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
- List functions of proteins

Haemoglobin

Structure of Hemoglobin (HbA – adult hemoglobin)

Hemoglobin is a conjugated protein:

Globin

the protein part

Heme

a prosthetic group that contains iron (Fe^{2+}) and binds oxygen

Adult hemoglobin (HbA1) has 4 polypeptide chains:

2 α-chains (each with 141 amino acids)

2 β-chains (each with 148 amino acids)

01

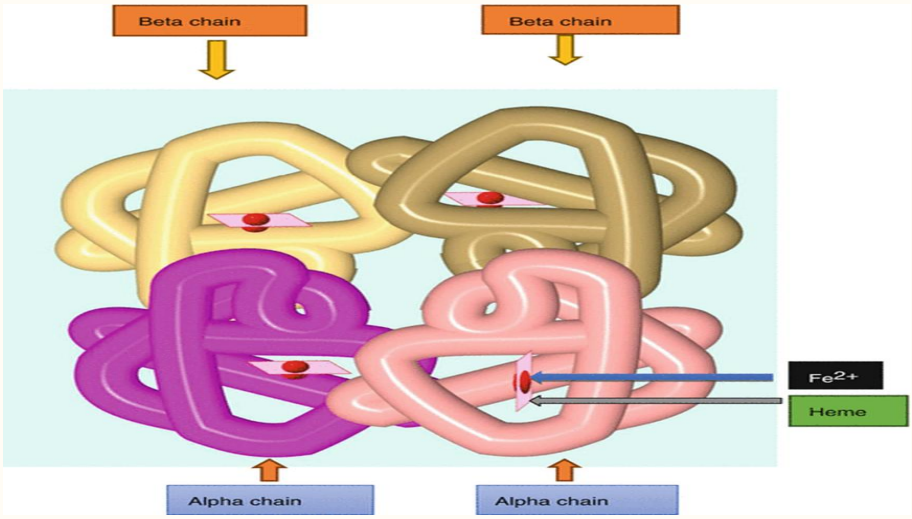
Each chain contains 8 α-helices arranged in a 3D structure

02

Together they form a quaternary structure (tetramer)

03

Each chain carries one heme group → so hemoglobin carries up to 4 oxygen molecules



Cooperative Binding of Oxygen

Key idea: Hemoglobin doesn't bind all oxygen molecules equally.

When one O_2 binds to a heme group, it causes a conformational change → this makes it easier for the next O_2 to bind.

This is called positive cooperativity.

The oxygen-binding curve is sigmoidal (S-shaped):

Myoglobin (one chain, no cooperativity) has a hyperbolic curve

Hemoglobin's curve allows it to load oxygen efficiently in the lungs and release it efficiently in tissues

Sickle Cell Anemia (HbS mutation)

Cause: A point mutation in the β-chain.

Normal	Mutated
Glutamate (a negatively charged amino acid) at position 6	Valine (a hydrophobic amino acid) at position 6

Consequences:

In deoxygenated HbS, the hydrophobic valine interacts abnormally with other HbS molecules → polymerization

