COURSE CODE: SC202(CHEMISTRY)

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BIOORGANIC CHEMISTRY: AMINO ACID-PEPTIDE-PROTEIN

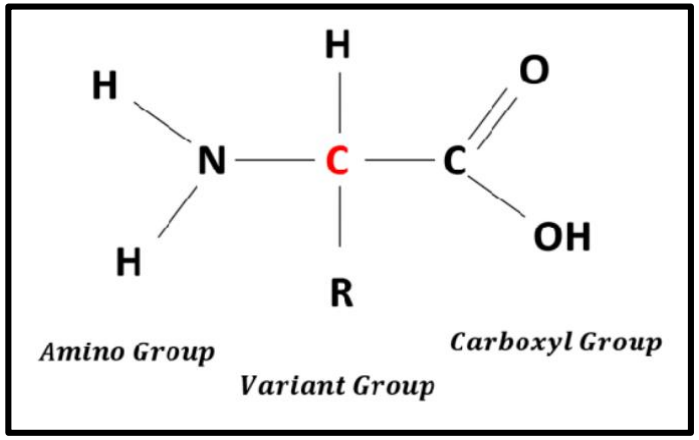
DEPT. OF SCIENCE AND MATHEMATICS

IIITG, GUWAHATI

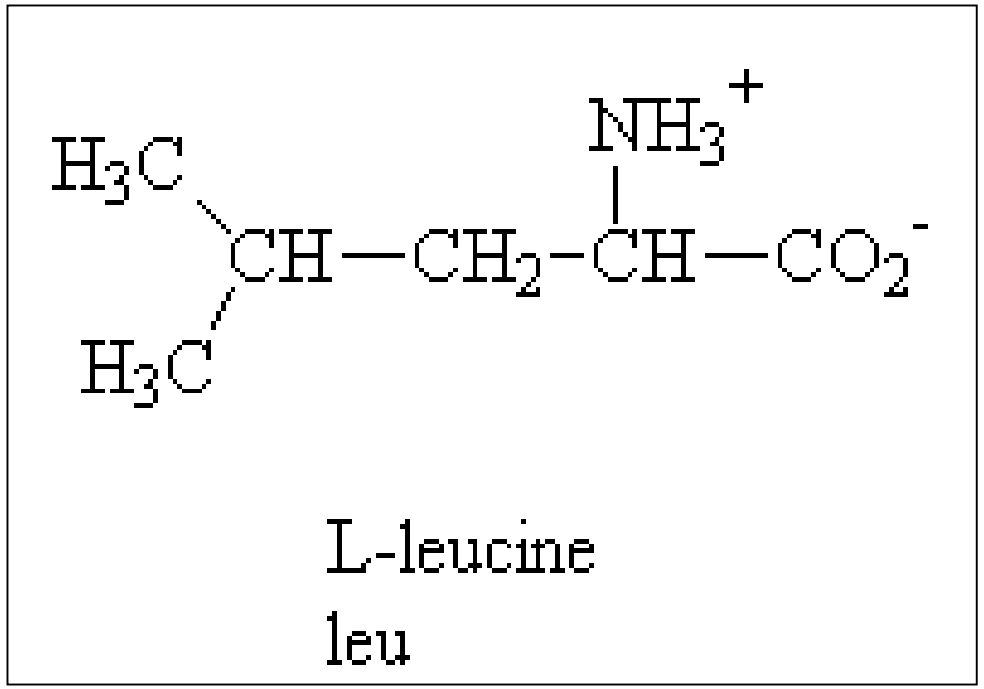
LECTURE DATES: 25/1/2023 & 01/02/2023

Amino Acid (AA)

- Amino Acids are the building blocks of protein. Proteins are polymers of AA linked together by peptide bond.
- There are 300 AA occurring in nature, but only 20 of them occurs in protein.
- An amino acid is a compound having both a carboxyl group(-COOH) and an amino group(-NH_2).
- All α-amino acids have the -NH_2 attached at the Cα to the –COOH, as well as H- & -R.



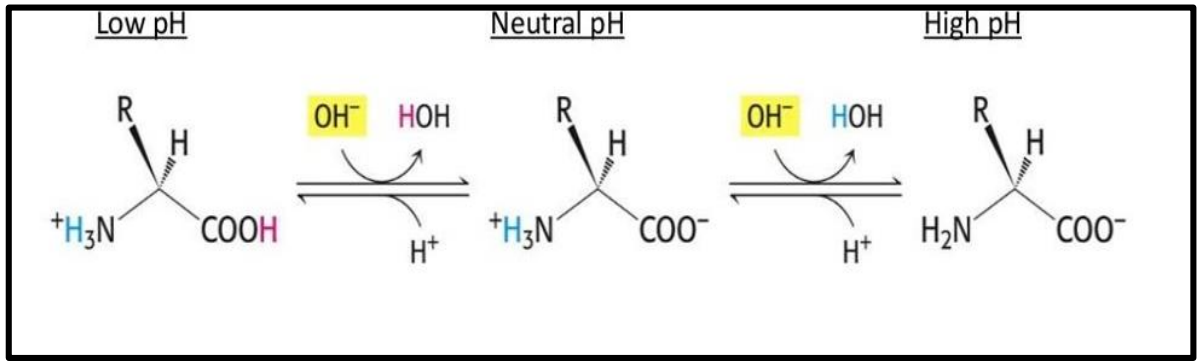
- All naturally occurring AA except glycine (R=H), are chiral.
- At physiological pH (7.4), -COOH group is dissociated forming negatively charged carboxylate ion (COO^-), and $-NH_2$ is protonated to give aminium ion (NH_3^+). This structure is known as Zwitterion.
- The following is the zwitterionic structure of Leucine.



