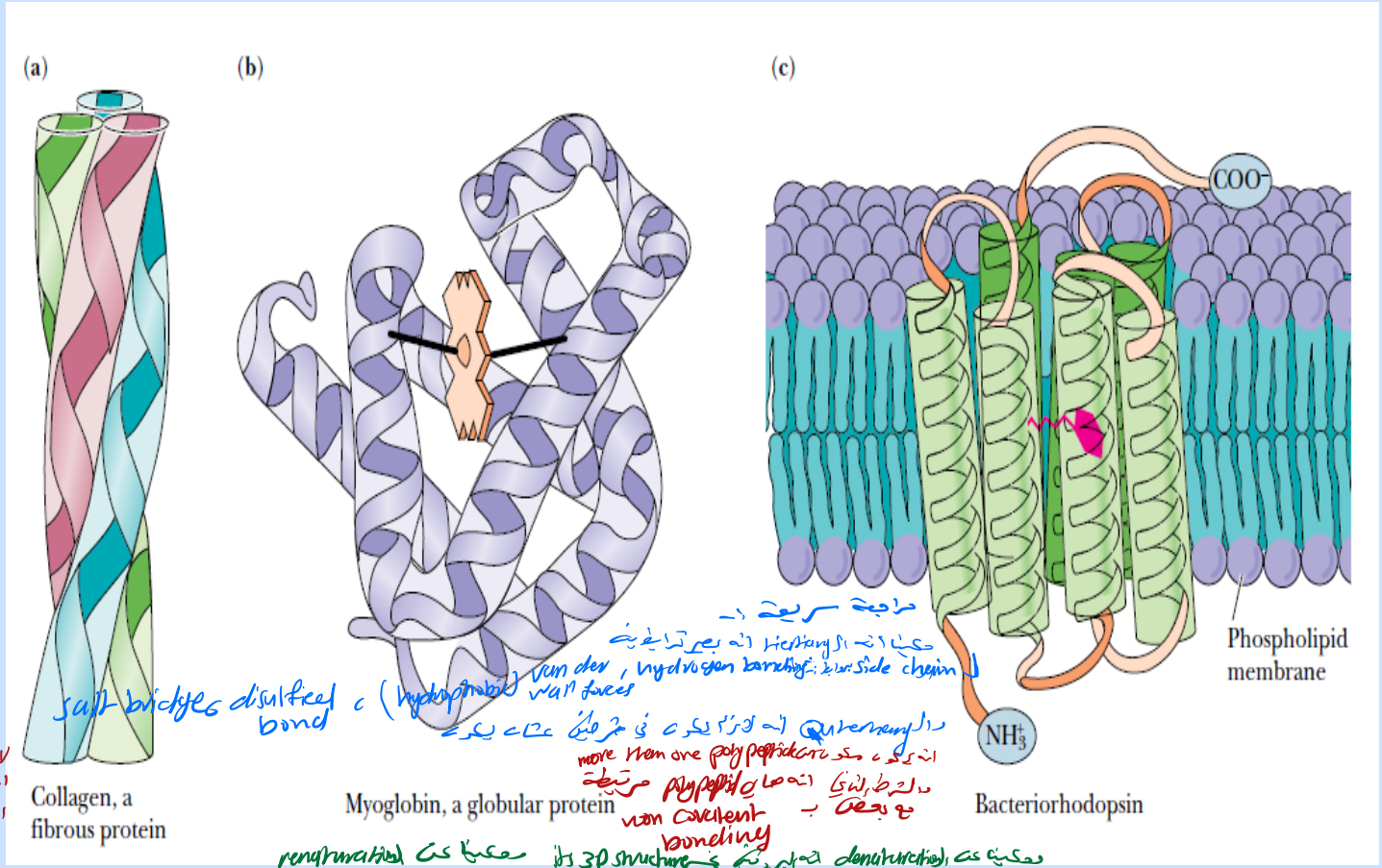
Classification of Proteins



Classification of Proteins

Proteins can be classified based on their shape and solubility into three groups:

1- **Fibrous proteins**: These proteins have a rod like structure. They are not soluble in water. Collagen is an example
these proteins often serve structural roles in cells.

2- **Globular proteins**: Due to their distribution of amino acids (hydrophobic inside, hydrophillic outside) they are very soluble in aqueous solutions (e.g Myoglobin)
these proteins serve metabolic functions

3- **Membrane proteins**: Those membrane proteins that are embedded in the lipid bilayer have extensive hydrophobic amino acids that interact with the non-polar environment of the bilayer interior. Membrane proteins are not soluble in aqueous solutions.
e.g: Rhodopsin
Membrane proteins carry out transport activities, receptor functions, and other related processes

Fibrous Proteins

General characteristics

1-Serve structural roles in cells

•Fibrous proteins are often mechanically strong & highly cross-linked

2-Insoluble in water

3-Secondary structure is simple based on one type only

Fibrous proteins have high alpha-helix or beta-sheet content.

4-Functions in structure of the body or cell (tendons, bones, muscle, hair, skin)

Most are structural proteins.

