PROTEIN

MEDICAL AND BIOLOGICAL IMPORTANCE

- Amino acids serve as building blocks of proteins. Some amino acids are found in free form in human blood
- They also serve as precursors of hormones, purines, pyrimidines, porphyrins, vitamins and biologically important amines like histamine.
- Peptides have many important biological functions. Some of them are hormones. They are used as anti-biotics and antitumor agents.
- Some peptides are required for detoxification reactions. Some peptides serve as neurotransmitters.
- Amino acid proline protects living organisms against free radical induced damage.

- Some peptides are involved in regulation of cell cycle and apoptosis.
- Peptides of vertebrates and invertebrates act as antimicrobial agents. They are part of innate immunity. Bacterial infections at epithelial surface induce production of antimicrobial peptides, which cause lysis of microbes.
- Peptides are enzyme inhibitors. Natural and synthetic peptide inhibitors of angiotensin converting enzyme (ACE) act as a anti hypertensives. Peptide inhibitors of ACE present in physiological foods, lowers blood pressure after they are absorbed from intestine. Lisinopril, Enalapril etc. are synthetic peptide inhibitors of ACE that are used as drugs in the treatment of hypertension.
- Some synthetic peptides are used as enzyme substrates

CLASSIFICATION

- Based on side chain and ring structure present, amino acids are classified into 7 major classes
- according to the reaction in solution or charge
- based on the number of amino and carboxyl groups present in the molecule
- according to their nutritional importance
- According to metabolic fate

Based on side chain and ring structure

- Amino acids with aliphatic side chain e.g. : glycine, alanine, valine, leucine and isoleucine
- with side chain containing hydroxyl groups e.g.: serine and threonine
- with side chain containing sulfur atoms e.g.: cysteine, methionine and cystine
- with side chain containing acidic groups or their amides e.g. : aspartic acid, aspargine, glutamic acid and glutamine
- with side chain containing basic groups e.g.: arginine, lysine, hydroxy lysine and histidine
- containing aromatic rings e.g.: phenylalanine, tyrosine and tryptophan
- Imino acids e.g.: proline and hydroxy proline

reaction in solution or charge

- Acidic : aspartic acid, glutamic acid
- basic : arginine, lysine and histidine
- neutral amino acids: Rest of the amino acids

number of amino and carboxyl groups

- Mono-amino mono-carboxylic acid: Glycine
- Mono-amino dicarboxylic acid: Glutamate

nutritional importance

Essential amino acids:

- methionine (M), arginine (A),
- tryptophan (T), threonine (T),
- valine (V), isoleucine (IL),
- leucine (L), phenyl alanine (P),
- histidine (H) and Lysine (L)

Non-essential amino acids

- alanine, glycine,
- serine, tyrosine,
- glutamate, glutamine,
- aspartate, aspargine,
- Cysteine and proline

Nutritional fate

Ketogenic

- Those which on catabolism gives ketone bodies e.g. leucine and lycine

Glucogenic

- That can serve as precursor for the formation of glucose or glycogen e.g.: alanine, aspartate, glycine etc

- Some are both ketogenic and glycogenic : isoleucine, phenylalanine, tryptophan, tyrosine

Rare Amino Acids or Unusual Amino Acids

- Ornithine, citrulline and arginino succinic acid of urea cycle.
- β-alanine is part of co-enzyme A
- Taurine is part of bile acids
- γ-aminobutyric acid is a neurotransmitter
- Mono- and di-iodotyrosine are precursors of thyroxine.
- Pantothenic acid is a water-soluble vitamin.
- Homoserine is an intermediate of methionine catabolism
- Homocysteine. It is also an intermediate of methionine catabolism. It is a atherothrombogenic agent. It triggers platelet adhesion. Hence, it is considered as a risk factor for development of coronary artery disease (CAD).
- S-allylcysteine sulfoxide. It is an amino acid obtained from garlic. It has many therapeutic effects. It is commonly called as alliin.

