Structural Bioinformatics- Nucleic acid data Bank, Molecular modelling databank.

- Branch of bioinformatics thar referred to as Structural Bioinformatics.
- Analysis and Prediction of 3D structure of biological macromolecules such as Protein, DNA and Rna.
- Main objective :
  - creation of new methods of analysis.
  - manipulating biological macromolecules data’s
  - to solve problem in biology
  - generate new knowledge
- Play important role in solving problem of evolutionary biology, drug discovery

Protein Data Bank(PDB) :

- PDB databases for 3D- Structural Data of large biological molecules, such as protein and nucleic acid
- Obtain by using techniques such as X- ray crystallography, NMR spectroscopy, cryo- electron microscopy.
- Structure and an stored information are freely available like; PDB like RCSB, PDBs and PDB etc
- Announced in 1971- joint venture between Cambridge crystallography Data centre UK and Brookhaven National Laboratory US
- In 2003, website formation.

www.wwpdb.org

www.rcs.org/pdb

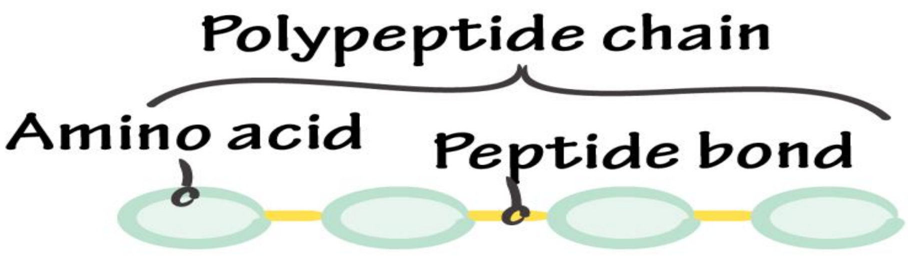
Basic of Protein Structure

- Protein is the three dimensional arrangement of atoms in an amino- acid chain molecules
- Polymers of amino acid(polypeptide chain), undergoes condensation reaction- each other with a peptide bond.
- Chain under 30 amino acid residue termed as peptide, rather than a protein.
- Level of protein structure – four distinct level of protein structure

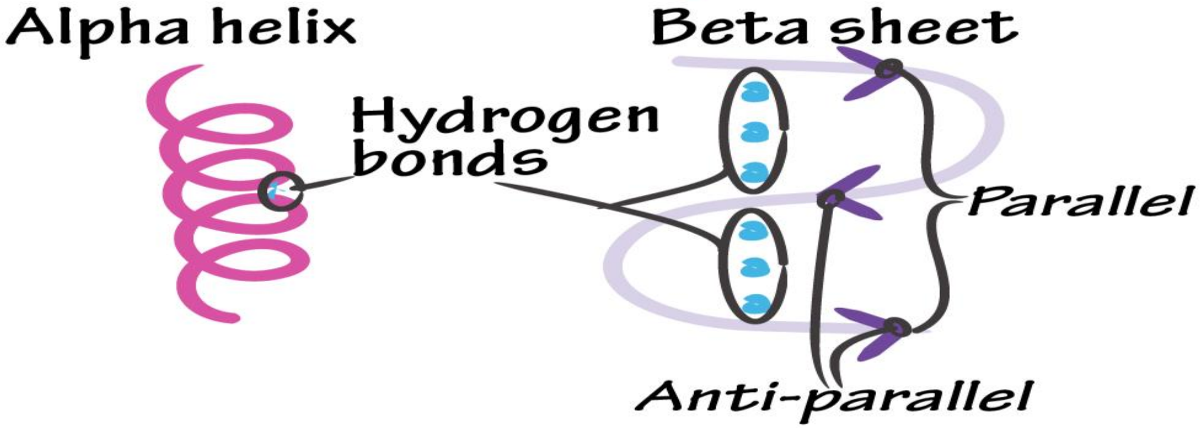
1. Primary level
2. Secondary level
3. Tertiary level
4. Quaternary level

