Structure-function relationship: Fibrous proteins

Prof. Mamoun Ahram
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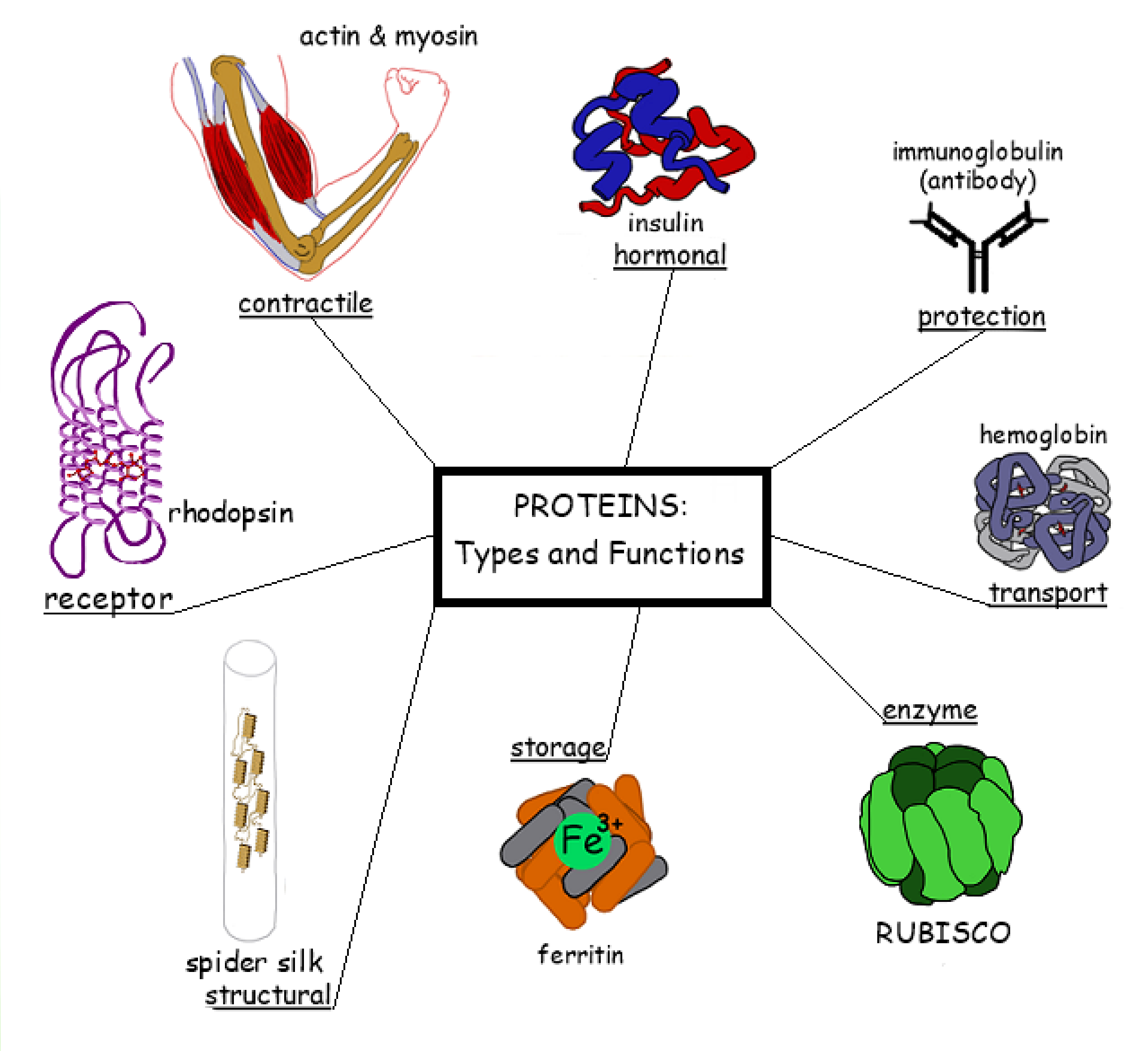
Biological Functions of Proteins

- Enzymes--catalysts for reactions
- Transport molecules—
  - hemoglobin; channel proteins
- Contractile/motion—
  - myosin; actin
- Structural—
  - collagen; keratin, actin
- Defense--antibodies
- Signaling—hormones, receptors
- Toxins--diphtheria; enterotoxins

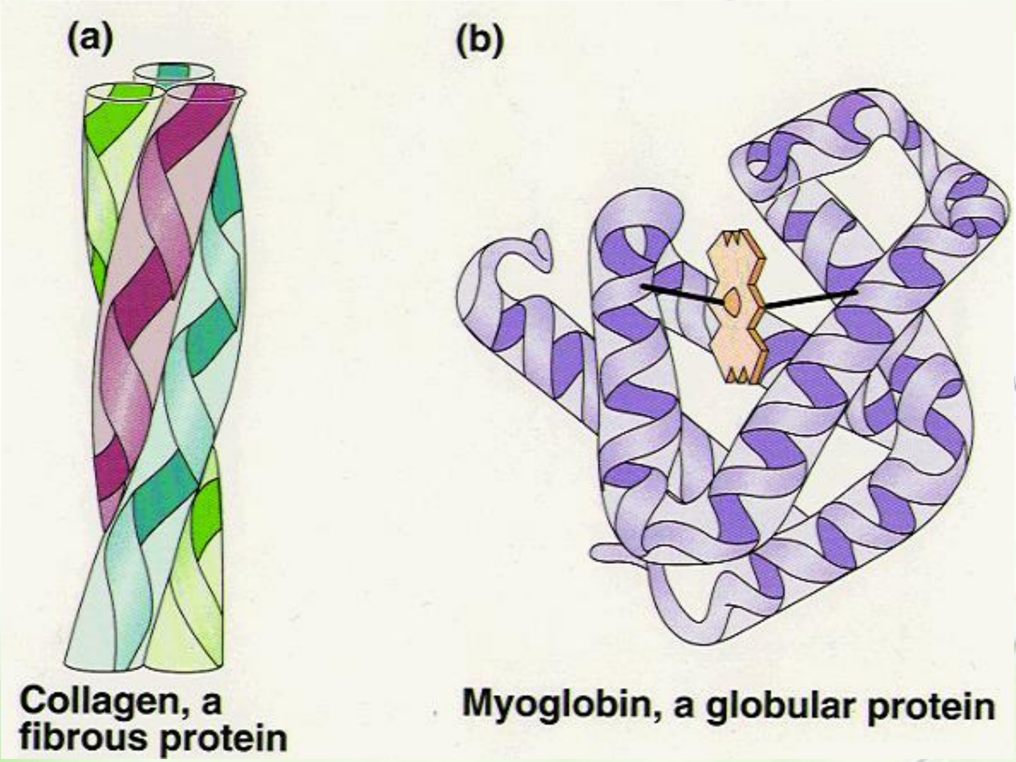


Types of proteins

- Proteins can be divided into two groups according to structure:
  - fibrous (fiber-like with a uniform secondary-structure only)
  - globular (globe-like with three-dimensional compact structures)

