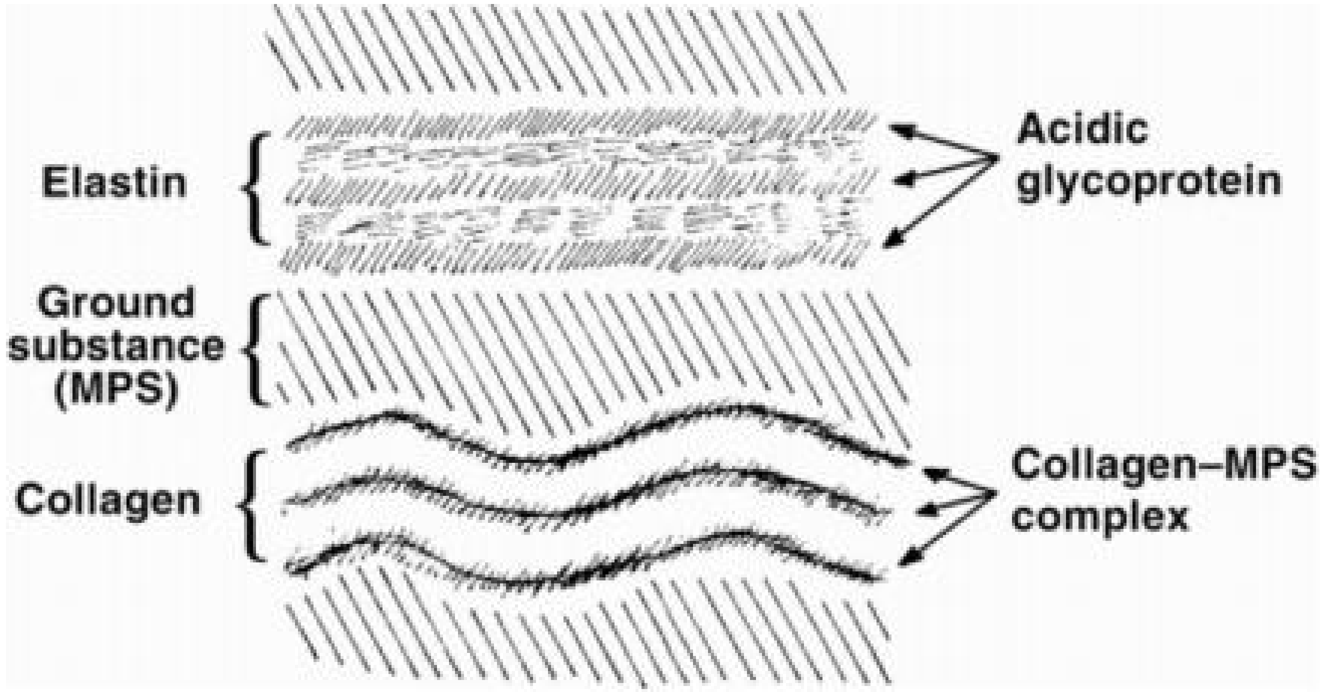
Module3

Biological materials-proteins, polysaccharides, Structure and property relation of Tissues- Mineralized tissues, collagen rich tissues and elastic tissues

Biological materials

- Structurally, biological tissues consist of a vast network of intertwining fibers with polysaccharide ground substances immersed in a pool of ionic fluid.
- Cells that comprise the living tissues are attached to the fibers
- Physically, ground substances (polysachharides) function as a glue, lubricant, and shock absorber in various tissues.
- Neural tissues consist almost entirely of cells, while bone is composed of organic materials and calcium phosphate minerals with minute quantities of cells and ground substances as a glue
- The major difference between biological materials and biomaterials (implants) :
- First, most biological materials are continuously bathed with body fluids. Exceptions are the specialized surface layers of skin, hair, nails, hooves, and the enamel of teeth. Second, most biological materials can be considered as *composites*



Schematic representation of mucopolysaccharides—protein molecules in connective tissues.