Examples include:

•Collagen

•Elastin

•Keratin

•Fibroin

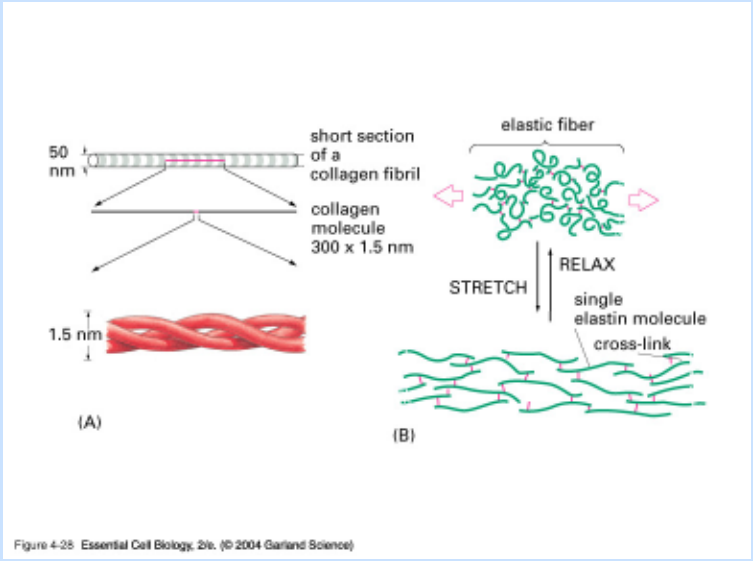
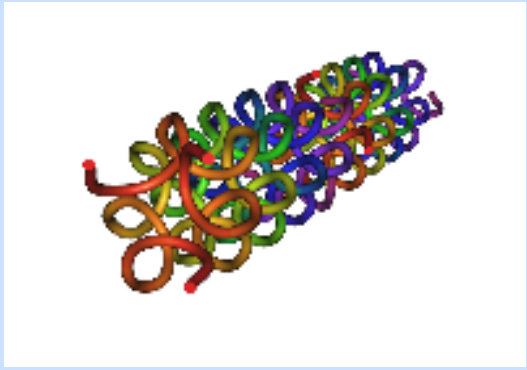


Figure 4-28 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Collagen

is the main structural protein of the various connective tissues in animals.



The collagens are the most abundant proteins in the body. make up from 25% to 35% of the whole-body protein content

- They occur in connective tissues where tensile strength is needed.
- Examples: skin, tendons, cartilage, bones.

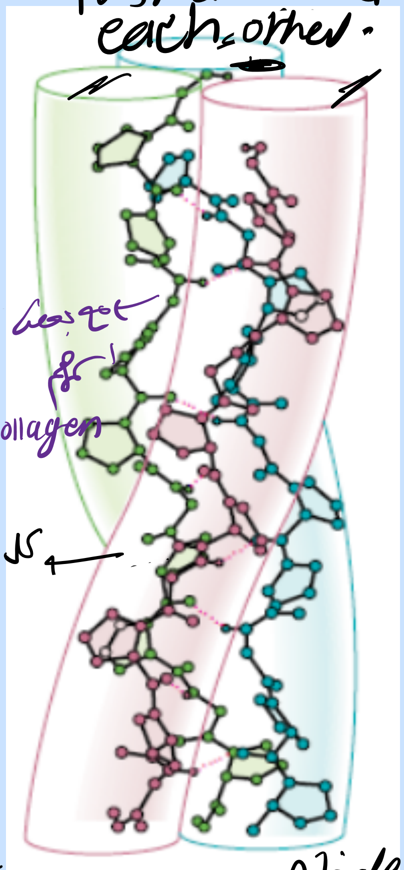
Tensile strength results from the use of:

(a) The triple helix secondary structure
(b) The assembly of tropocollagen subunits into a fibre
(c) Chemical cross linking to strengthen the fibre

Structure of collagen

Collagen is made up of three polypeptides (referred to as "α-chains") that are twisted around one another (tropocollagen) in a rope-like triple-helix and are held together by hydrogen bonds.

Collagen is formed from tropocollagen subunits. The triple helix in tropocollagen is highly extended and strong.



Features:

(1) Three separate polypeptide chains arranged as a left-handed helix (note that an alpha-helix is right-handed).

(2) 3.3 residues per turn

(3) Each chain forms hydrogen bonds with the other two

Types of collagen

In humans at least there are 19 different collagens. Within these 19 structural types, four major classes are generally identified.

Collagen type I
i)The fibers have diameter between 80 to 160nm.
ii)Found in bone, dentin, skin, tendon, muscles and walls of blood vessels.

Collagen type II
i)have a diameter <80nm
ii)found in invertiberal discs and hyaline cartilage.

Collagen type III
Found in spleen, muscle, and aorta.

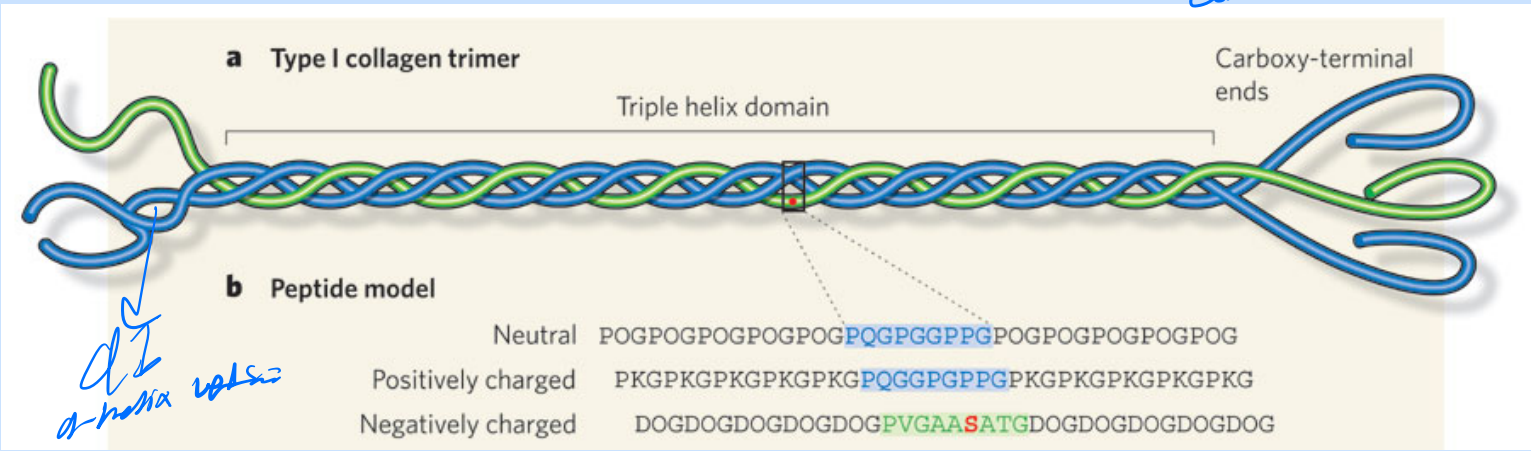
Collagen type IV
Found around different types of the basement membranes and muscles.

