Biochemistry of amino acids, proteins structure and function-I&II

year 1 med-students 2025/2026 (CBF-103)
(3&6)

by
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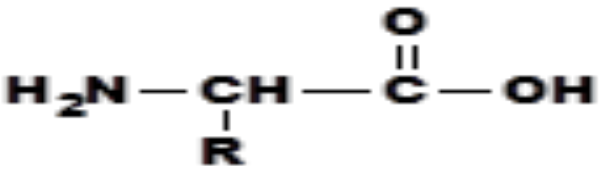
Objectives

- Illustrate amino acid structure
- Describe different classifications of amino acids
- Describe structural organization of proteins. Discuss with examples protein folding/Misfolding
- Define proteins of high and low biological value Discuss examples of medically and structurally important proteins
- List functions of proteins

- Amino acids are the building units (blocks /RESIDUES) of proteins
- **Definition of amino acids:**
  - Amino acids are organic acids that contain NH_2 group. They are the structural units of proteins and are obtained from them by hydrolysis. The general formula of any amino acid is as follows:



20 amino acids are occurring in human body differ from each other by the R-groups

All these amino acids are alpha-amino acids. This means that the amino group is attached to the α-carbon atom (next to the carboxyl group).

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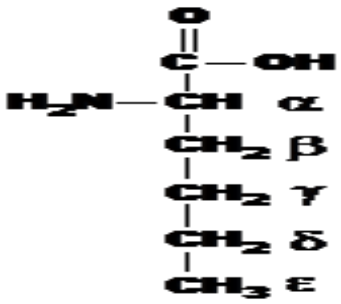


• The metabolizable form of them are **L-amino acids** (amino group is on the left side configuration). All amino acids present in mammals are L-amino acids.

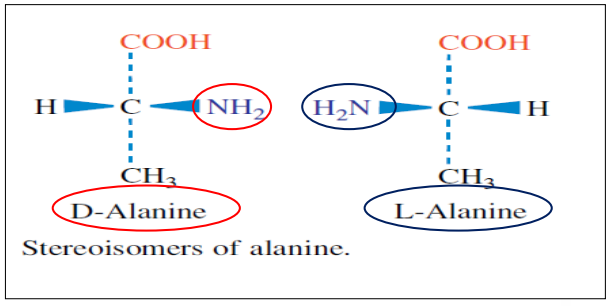
• D-amino acids are found in the cell walls of bacteria.

• All of the 20 amino acids are of the **L- α amino acid**.

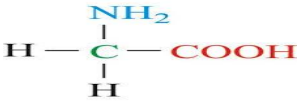
• Except

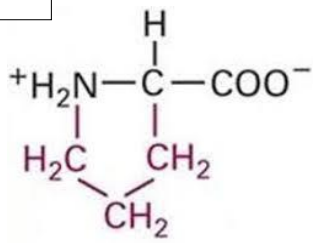
• **Glycine**, because glycine does not contain an asymmetric carbon atom, it is not optically active, and thus, it is neither D nor L.

• **Proline**, in which the nitrogen is part of a ring, is an imino acid.



Stereoisomers of alanine.





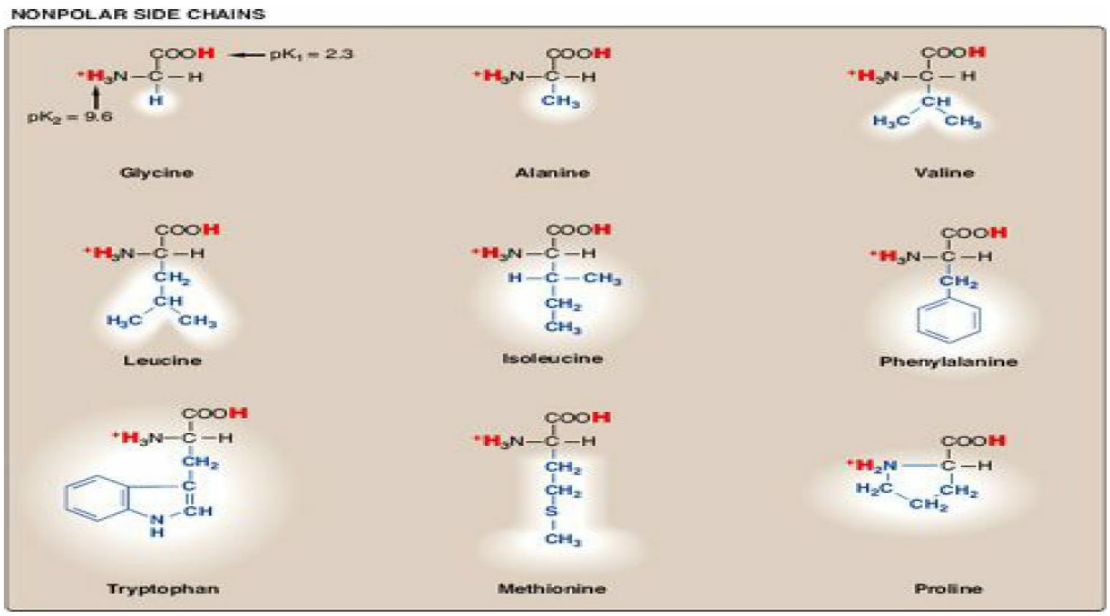
Classification of amino acids

I-Chemical classification:

