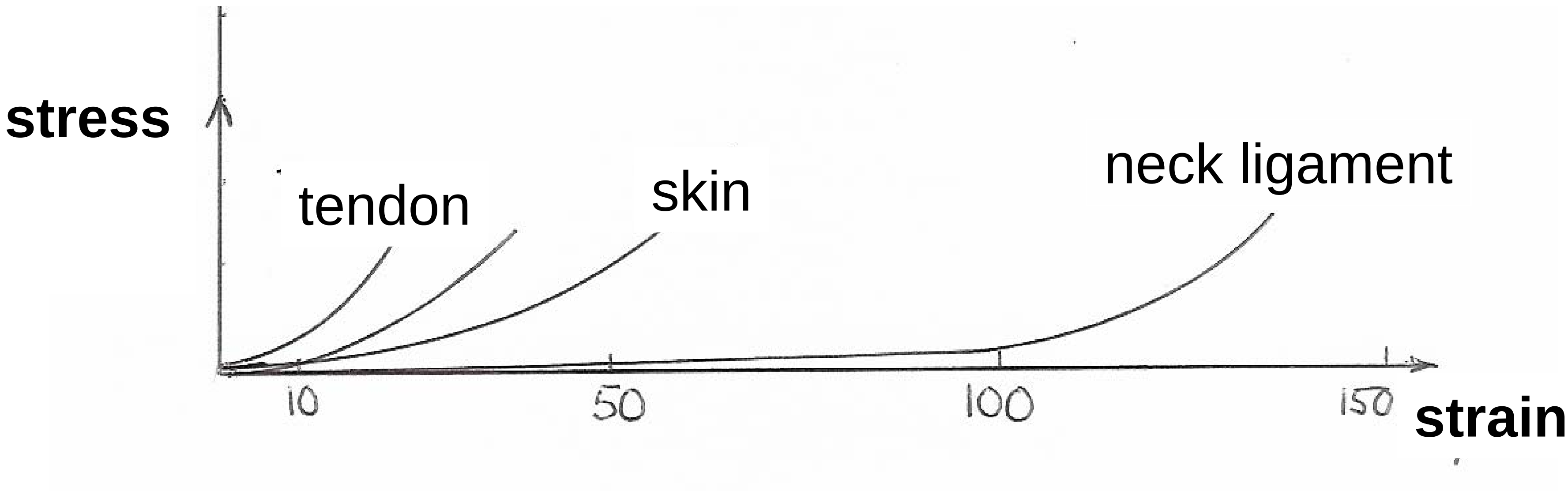
Outline of today's class:

STRESS-SUPPORTING STRUCTURES

1. Tissues and organs differ greatly in deformability even though made up of few components.
2. Collagen fibers: Orientation patterns in different organs match mechanical function.
3. Collagen fibers: Periodic structure of crystalline fibers at different scales.
4. Elastin fibers are amorphous and rubber-like.
5. Glycosaminoglycans (GAGs) are polysaccharides that keep water inside tissues.

1. Tissues and organs differ greatly in compliance (deformability).

Stress-strain curves (constitutive relations) for various tissues and organs:

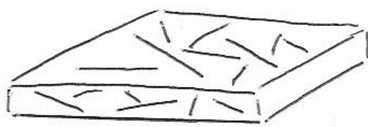


Are the basic rules of linear elastic mechanics obeyed by most tissues?

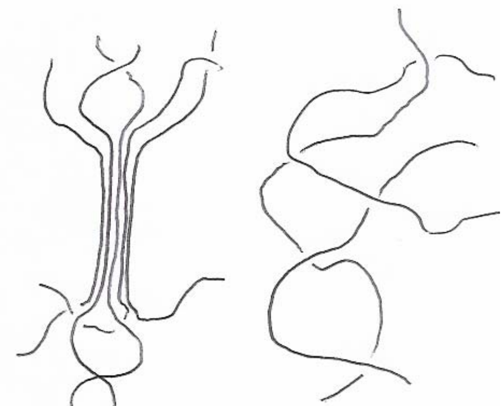
- **Matter is a continuum.**
- **Linearity. Directly proportional relation between stress and strain. No terms with exponent higher than 1.**
- **Elasticity. Time-independent mechanical behavior. Loading and deformation independent of time.**
- **Isotropy. The elastic constants are independent of loading direction.**
- **Conservation of mass.**

Tissues and organs differ greatly in deformability due to:

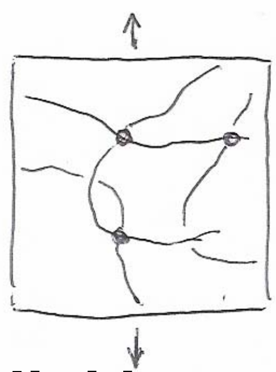
•molecular configuration
(collagen vs GAG)



•fiber reinforcement
(tendon vs liver)



•crystalline vs. amorphous fibers
(collagen vs elastin fibers)



•crosslinking
(newborn vs aged)

•ceramic content
•(bone vs cartilage)

Three basic structural families of macromolecules: Collagens, elastins and polysaccharides (GAGs)

- Diversity in mechanical behavior among tissues due primarily to variations in the organization of <u>fibers</u> of these macromolecular substances.