Collagen type V
It is found in embryonic cell cultures and the basement membranes.

Collagen type VI
It is ~~found in muscle and skin~~ ir is found in muscle and skin

Types of collagen

Type I collagen, which is the most common, is made up of:
(a) two identical peptide chains designated α1;
(b) one different chain designated α 2



Both type II & III consist of three identical polypeptide chains.

- Compared to the α -helix, the collagen helix is much more extended. There are about 3.3 residues per turn of each of these helices.

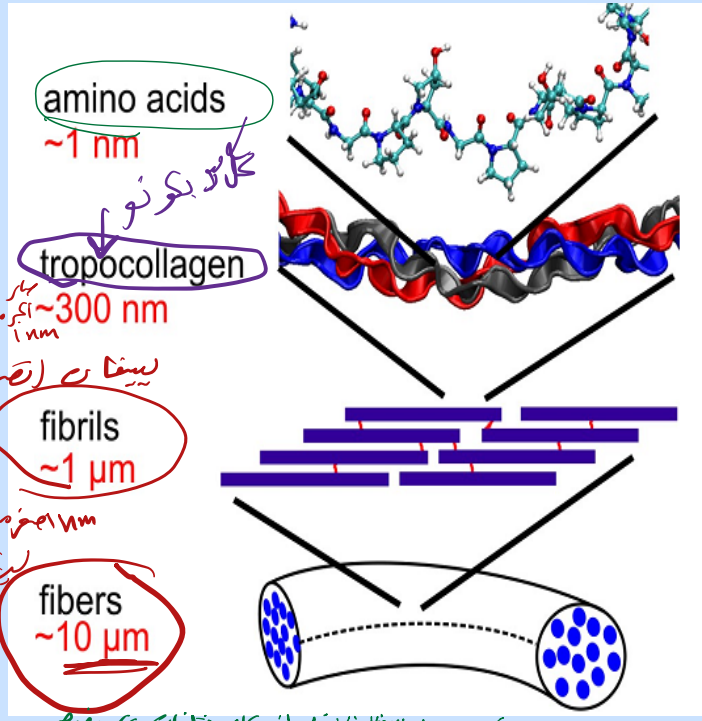
Collagen Amino Acid Composition

- Nearly one residue out of three is Gly
- Proline content is unusually high
- Proline facilitates the formation of the helical conformation of each α-chain because its ring structure causes "kinks" in the peptide chain.

- Many modified amino acids are present:
  - 4-hydroxyproline
  - 3-hydroxyproline
  - 5-hydroxylysine

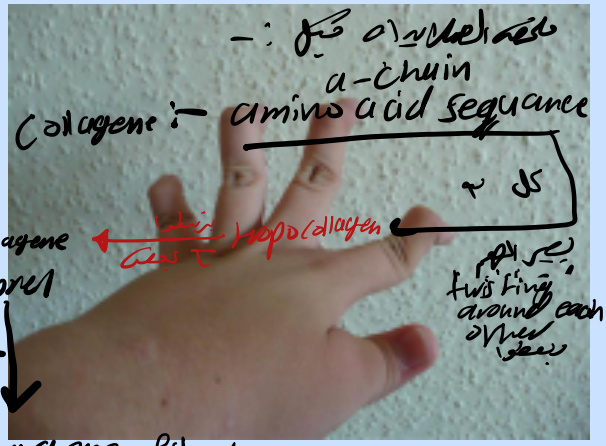
The hierarchical design of collagen.

The structural features of collagen ranges from the amino acid sequence, tropocollagen molecules, collagen fibrils to collagen fibers.



Ehlers-Danlos syndrome (EDS)

Connective tissues are proteins that support skin, bones, blood vessels and other organs.



EDS usually affects your skin, joints and blood vessel walls.

EDS is a group of inherited connective tissue disorders, caused by a defect in the synthesis of collagen (Type I or III).

There is no cure, and treatment is supportive, including close monitoring of the digestive, excretory and particularly the cardiovascular systems.

The fragile skin and loose joints is often a result of abnormal genes that produce abnormal proteins that confer an inherited frailty of collagen (the normal protein "glue" of our tissues).

Collagenopathy

eleven

The type II and XI collagenopathies are a group of disorders that affect connective tissues.

These disorders are caused by defects in type II or type XI collagen.

Type II and type XI collagen disorders are grouped together because both types of collagen are components of the cartilage found in joints and the spinal column, the inner ear, and the jelly-like substance that fills the eyeball

Causes

Mutations in the *COL11A1*, *COL11A2*, and *COL2A1* genes cause collagenopathy, types II and XI.