- Based on the solubility and ionization of the amino acid in aquas solution at physiological pH (7.4) as determined by the side chains (R-groups)

A. NON-Polar (hydrophobic)

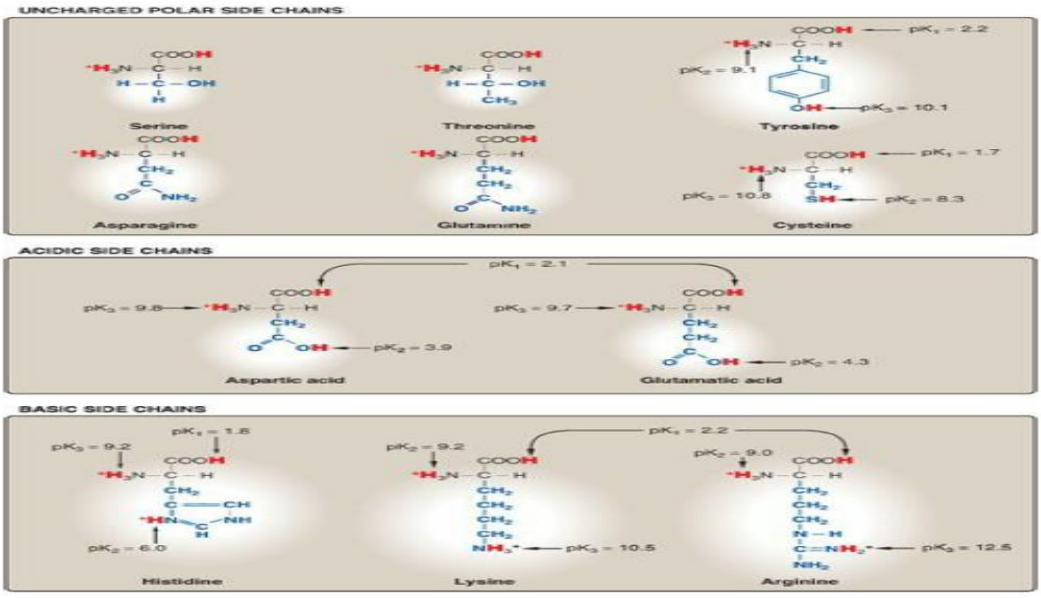
- Amino acids that do not prefer functioning in an aqueous environment-neutral
- Hydrophobic amino acids have side chains that contain Hydrocarbon or alkyl side chain (aliphatic side chain) SUCH AS glycine, alanine, branched chain amino acids (valine, leucine, and isoleucine), and proline
- Aromatic side chain (phenylalanine, and tryptophan)
- Methionine, it has sulphur group but its end is CH3.
- In general, proteins fold so that amino acids with hydrophobic side chains are in the interior of the molecule



B. Hydrophilic (polar)

Amino acids that prefer to function an aquas environment

1. **Polar neutral (un-charged).** Serine , threonine,(OH) cysteine (SH), asparagine and glutamine (carboxy-amide group)
2. **Polar negatively charged (acidic):** it includes glutamic and aspartic amino acids
3. **Polar positively charged (basic):** it includes lysine, arginine and histidine amino acids
4. In general, proteins fold so that amino acids with hydrophilic side chains are in the surface of the molecule



II. Biological classification:

1 Essential (indispensable), can not be synthesized in the human body and must be supplied in the diet. The deficiency of any of these amino acids leads to disturbed health and growth.

8-10 essential amino acids

VITTAL LyMPH

V= VALINE	I= ISOLEUCINE
T= THERIONINE	T= TRYPTOPHAN
A= ARGININE	L= LEUCINE
Ly= LYSINE	M= METHIONINE
P=PHENYLE ALANINE	H= HISTIDINE

A, H, are semi-essential, under increased body demands (Positive nitrogen balance), as in pregnancy , lactation, disease , and growth.

Also tyrosine and cysteine become essential under low supply from P .alanine and methionine respectively

2. Non essential (dispensable): can be synthesized in the human body and must NOT be supplied in the diet.

III. Metabolic classification:

- Depends on the catabolic fate of the carbon skeleton of the amino acid inside the human body.

