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Structure-Function relationship

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

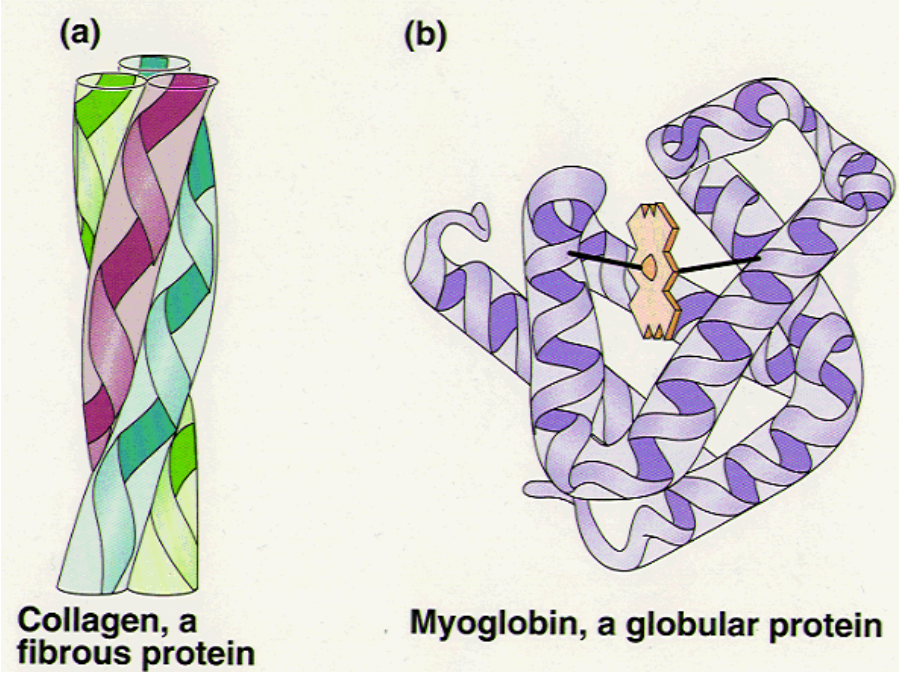
Types of proteins

- 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, elastins, & keratins

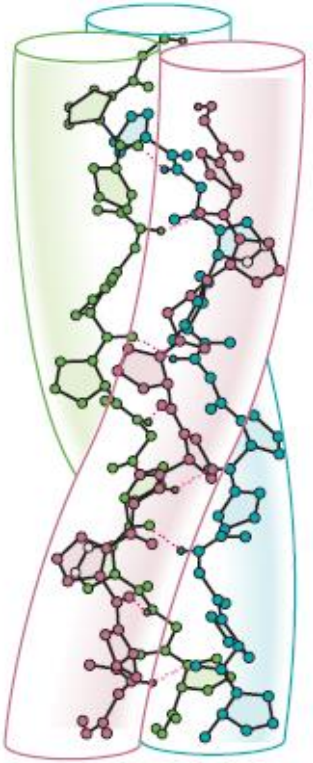
- Globular proteins: myoglobin, hemoglobin, & immunoglobulin



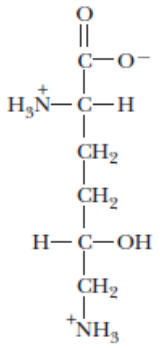
Collagen
Elastin
Keratin

Fibrous Proteins

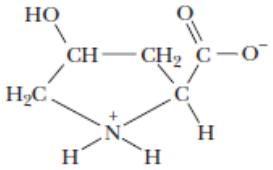
Collagen



- The most abundant protein in vertebrates
  - (25% of mammals protein)
- 25 different types (I, II, III, IV, … etc.)
- Found in all multicellular animals
- Organized in water-insoluble fibers
- Have a great strength
- Consists of 3 polypeptide chains wrapped around each other in a ropelike twist, or triple helix (tropocollagen)
- Has a repeating sequence of the amino acids;
  - Gly (33%) — X2(Pro 13%)—X3
  - Gly (33%) — X2— X3 (ProOH 9%)
  - Hydroxy-lysine frequently occurs in collagen