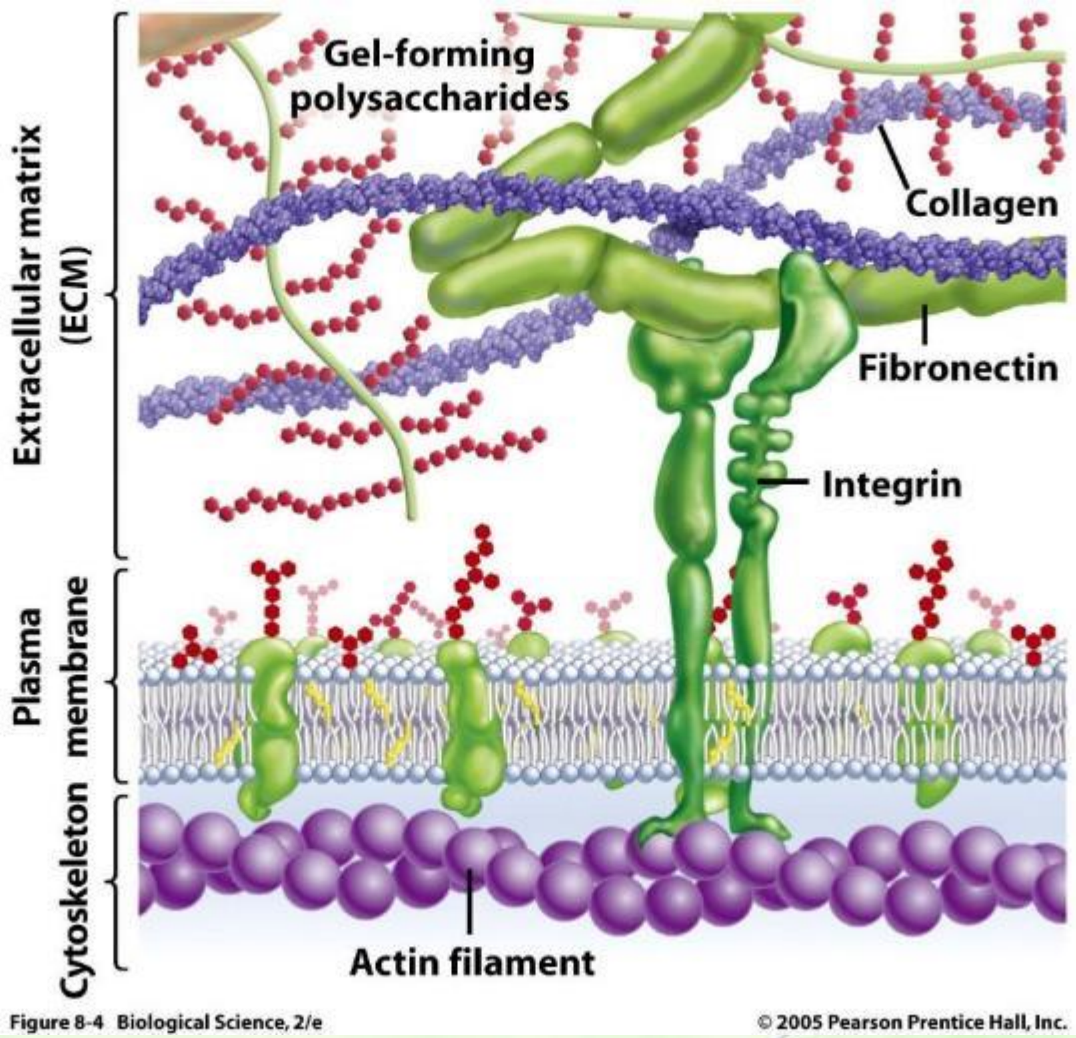
<u>Examples</u>

- Fibrous proteins: collagens, elastin, and keratins
- Globular proteins: myoglobin, hemoglobin, and immunoglobulin

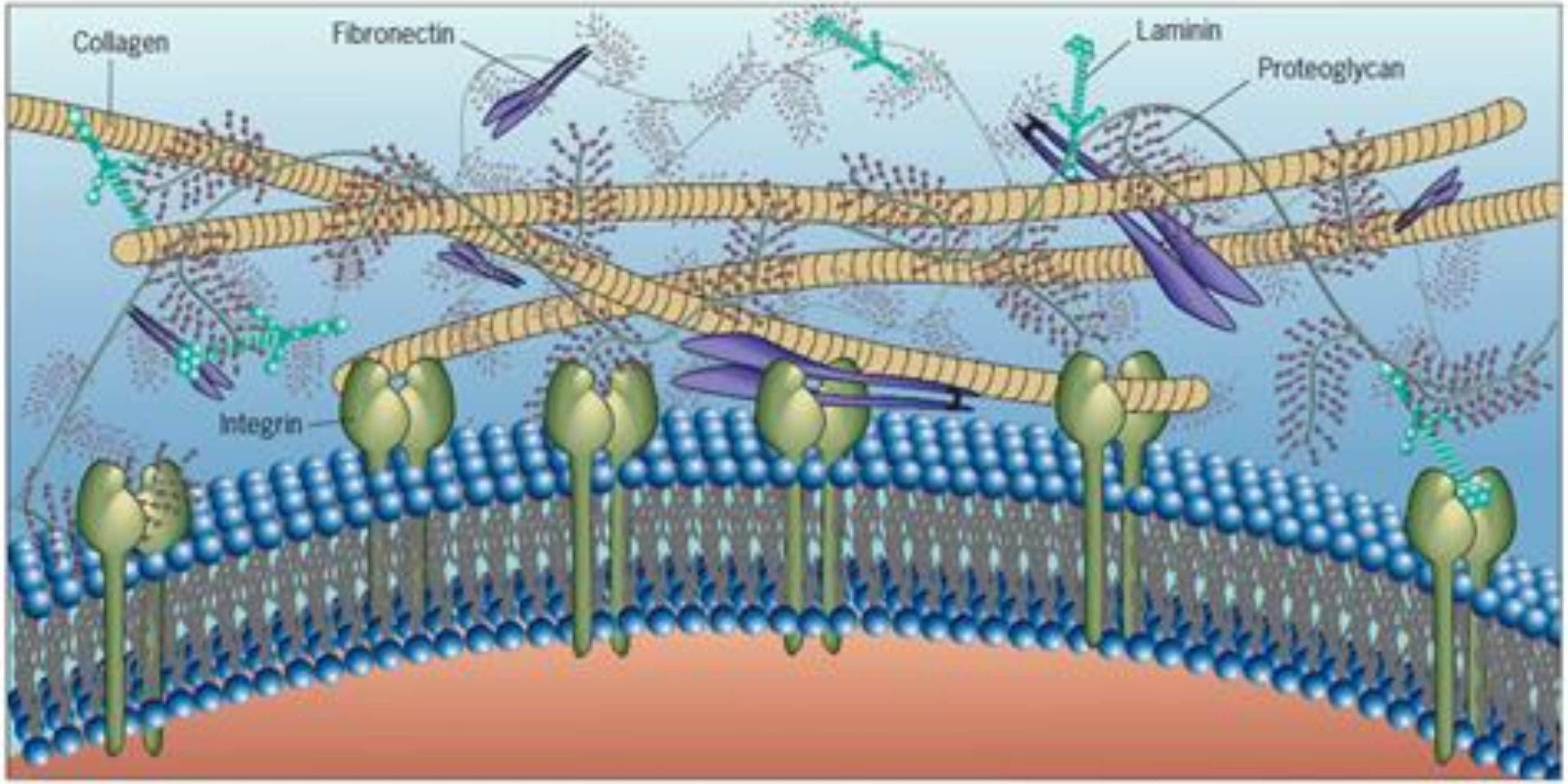


The extracellular matrix

- The extracellular space is largely filled by an intricate network of macromolecules including proteins and polysaccharides that assemble into an organized meshwork in close association with cell surface.

