Protein structure

* Primary : Amino acid sequence – order of amino acids
↓
* Secondary : α-Helix, β-sheet, Turns – due to interaction of backbo
↓
* Tertiary : 3D structure – due to interactions of side chains
↓
* Quaternary : Multiple peptide chains arrangement

Primary structure : The order and type of amino acids are importa to have a normal functioning protein

E.g. substitution of valine for glutamic acid in β-chain of HbA results in sickle cell anemia

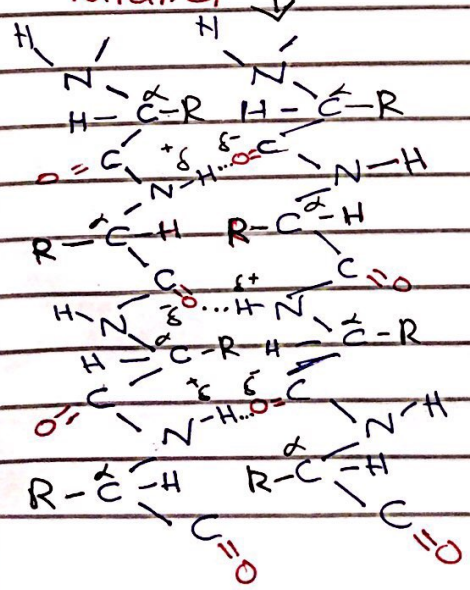
Secondary structure :

It is the twisting (folding) of the polypeptide chain into specific coiled structure held together by disulfide and hydrogen bonds.

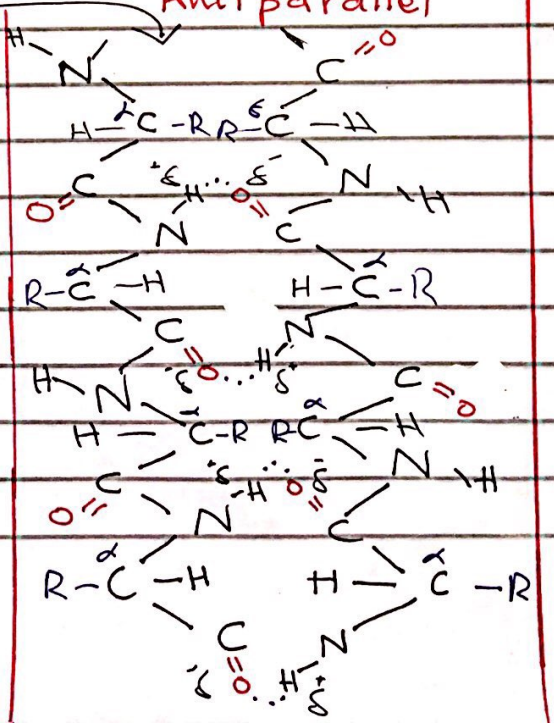
There are two main forms of secondary structure

β - pleated

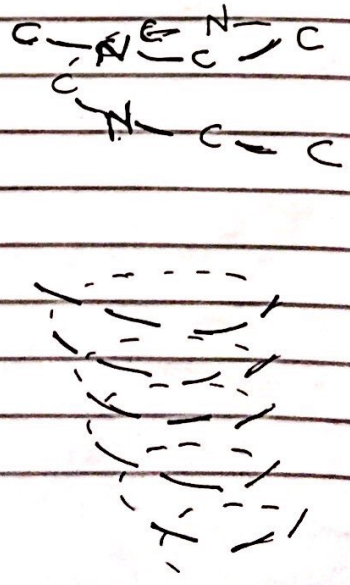
Parallel



Antiparallel



α - helix



Secondary structure :

	α - Helix	β - pleated sheets
Bond type	hydrogen bonds between peptide bonds in the same chain	hydrogen bonds formed between peptide bonds in different chains
Shape	Right handed helix	same direction : Parallel opposing direction : Anti parallel
Formed in (found in)	myosin, α keratin	silk, β-keratin

Note : Hydrogen bonds formed between peptide bonds تـوضـيـح
⟹ formed between functional -NH and functional $-\overset{O}{\overset{\|}{C}}-$, not between side chains

Note 2 : The type of the amino acids (side chains) and the order of them in the primary structure affect the type of the structure that this part of the protein will undergo during secondary, tertary and quaternary folding.