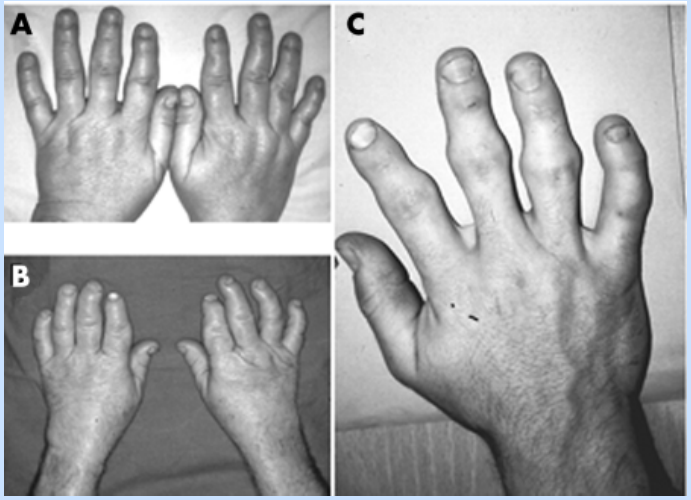
Collagenopathy, type 2 alpha 1:

refers to a wide range of conditions that can result from problems with cartilage collagen tissue due to a defect in the COL2A1 gene.

Defects in the COL2A1 gene result in defective or reduced collagen production which in turn affects the development of connective tissues including bones.

Symptoms of Collagenopathy, type 2 alpha 1

- Abnormal bone development
- Short stature
- Enlarged joints
- Curved spine
- Premature arthritis
- Vision problems
- Hearing problems
- Cleft palate
- Small lower jaw
- Various facial anomalies



Keratin

Keratin is the key structural material making up the outer layer of human skin.

يكون الطبقة الخارجية للجلد

- Tough and insoluble in water
- Main constituent of hair, nails and tooth enamel

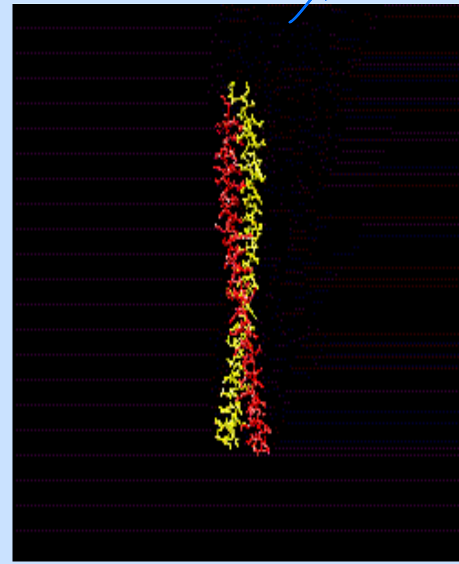
- Two major conformational groups
- (a) alpha-keratin whose peptide backbone forms a α-helix
- (b) β-keratin whose backbone forms a β-sheet structure.

α-Keratin

Made up of α-helix

alpha-keratin is found in hair, nails, outer layer of skin. It forms almost the entire dry weight of these materials.

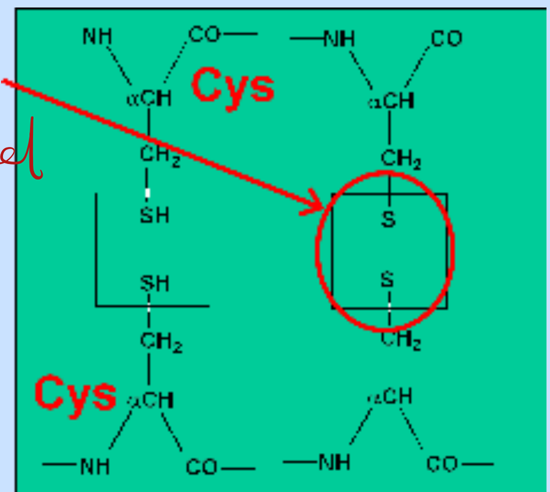
The entire secondary structure is a dimer of two alpha-helices.



It is rich in amino acids that favours alpha-helix formation
These hydrophobic side chains are on the alpha-helix surface-explaining its insolubility.

It is also rich in Cys residues.

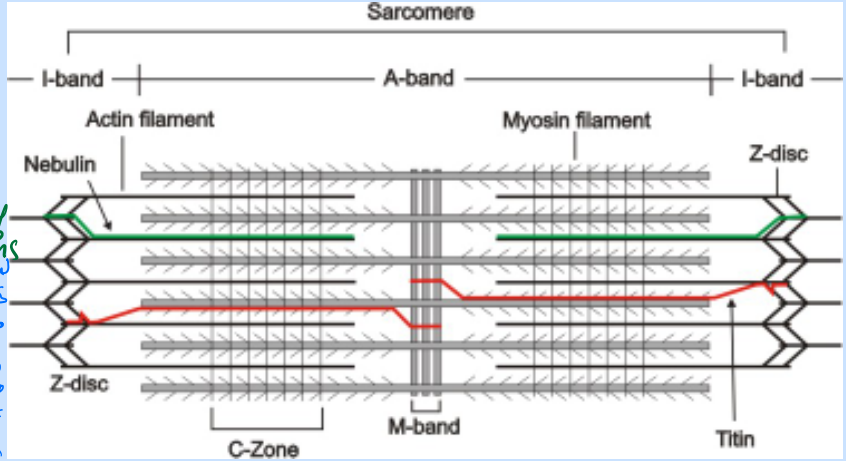
Two Cys residues form disulphide bridges in alpha-keratin, and link the alpha-helices together.



The more disulphides, the stronger the alpha-keratin.

