IIT Guwahati

Lecture 1

Course BT 631

Protein Structure, function and Crystallography

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Course BT 631
Protein Structure, function and Crystallography

Course content

- Introduction to protein structure and function; amino acids: building blocks of proteins, peptide bonds, polypeptides and its conformation;
- structural elements of protein structure: primary structure, secondary structure, irregular secondary structure, super secondary structure, motifs, tertiary structure, bonds stabilizing tertiary structure and quaternary structure;
- relation between fold and function: protein taxonomy, divergence and convergence;
- protein crystallography: x-ray diffraction, Bragg's law, crystal geometry, phasing problem, protein crystallization, crystallization techniques, instrumentation for x-ray diffraction; crystal harvesting and mounting; data collection, model building,
- challenges of crystallography; ultra-high resolution protein structures;
- protein database: UniProt database, protein data bank;
- structure and function of keratins, collagens, ATPase, hydrolases, dehydrogenase and protease.

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Protein Structure, function and Crystallography

Text Books/Reference Books:

1. C. Branden and J. Tooze, Introduction to Protein Structure, Garland Science, 1999.
2. D. Whitford, Proteins: Structure and Function, and J. Wiley, 2005.
3. A. Kessel and N. Ben-Tal, Introduction to Proteins: Structure, Function and Motion, 1st Edn., CRC Press, 2010.
4. B. Rupp, Biomolecular Crystallography (Principles, Practice and application to Structural Biology), Garland Science, Taylor and Francis Group, 2010.
5. M. Williamson, How proteins work?, Garland Science, 2011.

Protein

Proteins are the polymer of amino acids linked by the peptide bond and in native state show biological function.

Biological Function of Protein:

The biological function of protein depends on its unique 3-D Structure.

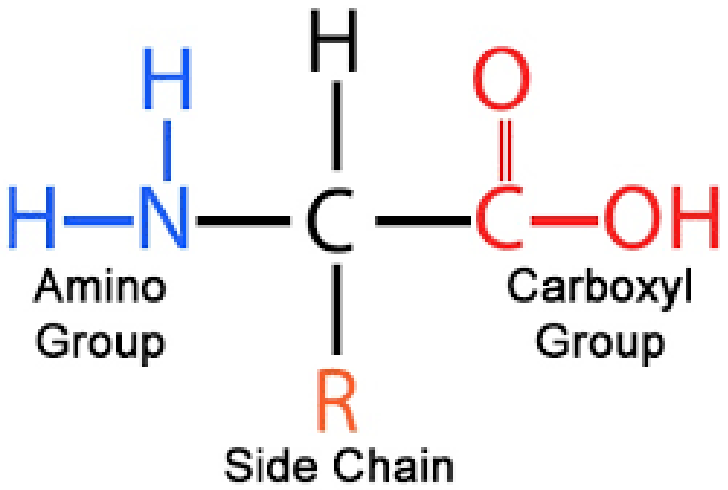
Protein plays a crucial role in all biological processes.

1. **Enzyme Catalysis**
2. **Signaling messenger**
3. **Structural elements of cells/tissues.**

Amino Acids

Amino acids are the bi-functional compounds containing-

- **Amino Group**
- **Carboxyl Group**
- **H-atom**
- **Side Chain (R= Alkyl Group)**



Amino Acids

Amino Acids are the building blocks of protein.

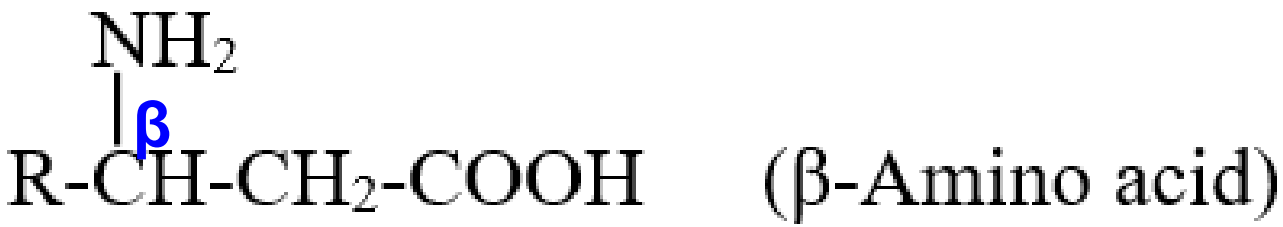
They are:

- **Colorless, crystalline, water soluble substances.**
- **Distinguishing feature is, a -COOH group and a $-NH_2$ group attached to the same carbon.**
- **R group gives individuality.**
- **R group varies from a simple H to a complex phenyl ring.**

Amino Acids

- **Amino acids found in Protein are α-amino acid.**
- **α-amino acid = -NH_2 group attached at α-carbon.**

e.g.



