Values of the elastic or Young's modulus for various materials
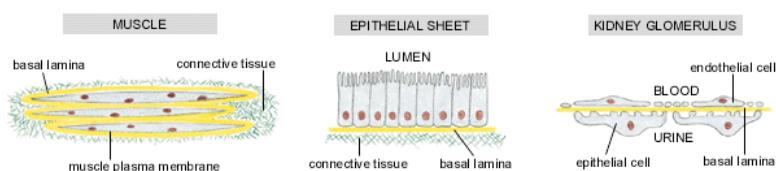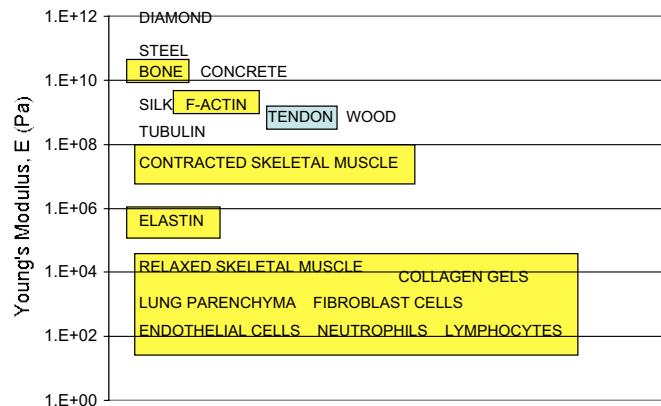

Figure 19-53. **Three ways in which basal laminae (*yellow lines*) are organized.** They surround certain cells (such as muscle cells), underlie epithelial cell sheets, and are interposed between two cell sheets (as in the kidney glomerulus). Note that in the kidney glomerulus both cell sheets have gaps in them, so that the basal lamina serves as the permeability barrier determining which molecules will pass into the urine from the blood.

Right tibia (somewhat non-isotropic and nonlinear)

Longitudinal direction

Radial direction
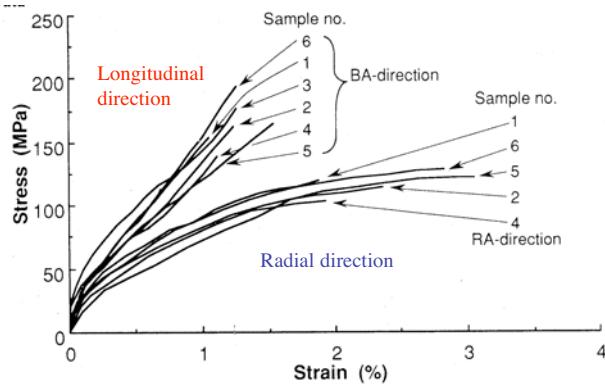
Comments
None.

Reference(s)
Kobayashi K, Tanabe Y, Koga Y, Hara T (1993) Identification of the dynamic properties of human compact bone. Theor Appl Mech 42:313–318


Striated muscle

A - resting
B - max contraction
C - active component

Macroscopic view

Microscopic - sarcomere level
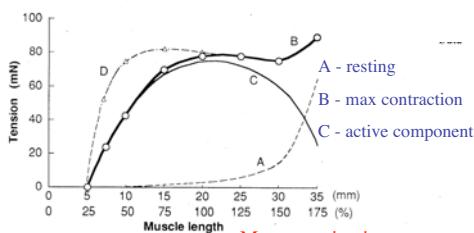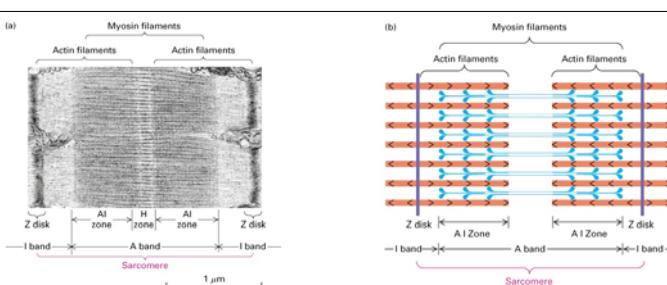
Comments
• Caption:
A, resting tension; B, maximum tension produced by the optimum stimulus; C, active tension (= B − A); D, potentiated tension produced by successive stimuli.
• The slightest resting tension was produced at 75% of the in situ length (20 mm).
• The optimum length, at which the active tension became maximum, is between 100% and 125% of the in situ length.
• The active tension declines almost symmetrically on either side of the optimal length.
• The maximum tension potentiated by successive stimuli was attained at 75% of the in situ length.