1. **Ketogenic amino acids:**
   - They give rise to acetate or acetoacetate on catabolism.
   - Two amino acids **lysine and leucine** are purely ketogenic in nature
2. **Glucogenic amino acids:**
   - converted into glucose
   - they give inter mediates of glycolysis or kerbs cycle
   - (pyruvate, oxaloacetate, a-ketoglutarate, propionate), can be converted into glucose.
   - 14 amino acids are pure glucogenic
3. **Mixed amino acids:**
   - Can be converted into glucose precursors or acetate on catabolism.
   - **Isoleucine , phenyl alanine , tyrosine and tryptophan**

Nitrogen Balance

Nitrogen Balance (Equilibrium)

- Nitrogen balance is the (normal) condition in which the amount of nitrogen incorporated into the body each day exactly equals the amount excreted.
- Normal healthy adults

Negative nitrogen balance

- when nitrogen loss exceeds incorporation.
- It is associated with:
  - Protein malnutrition (kwashiorkor)
  - Dietary deficiency of even 1 essential amino acid
  - Starvation
  - Uncontrolled diabetes
  - Infection

Positive nitrogen balance

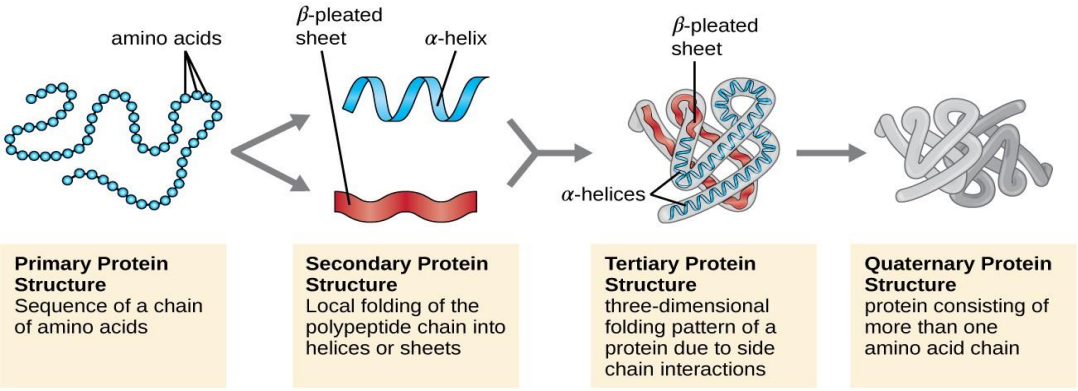
- when the amount of nitrogen incorporated exceeds the amount excreted.
- It is associated with:
- Growth
- Pregnancy AND lactating women
- Convalescence (recovery phase of injury or surgery)
- Recovery from condition associated with negative nitrogen balance

Biological value of proteins

- Depends on their digestibility and amino acid composition
- **High biological value (class I protein) are**
  - digestible
  - contain all essential amino acid
  - in balanced form
  - proteins of animal origin (red, white meat, fishes, liver, dairy products and eggs) and some plant origin like lentils
- **Low biological value (Class II proteins) they are**
  - indigestible
  - low content of essential amino acids
  - Imbalanced content of essential amino acids
  - proteins of plant origin
- **Mixed low** biological value proteins can complement each other making high biological proteins, (lentils and rice).

Protein structure

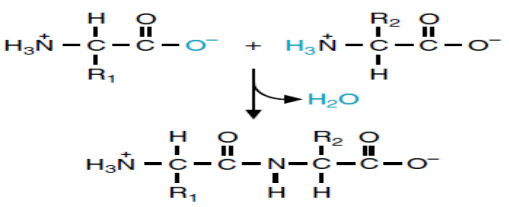
- The protein structure and function are defined based on the four levels of structures: primary, secondary, tertiary, and quaternary.

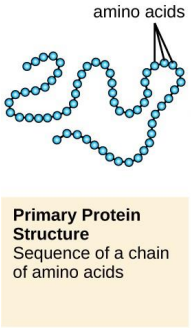


Figurs are nice to know

The primary protein structure

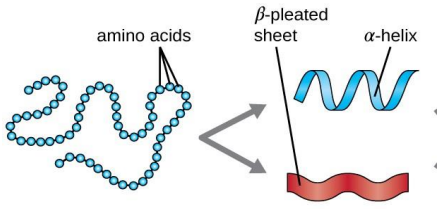
- The primary protein structure is the **linear sequence of amino acids** held together by peptide bond making a polypeptide chain.
- Amino acid sequence is determined by the genetic code of the protein
- Amino acid polymerization requires the carboxyl group of one amino acid to react with the amino group of another (subsequent) amino acid to form a covalent amide bond. **PEPTIDE BONDS**





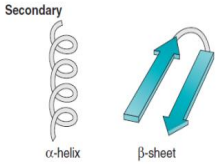
Secondary Protein Structure.