Amino Acids

Nature selects α-amino acid over β-amino acid because β-amino acid provides conditional flexibility to folded structure which is unfavorable.

Q. *Why branched Amino Acid are selected over unbranched amino acid?*

Ans. Because the branched side chain of amino acids provides extra stability to the folded state of the protein.

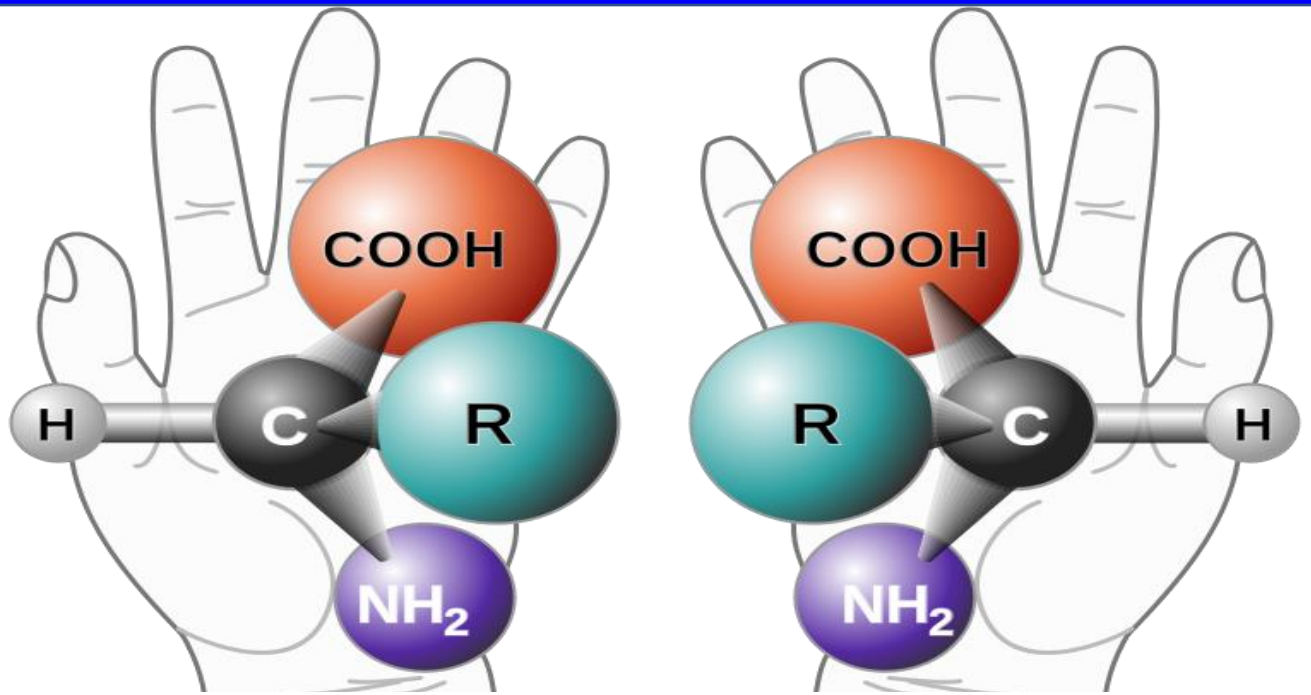
Stereoisomerism

Asymmetric α-Carbon gives rise to chiral center and the presence of two isomers (D and L).

All naturally occurring amino acids are L-amino acid.

D- and L-amino acids have identical properties with two exceptions:

- **They rotate plane polarized light in opposite direction.**
- **They exhibit different reactivity with asymmetric reagent.**



D-Amino Acid L-Amino Acid

Structurally, stereoisomers are defined as non-superimposable chemical isomers that have identical covalent structures.

This is important in protein synthesis as D-amino acids are effective inhibitors.

Stereoisomerism

Amino Acid (AA) Stereoisomers

All standard AAs have an asymmetric or chiral α-carbon, except for one AA.