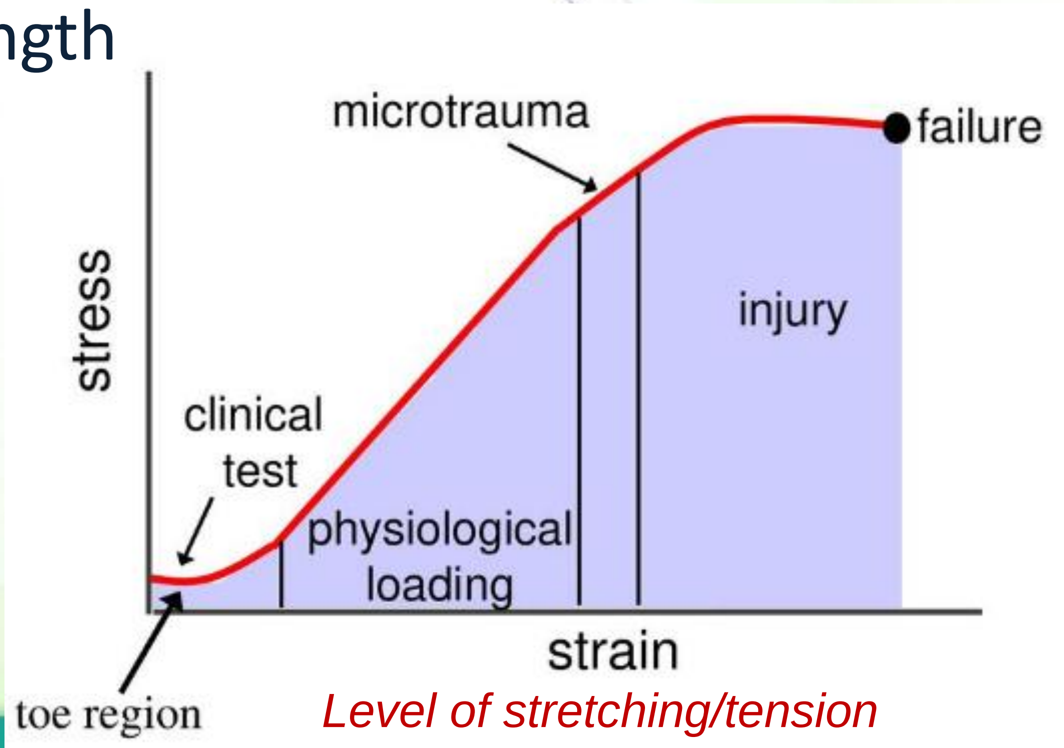


Collagens



Collagens and their properties

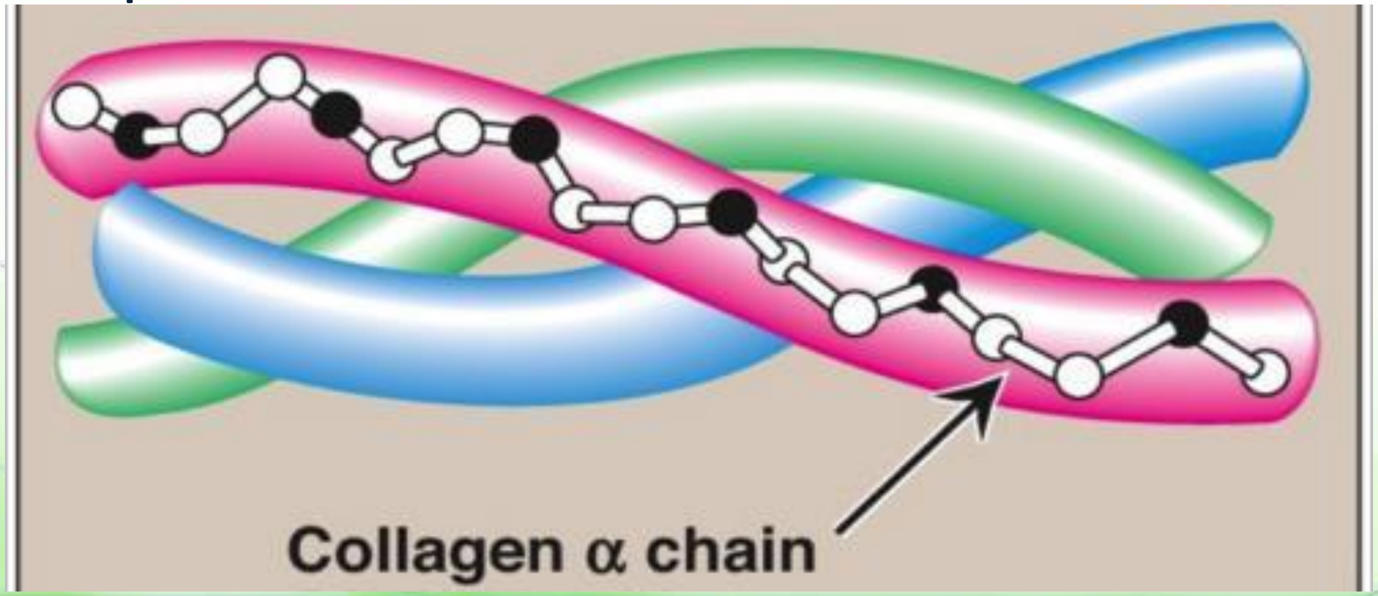
- A family of fibrous proteins of 40 types found in all multicellular animals
- Most abundant proteins in mammals (25% of he total protein mass)
- Named as type I collagen, type II collagen, type III collagen, and so on
- Main function: structural support to tissues
- Primary feature: stiffness and tensile strength



Level of stretching/tension

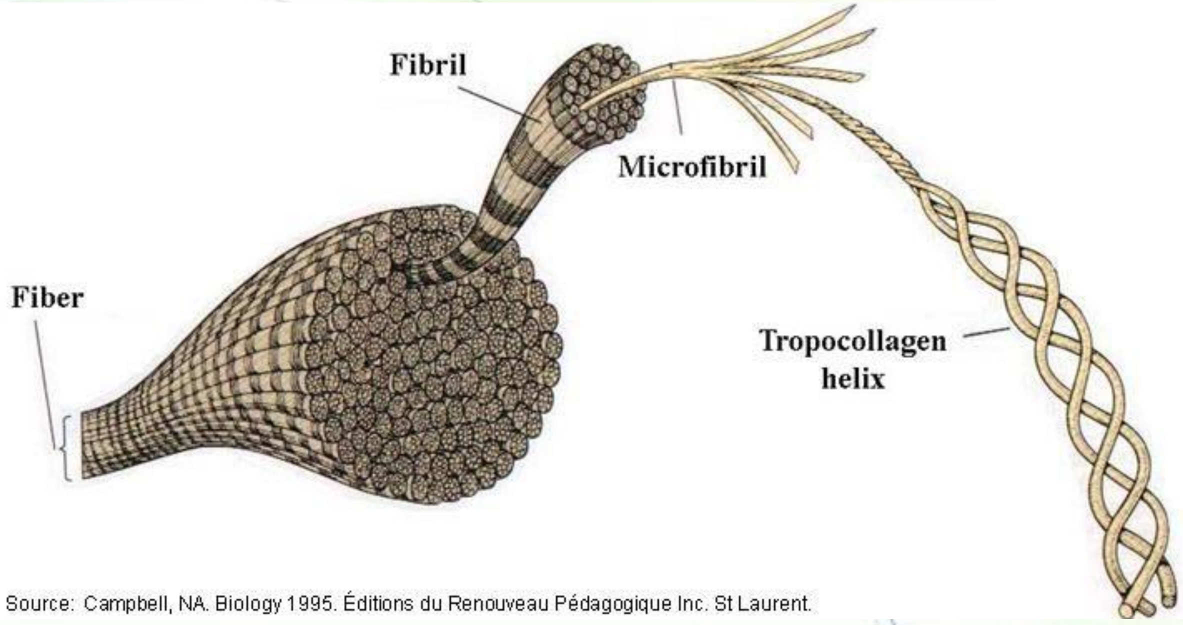
Structure

- It is a triple-stranded, helical protein, in which three collagen polypeptide chains, called α chains, are wound around one another in a ropelike superhelix.
- This basic unit of collagen is called tropocollagen.
- Compared to the α -helix, the collagen helix is much more extended with 3.3 residues per turn.



Formation of collagen fibers

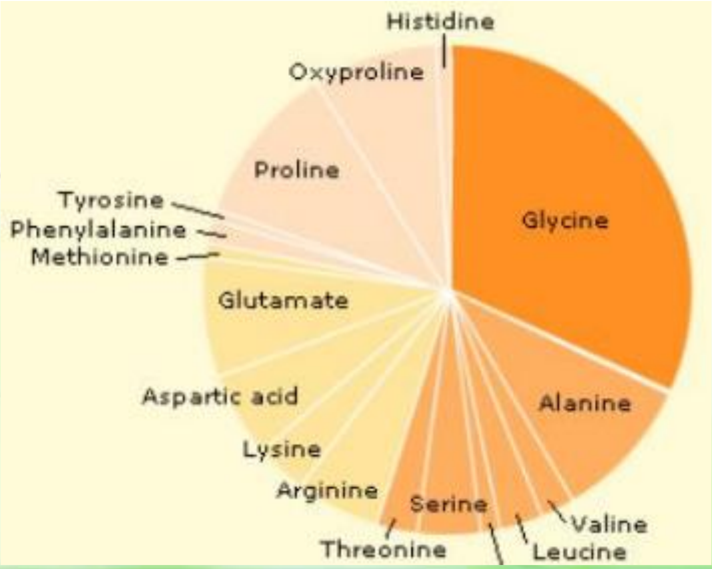
- Following cellular release of protocollagen, 5 of them polymerize into a microfibril, which are connected with each other via aldehyde links.
- Microfibrils align with each other forming larger collagen fibrils, which are strengthened by the formation of covalent cross-links between lysine residues.
- Fibrils assemble into collagen fibers.

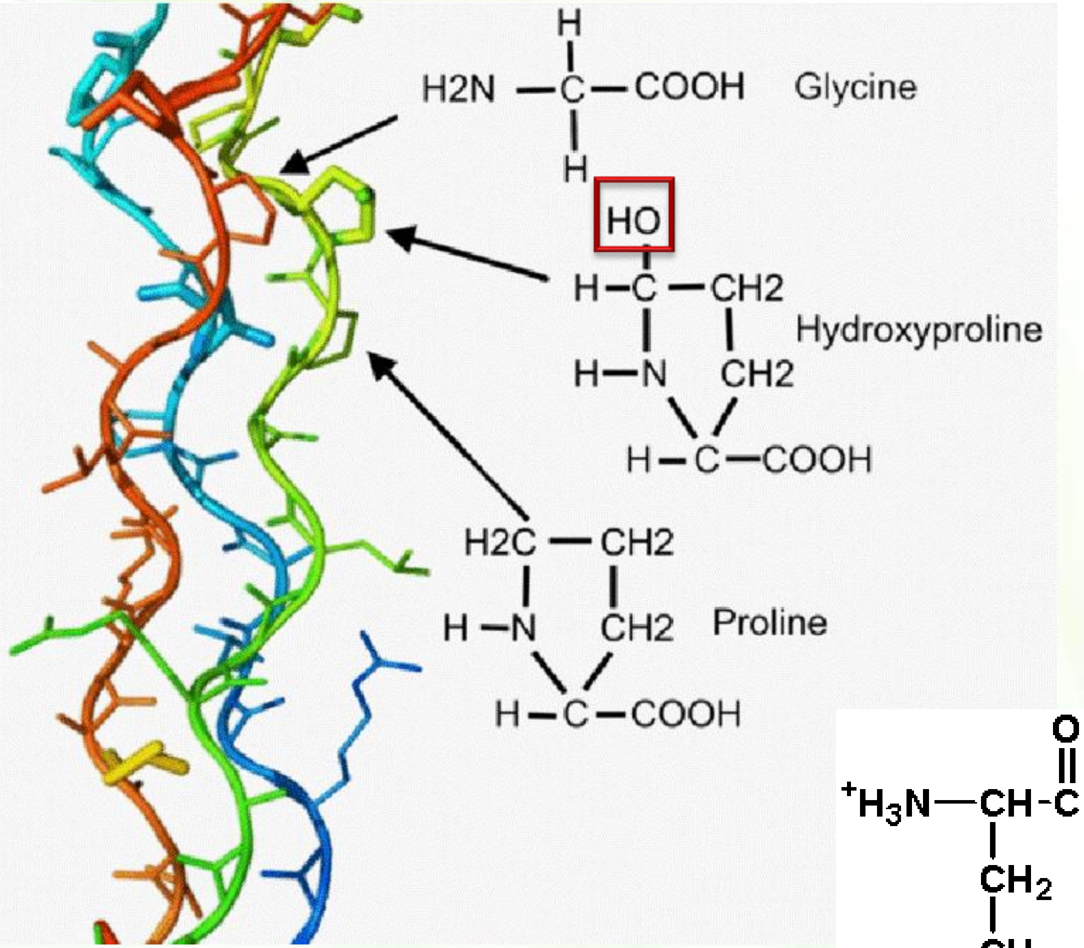


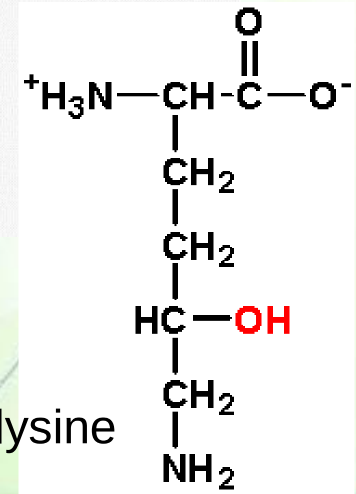
Source: Campbell, NA. Biology 1995. Éditions du Renouveau Pédagogique Inc. St Laurent.

