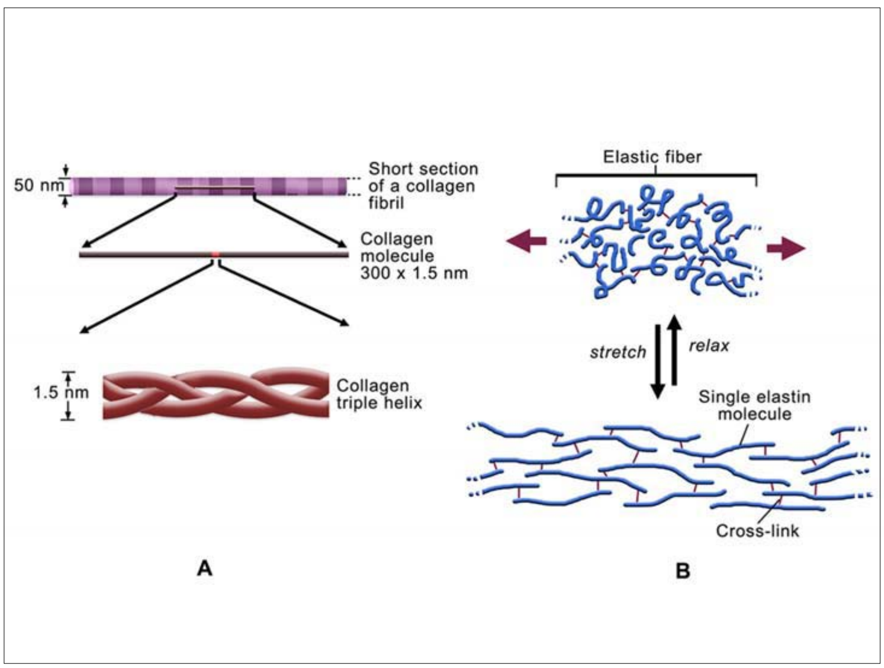
50 nm
Short section of a collagen fibril
Collagen molecule 300 x 1.5 nm
1.5 nm
Collagen triple helix
A
Elastic fiber
stretch
relax
Single elastin molecule
Cross-link
B

Entropic elasticity

Image removed due to copyright considerations.

See Figure 19-50 in: Alberts, Bruce, et al. *Molecular Biology of the Cell*. 4th ed. New York: Garland Publishing, 2002.

Image may be viewed online at the NIH's PubMed Bookshelf.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books

Elastin -- note linearity, small hysteresis.

Normally found intertwined with collagen.

Provides the "stretchiness" of tissues.

Combination of single-molecule characteristics and microscale structure.

Image removed due to copyright considerations.

See Figure 7.2:1 in: Fung, Y. C. *Biomechanics: Mechanical Properties of Living Tissues*. New York: Springer-Verlag, 1993

Canine aorta showing elastic fiber content.

Image removed due to copyright considerations.

See Figure 19-49 in: Alberts, Bruce, et al. *Molecular Biology of the Cell*. 4th ed. New York: Garland Publishing, 2002. Image may be viewed online at the NIH's PubMed Bookshelf. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books

Image removed due to copyright considerations.

Histological cross-section of a diseased carotid artery stained for smooth muscle cells.

Elastic response initially, then stiff, collagen response at high degrees of extension.

Image removed due to copyright considerations.

H=hypertensive

High wall stress leads to functional remodeling!

Lung parenchyma

Image removed due to copyright considerations

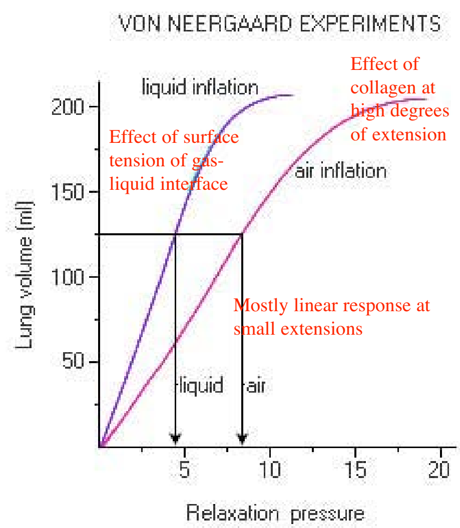

Image removed due to copyright considerations

Mostly air, parenchyma mostly elastin and collagen.