Eg. 1. Proline and Glycine : "Helix breakers" : found in turns
2. Large aromatic residues : prefer to adopt "β-strand conformations"

Secondary folding امثلة اللين السابقين عن

Motifs (super secondary structures)

* Motifs describes the connectivity between secondary structural elements.
* An individual motif usually consists of only a few elements.
* Protein structural motifs often include loops of variable lengh and unspecific structure

E.g. Alpha - alpha : 2 α-helix conected with a loop
Beta - Beta : 2 β-strands conected with a loop
β - α - β : β-strand - loop - α-helix - loop - β-strand
Helix - turn - helix : 2 α-helix conected with a short AAs strand
Helix - loop - helix : α-helices conected with a looping streatch of amino acids
Zinc finger motif : consist of an α-helix and a β-sheet
Leucine zipper : α-helix of 30 to 40 AAs residues ; It contain leucine every seven amino acids

Motifs :

α - α : Helix - loop - Helix , Helix - turn - Helix , α - α corner

β - β : Beta hairpin , Greek key

Other : Omega loop , zinc finger , leucine zipper , Nest , Niche

Tertiary structure :

Tertiary structure is the functional , 3D structure of proteins (polypeptide chain)

Motifs and domains are recognizable tertiary structures which serve as molecular building blocks

Note: Tertiary structure is considered to be largely determined by primary structure (its sequence of amino acids)

Tertiary structure formation

* Tertiary structure is formed due to interactions between side chains.

Interactions which occur between side chains are: Hydrogen, Ionic, Disulphide and hydrophobic interactions.

The interactions between side chains are sometimes stronger than interactions between peptide bonds (those which stabilize 2° structure). As a result the interactions between the side chains may cause a number of folds, bends, and loops in the protein chain

* E.g. Proline and glycine kink the α-helix (thus called helix breakers) to facilitates the formation of the helical conformation of each α-chain of collagen protein

E.g. 2 In the zinc finger motif : zinc bound at four positions to maintain the tertiary structure of this domain.

* Remember :

Amino acids with non-polar R groups : Hydrophobic interactions

Amino acids with charged polar R groups : Ionic interactions

Amino acids with uncharged polar R groups : Hydroxyl : Hydrogen bonds

Amide : Hydrogen interactions

Thiol : Disulfide bonds

Domains :

راجع السلايد

* A domain is a section of protein sufficient to preform a particular task

* The core of a domain is built from combinations of motifs

Folding of the peptide chain within a domain usually occurs independently of folding in other domains

Quaternary structure :

* Only big proteins undergo quaternary structure
* Definition : It is the aggregation of several polypeptide chains to form a protein molecule
* It describes the spatial relationships between the separate subunits
* The interactions that stabilize the 3° struture are the same that stabilize 4° structure

E.g. Insulin : 2 polypeptide chains (A and B) connected by disulfied bond

Globin of Hb : 4 chains (2 α and 2 β)

Notes :

* 1°, 2°, and 3° structures : folding of a single polypeptide chain
* 4° structure : binding of multiple subunits (polypeptide chains) togther
* Interactions (bonds) in the proteins :

Covalent Bonds : In 1° structure between amino acids

Disulphide Bridges : In 3°, 4° between sidechains (R)

Ionic Bonds : In 3°, 4° between sidechains (R)

Hydrophobic interactions : In 3°, 4° between side chains (R)

Hydrogen bonds : 1. In 2° between functional groups of the peptide bonds

2. In 3°, 4° between sidechains (R)

Protein folding

* The process by which a polypeptide folds into its characteristic and functional 3D structure (3° structure) From a random coil (1° structure)
* Chaperones : 1. assist in the folding of other proteins

2. Used to prevent misfolding and aggregation

3. Refold misfolded proteins

* Failure to fold into native structure produces inactive proteins that are usually toxic

Misfolded proteins is refolded by chaperons, degradated by proteosomes, or aggregate and accumulate forming amyloid fibrils

Protein denaturation :

The destruction of the organization of the protein molecule (2°, 3°, 4°). So, the polypeptide chain become unfolded and irregularly arranged.

Note : The higher the specificity of a domain the more it's effected by denaturation