Diversity and classification of PROTEINS

Biologically Active Peptides

(PEPTIDES - short polymers of amino acids)

Exhibit a number of specific functions. Even the smallest peptides can have biologically important effects

Some small peptides which have significant biological activity are formed as a

- **result of hydrolysis of large proteins**
- **while some are formed by synthesis.**

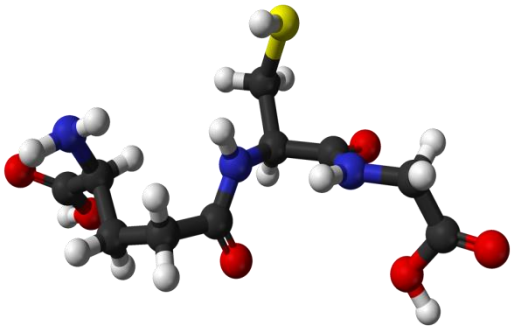
Classification of peptides

- **Regulatory peptides** ***(glutathione, angiotensin, bradykinin)***
- **Peptides with hormonal activity** ***(oxytocin, vasopressin)***
- **Peptides involved in digestion** ***(gastrin, secretin)***

Classification of peptides

- **Neuropeptides**
- **Alkaloids (*Nummularine C, ziziphine A)***
- **Antibiotics (*polymyxin B, gramicidin S, melittin, bombinin*)**
- **Toxines *(some extremely toxic mushroom poisons, such as amanitin*)**

Biologically Important Peptides



Glutathione: a tripeptide consisting of glutamic acid, cysteine and glycine.

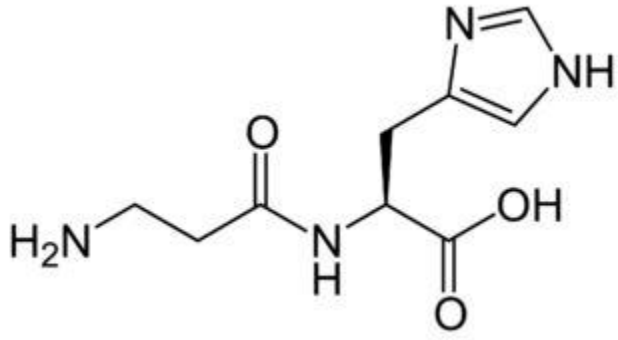
By its ability of easy dehydrogenation it gets converted to disulphide form and function in oxidation-reduction systems.

- **is one of the major endogenous antioxidants**
- **is used in DNA synthesis and repair, protein synthesis, prostaglandin synthesis, amino acid transport, and enzyme activation.**
- **is known as a substrate in conjugation reactions**
- **has roles in progression of the cell cycle, including cell death**

Biologically Important Peptides

Carnosine: a dipeptide of β-alanine and histidine. It is a water soluble dipeptide of voluntary muscle.

has a number of antioxidant properties, reduce the telomere shortening rate, considered as a geroprotector



Bradykinin: has relaxant effects on smooth muscle

Biologically Important Peptides

- **Angiotensins: the enzyme renin is released from kidneys and acts on globulin fraction of plasma to release a peptide Angiotensin I (10 amino acids). Angiotensin I is then converted to Angiotensin II by splitting off two amino acids, has greater effect on blood pressure. Removal of one residue from Angiotensin II results in formation of Angiotensin III (7 amino acids) which plays role in pathology of hypertension**

Biologically Important Peptides

Oxytocin *(nonapeptide - made up of 9 amino acids)* is normally produced by hypothalamus and released by the posterior pituitary. It plays a role in social bonding, sexual reproduction in both sexes, and during and after childbirth.

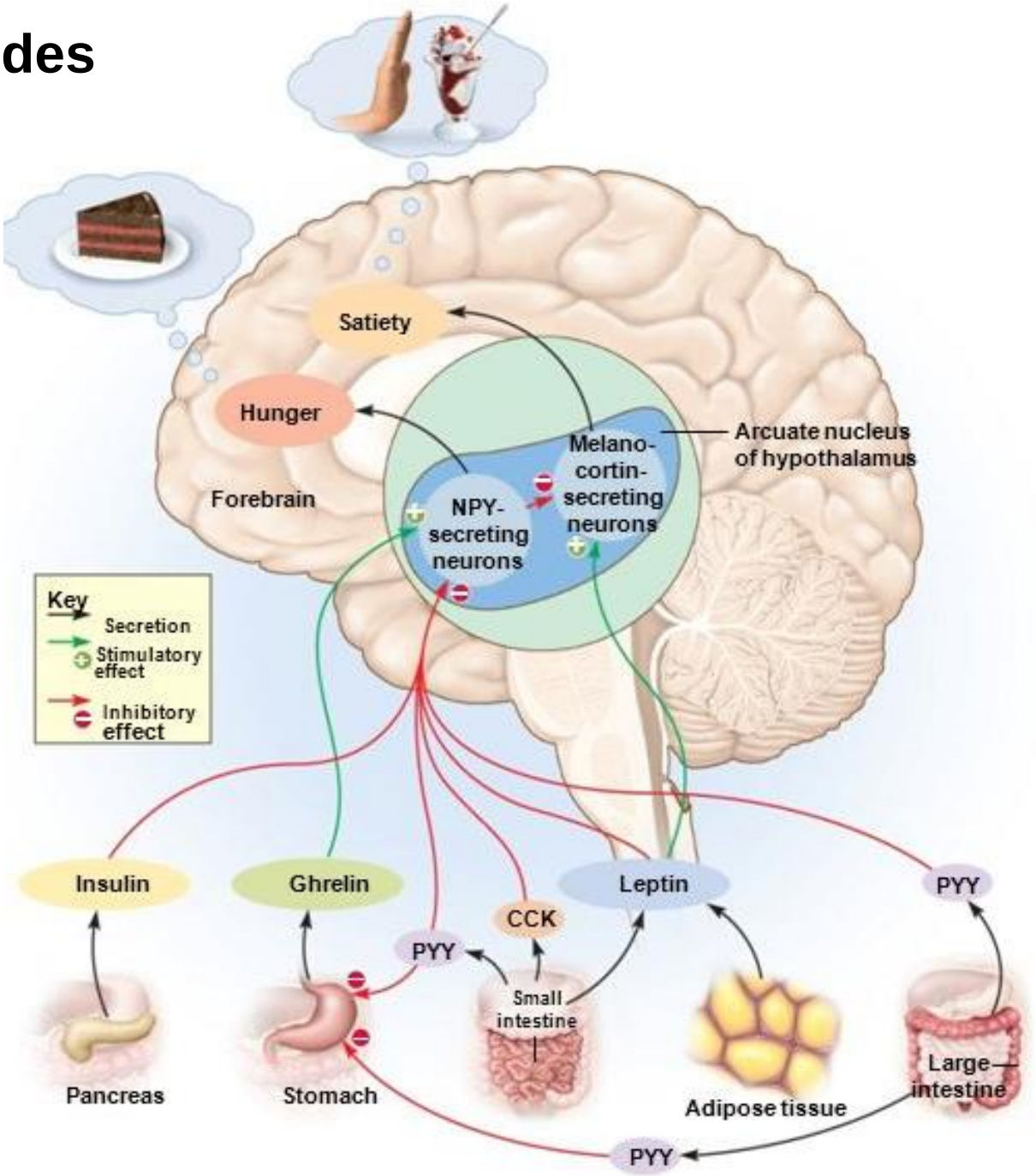
Vasopressin:

- **it increases the amount of water reabsorbed back into the circulation from the filtrate in the kidney tubules**
- **it constricts arterioles and raises arterial BP**
- **vasopressin may be released directly into the brain from the hypothalamus, and may play an important role in social behavior, sexual motivation and pair bonding, and maternal responses to stress.**

Biologically Important Peptides

Gastrin, Secretin and Pancreozymin: are gastrointestinal peptides which act as hormones which stimulate secretion of bile and other enzymes of digestive juices

Gut-brain peptides in appetite regulation

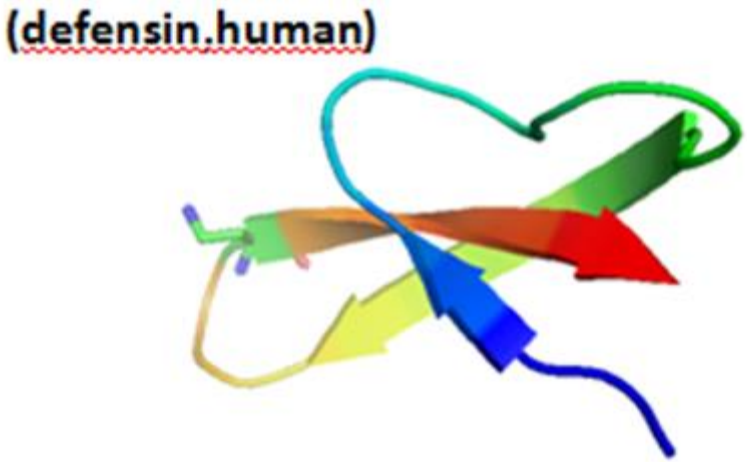


Biologically Important Peptides

Antibiotics

Anti Microbial Peptides isolated from a full range of organisms

cecropins, defensins, thionins



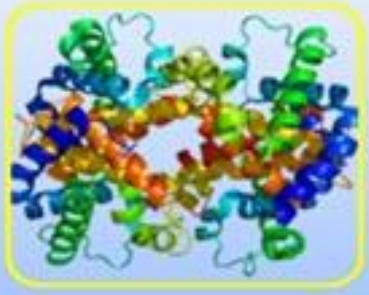
Brain Peptides

certain brain cells have receptors that bind opiates like morphine and have been termed endorphins (endogeneous morphine).

Dynorphin is a peptide of 13 amino acids which is called superopioate since it is significantly potent. Peptide fragments from brain that reduce intestinal motility are met-enkephalins and leuenkephalin.


haoxote.com

CLASSIFICATION OF PROTEINS

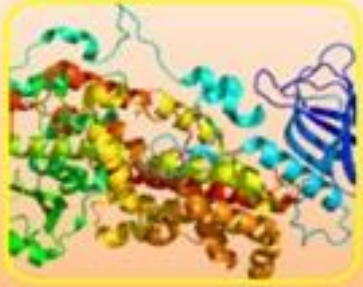


Classification Based on Structure

- *Fibrous Proteins*
- *Globular Proteins*
- *Intermediate Proteins*

Classification Based on Composition

- *Simple Proteins*
- *Conjugated Proteins*



Classification Based on Functions

- *Structural Proteins, Enzymes, Hormones*
- *Pigments, Transport Proteins, Contractile Proteins*
- *Storage Proteins, Toxins*

Classification of proteins
(depending on their composition)

PROTEINS

Simple

composed of amino acid residues only

Conjugated

two-component species whose constituents are

- **a simple protein and**
- **a non-protein moiety**

The non–amino acid part of a conjugated protein is usually called its

prosthetic group

Simple proteins

- **Protamines**

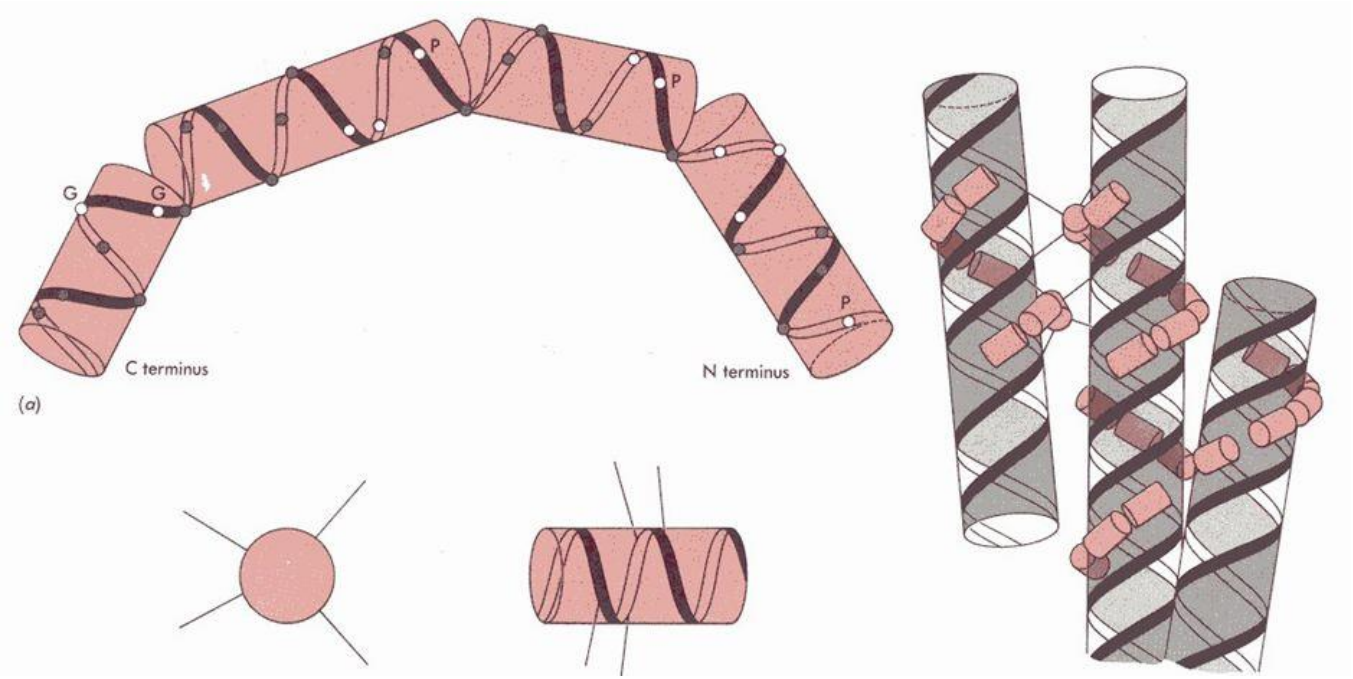
(***proteins of a small molecular size***)