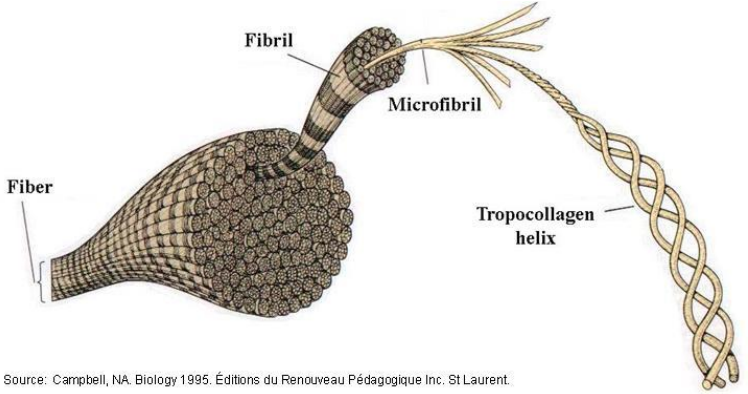


Hydroxylysine



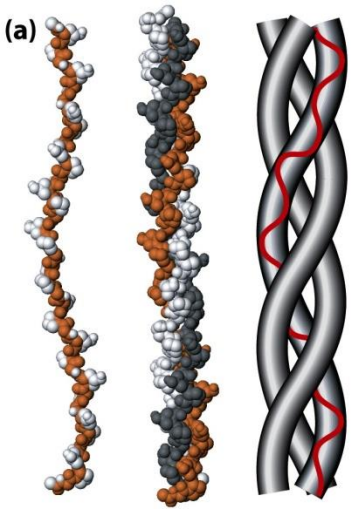
Hydroxyproline

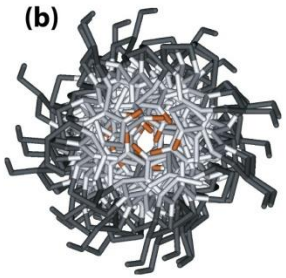
Collagen

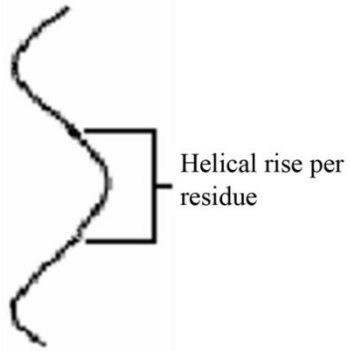


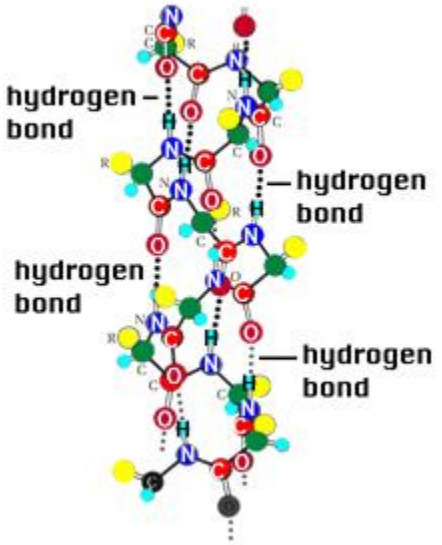
Source: Campbell, NA. Biology 1995. Éditions du Renouveau Pédagogique Inc. St Laurent.

- The triple helix (*tropocollagen)* is:
  - 300 nm long and 1.5 nm in diameter
  - left-handed, triple-stranded (α-chains), ropelike superhelix
  - Held together by H-bonding
  - Each strand have ≈ 800 amino acids (300 kDa)
- Compared to the α-helix (3.6 residues), the collagen helix is more extended with 3.3 residues per turn