CLASSES OF PROTEIN STRUCTURE

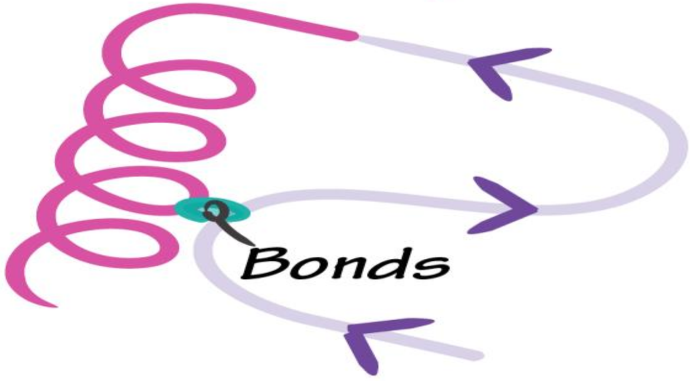
Primary



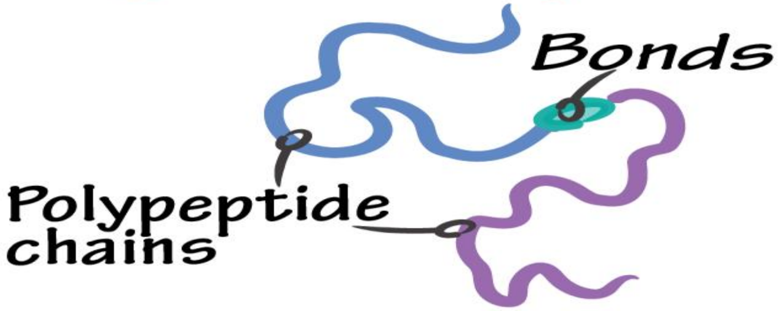
Secondary



Tertiary

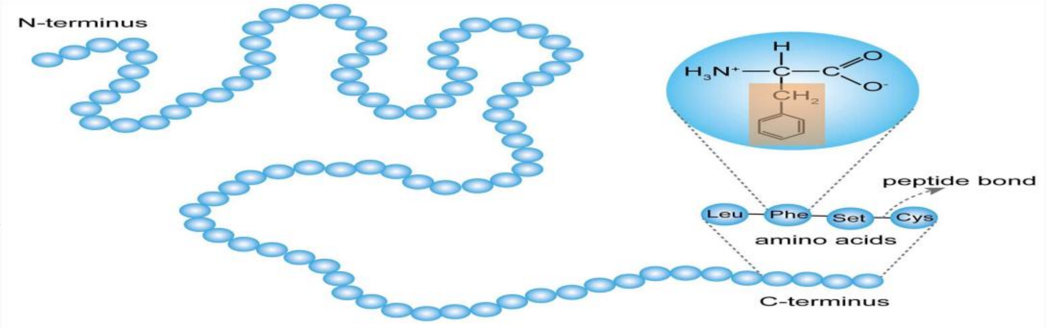


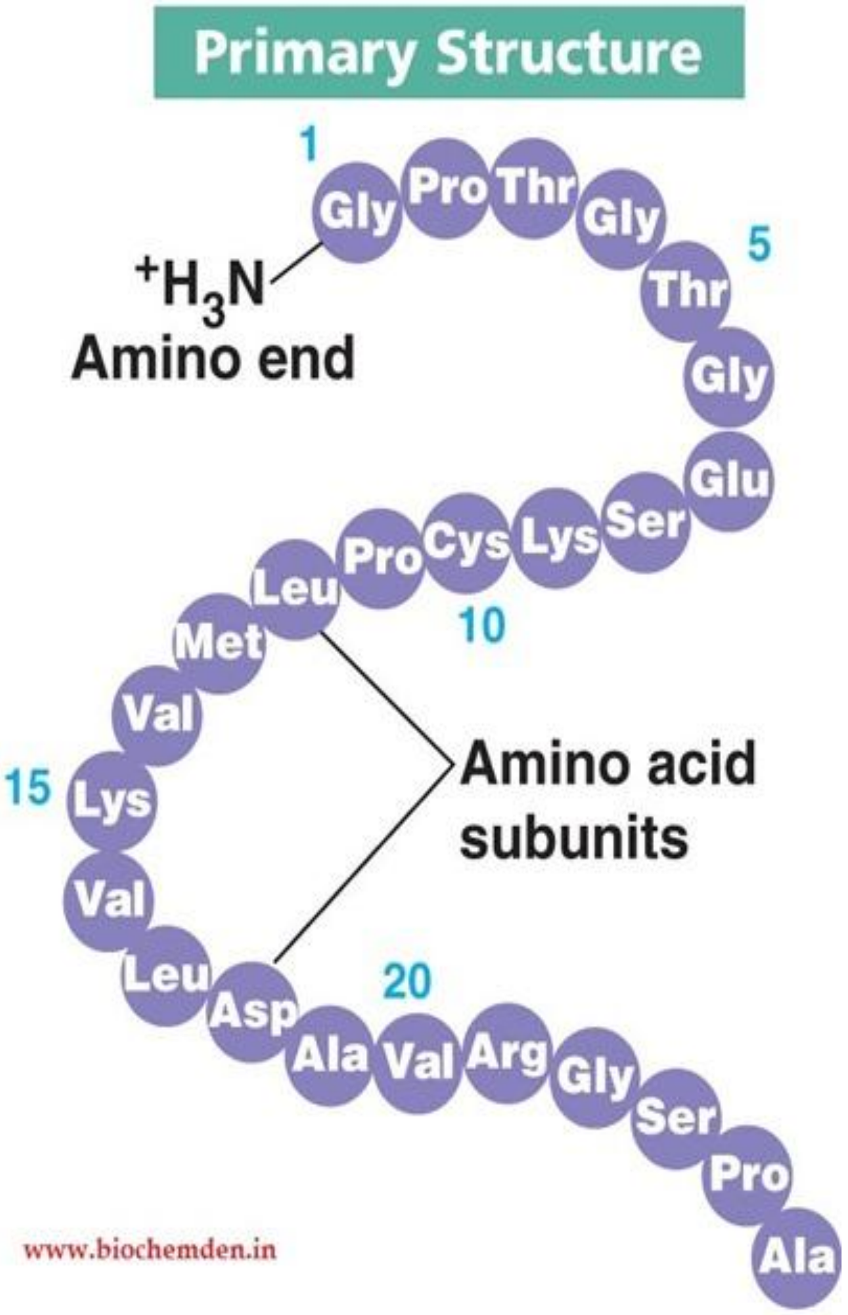
Quaternary



Primary level

- Simplest level of protein structure, primary structure is simply the sequence of amino acids in a polypeptide chain.
- Individual amino acid residues are held together by peptide bonds in polypeptide.
- Each protein or polypeptide has its own set of amino acids, assembled in a particular order. This order is determined by the particular gene coding for the protein.
- Each polypeptide chain has an N-terminus and C-terminus.
- For examp
polypeptid





