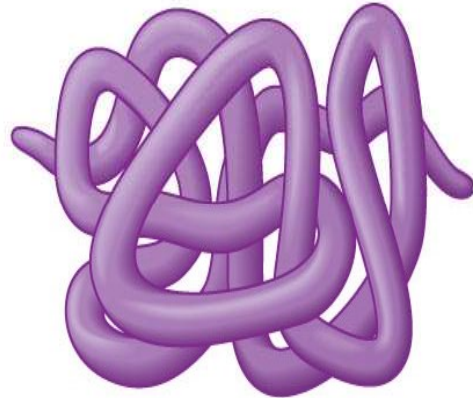
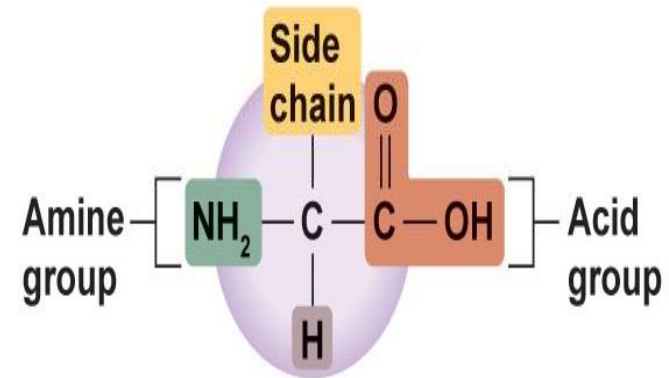


# Proteins and Amino Acids



Normal protein



Amino acid structure

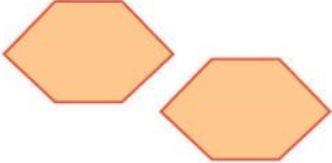
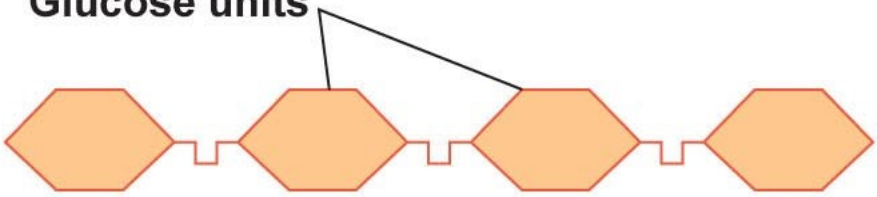

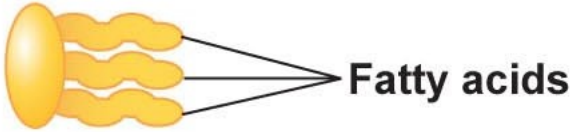
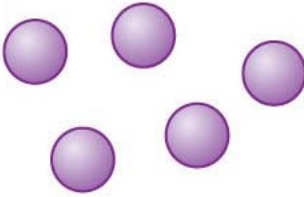
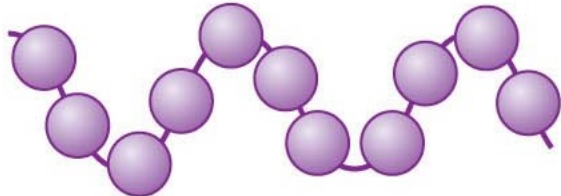
# What Are Proteins?

- Large molecules
- Made up of chains of amino acids
- Are found in every cell in the body
- Are involved in most of the body's functions and life processes
- The sequence of amino acids is determined by DNA

# Structure of Proteins

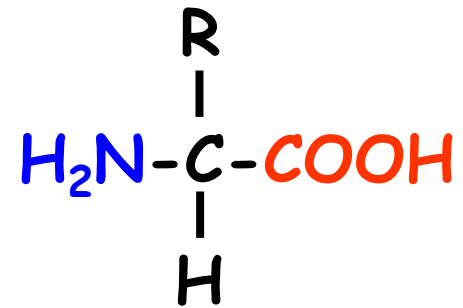
- Made up of chains of amino acids; classified by number of amino acids in a chain
  - Peptides: fewer than 50 amino acids
    - Dipeptides: 2 amino acids
    - Tripeptides: 3 amino acids
    - Polypeptides: more than 10 amino acids
  - Proteins: more than 50 amino acids
    - Typically 100 to 10,000 amino acids linked together
- Chains are synthesized based on specific bodily DNA
- Amino acids are composed of carbon, hydrogen, oxygen, and nitrogen

# Structural Differences Between Carbohydrates, Lipids, and Proteins

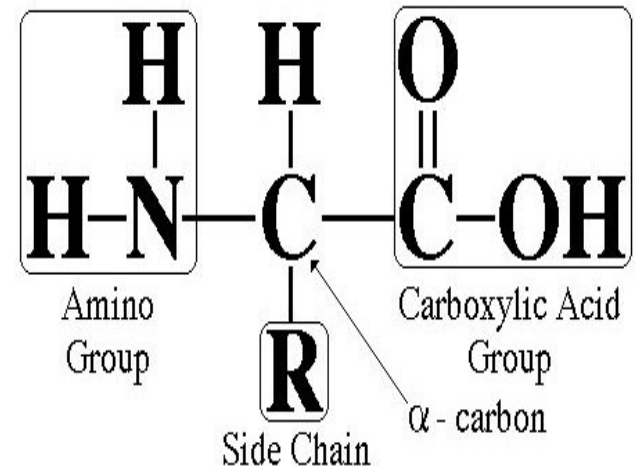
Macronutrients	Chains of	Example
Carbohydrates	Glucose 	Glucose units 
Lipids	Fatty acids 	Triglyceride 
Proteins	Amino acids 	Amino acids 

# Amino acids

- Amino acids are the "building blocks" of proteins.
- Amino acids are a group of organic compounds containing two functional groups **amino group** and **carboxyl group**, hydrogen and a **variable** side group (residue) each joined to a central carbon atom
- general formula  $H_2NCHR\text{COOH}$ , where R is an organic substituent.
- The amino group(-NH<sub>2</sub>) is basic while the carboxyl (-COOH) is acidic in nature.



## Amino Acid Structure



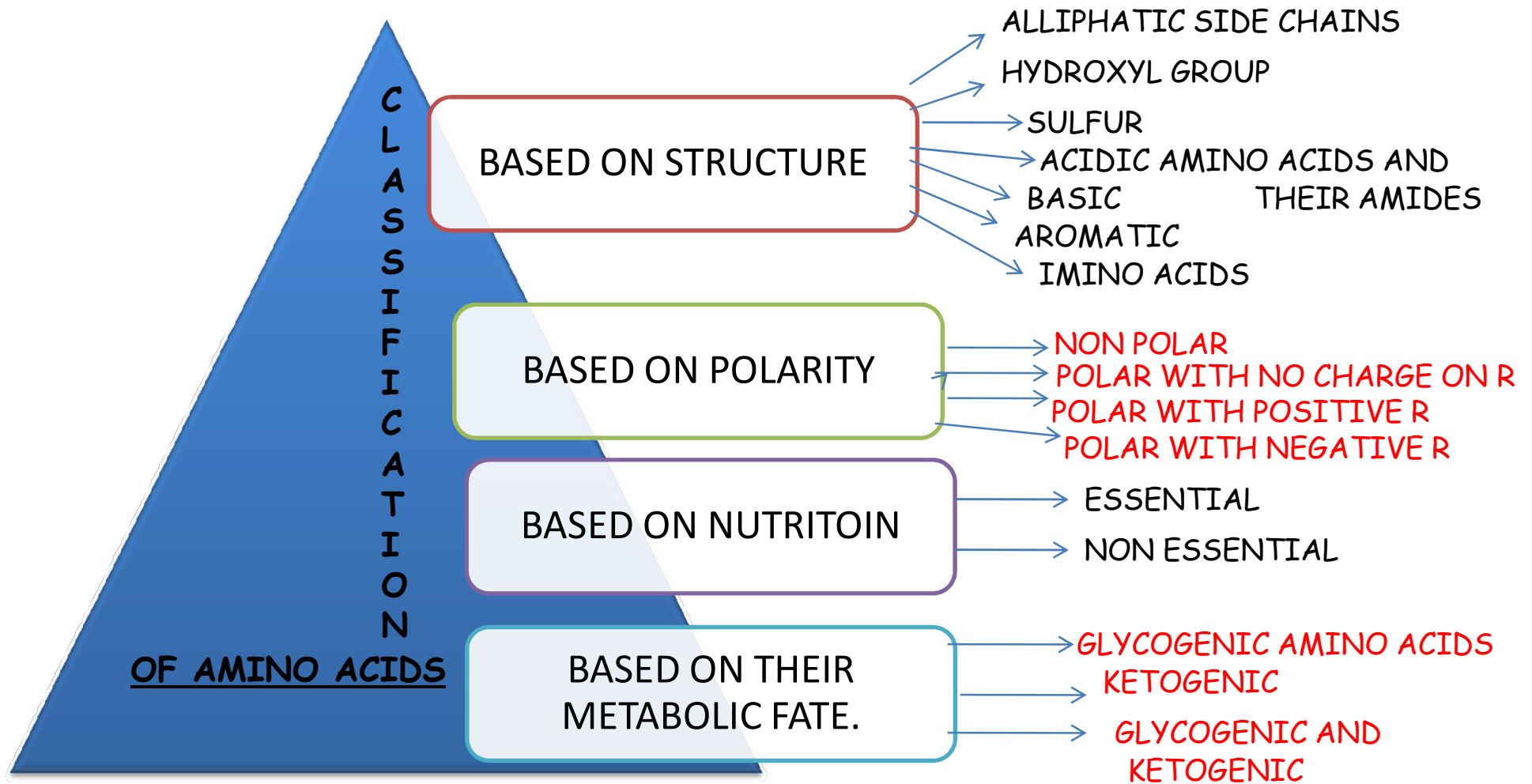
# Types and Functions of AMINO ACIDS

- There are **twenty** different amino acids that are used to form proteins in the human body, these are called the *proteinogenic* amino acids.
- The residues are side chains which give the individual properties to the amino acid (acidic, basic, neutral and nonpolar).