Reference(s)
Mashima H, Yoshida T (1965) Effect of length on the development of tension in guinea-pigs Taenia coli. Jpn J Physiol 15:463–477
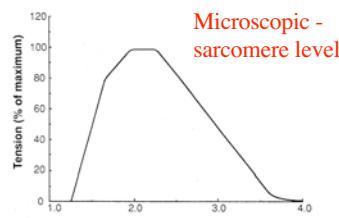
Comments
• Many features of the length-tension relation are simply explained by the sliding-filament theory.
• The peak of the curve consists of a plateau between sarcomere lengths of 2.05 and 2.2 μm.

Reference(s)
Gordon AM, Huxley AF, Julian FJ (1966) The variation in isometric tension with sarcomere length in vertebrate muscle fibres. J Physiol 184:170–192 (with permission)

Collagen -- single molecule characteristics
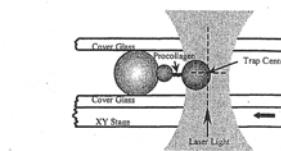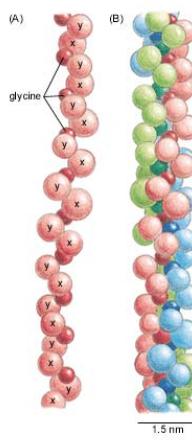
Fig. 1. Stretching a procollagen II molecule with an optical tweezers.

Type II procollagen.

Curve-fit: Marko-Siggio WLC
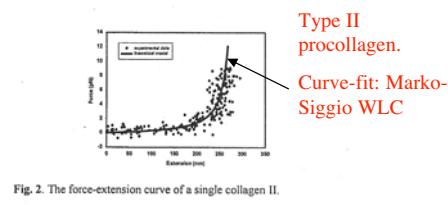
Fig. 2. The force-extension curve of a single collagen II.

1.5 nm

Figure 19-40. The structure of a typical collagen molecule. (A) A model of part of a single collagen a chain in which each amino acid is represented by a sphere. The chain contains about 1000 amino acid residues and is arranged as a left-handed helix with three amino acid residues per turn and with glycine as every third residue. Therefore an a chain is composed of a series of triplet Gly-X-Y sequences in which X and Y can be any amino acid (although X is commonly proline and Y is commonly hydroxyproline). (B) A model of a part of a collagen molecule in which three α chains, each shown in a different color, are wrapped around one another to form a triple-stranded helical rod. Glycine is the only amino acid small enough to occupy the crowded interior of the triple helix. Only a short length of the molecule is shown; the entire molecule is 300 nm long. (From model by B.L. Trus.)

Table 22-3. Major Collagen Molecules

Type	Molecule Composition	Structural Features	Representative Tissues
Fibrillar Collagens			
I	$[\alpha 1(I)]_2[\alpha 2(I)]$	300-nm-long fibrils	Skin, tendon, bone, ligaments, dentin, interstitial tissues
II	$[\alpha 1(II)]_3$	300-nm-long fibrils	Cartilage, vitreous humor
III	$[\alpha 1(III)]_3$	300-nm-long fibrils; often with type I	Skin, muscle, blood vessels
V	$[\alpha 1(V)]_3$	390-nm-long fibrils with globular N-terminal domain; often with type I	Similar to type I; also cell cultures, fetal tissues
Fibril-Associated Collagens			
VI	$[\alpha 1(VI)][\alpha 2(VI)]$	Lateral association with type I; periodic globular domains	Most interstitial tissues
IX	$[\alpha 1(IX)][\alpha 2(IX)][\alpha 3(IX)]$	Lateral association with type II; N-terminal globular domain; bound glycosaminoglycan	Cartilage, vitreous humor;
Sheet-Forming Collagens			
IV	$[\alpha 1(IV)]_2[\alpha 2(IV)]$	Two-dimensional network	All basal laminaes