- Model of supporting tissues as fiber-reinforced composite materials. A soft, aqueous GAG "matrix" gel is reinforced with fibers of collagen and elastin. [Bone is further reinforced with ceramic particles.] The model illuminates the critical importance of fiber orientation on stiffness and strength of tissues.

2. Collagen fibers: Orientation pattern in various organs match mechanical function.

- **<u>Tendons</u>. Thick fibrous bundles that connect muscle to bone. Support axial forces. Collagen fibers are uniaxially oriented.**
- **<u>Ligaments</u> are similar to tendon in structure but connect bone to bone.**
- **<u>Cornea</u>. Membrane protects curved eye surface from tangential forces. Planar orientation of collagen fibers.**
- **<u>Dermis (skin)</u>. Collagen fibers nearly randomly oriented (some orientation in plane of epidermis).**
- **<u>Articular cartilage</u>. Membrane between apposed bones in joints. It “lubricates” joints. “Cathedral” architecture of collagen fibers.**

Tendon connects muscle to bone and supports axial forces

Image removed due to copyright restrictions.
Diagram of human arm bone, muscle and tendon structure, showing elbow flexion and extension.

Quaternary structure of collagen. Fibers are probably single crystals, about 100 nm diameter, with a 64-nm periodicity ("banding").

Image removed due to copyright restrictions.
Electron microscope photograph of collagen fibers.

What is the orientation of 100-nm thin collagen fibers in 200-μm thick tendon fibers? Do they form helix round axis of tendon fiber? Or is their axis parallel to tendon fiber axis?

Image removed due to copyright restrictions.
Electron microscope photograph.

Tendon fibers

Effort to identify orientation of 100-nm collagen fibers by dissolution in aqueous acetic acid. However, collagen fiber orientation is not clearly shown in this experiment.

Image removed due to copyright restrictions.
Electron microscope photograph.

100 μm

Effort to identify orientation of collagen fibers by fracture. Wet tendon fibers fracture in "fibrillar" mode. 100-nm collagen fiber orientation not shown.

Image removed due to copyright restrictions.
Electron microscope photograph.

40 μm

Try a different approach. Dehydrate first, and then fracture tendon.

Image removed due to copyright restrictions.
Electron microscope photograph.

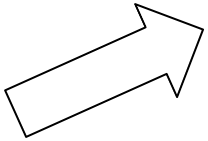
20 μm

Fracture surface of dry tendon

Detail of fracture surface for dry tendon showing parallel arrangement of fibers along major fiber axis. Individual fibers, about 100 nm diameter, are single crystals of collagen.

Image removed due to copyright restrictions.
Electron microscope photograph.

2 μm



normal to
fracture surface

Research question: how are collagen crystals bound to each other?