Types

- **PROTEINS-collagen,elastin**
- **POLYSACCHARIDES-Hyaluronic Acid and Chondroitin , Chondroitin Sulfate**

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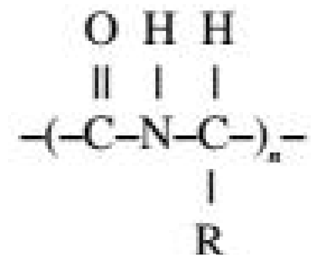
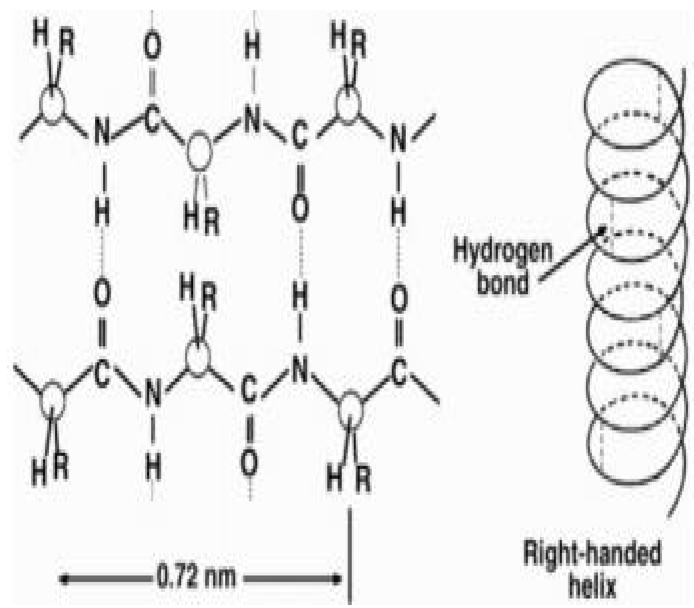
PROTEINS

- Proteins are polyamides formed by step-reaction polymerization between amino and carboxyl groups of amino acids:

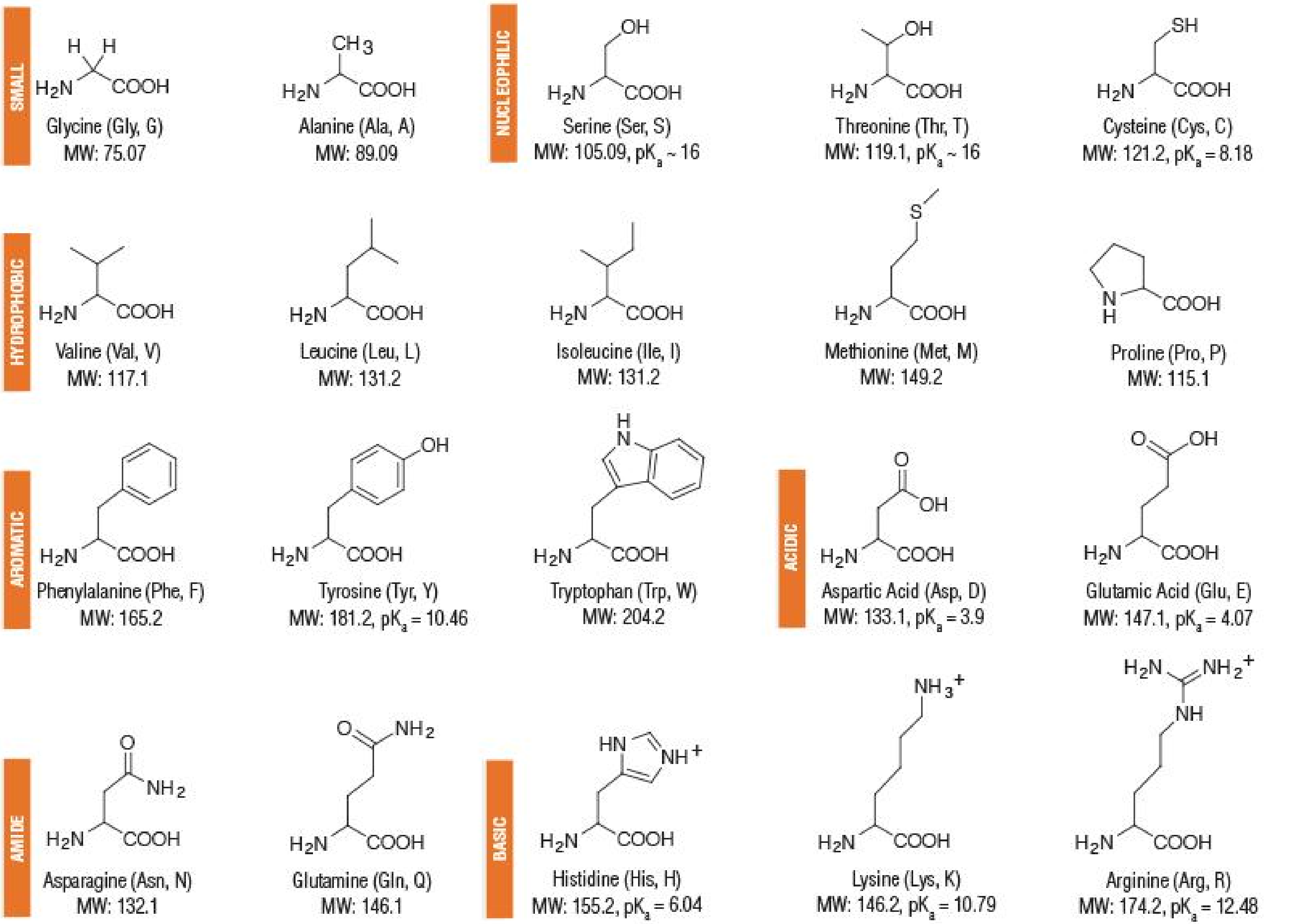
Depending on the side group(R), the molecular structure changes drastically. The structure has a repeating distance of 0.72 nm, and the side groups (R) are crowded, except for polyglycine, which has the smallest atom for the side group, H.