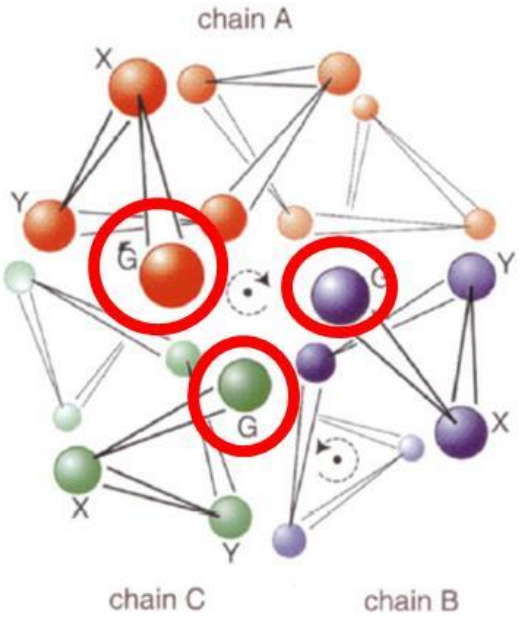


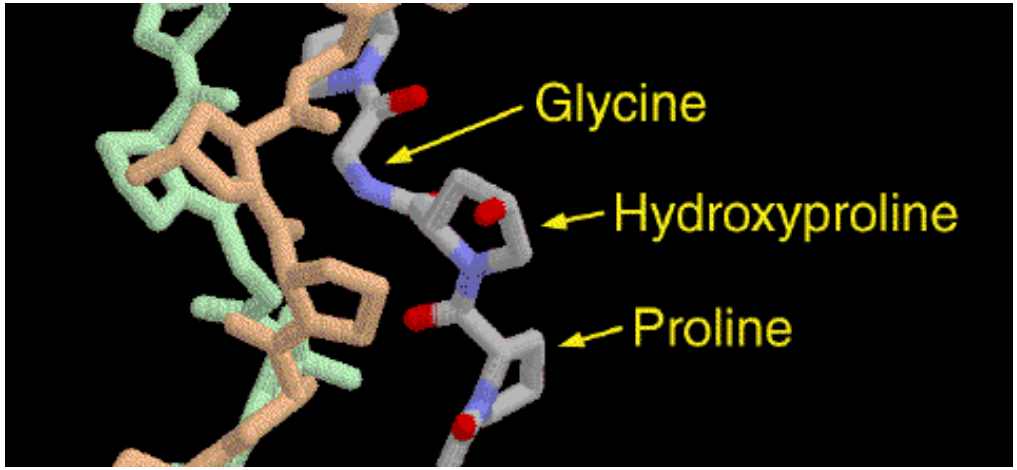




Functional purposes of amino acids

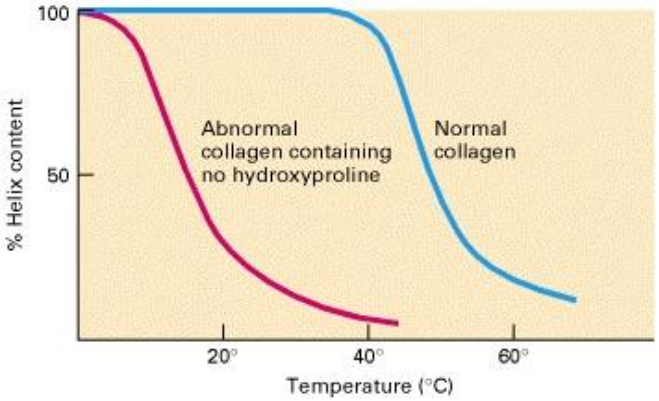
- Glycine: allows the three helical α-chains to pack tightly
- Proline: creates the kinks & stabilizes the helical conformation