SOURCE: K. Kuhn, 1987, in R. Mayne and R. Burgeson, eds., *Structure and Function of Collagen Types,* Academic Press, p. 2; M. van der Rest and R. Garrone, 1991, *FASEB J.* **5:**2814.
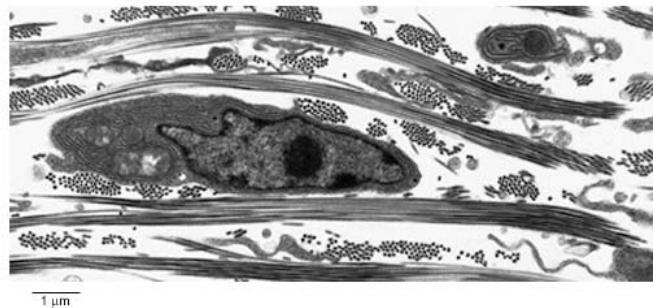
Figure 19-41. Electron micrograph of fibroblasts surrounded by collagen fibrils in the connective tissue of embryonic chick skin. The fibrils, which are organized into bundles that run approximately at right angles to one another, are produced by the fibroblasts. These cells contain abundant endoplasmic reticulum, where secreted proteins such as collagen are synthesized. (From C. Ploetz, E.I. Zycband, and D.E. Birk, *J. Struct. Biol.* 106:73-81, 1991.)
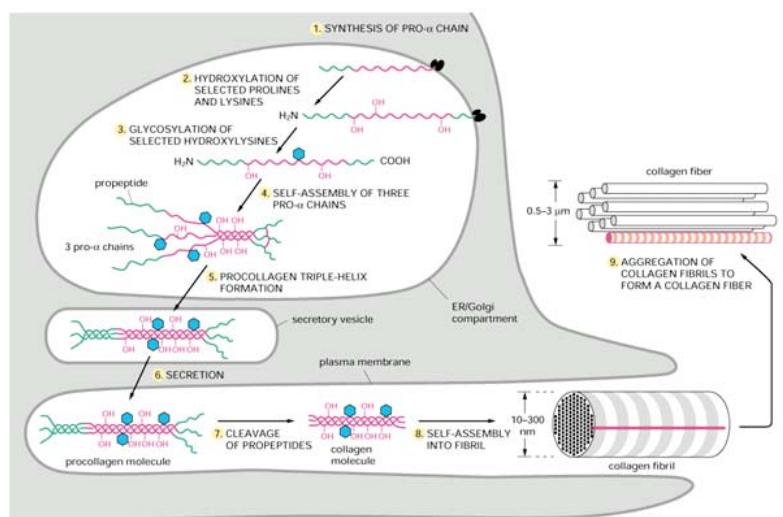
Figure 19-43. The intracellular and extracellular events involved in the formation of a collagen fibril. Note that collagen fibrils are shown assembling in the extracellular space contained within a large infolding in the plasma membrane. As one example of how the collagen fibrils can form ordered arrays in the extracellular space, they are shown further assembling into large collagen fibers, which are visible in the light microscope. The covalent cross-links that stabilize the extracellular assemblies are not shown.

4
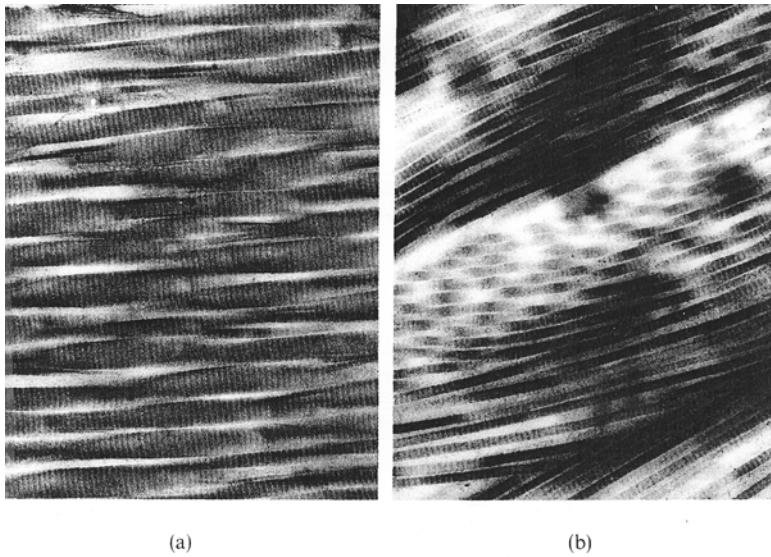
Figure 7.3:4 Electron micrographs of (a) parallel collagen fibrils in a tendon, and (b) mesh work of fibrils in skin (× 24 000). From Viidik (1973), by permission.