If the side groups are larger, then the resulting structure is an D-*helix*, where the hydrogen bonds occur between different parts of the same chain and hold the helix together, as shown in Figure .



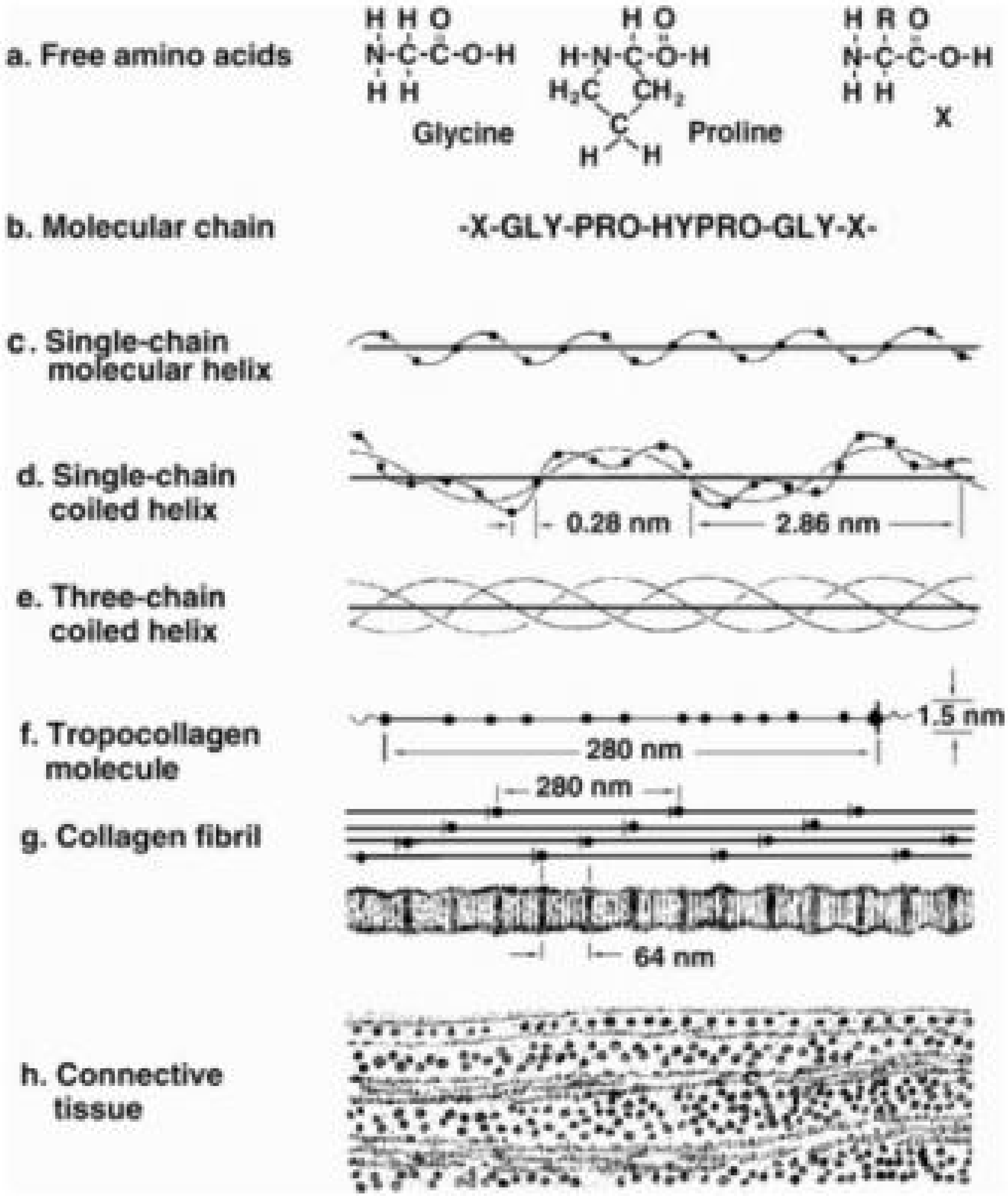


Chemical structure of amino acids



Collagen

- Collagen is a structural protein found in bone, cartilage, tendon, ligament, skin, and in the structural fibers of various organs.
- One of the basic constituents of protein is collagen, which has the general amino acid sequence–X–Gly–Pro–Hypro–Gly–X– (X can be any other amino acid) arranged in a triple D-helix. It has a high proportion of proline (Pro) and hydroxyproline (Hypro)
- Three left-handed-helical peptide chains are coiled together to give a right-handed coiled superhelix with periodicity of 2.86 nm.
- This triple super helix is the molecular basis of ***tropocollagen***, the precursor of collagen .
- The three chains are held strongly to each other by H bonds between glycine residues and between hydroxyl (OH) groups of hydroxyproline.
- In addition, there are crosslinks via lysine among the (three) helices.
- The side groups of some amino acids are highly non-polar in character and hence *hydrophobic*; therefore, chains with these amino acids avoid contact with water molecules
- If the collagen is dehydrated completely (lyophilized), then the solubility also decreases (so-called in vitro aging of collagen).



a. Free amino acids
Glycine
Proline
X
b. Molecular chain
-X-GLY-PRO-HYPRO-GLY-X-
c. Single-chain molecular helix
d. Single-chain coiled helix
0.28 nm
2.86 nm
e. Three-chain coiled helix
f. Tropocollagen molecule
1.5 nm
280 nm
280 nm
g. Collagen fibril
64 nm
h. Connective tissue

Composition of Collagen

A.A. and component	Content (mol/100 mol amino acids)
Gly	31.4–338
Pro	11.7–13.8
Hypro	9.4–10.2
Acid polar a.a.s. (aspt. glut. asparagine)	11.5–12.5
Basic polar a.a.s. (lys. agr. his.)	8.5–8.9