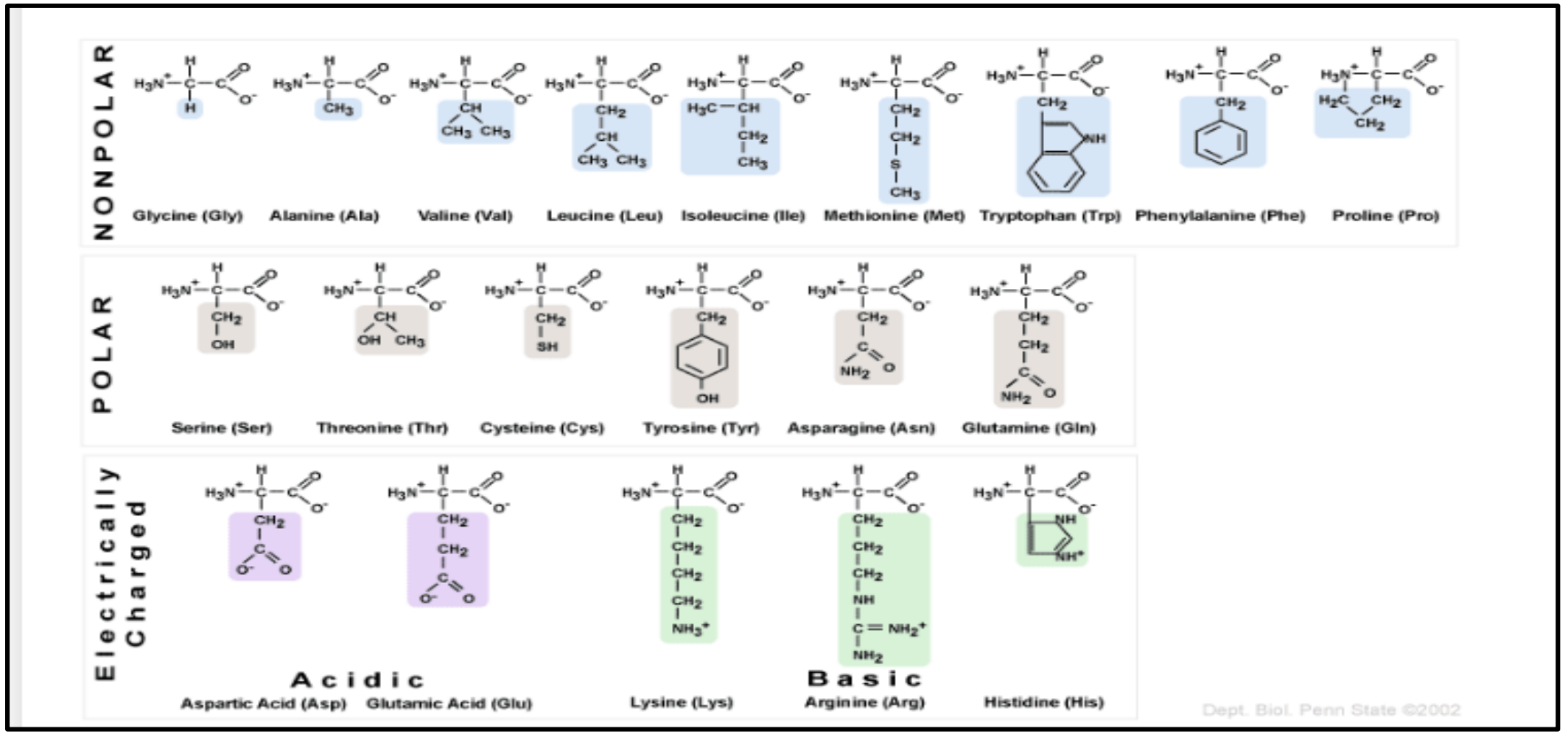
L-leucine

leu

- At low pH, when the proton concentration is high, then -NH_2 and -COOH of an AA, both remain protonated, i.e., -NH_3^+ and -COOH, respectively.
- At neutral pH, the –NH_2 group remains as -NH_3^+ ion and –COOH group remains as –COO^- ion.
- At high pH, when the proton concentration is very low, then the -NH_2 group remains as it is and –COOH group remains as –COO^- ion.



Classification of 20 common AA on the basis of –R group

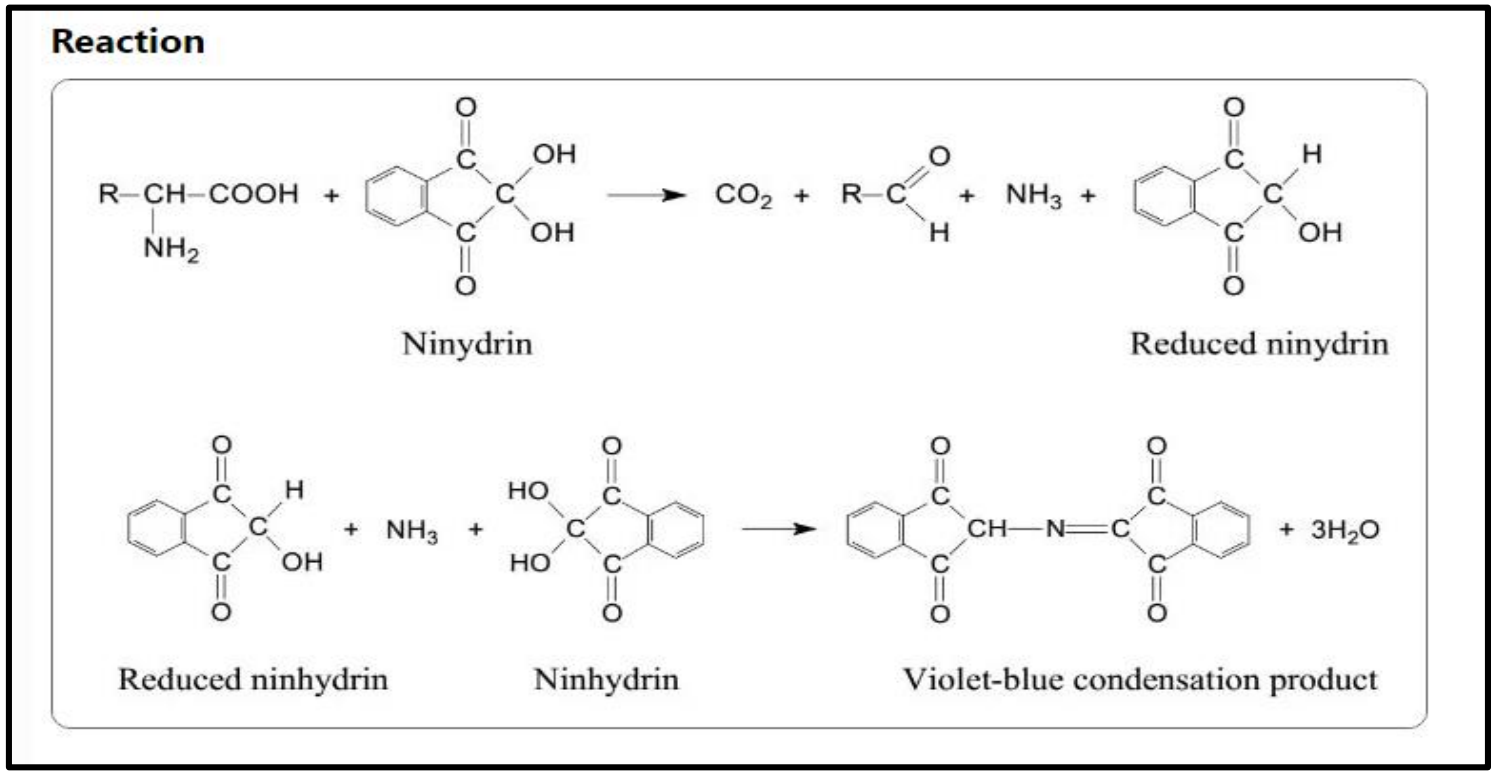


- Essential amino acid: The AA which cannot be synthesized in animal body and must be obtained through diet, e.g., valine, isoleucine, lysine, etc.

- Non-essential amino acid: The AA which are synthesized in animal body e.g., alanine, tyrosine, serine, etc.