salmin, clupein

- display pronounced basic properties due to the occurrence of large amounts of arginine

- readily soluble in water, noncoagulable by heat.

PROTAMINES



replace histones late in the haploid phase of spermatogenesis and are believed essential for sperm head condensation and DNA stabilization. In humans 10-15% of the sperm's genome is packaged by histones

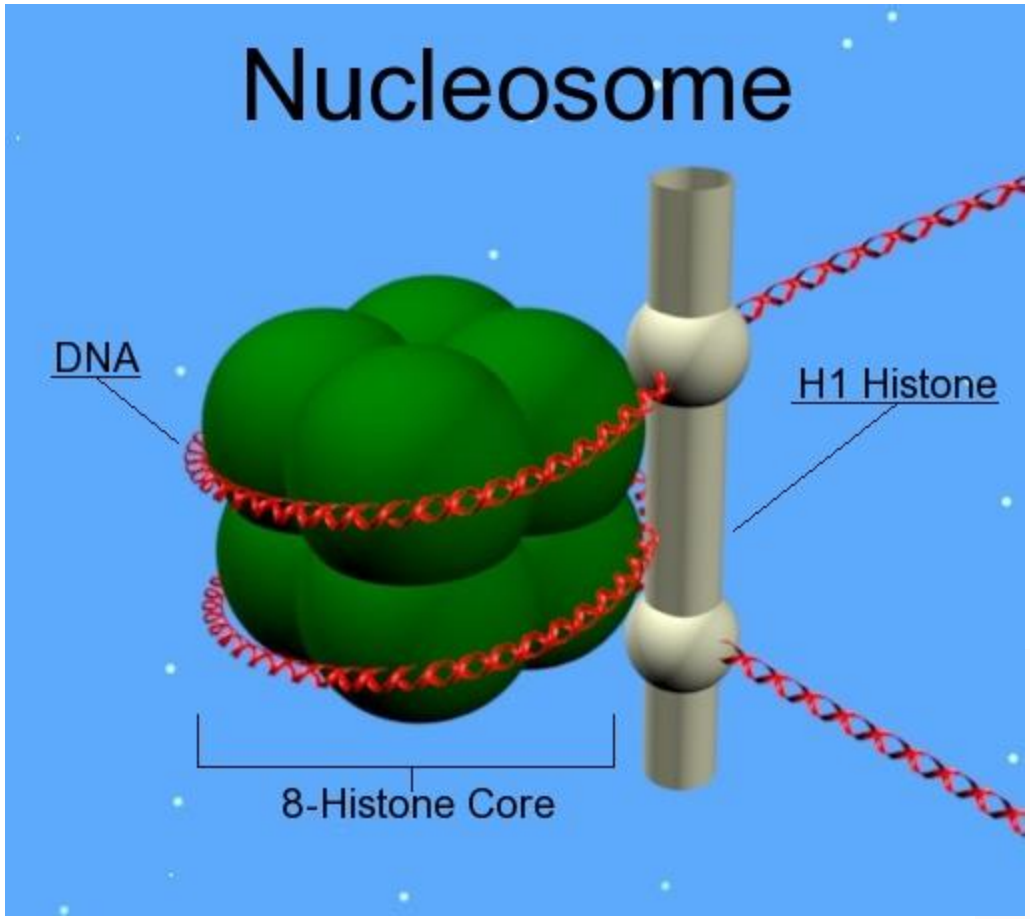
Simple proteins

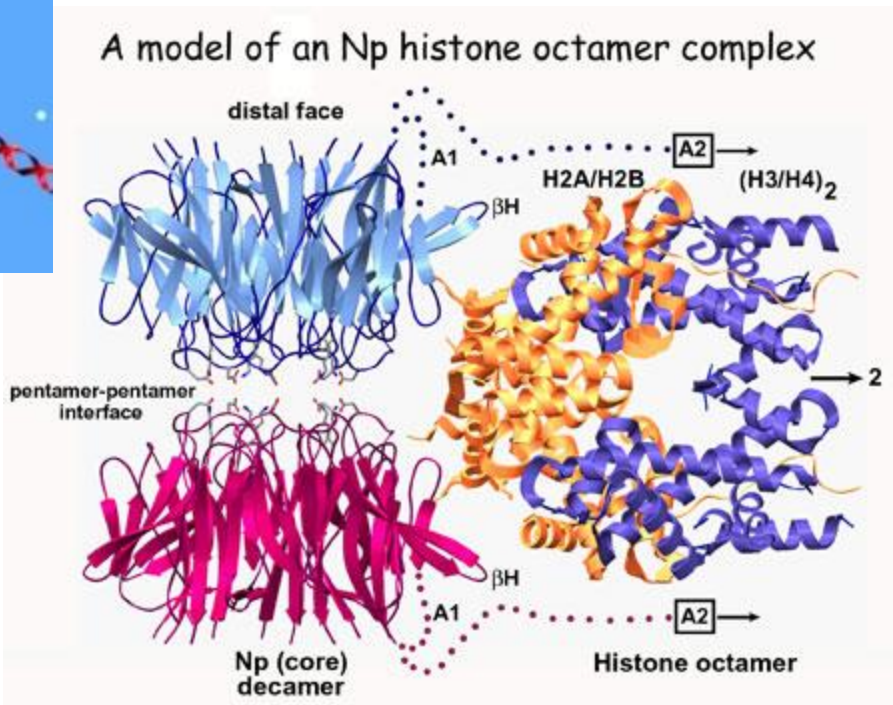
Histones

proteins of a small molecular size

-basic properties (major constituents – arginine and lysine)

- located in the cell nuclei and make part of deoxyribonucleoproteins. They act as repressors of template activity of DNA in the synthesis of RNA.