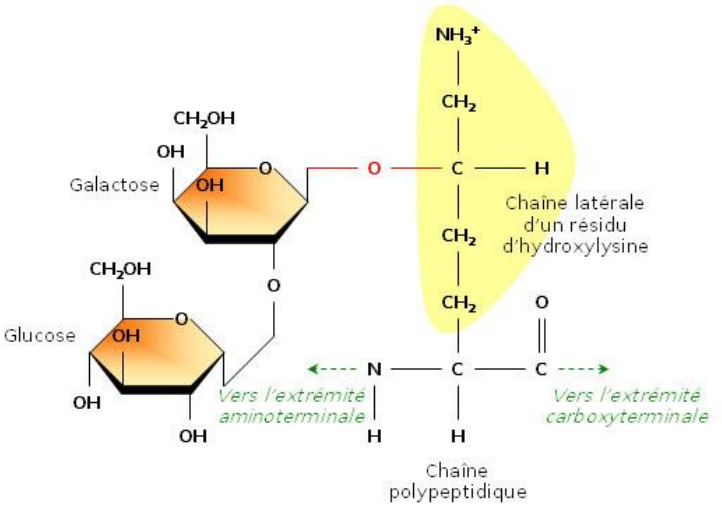


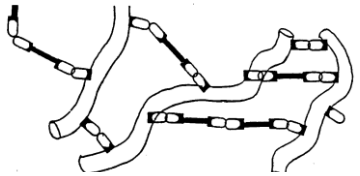


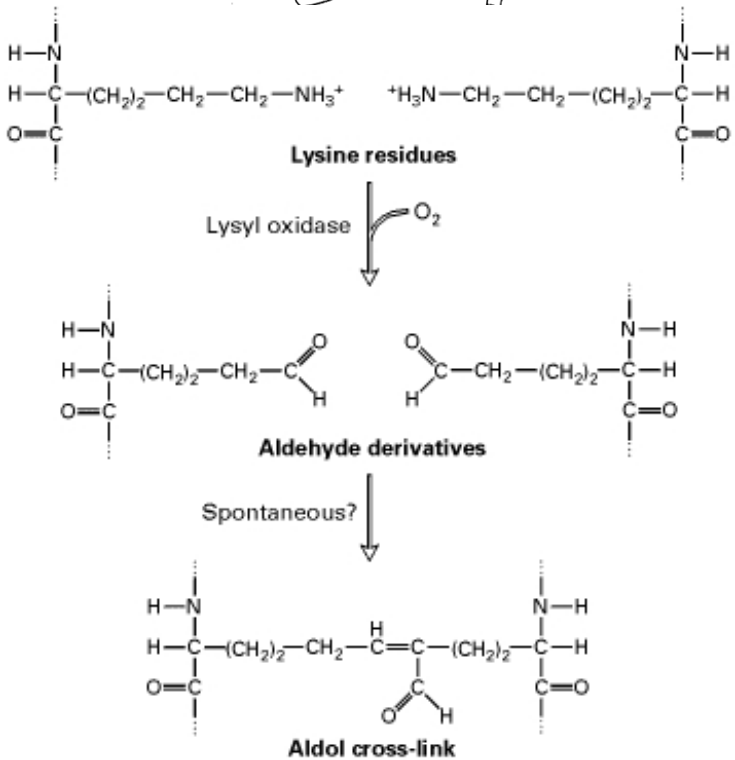
Functional purposes of amino acids

- Hydroxylysine:
  - Attachment sites of polysaccharides
  - Oxidation: to aldehyde followed by Covalent aldol cross-links form between hydroxylysine residues and lysine or another oxidized lysine
- Hydroxyproline:
  - Hydrogen bonding, Helical formation



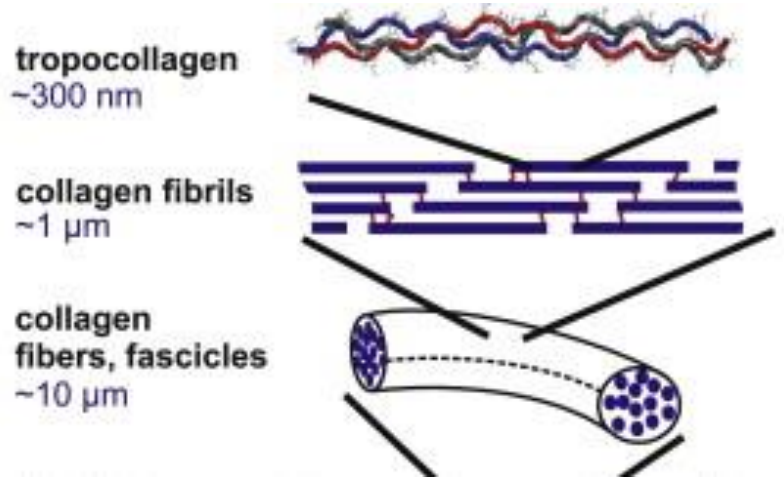


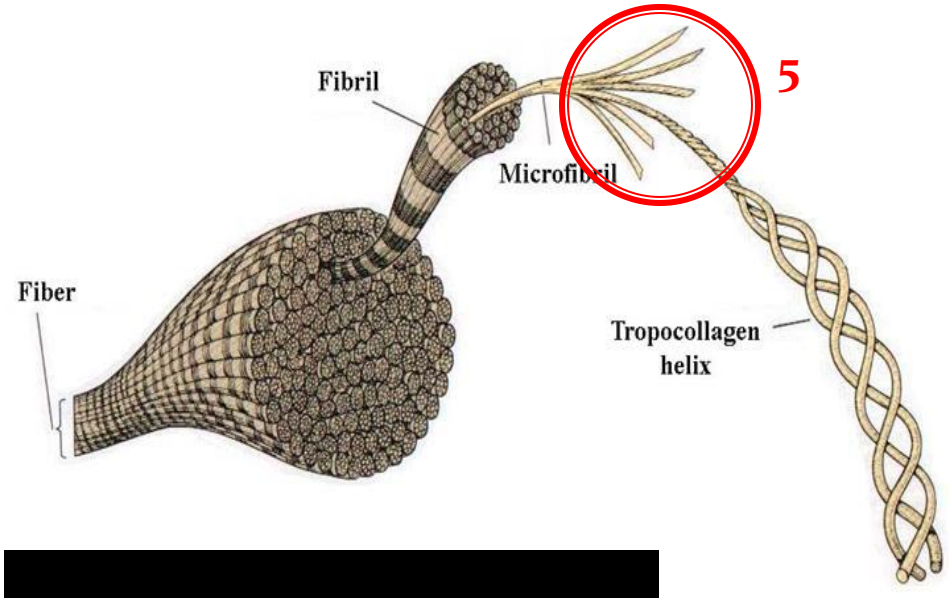




Formation of collagen fibers

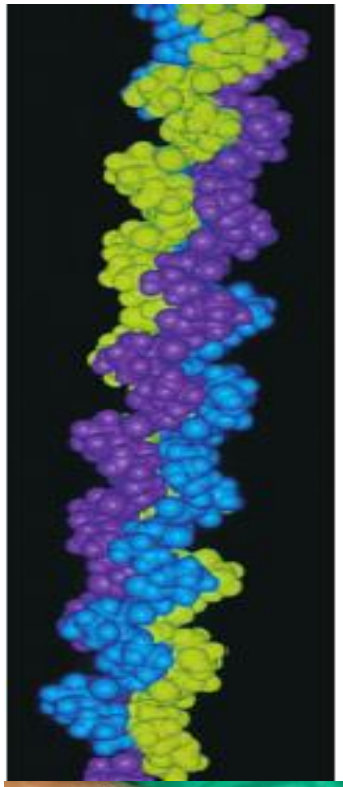
- Tropocollagen (5 of them) → microfibril → aldehyde links
- Microfibrils → fibrils → covalent cross links between lysine residues
- Fibrils → fibers

