CHAPTER 9
STRUCTURE-PROPERTY RELATIONSHIPS OF BIOLOGICAL MATERIALS
Table 5-1. Distribution of Various Tissues and Physiological Condition of Western Man\textsuperscript{a}

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>43%</td>
</tr>
<tr>
<td>Bone</td>
<td>30%</td>
</tr>
<tr>
<td>Skin</td>
<td>7%</td>
</tr>
<tr>
<td>Blood</td>
<td>7.2%</td>
</tr>
</tbody>
</table>

Organs:
- Spleen (0.2%)
- Heart (0.4%)
- Kidneys (0.5%)
- Lungs (1.0%)
- Liver (2%)
- Brain (2.3%)
- Viscera (5.6%)

Water 60%, solids 40%

Average body weight: 70 kg (155 lbs)

Medium height: 1.8 m (5.91 ft)

Basic metabolic rate 68 kcal/h

pH: Gastric contents (1.0), urine (4.5-6.0), intracellular fluid (6.8), blood (7.15-7.35)
P0\textsubscript{2} (mm Hg): Interstitial (2-40), venous (40), arterial (100), atmospheric (160)
PCO\textsubscript{2} (mm Hg): Alveolar (40)

\textsuperscript{a} From Ref. 1.
9.1 Proteins

- Polyamides formed by step reaction polymerization between amino & carboxyl groups of amino acids,

\[
H_2N \biggarrow R \biggarrow C \biggarrow C \biggarrow OH^n (9-1)
\]
• Step-reaction polymerization between amino & carboxyl groups of amino acids

\[
\begin{align*}
&\text{O} \\
&\text{C} \\
&\text{H} \\
&\text{H} \\
&\text{N} \\
&\text{C} \\
&\text{R} \\
&\text{n}
\end{align*}
\] (9-2)
• Simplest side group, hydrogen (H): glycine (Gly) [Fig. 9-1a] Repeating distance, 0.72 nm.
• If side groups are larger — helix where H-bonds occur between different parts of same chain & hold helix together [Fig 9-1b].
9.1.1 Collagen

- Sequence: -Gly-Pro-Hypro-Gly-X- (X: any other a.a.), triple helix.
- High proportion of proline (Pro) & hydroxyproline (Hypro) [Table 9-1].

**TABLE 9-1. AMINO ACID CONTENT OF COLLAGEN (1)**

<table>
<thead>
<tr>
<th>A.A. and Component</th>
<th>Content (mol/100 mol amino acids)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gly</td>
<td>31.4 - 338</td>
</tr>
<tr>
<td>Pro</td>
<td>11.7 - 13.8</td>
</tr>
<tr>
<td>Hypro</td>
<td>9.4 - 10.2</td>
</tr>
<tr>
<td>Acid polar a.a.s.</td>
<td></td>
</tr>
<tr>
<td>(Aspt. Glut. Asparagine)</td>
<td>11.5 - 12.5</td>
</tr>
<tr>
<td>Basic polar a.a.s.</td>
<td></td>
</tr>
<tr>
<td>(Lys. Agr. His.)</td>
<td>8.5 - 8.9</td>
</tr>
<tr>
<td>Other a.a.s.</td>
<td></td>
</tr>
</tbody>
</table>

1. A.A. and Component refers to amino acids and their components.
• Three left-handed-helical peptide chains right-handed coiled super helix periodicity of 2.86 nm. *tropocollagen* [Fig 9-2].
• H-bonds between glycine & hydroxyl (OH) groups of hydroxyproline. Cross-links via lysine among (three) helices.
• Primary factors stabilizing collagen molecules
  – H-bonding between the C=O & NH groups,
  – Ionic bonding between side groups of polar a.a.
  – Interchain cross-links between helices.
• Collagen fibrils (20-40nm dia) form fiber bundles, 0.2-1.2\,\mu m dia.
• SEM pictures of collagen fibrils in bone, tendon & skin[Fig 9-3]
• Side groups of some a.a. are highly non-polar hydrophobic;
• Stability of collagen fibers by forming mucopolysaccharide-protein complexes.
9.1.2 Elastin

- Structural protein found in elastic tissues, ligamentum nuchae, aortic wall, skin, etc.
- High elasticity, due to cross-linking of lysine residues via *desmosine, isodesmosine & lysinonorleucine* [Fig 9-4].