Other a.a.s.	Residue

Elastin

- Elastin is another structural protein found in a relatively large amount in elastic tissues such as *ligamentum nuchae* (major supporting tissue in the head and neck of grazing animals), aortic wall, skin, etc.
- The chemical composition of elastin is somewhat different from that of collagen.
- The high elastic compliance and extensibility of elastin is due to the crosslinking of lysine residues via *desmosine, isodesmosine*, and *lysinonorleusine*
- The formation of desmosine and isodesmosine is only possible by the presence of copper and lysyl oxidase enzyme; hence, deficiency of copper in the diet may result in non-crosslinked elastin.
  This, in turn, will result in tissue that is viscous rather than normal rubber-like elastic tissue,and abnormality that can lead to rupture of the aortic walls.
- Elastin is very stable at high temperature in the presence of various chemicals due to the very low content of polar side groups (hydroxyl and ionizable groups)
- Elastin contains a high percentage of amino acids with aliphatic side chains such as *valine* (6 times that of collagen) , very few ionizable groups

Composition of Elastin

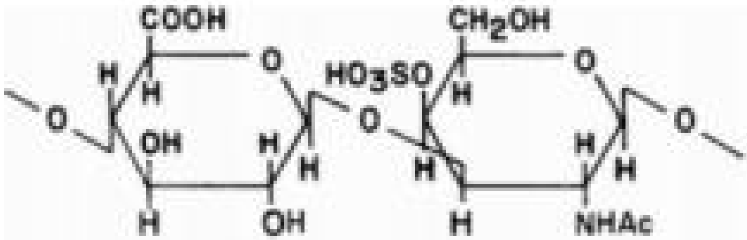
Content	Amount (residues/1000)
Gly	324
Hypro	26
Cationic residues (Asp, Glu)	21
Anionic residues (His, Lys, Arg)	13
Nonpolar residues (Pro, Ala, Val, Met, Leu, Ile, Phe, Tyr)	595
Half-cystine	4

POLYSACCHARIDES

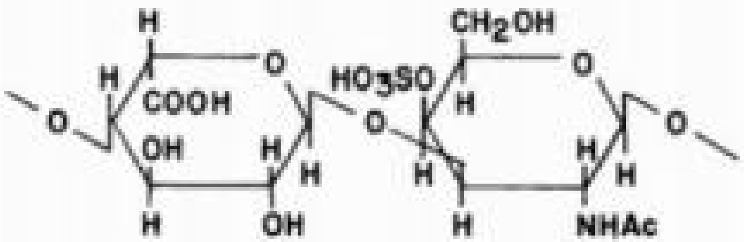
- Polysaccharides are polymers of simple sugars. They exist in tissues as a highly viscous material that interacts readily with proteins, including collagen, resulting in *glycosamino–glycans (*also known as *mucopolysaccharides)* or *proteoglycans*.
- These molecules readily bind both water and cations due to the large content of anionic side chains.
- They exists as viscoelastic gels
- They act as glue to bind the layers of collagen and elastin in connective tissue