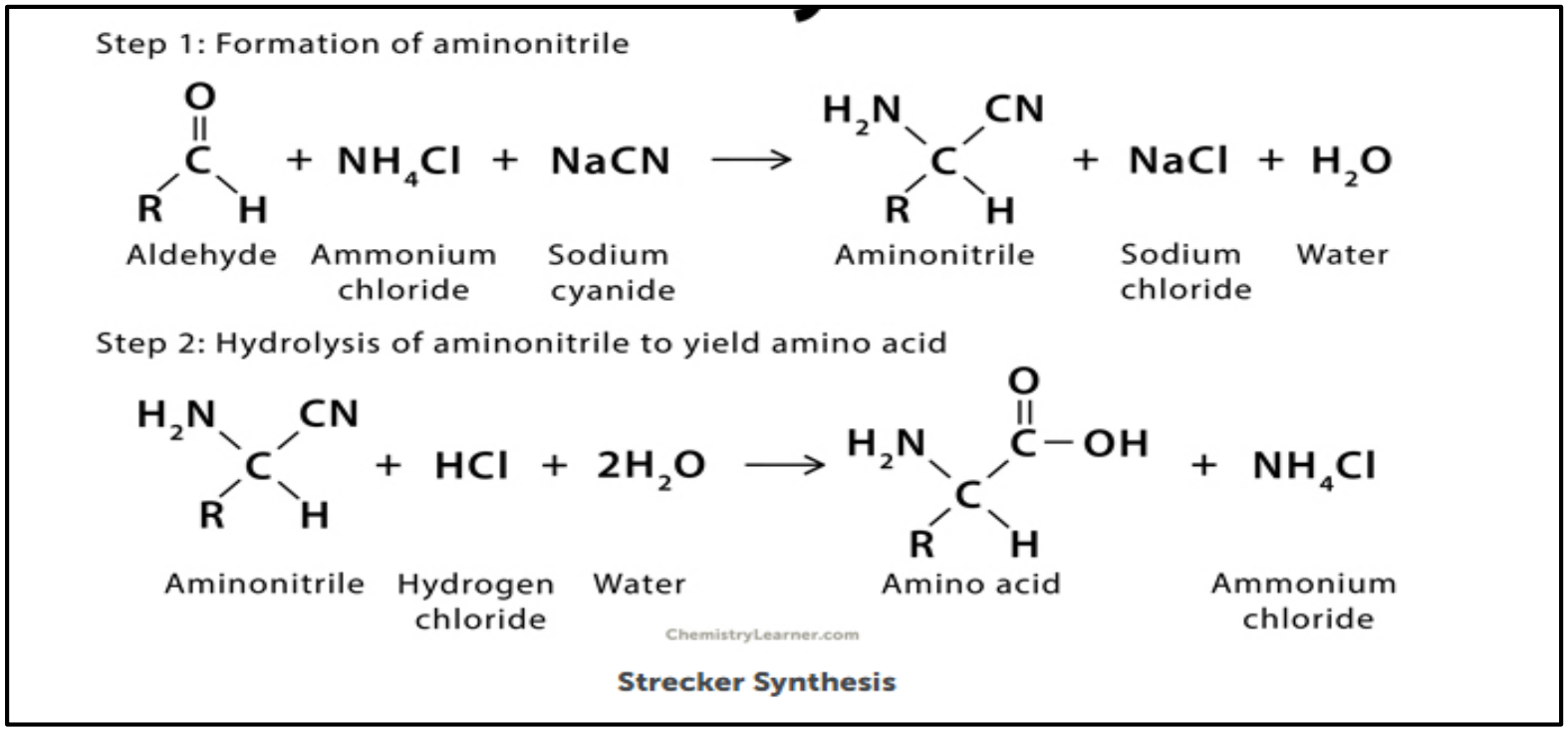
Ninhydrin reaction of AA

- Ninhydrin test is a chemical test performed to detect the presence of ammonia, primary/secondary amines, or **amino acids**. This test involves the addition of ninhydrin reagent to the test sample that results in the formation of deep blue colour in presence of AA. Proline and hydroxy proline gives yellow colour.

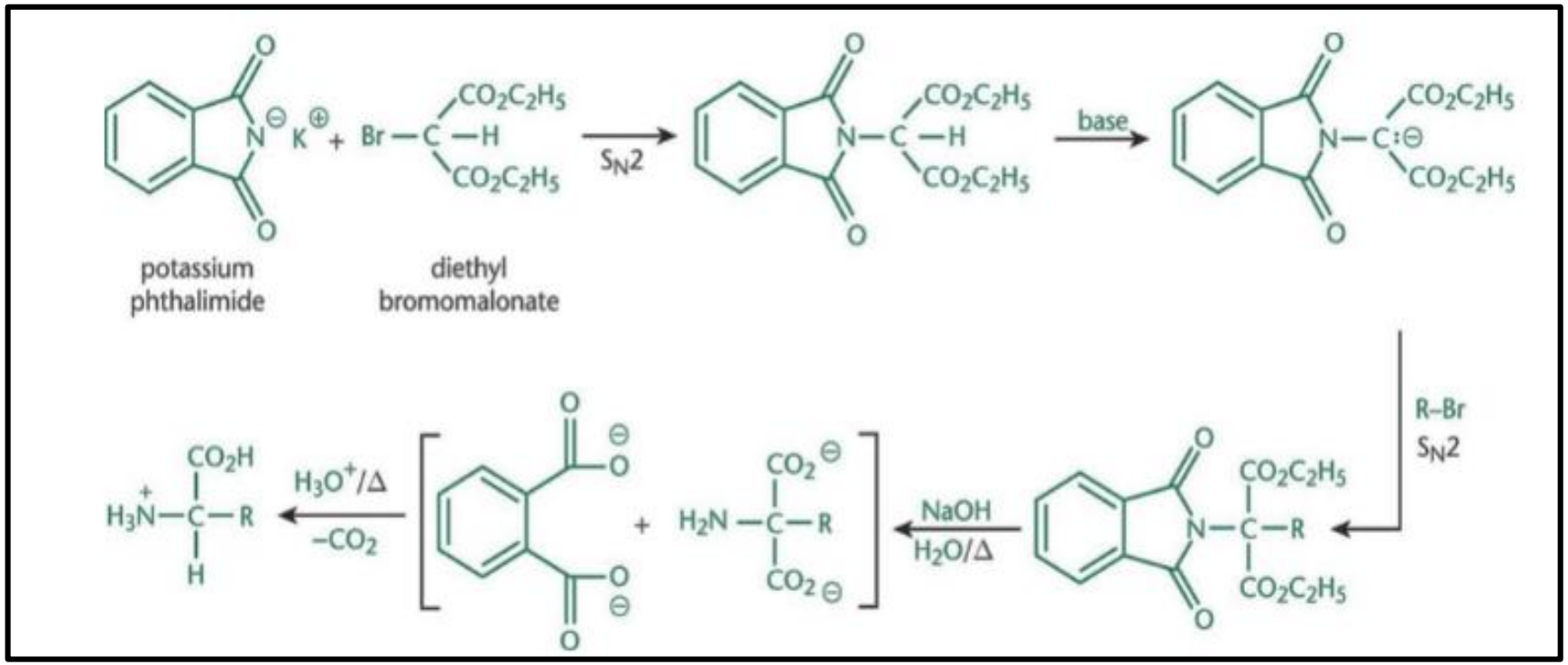


Synthesis of AA

- Strecker synthesis



- Gabriel synthesis



Chemical reactions of amino acid

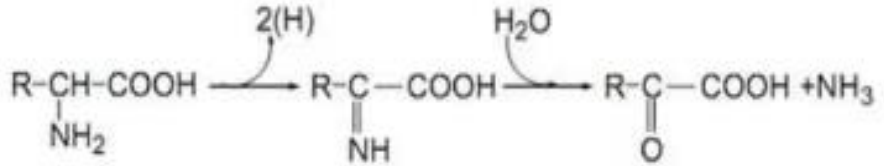
Three types of reactions are possible:-

- Reaction due to $-NH_2$ group
- Reaction due to –COOH group
- Reaction due to both $-NH_2$ and –COOH group