- **Secondary structure** describes the local regular **arrangement of nearby amino acids** of the polypeptide CHAIN
- The TWISTING of the polypeptide into its secondary structure is
  - determined by the primary structure,
  - maintained by repetitive hydrogen bonding between the peptide bonds
  - side chains are not involved.
- Common forms of secondary structure:
  - α-helix
  - β-pleated sheet (also known as β-structures and β-sheet),



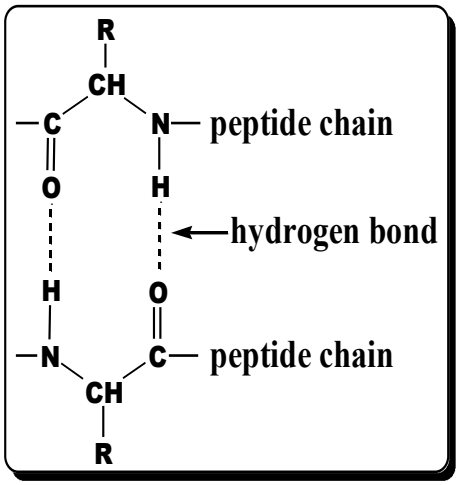
Primary Protein Structure
Sequence of a chain of amino acids

Secondary Protein Structure
Local folding of the polypeptide chain into helices or sheets



Hydrogen bonds:

- Hydrogen bond is a weak bond formed between the hydrogen atom of –NH of a peptide bond on one peptide chain and the oxygen of C=O of another peptide bond on an adjacent peptide chain or a loop belongs to same peptide chain.



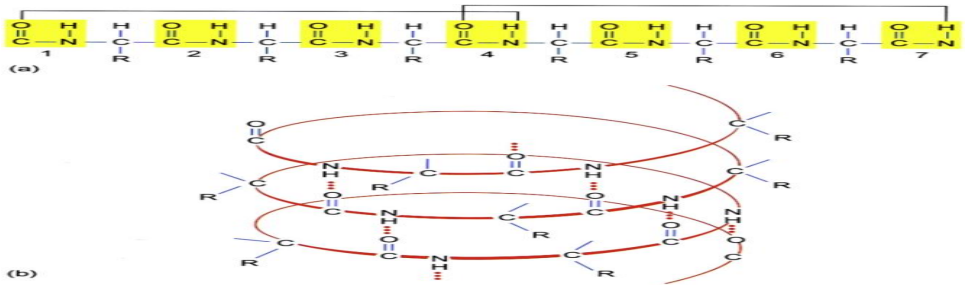
α-Helix

The most common secondary protein structures

- It is a spiral tightly packed polypeptide chain forming a helix shaped structure
- the side chains of the component amino acids extending outward from the central axis
- The helical structure is stabilized by **intra-chain hydrogen** bonds involving each a NH and a CO group of every 4th peptide bond so that each turn of an α-helix contains 3.6 amino acids.
- The hydrogen bonds extend up and are parallel to the helix

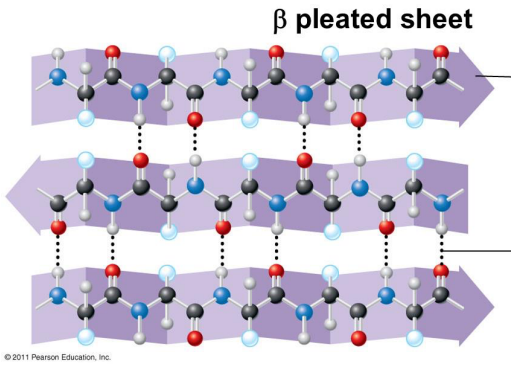
•Charges and Bulkiness of adjacent R groups Pro or Gly reduce the stability of a- helix

- α-helices is a common secondary structure in α-keratin, myoglobin, and hemoglobin
- It is absent in collagen and elastin



β-Pleated Sheet

- The β-structure has the amino acids in an extended conformation
- Between separate peptide chains or between segments of the same peptide chain.
- The structure is stabilized by **hydrogen bonds** between the a NH and a CO groups of adjacent polypeptide chains **(Inter -chain**).
- Hydrogen bonds are perpendicular to the polypeptide backbone in β-sheets
- Some amino acid residues such as glycine and alanine promote the formation of β-pleated sheets.