Proteoglycans (PGs) and glycosaminoglycans (GAGs)

a) GLYCOSAMINOGLYCANS (GAGs) form gels
- i) polysaccharide chains of disaccharide units
- ii) too inflexible and highly charged to fold in a compact way
- iii) strongly hydrophilic
- iv) form extended conformations and gels
- v) osmotic swelling (charge repulsion)
- vi) usually make up less than 10% of ECM by weight
- vii) fill most of the ECM space
- viii) four main groups
  - a. hyaluronan
  - b. chondroitin sulfate and dermatin sulfate
  - c. heparin sulfate and heparin
  - d. keratin sulfate

b) Proteoglycans (PGs)

i) form large aggregates
ii) aggrecan is a large proteoglycan in cartilage
iii) decorin is secreted by fibroblasts
iv) PGs have varying amounts of GAGs.
v) PGs are very diverse in structure and content
vi) PGs and GAGs can also complex with collagen
vii) secreted proteoglycans have multiple functions
viii) some PGs are not secreted
ix) PG/GAGs have important roles in cell-cell signaling

See Figure 19-39 in: Alberts, Bruce, et al. *Molecular Biology of the Cell*. 4th ed. New York: Garland Publishing, 2002.
Image may be viewed online at the NIH's PubMed Bookshelf.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books

Quick-freeze, deep-etch TEM of cornea (100,000x)

M. Johnson, J. Ruberti

Image removed due to copyright considerations.

Striations can be seen on the collagen fibers. PGs can be seen bridging between the collagen fibers.

Image removed due to copyright considerations.

See Figure 19-37 in: Alberts, Bruce, et al. *Molecular Biology of the Cell*. 4th ed. New York: Garland Publishing, 2002.

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See Figure 19-36 in: Alberts, Bruce, et al. *Molecular Biology of the Cell*. 4th ed. New York: Garland Publishing, 2002.