Motor Proteins →

- The most prominent example of a motor protein is the muscle protein myosin and actin which performs the contraction of muscle fibers in animals.



- Sarcomer is the smallest functional structure of the muscle.
- Sarcomere is made up of three different filament:

1- Myosin the thick filaments
2- Actin the thin filaments.
3- Proteins that stabilize the positions of the thick and thin filaments, and proteins that regulate the interactions between thick and thin filaments.

= The myosin head attaches to an actin filament within the sarcomere of a myofibril then pull towards the centre of the sarcomere. In the process, the sarcomere length shortens and the muscle contracts.

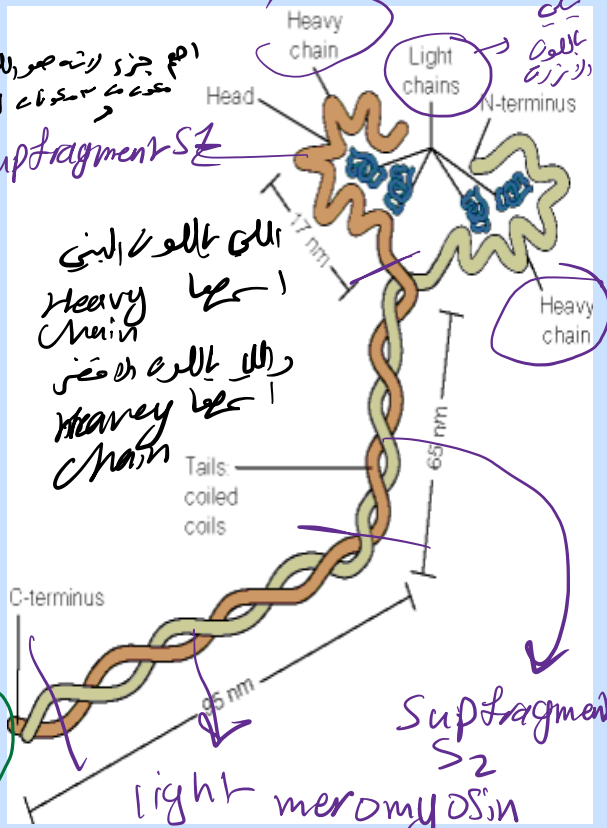
Myosin structure

Myosins are motor proteins that interact with actin thin filament and hydrolyse ATP to generate movement.

Myosin is a hexamer that consists of two heavy chains (220 kDa), and four light chains (~ 20 kDa each) paired into two regulatory light chains and two essential light chains.

The heavy chain consists of three proteolitically defined domains:
1- subfragment 1 (S1) 2- subfragment 2 (S2) and 3- light meromyosin (LMM).

The globular head (S1) forms the actin binding site and the ATPase site and can be further divided into 3 subdomains:
1-the N-terminal 25 kDa nucleotide binding domain
2-the central 50 kDa actin binding domain
3-C-terminal 20 kDa actin binding domain

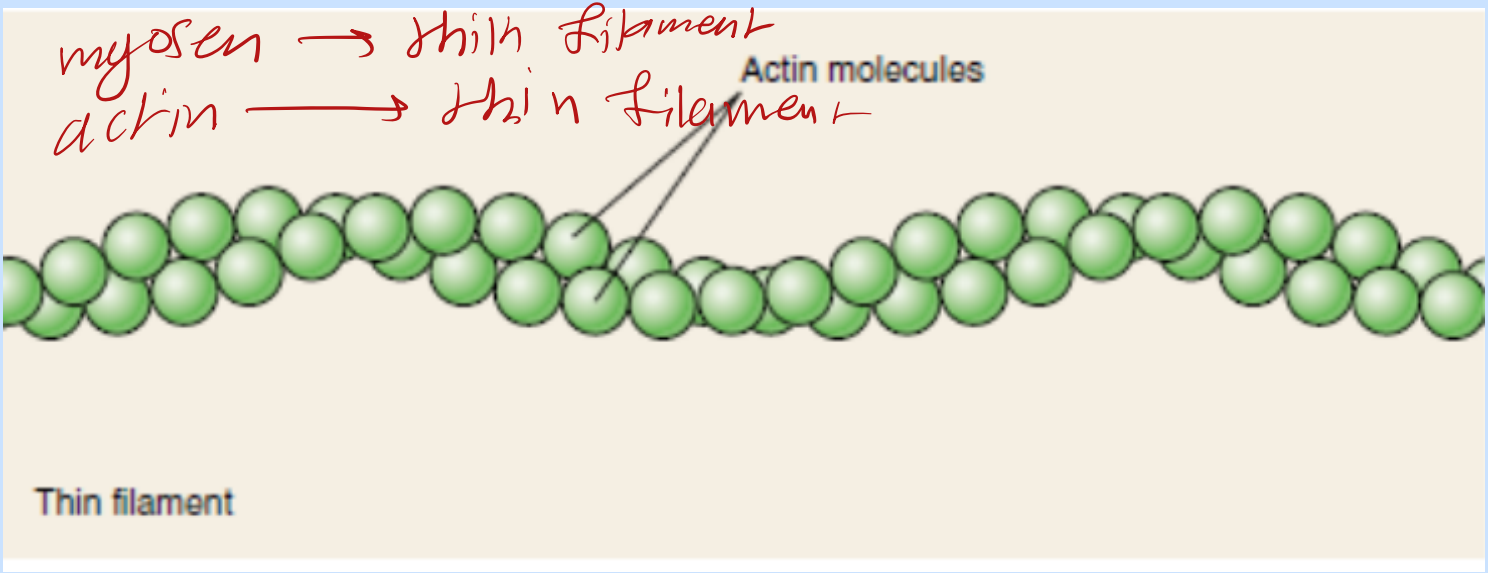


Actin

Actin is a 42 kDa adenine nucleotide-binding protein that made of 375 amino acids, and it is essential for so many cell functions.