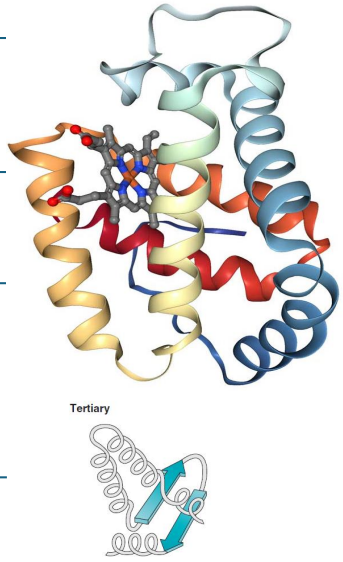
Tertiary protein structure

Tertiary structure is formed by combinations of secondary structural elements into a **three-dimensional organization** known as the **native** conformation

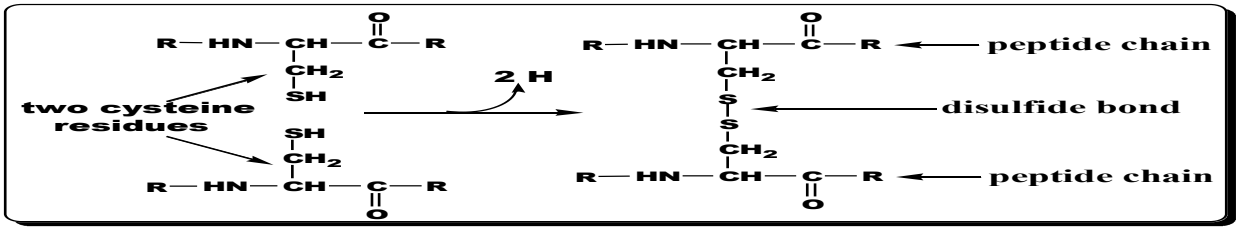
The **function** of a protein depends on its tertiary structure. If this is disrupted, it loses its activity.

Molecular chaperones مرافق (are defined as proteins that assists in the folding, assembly and conformational maintenance other proteins without becoming part of its final structure) bind reversibly to unfolded polypeptide segments and prevent their misfolding and premature aggregation such as heat-shock proteins (HSP).

IT is mainly stabilized by noncovalent interactions of the side chains

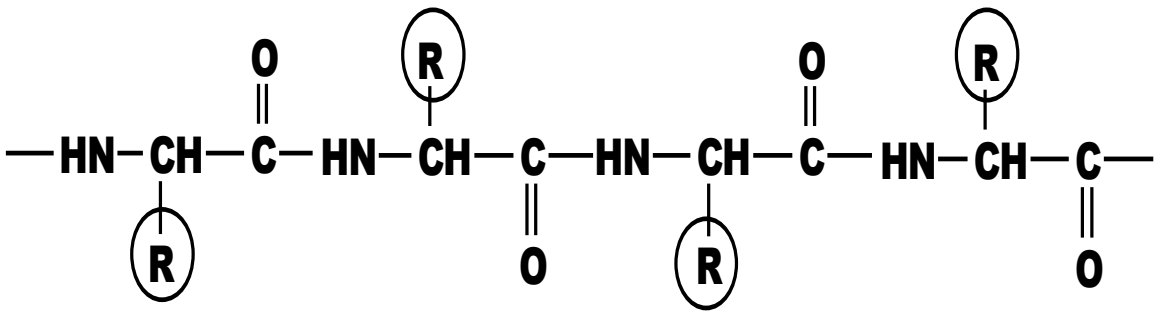


- Non-covalent interactions between amino acid residues produce the three dimensional shape of a protein and include
  - hydrophobic interactions,
  - electrostatic (ionic) interactions,
  - hydrogen bonds between side chain
- Also Covalent disulfide bonds also occur in tertiary structure.



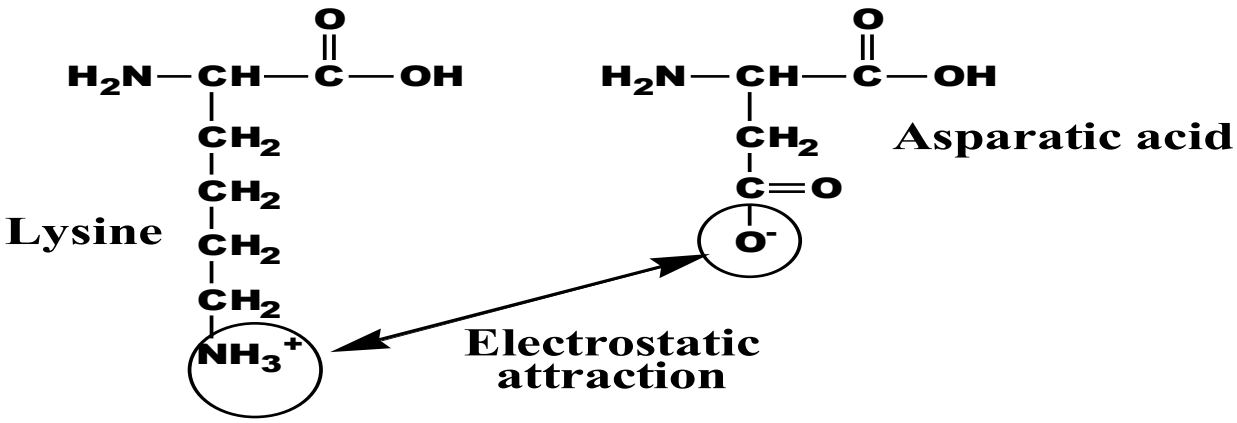
Hydrophobic bonds:

- The non polar side chains of neutral amino acids tend to associate in hidden core of protein molecule away from solvent.