PROPERTIES OF AMINO ACIDS

- *Optical isomerism*

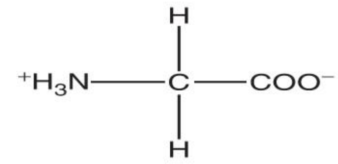
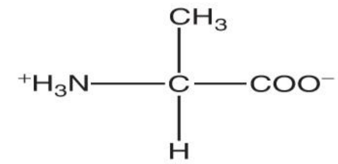
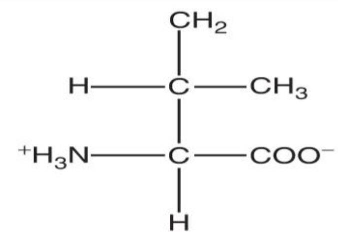
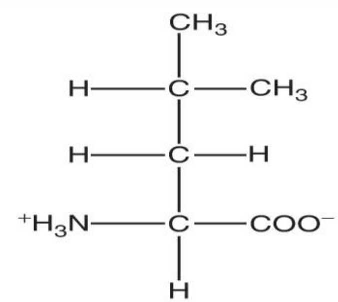
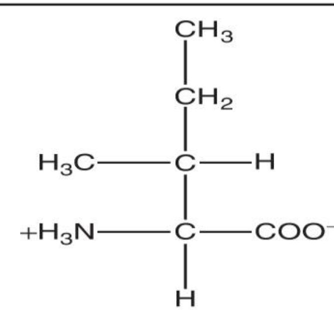
- *Acid-base or charge properties of amino acids:* Amino acids act as acids and bases. So they are called as ***ampholytes or amphoteric substances***.

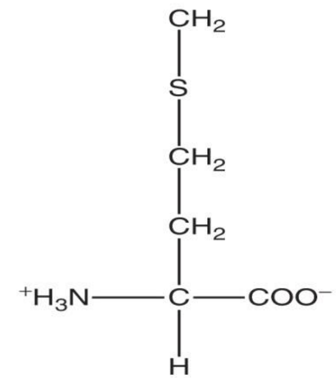
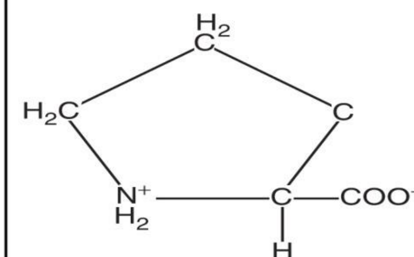
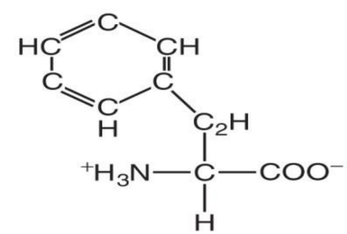
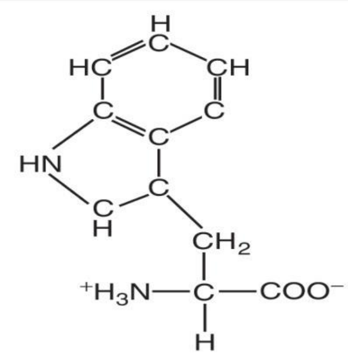
- At neutral pH both groups are ionized, this doubly charged molecule of amino acid containing positive and negative charges is called as **zwitter ion**

- ***Isoelectric pH****: It is the pH at which the net charge of an amino acid is zero or when* the number of positive charges are equal to number of negative charges. At isoelectric pH amino acids have minimum solubility.

- *Buffering action of amino acids:* Since amino acids are ampholytes they act as buffers.