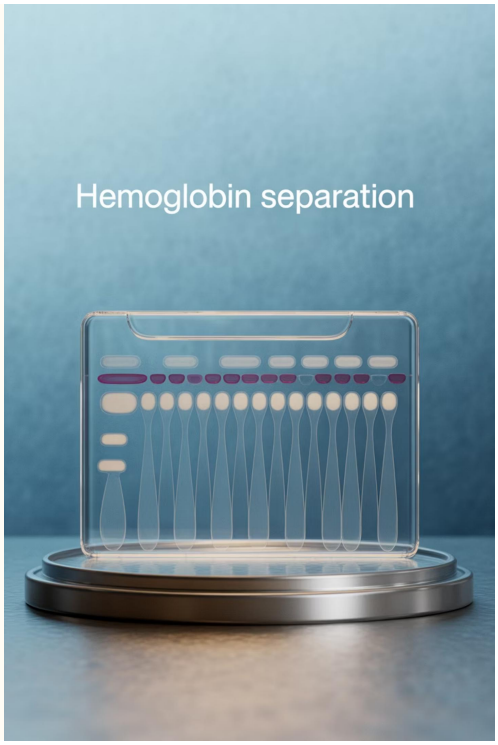
This distorts RBCs into a sickle shape

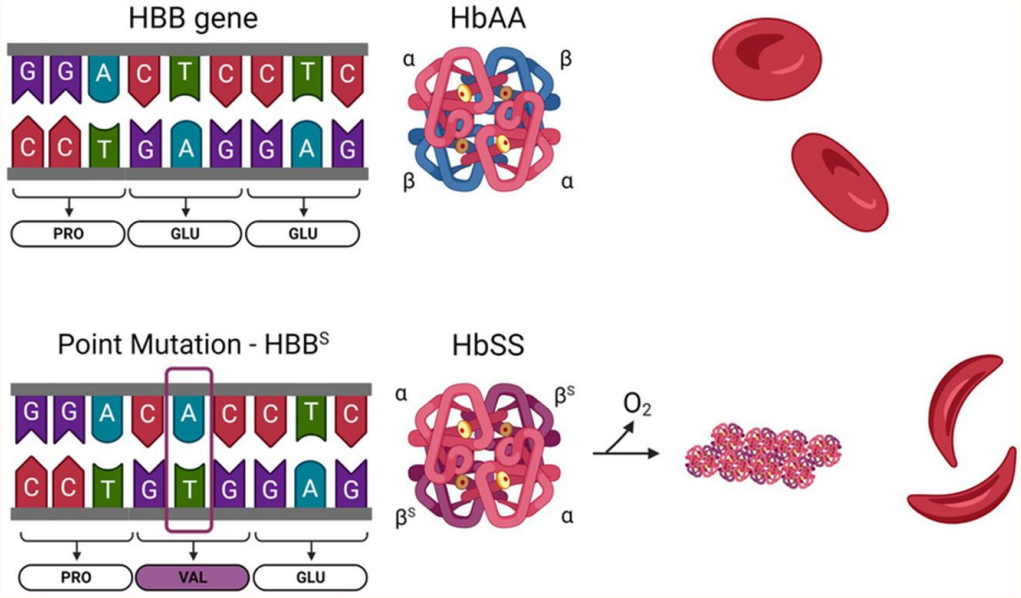
Sickled cells are stiff, fragile, and can block blood vessels

Symptoms: anemia, pain crises, organ damage.

Diagnosis: Hemoglobin electrophoresis distinguishes HbA from HbS (HbS moves differently because it has one less negative charge)

In mutant hemoglobin (HbS), a hydrophobic amino acid replaces a negatively charged one. As a result, HbS carries one less negative charge than normal hemoglobin (HbA). This difference in charge allows the two types of hemoglobin to be separated by electrophoresis.




HBB gene
G G A C T C C T C
C C T G A G G A G
PRO GLU GLU
HbAA
α β β α
Point Mutation - HBB^S
G G A C A C C T C
C C T G T G G A G
PRO VAL GLU
HbSS
α β^S β^S α
O_2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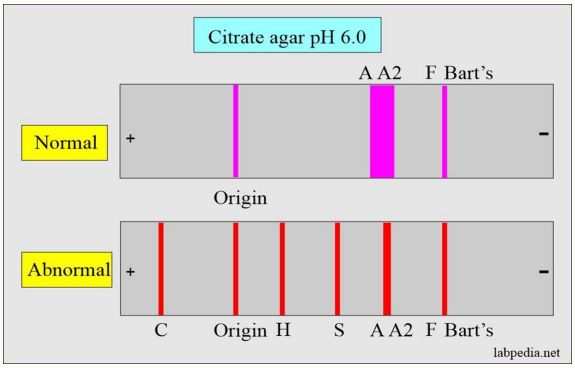
Hemoglobin electrophoresis

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

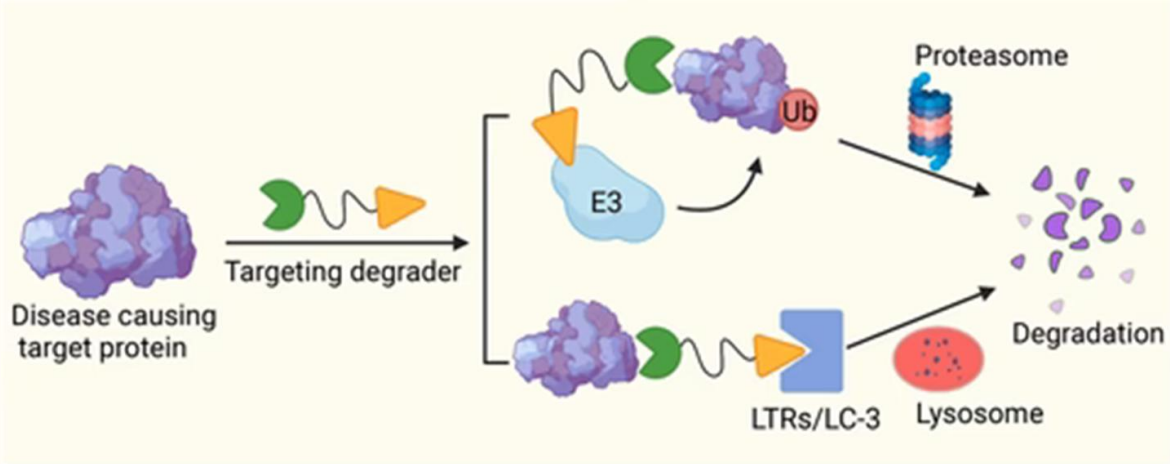
Normally folded protein that finished its function and reached its half life / or protein that are misfolded should be eliminated from the cells. Or protein that are misfolded.