Nucleosome
DNA
H1 Histone
8-Histone Core

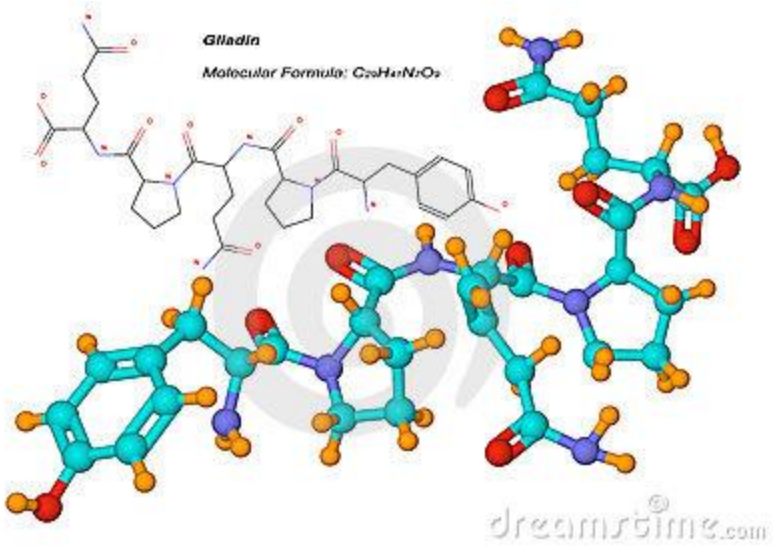

A model of an Np histone octamer complex
distal face
A1
A2
H2A/H2B
(H3/H4)2
βH
pentamer-pentamer interface
2
βH
A1
A2
Np (core) decamer
Histone octamer

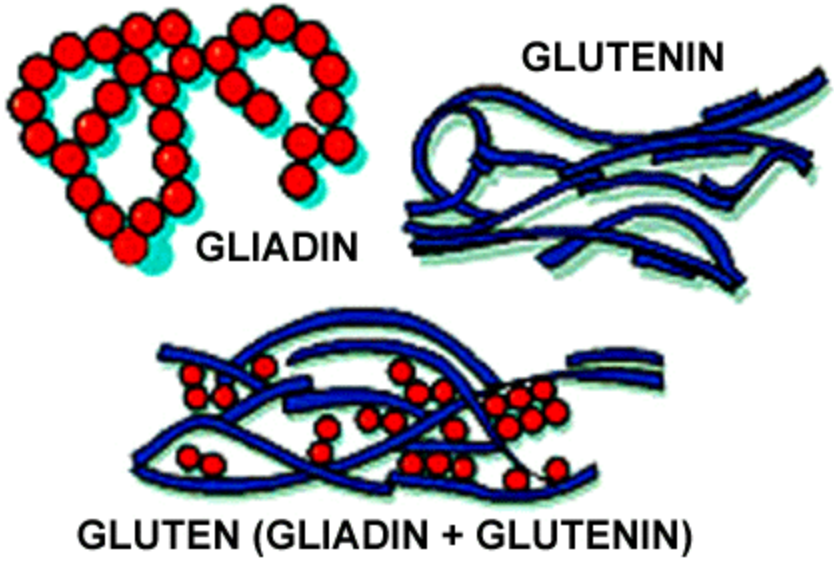
Simple proteins

- **Prolamines and Glutelins**
  (oryzenin, glutenin, gliadin, zein, hordein)

- proteins of vegetal origin

- soluble in 60-80% ethanol solution





Simple proteins

Albumins and Globulins

- widely occur in animal organs and tissues

Albumins and globulins differ in molecular size

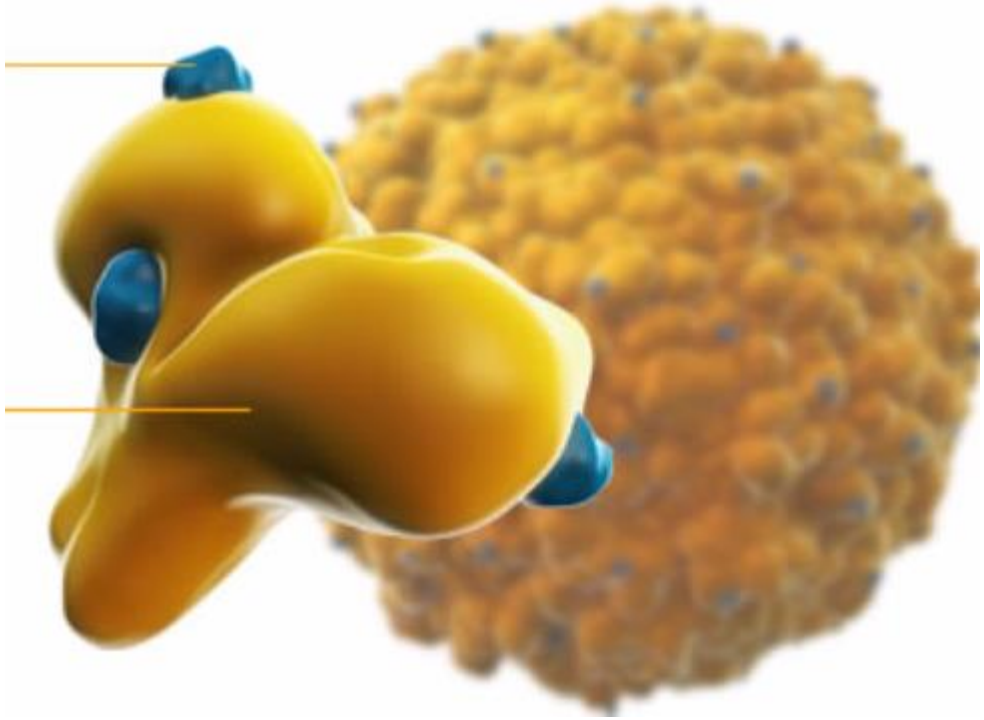
- albumins 40-70 kDa, globulins 150 kDa

- differ solubility *(widely used in clinical practice for their fractionation.*

The albumins may be *precipitated of solution by saturating the solution with ammonium sulphate.)*