![Chemical structures of desmosine, isodesmosine, and lysinonorleucine](image)

*Figure 9-4. Structure of desmosine, isodesmosine, and lysinonorleucine.*
• Presence of copper & lysyl oxidase enzyme.
• Elastin is very stable at high temp & chemicals due to very low content of polar side groups (hydroxyl & ionizable groups).
• It lacks all basic & acidic a.a. => very few ionizable groups.

**TABLE 9-2. AMINO ACID CONTENT OF ELASTIN**

<table>
<thead>
<tr>
<th>Content</th>
<th>Amount(residues/1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gly</td>
<td>324</td>
</tr>
<tr>
<td>Hypro</td>
<td>26</td>
</tr>
<tr>
<td>Cationic residues(Asp, Glu)</td>
<td>21</td>
</tr>
<tr>
<td>Anionic residues(His, Lys, Arg)</td>
<td>13</td>
</tr>
<tr>
<td>Nonpolar residues (Pro, Ala, Val, Met, Leu, Ile, Phe, Tyr)</td>
<td>595</td>
</tr>
<tr>
<td>Half-cystine</td>
<td>4</td>
</tr>
</tbody>
</table>
9.2 Polysaccharides

- Polymers of simple sugars.
- Highly viscous material interacts readily with proteins, including collagen, resulting in glycosaminoglycans (also known as mucopolysaccharides) or proteoglycans.
- Readily bind both water & cations due to large content of anionic side chains.
- Also exist at physiological concentrations not as viscous solids but as viscoelastic gels.
- All polysaccharides are disaccharide units unbranched macromolecules [Fig 9-5].

**Isomer A**

**Isomer B**

**Isomer C**

**Hyaluronic acid**

**Chondroitin**

**Chondroitin sulfate**

*Figure 9-5. Structure of hyaluronic acid, chondroitin, and chondroitin sulfates.*
• 9.2.1 Hyaluronic acid and chondroitin

• N-acetylglucosamine and D-glucuronic acid, but lacks the sulfate residues.
• Animal HA contains a protein component (>0.33 % chemically bound to at least one protein or peptide which cannot be removed) proteoglycan molecules behave differently from pure PS.
• Found in the vitreous humor of the eye, synovial fluid, skin, umbilical cord and aortic walls.
• Chonodroitin is similar to HA in its structure and properties and is found in the cornea.
9.2.2 Chondroitin sulfate

- Sulfated MPS which resists hyaluronidase enzyme.
- Three isomers [Fig 9-5]. Isomer A (chondroitin 4-sulfate), cartilage, bones & cornea, isomer C (chondroitin 6-sulfate), cartilage, umbilical cord & tendon. Isomer B (dermatan sulfate), skin & lungs.

Figure 9-5. Structure of hyaluronic acid, chondroitin, and chondroitin sulfates.
• Complexes of protein & MPS (ground substance) physical behavior of connective tissues either as lubricating agents between tissues (e.g. joints) or between elastin & collagen micro-fibrils [Fig 9-6].

Figure 9-6. A schematic representation of mucopolysaccharide–protein molecules in connective tissues. Note the wavy nature of collagen fibers and straighter form of elastin.
9.3 Structure-Property Relationship of Tissues

- Property measurements of any tissues have the following limitations & variations:
  - Limited sample size,
  - Original structure can undergo change during sample collection or preparation,
  - Inhomogeneity,
  - Difficult to obtain fundamental physical parameters,
  - Tissue cannot be frozen or homogenized w/o altering its structure or properties.
  - *In vitro & in vivo* properties, difficult to correlate.
• Property-structure relation of tissues design better performing implants.
• "What kind of physiological functions are being performed by the tissues or organs under study \textit{in vivo} and how can one best assume their lost function?"
9.3.1 Mineralized Tissue (Bone and Teeth)
a. Composition and Structure

- Primary function: "load-carrying."
- Long bone [Fig 9-7].
Wet cortical bone, 22% organic matrix of which 90-96% is collagen; mineral, 69%; & water, 9% [Table 9-3].

TABLE 9-3 COMPOSITION OF BONE(3)

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mineral (apatite)</td>
<td>69</td>
</tr>
<tr>
<td>Organic matrix</td>
<td>22</td>
</tr>
<tr>
<td>collagen (90-96% of organic matrix)</td>
<td></td>
</tr>
<tr>
<td>others (4-10% of organic matrix)</td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>9</td>
</tr>
</tbody>
</table>
• Mineral: submicroscopic crystals of apatite of calcium & phosphate, resembling hydroxyapatite in its crystal structure \((\text{Ca}_{10}\text{(PO}_4\text{)}_6\text{(OH)}_2)\).