Actin is found in two major forms:

Globular which is the monomeric form (G-actin) that can spontaneously polymerise into the filamentous form (F-actin) at physiological salt concentration.



Actin monomers are arranged in a two-strand helix.

Tropomyosin (Tm)

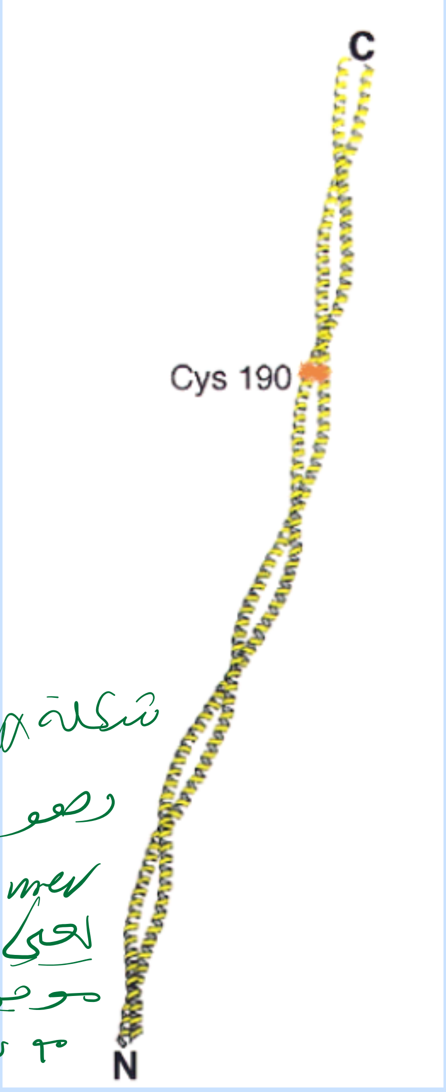
regulatory proteins — دائماً مرتبط مع الأكتين

Tropomyosin (Tm) is a right-handed helical protein which forms a coiled dimer that cooperatively (بشكل تعاوني) binds with actin thin filament.

Each Tm chain is composed of 284 amino acids, and a tight hydrophobic interaction between two chains holds them together

Tropomyosin is always found associated with actin.

Each tropomyosin spans the length of seven actin monomers.



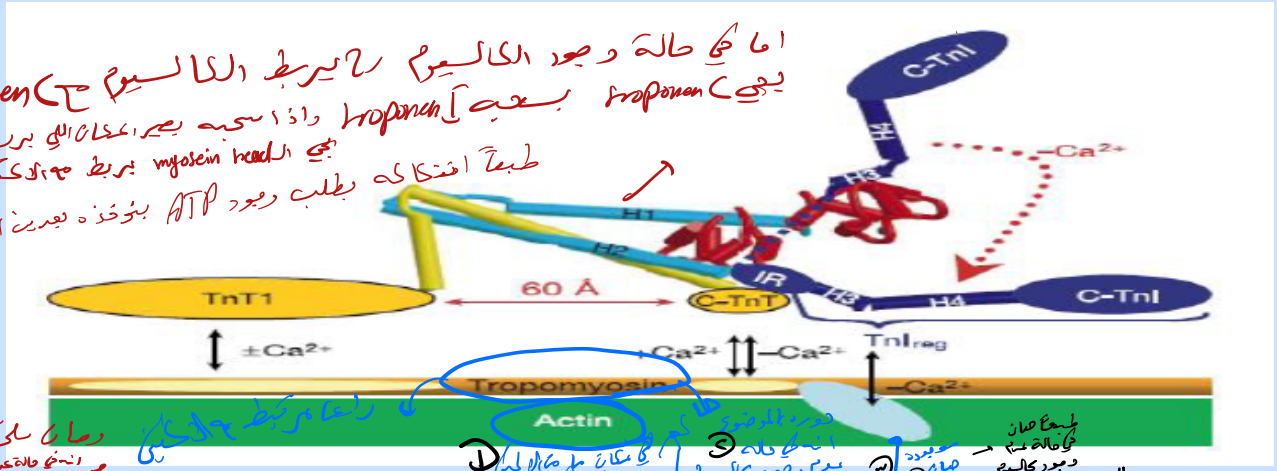
α-helix شكله
وهو موجود as dimer
يعني كماله ما يكون موجود كل تنتين tropomyosin بيرتبطوا dimer

يعني كل ٧ حبات من الأكتين
one tropomyosin
as dimer tropomyosin

Troponin complex (Tn)

Troponin is the calcium-based regulator of striated muscle contraction.

Troponin is a heterotrimeric complex that is composed of three interacting subunits: Troponin C, which is the calcium sensor subunit (18 kDa), Troponin I which is the inhibitory subunit (24 kDa) and Troponin T which is the tropomyosin binding subunit (37 kDa).

