-P Dehydrogenase Tertiary Structure

β-sheet

α-helix

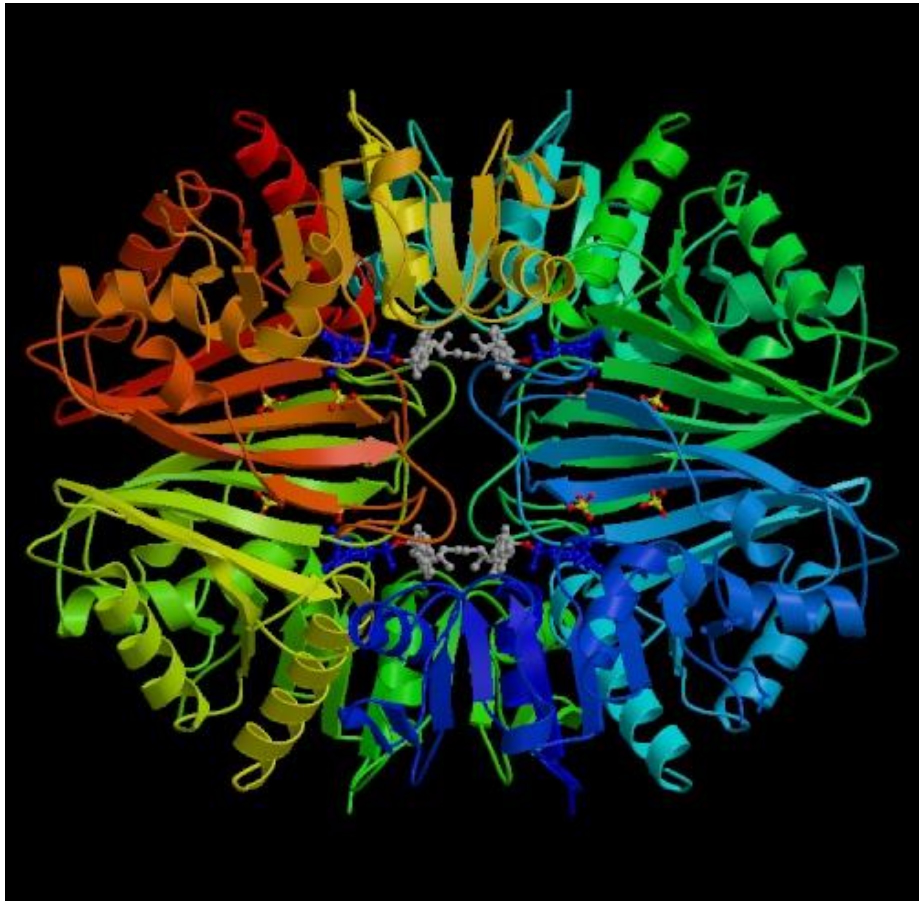


Quaternary Structure

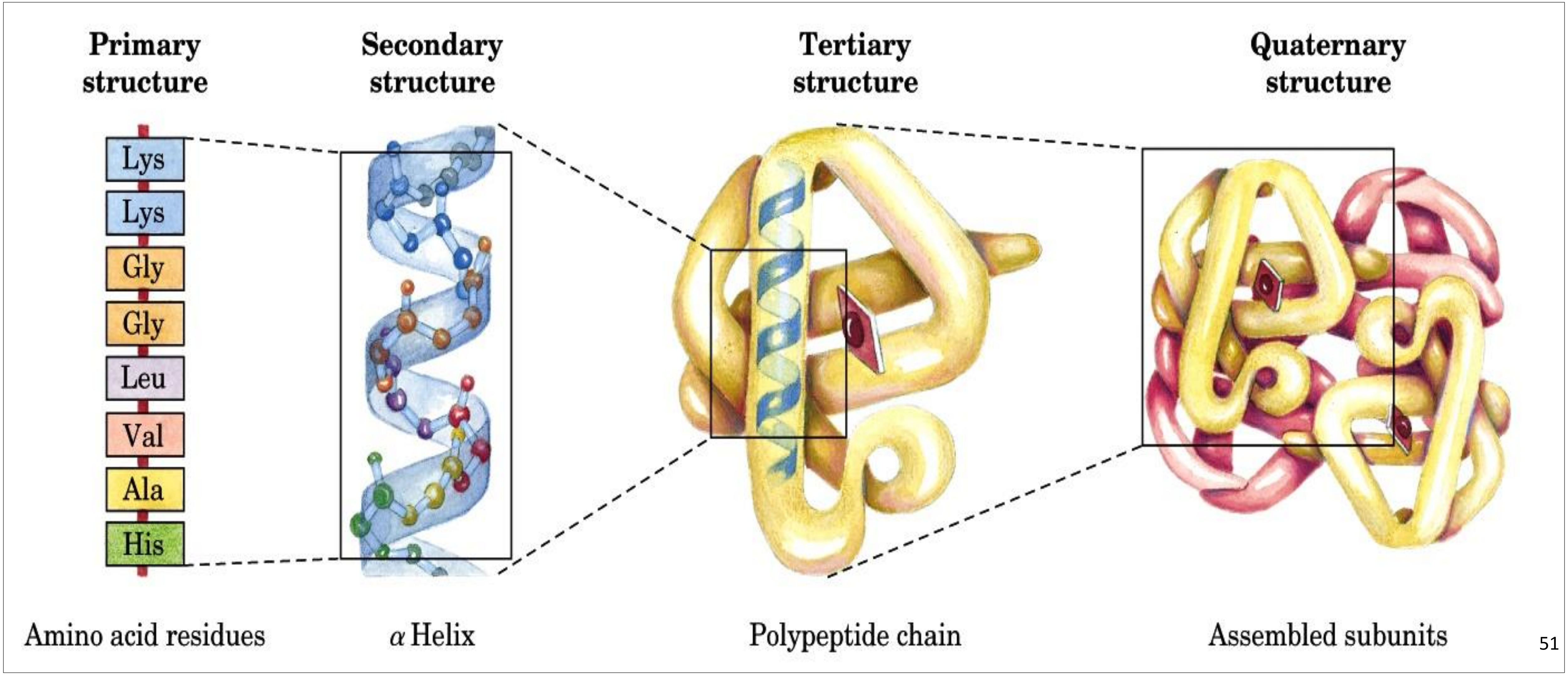
Quaternary structure results from the **interaction** of independent polypeptide chains.

- Factors influencing quaternary structure include:

✓ **Hydrophobic interactions**