Striated
appearance of
collagen fibrils
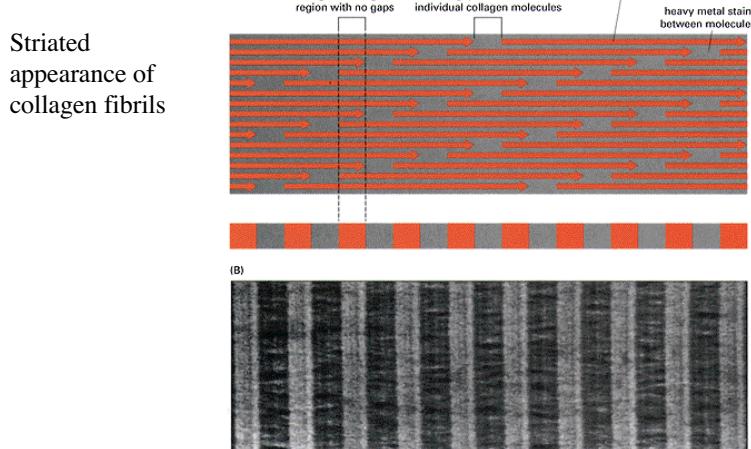
Figure 19-44. How the staggered arrangement of collagen molecules gives rise to the striated appearance of a negatively stained fibril. (A) Since the negative stain fills only the space between the molecules, the stain in the gaps between the individual molecules in each row accounts for the dark staining bands. An electron micrograph of a portion of a negatively stained fibril is shown below (B). The staggered arrangement of the collagen molecules maximizes the tensile strength of the aggregate. (B, courtesy of Robert Horne.)
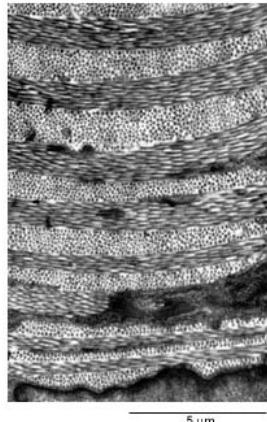
Collagen fiber arrangement in skin and cornea with alternating directions

Figure 19-46. Electron micrograph of a cross-section of tadpole skin. Note the plywoodlike arrangement of collagen fibrils, in which successive layers of fibrils are laid down nearly at right angles to each other. This arrangement is also found in mature bone and in the cornea. (Courtesy of Jerome Gross.)
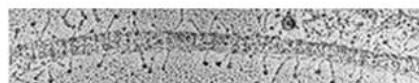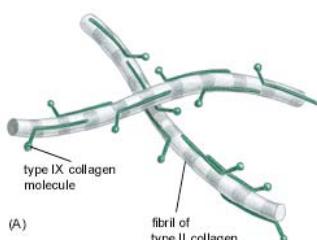
Figure 19-47. Type IX collagen. (A) Schematic drawing of type IX collagen molecules binding in a periodic pattern to the surface of a type-II-collagen-containing fibril. (B) Electron micrograph of a rotary-shadowed type-II-collagen-containing fibril in cartilage sheathed in type IX collagen molecules; an individual type IX collagen molecule is shown in (C). (B and C, from L. Vaughan et al., *J. Cell Biol.* 106:991-997, 1988, by copyright permission of the Rockefeller University Press.)

TENDON HIERARCHY

Figure 7.3:6 Hierarchy of structure of a tendon according to Kastelic et al. (1978). Reproduced by permission. Evidences are gathered from X ray, electron microscopy (EM), scanning electron microscopy (SEM), and optical microscopy (OM).

ACL -- different strain rates

Range of linearity.

E = d(stress)/d(strain) = 10^9 Pa

Comments
* Ninety percent of the ACL specimens failed by avulsion at the insertion site (72% at the tibial insertion and 18% at the femoral insertion), and 10% failed in the midsubstance.