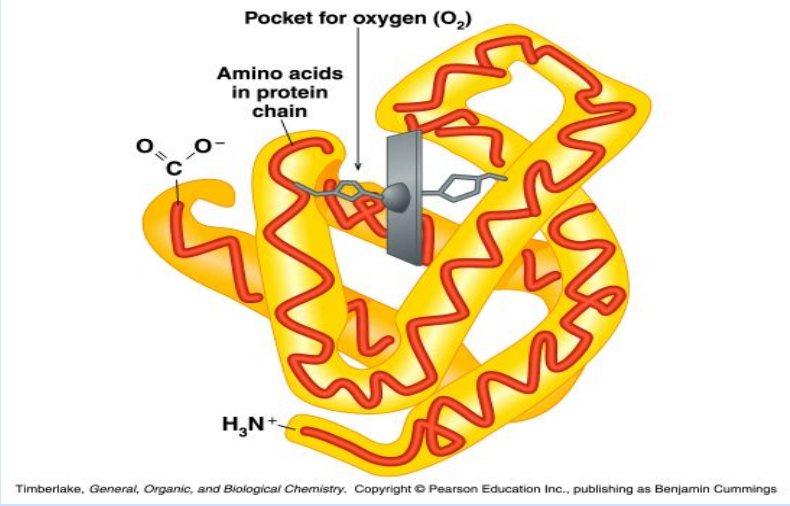


A schematic representation of the interaction between the troponin complex and the rest of the thin filament. The black arrows indicate the interaction between actin-tropomyosin and troponin in the presence and absence of calcium

Globular Proteins

Globular proteins, also known as sphero-proteins, are proteins formed by compacted amino acid chains, which are folded into intricate shapes that often roughly resemble spheres.

A key difference between globular proteinsand fibrous proteins is that the former type of protein is usually soluble in water, while the latter type is not.



- Globular proteins comprise the most varied type of proteins. Globular proteins are soluble in aqueous solution. To achieve this, globular proteins generally have polar residues on the surface and hydrophobic residues on the interior.
- Globular proteins include enzymes, transport proteins, regulatory proteins, proteins with many other functions.

Classification of Globular Proteins According to Secondary Structure

All alpha: Proteins that contain only alpha helical secondary structure. Myoglobin is an example of an all alpha protein.

All beta: Protein that contain only beta-sheet secondary structure. Tenascin is an example of an all beta protein.

Alpha/beta: Proteins that contain alternating alpha-helical and beta-sheet secondary structure elements. Triose Phosphate Isomerase is an example of an alpha/beta protein.

Alpha + Beta: In these proteins the alpha helical and beta sheet regions occur in independent regions of the molecule. Ribonuclease A is an example of an alpha+beta protein.

Oxygen-binding proteins

Globular protein ← شكله كروي

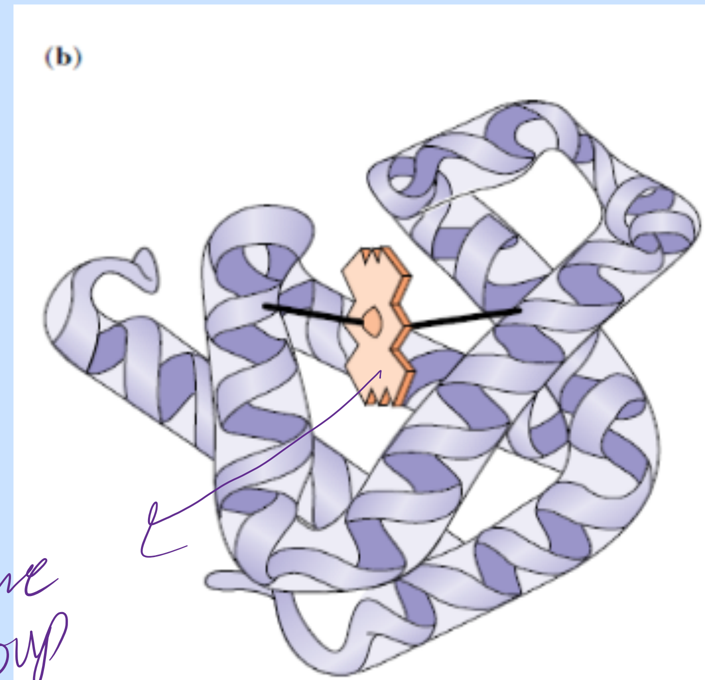
- Myoglobin and Hemoglobin are the two oxygen-binding proteins present in large multicellular organisms.

Myoglobin stores the oxygen in the muscles.

مستودع يخزن الاكسجين في العضلة

Hemoglobin transports oxygen in the blood and is located in the red blood cells

هو الي بنقل الاكسجين هو يستخدم في العضلات او هو يخزن او لكل الجسم



Heme group

Myoglobin (Mb)

- 75% of structure is α-helix in 8 regions, these are termed helices A, B, C, D, E, F, G, and H.
- Myoglobin consists of a single polypeptide chain of 153 amino acids attached to a single heme group

Myoglobin interior almost entirely nonpolar residues

- Mb Stores and facilitates oxygen diffusion in muscles especially in heart and skeletal muscle.