✓ **Hydrogen bonding**
✓ The **shape** and **charge distribution** on amino acids of associating polypeptides



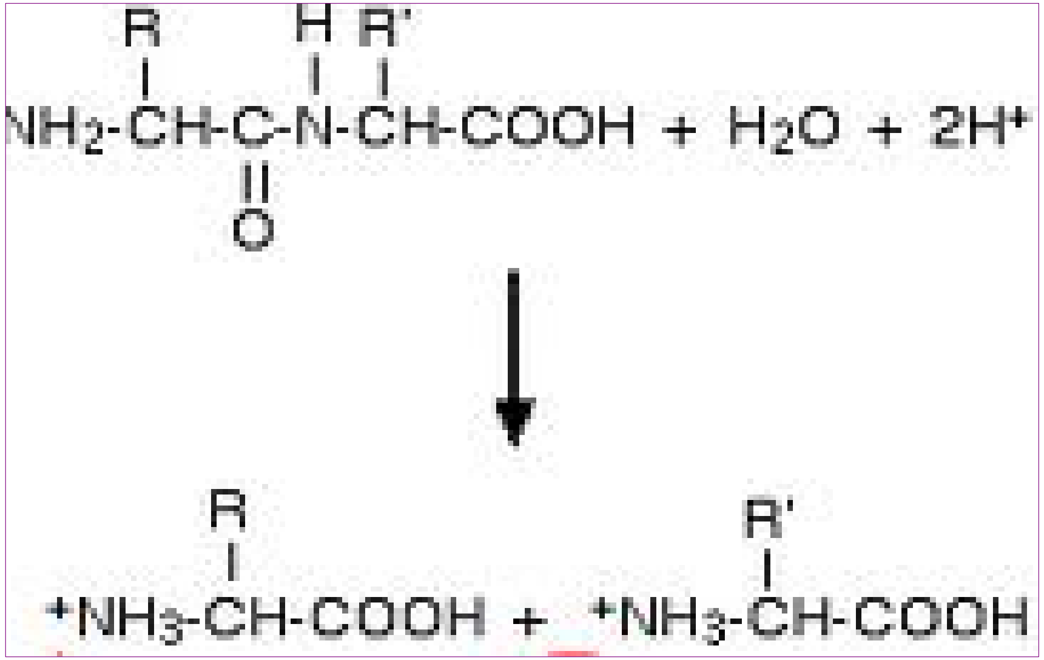
Levels of Protein Structure



Chemical properties of protein

1. Hydrolysis:

Protein hydrolysis is the **reverse** of **peptide bond formation** and the peptides are broken down to amino acids.



