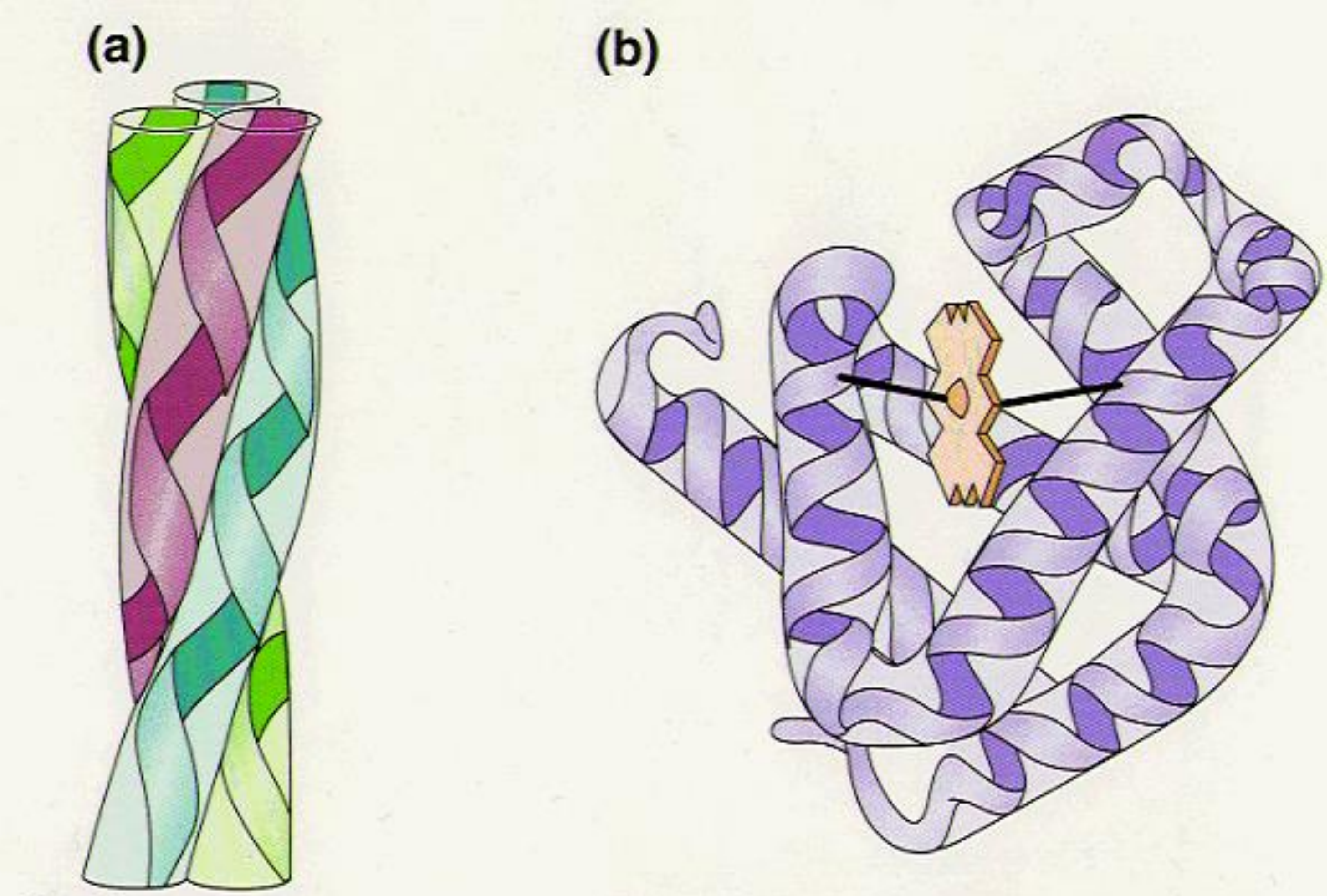
STRUCTURE-FUNCTION RELATIONSHIP: FIBROUS PROTEINS

BIOLOGICAL FUNCTIONS OF PROTEINS

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

TYPES OF PROTEINS

- Structure:
  - Fibrous (fiber-like with a uniform secondary-structure only)
  - Globular (globe-like with three-dimensional compact structures)
- Examples
- Fibrous proteins: collagens, elastins, and keratins
- Globular proteins: myoglobin, hemoglobin, and immunoglobulin

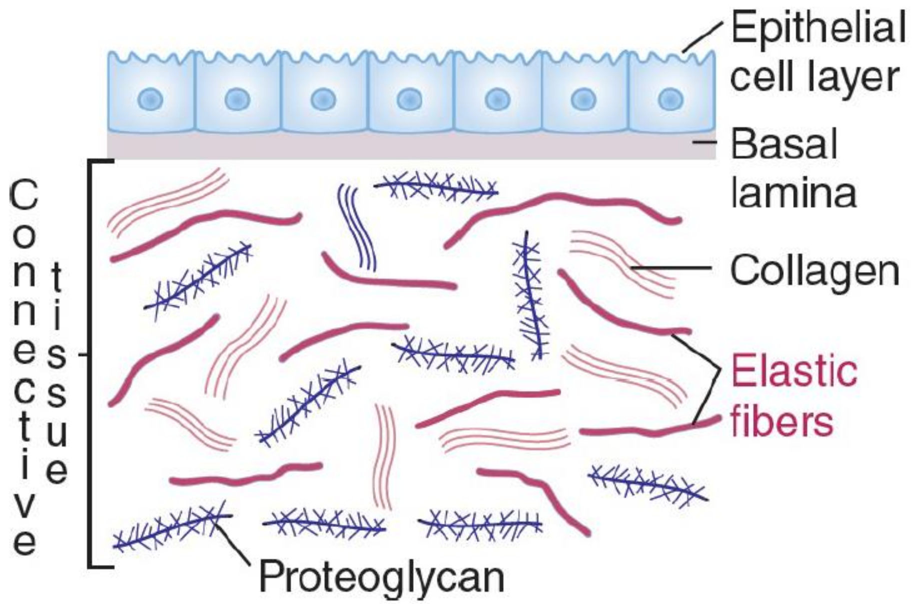


Collagen, a fibrous protein

Myoglobin, a globular protein

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.



