Proteins

- Fibrous ⇝ uniform secondary structure
- Globular ⇝ many secondary structures

Fibrous Proteins

1) Collagen

⇝ most abundant protein (25%)

↳ Provide support, stiffness and tensile strength

3 α-chains → Tropocollagen → microfibril → fibril → Fiber

↳ Triple helix → basic unit

Fibril forming Collagens:

Collagen I, II, III, V, XI, XXIV, XXVII

Glycine (33%)	Proline	Hydroxylysine	Hydroxyproline	Allysine
Small, flexible	Stabilize the structure	attachment of sugar	Can form	☆ produced by lysine
can form H-bonds	and gives rigidity	aiding in recognition	H-bonds	oxidase
↳ Tight packing	☆ X H-bonds	interaction and signaling		☆ form aldol cross link with Allysine

Hydroxylase requires Vitamin C

Lysine, Hydroxylysine

Packing of collagen depends on: H-bonds, cross links (increase with age)

↳ X Hydroxylation → Cause Ehlers-Danlos syndrome, Scurvy

deficiency of vitamin C

☆ Glycosylation of Collagen, increases cross links

↳ Hyperglycemia ⇝ formation of AGEs ⇝ increase oxidative stress and cytokines

☆ Collagen is synthesized as Preprocollagen then modified (Hydroxylation, Glycosylation) in the ER and Golgi forming Procollagen ⇝ secreted and cleave pro-region

2) Elastin

- ☆ Flexible and resilient
- ☆ interwoven with collagen, prevent tearing
- ☆ Basic unit: Tropoelastin

It consists of: Hydrophillic domain (Lysine, alanine) and Hydrophobic domain (Valine, Proline, Glycine)

↳ Reformation after stretching

- ☆ No Hydroxylysine (X glycosylated)
- ☆ Contain aldol cross link

3) Keratin

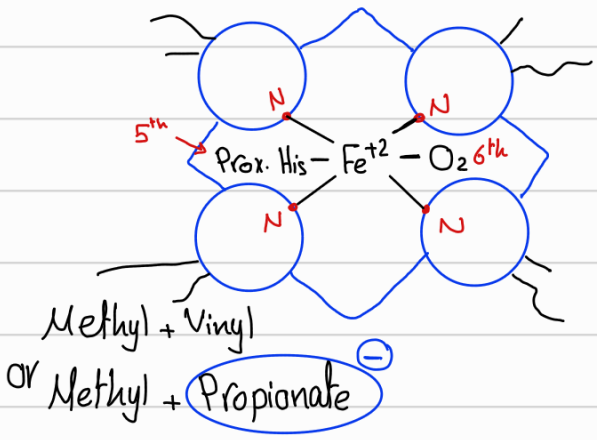
- ☆ Form intermediate filaments
- ☆ Present in hair, fingernails and skin
- ☆ high content of Cys ⇝ disulfide cross links
- ☆ Basic unit ⇝ protofilament

dimer → tetramer (protofilament) → protofibril → microfibril → macrofibril → filament

- ☆ Temporary hair waving: H bonds (non covalent)
- ☆ Permanent: disulfide (covalent)

Globular → Hemoglobin → Transport O_2 in RBC
→ Myoglobin → Store O_2 in muscles

Heme → Protoporphyrin IX + Ferrous (Fe^{+2})
(Protoporphyrin IX: Hydrophobic)

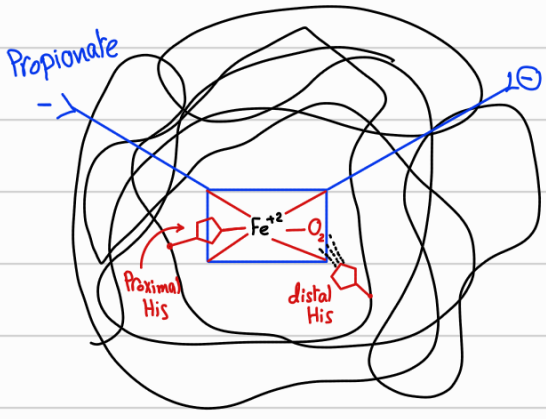


when heme is oxygenated ⇝ deep red

Hemoproteins:
1) Hemoglobin, Myoglobin
2) NOS, Cytochrome P450
3) Cyt c, Cyt b
4) Sensor proteins

Myoglobin (Mb)

☆ Monomer, 8 α-helices



☆ Globin fold is hydrophobic to prevent oxidation of $Fe^{+2} \rightarrow Fe^{+3}$

☆ E7: distal His, gate for O_2 entry
- → Prevent binding of CO
- → Stabilize O_2 by H-bonds