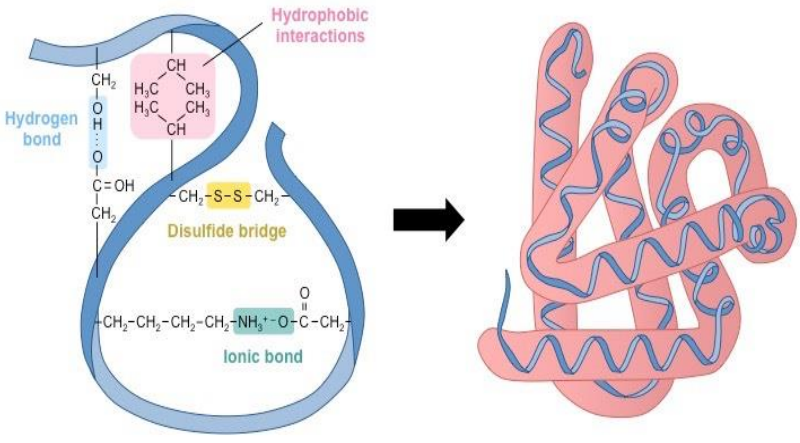


Electrostatic bonds:

- These are salt bonds formed between oppositely charged groups in the side chains of amino acids e.g. ε-amino group of lysine and the carboxyl group of asparatic acid.



Tertiary protein structure

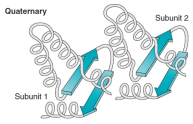


Types of side chain interactions

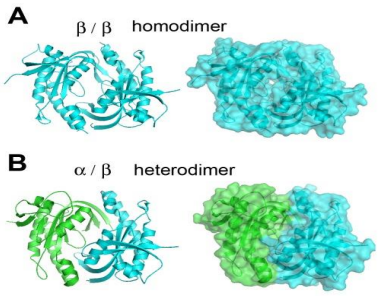
Overall 3D shape (3° Structure)

Quaternary protein structure:

Quaternary structure refers to the spatial arrangement of two or more polypeptide chains, **oligomeric** proteins (a molecule that consists of a few repeating units) .

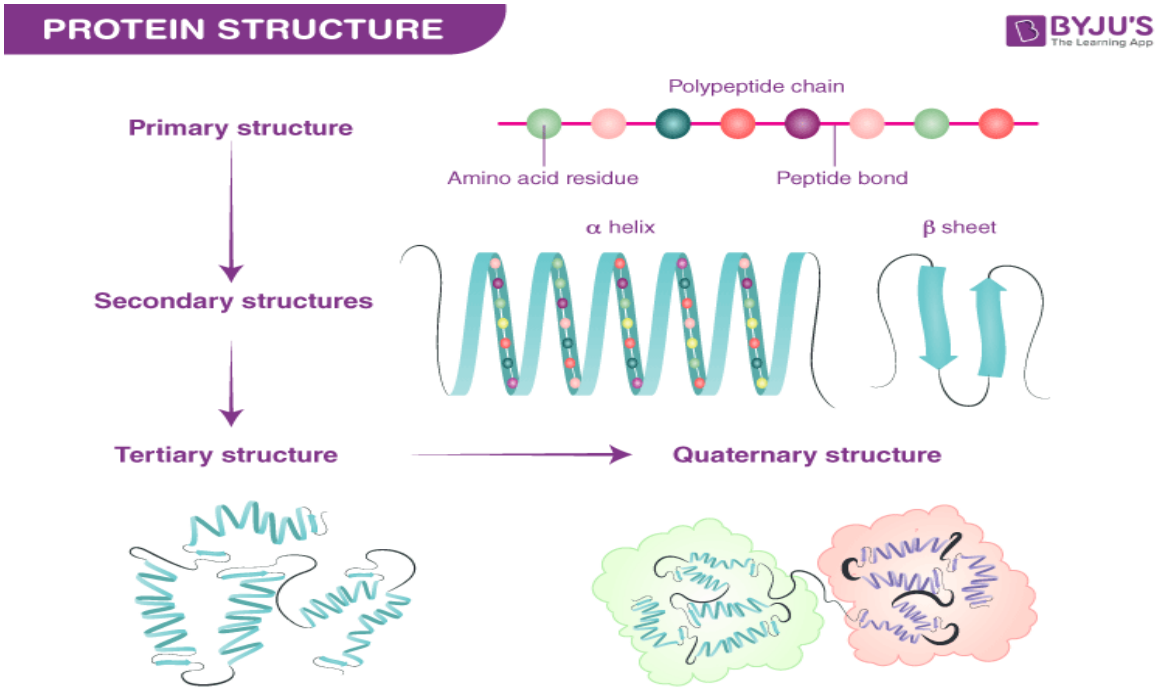


- Homo-oligomers (made up of a number of identical subunits),
- Hetero-oligomers (made up of different subunits).