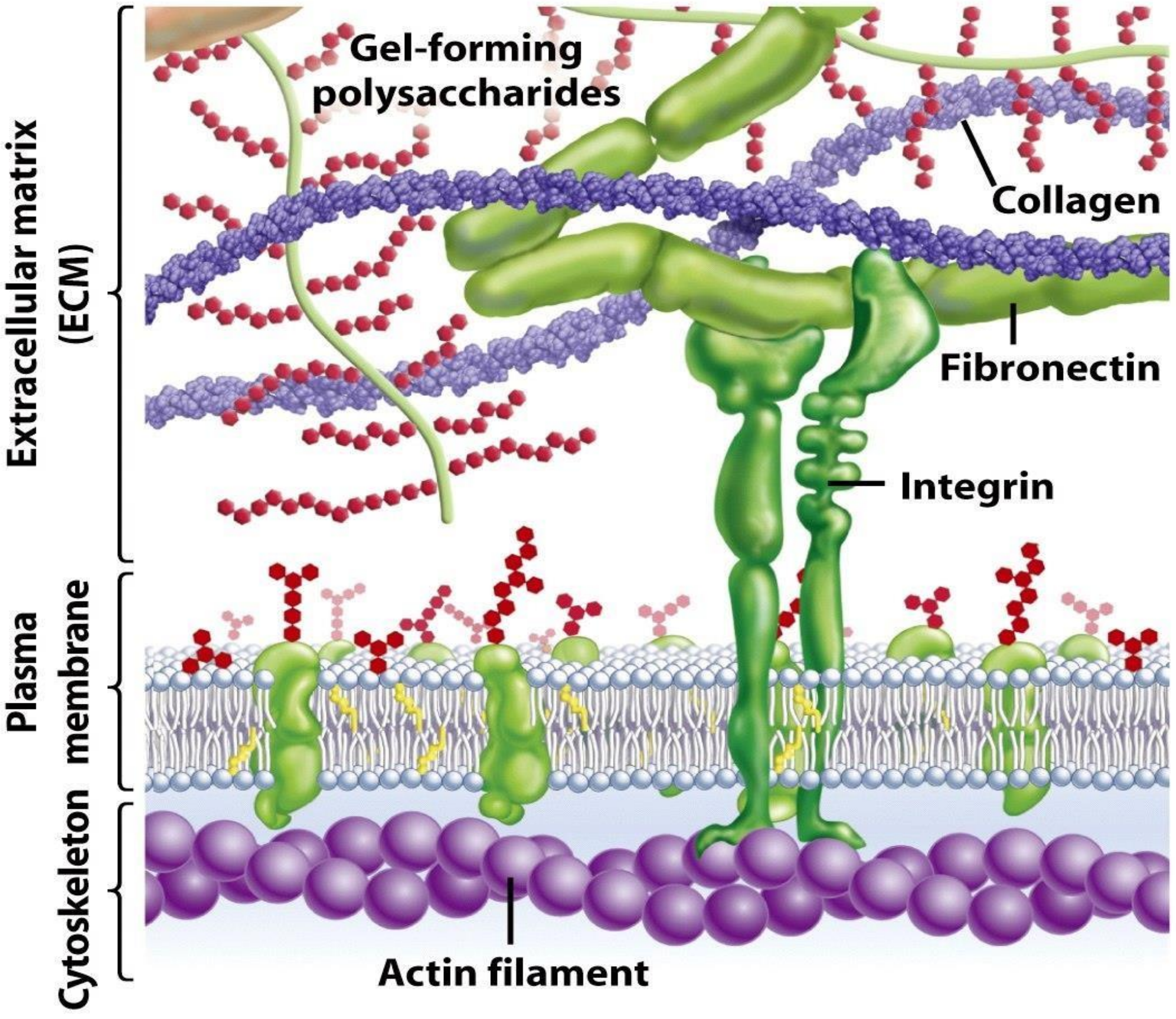


Figure 8-4 Biological Science, 2/e

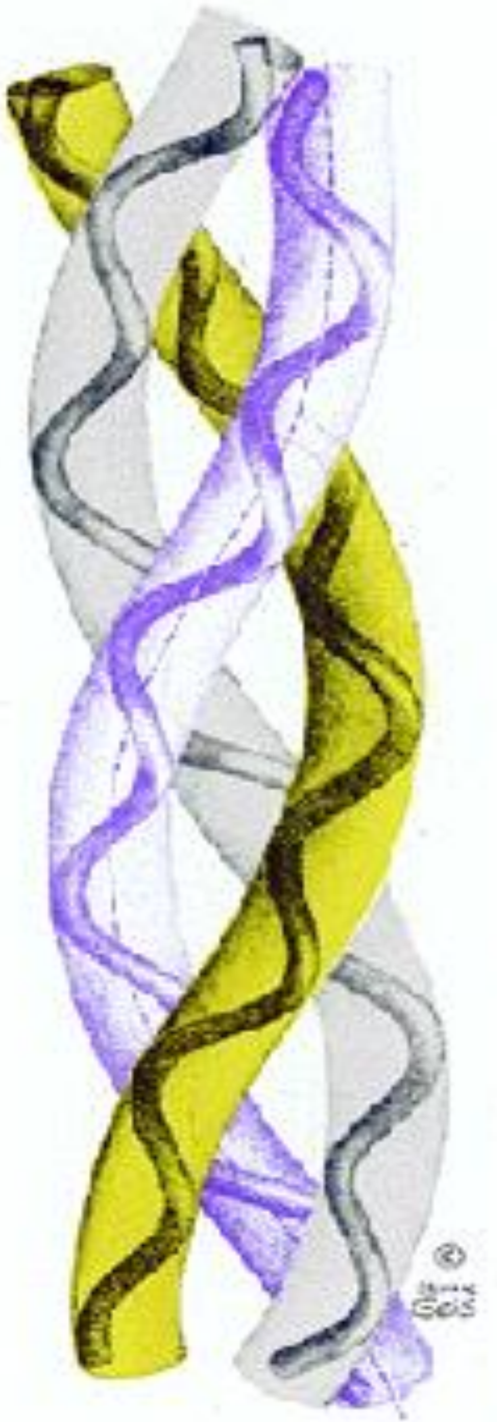
COLLAGENS

COLLAGENS AND THEIR PROPERTIES

- The collagens are a family of fibrous proteins with 25 different types found in all multicellular animals.
- They are the most abundant proteins in mammals, constituting 25% of the total protein mass in these animals.
- Collagen molecules are named as type I collagen, type II collagen, type III collagen, and so on.
- The main function of collagen molecules is to provide structural support to tissues.
- Hence, the primary feature of a typical collagen molecule is its stiffness.

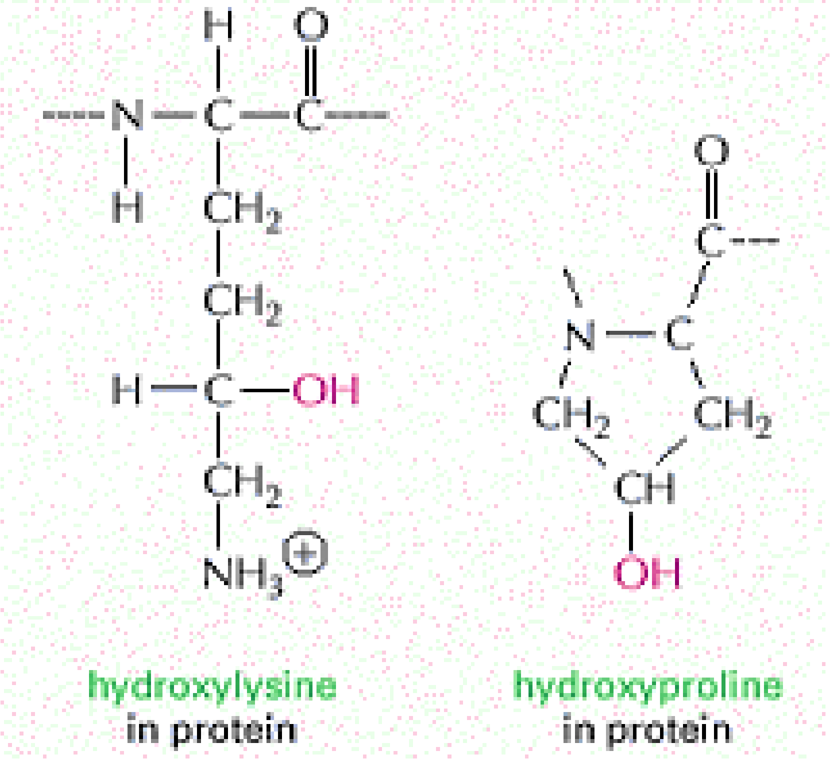
STRUCTURE

- It is a left-handed, 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.