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

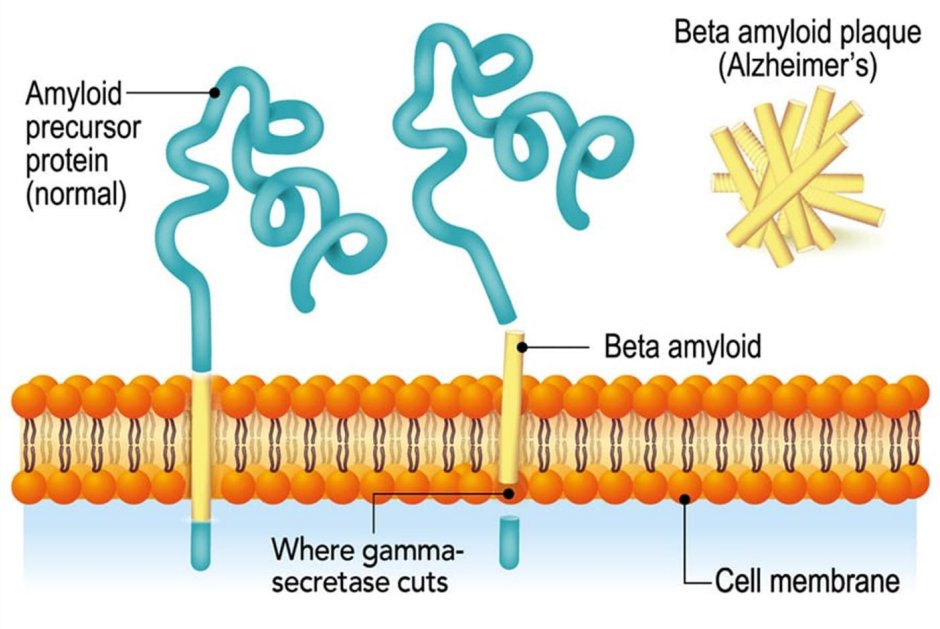
Alzheimer's disease

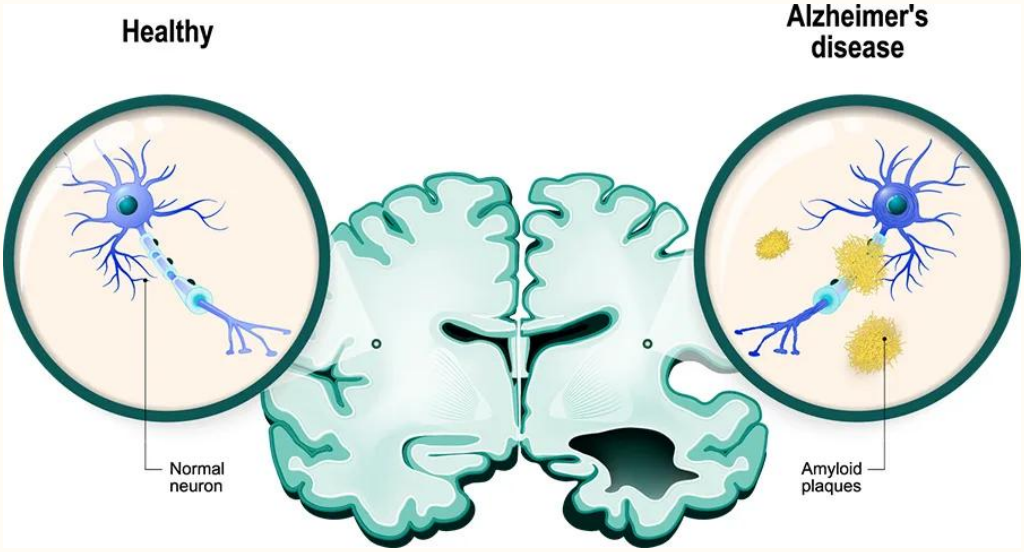
It is progressive neuro-degenerative disease with dementia.