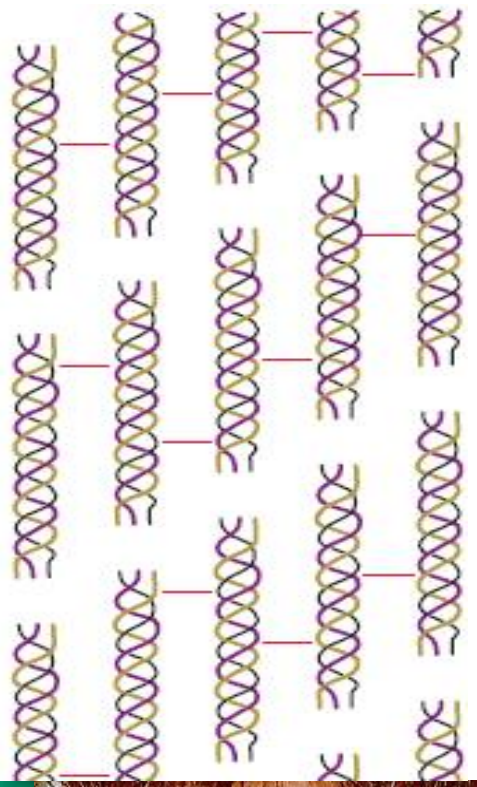


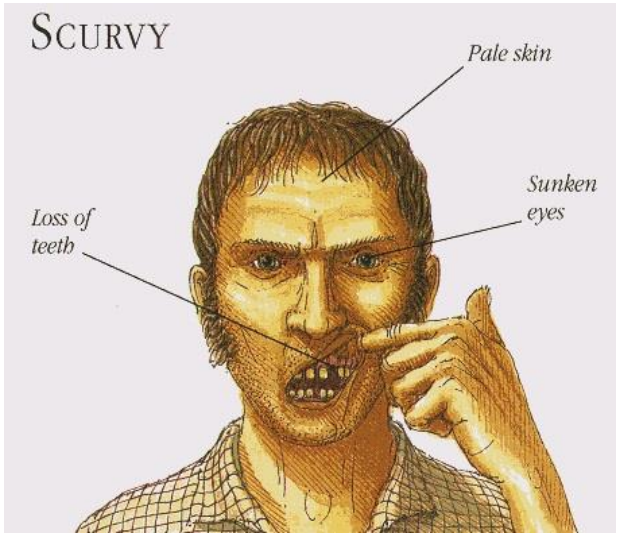


Collagen; Diseases

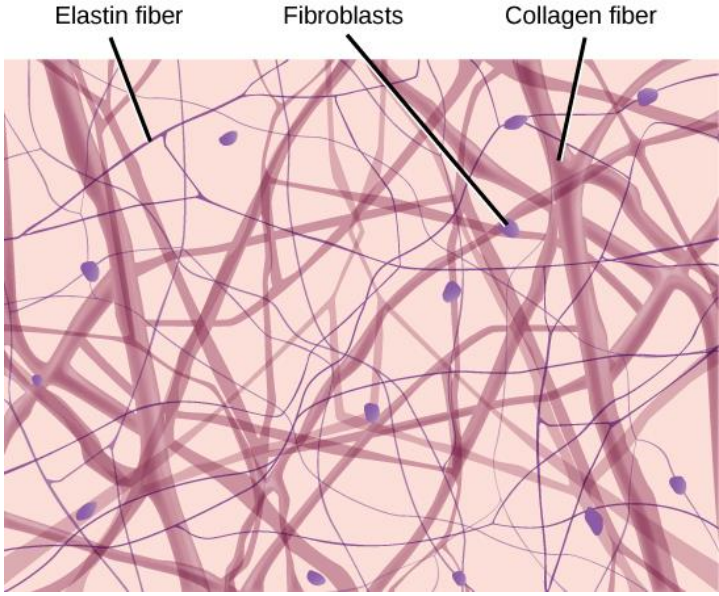
- Cross-linked intra- & inter-molecularly
- Cross-linking amounts varies according to tissue & increases with age (meat)
- Deficiency of cross-linking (Scurvy & osteogenesis imperfecta)