• Other ions; citrate \((\text{C}_6\text{H}_5\text{O}_7^{-4})\), carbonate \((\text{CO}_3^{-2})\), fluoride \((\text{F}^{-})\) & hydroxyl ions \((\text{OH}^{-})\)

• Apatite crystals slender needles, 20-40 nm length, 1.5-3 nm in thickness, in collagen fiber matrix. [Extra Fig 1]
• Mineral containing fibrils => lamellar sheets (3-7 \( \mu \text{m} \)), run helically w.r.t. long axis of cylindrical osteons (Haversian systems).

• **Osteon**: 4~20 lamellae, concentric rings around Haversian canal.

• Osteons: 150~250 \( \mu \text{m} \) dia.

• Between osteons; interstitial systems are sharply divided by cementing line.

• Intercommunicating pore systems: canaliculi, lacunae & Volkmann's canals. 18.9±0.45v/o, compact beef bone.
• External & internal surfaces of bone: periosteum & endosteum; **osteogenic**.

• Mineral phase; not completely discrete aggregation of calcium phosphate mineral crystals[^Fig 9-8^].

• **Cancellous (or spongy):** consists of 3-D branches or bony trabeculae interspersed by bone marrow.
• Deciduous or primary & permanent teeth
• Two portions: crown & root, demarcated by gingiva
• Root is placed in alveolus in maxillary or mandibular bones [Fig 9-9]
• **Enamel**: hardest substance found in body, almost entirely of calcium phosphate salts (97%), large apatite crystals.

• **Dentin**: mineralized tissue similar to compact bone. Physical properties are similar.

• **Collagen matrix of dentin** is more **cross-linked** than other tissues.

• **Dentinal tubules** (3-5 µm thick) penetrate every part of dentin. Contain collagen fibrils (2-4 µm thick), interface is **cemented** by a protein-PS complex substance, & processes of **odontoblasts**, which are cells lining pulp cavity.
• **Cementum** covers tooth root with a coarsely fibrillated bone-like substance

• **Pulp** occupies cavity & contains thin collagenous fibers running in all directions & not aggregated into bundles. Ground substance, nerve cells, blood vessels, etc. also contained in pulp.

• **Periodontal membrane** anchors root firmly into alveolar bone, made of mostly collagenous fibers plus glycoproteins (protein-PS complex).
• Strength; the highest for enamel & dentin is between bone & enamel. Thermal expansion & conductivity are higher for enamel than dentin [Table 9-4].

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Density (g/cm³)</th>
<th>Modulus of Elasticity (GPa)</th>
<th>Compressive Strength (MPa)</th>
<th>Coefficient of Thermal Expansion (°C)</th>
<th>Thermal Conductivity (W/m°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enamel</td>
<td>2.2</td>
<td>48</td>
<td>241</td>
<td>11.4 x 10⁻⁶</td>
<td>0.82</td>
</tr>
<tr>
<td>Dentin</td>
<td>1.9</td>
<td>13.8</td>
<td>138</td>
<td>8.3 x 10⁻⁶</td>
<td>0.59</td>
</tr>
</tbody>
</table>
• Example 9-2.
• Calculate the volume percentage of each major component of a wet bone based on the weight percentage i.e., 9, 69 and 22 % for water, mineral and organic phase respectively. Assume the densities of mineral and organic phase 3.16 and 1.03 g/cm³ respectively.

Answer

Based on 100 g of bone the volume of each component can be calculated dividing the weight by its density:

<table>
<thead>
<tr>
<th>Component</th>
<th>%</th>
<th>Wt(g)</th>
<th>V(cm³)</th>
<th>v/o</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mineral</td>
<td>69</td>
<td>69</td>
<td>21.8</td>
<td>41.8</td>
</tr>
<tr>
<td>Organic</td>
<td>22</td>
<td>22</td>
<td>21.4</td>
<td>41.0</td>
</tr>
<tr>
<td>Water</td>
<td>9</td>
<td>9</td>
<td>9.0</td>
<td>17.2</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>52.2</td>
<td>100</td>
</tr>
</tbody>
</table>
b. Mechanical Properties of Bone & Teeth