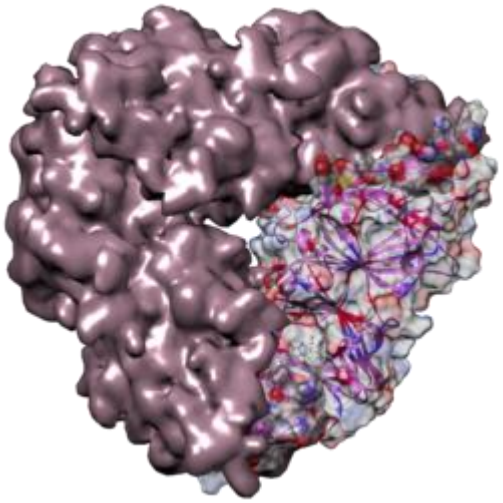
Albumins

-important for oncotic pressure (colloid osmotic pressure) of blood serum

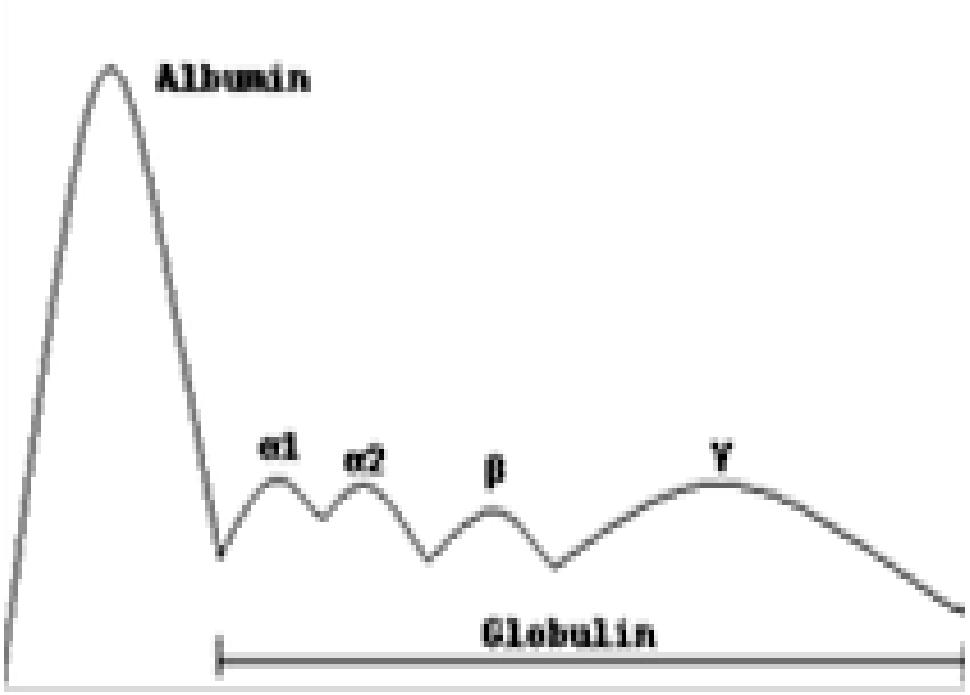


- transport
fatty acids
thyroid hormones
steroid hormones

Globulins



- **are insoluble in pure water but dissolve in dilute salt solutions. Some globulins are produced in the liver, while others are made by the immune system**



Globulins exist in various sizes. The lightest globulins are the alpha globulins, while the heaviest class of globulins are the gamma globulins. Being the heaviest, the gamma globulins are among the slowest to segregate in gél electrophoresis.

The immunologically active gamma globulins are also called "immunoglobulins" or "antibodies"

In health the albumin-to-globulin ratio in blood plasma is maintained at a constant level commonly referred as the

protein quotient.

In many diseases this quotient is liable to variation.

So, the determination of protein quotient in the patients blood is of important diagnostic value

The classification of conjugated proteins is based on the chemical nature of their non-protein components

Chromoproteins

Lipoproteins

Glycoproteins

Phosphoproteins

Nucleoproteins

Metalloproteins

Chromoproteins:

These are proteins in combination with a proshetic group that is a pigment (coloured substance).

Examples are the respiratory pigment hemoglobin , visual purple or rhodopsin found in the rods of the eye, flavoproteins and cytochromes.

Chromoproteins:

- **hemoproteins**

(containing heme as prostetic group)

Hemoglobin: ***respiratory protein found in RBC***

Cytochromes: ***mitochondrial enzymes*** **of the respiratory chain.**

Catalase: ***the enzyme that decomposes*** H_2O_2

Peroxidase: ***an oxidative enzyme.***

Chromoproteins:

flavoproteins

(FMN, FAD as prostetic group)

constituents of oxidoreductases – enzymes that catalyze reduction-oxidation reactions in the cells)

visual purple ***It is a protein of the retina in which the prosthetic group is a carotenoid pigment which is purple in colour.***

Lipoproteins:

These are proteins conjugated with lipids.
There are five types of lipoproteins:

- **high density lipoproteins (HDL),**
- **intermediate density lipoproteins (IDL),**
- **low density lipoproteins (LDL),**
- **very low density lipoproteins (VLDL)**
- **chylomicrons.**

Glycoproteins

(Protein+Carbohydrate)

Glycoproteins are of two main categories, intracellular and secretory.

Intracellular glycoproteins are present in cell membranes and have an important role in membrane interaction and recognition.

- **Secretory glycoproteins are:**

  plasma glycoproteins, secreted by the liver,

  thyroglobulin, secreted by the thyroid gland,

  immunoglobins, secreted by plasma cells,
  ovoalbumins, secreted by the oviduct in the hen,

  ribonuclease, the enzyme which breaks down RNA,

  deoxyribonuclease, which breaks down DNA.

Phosphoproteins

(Protein+phosphate):
Phosphoproteins are proteins in combination with a phosphate-containing radical other than a nucleic acid or a phospholipid.

Examples of phosphoproteins are casein of milk and ovovitelline in eggs.

Nucleoproteins:

(Protein + nucleic acid).

Nucleoproteins are proteins in combination with nucleic acids.

Deoxyribonucleoproteins (chromatin)

Ribonucleoproteins (ribosomes)

Metalloproteins:

These are proteins conjugated to metal ion(s) which are not part of the prosthetic group.

They include cearuloplasmin, an enzyme with oxidase activity that may transport copper in plasma, siderophilin, ferritin

Protein function often entails interactions with other molecules.