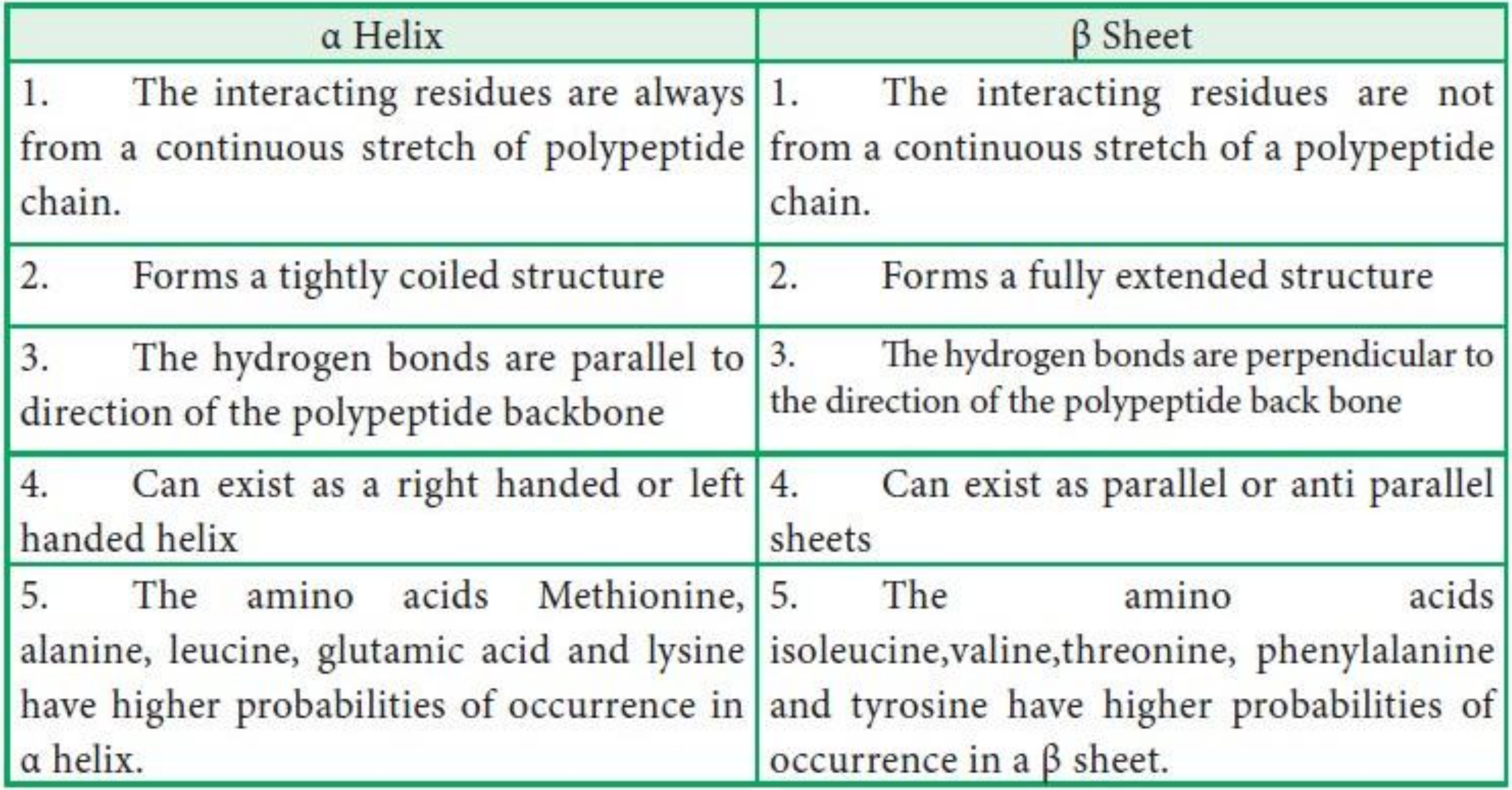
Secondary structure

- Next level of protein structure, secondary structure refers to local folded structures that form within a polypetide due to interactions between the atoms of the backbone.
- Refers to polypeptide chain apart from the R- group
- Most common types are –