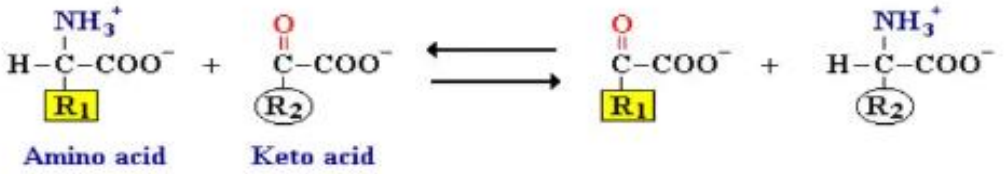
Reaction due to amino group

i) Oxidative deamination-An amino group is removed and corresponding α-keto acid is formed.

α -keto acid produced is either converted to glucose or ketone bodies or is completely oxidized.



ii) Transamination-Transfer of an α amino group from an amino acid to an α keto acid to form a new amino acid and a corresponding keto acid.



Reaction due to –COOH group

i) Decarboxylation- Amino acids undergo alpha decarboxylation to form corresponding amines.

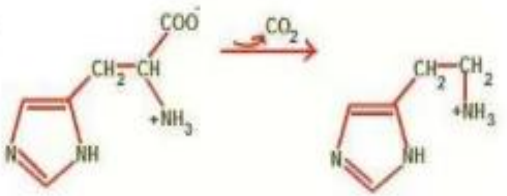
Examples-

Glutamic acid ⟶ GABA

Histidine ⟶ Histamine

Tyrosine ⟶ Tyramine

Histidine Histamine

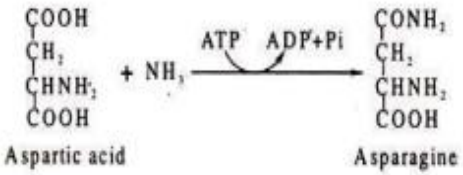


ii) Formation of amide linkage

Non α carboxyl group of an acidic amino acid reacts with ammonia by condensation reaction to form corresponding amides

Aspartic acid ⟶ Asparagine

Glutamic acid ⟶ Glutamine

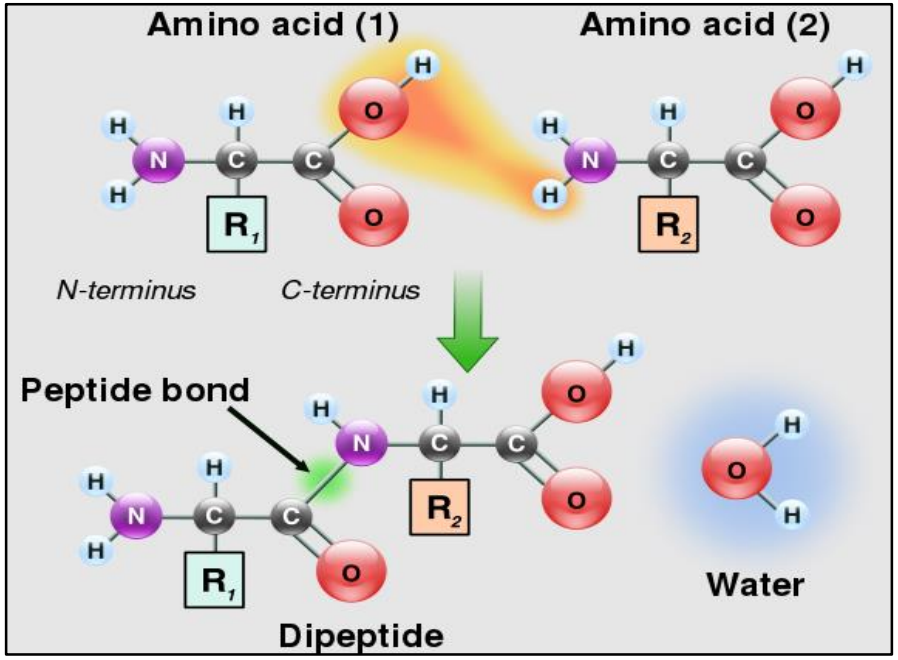


Reaction due to both $–NH_2$ and –COOH groups

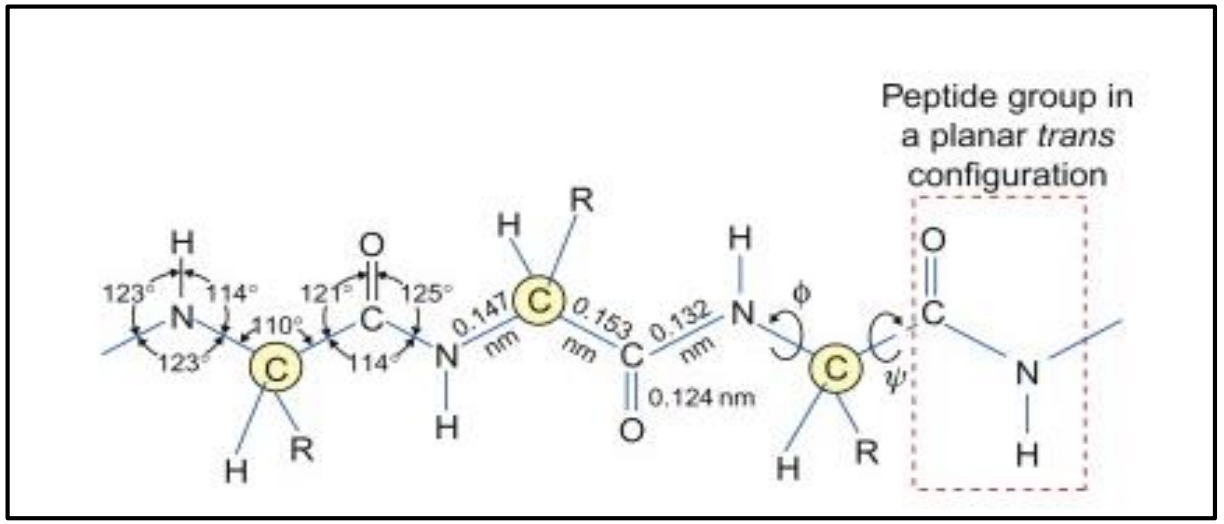
Peptide bond formation (discussed in the next slide)

Peptide

- Amino acids are linked together by amide bond to form peptide. When two AA are combined then it is called dipeptide, when three are combined then tripeptide and so on..
- Polypeptide is a polymer of large number of AA joined together by peptide bonds.



Peptide bonds have a planar, trans configuration and undergo very little rotation or twisting around the amide bond that links the α-amino nitrogen of one amino acid to the carbonyl carbon of the next. This effect is due to amido-imido tautomerization. The partial double-bond character of the N—C bond in the transition state probably best represents what exists in nature. Electrons are shared by the nitrogen and oxygen atoms, and the N—C and C—O bonds are both “one-and-one-half” bonds (intermediate between single and double). The short carbonyl carbon–nitrogen bond length, 0.132 nm (the usual carbon–nitrogen single bond length is 0.147 nm), is consistent with the partial double-bond character of the peptide linkage. The planarity and rigidity of the peptide bond are accounted for by the fact that free rotation cannot occur around double bonds.