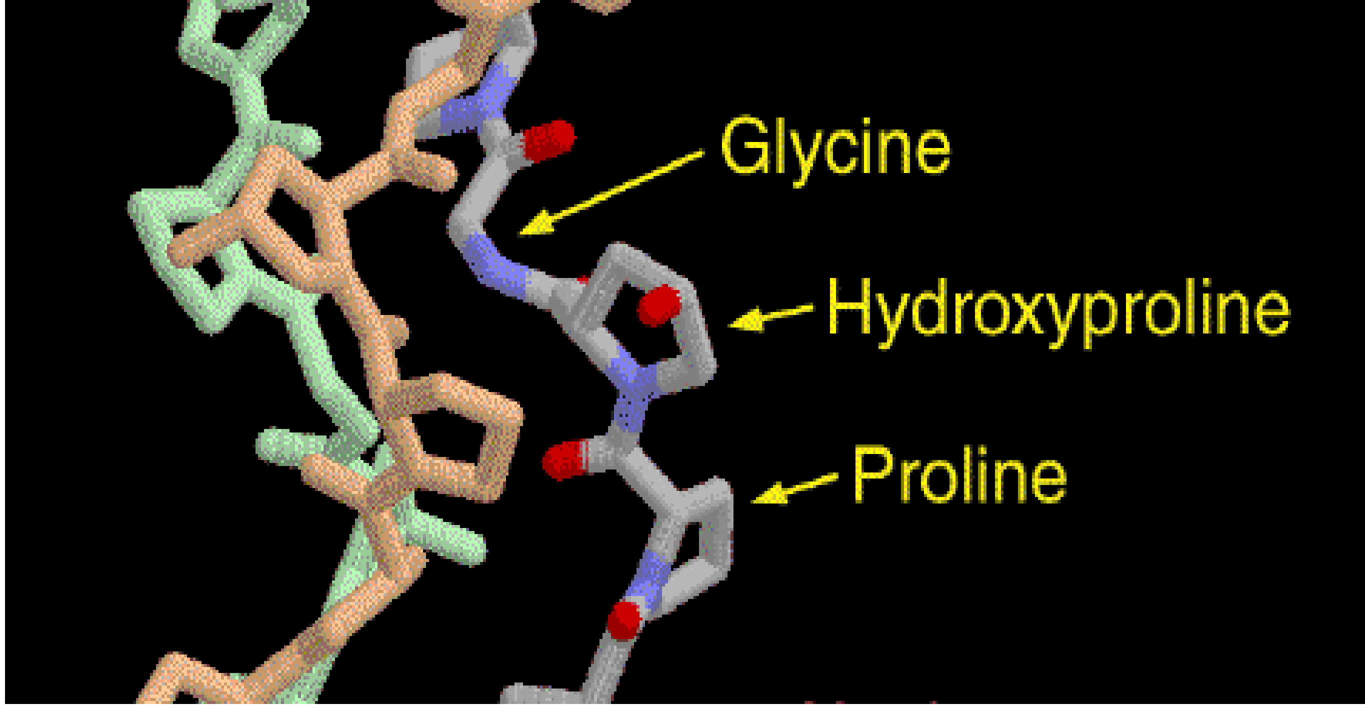
COMPOSITION OF COLLAGENS

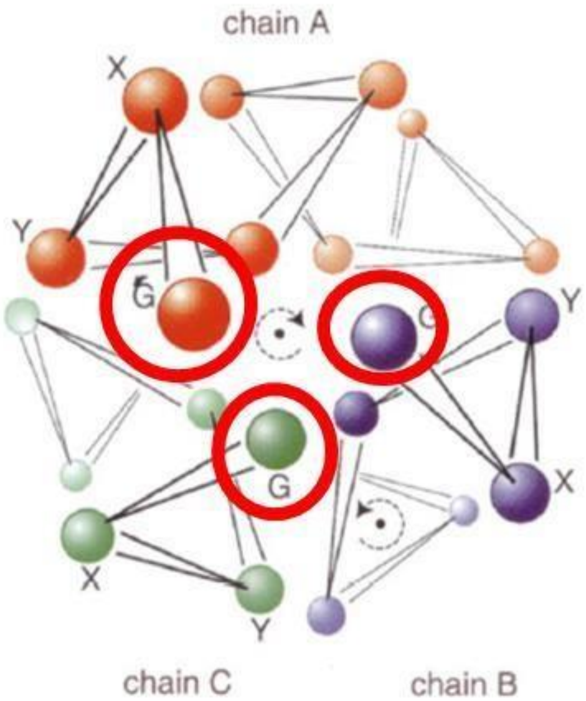
- Collagens are rich in glycine (33%) and proline (13%).
- It is also unusual in containing hydroxyproline (9%) and hydroxylysine.
- Every third residue is glycine, which, with the preceding residue being proline or hydroxyproline in a repetitive fashion as follows:
- Gly-pro-Y
- Gly-X-hydroxyproline



FUNCTIONAL PURPOSE OF AMINO ACIDS

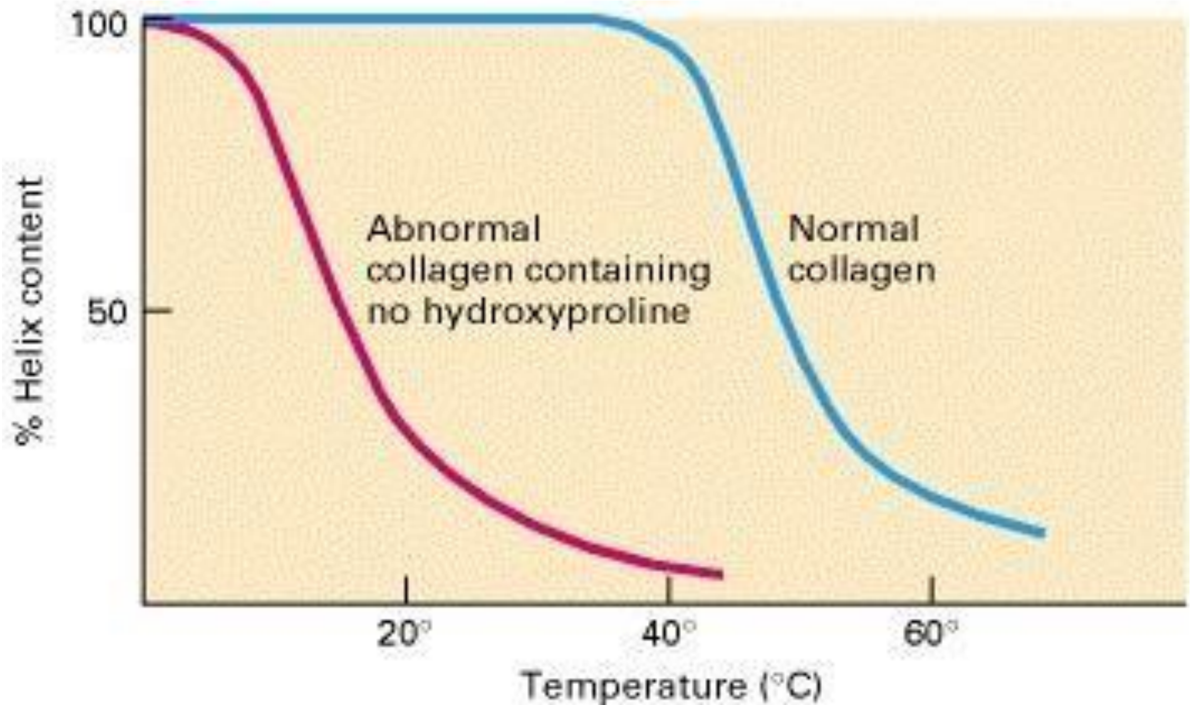
- Glycine allows the three helical a chains to pack tightly together to form the final collagen superhelix.
- Proline creates the kinks and stabilizes the helical conformation in each a chain.