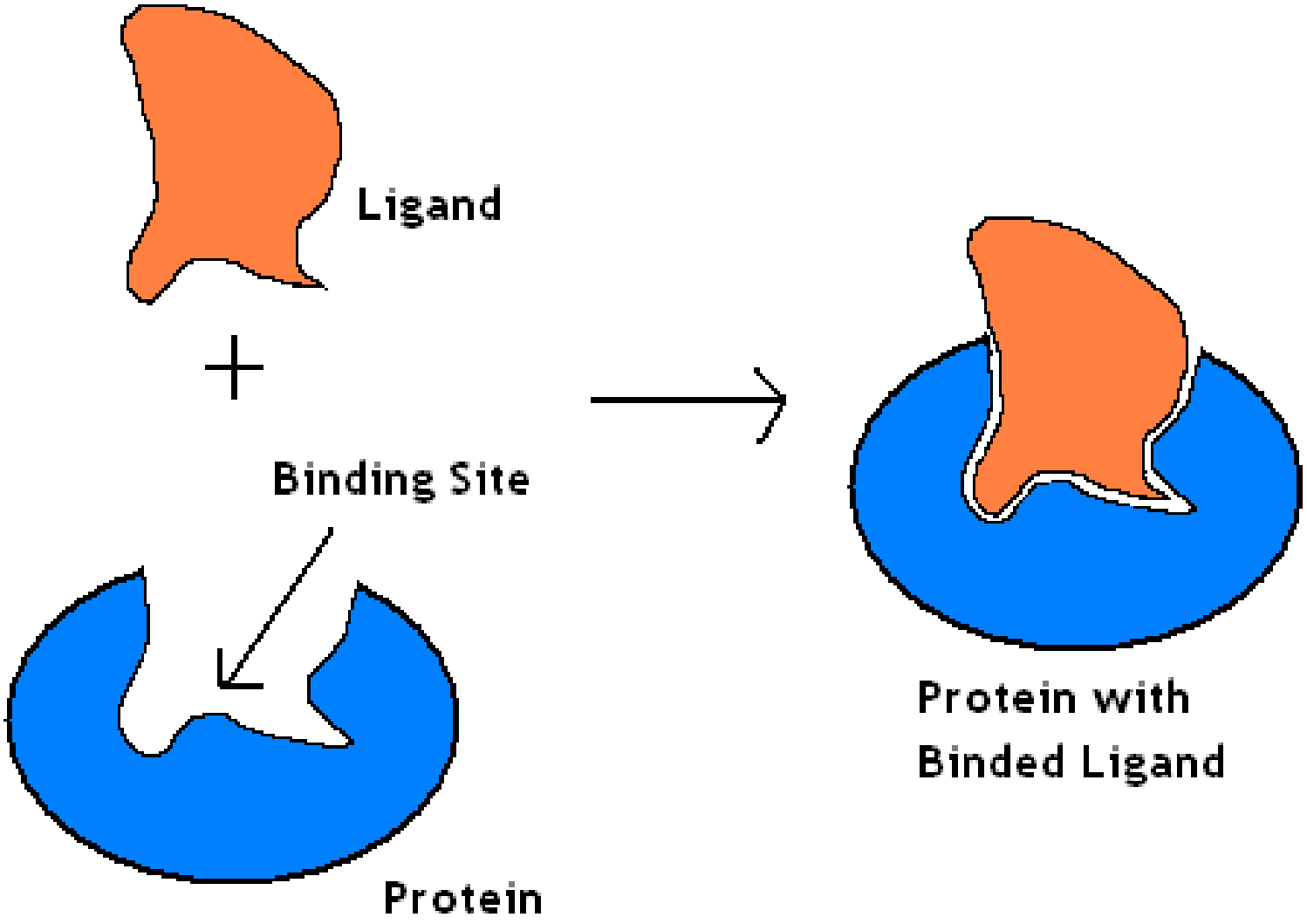
A molecule bound by a protein is called a