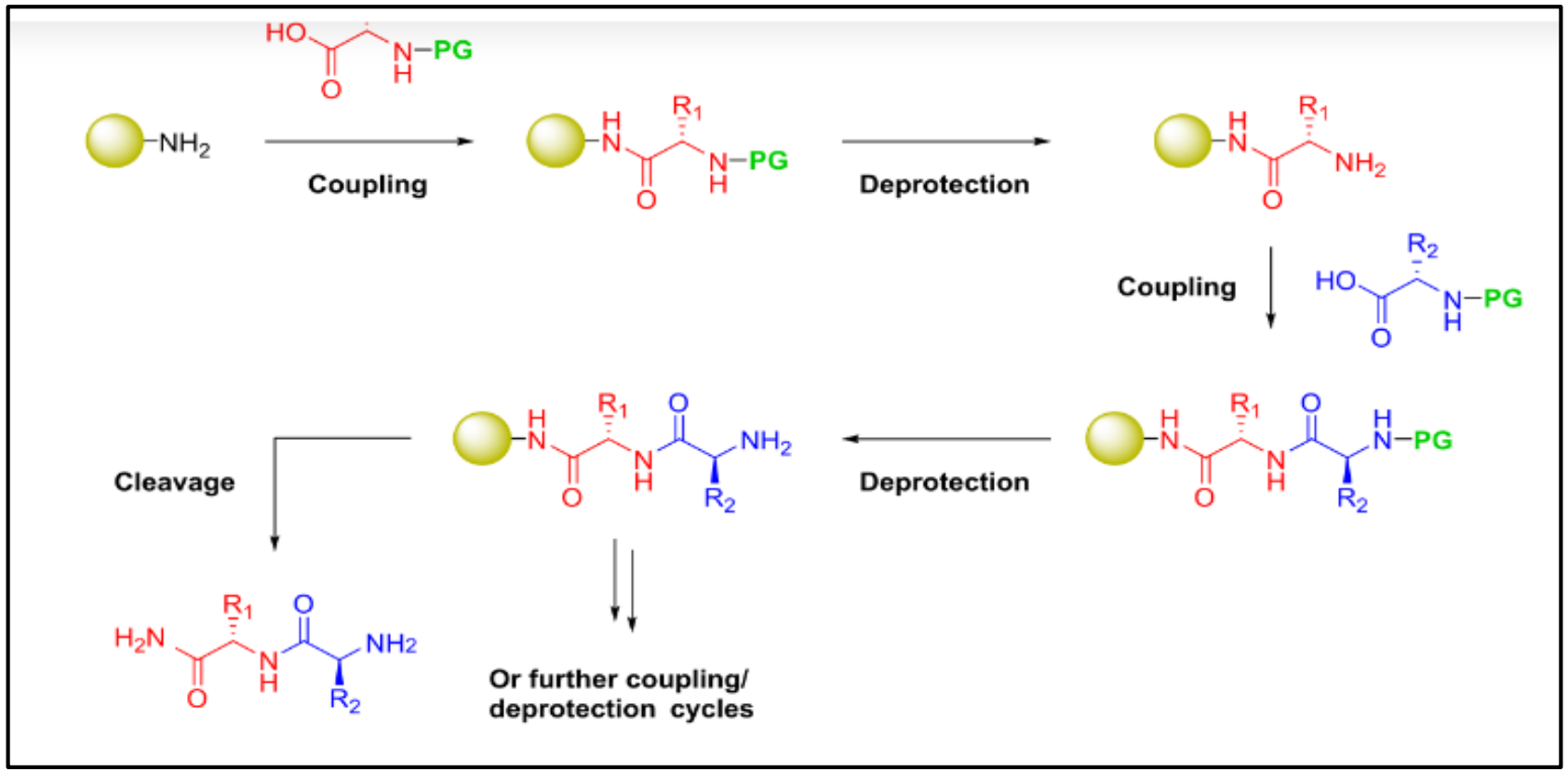


Solid phase peptide synthesis

Solution phase peptide synthesis is typically very arduous and laborious - requiring long coupling reaction time and a need for recrystallization or column chromatography between each amino acid coupling.

After making several analogues of bradykinin (9 amino acids), Bruce Merrifield sought an alternative and began developing methods for solid phase peptide synthesis, efforts for which he later won the Nobel Prize in Chemistry. The beauty of Merrifield's strategy is that chemical reagents can be reacted with a reactive moiety on a solid support, then removed by a simple filtration step, improving the throughput of peptide synthesis.

Schematic diagram of solid phase peptide synthesis

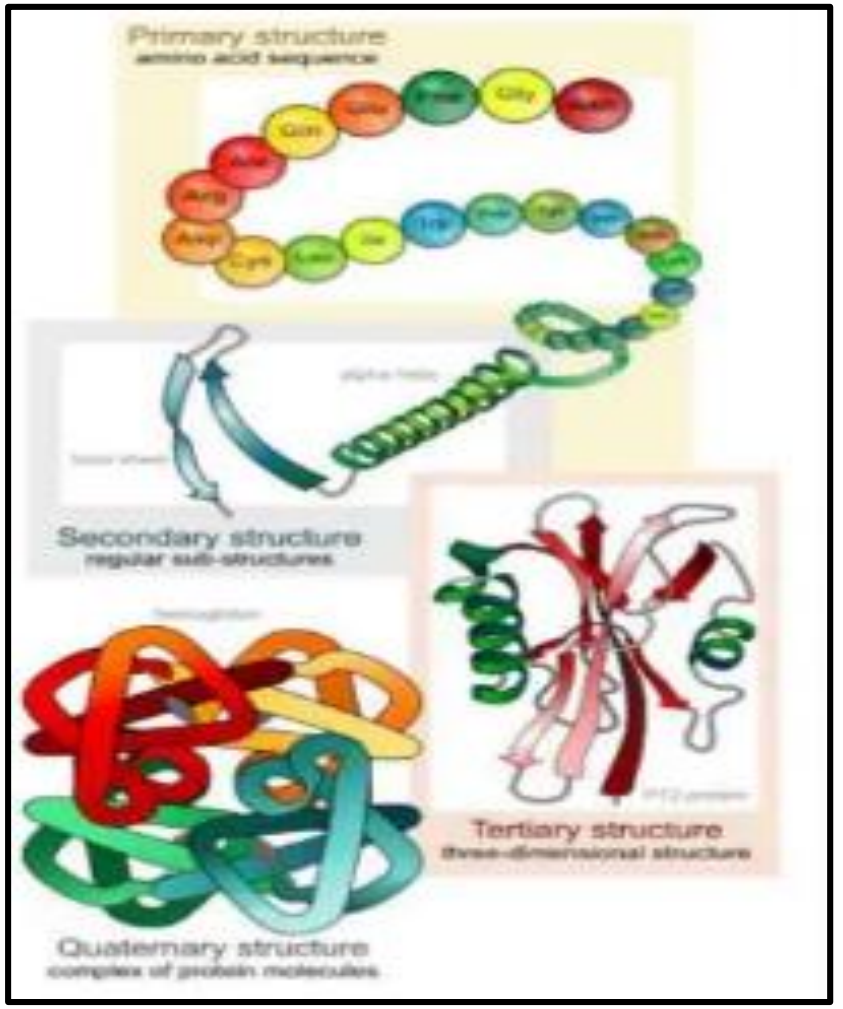


Proteins

Proteins are an important class of biological macromolecules which are the polymers of amino acids.