## Functions:

- ✓ Protein synthesis, energy reserves, hormones (thyroxin)
- ✓ **20 different amino acids** used in protein synthesis though others do occur in nature
- ✓ Essential amino acids cannot be synthesised by the organism and must form part of their diet.

# CLASSIFICATION OF AMINO ACIDS:-



<b>Classification</b>	<b>Amino Acid</b>
Nonpolar	Glycine Alanine Valine Leucine Isoleucine Proline Methionine Phenylalanine Tryptophan
Polar	Serine Threonine Asparagine Glutamine Cysteine Tyrosine
Acidic (Polar)	Aspartic Acid Glutamic Acid
Basic (Polar)	Lysine Arginine Histidine



# Physical properties

1. SOLUBILITY
2. MELTING POINTS.
3. TASTE.
4. OPTICAL ACTIVITY.
5. ZWITTERION.
6. ISOELECTRIC POINT.

## Solubility:-

Amino acids are generally **soluble in water** and insoluble in non-polar organic solvents such as hydrocarbons.

## Melting points:-

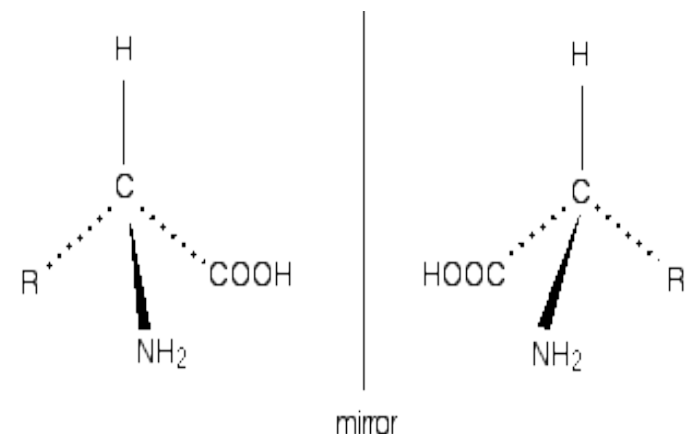
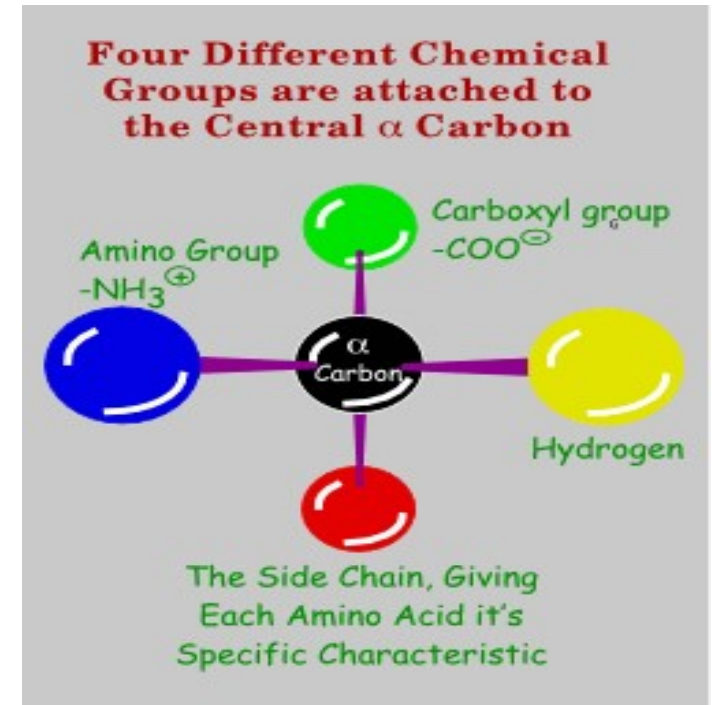
The amino acids are crystalline solids with surprisingly **high melting points**. Decomposition and melting tend to be in the 200 - 300°C range.

## TASTE:-

May be **sweet ,tasteless or bitter**.

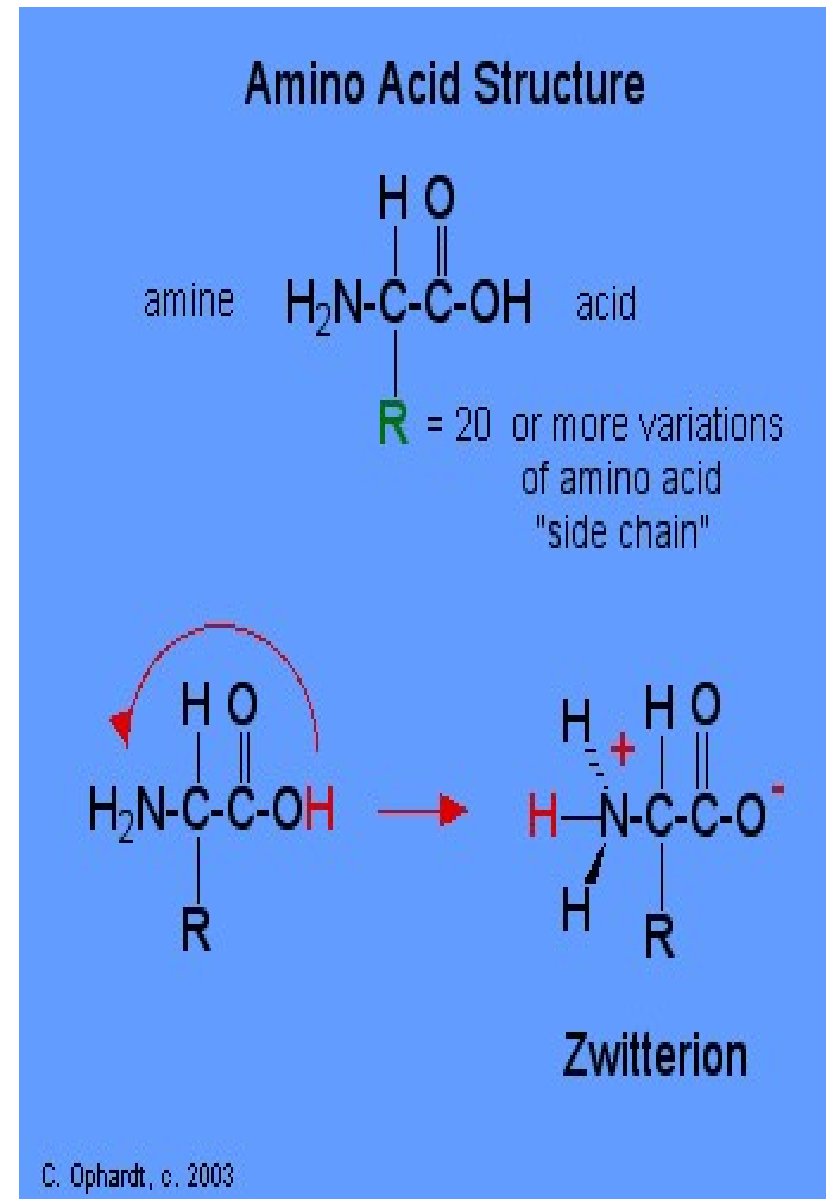
# Optical Activity:-

- If you look again at the general formula for an amino acid, you will see that the carbon at the centre of the structure has **four different groups** attached. In glycine, the "R" group is another hydrogen atom.
- Because of these four different groups attached to the same carbon atom, amino acids (apart from glycine) are **chiral or assymmetric**.
- The lack of a plane of symmetry means that there will be two **stereoisomers** of an amino acid (apart from glycine) - one the **non-superimposable** mirror image of the other.
- For a general 2-amino acid, the isomers are:



# Zwitterion

- Amino acid physical properties indicate a "salt-like" behavior.
- An intramolecular neutralization reaction leads to a salt-like ion called a zwitterion. The accepted practice is to show the amino acids in the zwitterion form.
- (1) The carboxyl group can lose a hydrogen ion to become negatively charged.
- (2) The amine group can accept a hydrogen ion to become positively charged.



# The Isoelectric Point

- The isoelectric point, pI, is the pH of an aqueous solution of an amino acid (or peptide) at which the molecules on average have no net charge. In other words, the positively charged groups are exactly balanced by the negatively charged groups.

# CHEMICAL PROPERTIES OF AMINO ACIDS

## REACTION DUE TO -COOH GROUP:-

- ✓ Amino acid+bases=salts(-COONa)  
Amino acids+alcohol=esters.
- ✓ DECARBOXYLATION:-  
Produces amines.  
Amino acids+NH<sub>3</sub>=Glutamine.