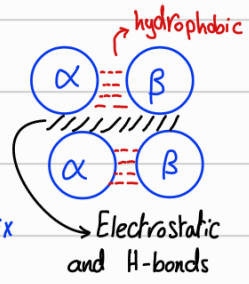
☆ F8: Proximal His, bind iron covalently

☆ Heme form hydrophobic interactions with globin fold

☆ Propionate form electrostatic with protein surface

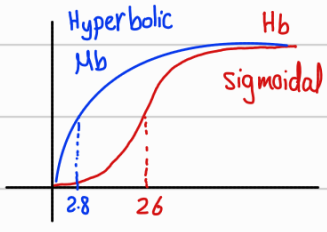
☆ P50 = 2.8 ⇝ ↑ affinity to O_2
⇒ normal condition, bind O_2 ⇝ saturated
⇒ Hypoxia, release O_2 ⇝ unsaturated
⇒ Hyperbolic curve

Hemoglobin (Hb)



☆ Heterotetramer (2α, 2β) (Protomer)
- 7 α-helix
- 8 α-helix

☆ Sigmoidal curve
→ Allosteric, Positive Cooperative



☆ Affinity$_{Mb}$ > Affinity$_{Hb}$

Hb → intermediate affinity
- → R state → ↑ affinity → lungs (saturated)
- → T state → ↓ affinity → Tissues (Release, unsaturated)

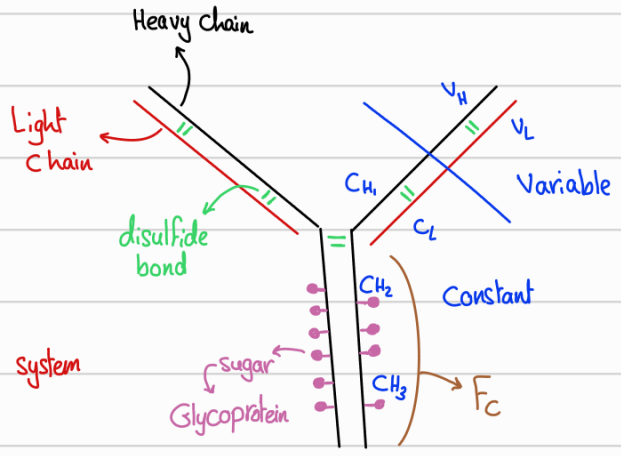
☆ Allosteric → binding of O_2 to 1 subunit affects others
- → Binding O_2 to a subunit induces movement (15°, 0.4 Å) (domed structure → flat structure)
- → This movement breaks electrostatic and H-bonds converting it from T → R state

☆ In Mb ⇝ This movement do not affect its function

☆ Distal His decreases the affinity of CO but it still more than affinity of O_2
- → by bending the bond
- → Smoking and heaters cause irreversible binding of CO to Fe^{+2}

Immunoglobulins ⇝ antibodies ⇝ produced by B cells (Adaptive Humoral immunity)

Functions: 1) Neutralization (prevent entry to cells)
2) Activate phagocytes (such macrophages)
3) Activate the complementary protein system



☆ Antibodies are Heterotetramers

Constant domain: Uniform for antibodies of the same isotype
→ bind immune cells to activate phagocytosis and complementary system

Variable domain: vary between different antibodies
→ bind the antigen (epitope)

Each B cell produces one type of antibodies only

Each antibody binds 2 antigens

Hypervariable region (CDR): 3 loops in variable domain
→ The most specific and highest affinity binding site for the antigen

Hinge region: gives flexibility and enhances affinity

Immunoglobulin motif
→ antiparallel β sheets + 3 loops → Hypervariable Region

Immunoglobulin fold
→ 2 motifs, stabilized by disulfide bonds
→ β-Barrel

Antibody - Antigen interactions: Non-Covalent
↑affinity = many interactions

☆ Light chain can be Lambda or Kappa

☆ Heavy chain can be alpha, Gamma, Mu, Epsilon or Delta

Classes: 1) IgM ⇝ Pentamer → bind 10 epitopes
→ The first type to be produced

2) IgG ⇝ The most abundant
→ cross the placenta

3) IgE ⇝ Allergic reaction
→ Mast cells

4) IgD

5) IgA ⇝ Mucosal membrane
→ breast milk
→ Dimer → 4 epitope

DNA rearrangement of:
Variable: change specificity and affinity to antigen
Constant: class switching

Polyclonal antibodies: from different B cells
Monoclonal antibodies: from the same B cell
Hybridoma: B cell fused with myeloma
→ immortal B cell

Idiotype: different variable
Isotypes: different class (constant of Heavy Chain)
Allotype: slight difference in the constant region between individuals