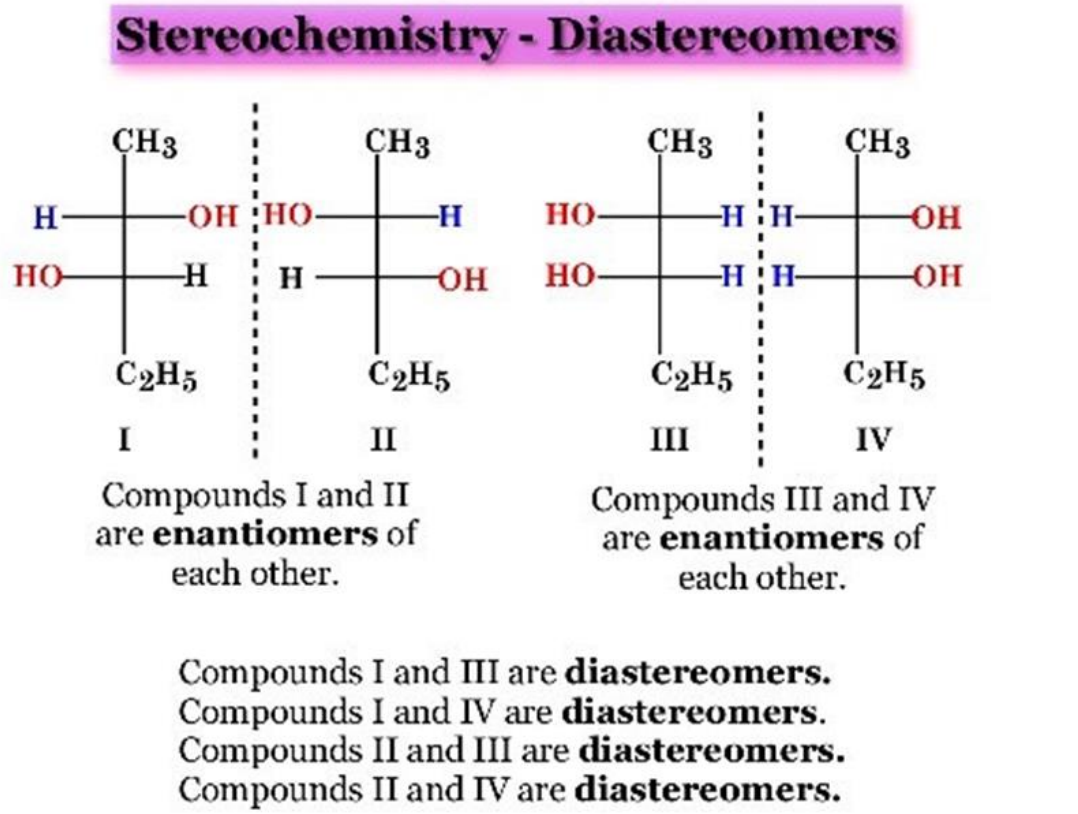
Thus, stereochemical isomers exist for all but one of the standard amino acids.

There are 2 classes of stereoisomers:

Enantiomers and Diastereoisomers.

a) Enantiomers are *mirror image* chemical isomers.

b) Diastereoisomers are *non-mirror image* chemical isomers.

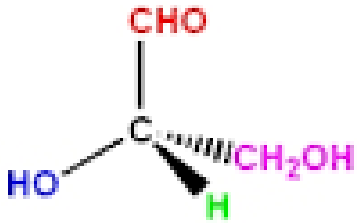


Amino Acids

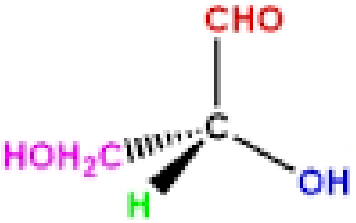
The convention used to define the Cα carbon stereochemistry of amino acids is based on the mirror image enantiomers of glyceraldehyde, which is a three carbon structure having a central chiral carbon. The two enantiomers of glyceraldehyde are designated "D" and "L" by reference to their unique optical activities.

When a plane-polarized light beam passes through a pure solution of D-glyceraldehyde the emergent beam will be rotated the light plane to the right, and hence is the enantiomer is considered to be dextrorotatory ("dextra" is Latin for right) and is designated the "D" enantiomer.

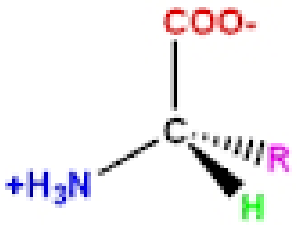
However, if beam of plane polarized light passes through a pure solution of L-glyceraldehyde, the emergent light beam will be rotated in the opposite direction to the left, and hence the enantiomer is considered to be levorotatory (laevus is Latin for left) and is designated the "L" enantiomer.



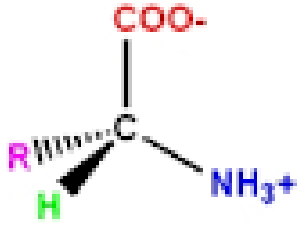
L-Glyceraldehyde



D-Glyceraldehyde



L-Amino acid



D-Amino acid