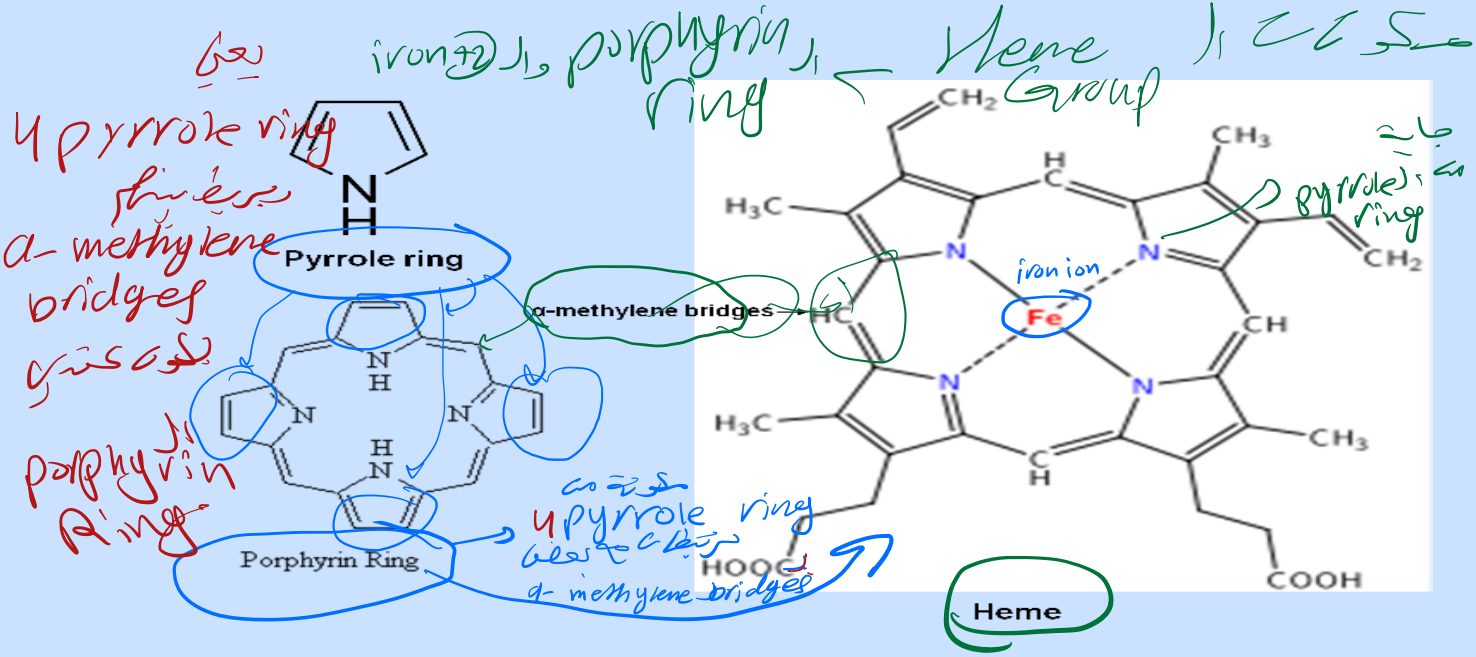
- The eight α helical segments are folded into a globular structure, creating a cradle (box) and within this cradle lies a single heme group and the binding site of O2.

The heme of myoglobin lies between helices E and F.

- Three critical functions for Mb: 1- it holds the heme group, 2- it protects the heme iron atom from oxidation, and 3- it provides a pocket into which the O_2 can fit.

Structure of heme in myoglobin

- Heme is a complex of porphyrin and ferrous iron (Fe^{2+}).
- Porphyrins are a group of organic compound that have four pyrrole subunits interconnected via α-methylene bridges (=CH–)



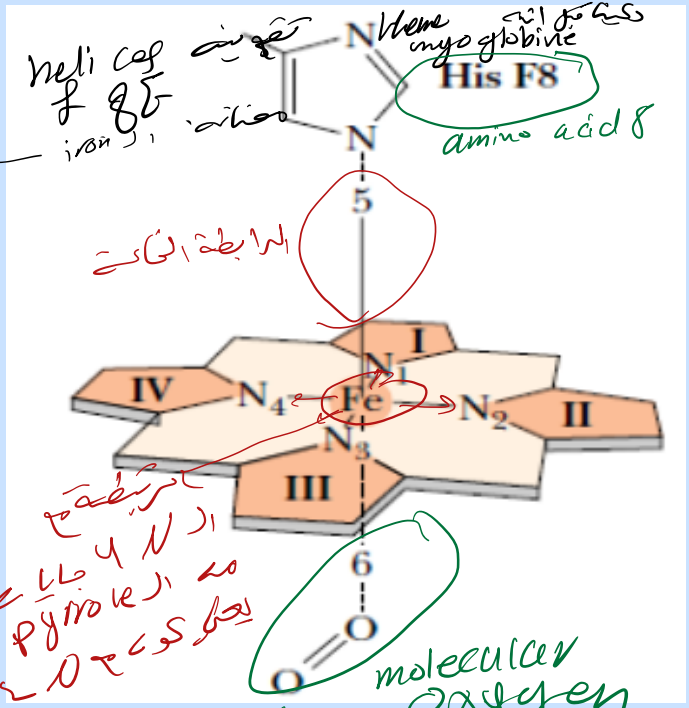
The hydrophobic environment in the interior of myoglobin or hemoglobin prevents the oxidation of iron.

Heme structure

- The iron is held in the center of the porphyrin ring.
- Iron ions prefer to interact with six ligands.
- Four of the ligands to this iron ion are provided by nitrogen atoms in the pyrrole ring system.

-The fifth ligand is provided by a nitrogen atom from the imidazole group of His 93 (proximal histidine) (also known as His F8 the eighth residue of the 'F helix' of myoglobin).

The sixth ligand to iron is provided by molecular oxygen, which binds to the heme group in a pocket formed by Mb.



وبنروح نمه

والرابطة السادسة مع ال molecular oxygen

طبعاً المرة الجاي بدنا نعرف انه اذا الاكسجين ربط شو بأثر 4 على شكل البروتين واذا فك شو بأثر على شكل البروتين

وبعدين نحكي انه مجرد ما يرتبط ال iron ب fe الاكسجين

2 بسبب الاكسجين ال iron عليه وبكا بتحب

ال iron مغناطيس

2 بحكي البروتين

بيصير rubchring بشكل الهيموغلوبين

الحمد لله

صلوا عالنبي ♥