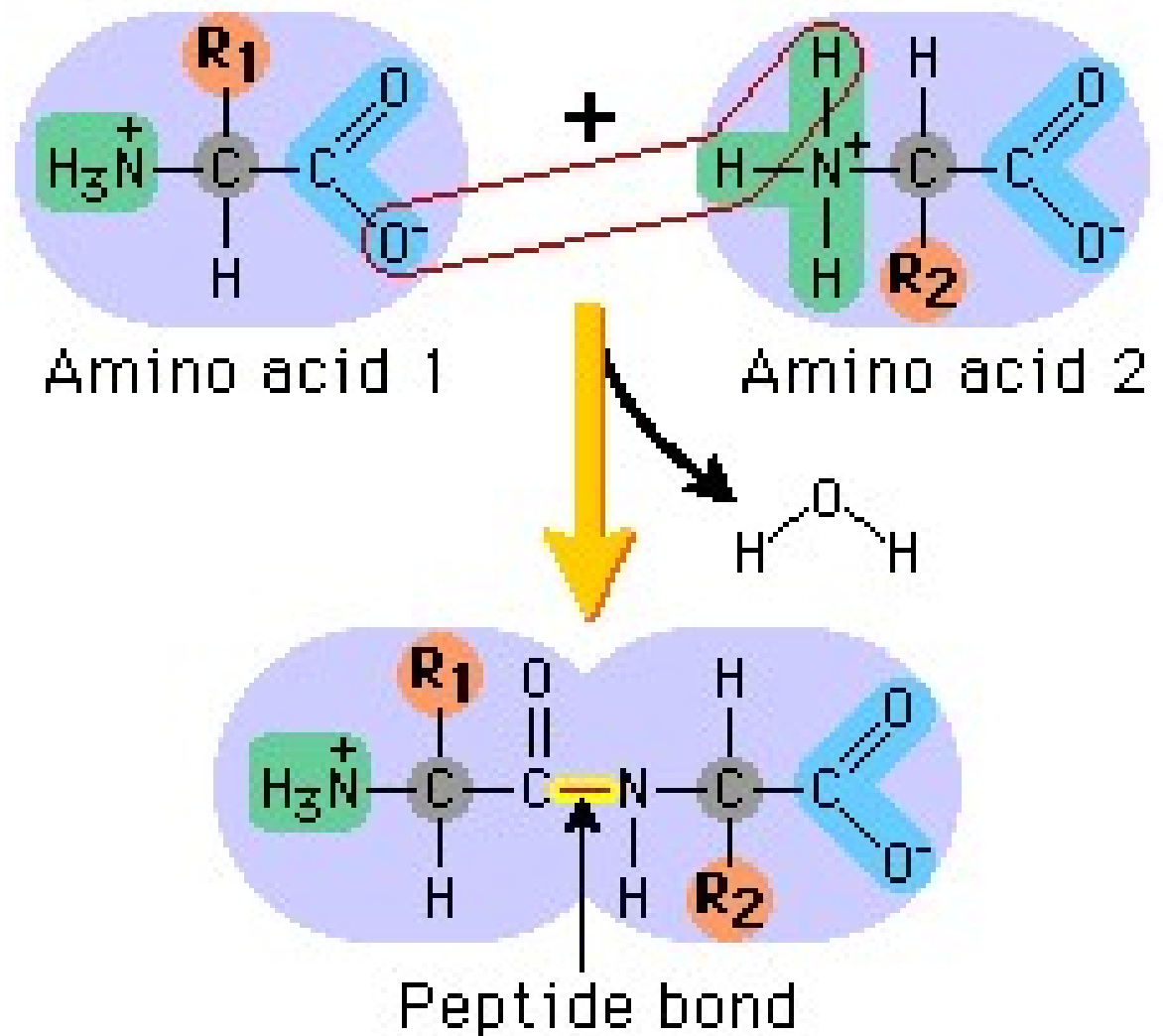
## REACTION DUE TO -NH<sub>2</sub> GROUP:-

- ✓ Amino acids+acids=salts
- ✓ Transamination
- ✓ Oxidative deamination.

# The Peptide Bond

Amino acids are joined together **in proteins** by peptide bonds.

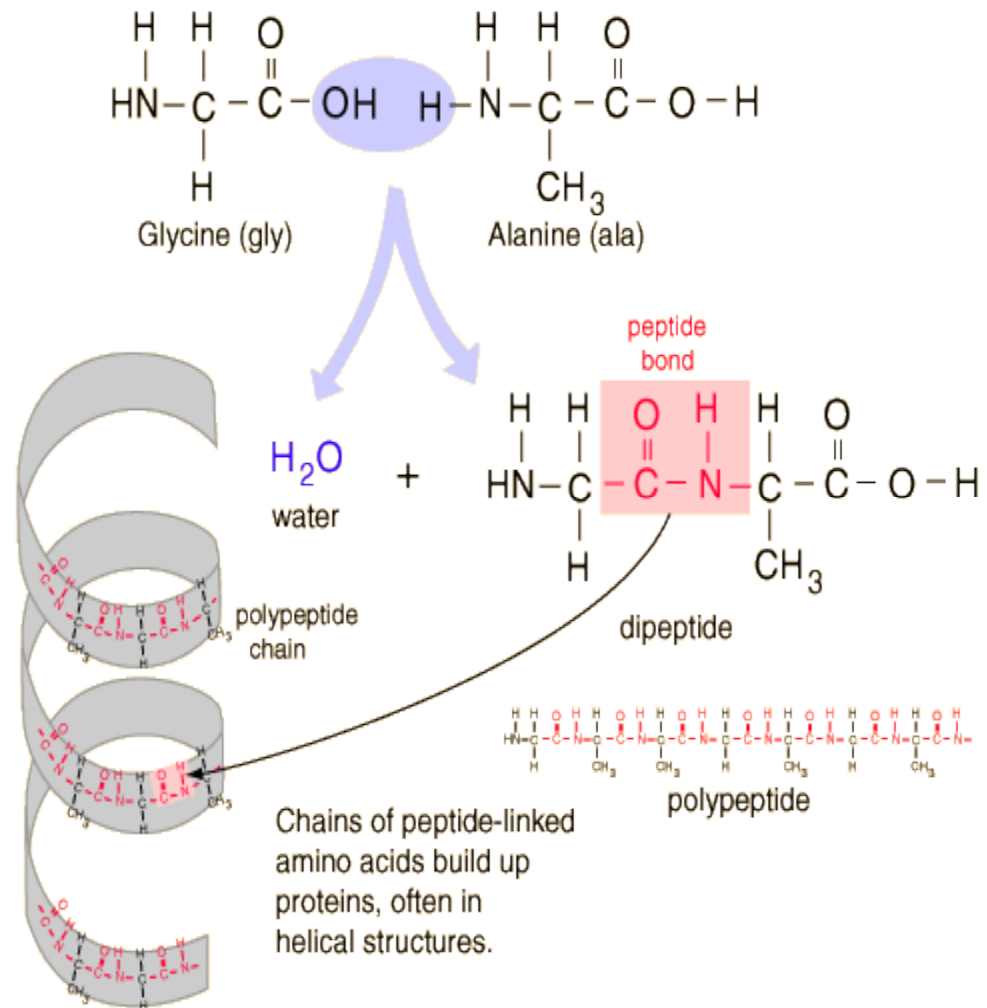
A peptide bond forms between the **carboxyl group** of one amino acid (amino acid 1 in the figure below) and the **amino group** of the adjacent amino acid (amino acid 2).



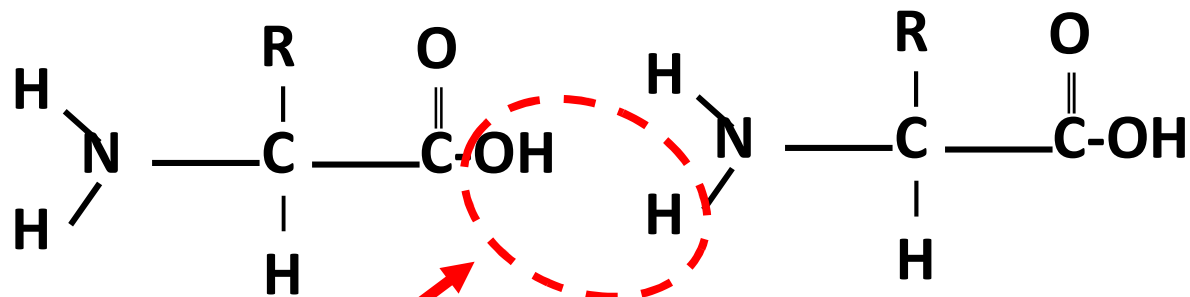
## PEPTIDE BOND

➤ Carboxyl group + amino group form a strong covalent bond releasing water in the process = a **condensation reaction** (the reverse is hydrolysis/ removal of H<sub>2</sub>O)

➤ Amino acids join together in a long chain: **N** terminal end to **C** terminal end = a **polypeptide**.