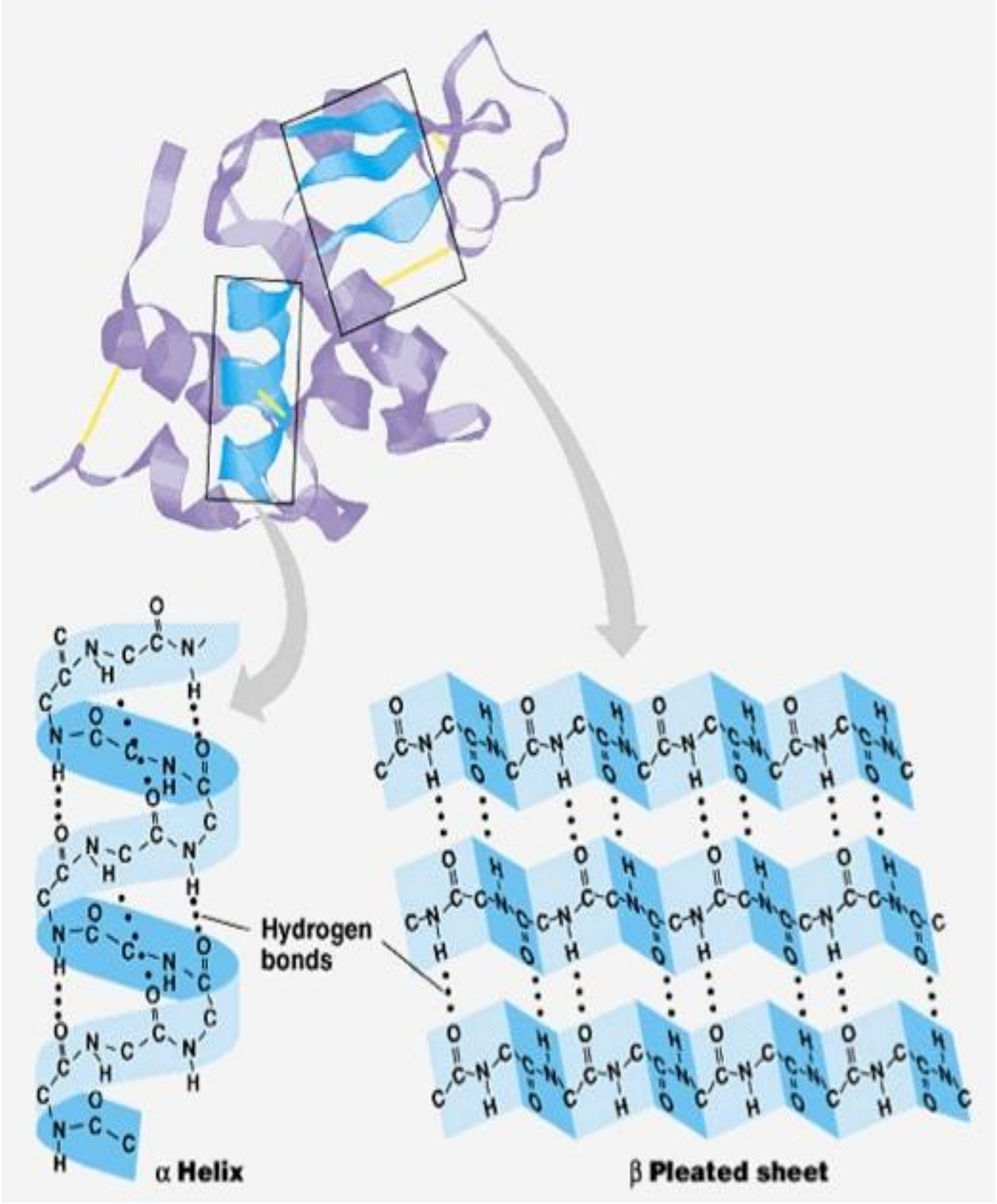
  1. a- helix and

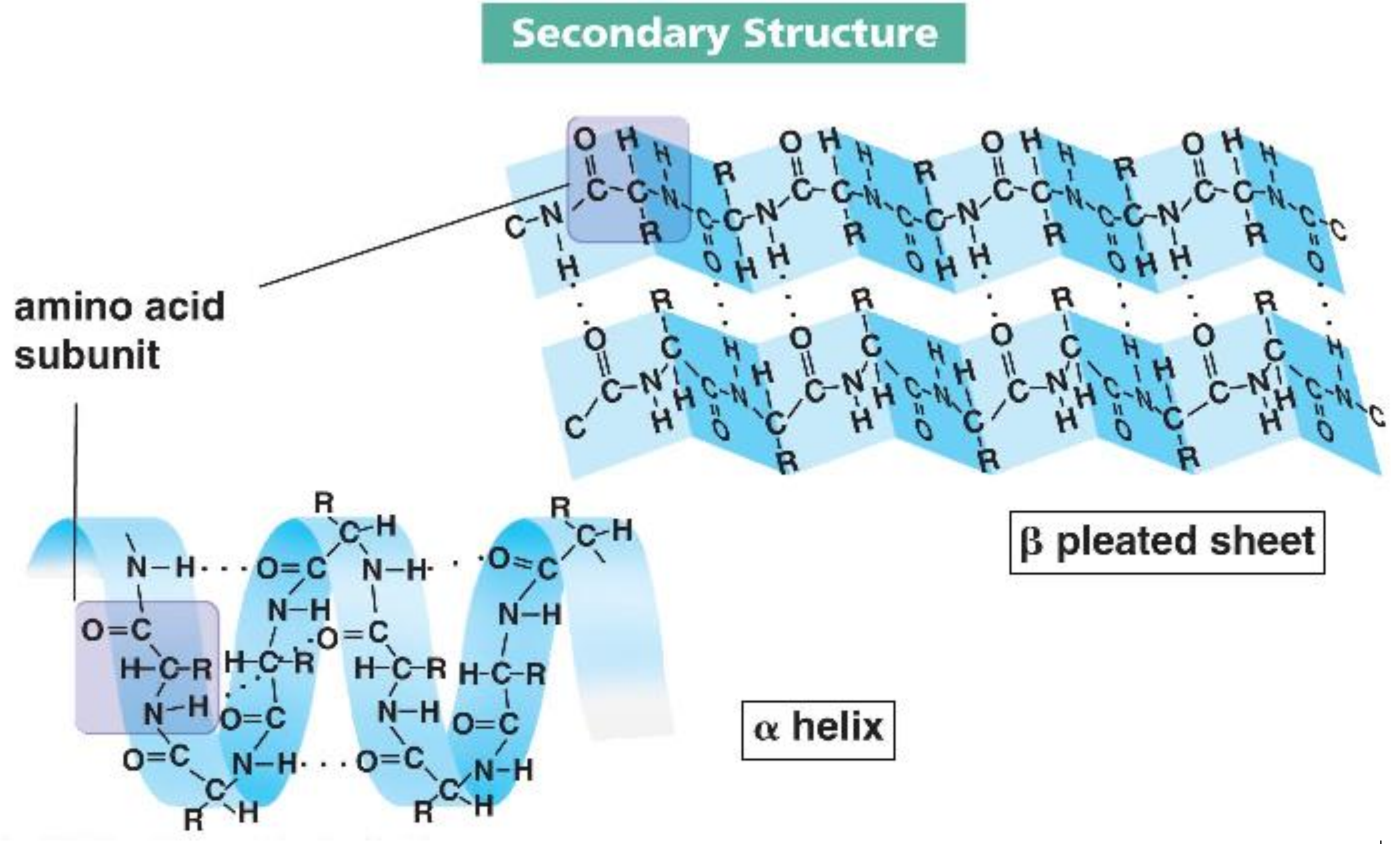
  2. B(beta) – sheet
- both are held in shape by hydrogen bonds, which from between the carbonyl O of one amino acid and the amino H of another