Properties depend on humidity, type of load (compressive or tensile), rate of loading, & direction of applied load w.r.t. orientation of microstructure.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Direction of Test</th>
<th>Modulus of Elasticity (GPa)</th>
<th>Tensile Strength (MPa)</th>
<th>Compressive Strength (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leg Bone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femur</td>
<td>longitudinal</td>
<td>17.2</td>
<td>121</td>
<td>167</td>
</tr>
<tr>
<td>Tibia</td>
<td>&quot;</td>
<td>18.1</td>
<td>140</td>
<td>159</td>
</tr>
<tr>
<td>Fibula</td>
<td>&quot;</td>
<td>18.6</td>
<td>146</td>
<td>123</td>
</tr>
<tr>
<td>Arm Bone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humerus</td>
<td>longitudinal</td>
<td>17.2</td>
<td>130</td>
<td>132</td>
</tr>
<tr>
<td>Radius</td>
<td>&quot;</td>
<td>18.6</td>
<td>149</td>
<td>114</td>
</tr>
<tr>
<td>Ulna</td>
<td>&quot;</td>
<td>18.0</td>
<td>148</td>
<td>117</td>
</tr>
<tr>
<td>Vertebra</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>longitudinal</td>
<td>0.23</td>
<td>3.1</td>
<td>10</td>
</tr>
<tr>
<td>Lumbar</td>
<td>&quot;</td>
<td>0.16</td>
<td>3.7</td>
<td>5</td>
</tr>
<tr>
<td>Spongy bone</td>
<td>&quot;</td>
<td>0.09</td>
<td>1.2</td>
<td>1.9</td>
</tr>
<tr>
<td>Skull</td>
<td>tangential / radial</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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- 97
Effect of drying [Fig 9-10]
• **Effect of anisotropy**: Young's modulus & tensile & compressive strengths in longitudinal direction are 2 & 1.5 times higher than those in radial or tangential directions respectively.

• **Effect of the rate of loading** [Fig 9-11]. Young's modulus, ultimate compressive & yield strength increase with increased rate of loading. Failure strain & fracture toughness of bone reach a maximum then decrease.
**Effect of mineral content** [Table 9-6]. More mineralized bone has higher modulus of elasticity & bending strength but lower toughness.

**TABLE 9-6. PROPERTIES OF THREE DIFFERENT BONES WITH VARYING MINERAL CONTENTS (10)**

<table>
<thead>
<tr>
<th>Type of Bone</th>
<th>Work of Fracture (J/m²)</th>
<th>Bending Strength (MPa)</th>
<th>Young’s Modulus (GPa)</th>
<th>Mineral Content (%)</th>
<th>Density (g/cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deer Antler</td>
<td>6190</td>
<td>179</td>
<td>7.4</td>
<td>59.3</td>
<td>1.86</td>
</tr>
<tr>
<td>Cow Femur</td>
<td>1710</td>
<td>247</td>
<td>13.5</td>
<td>66.7</td>
<td>2.06</td>
</tr>
<tr>
<td>Whale Tympanic Bulla</td>
<td>200</td>
<td>33</td>
<td>31.3</td>
<td>86.4</td>
<td>2.47</td>
</tr>
</tbody>
</table>
• **Effect of viscoelasticity** includes loading rate effect
• Viscoelastic properties of bone; mechanical models [Fig 9-12].
- **Effect of frequency of loading;** stiffness & dynamic mechanical damping of compact bone, Fig 9-13.

- Simple spring-dashpot model (Fig 9-12) give substantial loss & modulus variation only over about a factor ten in time or frequency Fig 9-13.

- Stiffness increases with frequency (also with rate of loading), while damping (loss tangent) has a minimum at frequencies associated with walking, running, & other activities.

• **Effect of density** \((\rho, \text{ g/cm}^3)\) & **strain rate** \((d\varepsilon/dt, \text{ sec}^{-1})\) upon **compressive strength** \(\sigma_{\text{ult}}, \text{ MPa}\) of bone is,

\[
\sigma_{\text{ult}} = 68\rho^2(d\varepsilon/dt)^{0.06} \quad (9-2)
\]

• This includes compact & trabecular bone.
• Strength of bone; depend strongly upon its density & weakly upon strain rate as shown in Fig 9-14.