- *Ultra violet light (UV) absorption of amino acids:* Aromatic amino acids absorb ultraviolet light. Tryptophan absorb ultra violet light at 280 nm. The ultra violet light absorption is also exhibited by proteins containing tryptophan. Hence, it is used for quantitative estimation of proteins

Name	Abbreviation(s)	Unique Features	Structure
Nonpolar, hydrophobic side chains—found in protein interiors			
Glycine	Gly, G	• Smallest • R is a single proton • Flexible • Neuroinhibitor • Role in biosynthesis of many compounds, such as purines	
Alanine	Ala, A	• Methane • α-Keto homologue is pyruvate • Role in nitrogen transport from tissues to the liver	
Valine	Val, V	• Butyl group • Branched chain amino acid found in high concentration in muscles	
Leucine	Leu, L	• Branched chain amino acid found in high concentration in muscles	
Isoleucine	Ile, I	• Isomer of leucine • Branched chain amino acid found in high concentration in muscles	

Name	Abbreviation(s)	Unique Features	Structure
Nonpolar, hydrophobic side chains—found in protein interiors			
Methionine	Met, M	• One of two amino acids containing sulfur • Contains a sulfur as an ester • Sulfur easily oxidized • As S-adenosyl-L-methionine (SAM), a methyl donor in many bioreactions	
Proline	Pro, P	• α-Carbon forms a ring containing primary amine • Inflexible • Forms kinks in secondary structures	
Phenylalanine	Phe, F	• Alanine plus a phenyl • Converted to tyrosine, which is, in turn, converted to L-dopa • Interferes with the production of serotonin	
Tryptophan	Trp, W	• Bulky, aromatic side chains • Indole group • Precursor for serotonin and niacin	

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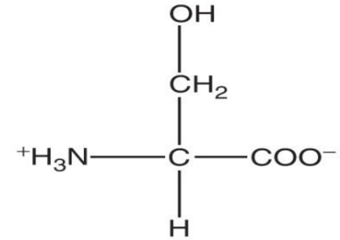
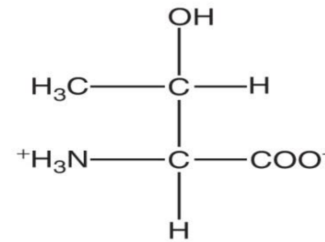
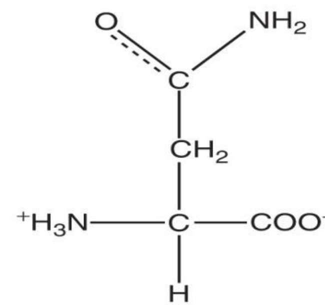
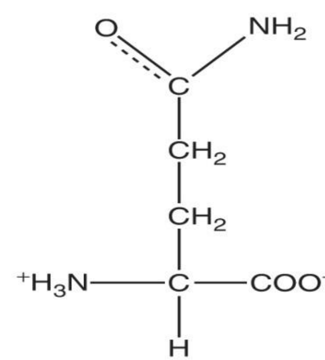
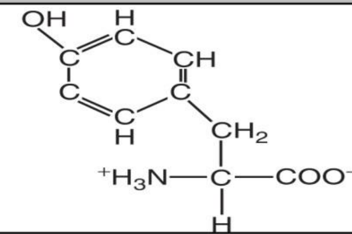
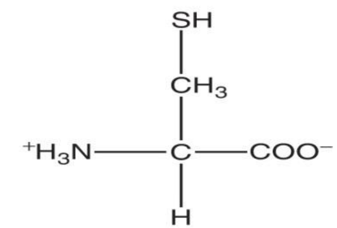
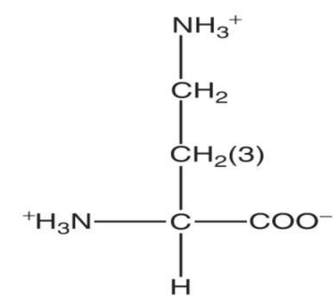
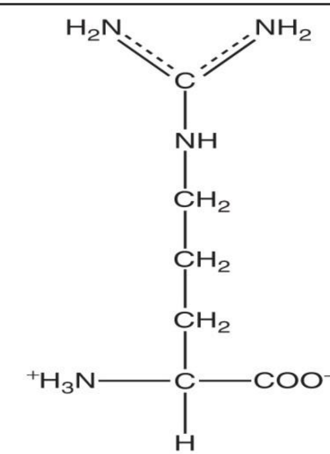
Name	Abbreviation(s)	Unique Features	Structure
Uncharged polar side chains—metabolically active and located on the exterior of proteins			
Serine	Ser, S	• Hydroxyl group • Found at the active site of enzymes • Aids in glycoprotein formation	
Threonine	Thr, T	• Methyl and hydroxyl group • Found at the active site of enzymes • Aids in glycoprotein formation	
Asparagine	Asn, N	• Methyl group and carboxyl group with a highly polar uncharged amine that readily forms hydrogen bonds • Found at the ends of alpha helices and beta sheets • Aids in formation of glycoproteins • Input to urea cycle • α-Keto homologue is oxaloacetate	
Glutamine	Gln, Q	• Two methyl groups and carboxyl group with a highly polar uncharged amine • Central role as nitrogen donor in synthesis of nonessential amino acids • Provides nitrogen transport to the liver	