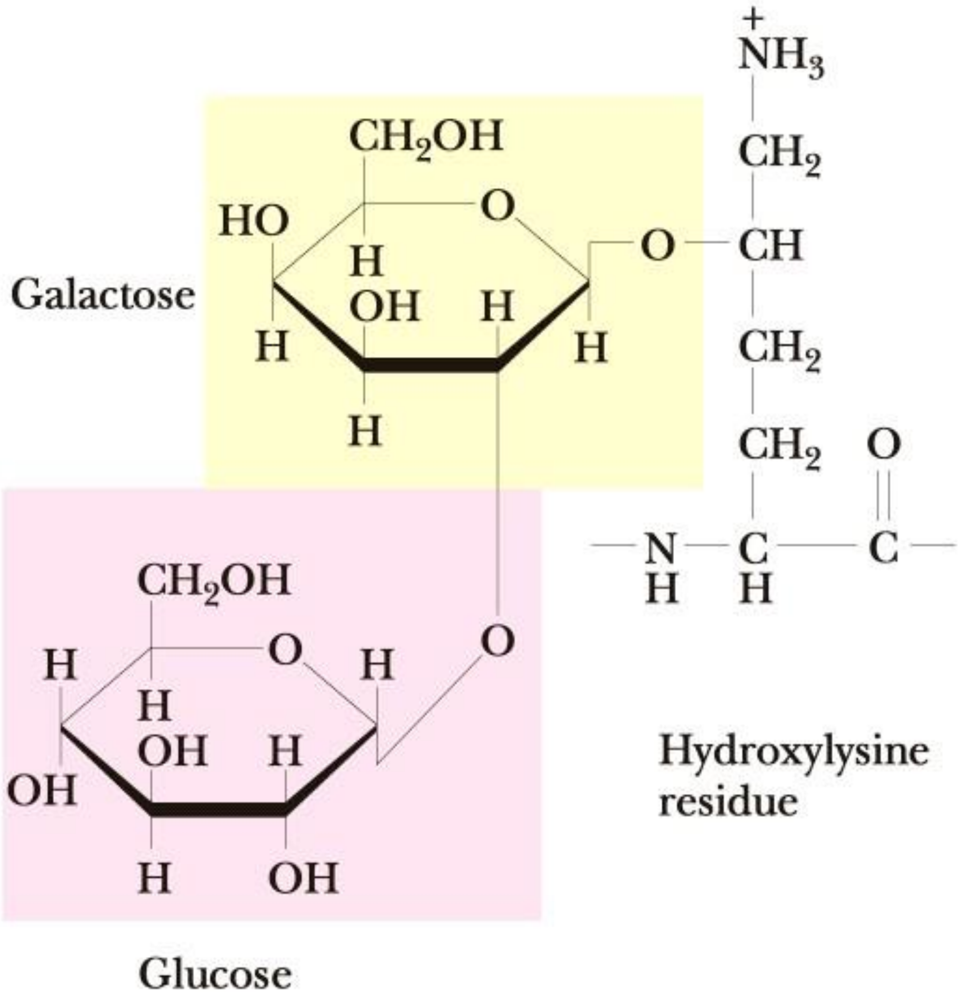
PURPOSE OF HYDROXYPROLINE

- 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



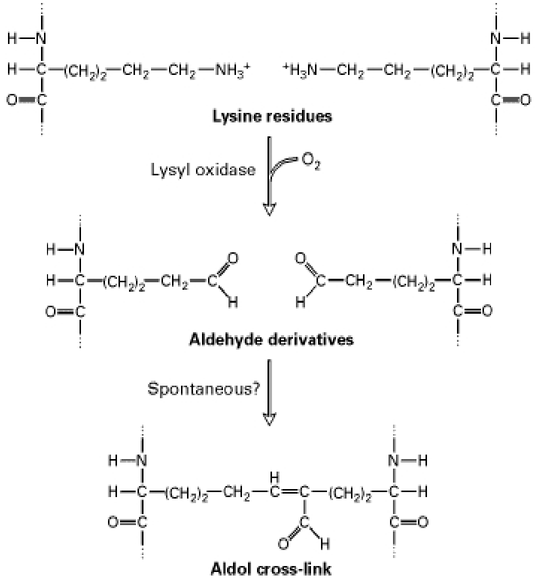
HYDROXYLYSINE

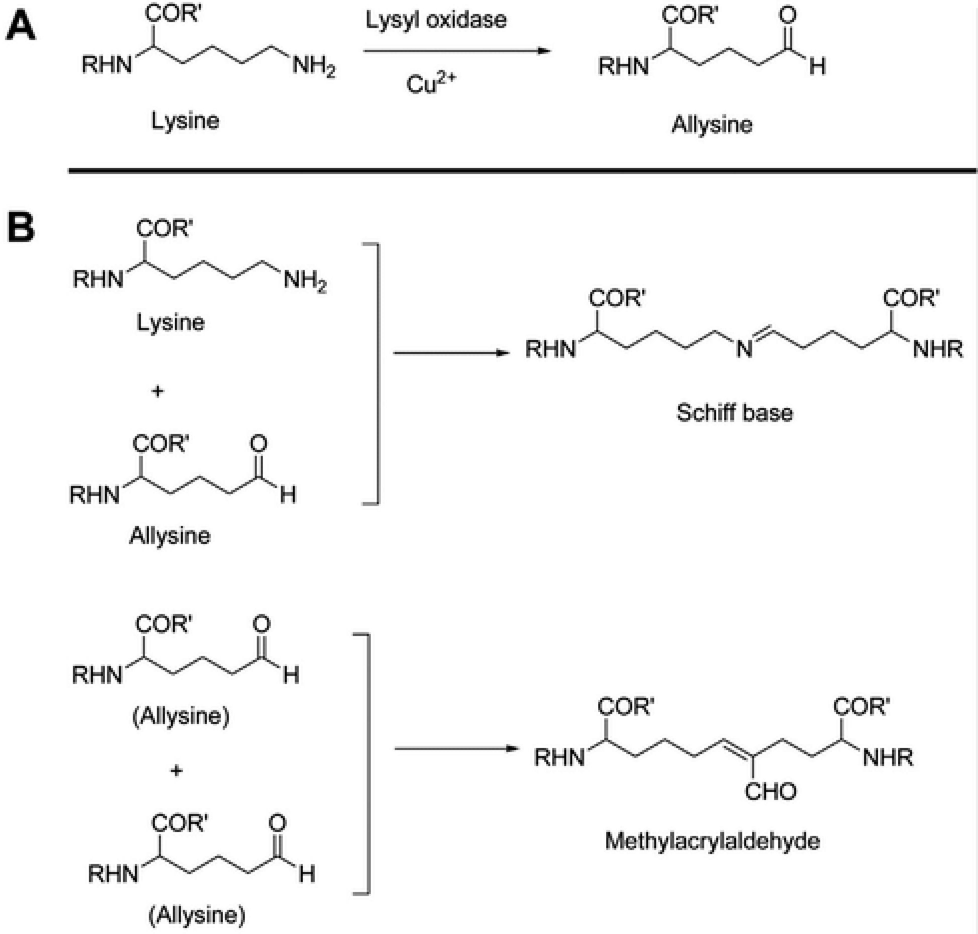
- Hydroxylysine serves as attachment sites of polysaccharides making collagen a glycoprotein.

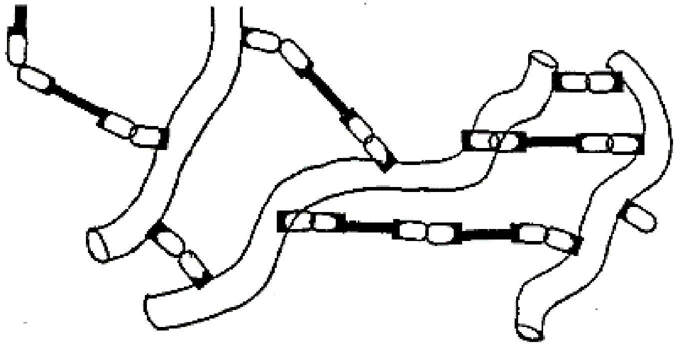


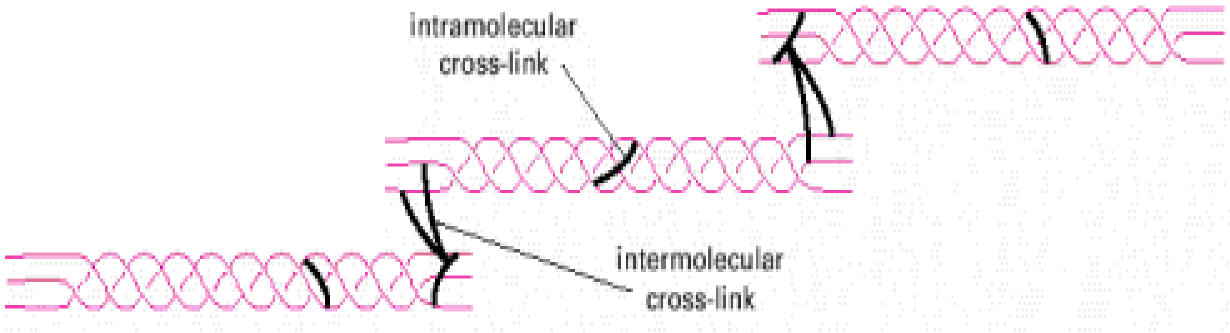
OXIDATION OF LYSINE

- Some of the lysine side chains are oxidized to aldehyde derivatives known as allysine.
- Covalent aldol cross-links form between hydroxylysine residues and lysine or another oxidized lysine.