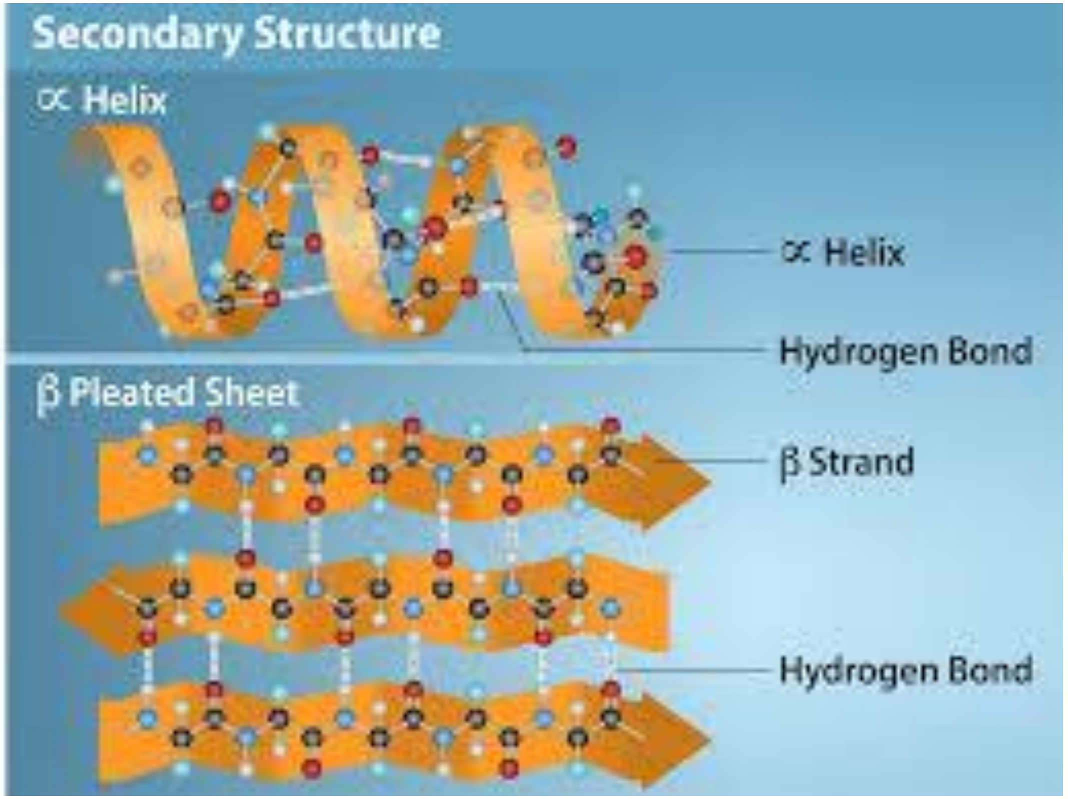
a – helix **B - sheet**

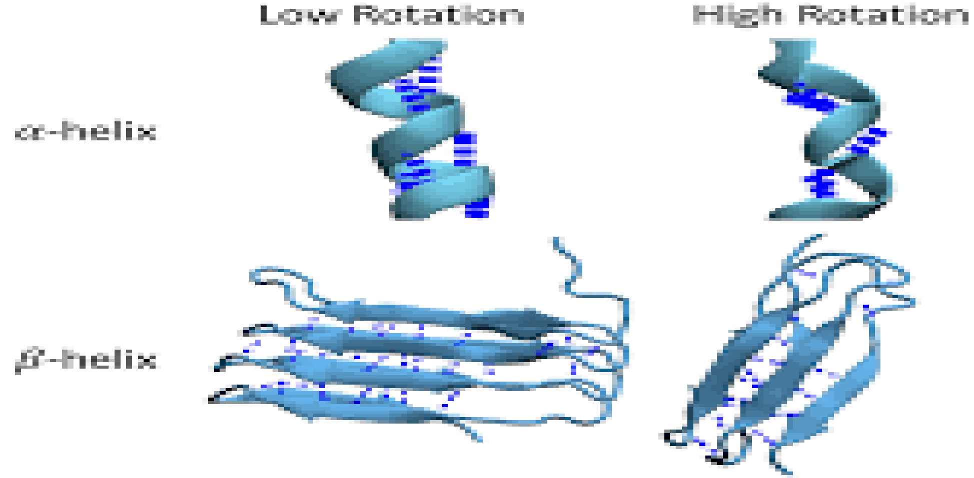


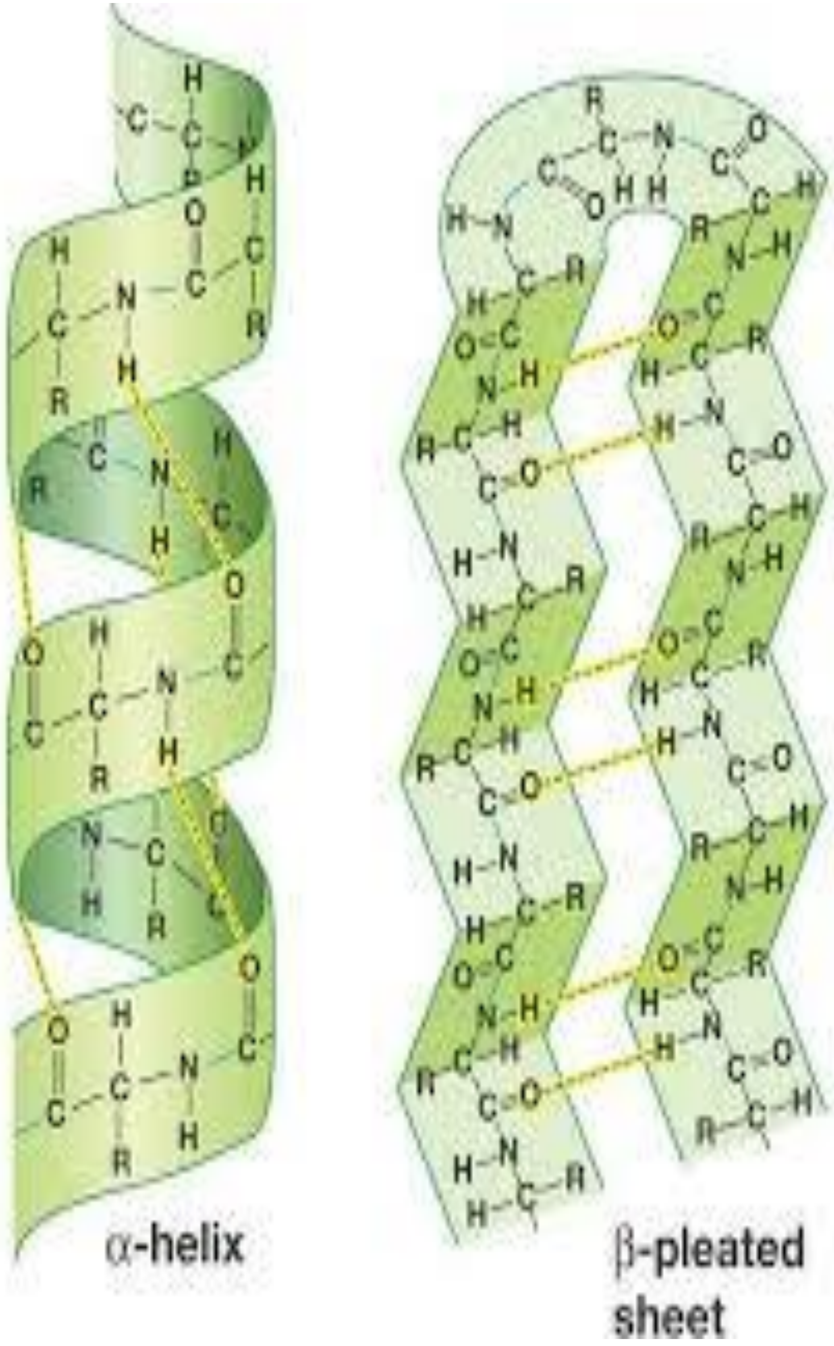
α Helix	β Sheet
1. The interacting residues are always from a continuous stretch of polypeptide chain.	1. The interacting residues are not from a continuous stretch of a polypeptide chain.
2. Forms a tightly coiled structure	2. Forms a fully extended structure
3. The hydrogen bonds are parallel to direction of the polypeptide backbone	3. The hydrogen bonds are perpendicular to the direction of the polypeptide back bone
4. Can exist as a right handed or left handed helix	4. Can exist as parallel or anti parallel sheets
5. The amino acids Methionine, alanine, leucine, glutamic acid and lysine have higher probabilities of occurrence in α helix.	5. The amino acids isoleucine,valine,threonine, phenylalanine and tyrosine have higher probabilities of occurrence in a β sheet.