The eye

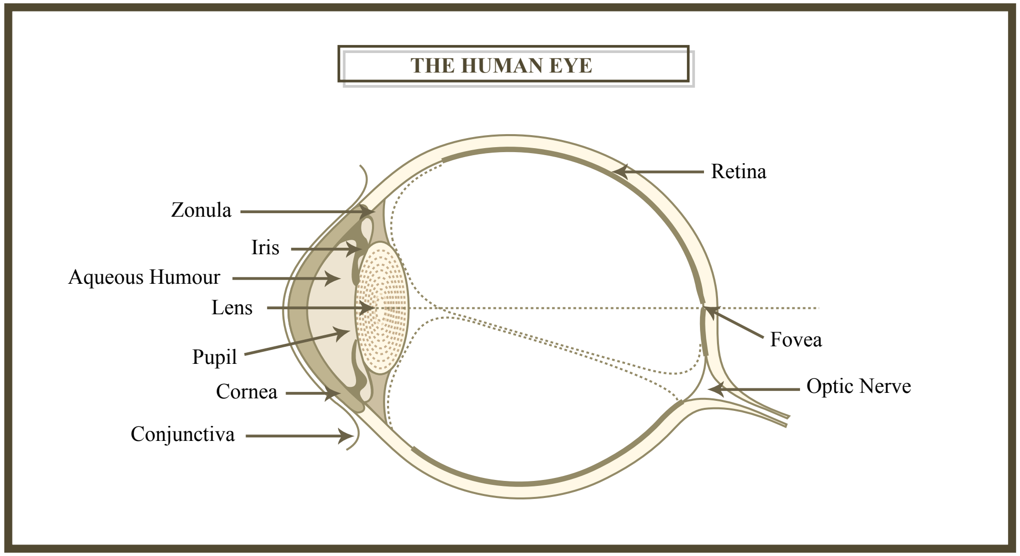


Figure by MIT OpenCourseWare.

CORNEA. Membrane protects curved eye surface from tangential forces. Planar orientation of collagen fibers.

Image removed due to copyright restrictions.

Tadpole cornea

Research question: how can the cornea, a two-phase material, be transparent?

Image removed due to copyright restrictions.

Fish cornea

Detailed view of skin

Image removed due to copyright restrictions.
Medical illustration (by Frank Netter) of the structure of human skin.

SKIN

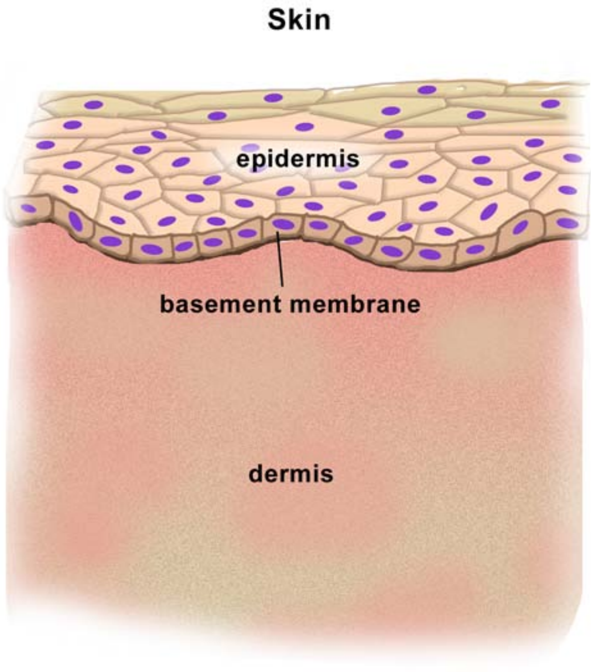


Figure by MIT OpenCourseWare.

Dermis

A, arterioles
N, peripheral
nerve
Almost all else
is quasi-random
assembly of
collagen fibers

Histology photo removed due to copyright restrictions.

100 μm

DERMIS (Skin). Collagen fibers nearly randomly oriented (there is some orientation in plane of epidermis). Supports forces along all three axes.

Microscope photo removed
due to copyright restrictions.

20 μm

Collagen fibers in human dermis: 4 magni-fications

Microscope photos removed due to copyright restrictions.

Banding visible on individual fibrils (quaternary structure)

Gibson and Kenedi

right nipple

Diagram removed due to copyright restrictions.

Skin extensibility varies over right side of chest. Langer's lines coincide with axis of minimum extensibility.