Name	Abbreviation(s)	Unique Features	Structure
Uncharged polar side chains—metabolically active and located on the exterior of proteins			
Tyrosine	Tyr, Y	• Similar to phenylalanine but with polar hydroxyl group on phenyl ring • Important metabolically because ionization altered by micro pH changes	
Charged polar side chains—reactive			
Cysteine	Cys, C	• Sulfhydryl (thiol) group • Forms disulfide bridges • Found at the active site of enzymes • Binds iron	
Lysine	Lys, K	• Long aliphatic chain terminating in an amine • Nucleophilic • Forms ionic bonds	
Arginine	Arg, R	• Long aliphatic chain containing an amine and terminating in two amines • Nucleophilic • Forms ionic bonds • Generated in the urea cycle	

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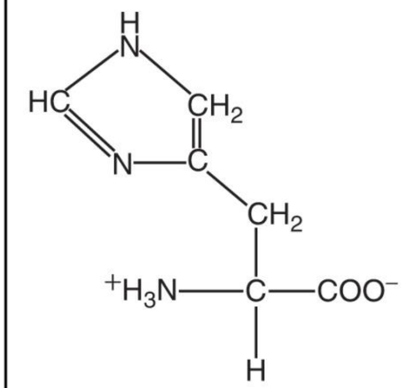
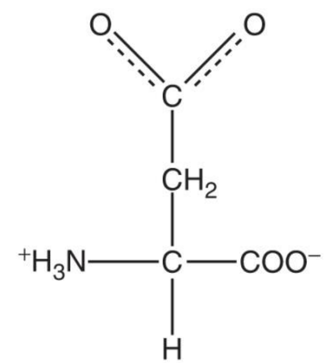
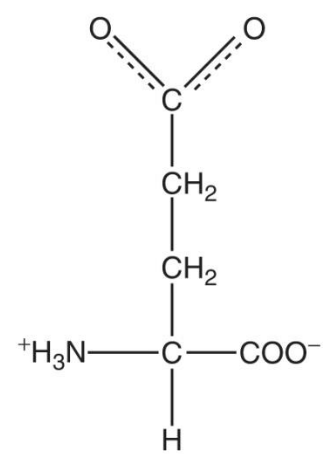
Name	Abbreviation(s)	Unique Features	Structure
Charged polar side chains—reactive			
Histidine	His, H	• Methyl • Imidazole group • Ionic bonds found at the active site of enzymes • Crucial in the structure of hemoglobin	
Aspartate or aspartic acid	Asp, D	• Donates an amine to become oxaloacetate • Active in proteolytic enzymes	
Glutamate or glutamic acid	Glu, E	• Central role as nitrogen donor in synthesis of nonessential amino acids • Provides nitrogen transport to the liver	

PROTEIN STRUCTURE

Primary Structure

- The linear sequence of amino acid residues in a polypeptide chain is called as primary structure. Generally disulfide bonds if any are also included in the primary structure