Digestion is an example of **protein hydrolysis**.

Note: In the laboratory the Protein can be hydrolyses by heating with hydrochloric acid.

Chemical properties of protein

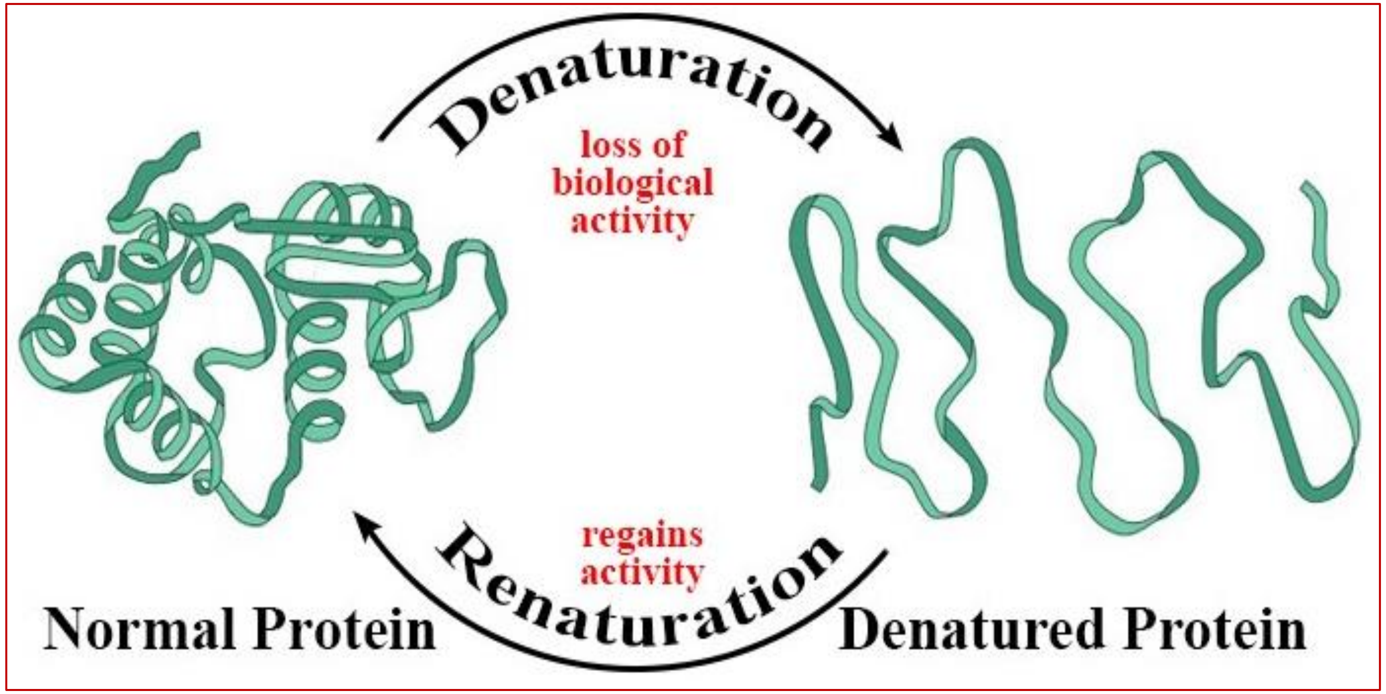
2. Denaturation:

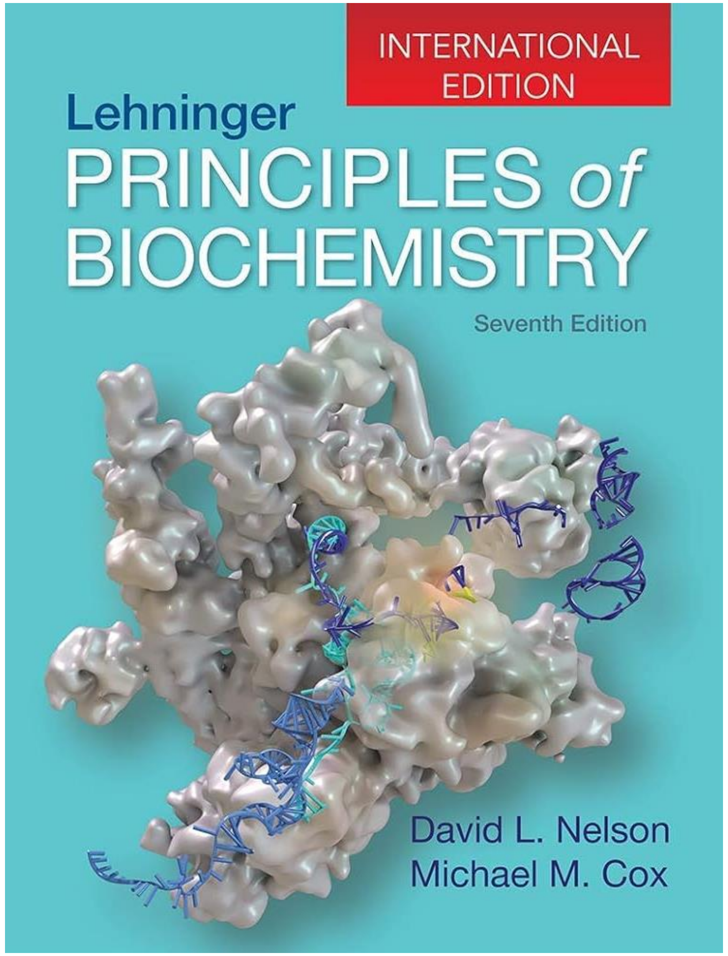
Denaturation of proteins refers to the unfolded and rearrangement of the **secondary**, **tertiary**, and **quaternary** without breaking the peptide bonds (**primary structure will remain**).

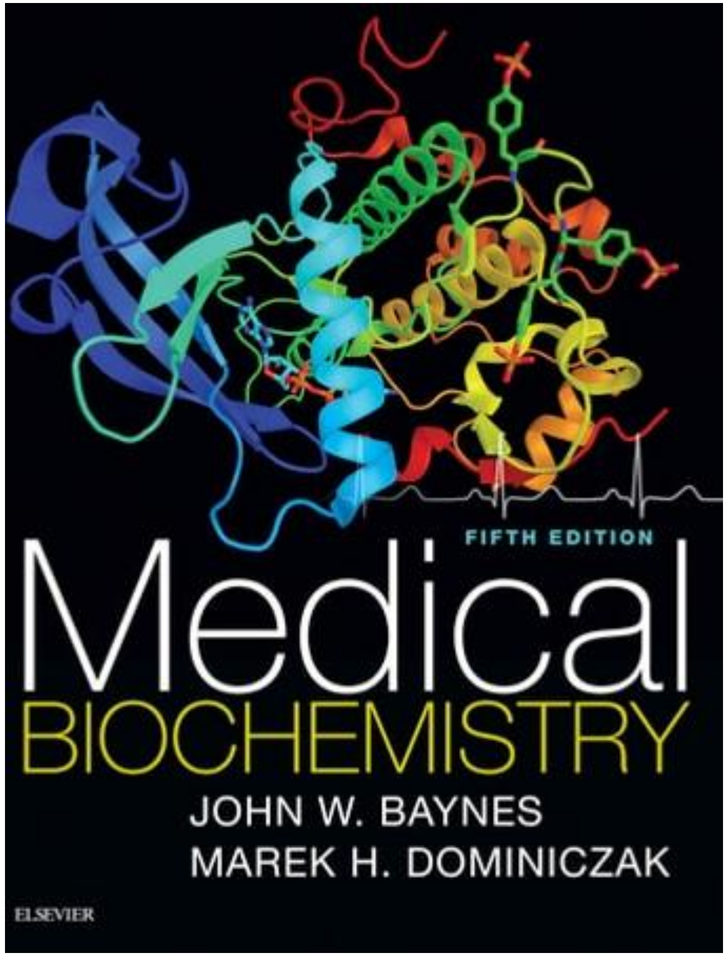
A protein that is denatured loses its biological activity.

3. Renaturation:

Is the process of returning a **denatured protein structure** to its original structure and normal level of biological activity.







- **Lehninger Principles of Biochemistry (International Edition), 2021, David L. Nelson, Michael M. Cox.**
- **Medical Biochemistry E-Book, Marek H. Dominiczak, John W Baynes.**