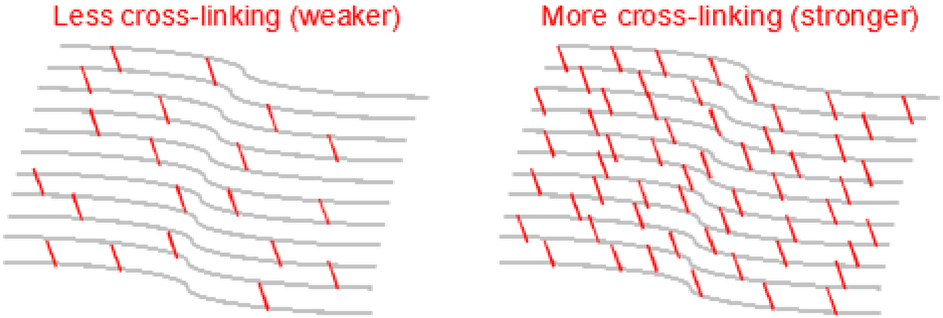






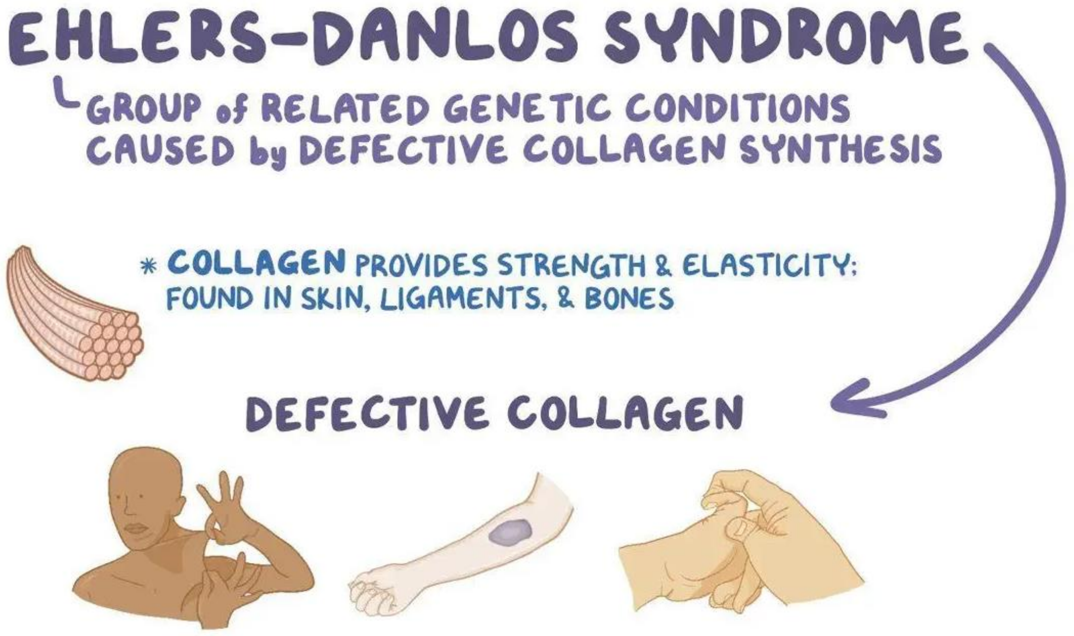
FUNCTION OF CROSS-LINKING

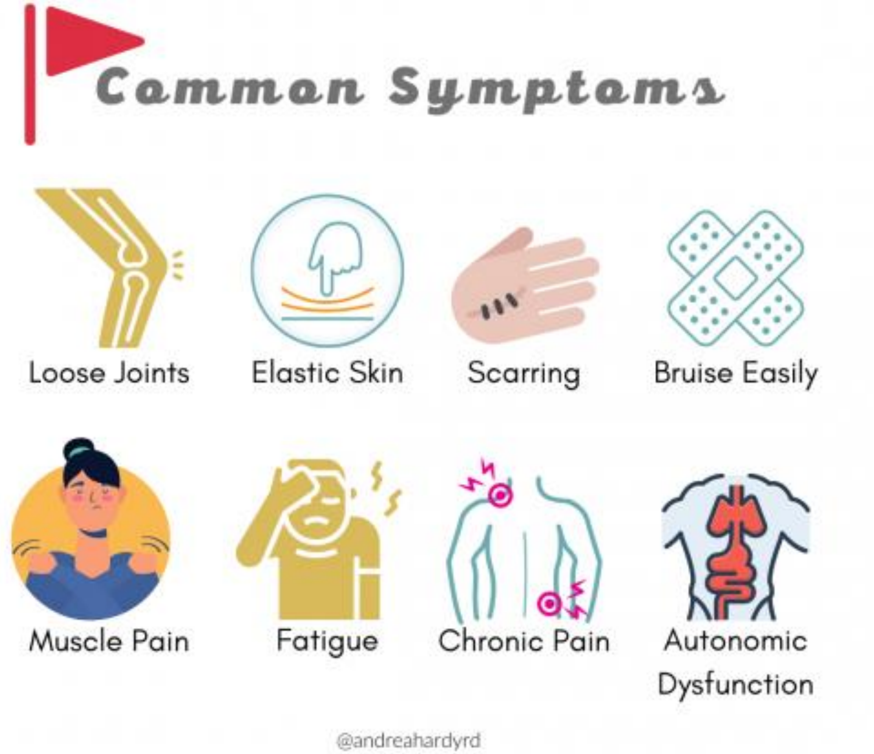
- These cross-links stabilize the side-by-side packing of collagen molecules and generate a strong fibril
- If cross-linking is inhibited, the tensile strength of the fibrils is drastically reduced; collagenous tissues become fragile, and structures such as skin, tendons, and blood vessels tend to tear.
- 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.



DEFICIENT CROSS-LINKING

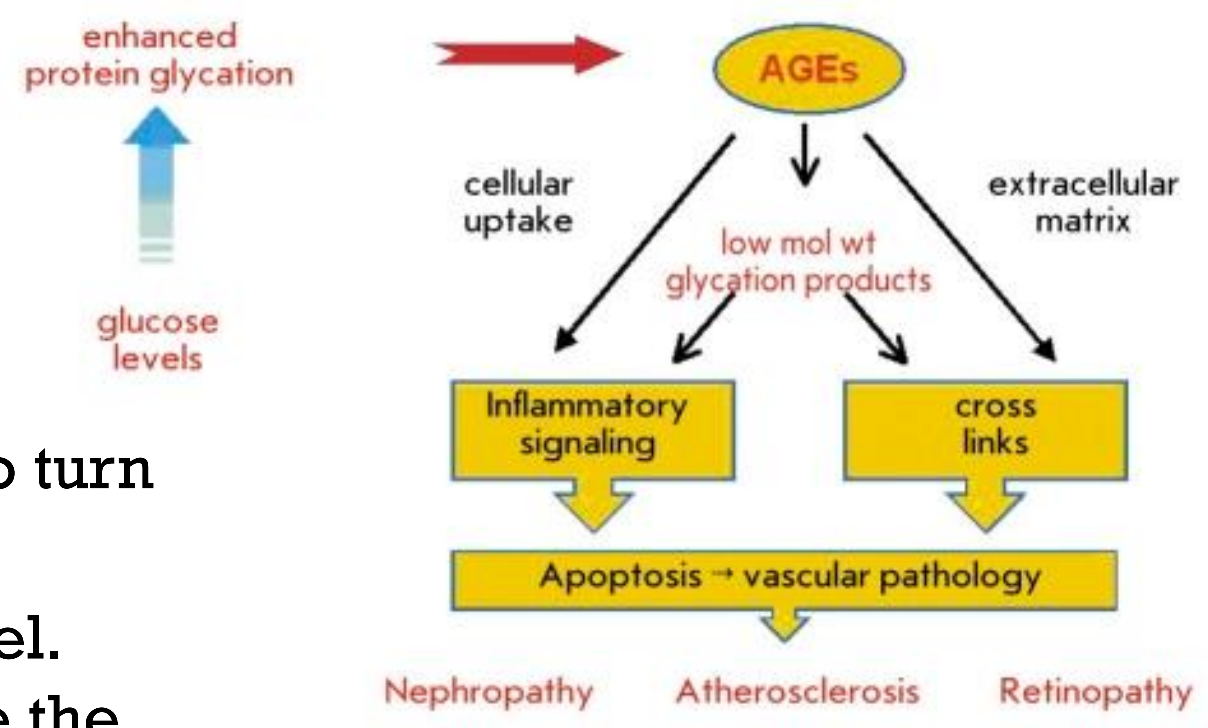
- If cross-linking is inhibited, the tensile strength of the fibrils is drastically reduced; collagenous tissues become fragile, and structures such as skin, tendons, and blood vessels tend to tear.
- Deficiency of hydroxylation can cause diseases such as Ehlers-Danlos syndrome.





ADVANCED GLYCATION END PRODUCTS (AGES)

- Proteins (e.g., collagen) can be nonenzymatically glycated producing glycosylated proteins that are difficult to turn over (to be degraded).
- Glycation is proportional to glucose level.
  - Hyperglycemia and diabetes increase the levels of glycated proteins.