scar

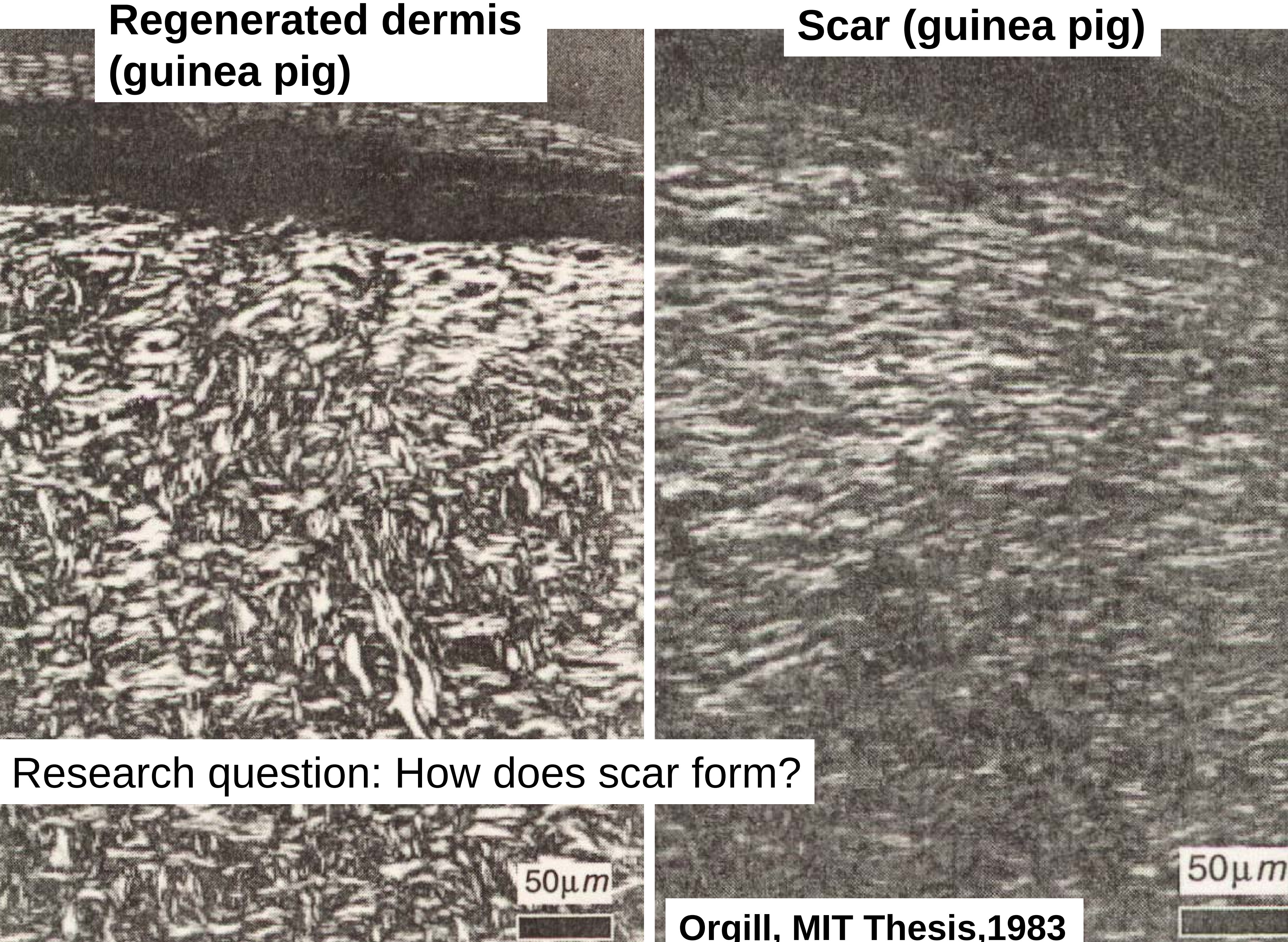
normal dermis

Image removed due to copyright restrictions.

light scattering pattern shows axial orientation for scar

Regeneration of the dermis in guinea pig skin wounds. Studied by histology (up) and laser light scattering (down).

Image removed due to copyright restrictions.



Research question: How does scar form?

Orgill, MIT Thesis,1983

ARTICULAR CARTILAGE. Membrane between apposed bones in joints (arrow). It “lubricates” joints. Does not “damp” impact forces.

Photo removed due to copyright restrictions.

<u>ARTICULAR CARTILAGE</u>. It “lubricates” joints partly through a “weeping” mechanism in which synovial fluid is squeezed out of cartilage during compression.

Diagram removed due to copyright restrictions.

ARTICULAR CARTILAGE. Collagen fiber orientation varies greatly from surface to interior. Fiber orientation resembles arcing struts in cathedral architecture.

Histology image removed due to copyright restrictions.

Research question: How does cartilage maintain the lowest known coefficient of friction?

Abnormally stretchy skin

Three photos removed due to
copyright restrictions.

a baby inside the uterus about to be born

Diagram removed due to copyright restrictions.

cervix

From Sci. American

Viscoelasticity of uterine cervix

From Harkness and Harkness

deformation

during childbirth

Graph removed due to copyright restrictions.

after

before

time, s

Chicken with normal bones

Collagen fibers in bones lack crosslinking

X-ray images removed due to copyright restrictions.

3. Collagen fibers: Periodic structure of crystalline fibers at different scales.

- **Protein fibers typically comprise a hierarchy of "ordered" structures; each member of the hierarchy is characterized by repetititon of a structural motif (periodicity) either along the macromolecular chain or across a collection of chains.**
- **Primary structure is the complete amino acid sequence of each protein chain (no information on configuration).**
- **Secondary structure is the local 3-D configuration of a few (3-5) amino acid units (residues) along the chain (helix?)**

3. Collagen fibers: Structure at different scales (cont.)

- **Tertiary structure is the configuration of the entire molecule (triple helix).**
- **Quaternary structure refers to the crystalline structure formed by aggregation of many molecules ("banded" fiber). Crystalline structure of fibers restricts stretching to about 10% along axis.**
- **Architecture of fibers refers to orientation of fibers that comprise the macroscopic tissue or organ.**

primary

secondary

tertiary

quaternary

Hierarchy of collagen structures

Diagram removed due to copyright restrictions.