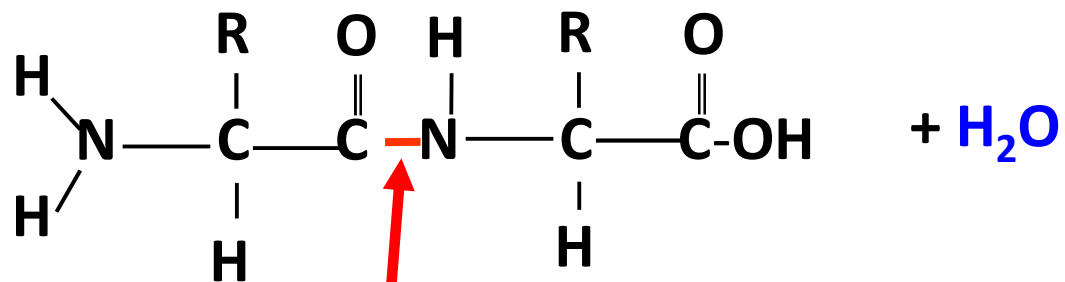






Condensation  
reaction

A dipeptide is formed



The peptide bond

# Structural organization of proteins

- **Primary (1°) Protein Structure**
  - linear sequence of amino acids.
- **Secondary (2°) Protein Structure**
  - localized regional structures
- **Tertiary (3°) Protein Structure**
  - overall shape of proteins
- **Quaternary (4°) Protein Structure**
  - interactions between proteins

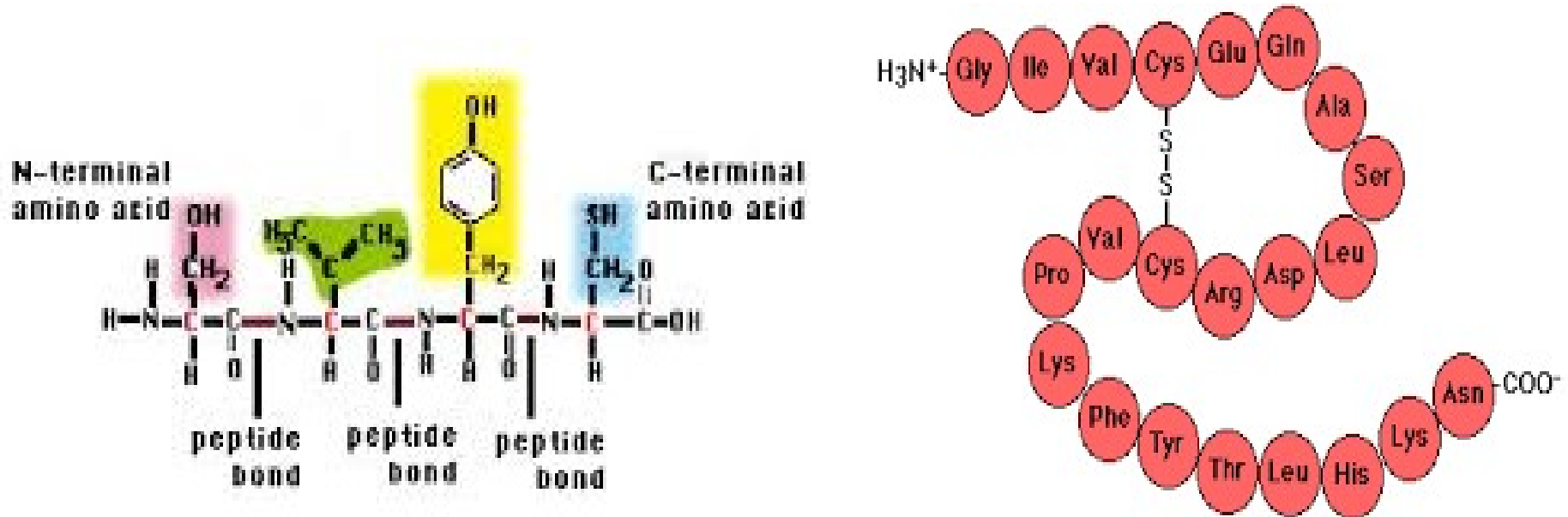
Native protein structure is essential for the biological function of a protein.

*Loss of structure results in loss of biological function.*

# Primary structure

Definition:

The linear sequence of amino acids forming the backbone of a protein.



- Peptides: di-, three-, tetra- peptides
- Oligopeptides: up to 20 amino acids
- Polypeptides: from 20 to 50 amino acids
- Proteins: > 50 amino acids

# Polypeptide name formation

## Naming of Peptide bond

H<sub>3</sub>N-Glutamate - cysteine - methionine - glycine-COO

N- terminal

Glu - cys - met- Gly

C- terminal

glutamyl - cystenyl - methionyl-glycine

- ✓ Amino acid sequence is read from N-terminal to C-terminal.
- ✓ Protein synthesis occurs in the same way.
- ✓ N-terminal a.a - "yl" ; C- terminal a.a - "ine" .

## Remember

- Every polypeptide chain has a unique amino acid sequence determined by genes.
- A single amino acid change in polypeptide chain may change or completely abolish protein function.
- Primary structure determines the higher levels of protein organization.

Bonds in primary structure: **Peptide bonds.**

# Secondary structure

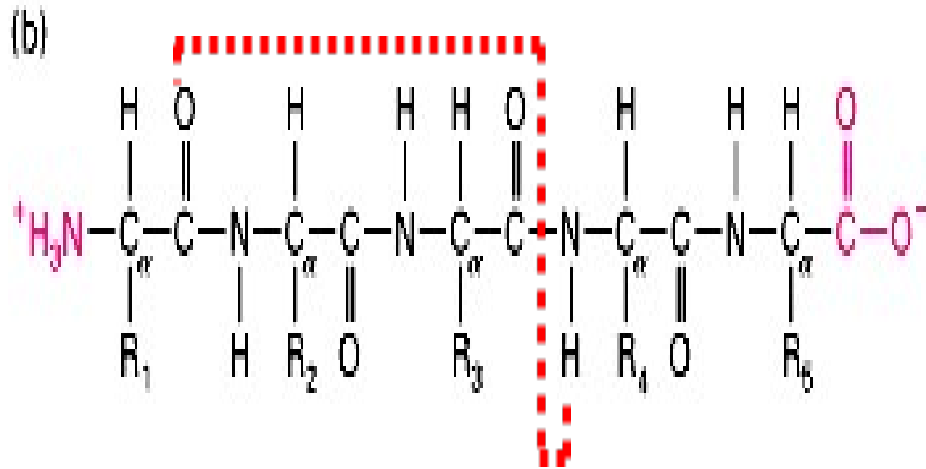
Definition: Spatial folding of the polypeptide chain in properly arranged, repetitive structures.

Three types of secondary structures:

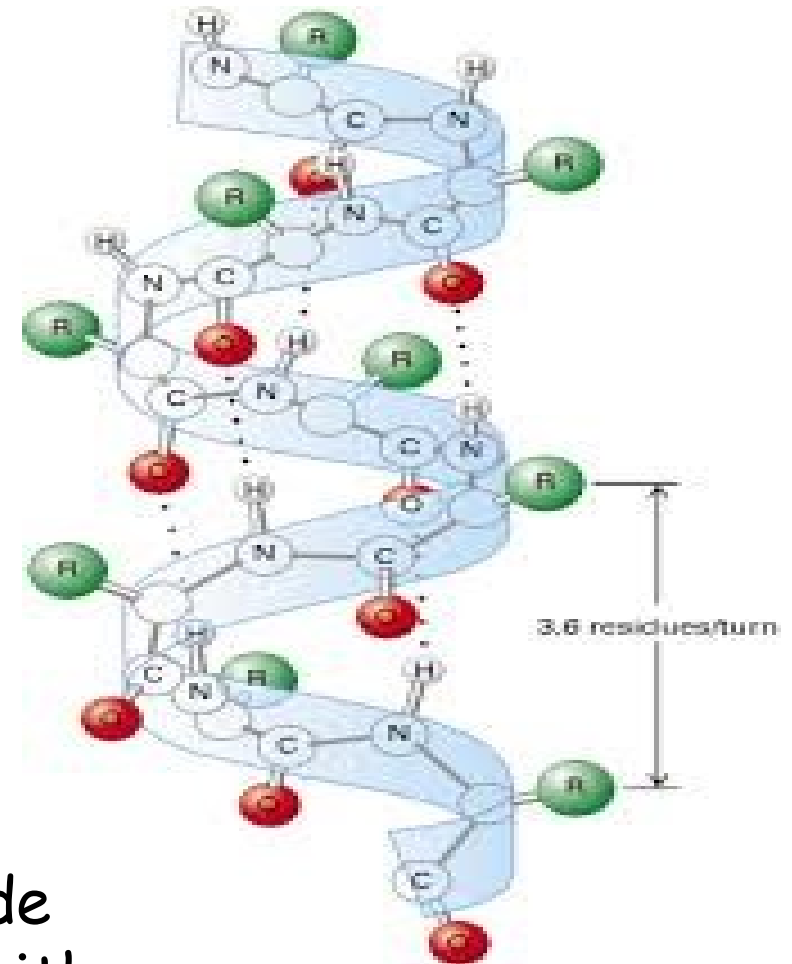
- $\alpha$ -helix,
- $\beta$ -sheet,
- $\beta$ -turn.

Formed as a result of hydrogen bonds between the carbonyl oxygen (C = O) and the amide hydrogen (N-H) of the polypeptide chain and does not depend on the side radicals.

## Alpha (α) helix



The carbonyl oxygen of each peptide bond is linked to a hydrogen bond with the amide hydrogen of the fourth amino acid towards the C-terminus.



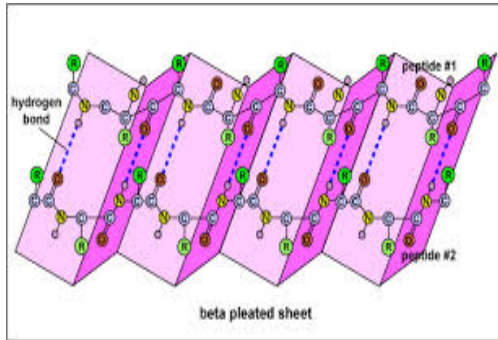
# Features of alpha helix

- Most common and stable conformation.
- Spiral structure: Polypeptide bonds form the backbone of the spiral. R-groups of the amino acids remain outwards of the spiral.
- Stabilized by H-bonds: Hydrogen bonds are weak but collectively determine the stability of  $\alpha$ -helix.