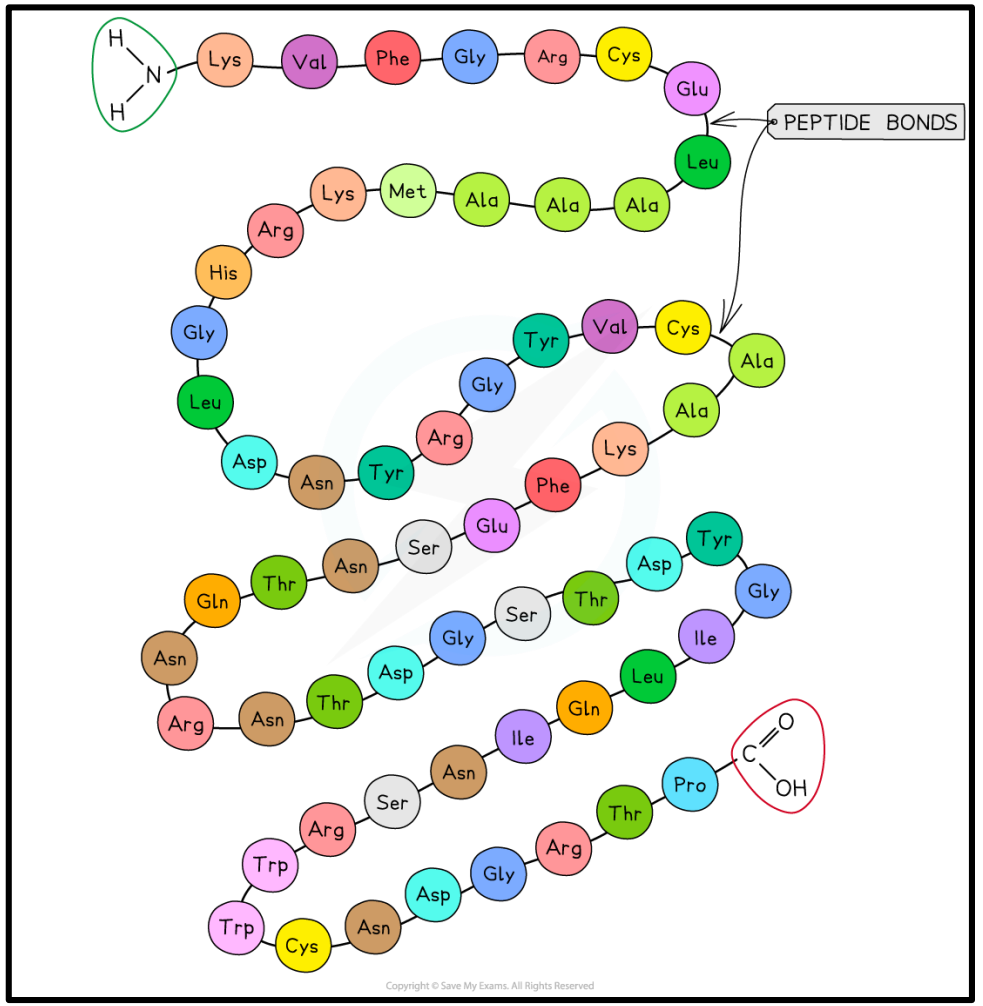
Biochemists have distinguished several levels of structural organization of proteins.

They are:
-Primary structure
-Secondary structure
-Tertiary structure
-Quaternary structure



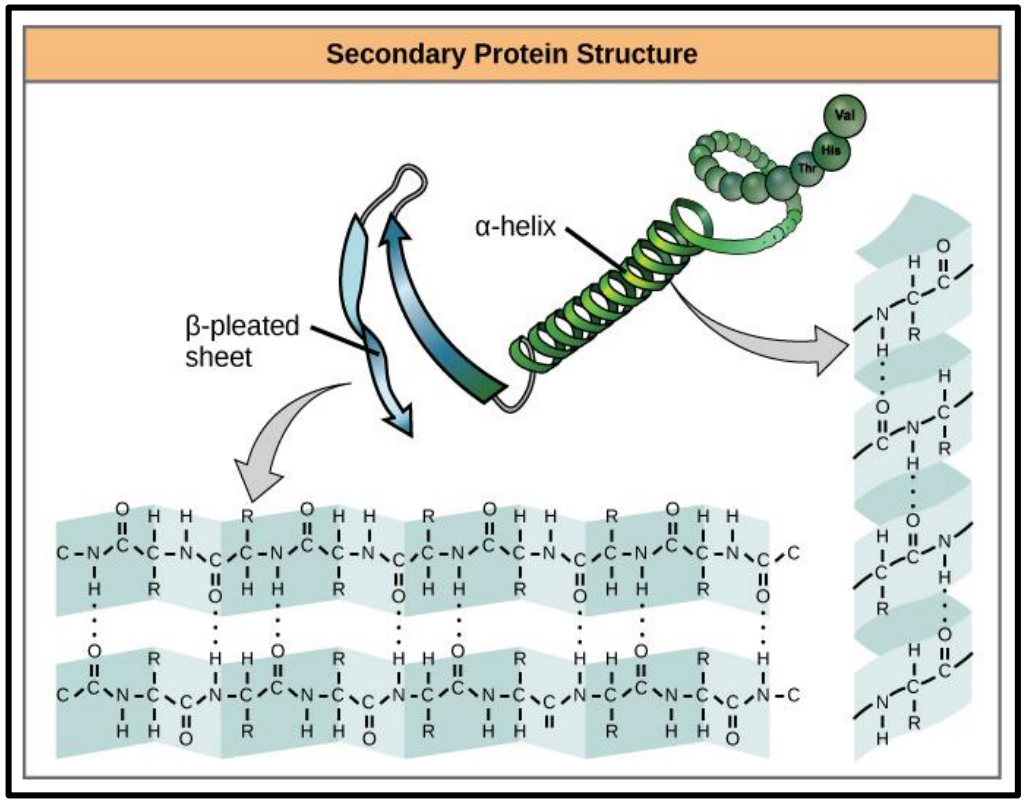
Primary structure

- The primary structure of protein refers to the sequence of AA in the polypeptide chain.
- AA are linked covalently by peptide bonds.
- Each component AA in a polypeptide is called a “ residue”.
- By convention, the 1º structure of a protein starts from the amino terminal end and ends in the carboxylic acid terminal end.



Secondary structure

- Secondary structure refers to the local folded structures that form within a polypeptide due to interactions between atoms of neighbouring AA.
- The most common types of secondary structure are α-helix and β-pleated sheet.
- Both the structures are held in shape by H-bonds which form between carbonyl O of one AA and amino H of another AA.