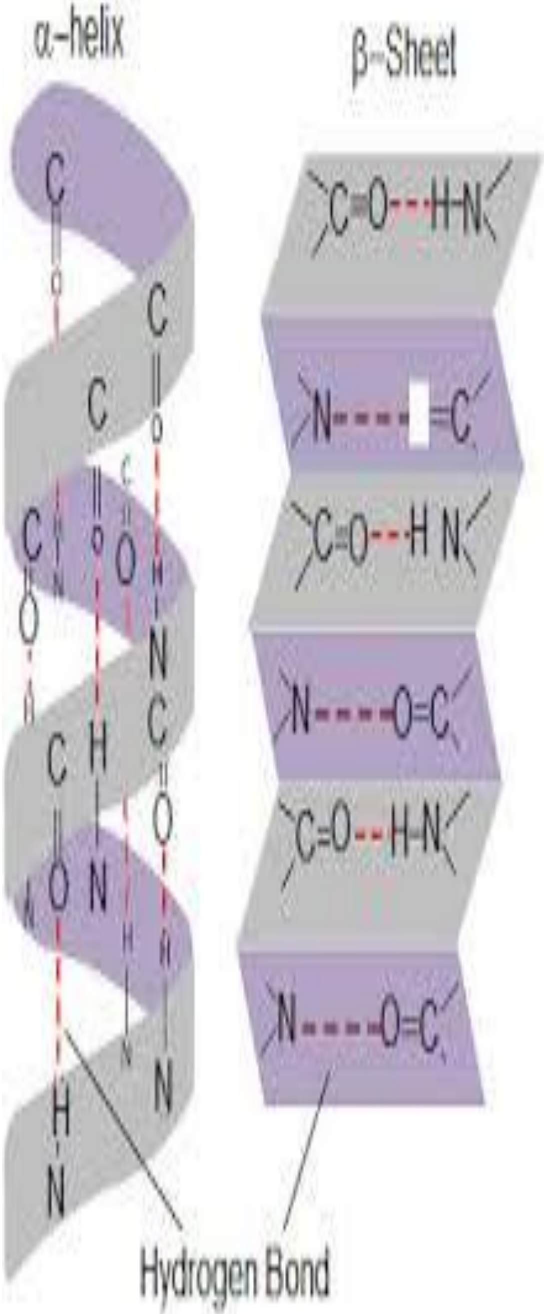

Hydrogen bonds
α Helix
β Pleated sheet


Secondary Structure
amino acid subunit
β pleated sheet
α helix


Secondary Structure
∝ Helix
∝ Helix
Hydrogen Bond
β Pleated Sheet
β Strand
Hydrogen Bond


Low Rotation
High Rotation
α-helix
β-helix


α-helix
β-pleated sheet


α-helix
β-Sheet
C=O---H-N
N----=C
C=O--H N
N----O=C
C=O--H-N
N----O=C
Hydrogen Bond

Tertiary structure

- The tertiary structure can be decribed as the complete three- dimensional assembly of all amino acids of a single polypeptide chain.
- The tertiary structure can come in various forms but is generally classifed as

1. Globular protein

Globular proteins are usually soluble and surrounded by water molecules. They tend to have an overall compact structure of sperical shape.