Composition of collagens

- Collagens are rich in glycine (33%) and proline (13%).
    - Every third residue is a glycine.
- They unusually in contain hydroxyproline (9%) and hydroxylysine.
- Primary structure: Gly X-Y
    - **X** is often proline and **Y** is often hydroxyproline.



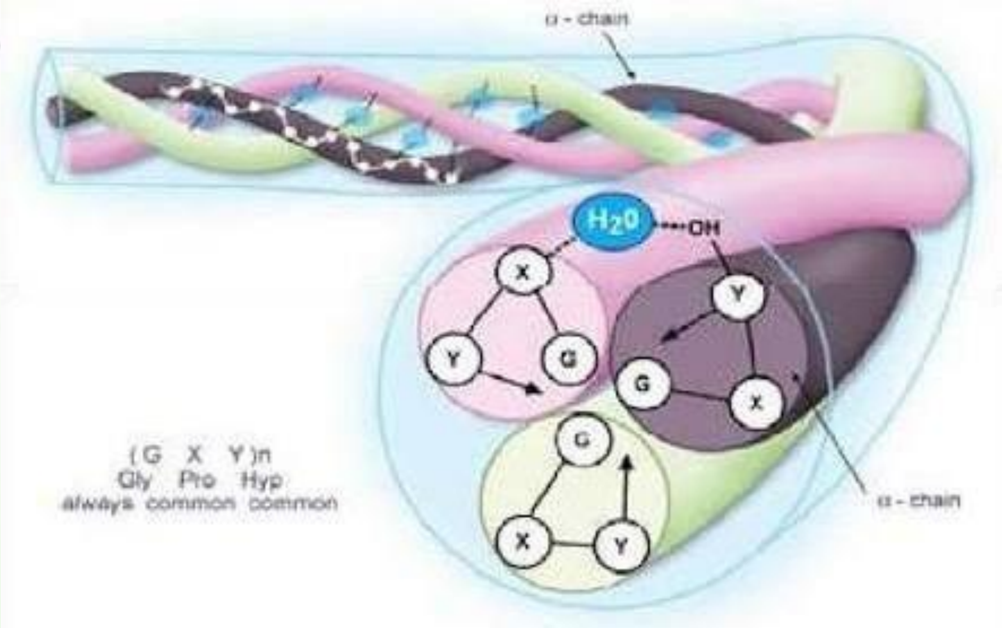


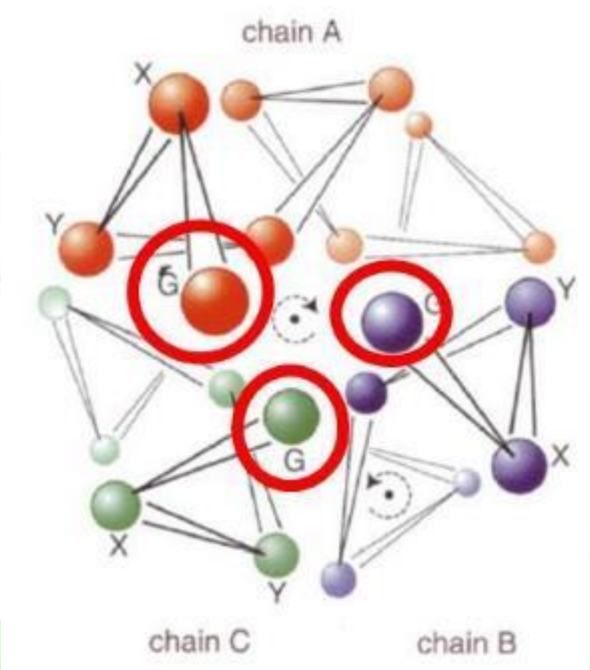


Hydroxylysine

Functional purpose of amino acids

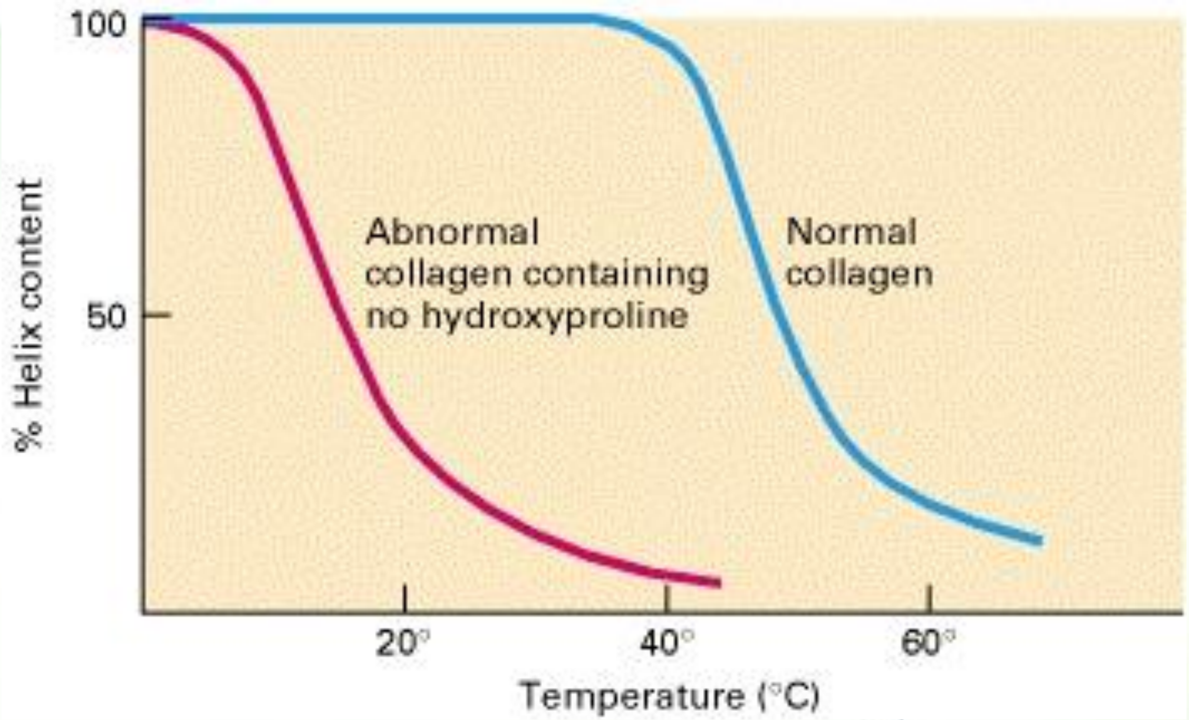
- Glycine allows the three helical a chains to pack tightly together to form the final collagen superhelix and provides flexibility to the molecule because it can rotate freely.
- Proline creates the kinks, stabilizes the helical conformation in each a chain, and provides rigidity to collagens.