Quaternary collagen structure
observed as banding with a 64-nm period

Image removed due to
copyright restrictions.

100 nm

Research question: How does
collagen banding induce clotting?

What is the water content in jello?

When collagen melts it becomes <u>gelatin</u>, an amorphous polymer

Chemical diagram removed due to copyright restrictions.

4. Elastin fibers are amorphous and rubber-like

- **Primary structure of this protein comprises mostly nonpolar amino acids (AA); weak forces between neighboring AA along chain (intramolecular interactions) as well as between AA in adjacent chains (intermolecular).**
- **No structural periodicity detected; therefore, no hierarchy of periodic motifs observed.**

Elastin

X-ray diffraction pattern is negative (amorphous)

Image removed due to copyright restrictions.

SKIN

Histology photo removed due to copyright restrictions.

P, papillary dermis
R, reticular dermis
<u>Elastin</u> fibers stain black

100 μm

4. Elastin fibers (cont.)

- <u>No interactions</u>. There is no crystallinity in elastin fibers (amorphous). Its macromolecules are free of interactions (either intra- or intermolecular) and are, therefore, capable of stretching out their coiled configurations all the way, until covalent bonds are stretched.
- <u>Mechanical behavior</u>. Rubber-like behavior, capable of extension by 150%, is observed; however, unlike tire rubber, elastin is a liquid-filled elastomer (it would make a terrible tire rubber). Amorphous elastin fibers in contrast to crystalline structure of collagen fibers (compare relatively stiff, crystalline Nylon fibers to stretchy, amorphous Spandex fibers).

4. Elastin fibers (cont.)

- **<u>Neck ligament</u>: free and easy movement of head around spinal column.**
- **<u>Aorta</u>: both collagen and elastin fibers reinforce blood vessel wall. Fibers in vessel wall become enriched in elastin the closer is vessel to the heart (increased distance from periphery); near heart, vessel wall becomes more stretchy and partly damps mechanical energy, probably contributing in converting the on-off pulsatile energy output of the heart to a more continuous flow pattern.**
- **<u>Skin</u>. Effects of ageing on stress-strain curve of skin. Loss of elastin?**

Aorta. Data on % elastin (as % elastin+ collagen) in this major blood vessel. Elastin content decreases from top (left) through chest diaphragm (right).

Four graphs removed due to copyright restrictions.

dog

elephant

hippo

giraffe

Aorta. Data on % elastin (as % elastin+ collagen) in this major blood vessel. Elastin content decreases from top (left) through chest diaphragm (right).

Four graphs removed due to copyright restrictions.

dog

elephant

hippo

giraffe

5. Glycosaminoglycans (GAGs) in tissues are polysaccharides.

- <u>Repeat units</u>: Macromolecular chain made up of sequence of sugar, not AA, units. GAGs are side chains of “core” protein chain: proteoglycan.
- Sequence of <u>fixed negative (electrostatic) charges</u> along chain axis stiffens it up due to repulsive interactions among charged ions. Highly ionic macromolecular network swells highly in water, occasionally increasing its dry mass by over 1000X. About two-thirds of body weight is water, most of it "trapped" by GAGs. (Proteins also immobilize water.)

5.Glycosaminoglycans(GAGs)(cont.).

- **Swollen GAGs serve as the soft "matrix" in the mechanical model of supporting tissues as fiber-reinforced composites. This matrix is stiffened and strengthened by collagen and elastin fibers.**
- **Stiffness of tissues with very high GAG content depends strongly on maintenance of ionic charges at "full strength". E.g., stiffness of articular cartilage drops by about 50% when the salt-free water that swells it is replaced with a high-salt water solution. Salt ions "screen" fixed charges on GAG chains, causing drop in repulsive forces among them. (Research question: What accounts for remainder 50% of stiffness of cartilage?)**

Summary

Tissues differ in deformability. They comprise fibers and gel-like matrix.

Orientation of crystalline collagen fibers in tissues roughly relates to mechanical function of tissue.

Hierarchy of structural order (periodicity) in collagen and other proteins.

Elastin fibers are amorphous and rubber-like.

Glycosaminoglycans (GAGs) are electrically charged polysaccharides. Charges retain much water. Charge repulsion straightens up chains.