• **Example 9-3.**

• Calculate the density of mineral phase of dried cow femur (c.f. Table 9-5) if the density of the organic phase and water is 1 g/cm³.
• **Answer**

• Using a simple mixture rule, neglecting water since it is dried;

\[ \bar{\rho} = \rho_1 V_1 + \rho_2 V_2 + \cdots + \rho_n V_n \]

\[ V_1 + V_2 + \cdots + V_n = 1 \]

• From Example 9-2, \( V_1 = V_2 = 0.5 \)

• Therefore, \( 2.06 = 1 \times 0.5 + \rho_m \times 0.5 \)

\[ \rho_m = 3.12 \text{ g/cm}^3 \]

• This value is close to the value of hydroxyapatite mineral as given in Ex 6-2.
c. Modeling of Mechanical Properties of Bone

- Composite material model: mineral (hydroxyapatite) & organic (collagen) phase.
- If load is independently borne by the two components then total load \( P_t \) is borne by mineral \( P_m \) and collagen \( P_c \),

\[
P_t = P_m + P_c
\]  
(9-3)
Since $\frac{P}{A} = E$, thus,

$$P_m = A_m \times E_m \times \phi_m \quad (9-4)$$

- where $A$, $E$, & $\phi$; area, modulus, & strain. Suppose that the strain of collagen can be assumed to be equal to that of mineral, that is

$$P_c = P_m \frac{A_cE_c}{A_mE_m}$$
therefore,

\[ P_m = \frac{P_t A_m E_m}{A_m E_m + A_c E_c} \]

If we express equation (9-3) in terms of Young's modulus, it becomes,

\[ E_t = E_m V_m + E_c V_c \]

where \( V \) is volume fraction. This is the "rule of mixtures" or Voigt model.
• If fibers are arranged in perpendicular direction,

\[
\frac{1}{E_t} = \frac{V_m}{E_m} + \frac{V_c}{E_c} \quad (9-8)
\]

Since not all collagenous fibers are exactly oriented in same direction, one can propose another model,

\[
\frac{1}{E_t} = \frac{x}{E_m V_m + E_c V_c} + (1+x)\left(\frac{V_m}{E_m} + \frac{V_c}{E_c}\right) \quad (9-9)
\]

where \( x \) is fraction of bone which conforms to parallel direction & \((1-x)\), rest.
d. Electrical Properties of Bone

- Late 1950's, dry bone is **piezoelectric** in classic sense.
- Hypothesized role in bone remodelling.
- Piezoelectric effects occur in kilohertz range.
- Both dielectric properties & piezoelectric properties of bone depend strongly upon frequency.
• 0.7 pC/N observed in bone, c.f. 0.7 & 2.3 pC/N for different directions in quartz, & 600 pC/N, some ceramics.

• Two different mechanisms are responsible for these effects: classical piezoelectricity due to molecular asymmetry of collagen in dry bone, fluid flow effects, streaming potentials.

• Electrical properties of bone are relevant not only as a hypothesized feedback mechanism for bone remodelling, but also in context of external electrical stimulation of bone to aid its healing & repair.
### Table 9-7. Electrical Properties of Bone

<table>
<thead>
<tr>
<th>Property</th>
<th>Condition</th>
<th>Value</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dielectric Permittivity</td>
<td>Radial, 78%rh, 37°C, 1 Hz</td>
<td>$10^5$</td>
<td>25</td>
</tr>
<tr>
<td>Resistivity (Ω m)</td>
<td>Longitudinal, 100%hydration, 0.1-30sec</td>
<td>45</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Radial, 100%hydration, 0.1-30sec</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Piezoelectric Coefficients (pC/N)</td>
<td>75%rh, 23.5°C, 100 Hz</td>
<td>$d_{11}=0.014$</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$d_{12}=0.026$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$d_{13}=-0.032$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$d_{14}=0.105$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$d_{15}=-0.013$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$d_{16}=-0.070$</td>
<td></td>
</tr>
</tbody>
</table>
9.3.2 Bone Remodeling

a. Phenomenology

- Galileo, balance of forces in beam bending & with applying this understanding to mechanical analysis of bone.
- **Julius Wolff**, 1892; observation that bone is reshaped in response to forces acting on it *Wolff's law*.
- Remodeling of cancellous bone structure followed mathematical rules corresponding to principal stress trajectories[Fig 9-15].
• Phenomenology of bone remodeling:

(1) Remodelling triggered not by principal stress but by 'flexure'.

(2) Repetitive dynamic loads on bone trigger remodelling; static loads do not.

(3) Dynamic flexure causes all affected bone surfaces to drift towards concavity which arises during act of dynamic flexure.

• These rules are essentially qualitative & they do not deal with underlying causes.
• Remodelling of Haversian bone influence **quantity** of bone, not quality, i.e. Young's modulus, tensile strength, & composition not substantially changed.