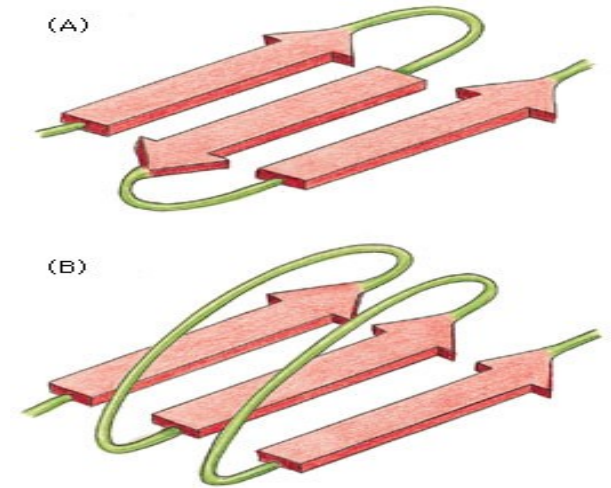


## Alpha helix is disrupted by:

- Presence of proline.
- Crowding of equally charged radicals, for example lysine, arginine, histidine
- Crowding of bulk R-groups (leucine, isoleucine, tyrosine). Spatial interference.
- Prevailing of amino acids with R-groups which are capable of forming H-bonds.
- Presence of chemicals tending to form hydrogen bonds (carbamide).

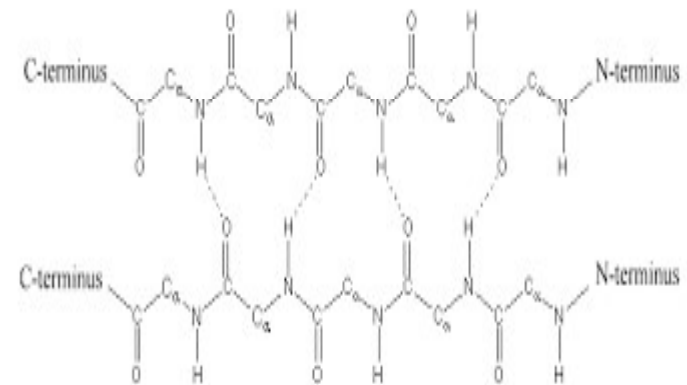


## Beta ( $\beta$ ) –pleated sheet

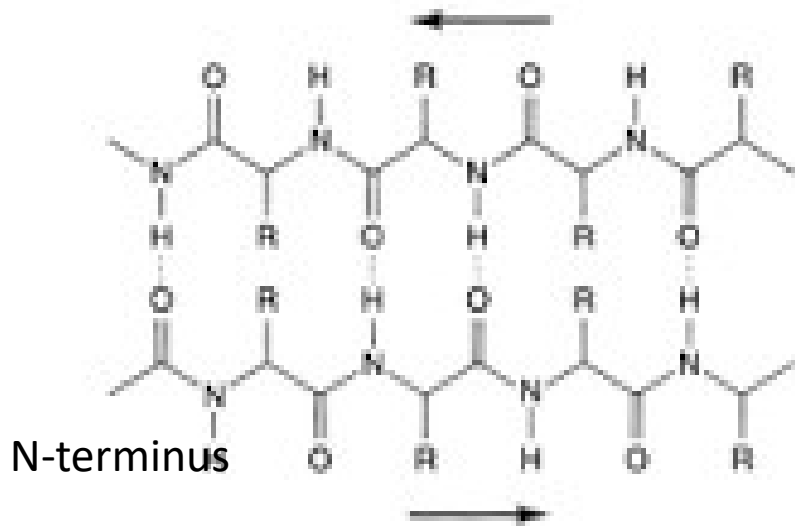


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### Parallel $\beta$ Sheet



Parallel - run in the same direction with longer looping sections between them



N-terminus

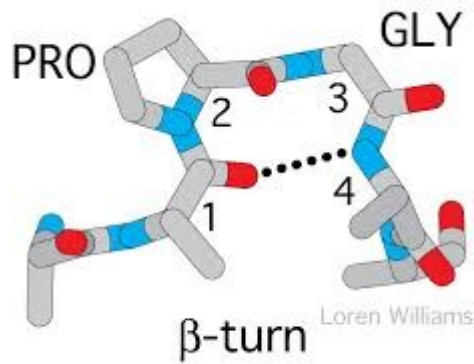
N-terminus

Anti-parallel beta sheets: polypeptide chains run in an opposite direction

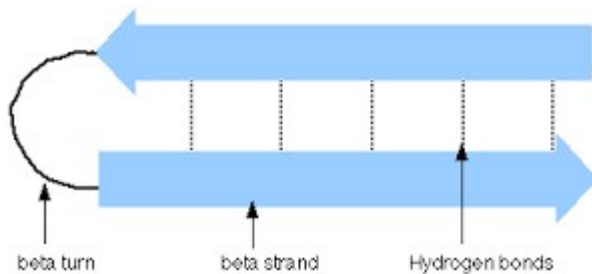
Both models are found in proteins, but the antiparallel structure is more stable than the parallel beta-sheet.

## $\beta$ - turns

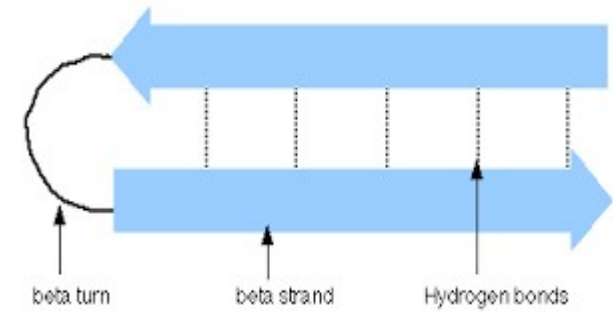
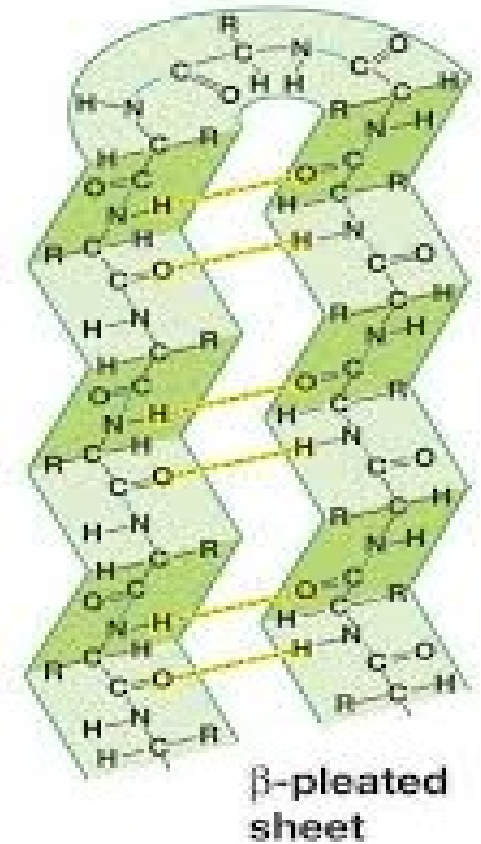
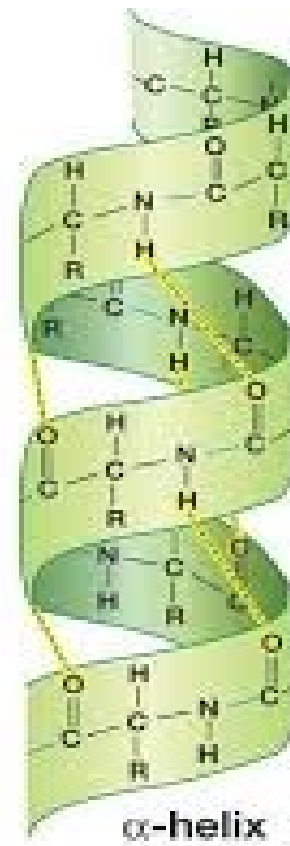
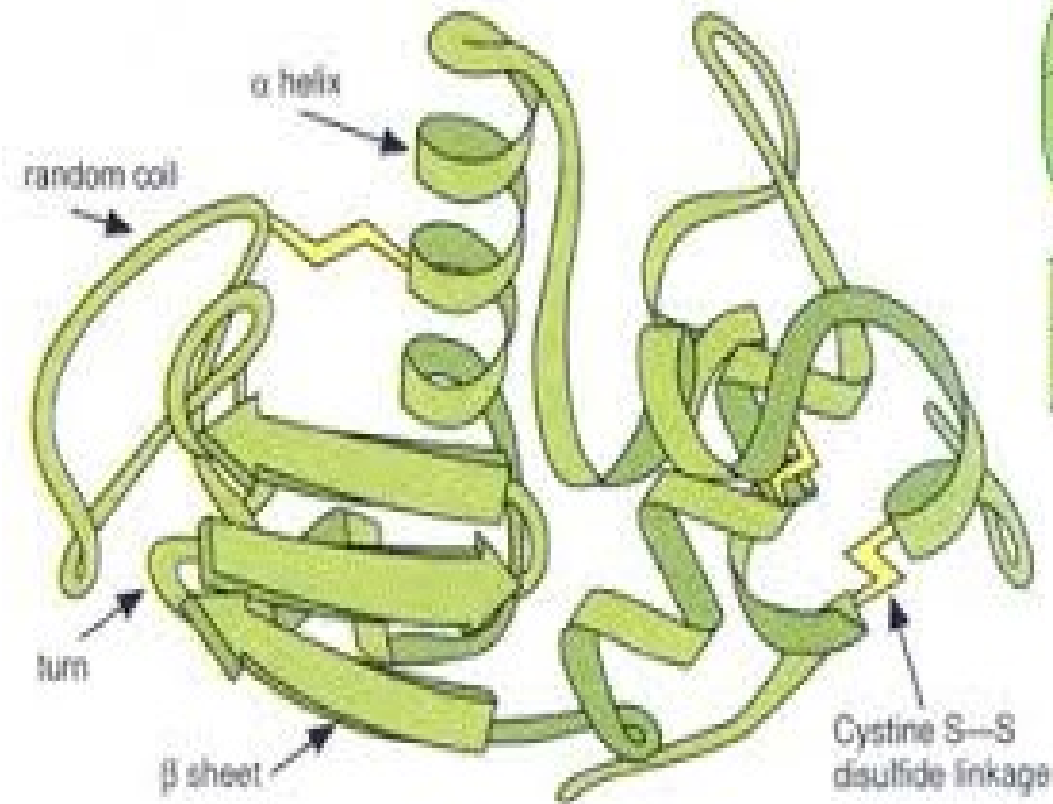
Permits the change of direction of the peptide chain to get a folded structure.