Hyaluronic Acid and Chondroitin

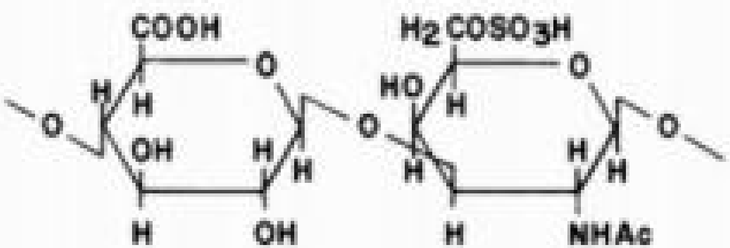
- Hyaluronic acid is found in the vitreous humor of the eye, synovial fluid, skin, umbilical cord,and aortic walls.
- Hyaluronic acid is made of residues of N-acetylglucosamine and Dglucuronic acid, but it lacks the sulfate residues.
- The animal hyaluronic acid contains a protein component (0.33 w/o or more) and is believed to be chemically bound to at least one protein or peptide that cannot be removed.
- Chondroitin is similar to hyaluronic acid in its structure and properties ecept the chemical linkage at one site (position of hydroxy group w.r.t. the interunit linkage
- It is found in the cornea of the eyes



Isomer A

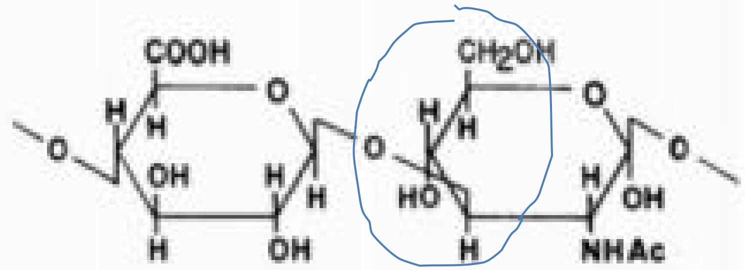


Isomer B

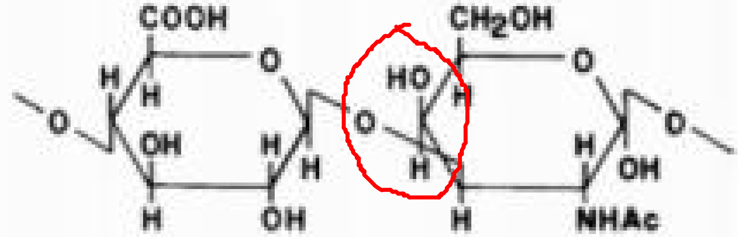


Isomer C

Chondroitin sulfate



Hyaluronic acid



Chondroitin

Chondroitin Sulfate

- Isomer A (chondroitin 4-sulfate) is found in cartilage, bones,and the cornea, while isomer C (chondroitin 6-sulfate) can be isolated from cartilage, umbilical cord, and tendon. Isomer B (dermatan sulfate) is found in skin and the lungs and is resistant to testicular hyaluronidase enzyme.
- The chondroitin sulfate chains in connective tissues are bound covalently to a polypeptide backbone through their reducing ends.
- Complexes of protein and mucopolysaccharides (ground substance) play an important role in the physical behavior of connective tissues either as lubricating agents between tissues (e.g., joints) or between elastin and collagen microfibrils

STRUCTURE–PROPERTY RELATIONSHIP OF TISSUES

- **Mineralized Tissue (Bone and Teeth)**
- Bone and teeth are mineralized tissues whose primary function is “load carrying.” Teeth are in more extraordinary physiological circumstances since their function is carried out in direct contact with ex-vivo substances, while the functions of bone are carried out inside the body in conjunction with muscles, ligaments, and tendons.