• Initial remodelling of primary bone reduction in strength.

• Intermittent deformation produce a marked adaptive response in bone, static deformation, little effect.

• Response of different bones in same skeleton to mechanical loads must differ, otherwise lightly loaded bones such as skull, or auditory ossicles, resorbed.
b. Feedback Mechanisms of Bone Remodeling

- Feedback system: bone cells sense state of strain in bone matrix around them & either add or remove bone to maintain strain within normal limits (Fig 13-1).

Example 9-4

- Calculate using a simple rule of mixture model the percentage of load borne by mineral phase of a cow femur which is subjected to 500 N of load. The Young's moduli of mineral and collagen are about 17 and 0.1 GPa respectively.
Answer

• Since the area is proportional to the volume percentage of each component hence from Example 9-2 and equation (9-6)

\[
\frac{P_m}{P_i} = \frac{0.44 \times 17}{0.44 \times 17 + 0.40 \times 0.1} = 0.9947
\]

99.47% of load borne by mineral phase. Actually strength of demineralized bone is 5%-10% of of whole bone. Rule of mixtures (Voigt model) represents upper bound on modulus of composite. It is appropriate for a composite with fibers or laminae oriented in the direction of the applied load. The structure of bone is considerably more complex than these, so that the analysis is an approximation.
9.3.3 Collagen-Rich Tissues

- Collagen-rich tissues function mostly in a load-bearing capacity skin, tendon, cartilage, the lens of the eye & shaping of ear, tip of nose, etc.
a. Composition and Structure

- Mostly made of collagen (over 75 % dry, Table 9-8).

**TABLE 9-8. COMPOSITION OF COLLAGEN-RICH SOFT TISSUES**

<table>
<thead>
<tr>
<th>Component</th>
<th>Composition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collagen</td>
<td>75(dry), 30(wet)</td>
</tr>
<tr>
<td>Mucopolysaccharides</td>
<td>20(dry)</td>
</tr>
<tr>
<td>Elastin</td>
<td>&lt; 5(dry)</td>
</tr>
<tr>
<td>Water</td>
<td>60-70</td>
</tr>
</tbody>
</table>
• Collagen, made of tropocollagen, made of three-chain coiled superhelix (Fig 9-2). Collagen fibrils aggregate fibers [Fig 9-16].

• Fibrils & fibers, stabilized through intra & inter molecular H-bonding (C=O--HN),

Figure 9-16. Diagram showing that the “reticular fibers” associated with the basal lamina of an epithelial cell (above) and the “collagen fibers” of the connective tissue in general (below) are both composed of unit fibrils of collagen. Those of the reticulum are somewhat smaller and interwoven in loose networks instead of in larger bundles. From W. Bloom and D. W. Fawcett, *A Textbook of Histology*, 9th ed., W. B. Saunders Co., Philadelphia, 1968.
b. Physical Properties

- When heated its specific volume increases (density decreases, $T_g \sim 40^\circ C$ & shrinkage, $T_s \sim 56^\circ C$).
- Shrinkage temp, denaturation point for collagen.
- Stress-strain curves; nonlinear behavior[Fig 9-17].

<table>
<thead>
<tr>
<th>Fibers</th>
<th>Modulus of Elasticity (MPa)</th>
<th>Tensile Strength (MPa)</th>
<th>Ultimate Elongation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elastic</td>
<td>0.6</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Collagen</td>
<td>1000</td>
<td>50-100</td>
<td>10</td>
</tr>
</tbody>
</table>
- Skin, felt-like structure consisting of continuous fibers, randomly arranged in layers or lamellae. Mechanical anisotropy [Fig 9-18].

Langer's lines [Fig 9-19].
Another feature of the stress-strain curve, extensibility under small load [Fig 9-20].
• **Cartilage:** two main physiological functions. Maintenance of shape (ear, tip of nose, & rings around trachea), & provide bearing surfaces at joints.

• Contains very large & diffuse protein-PS molecules which form a gel, collagen-rich molecules entangled

• Joint cartilage, **very low coefficient of friction** (< 0.01); squeeze-film effect between cartilage & synovial fluid.

• Modulus of elasticity (10.3 - 20.7 MPa) & tensile strength (3.4 MPa), quite low.
Example 9-5

• Estimate the wet % compositions of mucopolysaccharides (MPS) and elastin in Table 9-8 assuming the densities of collagen, MPS and elastin are about 1 g/cm$^3$ and water content is about 65%.
Answer

- Based on 100 g of wet tissue.