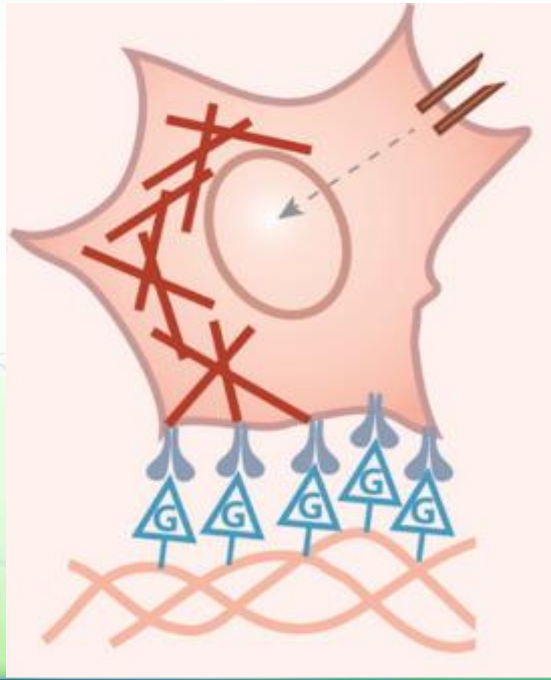
Purpose of hydroxyproline

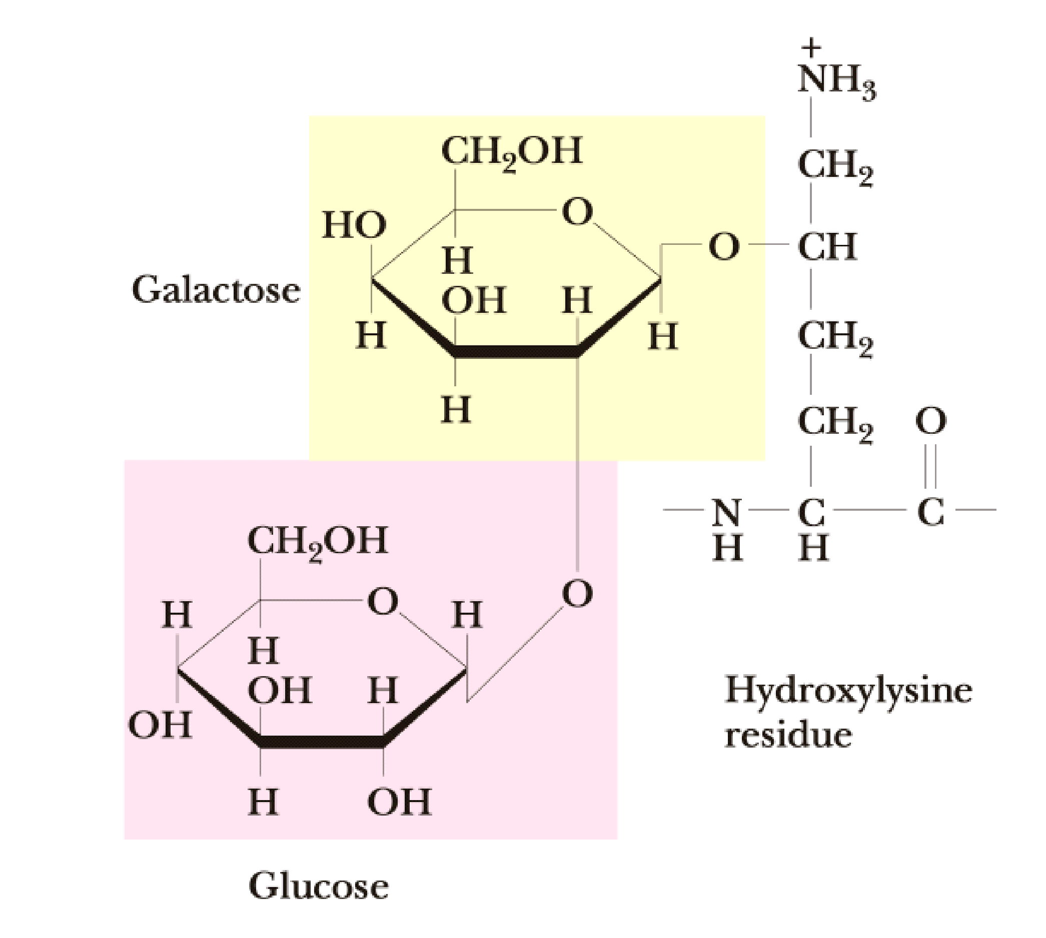
- Normal collagen is stable even at 40°C.
- Without hydrogen bonds between hydroxyproline residues, the collagen helix is unstable and loses most of its helical content at temperatures above 20°C



Hydroxylysine

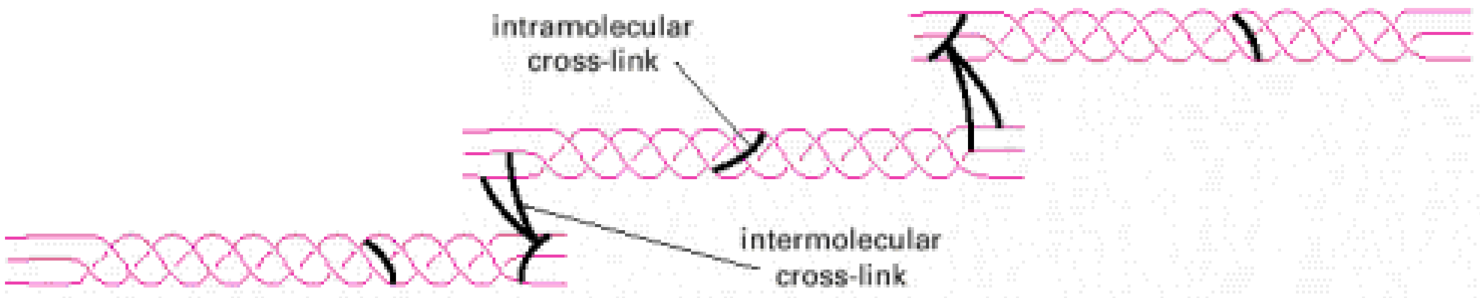
- Hydroxylysine serves as attachment sites of polysaccharides making collagen a glycoprotein.
- Sugars allows collagen to recognize and interact with cell surface receptors.

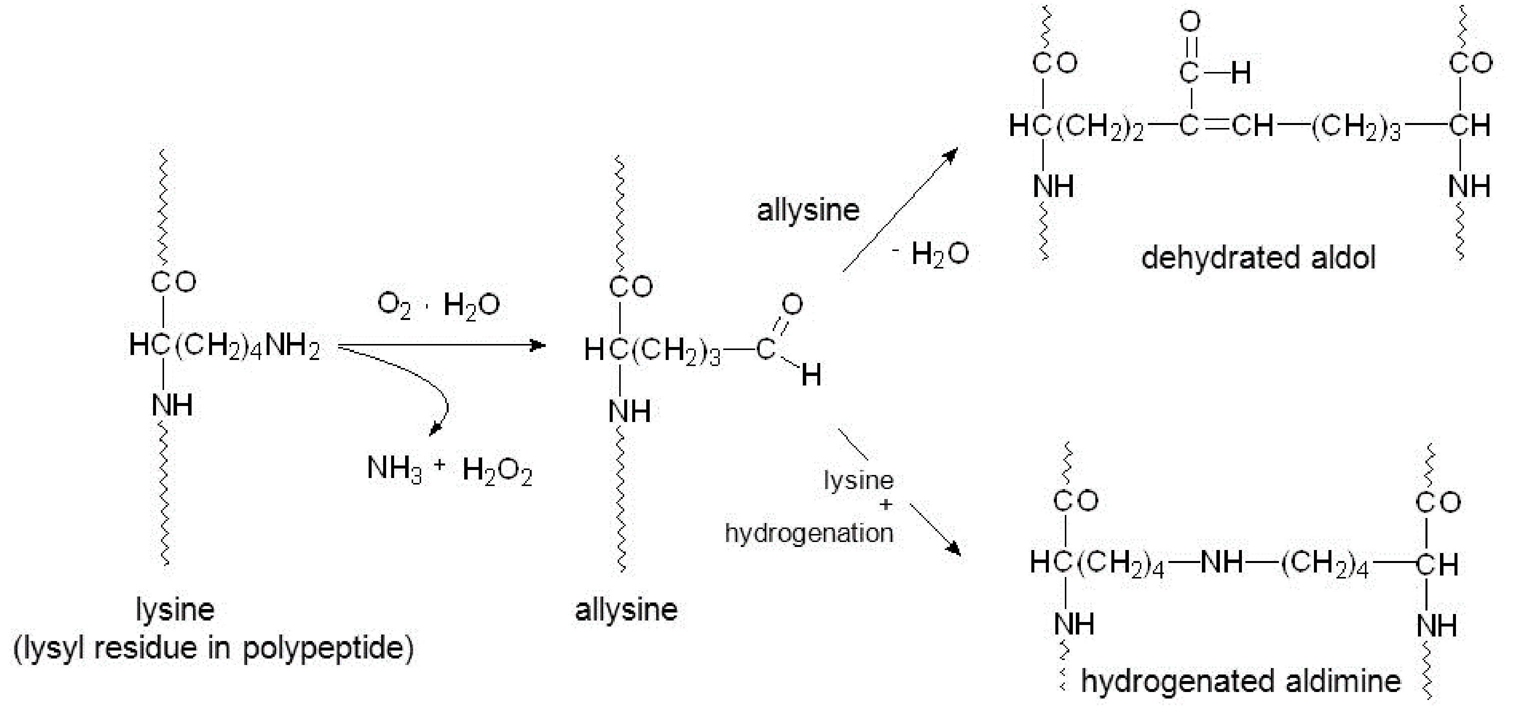




Oxidation of lysine

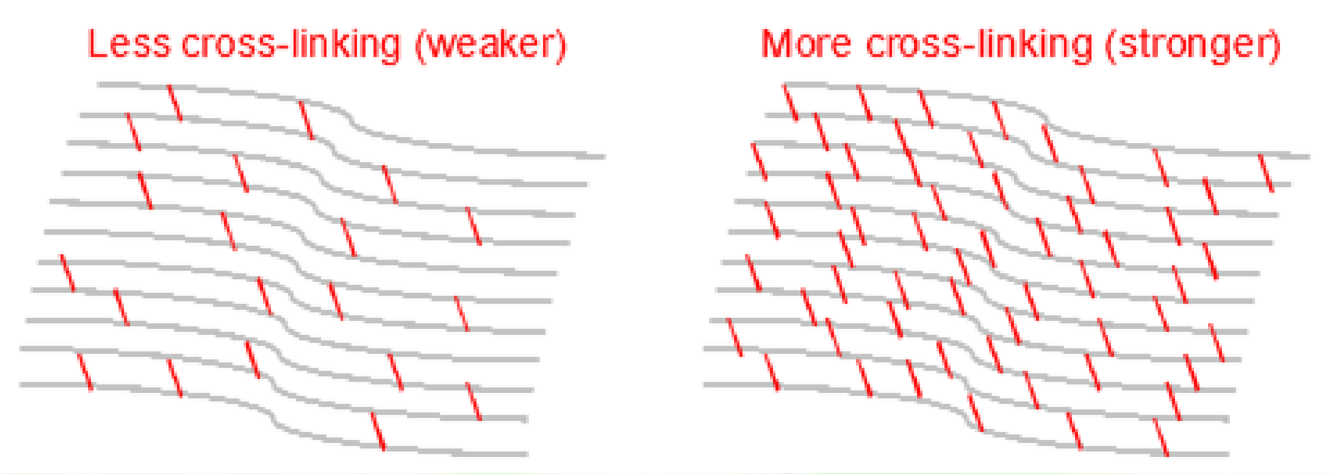
- Some of the lysine side chains are oxidized to aldehyde derivatives known as allysine.
- Allysine cross-links with another allysine, hydroxylysine, or lysine residues within the same or with another tropocollagen.
- These cross-links stabilize the side-by-side packing of collagen molecules and generate a strong fibril.