Composition of Bone

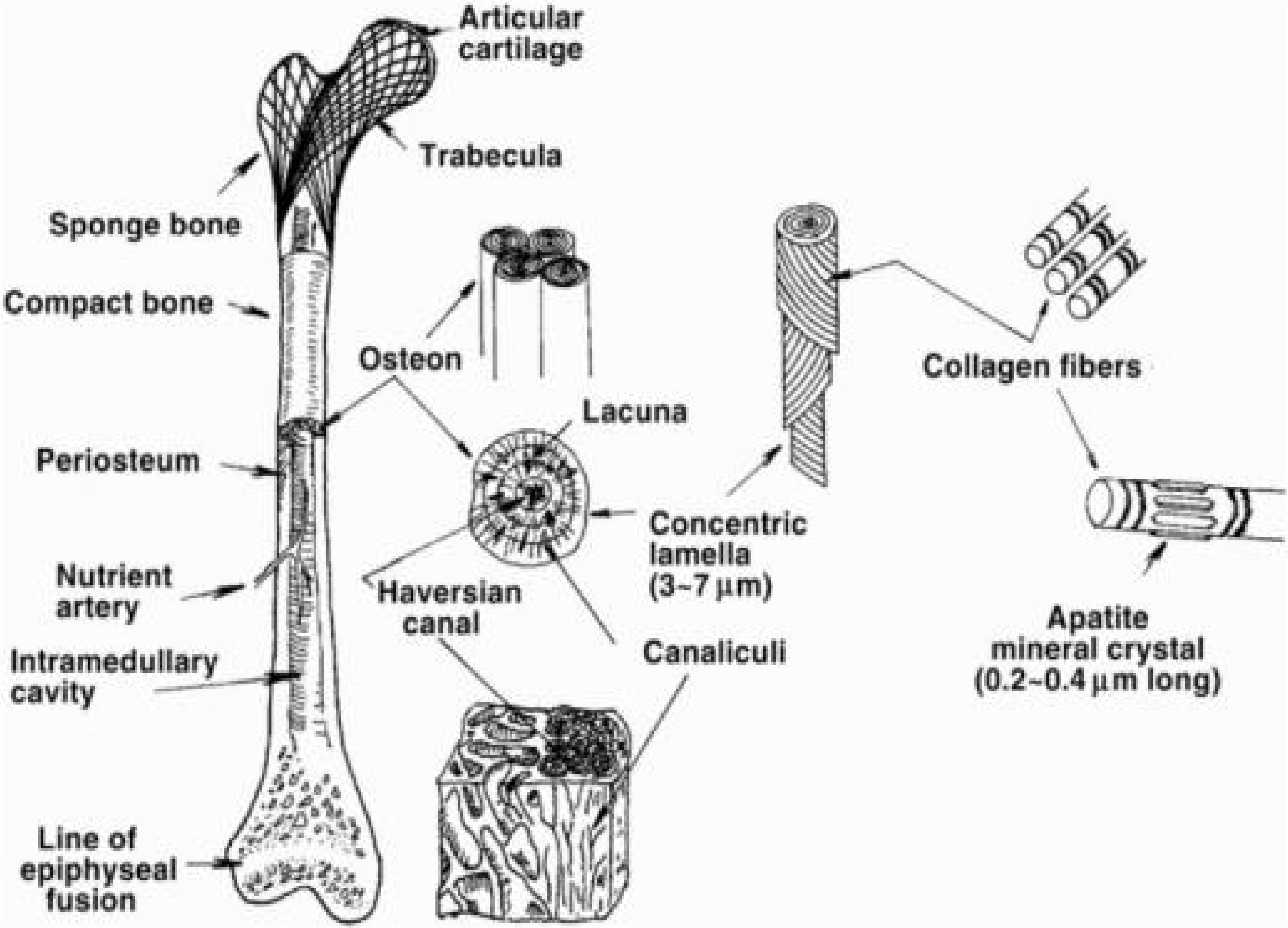
Component	Amount (w/o)
Mineral (apatite)	69
Organic matrix	22
collagen	(90–96% of organic matrix)
others	(4–10% of organic matrix)
Water	9

Wet cortical bone is composed of 22 w/o organic matrix, of which 90–96 w/o is collagen, mineral (69 w/o), and water (9 w/o),

Reference: J.B. PArk

Chemical structure of bone

- The major subphase of the mineral consists of submicroscopic (nanoscale) crystals of an apatite of calcium and phosphate, resembling hydroxyapatite in its crystal structure — ($Ca_{10}(PO_4)_6(OH)_2$).
- There are other mineral ions such as citrate ($C_6H_5O_7^{-4}$), carbonate (CO_3^{-2}), fluoride (F^-), and hydroxyl ions (OH^-), which may yield some other subtle differences in microstructural features of the bone.
- The apatite crystals are formed as slender needles, 20–40 nm in length by 1.5–3 nm in thickness, in the collagen fiber matrix. Plate-like crystals are also found in bone.
- Collagen fibrils, which contain mineral, are arranged into lamellar sheets (3-7 μm) that run helically with respect to the long axis of the cylindrical *osteons* (or sometimes called *Haversian systems*)