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

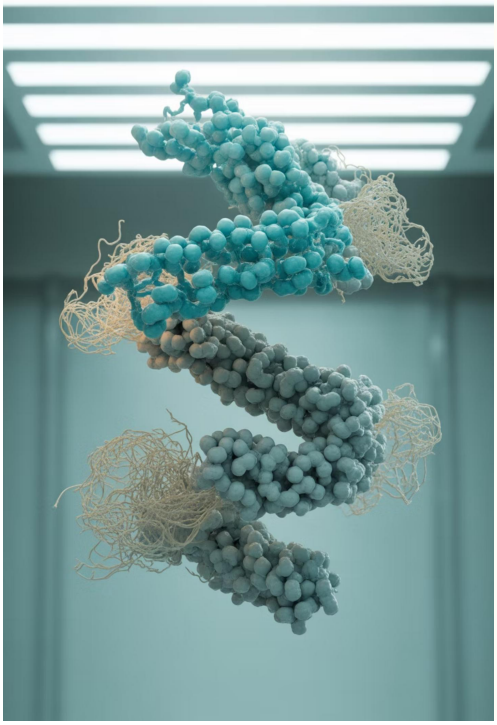
a condition that stops parts of the brain working properly over time. It's passed on (inherited) Autosomal dominant from a person's parents. It gets gradually worse over time and is usually fatal after a period of up to 20 years

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: Protein not DNA, Or RNA

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.

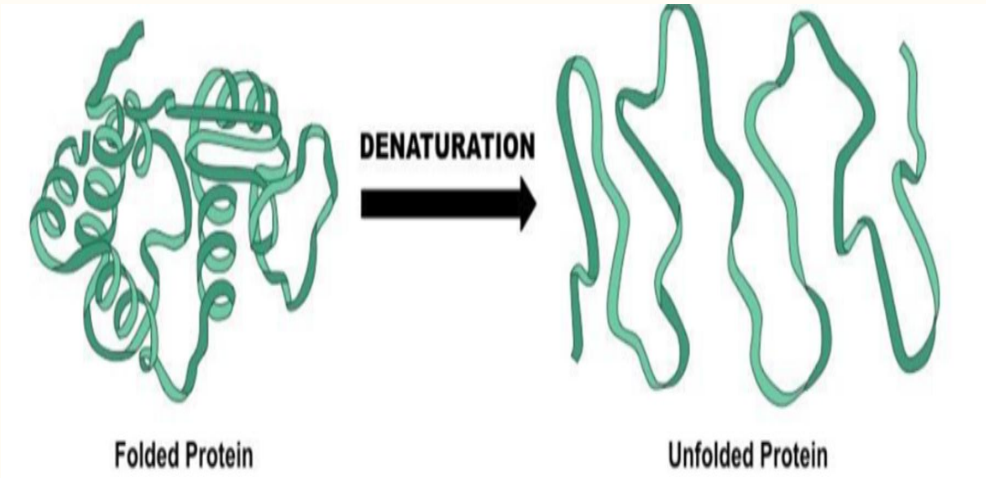
Result from transmission of an abnormal prion protein from affected individual or animal that leads to altering the a-helical arrangement of the normal prion protein and replacing it with b-pleated sheets.



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.

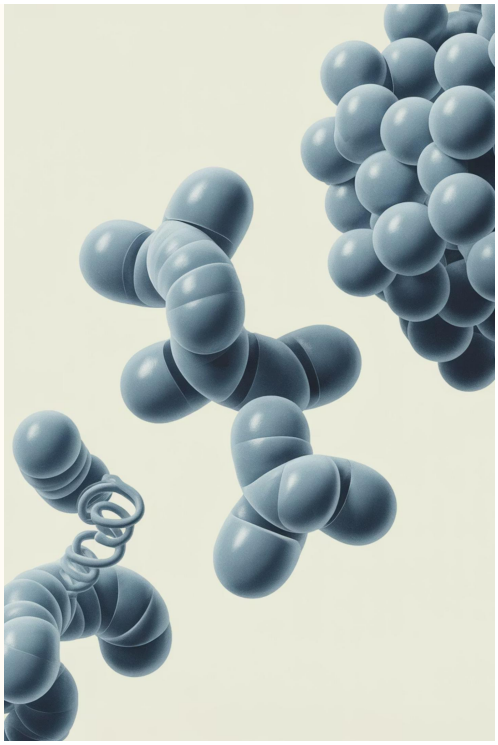
Denaturing agents include heat, organic solvents, strong acids or bases, detergents, and ions of heavy metals such as lead.



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

Proteins are the main structural component in bone, muscles, cyto-skeleton and cell membrane.

All enzymes are proteins in nature.

Most of hormones and all cellular receptors are protein in nature.

Transport role:

albumin – fatty acids, bilirubin, calcium, drugs

transferin – iron

cerulplasmin – copper

lipoproteins – lipids

haptoglobin – free hemoglobin

thyroxin binding globulin – thyroxin

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

Defensive role:

Immunoglobulins combine with foreign antigens and remove them.

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