Reference(s)
Danto MI, Woo SL-Y (1993) The mechanical properties of skeletally mature rabbit anterior cruciate ligament and patellar tendon over a range of strain rates. J Orthop Res 11:58–67 (with permission)

Collagen derives its stiffness, not from the single molecule characteristics of collagen, but rather from the straightening of "wavy" collagen fibers
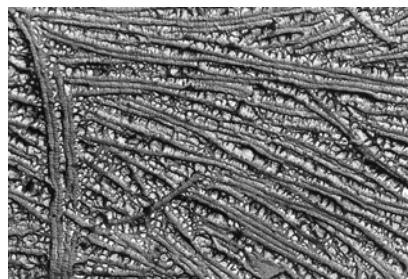
Cornea, M.
Johnson, J. Ruberti
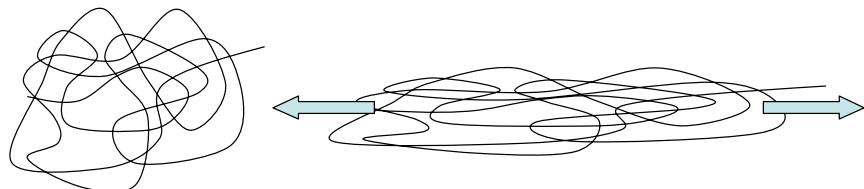
Start 3/12
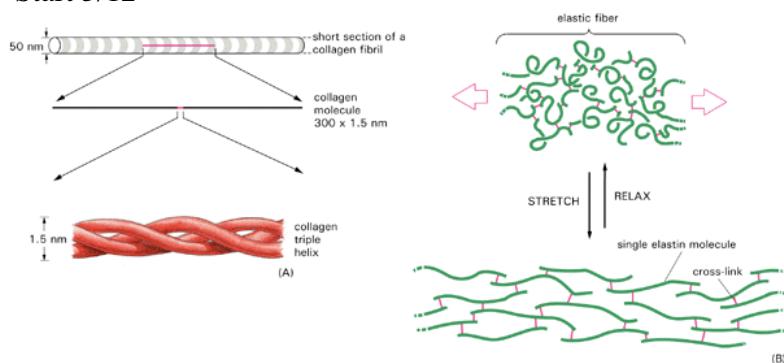
Figure 3-32. Contrast between collagen and elastin. (A) *Collagen* is a triple helix formed by three extended protein chains that wrap around each other. Many rodlike collagen molecules are cross-linked together in the extracellular space to form inextensible collagen fibrils (*top*) that have the tensile strength of steel. (B) *Elastin* polypeptide chains are cross-linked together to form elastic fibers. Each elastin molecule uncoils into a more extended conformation when the fiber is stretched. The striking contrast between the physical properties of elastin and collagen is due entirely to their very different amino acid sequences.

Entropic elasticity

Figure 19-50. Stretching a network of elastin molecules. The molecules are joined together by covalent bonds (indicated in *red*) to generate a cross-linked network. In the model shown each elastin molecule in the network can expand and contract as a random coil, so that the entire assembly can stretch and recoil like a rubber band.

Elastin -- note linearity, small hysteresis.

Normally found intertwined with collagen.

Provides the "stretchiness" of tissues.

Combination of single-molecule characteristics and microscale structure.

Figure 7.2:1 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 rectangular cross section. Loading is uniaxial. The curve labeled "control" refers to native elastin. The curve labeled "10% formalin" refers to a specimen fixed in formalin solution for a week without initial strain. From Fung and Sobin (1981). Reproduced by permission of ASME.

Canine aorta showing elastic fiber content.
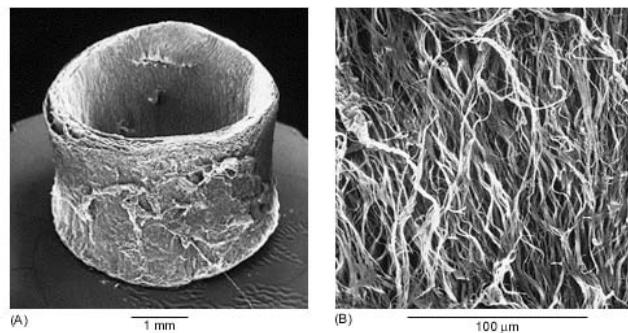
Figure 19-49. A network of elastic fibers. These scanning electron micrographs show a low-power view of a segment of a dog's aorta (A) and a high-power view of the dense network of longitudinally oriented elastic fibers in the outer layer of the same blood vessel (B). All of the other components have been digested away with enzymes and formic acid. (From K.S. Haas, S.J. Phillips, A.J. Comerota, and J.W. White, *Anat. Rec.* 230:86-96, 1991.)
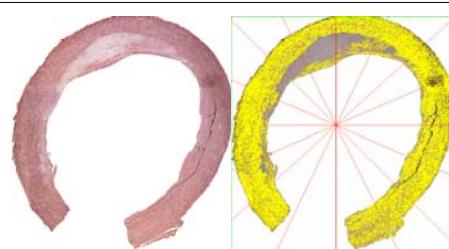
Histological cross-section of a diseased carotid artery stained for smooth muscle cells.