Articular cartilage
Trabecula
Sponge bone
Compact bone
Osteon
Lacuna
Periosteum
Concentric lamella (3~7 µm)
Nutrient artery
Haversian canal
Intramedullary cavity
Canaliculi
Line of epiphyseal fusion
Collagen fibers
Apatite mineral crystal (0.2~0.4 µm long)

- The osteon is made up of 4 to 20 lamellae that are arranged in concentric rings around the Haversian canal. Osteons are typically from 150 to 250 μm in diameter. Between these osteons the interstitial systems are sharply divided by the *cementing line*, or *cement line.*
- The metabolic substances can be transported by the intercommunicating pore systems, known as *canaliculi, lacunae*, and *Volksmann's canals,* which are connected with the marrow cavity. These various interconnecting systems are filled with body fluids.
- Long bones such as the femur contain cancellous (or spongy) and compact bone. The spongy bone consists of three-dimensional branches or bony trabeculae interspersed by the bone marrow.
- More spongy bone is present in the epiphyses of long bones and within vertebrae, while compact bone is the major form present in the diaphysis of a long bone

Teeth

- All teeth are made of two portions — the crown and the root — usually demarcated by the gingiva (gum). The root is placed in a socket called the alveolus in the maxillary (upper) or mandibular (lower) bones.
- The enamel is the hardest substance found in the body and consists almost entirely of calcium phosphate salts (97%) in the form of large apatite crystals.

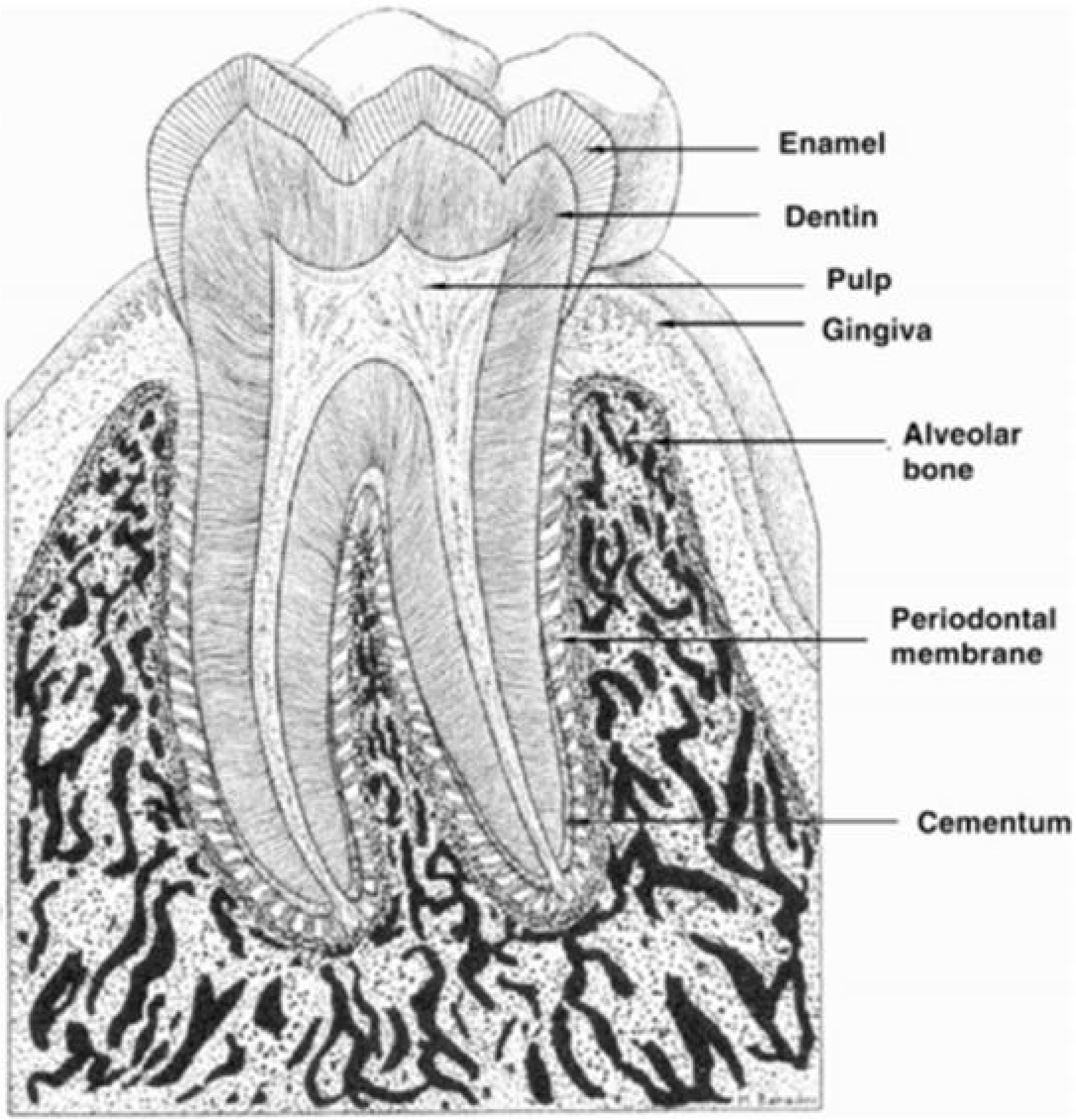
  The dentin is another mineralized tissue whose distribution of organic matrix and mineral is similar to that of compact bone.