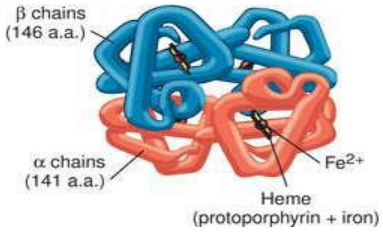
The subunits are joined together by the same types of noncovalent interactions as tertiary structure

- Subunits may either function independently of each other
- or may work cooperatively, as in **haemoglobin**, in which the binding of oxygen to one subunit of the tetramer increases the affinity of the other subunits for oxygen



Haemoglobin

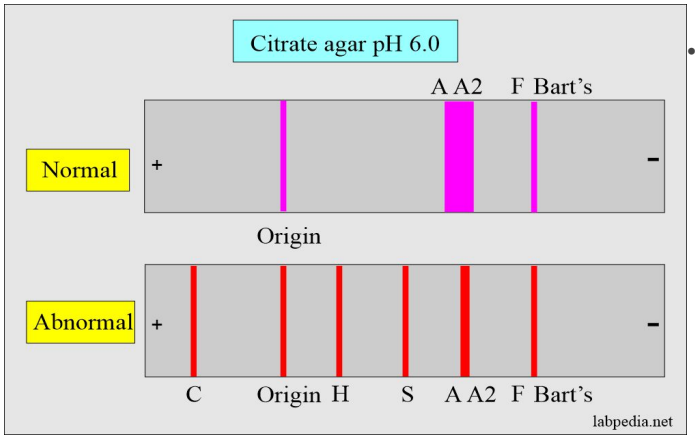
- Haemoglobin is a molecule composed of heme group (iron holding) and protein called globin participating in oxygen transport necessary for human life
- Adult haemoglobin (HbA1) consists of **four** polypeptide chains (two **α** and two **β** chains), so it has a **quaternary** protein form.
- **α chain has 141 amino acids, β chain has 148 amino acids**
- Eight **α** -helices occur in each chain.
- The **α** and β of HbA are similar in 3-D configuration to each other and to the single chain of muscle myoglobin.
- **α** and two β bind oxygen cooperatively



Haemoglobin S

- One common mutation results in **sickle cell anemia,** in which the beta chain of hemoglobin contains a valine rather than a glutamate at position 6.
- This change allows deoxygenated molecules of HbS to polymerize and occlude blood vessels.
- The mutant haemoglobin (HbS), a hydrophobic amino acid replaces an amino acid with a negative charge.
- Meaning that the HbS will have one less negative charge overall compared with HbA
- These 2 hemoglobins can be resolved by electrophoresis.

Hemoglobin electrophoresis



- A hemoglobin electrophoresis test applies an electric current to a blood sample. This separates the normal and abnormal types of hemoglobin. Each type of hemoglobin can then be measured individually and compared with the normal level.

Protein degradation

Normally folded protein that **finished** its function and reached its half life / or protein that are **misfolded** should be eliminated from the cells. Or protein that are misfolded .

Proteins from the intracellular environment may be targeted for degradation by the **ubiquitin–proteasomal pathway.**

Ubiquitin a compound found in living cells which plays a role in the degradation It is a single-chain polypeptide.

Autophagy: The ultimate degradation occurs via cleavage by lysosomal acid hydrolases.

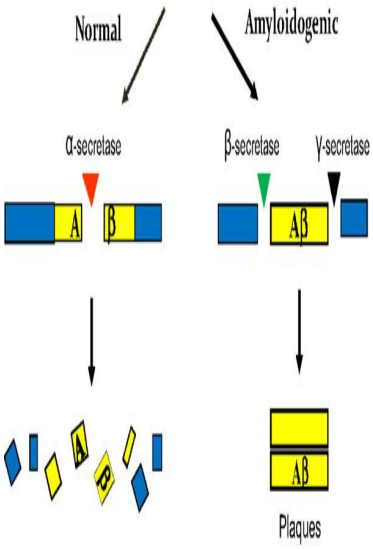
Autophagy is your body's cellular recycling system. It allows a cell to disassemble its junk parts into new, usable cell parts

Protein misfolding

- **Protein exposed to:**
  - Environmental toxins
  - Infectious agents
  - Translation errors and genetic mutations
- **Misfolded proteins are highly deleterious to the cell because**
  - They can form non-physiological interactions with other proteins
  - Can be targeted to inappropriate cellular locations
  - Can be resistant to proteolysis and form aggregates, such as amyloid plaques
- **Amyloidosis:** is accumulation of misfolded proteins that cannot be removed by ubiquitination or autophagy in the form of b-pleated fibrils (amyloid) both intra/ extracellularly leads to tissue degeneration.