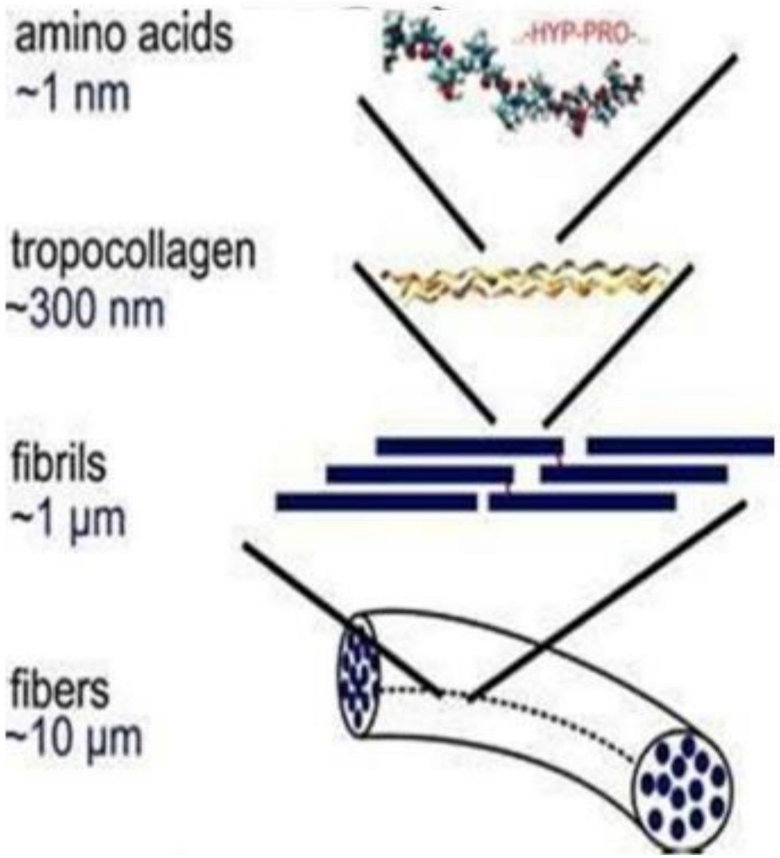


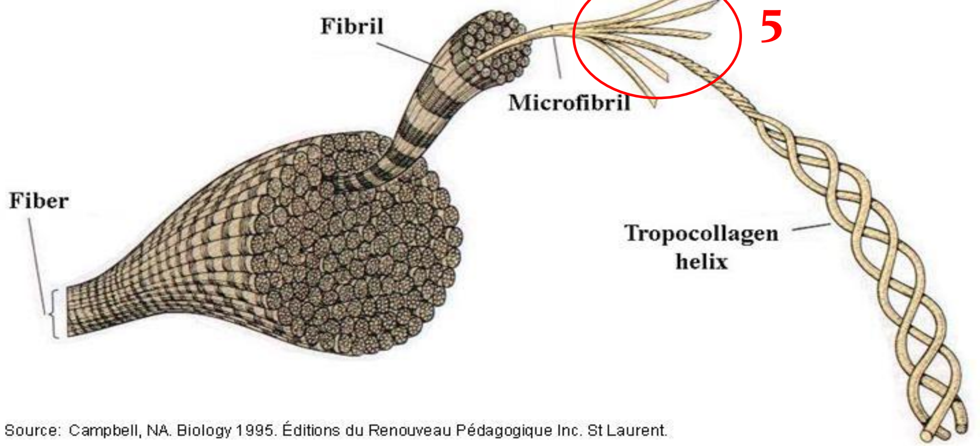
Uncontrolled diabetics suffer from cardiomyopathy

- Glycated proteins in tissues are further modified by nonenzymatic oxidation forming additional cross-links.
- The net result is the formation of large protein aggregates termed advanced glycation end products (AGEs), which increase cellular oxidative stress.

FORMATION OF COLLAGEN FIBERS

- Following cellular release of protocollagen, 5 of them polymerize into a microfibril, that get 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.
- Microfibrils assemble into collagen fibers.

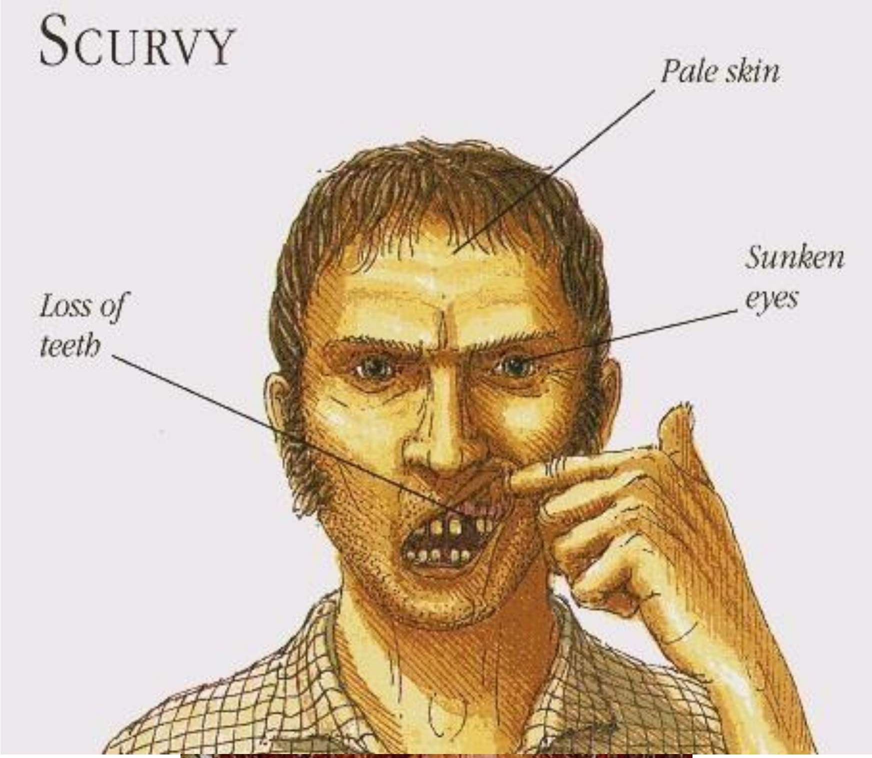




Source: Campbell, NA. Biology 1995. Éditions du Renouveau Pédagogique Inc. St Laurent.

SCURVY

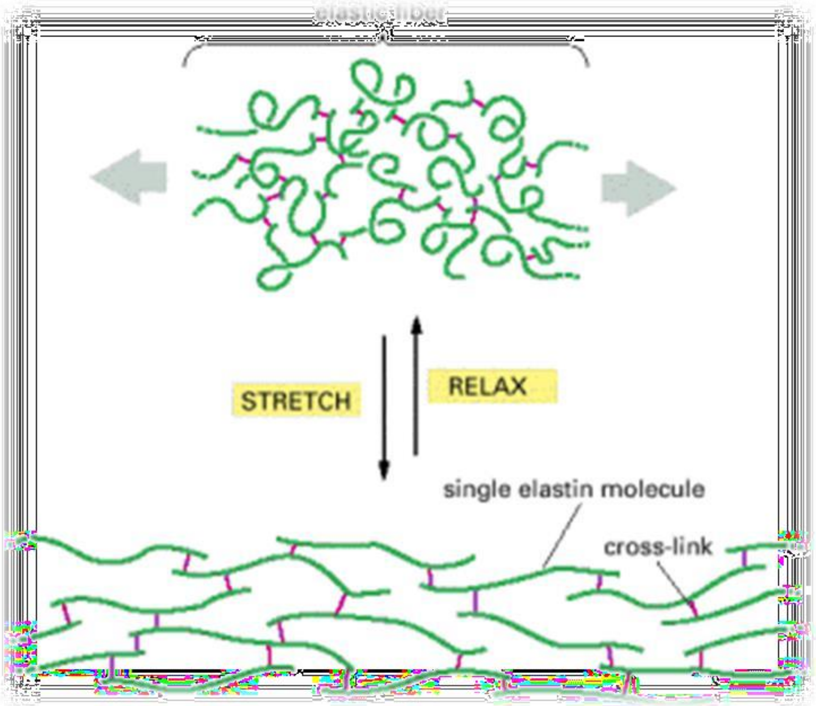
- Scurvy is a disease is caused by a dietary deficiency of ascorbic acid (vitamin C).
- Deficiency of vitamin C prevents
- proline hydroxylation.
- The defective pro-α chains fail to form a stable triple helix and are immediately degraded within the cell.
- Blood vessels become extremely fragile and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

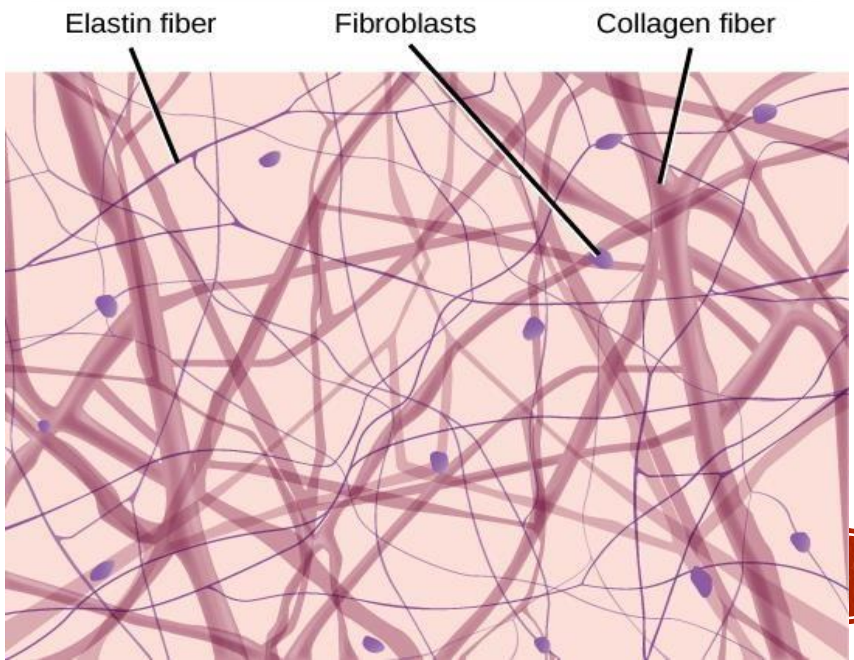


ELASTINS

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 these 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.