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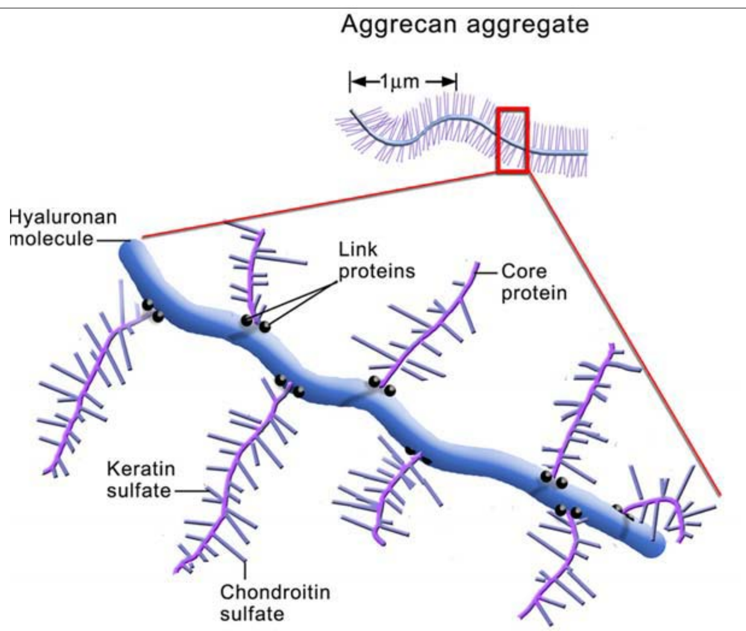
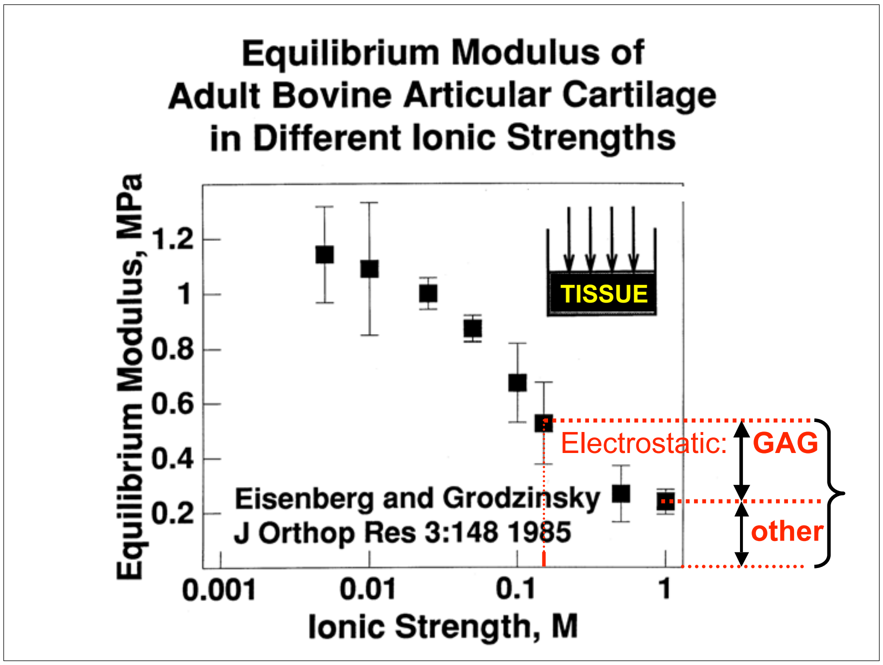
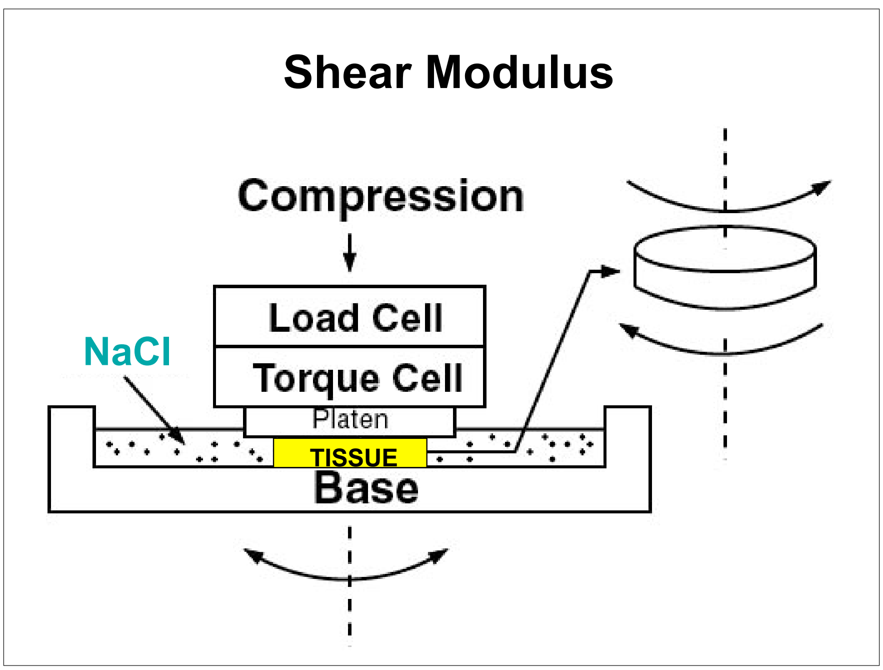
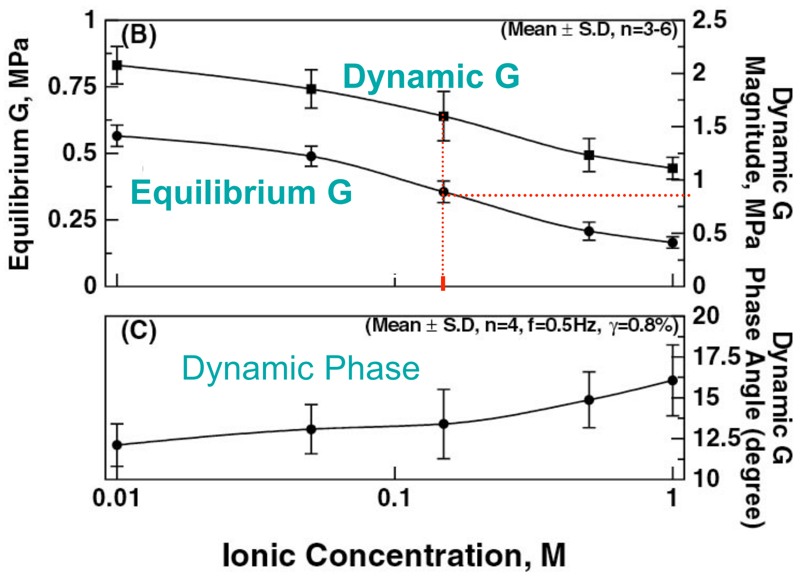


An aggrecan aggregate from fetal bovine cartilage.