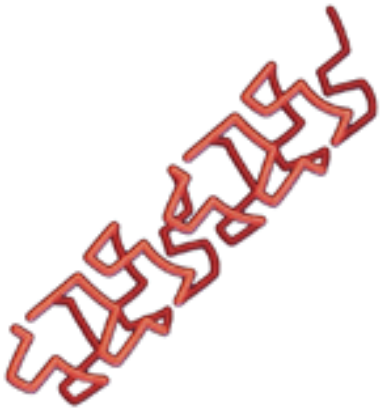


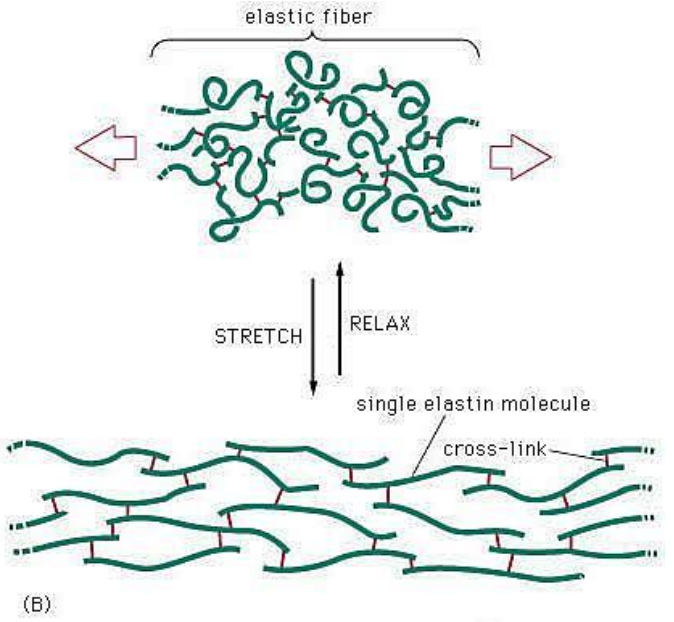


Elastin

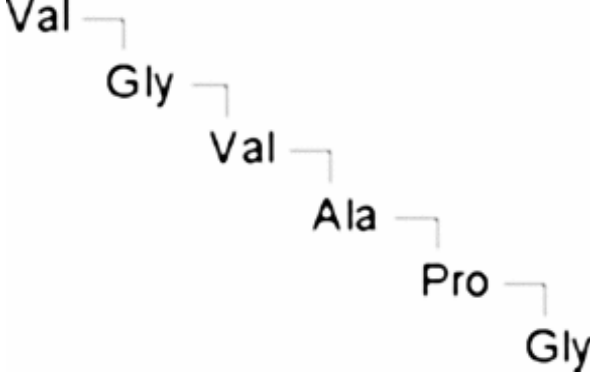


- Skin, blood vessels, and lungs
- Resilience vs. flexibility
- Long, inelastic <u>collagen fibrils are interwoven</u> with the elastic fibers to limit the extent of stretching and prevent the tissue from tearing
- It is <u>not glycosylated</u>