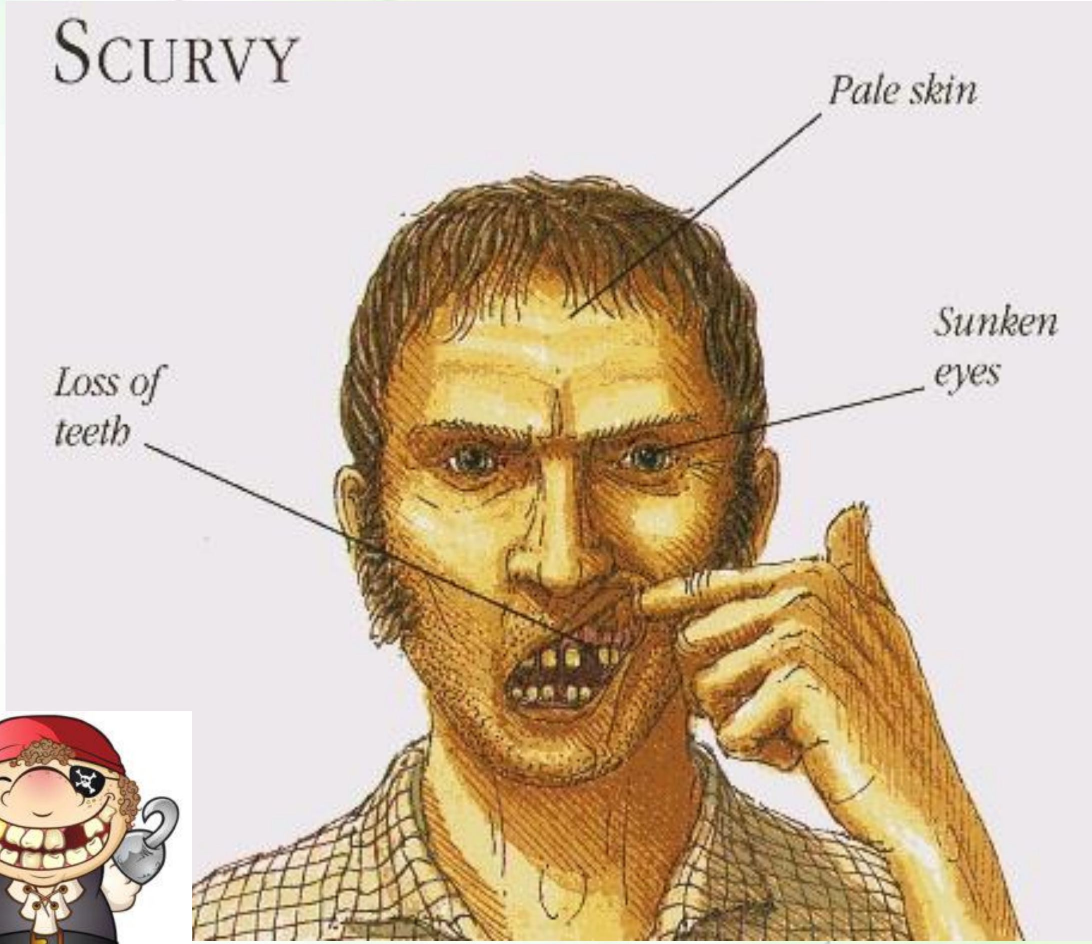
Function of cross-linking

- If cross-linking is inhibited, the tensile strength of the fibrils is drastically reduced; collagenous tissues become fragile, and structures such as skin, tendons, and blood vessels tend to tear.
- Deficiency of hydroxylation can cause diseases such as Ehlers-Danlos syndrome.
- The amount of cross-linking in a tissue increases with age. That is why meat from older animals is tougher than meat from younger animals.

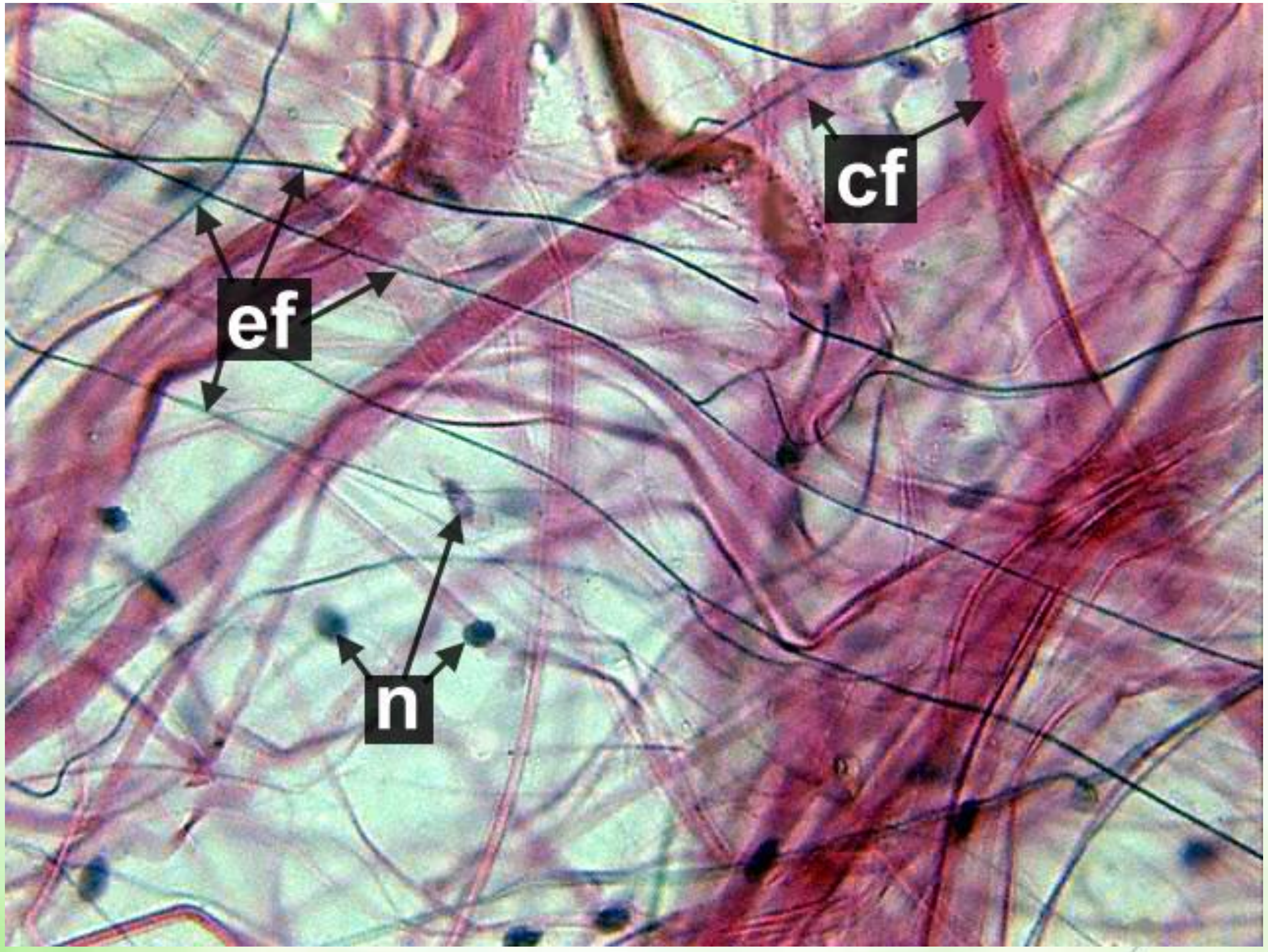


Scurvy

- Scurvy is a disease is caused by a dietary deficiency of ascorbic acid (vitamin C).
- Deficiency of vitamin C prevents proline hydroxylation.
- The defective pro-α chains fail to form a stable triple helix and are immediately degraded within the cell.
- Blood vessels become extremely fragile and teeth become loose in their sockets.