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

H=hypertensive

High wall stress leads to functional remodeling!
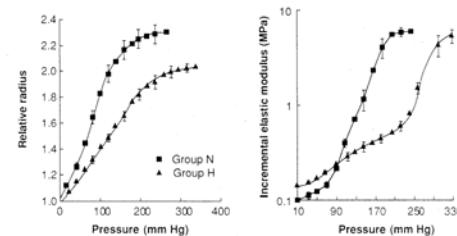
Comments

• Incremental elastic modulus, E_{inc}:

$E_{inc} = 0.75 \times \Delta P/(\Delta R/R) \times (R/h)$.

R, average radius; h, average wall thickness; ΔR, radius increment over pressure increment of ΔP.

• Relative wall thickness of the thoracic aorta at a pressure of 110 mmHg was 0.076 ± 5.2 (mean $\pm$ SE $\times 10^3$) for control and 0.136 ± 6.8 for hypertensive rats aged 20 weeks.

• Systolic blood pressure at the caudal artery: 110 mmHg for control and 180 mmHg for treated animals at the age of 20 weeks.

Lung parenchyma

VON NEERGAARD EXPERIMENTS

Effect of collagen at high degrees of extension

Effect of surface tension of gas-liquid interface

Mostly linear response at small extensions

Mostly air, parenchyma mostly elastin and collagen.
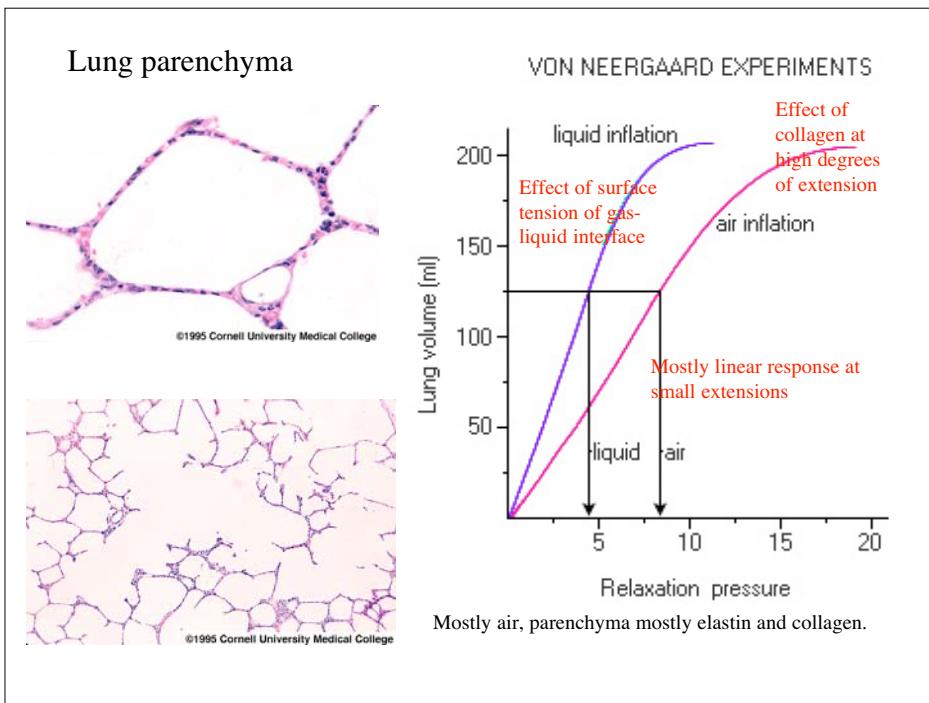
Proteoglycans (PGs) and glycosaminoglycans (GAGs)