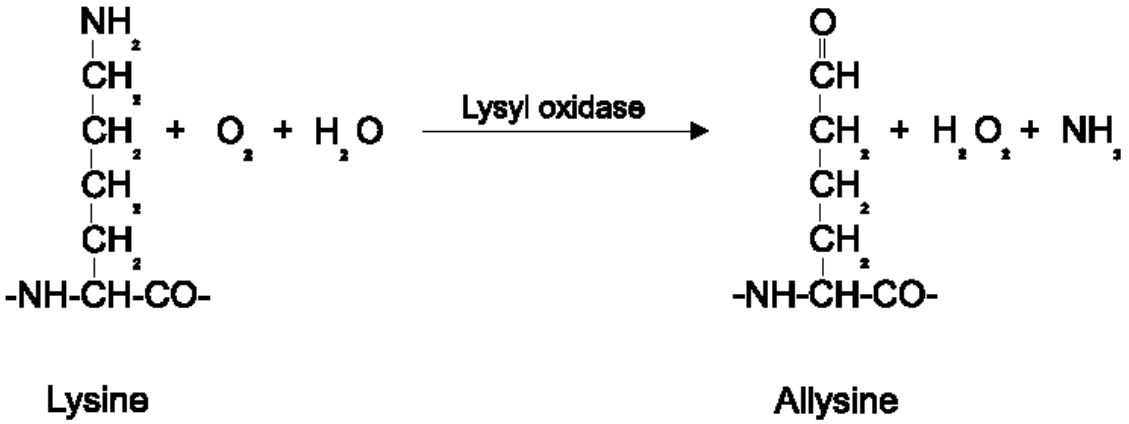


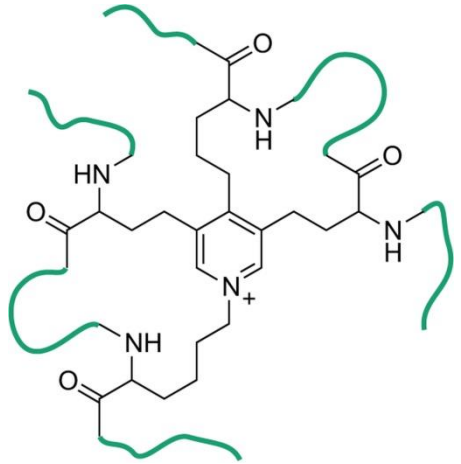


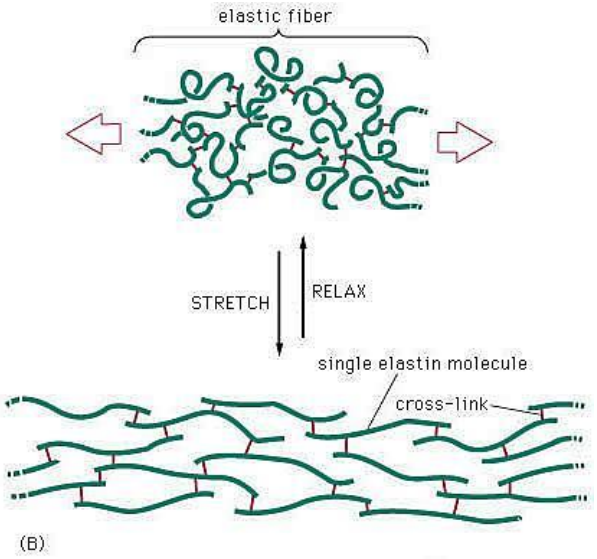
Elastin



- Rich in hydrophobic amino acids (ex. Gly, Val & Pro); mobile hydrophobic regions bonded by crosslinks between Lys
- Elastic fibers in arteries are composed mainly of elastin (≈70%)
- Tropoelastin → Elastin (Lysyl oxidase)
- Three allysyl side chains plus one unaltered lysyl side chain