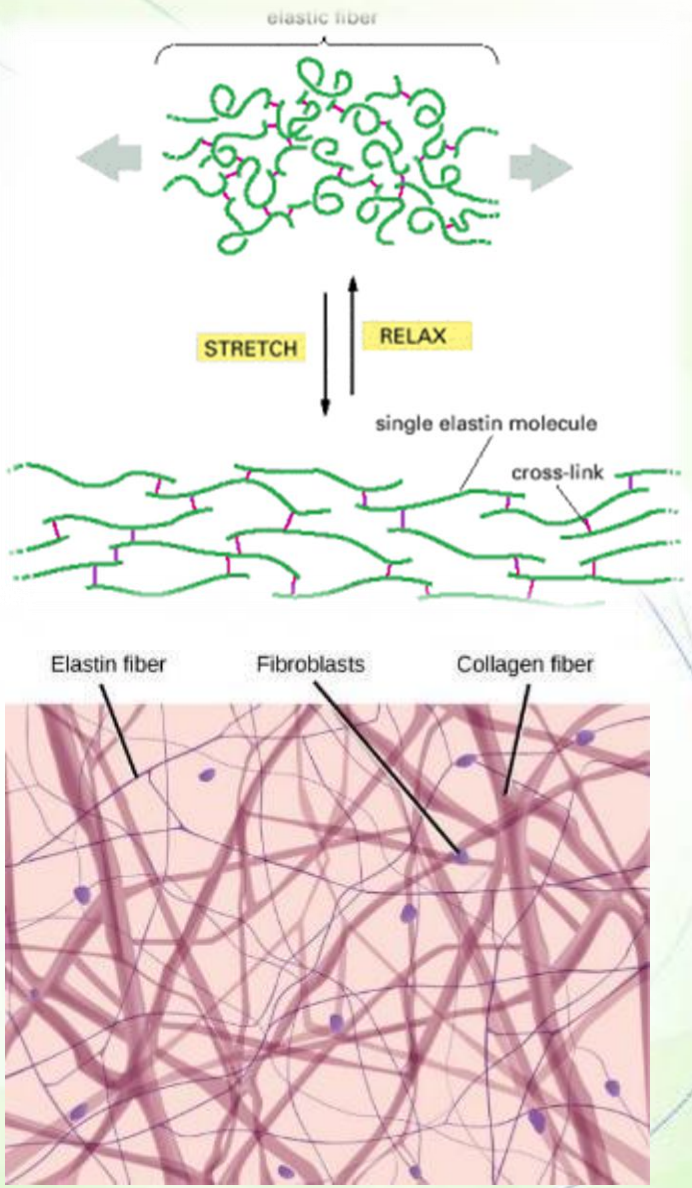


Elastin



Resilience vs. flexibility

- Many tissues, such as skin, blood vessels, and lungs, need to be both strong and elastic in order to function.
- A network of elastic fibers in the extracellular matrix of tissues gives them the required resilience so that they can recoil after transient stretch.
- Long, inelastic collagen fibrils are interwoven with the elastic fibers to limit the extent of stretching and prevent the tissue from tearing.



Elastin

- The main component of elastic fibers is elastin, which is a highly hydrophobic protein and is rich in proline and glycine.
- It contains some hydroxyproline, but no hydroxylysine.
  - It is not glycosylated.
- The primary component, tropoelastin molecules, is cross-linked between lysines to one another.

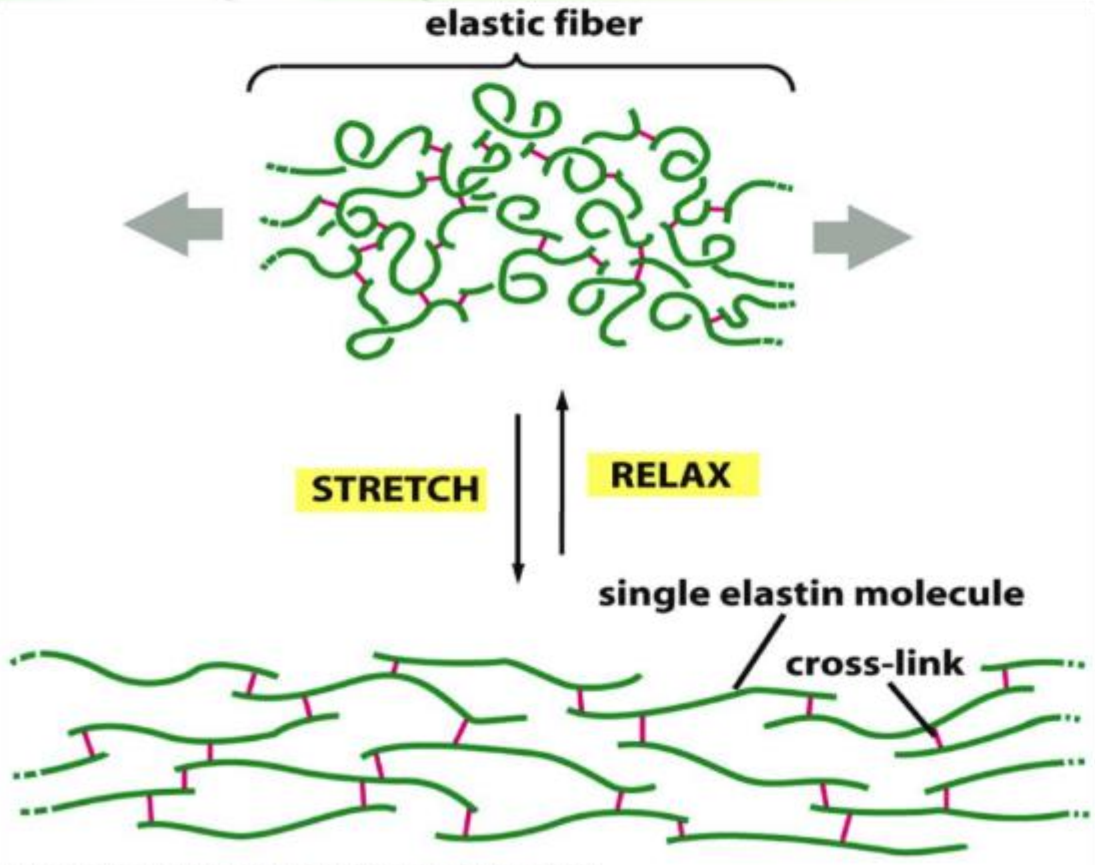
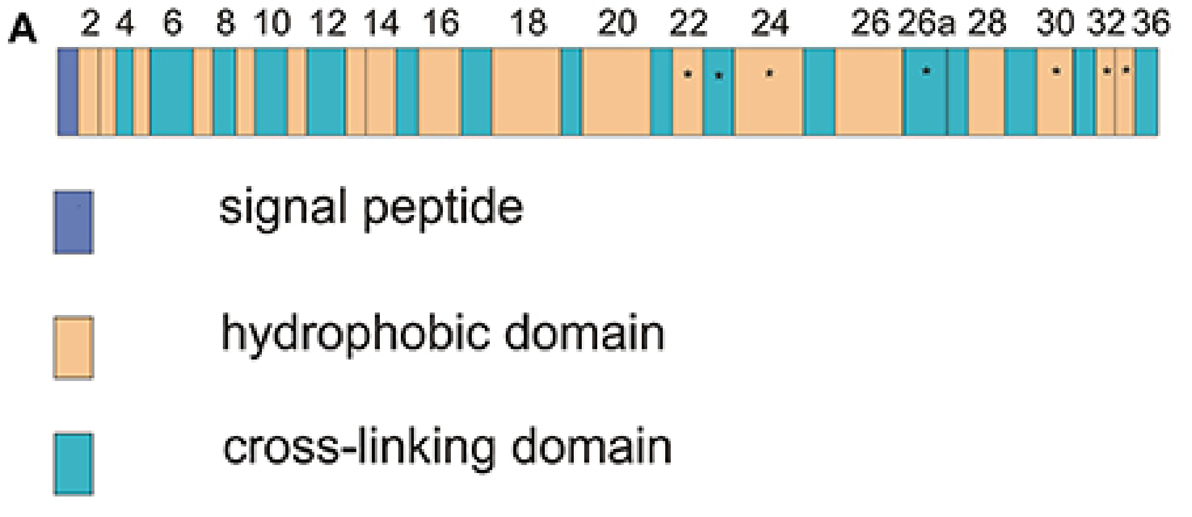


Figure 19-71 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Elastin structure

- The elastin protein is composed largely of two types of short segments that alternate along the polypeptide chain:
  - Hydrophobic segments, which are responsible for the elastic properties of the molecule; and
  - Alanine- and lysine-rich α-helical segments, which form cross-links between adjacent molecules.