Equilibrium Modulus of
Adult Bovine Articular Cartilage
in Different Ionic Strengths
Equilibrium Modulus, MPa
1.2
1
0.8
0.6
0.4
0.2
0.001
0.01
0.1
1
Ionic Strength, M
TISSUE
Electrostatic:
GAG
other
Eisenberg and Grodzinsky
J Orthop Res 3:148 1985


Shear Modulus
Compression
Load Cell
Torque Cell
Platen
TISSUE
Base
NaCl

Shear Modulus: (Dynamic @ 0.5Hz, 0.8% strain)



Like charge repulsion accounts for a large fraction (~50%) of the stiffness in tissues with high GAG content.

These effects can be eliminated either by shielding (importance of Debye length -- BE.430!) with counter-ions or neutralization by changing pH.

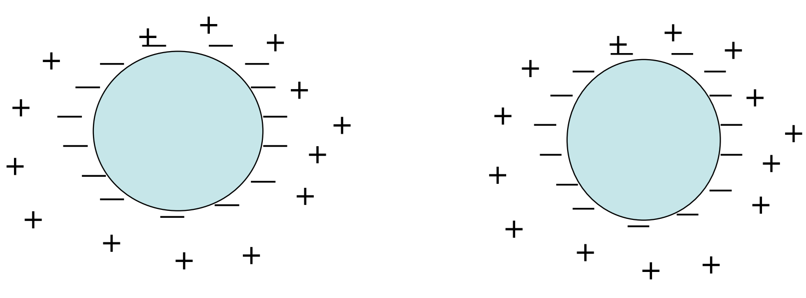
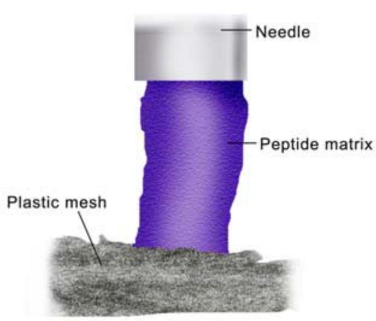


Table 19-3. Some Common Proteoglycans

Proteoglycan	Approximate Molecular Weight of Core Protein	Type of GAG Chains	Number of GAG Chains	Location	Functions
Aggrecan	210,000	chondroitin sulfate + keratan sulfate	~130	cartilage	mechanical support; forms large aggregates with hyaluronan
Betaglycan	36,000	chondroitin sulfate/ dermatan sulfate	1	cell surface and matrix	binds TGF-β
Decorin	40,000	chondroitin sulfate/ dermatan sulfate	1	widespread in connective tissues	binds to type I collagen fibrils and TGF-β
Perlecan	600,000	heparan sulfate	2-15	basal laminae	structural and filtering function in basal lamina
Serglycin	20,000	chondroitin sulfate/ dermatan sulfate	10-15	secretory vesicles in white blood cells	helps to package and store secretory molecules
Syndecan-1	32,000	chondroitin sulfate + heparan sulfate	1-3	fibroblast and epithelial cell surface	cell adhesion; binds FGF

Stress-Strain Behavior of KFE12

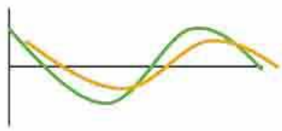


Leon, et al., 1998

Linear behavior up to fracture

Relatively low toughness due to small fracture strain

Rheological Measurements to Monitor Gelation



- Cone-plate rheometer oscillated over a range of frequencies (ω)
- Imposed: sinusoidal torque (τ)
- Measured: sinusoidal strain (ε)

ADHESION PROTEINS

a) fibronectin
   i) principal adhesion protein of connective tissues
   ii) fibronectin is a dimeric glycoprotein
   iii) fibronectin interacts with other molecules
b) laminin
   i) found in basal laminae
   ii) form mesh-like polymers
   iii) has various binding sites
   iv) assembles networks of crosslinked proteins
c) integrins
   i) cell surface receptor, for attachment of cells to ECM
   ii) family of transmembrane proteins
   iii) two subunits, alpha and beta
   iv) about 20 different integrins
   v) binding sites for ECM components
   vi) binding sites for the cytoskeleton and linkage to ECM