Protein misfolding

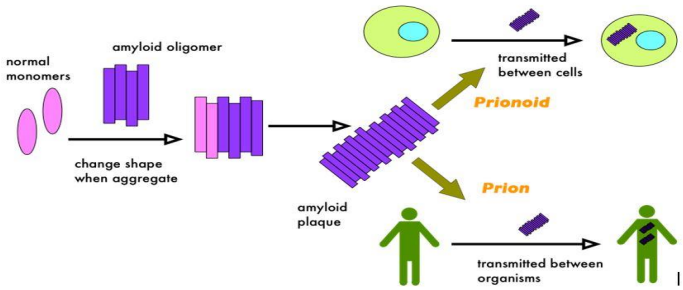
- **Alzheimer's disease**
- It is progressive neuro-degenerative disease with dementia.
- It is characterized by accumulation of amyloid β-protein (Aβ) as extracellular plaques,
- **Amyloid β-protein (Aβ)**, proteolytically derived from a transmembrane glycoprotein known as β-amyloid precursor protein (βAPP).
- Ageing, environmental toxin, familial, genetic
- **Huntington disease**
- a condition that stops parts of the brain working properly over time. It's passed on (inherited) from a person's parents. It gets gradually worse over time and is usually fatal after a period of up to 20 years
- The responsible gene contains an abnormally large number of **CAG** repeats. (Cytosine, Adenine, Guanine). This trinucleotide repeat expansion leading to **polyglutamine repeats** within the Huntington protein.

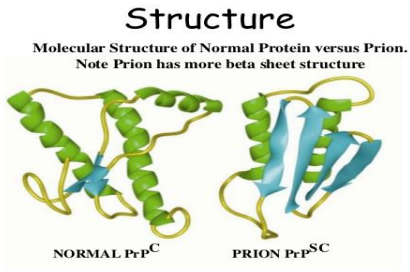


- **Prions disease:**

- like Creutzfeldt-Jakob disease كروتزفيلد-جاكوب(CJD), bovine spongiform encephalopathy (**mad cow disease).** A prion is a type of protein that can trigger normal proteins in the brain to fold abnormally.

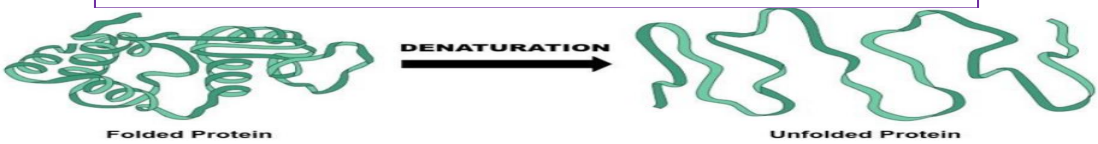
- Result from transmission of an abnormal prion protein from affected individual or animal that leads to altering the a-helical arrangement of the normal prion protein and replacing it with b-pleated sheets.





- Infectious prion proteins have a higher content of beta-pleated sheets, which increases stability hence more resistant to denaturation

Denaturation of proteins



- Protein denaturation results in the unfolding and disorganization of a protein's secondary and tertiary structures without the hydrolysis of peptide bonds leads to loss of native form and biological function.
- Denaturing agents include heat, organic solvents, strong acids or bases, detergents, and ions of heavy metals such as lead.
- Denaturation may, under ideal conditions, be reversible, such that the protein refolds into its original native structure when the denaturing agent is removed.
- However, most proteins, once denatured, remain permanently disordered.
- Denatured proteins are often insoluble and precipitate from solution.

Functions of proteins

- **Structural role:** Proteins are the main structural component in bone, muscles, cyto-skeleton and cell membrane.
- **Catalytic role:** All enzymes are proteins in nature.
- **Hormonal role:** Most of hormones and all cellular receptors are protein in nature.
- **Transport role:**

o albumin – fatty acids, bilirubin, calcium, drugs

o transferin – iron

o cerulplasmin – copper

o lipoproteins – lipids

o haptoglobin – free hemoglobin

o thyroxin binding globulin – thyroxin

o Hemoglobin (a chromo-protein) carries O2 from the lung to tissues is a protein.

- **Defensive role:**

o Immunoglobulins combine with foreign antigens and remove them.

o Complement system removes cellular antigens.

- Plasma proteins, specially albumin, are important for maintaining osmotic pressure of the blood.
- **Blood clotting:** coagulation factors are proteins.
- **Anticoagulant activity (thrombolysis)**
- **Buffering capacity:** Proteins in plasma help to maintain acid-base balance
- **Control of gene expression:** Most factors required for DNA replication, transcription and mRNA translation are protein in nature.

NB: FUNCTIONS FOR KNOWLDGE ONLY


Thank
you