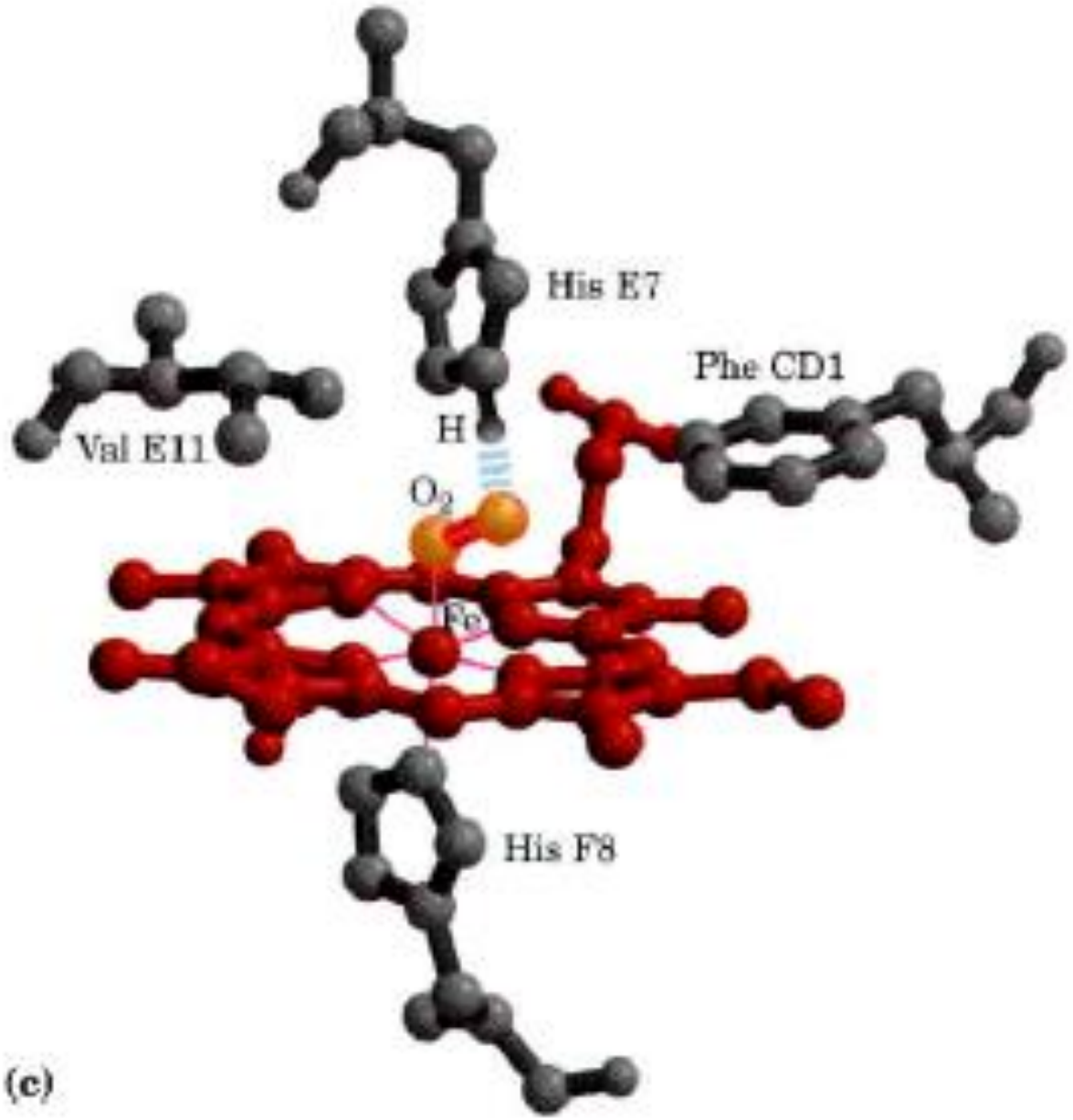
ligand

the site to which it binds is called the

binding site.

binding site is complementary to the ligand in size, shape, charge, and hydrophobic or hydrophilic character.


Ligand
Binding Site
Protein
Protein with
Binded Ligand



(c)

A ligand may be any kind of molecule, including another protein.

The transient nature of protein ligand interactions is critical to life, allowing an organism to respond rapidly and reversibly to changing environmental and metabolic circumstances.

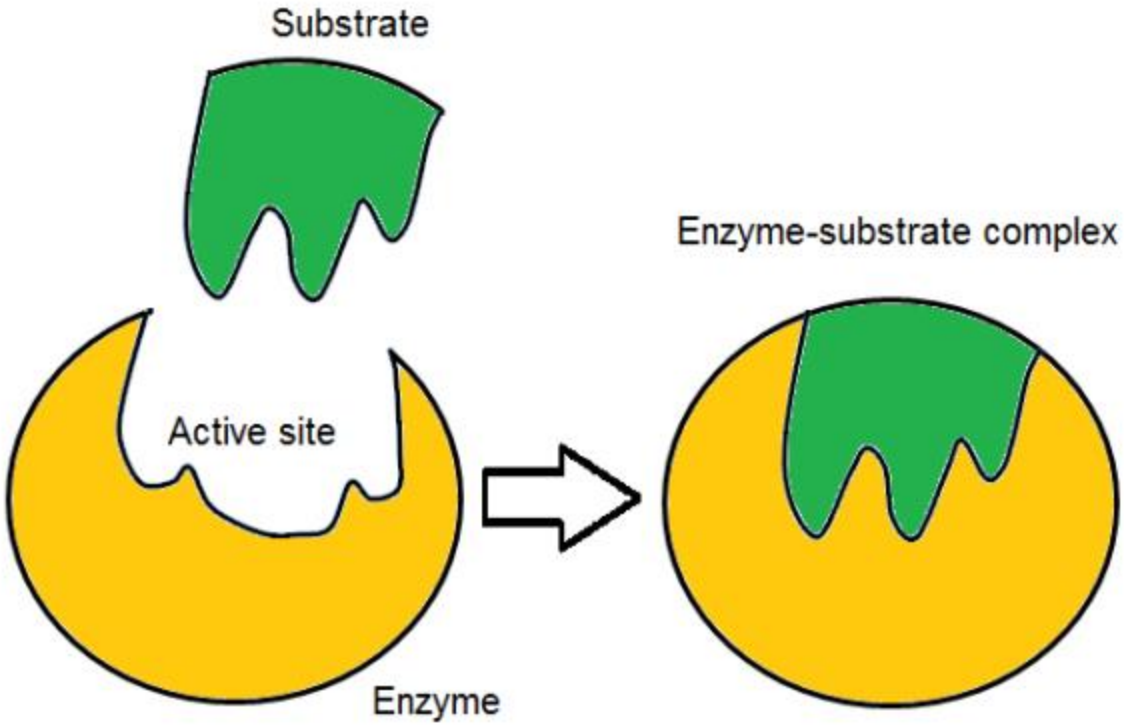
Interaction protein – ligand
is specific: the protein can discriminate among the thousands of different molecules in its environment and selectively bind only one or a few.
A given protein may have separate binding sites for several different ligands.

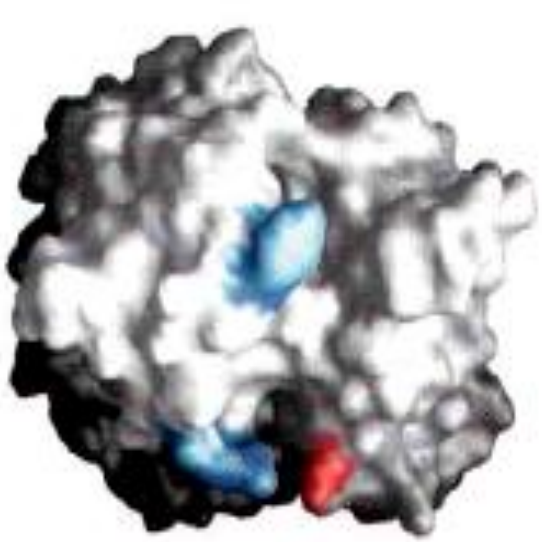
These specific molecular
interactions are crucial in maintaining the high degree of order in a living system.

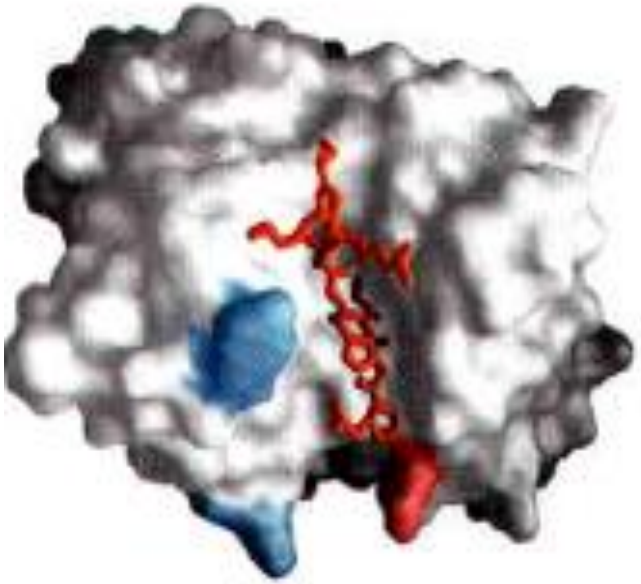
Proteins may undergo conformational changes when a ligand binds,

a process called induced fit.