<table>
<thead>
<tr>
<th>Composition</th>
<th>Weight (g)</th>
<th>Dry (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collagen</td>
<td>30</td>
<td>35 g x 0.75 = 26.25</td>
</tr>
<tr>
<td>MPS</td>
<td>x</td>
<td>35 g x 0.20 = 7.00</td>
</tr>
<tr>
<td>Elastin</td>
<td>y</td>
<td>35 g x 0.05 = 1.75</td>
</tr>
<tr>
<td>Water</td>
<td>65</td>
<td>0</td>
</tr>
</tbody>
</table>

x + y = 5 g  solving simultaneously yields:

x/y = 7/1.75 x=4 g & y=1 g, MPS:4%, Elastin:1%

- This indicates that a very small amount of elastin exists in the collagen-rich tissues.
9.3.4 Elastic Tissues

a. Composition & Structure

- "Protein rubber"
  Ligamentum nuchae contains 80% (dry) elastin.

- Blood vessel wall has three distinct layers viewed in cross section [Fig 9-21]:
(1) **Intima**: structural elements, oriented longitudinally,

(2) **Media**: which is the thickest layer of the wall and whose components are arranged circumferentially,

(3) **Adventitia**: connects vessels firmly to surrounding tissue via fascia. Intima & media, fenestrated by internal elastic membrane (*elastica interna*) which is predominant in arteries of medium size. Between the media & adventitia, thinner external elastic membrane (*elastica externa*) found. **Smooth muscle** cells found between adjacent elastic lamellae in helical array.
b. Properties of Elastic Tissues

- Chains in elastin are cross-linked by desmosine, isodesmosine & lysinonorleucine.

- Stress-strain curve of bovine ligamentum nuchae at low extension [Fig 9-22].

Figure 9-22. The stress–strain curve of elastin. The material is the ligamentum nuchae of cattle, which contains a small amount of collagen that was denatured by heating at 100°C for an hour. Such heating does not change the mechanical properties of elastin. The specimen is cylindrical with a rectangular cross section. Loading is uniaxial. The curve labeled “control” refers to native elastin. The curve labeled “10% formalin” refers to specimen fixed in formalin solution for a week without initial strain. From Y. C. Fung, Biomechanics: Mechanical Properties of Living Tissues, Springer-Verlag, Berlin, 1981.
Relative amount of elastin along blood vessel walls vary [Fig 9-23].

Figure 9-23. Variation of elastin percent per combined elastin and collagen content along the major arterial tree. From A. C. Burton, *Physiology and Biophysics of Circulation*, Year Book Medical Publ., Inc., Chicago, 1965.
• Anisotropy of mechanical properties is prominent in longitudinal & circumferential direction of blood vessel [Fig 9-24].

Figure 9-24. Stress–strain curves of human artery in the longitudinal and circumferential direction of the vessel (J. B. Park, unpublished data).
• Mean pressure of various blood vessels & approximate tension developed at normal pressur, Laplace equation,

\[ T = P_i \times r \quad (9-10) \]

T is wall tension, \( P_i \) is internal pressure, & \( r \) is radius of vessel.
### TABLE 9-10 WALL TENSION AND PRESSURE RELATIONSHIP OF VARIOUS SIZES OF BLOOD VESSELS (19)

<table>
<thead>
<tr>
<th>Type of Vessels</th>
<th>Mean Pressure (mm Hg)</th>
<th>Internal Pressure (dyne/cm²)</th>
<th>Radius (cm)</th>
<th>Wall Tension (dyne/cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta, large artery</td>
<td>100</td>
<td>$1.5 \times 10^5$</td>
<td>1.3</td>
<td>170,000</td>
</tr>
<tr>
<td>Small Artery</td>
<td>90</td>
<td>$1.2 \times 10^5$</td>
<td>0.5</td>
<td>60,000</td>
</tr>
<tr>
<td>Arteriole</td>
<td>60</td>
<td>$0.8 \times 10^5$</td>
<td>62 -150μm</td>
<td>500-1,200</td>
</tr>
<tr>
<td>Capillaries</td>
<td>30</td>
<td>$0.4 \times 10^5$</td>
<td>4μm</td>
<td>16</td>
</tr>
<tr>
<td>Venules</td>
<td>20</td>
<td>$0.26 \times 10^5$</td>
<td>10μm</td>
<td>26</td>
</tr>
<tr>
<td>Veins</td>
<td>15</td>
<td>$0.2 \times 10^5$</td>
<td>200μm</td>
<td>400</td>
</tr>
<tr>
<td>Vena Cava</td>
<td>10</td>
<td>$0.13 \times 10^5$</td>
<td>1.6 cm</td>
<td>21,000</td>
</tr>
</tbody>
</table>
• Muscle; another elastic tissue. "active"
• Passive tissue; stress-strain curve shows non-linear, viscoelastic behavior[Fig 9-25].