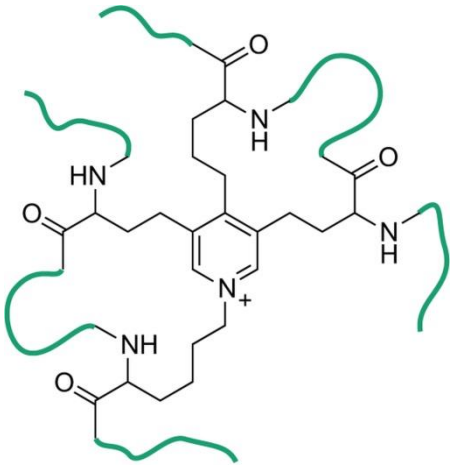


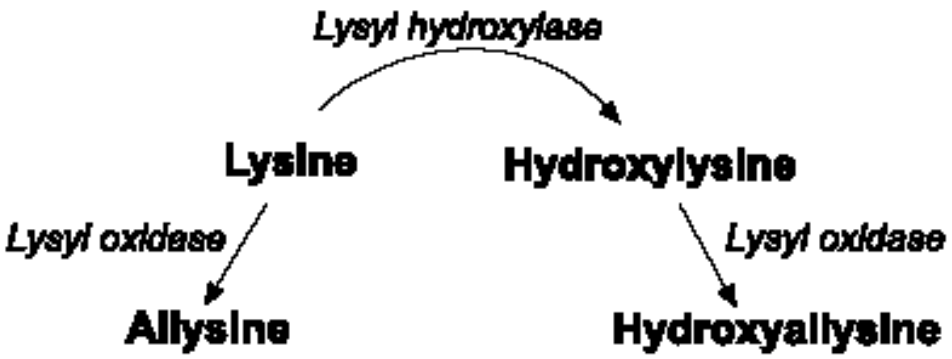


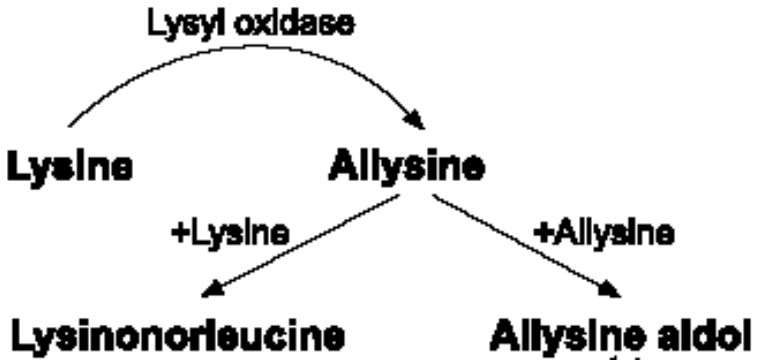


Elastin & hydroxylysine

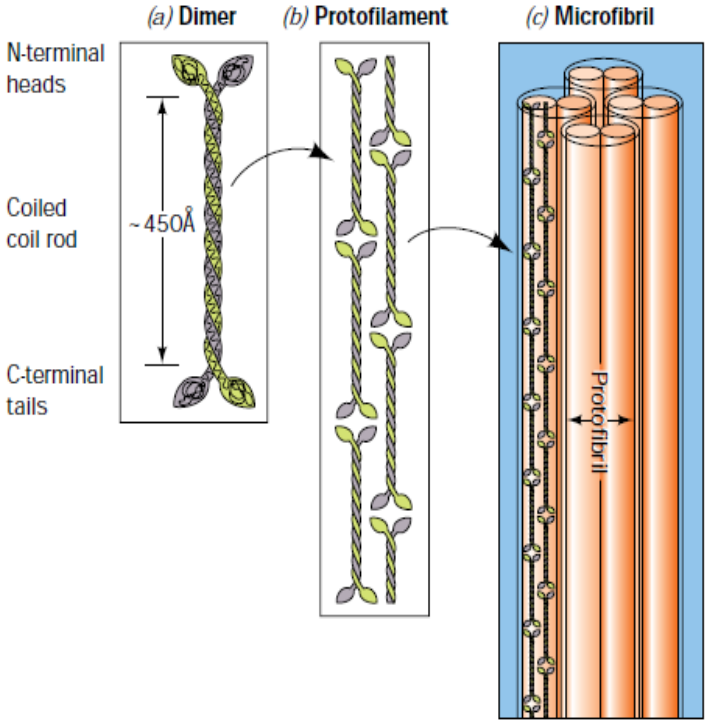
- Collagen contain lysine that can be hydroxylated by lysyl-hydroxylase to form hydroxyl-lysine or by lysyl-oxidase to form Allysine
- Cross-linking of elastin occurs through the enzyme lysyl-oxidase producing the Allysine, the pathway for oxidation through lysyl-hydroxylase does not occur in elastin





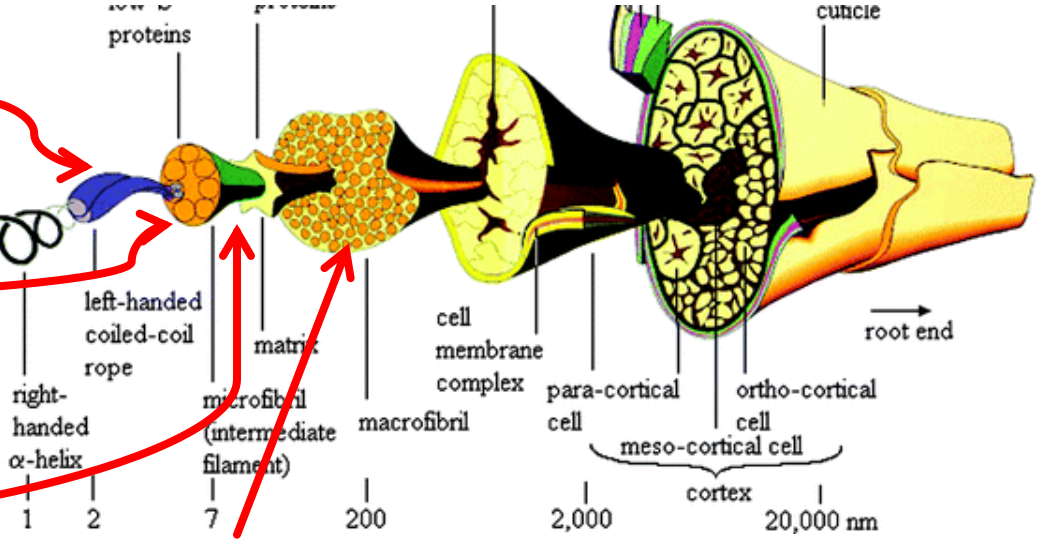


Keratin

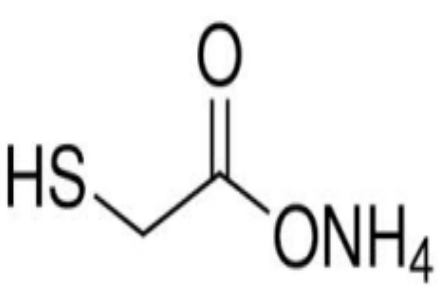


- Principal component of epidermis & related appendages (hair, horn, nails, & feathers)
- α (mammals) or β (birds & reptiles)
- Mammals: ≈30 types, tissue-specific

- Structure:
  - α-helix (1), Coiled coil (2)
  - Protofibril (4)
  - Microfibril (28-32) (7-8 proto), Macrofibril (1000_s) (100_s micro)



α-Keratin



- Unusual content of Cys
- Classified as "hard" or "soft" according to S content (Cys)
- How is a perm done?
  - A basic reducing substance (usually ammonium thioglycolate) is added to reduce and rupture some of the disulfide cross-links
  - Temporary Wave (affect H-bonding)
  - Vs. permanent wave (affect H & S-S bonding)