2. Membrane proteinss

Exist in lipid bilayers of cell meml

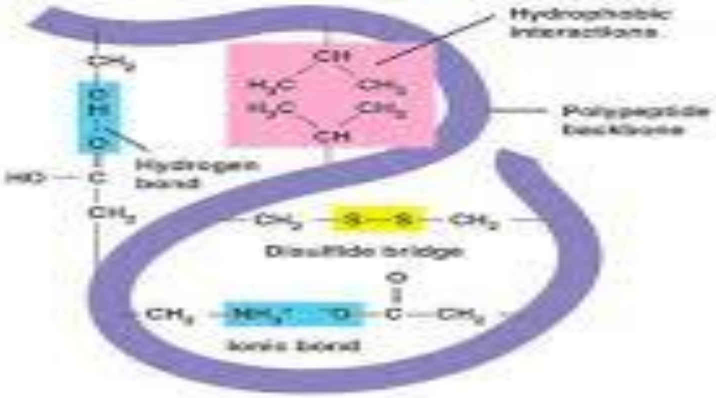
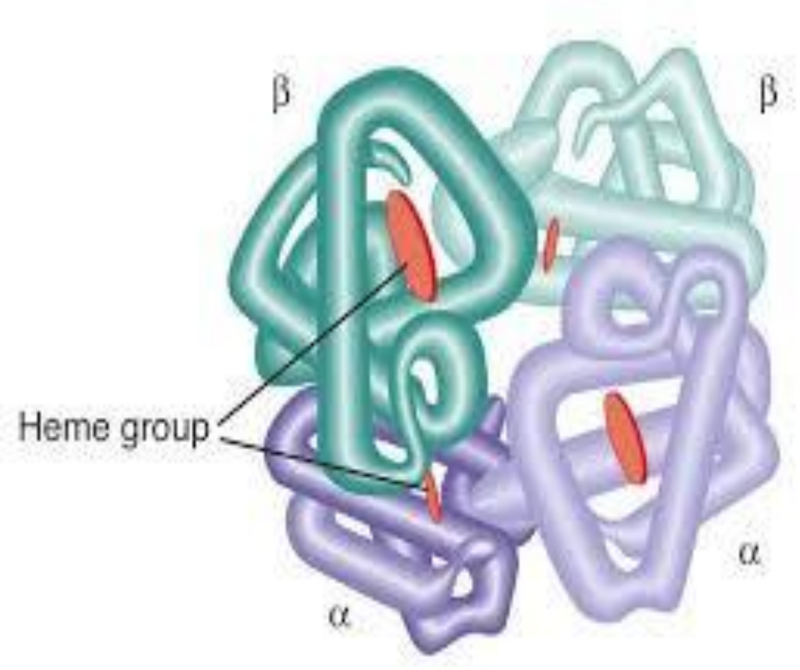
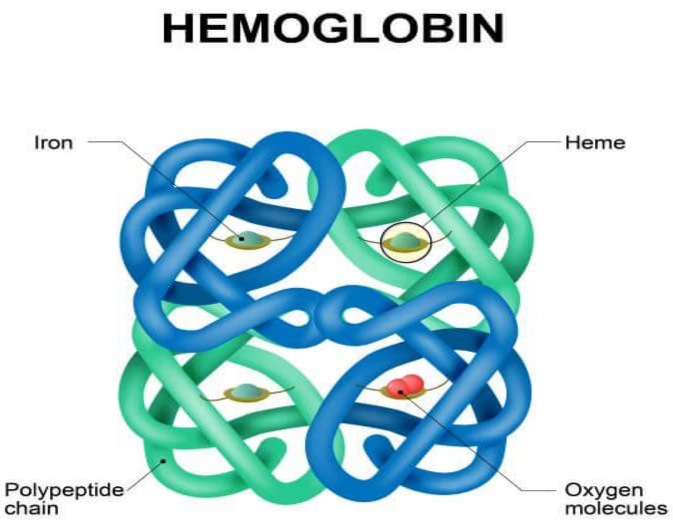


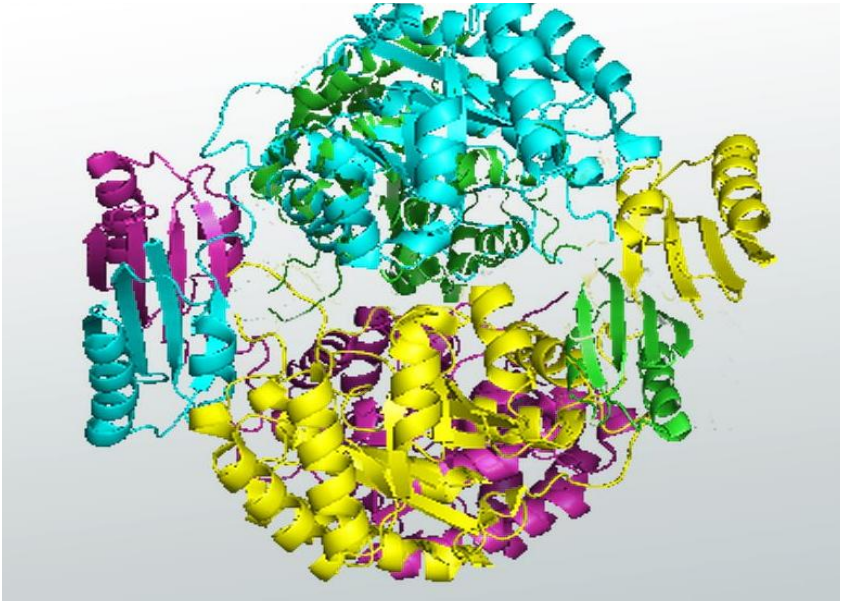
Fig 1. Tertiary Structure. This diagram illustrates some of the key bonds present in the tertiary structure.

Quaternary structure

- Some proteins are made up of multiple polypeptide chains, also known as subunits. When these subunits come together, they give the protein its quaternary structure.
- Very complex structure of proteins







Molecular modelling databases(MMDB)

- NCBI → search[insulin]

Molecular modelling and protein structure prediction

1. Process of creating 3D model of protein from amino acid composition.
2. Known as protein structure prediction or protein modelling

Uses

- to understand function at the protein
- Learn how they interact with protein, ligand and chemicals
- Use in docking analyses that identities chemicals into drug to treat diseases(computer aided drug discovery)
- Modelling depends upon secondary to tertiary structure
- Can be done by homology modelling

Homology modelling

- Comparative modelling procedure, 3D structure

Steps :

- Identifying best template for unknown sequence
- Best method for template identification
    - pair- wise sequence alignment
    - multiple- sequence alignment
- Degree of similarity between two sequence
- By using computer best model is constructed
    - stisfy all biological, physical and chemical requirement
    - stable conformational status