Structural features of teeth

- The collagen matrix of the dentin might have a somewhat different molecular structure than the normal bone: it is more crosslinked than that found in other tissues.
- Dentinal tubules (3–5 μm wide) radiate from the pulp cavity toward the periphery and penetrate every part of the dentin.
  The dentinal tubules contain collagen fibrils (2-4 Pm thick) in the longitudinal direction, and the interface is cemented by a protein–polysaccharide complex substance, as well as the processes of the odontoblasts, which are cells lining the pulp cavity.

Structural features of teeth

- Cementum covers most of the root of the tooth with a coarsely fibrillated bone-like substance devoid of canaliculi, Haversian systems, and blood vessels.
- The pulp occupies the cavity and contains thin collagenous fibers running in all directions and not aggregated into bundles.
- Ground substance, nerve cells, blood vessels, etc. are also contained in the pulp. The periodontal membrane anchors the root firmly into the alveolar bone and is made of mostly collagenous fibers plus glycoproteins (protein–polysaccharides complex) .



Sagittal section of a molar tooth.

Collagen-Rich Tissues

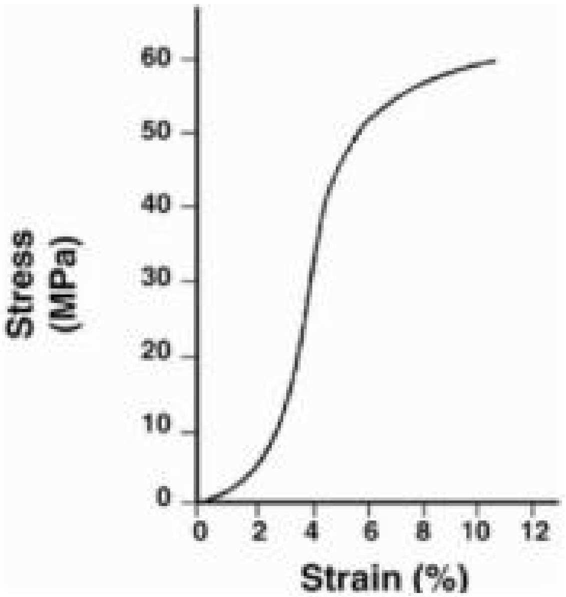
Physical properties

- Collagen-rich tissues function mostly in a load-bearing capacity. These tissues include skin, tendon, cartilage, etc. Special functions such as transparency for the lens of the eye and shaping of the ear, tip of the nose, etc. can be carried out also by the collagenous tissues.

Composition of Collagen-Rich Soft Tissues

Component	Composition (%)
Collagen	75 (dry), 30 (wet)
Mucopolysaccharides	20 (dry)
Elastin	< 5 (dry)
Water	60–70

- The collagen-rich tissues can be thought of as polymeric materials in which the highly oriented crystalline collagen fibers are embedded in the ground substance of mucopolysaccharides and amorphous elastin (a rubber-likebiopolymer)
- The stress–strain curves of a collagenous structure such as tendon exhibit nonlinear behavior
- The initial toe region represents alignment of fibers in the direction of stress, and the steep rise in slope represents the majority of fibers stretched along their long axes.
- As for the later decrease in slope, individual fibers may be breaking prior to final catastrophic failure.
- The highest slope of the stress–strain curve is about 1.0 GPa, which is close to the modulus of individual collagen fibers. The tensile strength is, however, much lower than that of the individual fibers.



A typical stress–strain curve for tendon. Reprinted with permission from Rigby et al. (1959). Copyright © 1959, Rockefeller University Press.

Cartilage is another collagen-rich tissue that has two main physiological functions. One is the maintenance of shape (ear, tip of nose, and rings around the trachea), and the other is to provide bearing surfaces at joints. It contains very large and diffuse protein–polysaccharide molecules that form a gel in which the collagen-rich molecules are entangled

Elastic Tissues