Tertiary structure

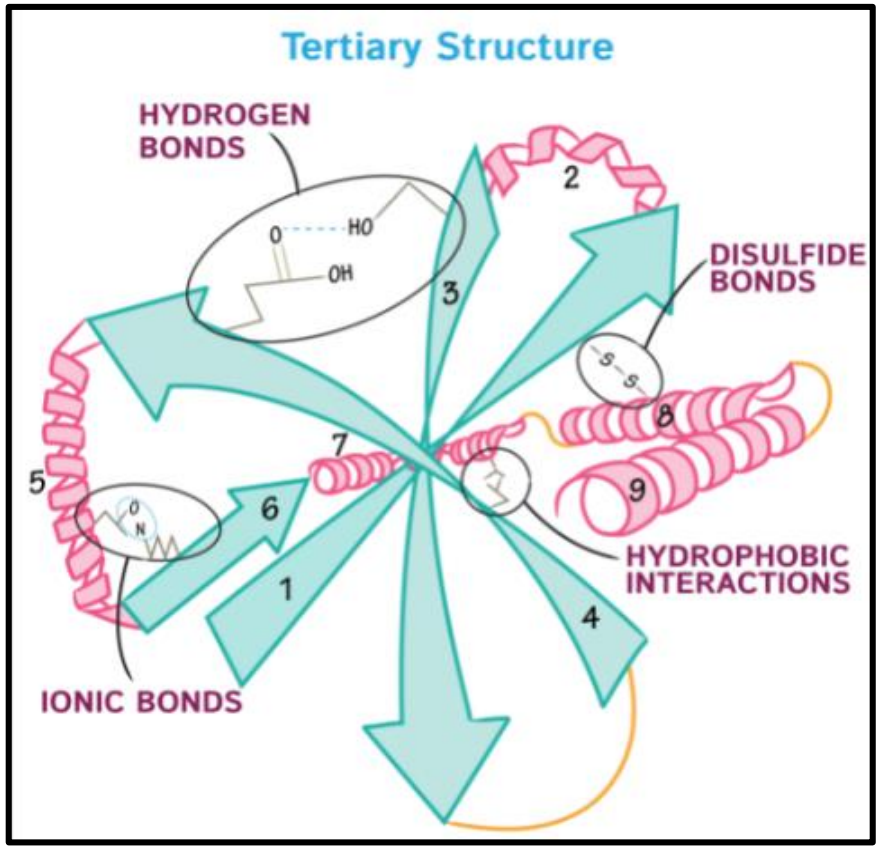
- The overall three-dimensional structure of a polypeptide is called the tertiary structure of a protein.
- Each protein has a unique tertiary structure which determines its function.
- The forces behind tertiary structure are:-

  a) hydrogen bond

  b) ionic interaction between polar groups of side chains

  c) hydrophobic interaction between nonpolar groups of side chains and

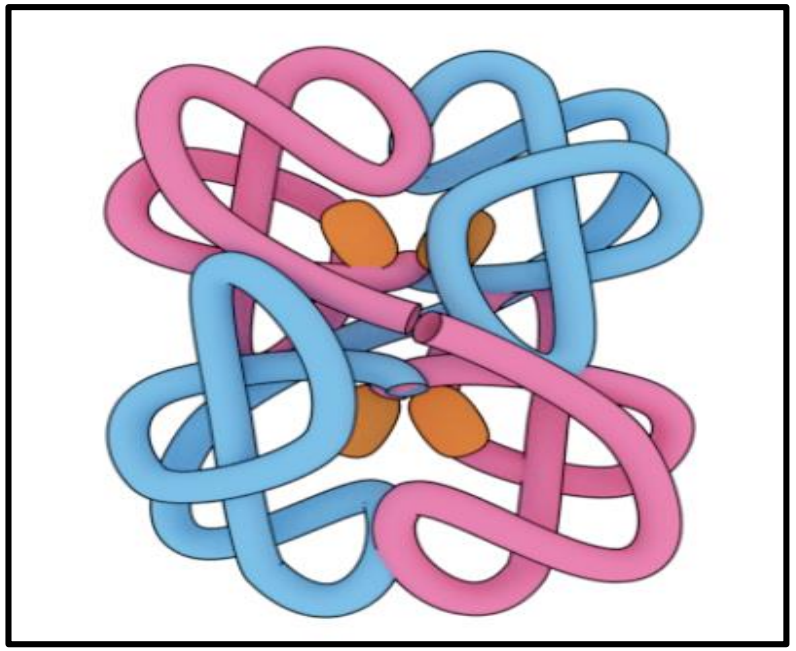
  d) disulphide linkage involving Cysteine residues.



Quaternary structure

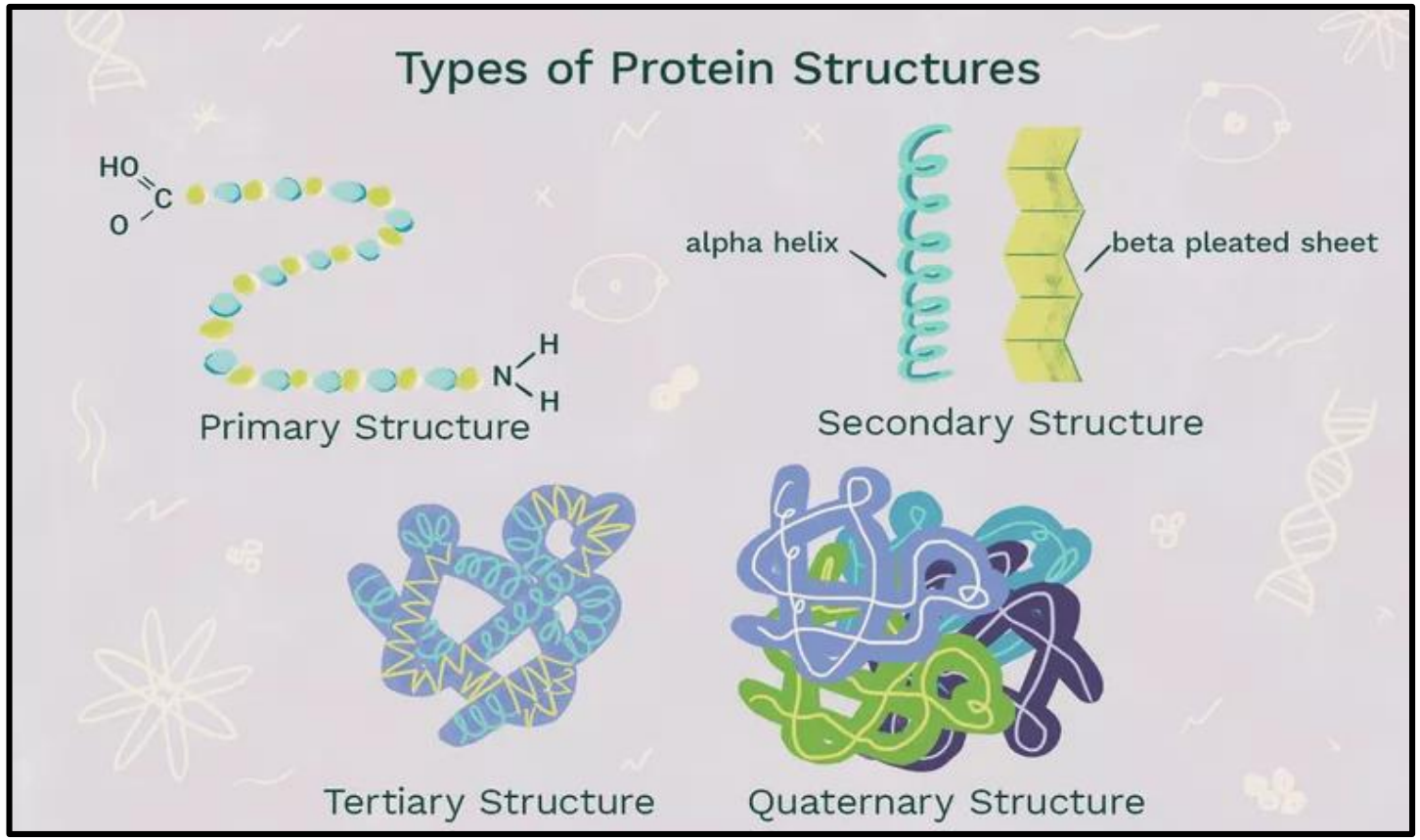
- When a protein contains more than one polypeptide chain, the arrangement of polypeptide chains with respect to one another is quaternary structure.