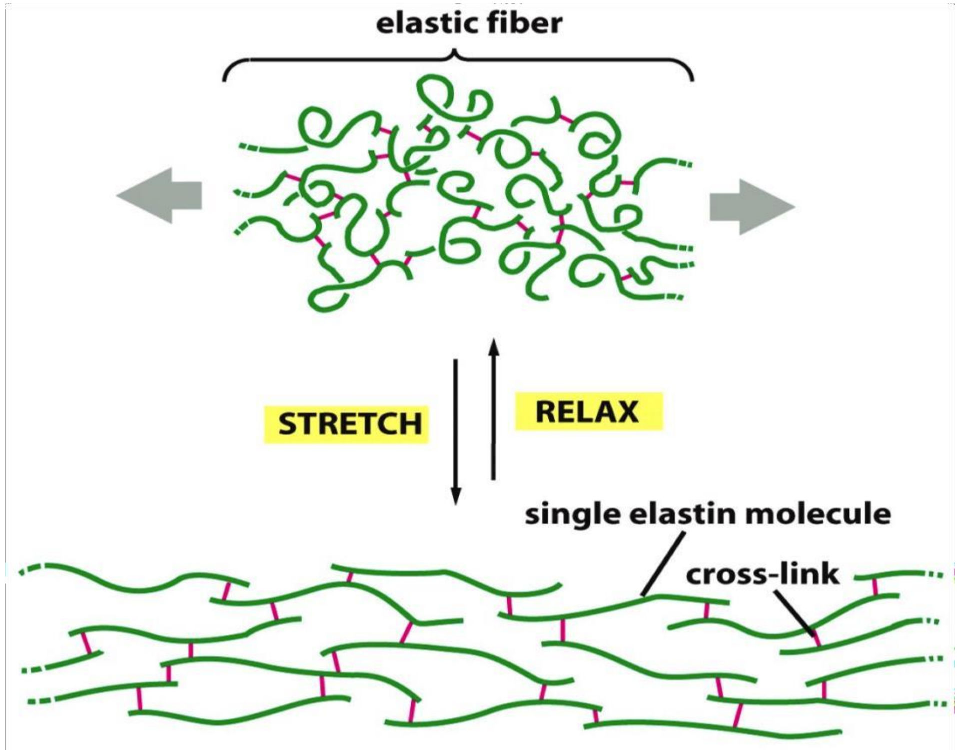
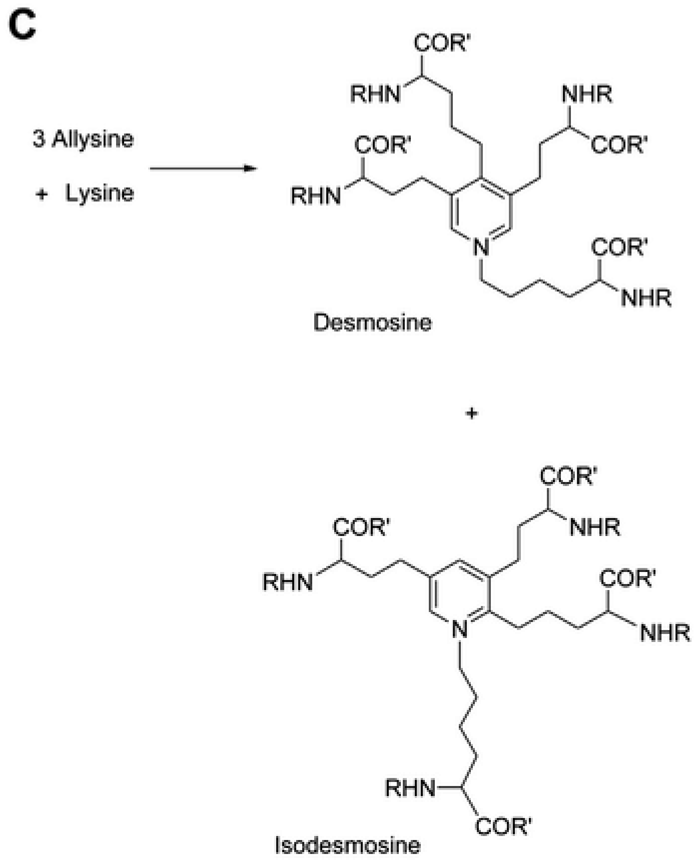
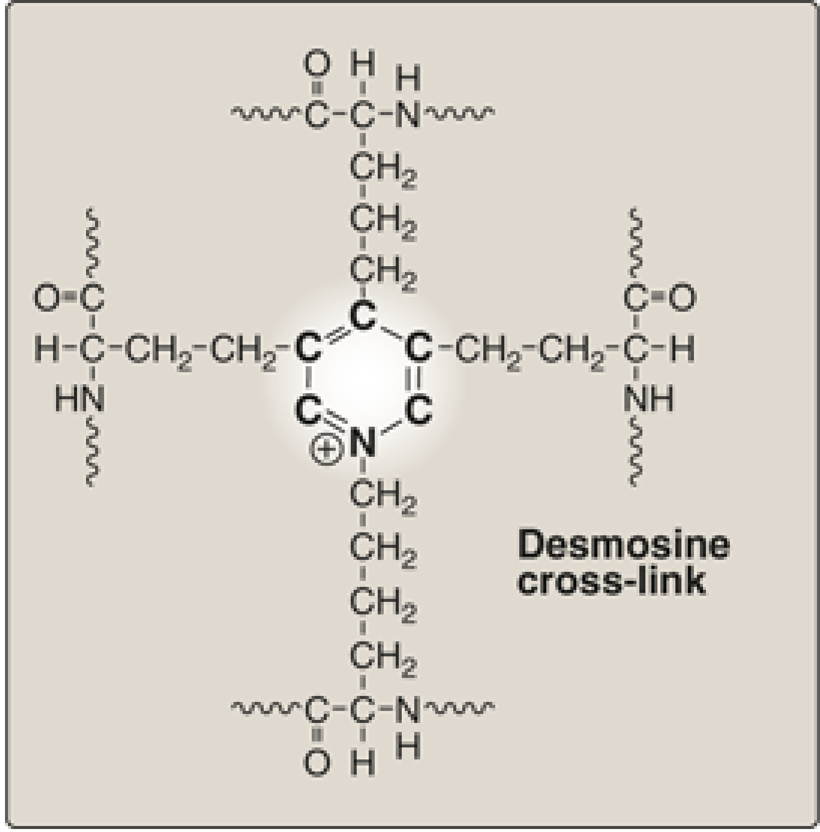


Figure 19-71 Molecular Biology of the Cell 5/e (© Garland Science 2008)

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
- Three allysyl side chains plus one unaltered lysyl side chain form a desmosine crosslink.