Secondary Structure

Main Features of α-Helix

- In α-helix polypeptide, backbone is tightly wound round (coiled) long axis of the molecule
- The distance between two amino acid residues is 1.5 Å.
- α-helix contain 3.6 amino acid residues per turn. The R-group of amino acids project outwards of the helix
- The pitch of the α-helix is 5.4 Å long and width is 5.0 Å
- The α-helix is stabilized by intra chain hydrogen bonds formed between –N–H groups and –C=O groups that are four residues back, *i.e.,* –N–H group of a 6th peptide bond is hydrogen bonded to –C=O group of 2nd peptide bond
- Each peptide bond participates in the hydrogen bonding. This gives maximum stability to α-helix

- α-helix present in most fibrous proteins is right handed. The right handed α-helix is more stable than the left handed helix.

- α-helix is hydrophobic in nature because of intra chain hydrogen bonds.

- An α-helix forms spontaneously since it is the most stable conformation of polypeptide chain.

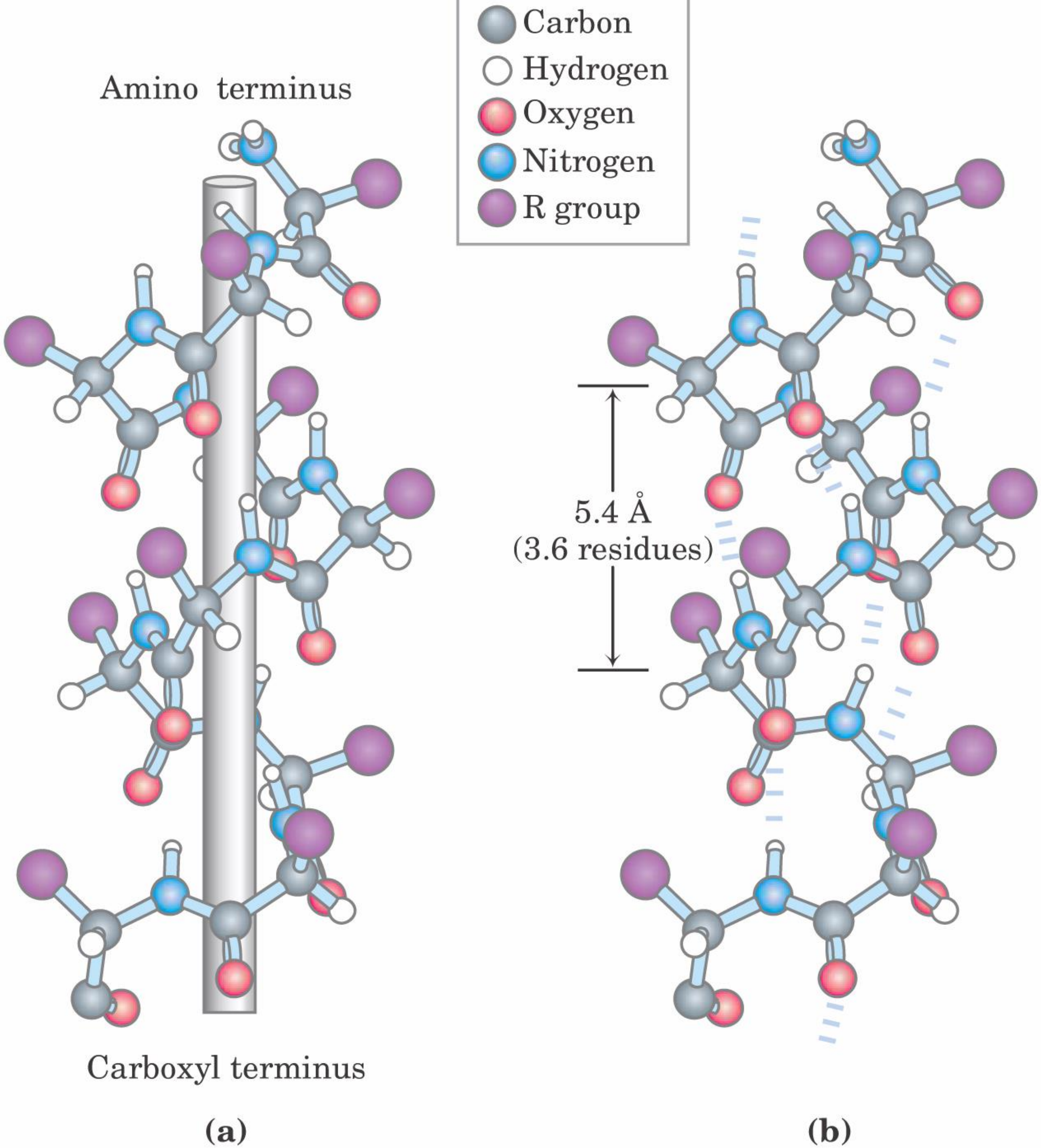
- Some amino acids act as terminators for α-helix.