  Example- Haemoglobin



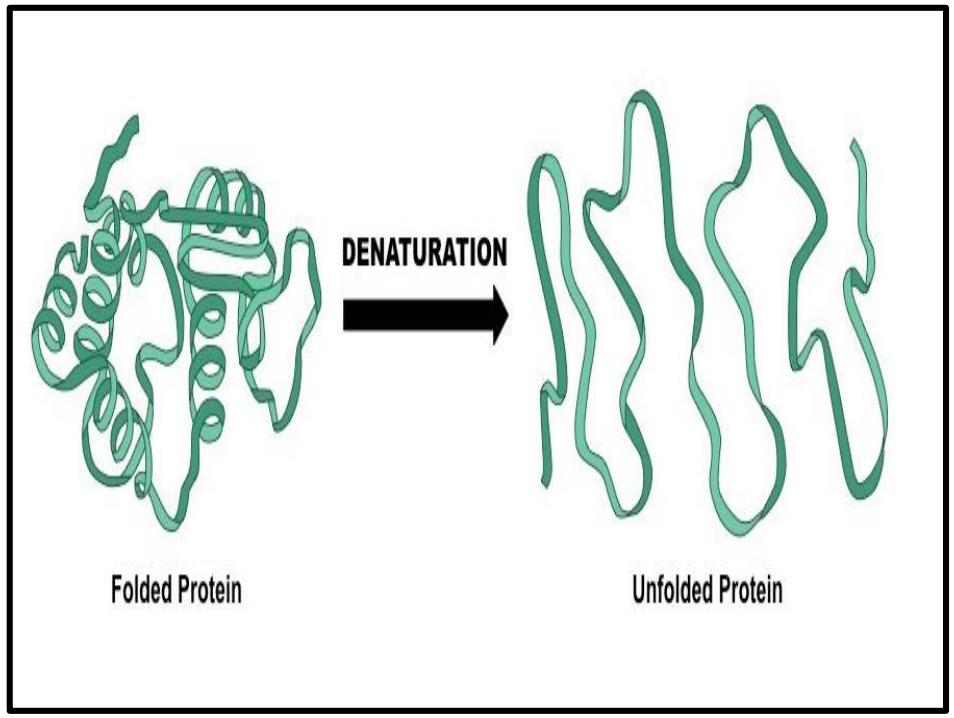
Quaternary structure

Levels of protein structure



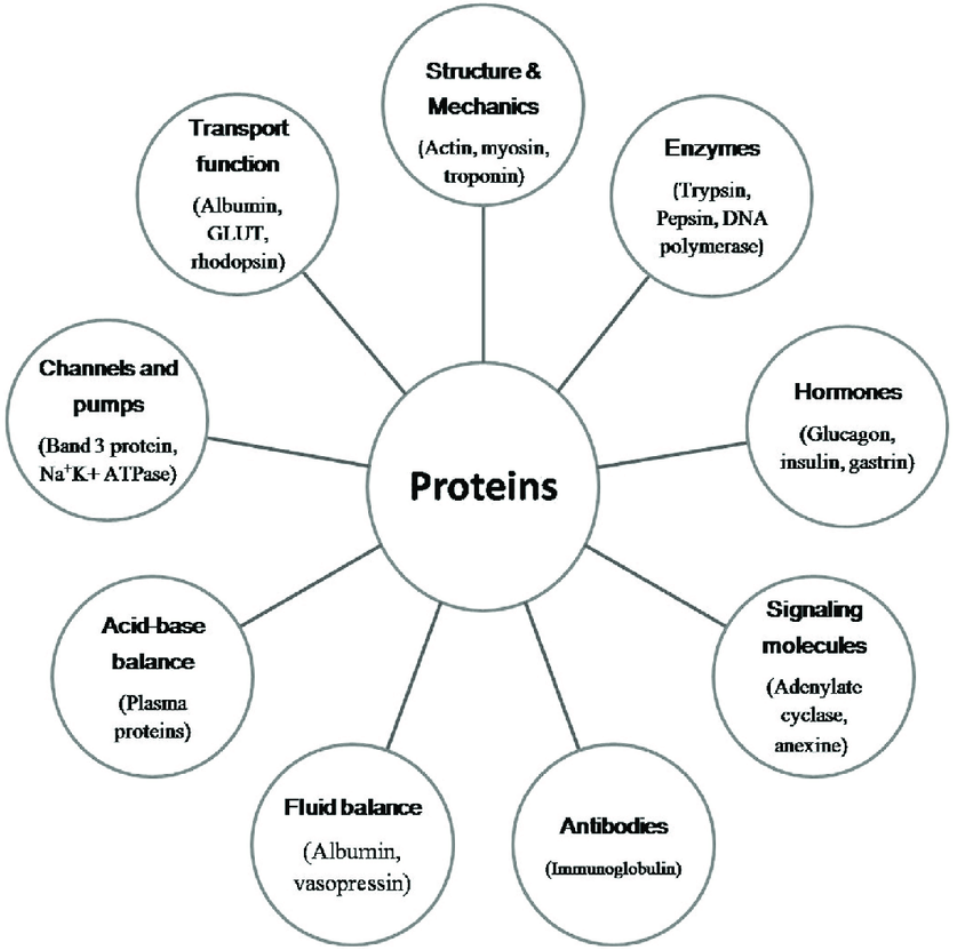
Denaturation and protein folding

- Each protein has its own unique shape. If the temperature or pH of protein's environment is changed, or if the protein is exposed to different chemicals or UV-rays, then the protein loses its three dimensional structure and turn back into an unstructured string of AA.
- When the protein loses its three dimensional structure, but does not lose its primary sequence, then it is said to be denatured.



Function of protein

- Protein is vital in the maintenance of body tissues including development and repair.
- Protein is the major source of energy.
- Protein is involved in the creation of many hormones.
- Protein creates enzymes that increases the rate of a chemical reactions occurring in the body.
- It takes part in the transport process of the living system.



Reference

- Principle of biochemistry by Lehninger
- www. Slideshare.net
- www. google.com