In a multi-subunit protein, the binding of a ligand to one subunit may affect ligand binding to other subunits.


Substrate
Enzyme-substrate complex
Active site
Enzyme





Interactions between ligands and proteins may be regulated, usually through specific interactions with one or more additional ligands.

These other ligands may cause conformational changes in the protein that affect the binding of the first ligand.

Hemoglobin molecules illustrate almost every aspect of that most central of biochemical processes: the reversible binding of a ligand to a protein. This classic model of protein function tells us a great deal about how proteins work.

Protein-Ligand Interactions Can Be Described Quantitatively

A quantitative description of this interaction is therefore a central part of many biochemical investigations.
In general, the reversible binding of a protein (P) to a ligand (L) can be described by a simple equilibrium expression:

$$P + L = PL$$

The reaction is characterized by an equilibrium constant, *K*a
The term *K*a is an association constant

Changes of proteins in ontogenesis

- **Embryonic hemoglobin with the structure α2 ε2 globin chain are formed in the first three months of embryonic development.**

Then predominates

- **Fetal Hb (HbF); its subunits are α-globin and γ-globin. HbF predominates in the fetus during the second and third trimesters of gestation and in the neonate.**

Embryonic and fetal hemoglobins have higher O_2 affinities than HbA, as they have to take up oxygen from the maternal circulation.

- **HbF is gradually replaced by HbA during the first few months of life. Over 95% of the Hb found in adult humans is HbA**

- **HbA2 accounts for 2-3% of the total and has an α2δ2 polypeptide composition. Functionally, these two adult Hbs are indistinguishable**

Changes of proteins in disease

PROTEOPATHIES

a class of diseases in which certain proteins become structurally abnormal, and thereby disrupt the function of cells, tissues and organs of the body.

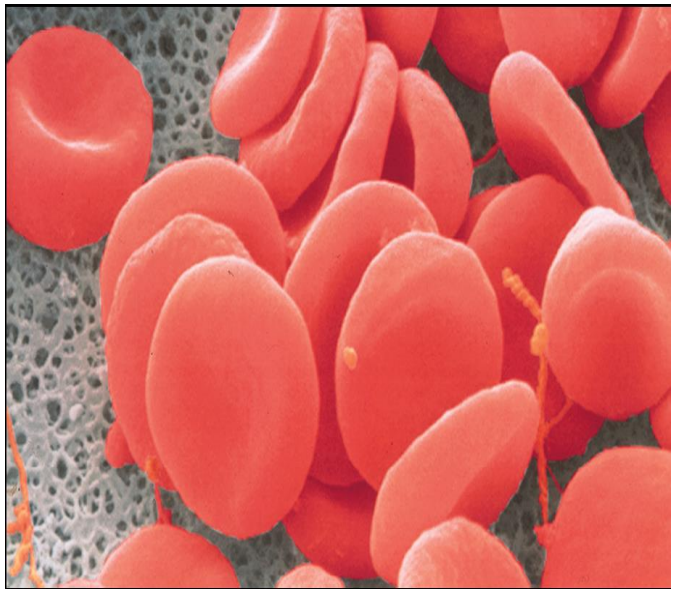
Often the proteins fail to fold into their normal configuration; in this misfolded state, the proteins can become toxic in some way or they can lose their normal function.

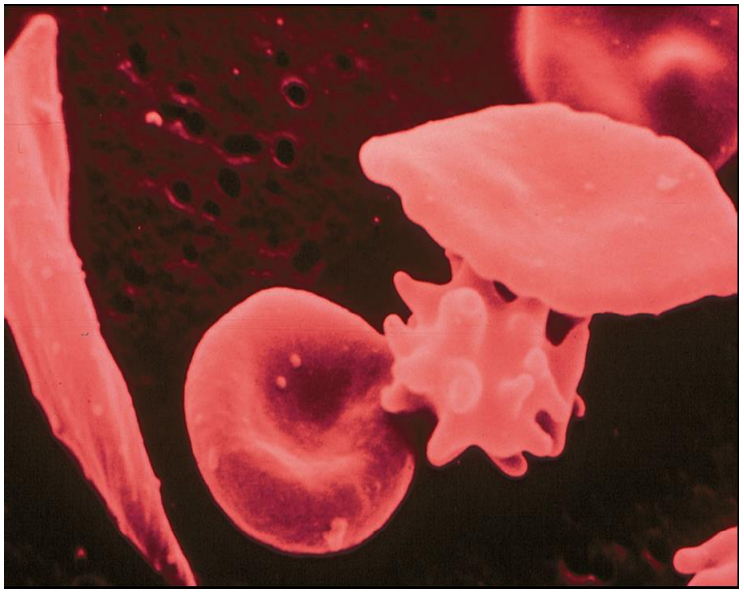
The proteopathies include such diseases as Alzheimer's disease, Parkinson's disease, prion disease, type 2 diabetes, amyloidosis, and a wide range of other disorders

Sickle-Cell Anemia Is a Molecular Disease of Hemoglobin

The great importance of the amino acid sequence in determining the secondary, tertiary, and quaternary structures of globular proteins, and thus their biological functions, is strikingly demonstrated by the hereditary human disease

sickle-cell anemia.





Sickle-cell anemia is a genetic disease caused by a single amino acid substitution (Glu 6 toVal 6) in each β-chain of hemoglobin.

The change produces a hydrophobic patch on the surface of the hemoglobin that causes the molecules to aggregate into bundles of fibers.

This homozygous condition results in serious medical complications.

Proteins as medications:

- **Blood coagulation factors** (factor VIII and factor IX)
- **Thrombolytic agents** (tissue plasminogen activator)
- **Hormones** (insulin, glucagon, growth hormone, gonadotrophins)
- **Haematopoietic growth factors** (erythropoietin, colony stimulating factors)
- **Interferons** (Interferons-α, -β, -γ)
- **Interleukin-based products** (Interleukin-2)
- **Vaccines** (hepatitis B surface antigen)
- **Monoclonal antibodies** (various)
- **Additional products** (tumour necrosis factor, therapeutic enzymes)