Figure 9-25. The length–tension curve of a resting papillary muscle from the right ventricle of the rabbit. Hysteresis curves at strain rates 0.09, 0.9, and 9% length/sec. Length at 9 mg = 0.936 cm at 37°C. From Y. C. Fung, Biomechanics: Mechanical Properties of Living Tissues, Springer-Verlag, Berlin, 1981.
Unbound 'free water' is squeezed out of the specimen since the laboratory preparation is an open system. It is not yet fully understood what is the role of the water in contributing to the mechanical properties of tissues.

**TABLE 9-11. MECHANICAL PROPERTIES OF SOME OF THE NON-MINERALIZED HUMAN TISSUES**

<table>
<thead>
<tr>
<th>Tissues</th>
<th>Tensile Strength (MPa)</th>
<th>Ultimate Elongation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>7.6</td>
<td>78</td>
</tr>
<tr>
<td>Tendon</td>
<td>53</td>
<td>9.4</td>
</tr>
<tr>
<td>Elastic Cartilage</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>Heart Valves (Aortic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radial</td>
<td>0.45</td>
<td>15.3</td>
</tr>
<tr>
<td>Circumferential</td>
<td>2.6</td>
<td>10.0</td>
</tr>
<tr>
<td>Aorta</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transverse</td>
<td>1.1</td>
<td>77</td>
</tr>
<tr>
<td>Longitudinal</td>
<td>0.07</td>
<td>81</td>
</tr>
<tr>
<td>Cardiac Muscle</td>
<td>0.11</td>
<td>63.8</td>
</tr>
</tbody>
</table>
Example 9-6.
From Figure 9-18, answer.

(a) How much stress will be developed if the abdominal skin was stretched 30% in the parallel and in the perpendicular direction to the cephalo-caudal direction of the body?

(b) What are the strains if the skin was stressed to 1 MPa?

(c) What are the moduli of elasticity in the two principal directions?
Answer

(a) From Figure 9-18, the stresses in the perpendicular and parallel to the cephalo-caudal direction of the main body are about 1 and 0.01 MPa respectively.

(b) 30% and 43% strain will be developed in the perpendicular and parallel to the cephalo-caudal direction of the body respectively.

(c) Perpendicular direction: \( E = \frac{(5.2 - 0)}{(0.41 - 0.31)} = 52 \text{ MPa} \)

Parallel direction: \( E = \frac{(4.6 - 0)}{(0.54 - 0.44)} = 46 \text{ MPa} \)
c. Further Considerations of the Mechanical Properties of Soft-Tissues

• Soft tissues exhibit **viscoelastic** behavior
• Modeling structure, Fig 9-26.
• Three major components: **smooth muscle** fibers in helical fashion; **elastic fibers** of elastin & **collagen** forming a crimped network structure extended at high load.
• **Stress-strain curves** after removal each major component [Fig 9-27].
• Ligamentum nuchae rubberlike elasticity up to 50% elongation.
• Removes collagen component from tissue by enzyme (collagenase) or autoclaving, behaves entirely like elastomer up to 100% elongation.
• Removes elastin component from same tissue then remaining tissue behaves as collagenous tissue
• Removal of ground substance did not alter basic stress-strain behavior.

![Stress-strain curves](image)


![Schematic representation](image)

**Figure 9-28.** A schematic representation of structure–property relationship of connective tissues. The collagen is represented by a loosely knitted fabric.
Example 9-7

• Calculate the modulus of elasticity of the bovine ligamentum nuchae (Fig 9-27).
Answer

There are two distinct regions demarcated at about 60-70% strain.

Initial region

\[ E = \frac{0.06 \text{ MPa}}{100\%} = 0.06 \text{ MPa} \]

Secondary region

\[ E = \frac{0.85}{0} \text{ MPa} \]

\[ E = \frac{1.77 \text{ MPa}}{120\% - 72\%} \]

These two values are lower and higher than the single value given in Table 9-8 for the elastic fibers.
The End