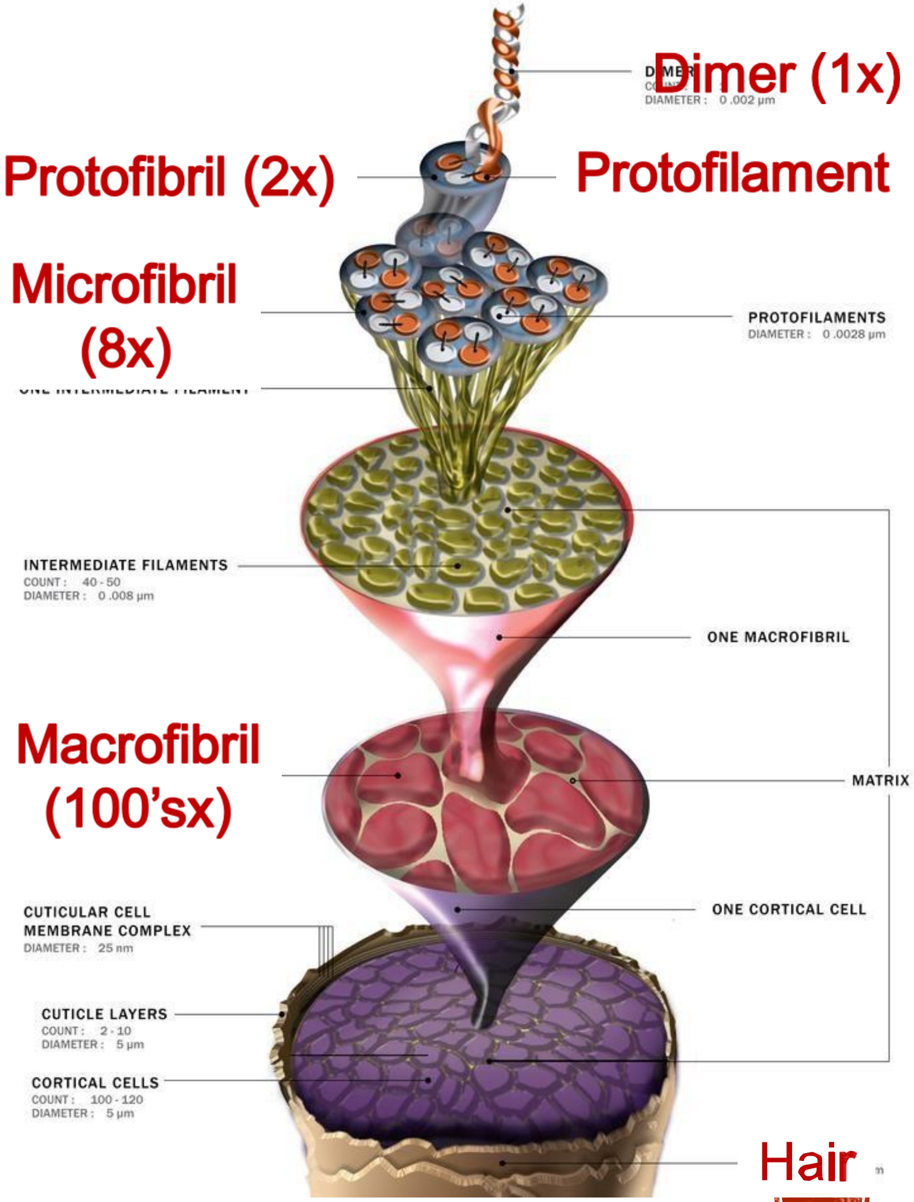
KERATINS

KERATINS

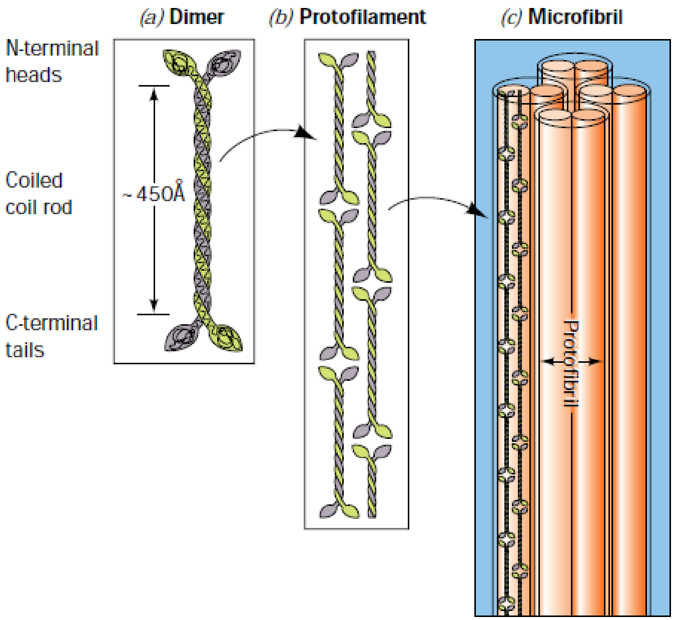
- Two important classes of proteins that have similar amino acid sequences and biological function are called α-and β-keratins, which as members of a broad group of intermediate filament proteins.
- α-keratin is the major proteins of hair and fingernails as well as animal skin.
- α-keratin has an unusually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

STRUCTURE

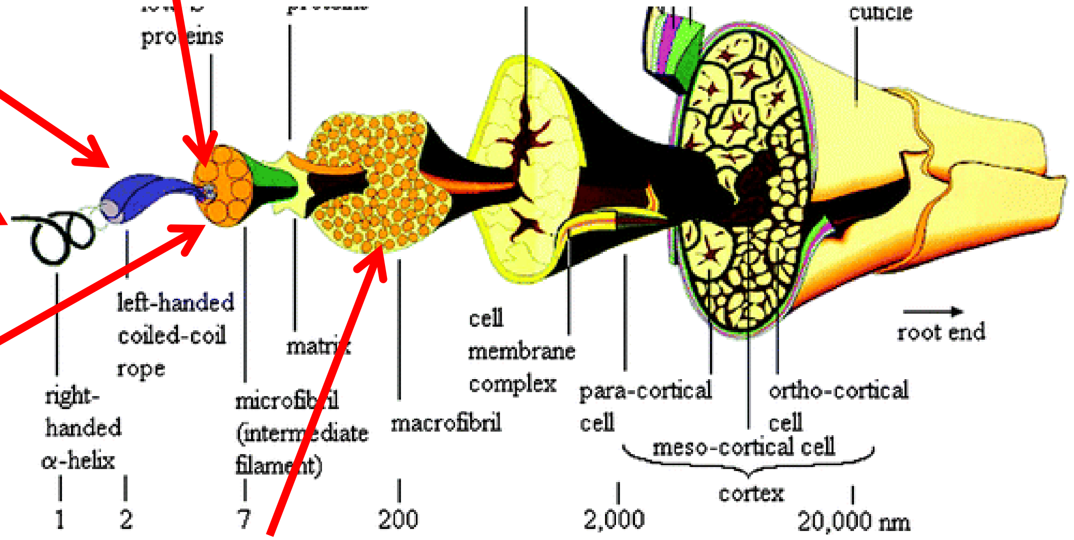
- Two helical α-keratin molecules (protofilaments) interwind forming a dimer.
- Two dimers twist together to form a 4-molecule protofibril.
- Eight protofibrils combine to make one microfibril.
- Hundreds of microfibrils are
- cemented into a macrofibril.



α-KERATINS STRUCTURE



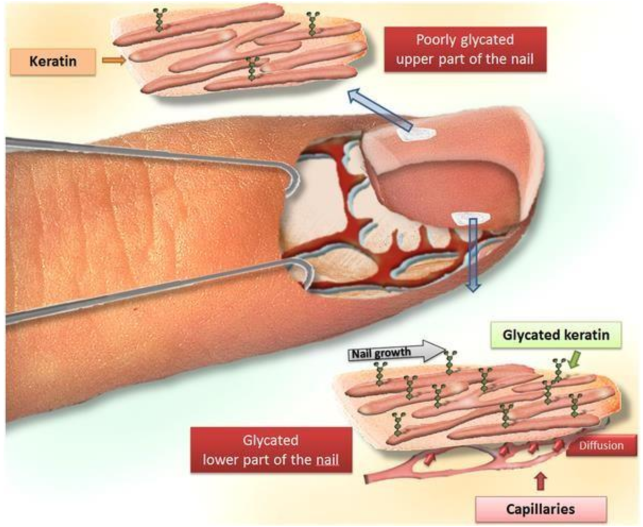
- α-helix (1), Coiled coil (2), Protofibril (4),

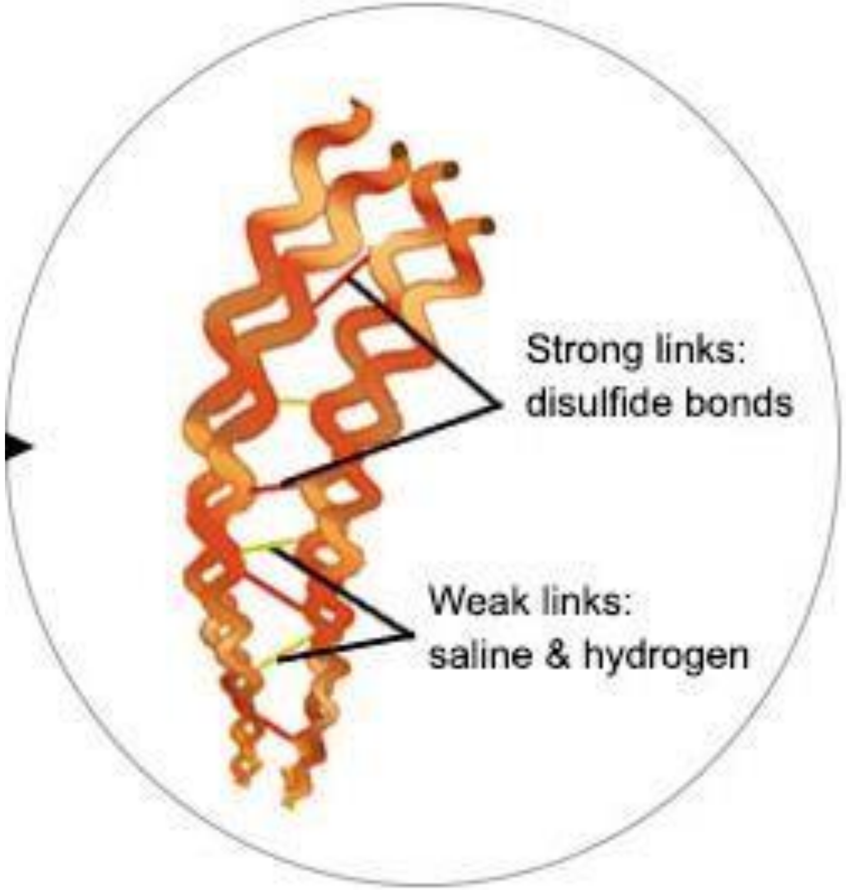


- Microfibril (28-32) (7-8 proto), Macrofibril (1000_s) (100_s micro)

KERATIN IN NAILS

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





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.