Beta-turn loops allow for protein compaction, since the hydrophobic amino acids tend to be in the interior of the protein, while the hydrophilic residues interact with the aqueous environment.



# Secondary structures: Summary



# Spatial relationship of the different secondary structures

myoglobin



75%  $\alpha$  – helix.  
No  $\beta$  – sheets.

lysozyme



40%  $\alpha$  – helix.  
12%  $\beta$  – sheets.

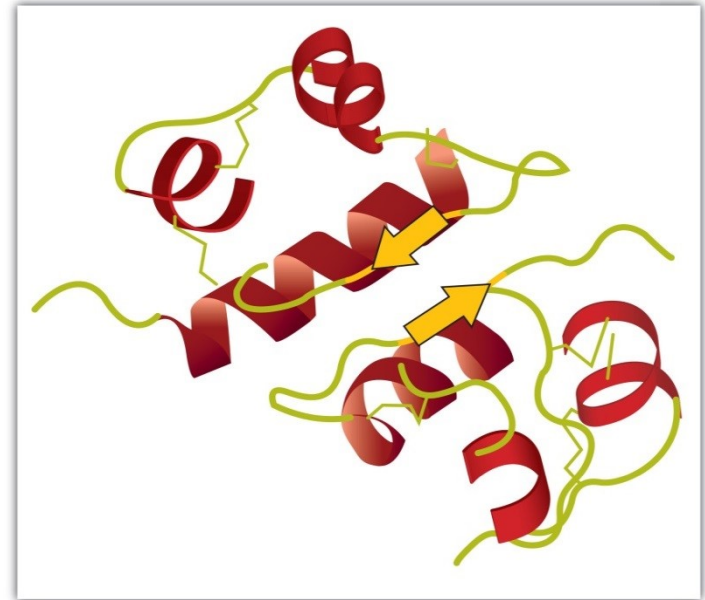
$\alpha$  – amylase inhibitor



Only  $\beta$  – sheets.  
No  $\alpha$  – spirals.

# Tertiary structure

- Complete three-dimensional shape of a given protein.  
Conformation.
- Represent the spatial relationship of the different secondary structures to one another within a polypeptide chain and how these secondary structures themselves fold into the three-dimensional form of the protein.

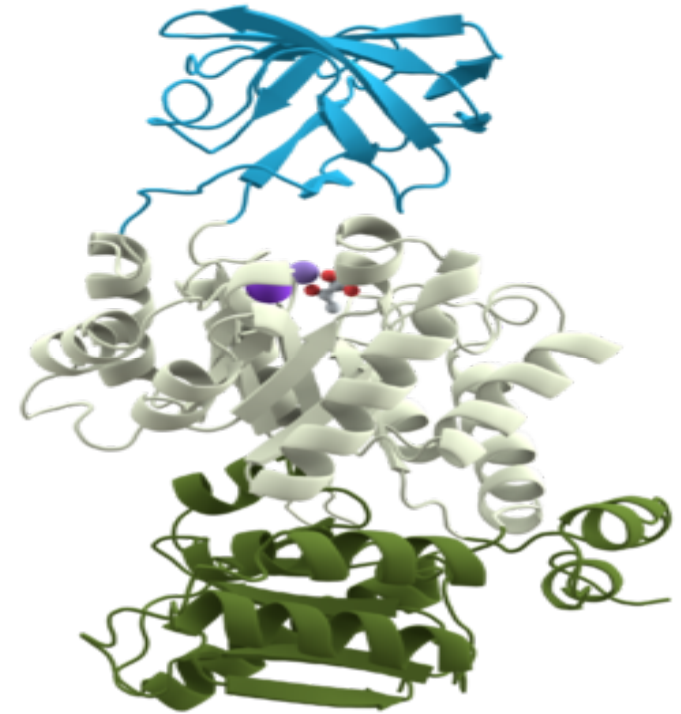


The spiral regions represent sections of the polypeptide chain that have an  $\alpha$ -helical structure, while the broad arrows represent  $\beta$ -pleated sheet structures.

**Tertiary structure:** Describes the relationship of different domains to one another within a protein.

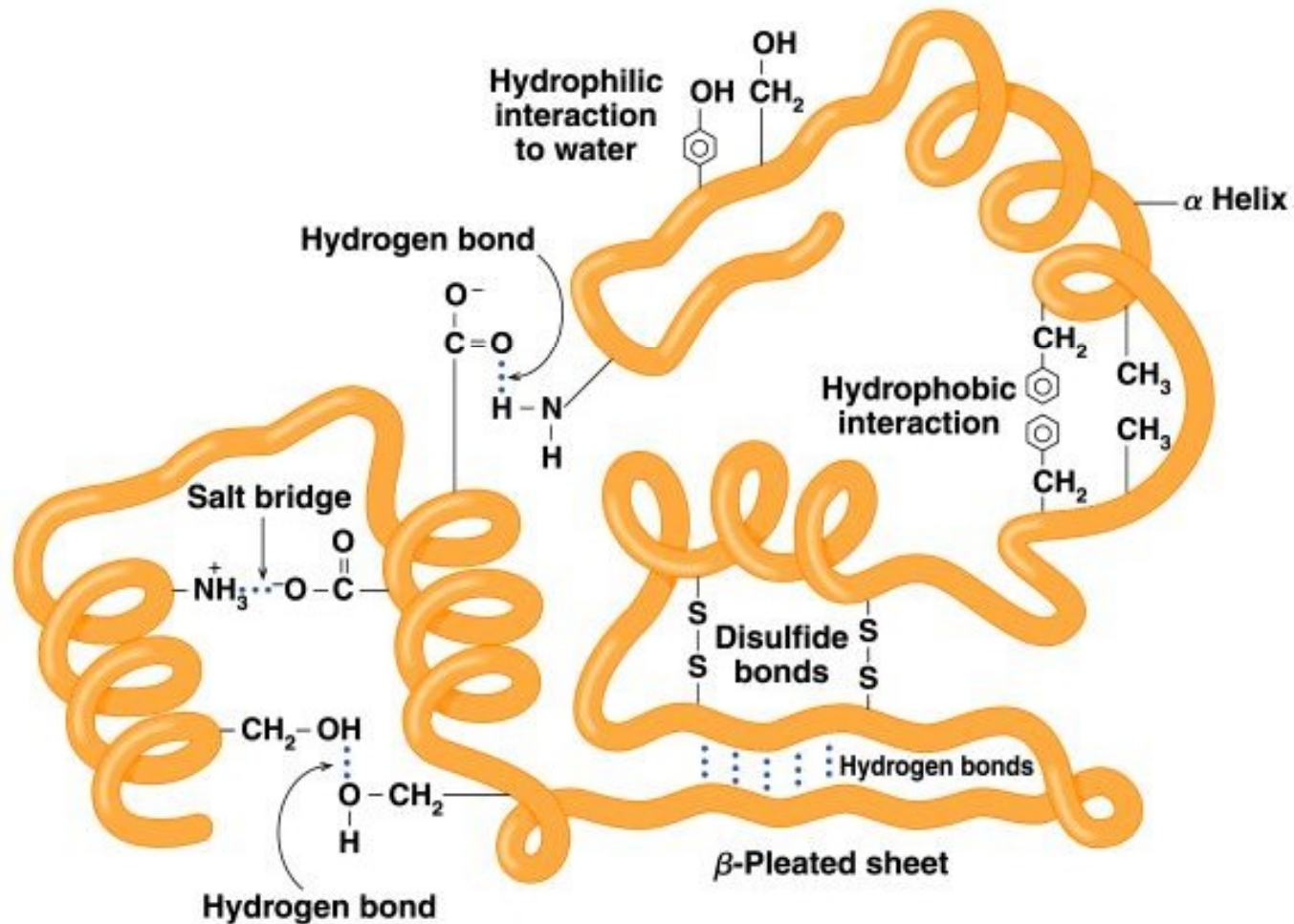
## Protein domain

- A **domain** is a basic structural unit within a protein molecule.
- Part of protein that can fold into a stable structure independently.
- Different domains can possess different functions.
- Proteins can have one to many domains depending on protein size.
- A polypeptide with 200 amino acids consists of two or more domains.
- Domains are usually connected with relatively flexible areas of protein.