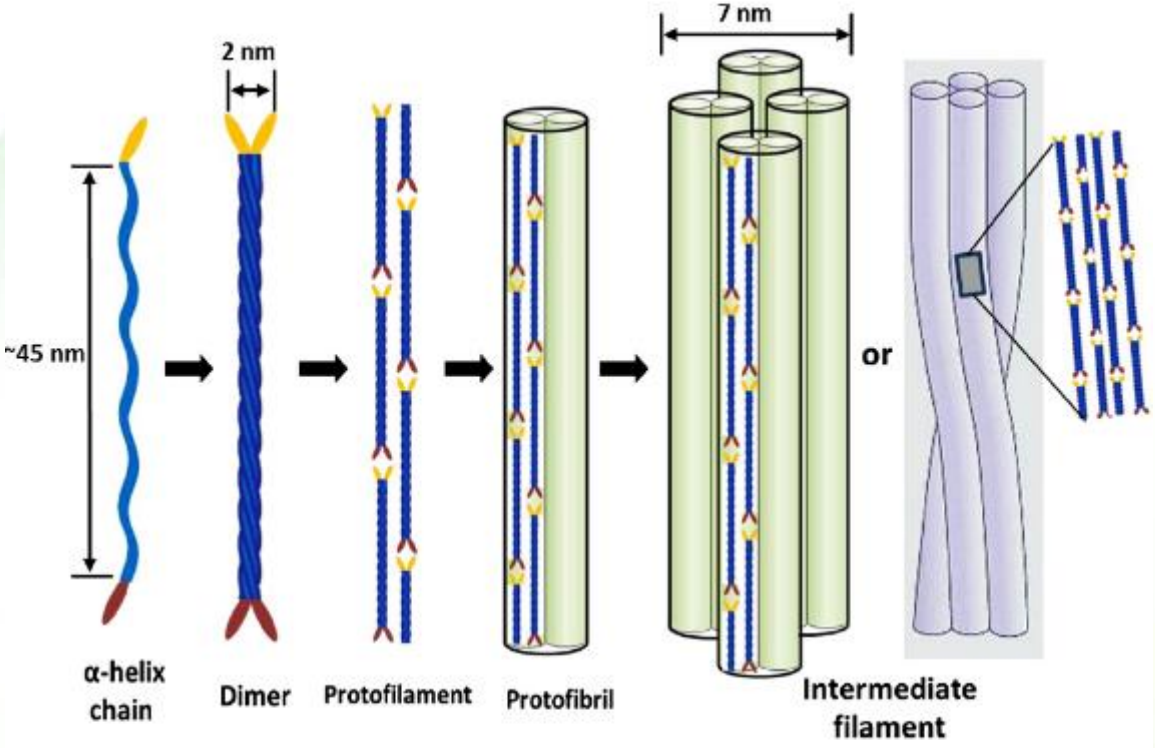
Keratins

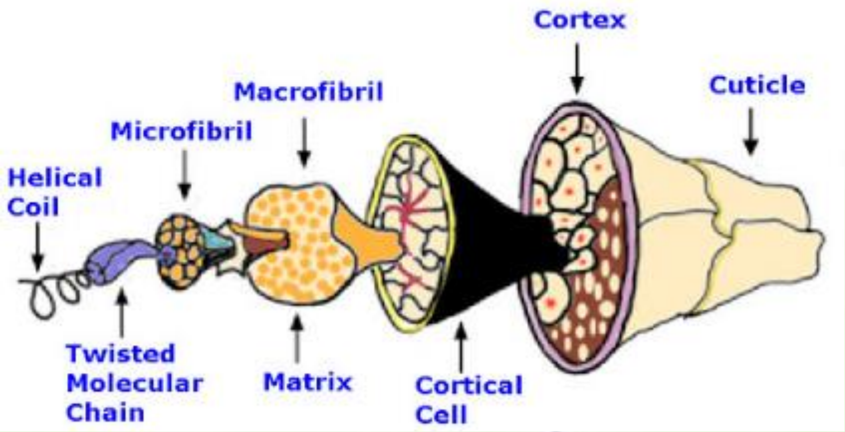
Keratins

- Two important classes of proteins that have similar amino acid sequences and biological function are called α-and β-keratins, which as members of a broad group of intermediate filament proteins.
- α-keratin is the major proteins of hair and fingernails as well as animal skin.
- α-keratin has an unusually high content of cysteine residues.

α-keratins structure (hair vs. fingernails)

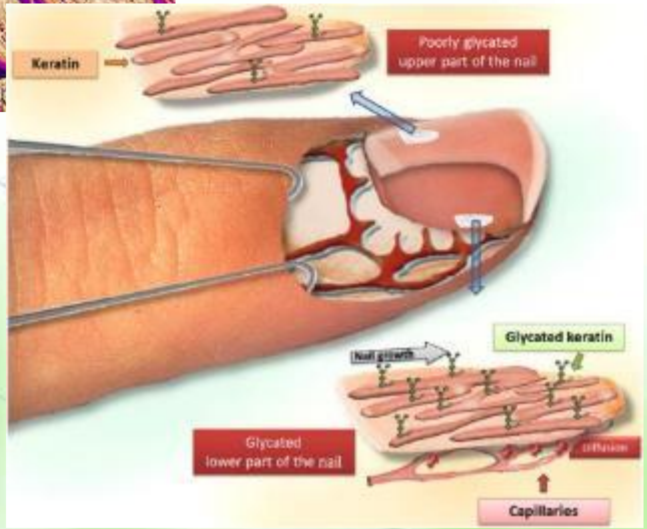
- Two helical α-keratin molecules form a coiled coil dimer.
- Two coiled coil dimers associate forming tetramer and tetramers associate head-to-tail forming a protofilaments.
- Two protofilaments twist together to form a protofibril.
- Four protofibrils form an intermediate filament.
- Eight intermediate filaments cluster to make a microfibril.
- Hundreds of microfibrils are cemented into a macrofibril.
- Many macrofibrils cluster to form a single hair.

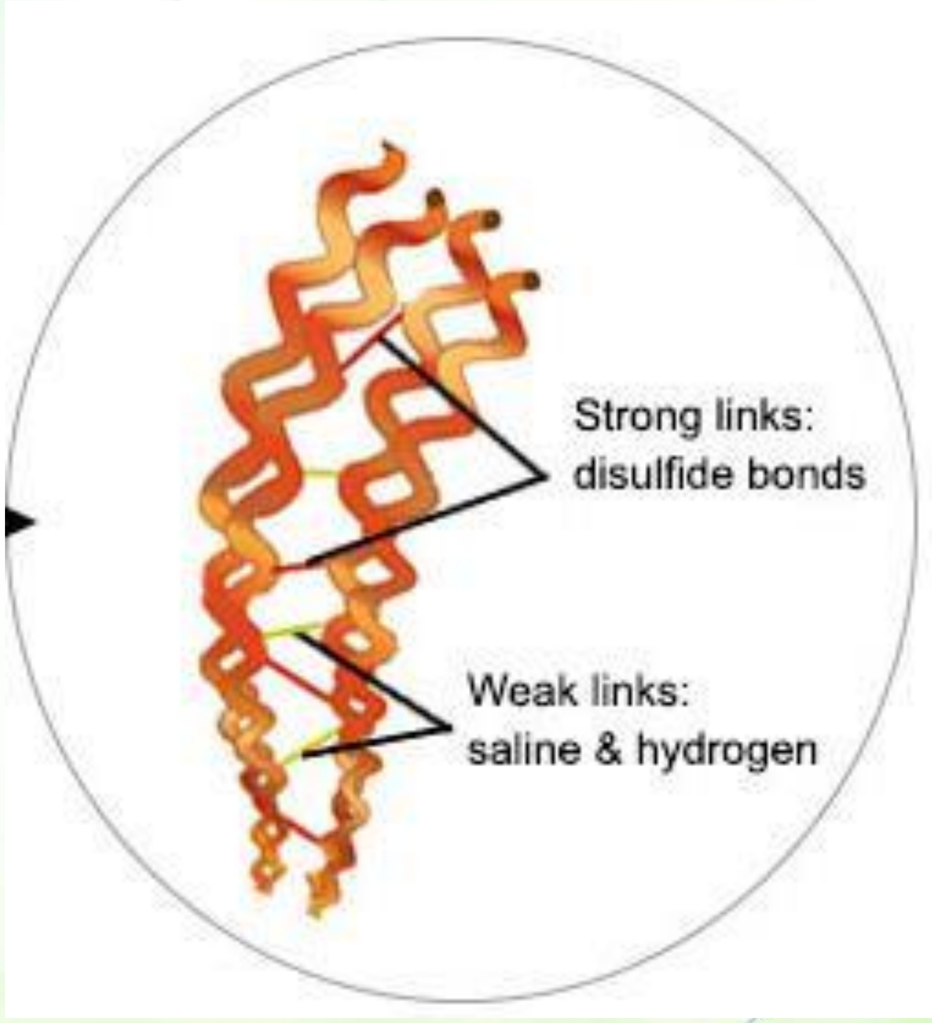




Keratin in nails

- α-keratin can be hardened by the introduction of disulfide cross-links (fingernails).



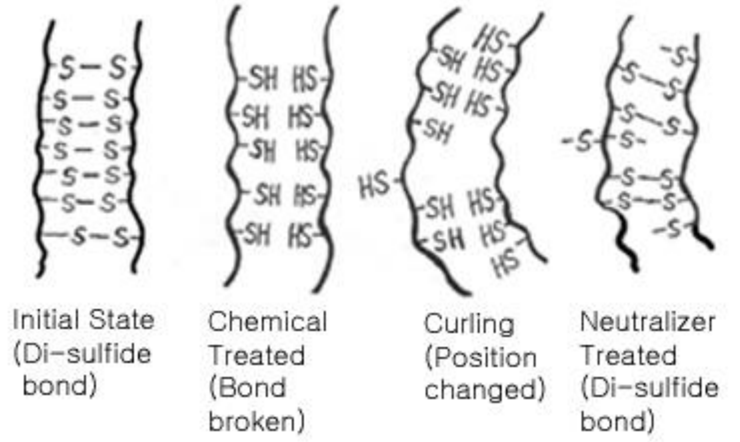


Looking beautiful?

Having a hair design?

Temporary Wave

- When hair gets wet, water molecules disrupt some of the hydrogen bonds, which help to keep the alpha-helices aligned. When hair dries up, the hair strands are able to maintain the new curl in the hair for a short time.



Permanent wave

- A reducing substance (usually ammonium thioglycolate) is added to reduce some of the disulfide cross-links. The hair is put on rollers or curlers to shift positions of alpha-helices. An oxidizing agent, usually hydrogen peroxide, is added to reform the disulfide bonds in the new positions until the hair grows out.