Example: Proline.

- Aromatic amino acids stabilizes α-helix.

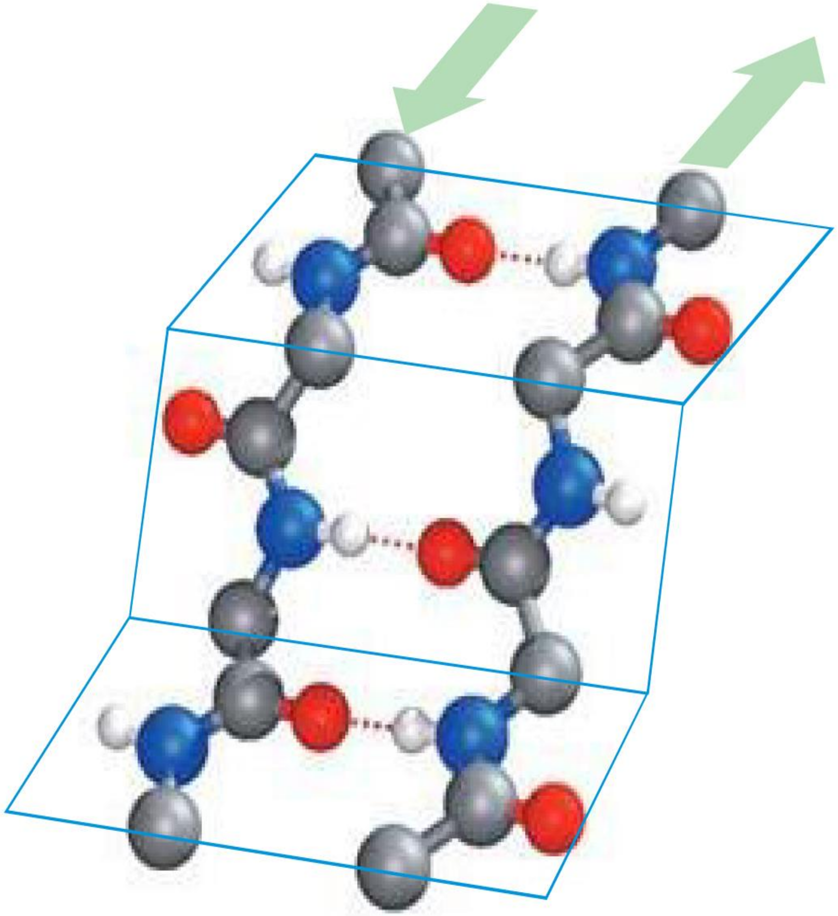
- Charged and hydrophobic amino acids destabilize α-helix.

- Content of α-helix varies from protein to protein.