Pyruvate kinase (a monomeric protein):  
three domains

Tertiary structure is based on various types of interactions between the side-chains of the peptide chain.





# STABILIZING INTERACTIONS OF TERTIARY STRUCTURES

**Table 20.5** Some Cross-Links in Tertiary Structures

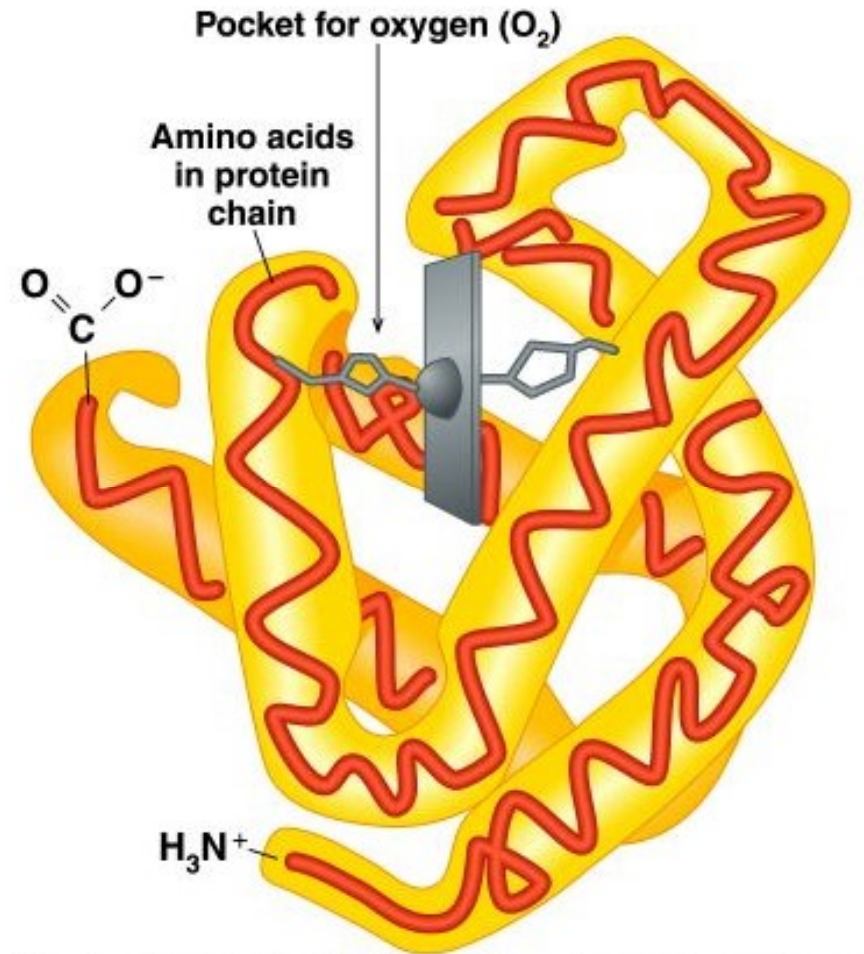
	Nature of Bonding	Example
<b>Hydrophobic interactions</b>	Attractions between nonpolar alkyl and aromatic groups form a nonpolar center that is repelled by water	$\begin{array}{c} \text{---CH}_3 \\ \text{CH}_3\text{---} \\ \text{---CH}_2\text{OH} \cdots \cdots \text{O---H} \\   \\ \text{H} \end{array}$
<b>Hydrophilic Interactions</b>	Attractions between polar or ionized R groups and water on the surface of the tertiary structure	
<b>Salt bridges</b>	Ionic interactions between ionized R groups of acidic and basic amino acids	$\begin{array}{c} \text{O} \\    \\ \text{---CO}^- \cdots \cdots \text{H---N}^+ \text{---} \\   \\ \text{H} \end{array}$
<b>Hydrogen bonds</b>	Occur between polar side groups of amino acids	$\begin{array}{c} \diagup \text{C}=\text{O} \cdots \cdots \text{HO---} \\ \diagdown \\ \diagup \text{C}=\text{O} \cdots \cdots \text{H---N---} \\ \diagdown \quad   \\ \quad \quad \text{H} \end{array}$
<b>Disulfide bonds</b>	Strong covalent links between sulfur atoms of two cysteine amino acids	$\text{---SH} + \text{HS---} \longrightarrow \text{---S---S---}$

# Globular Proteins

- Globular proteins fold up into compact, spherical shapes.
- Their functions are related to cell metabolism: biosynthesis and biodegradation, transport, catalytic function.
- Hydrophobic R-groups are oriented into inner part of the protein molecule, while hydrophilic R-groups are pointed towards molecule edges.
- Globular proteins are **water soluble**.

## Example: myoglobin

- Globular protein that stores oxygen in muscles
- A single peptide chain that is mostly  $\alpha$ -helix
- $O_2$  binding pocket is formed by a heme group and specific amino acid side-chains that are brought into position by the tertiary structure



# Fibrous proteins

- Much or most of the polypeptide chain is parallel to a single axis
- Fibrous proteins are often mechanically strong and highly cross-linked
- Fibrous proteins are usually insoluble
- Usually play a structural role

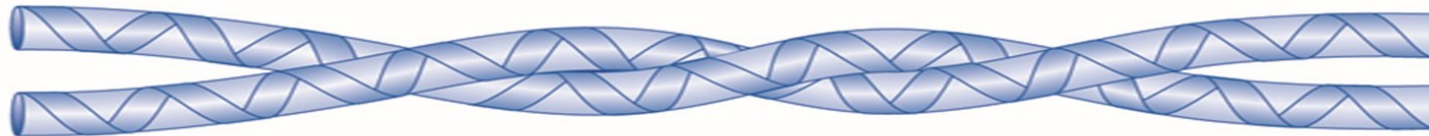
## Fibrous Proteins: Keratins

- For example,  $\alpha$ -keratins are fibrous proteins that make hair, fur, nails and skin
  - hair is made of twined fibrils
  - the  $\alpha$ -helices are held together by disulfide bonds

$\alpha$ -Helix



Coiled coil of two  $\alpha$ -helices



Protofilament (pair of coiled coils)

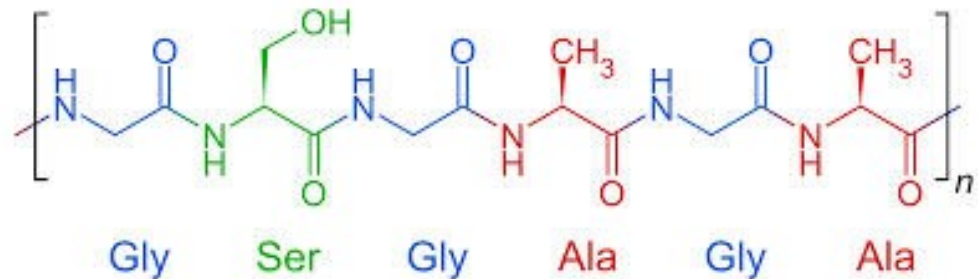
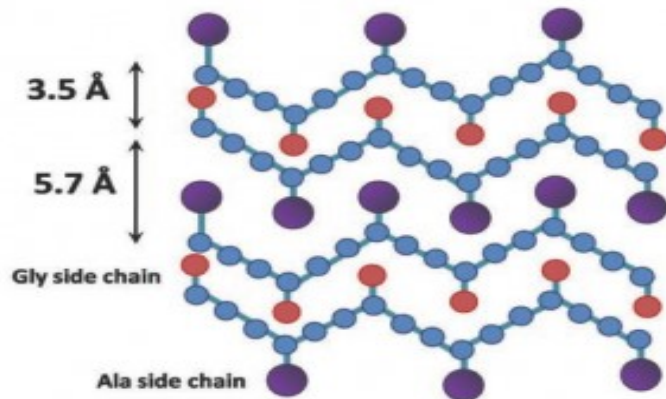


Filament (four right-hand twisted protofibrils)



# Fibrous proteins: Fibroin

- Fibroins are the silk proteins. They also form the spider webs
- Made with a  $\beta$ -sheet structures with Gly on one face and Ala/Ser on the other
- Fibroins contain repeats of [Gly-Ala-Gly-Ala-Gly-Ser-Gly-Ala-Ala-Gly-(Ser-Gly-Ala-Gly-Ala-Gly)<sub>8</sub>]
- The  $\beta$ -sheet structures stack on top of each other
- Bulky regions with **valine** and **tyrosine** interrupt the  $\beta$ -sheet and allow the stretchiness

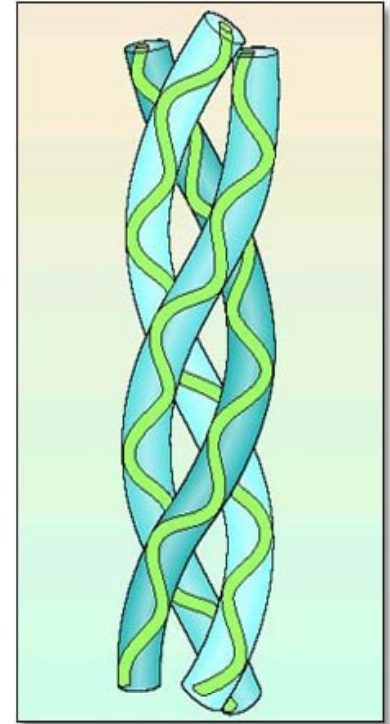


# Fibrous proteins: Collagen is a Triple Helix

Collagen is formed from tropocollagen subunits. The triple helix in tropocollagen is highly extended and strong.

Features:

- Three separate polypeptide chains arranged as a left-handed helix (note that an  $\alpha$ -helix is right-handed).
- 3.3 residues per turn
- Each chain forms hydrogen bonds with the other two: STRENGTH!



Collagen amino acid composition:

- Nearly one residue out of three is Gly
- Proline content is unusually high
- Many modified amino acids present:
  - 4-hydroxyproline
  - 3-hydroxyproline
  - 5-hydroxylysine
- Pro and HydroxyPro together make 30% of amino acids.

# Globular proteins vs Fibrous proteins

1. Compact protein structure

2. Soluble in water (or in lipid bilayers)

3. Secondary structure is a complex with a mixture of  $\alpha$ -helix,  $\beta$ -sheet and loop structures

4. Quaternary structure is held together by noncovalent forces

5. Functions in all aspects of metabolism (enzymes, transport, immune protection, hormones, etc).

Extended protein structure

Insoluble in water (or in lipid bilayers)

Secondary structure is simple with predominant one type only

Quaternary structure is usually held together by covalent bridges

Functions in structure of the body or cell (tendons, bones, muscle, ligaments, hair, skin)



# Quaternary structure of proteins

## Monomeric proteins:

- built of a single polypeptide chain.

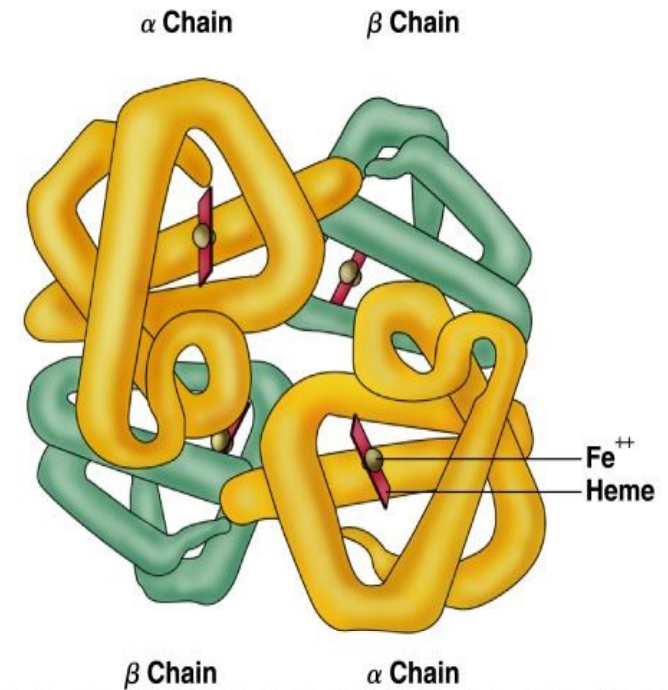
## Oligomeric proteins:

- built of more than one polypeptide chains called subunits or monomers.

- **Quaternary structure** describes the joining of two or more polypeptide subunits.
- The subunits each have their own tertiary structure.
- Bonds - non-covalent interactions.
- Subunits can either function independently or work co-operatively.
- Dissociation of a subunit results in loss of function.

# For example: Hemoglobin

- A globular protein that consists of four subunits (2 $\alpha$  and 2 $\beta$ , of two different types ( $\alpha$  and  $\beta$ ))
- Each subunit contains a heme group for O<sub>2</sub> binding
- Binding O<sub>2</sub> to one heme facilitates O<sub>2</sub> binding by other subunits
- Replacement of even one amino acid in primary structure with another amino acid is critical for the function of the protein.



Normal red blood cell



Sickled red blood cell

## NORMAL $\beta$ -GLOBIN

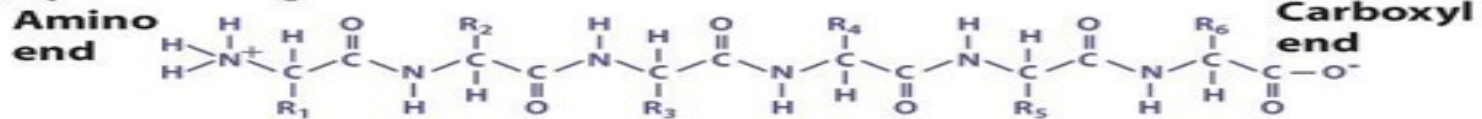
DNA.....TGA	GGA	CTC	CTC.....
mRNA.....ACU	CCU	GAG	GAG.....
Amino acid.....	thr	pro	glu

## MUTANT $\beta$ -GLOBIN

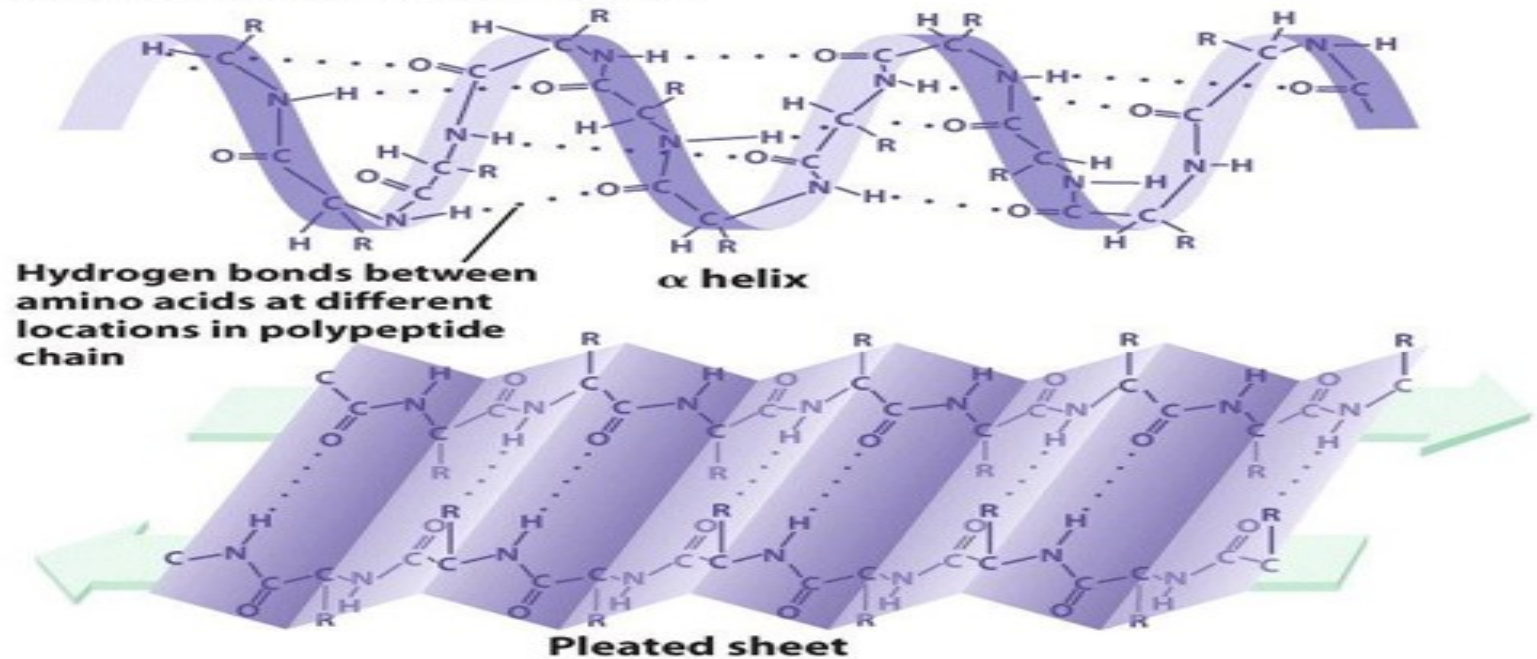
DNA.....TGA	GGA	CAC	CTC.....
mRNA.....ACU	CCU	GUG	CTC.....
Amino acid.....	thr	pro	val

# Structural organization of proteins: Summary

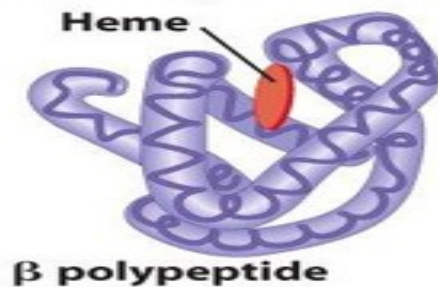
## (a) Primary structure



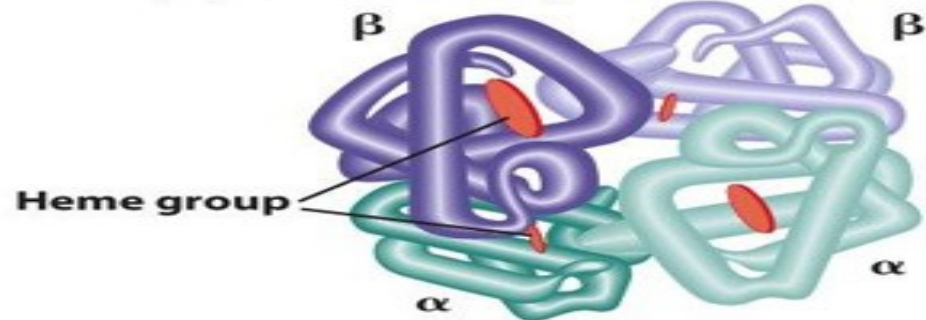
## (b) Secondary structure



## (c) Tertiary structure



## (d) Quaternary structure





*Thank  
You*