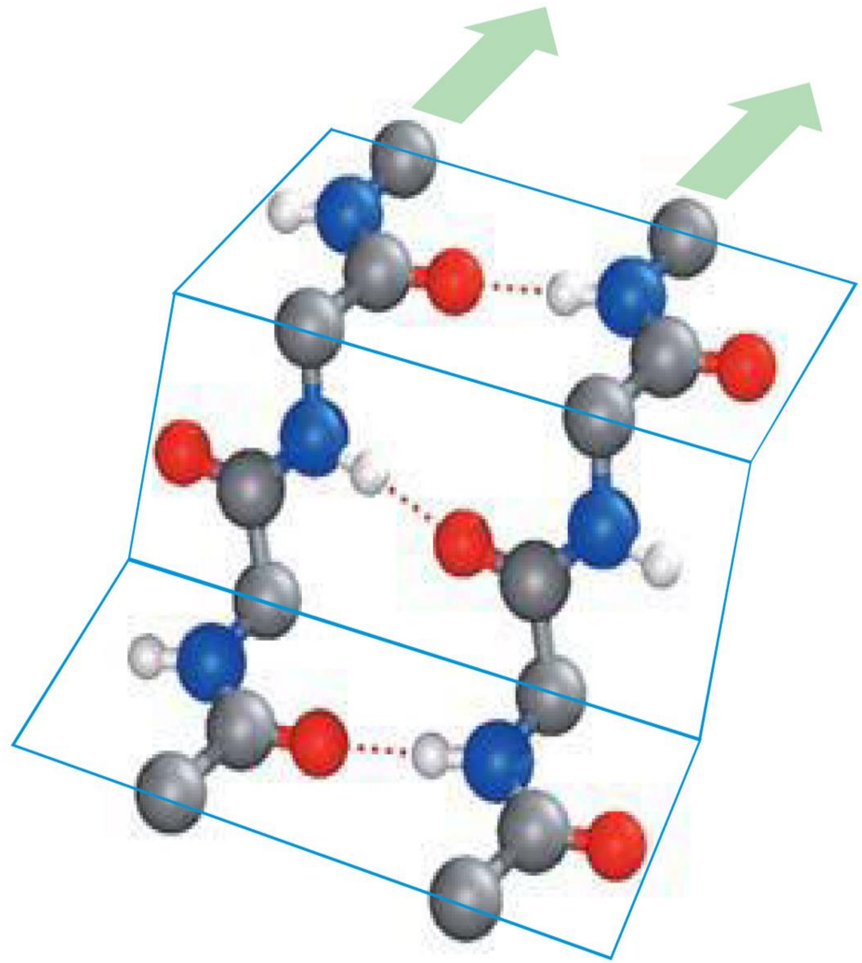

Carbon
Hydrogen
Oxygen
Nitrogen
R group
Amino terminus
Carboxyl terminus
5.4 Å
(3.6 residues)
(a)
(b)

β-Pleated Sheet Features

- In β-pleated sheet, the polypeptide chain is fully extended.
- In β-pleated sheet, polypeptide chains line up side by side to form sheet. The side chains are above or below the plane of the sheet.
- When the adjacent polypeptide chains run in same direction (N to C terminus) the structure is termed as parallel β-pleated sheet.
- When the adjacent polypeptide chains run in opposite direction the structure is termed as anti-parallel β-pleated sheet
- The β-pleated sheet is stabilized by inter chain hydrogen bonds
- β-keratin contains anti parallel β-pleated sheet.
- Both parallel and anti-parallel β-pleated sheet occur in other proteins. Amyloid protein present in Alzheimer's disease has anti parallel β-pleated sheet. It accumulates in the CNS.



1. Antiparallel



2. Parallel

Tertiary Structure

- Three-dimensional folding of polypeptide chain is called as tertiary structure. It consists of regions of α-helices, β-pleated sheet, β-turns, motifs and random coil conformations

Quaternary Structure

- Proteins containing two or more polypeptide chains possess quaternary structure. These proteins are called as *oligomers*. The individual polypeptide chains are called as protomer, *monomers* or *subunits*