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


collagen fibril

0.5 μm
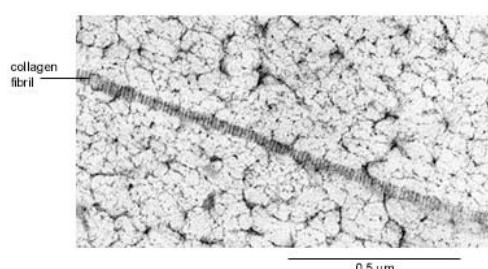
Figure 19-39. Electron micrograph of proteoglycans in the extracellular matrix of rat cartilage. The tissue was rapidly frozen at -196°C and fixed and stained while still frozen (a process called *freeze substitution*) to prevent the GAG chains from collapsing. The proteoglycan molecules are seen to form a fine filamentous network in which a single striated collagen fibril is embedded. The more darkly stained parts of the proteoglycan molecules are the core proteins; the faintly stained threads are the GAG chains. (Reproduced from E.B. Hunziker and R.K. Schenk, *J. Cell Biol.* 98:277-282, 1985, by copyright permission of the Rockefeller University Press.)

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

M. Johnson, J. Ruberti
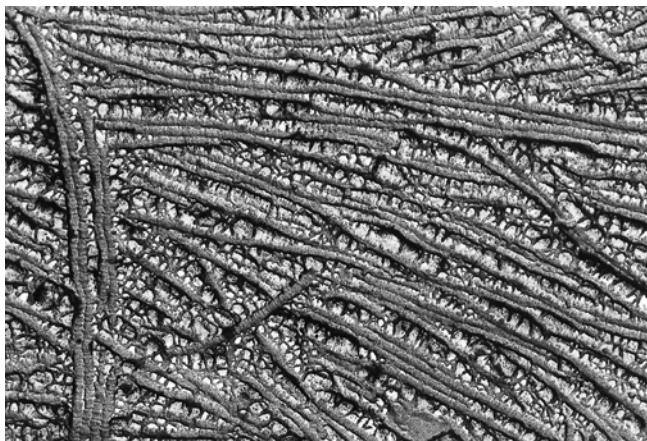
Striations can be seen on the collagen fibers. PGs can be seen bridging between the collagen fibers.


| DECORIN (MW ~ 40,000) | AGGRECAN (MW ~ 3 x 10⁶) | RIBONUCLEASE (MW ~ 15,000) |

core protein

GAG

100 nm

short, branched oligosaccharide side chain

polypeptide chain
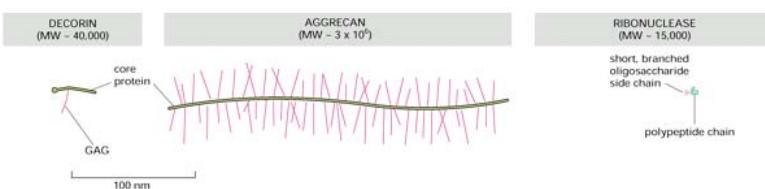
Figure 19-37. Examples of a large (aggrecan) and a small (decorin) proteoglycan found in the extracellular matrix. They are compared to a typical secreted glycoprotein molecule (pancreatic ribonuclease B). All are drawn to scale. The core proteins of both aggrecan and decorin contain oligosaccharide chains as well as the GAG chains, but these are not shown. Aggrecan typically consists of about 100 chondroitin sulfate chains and about 30 keratan sulfate chains linked to a serine-rich core protein of almost 3000 amino acids. Decorin "decorates" the surface of collagen fibrils, hence its name.
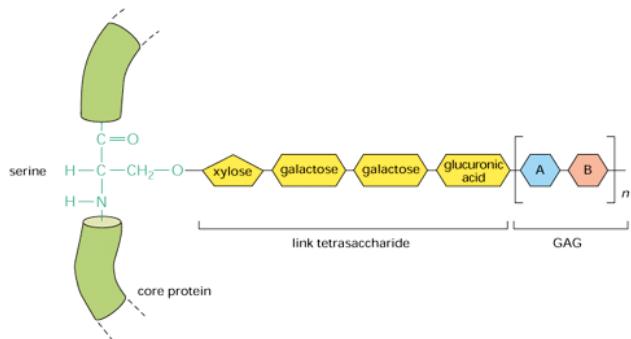
Figure 19-36. The linkage between a GAG chain and its core protein in a proteoglycan molecule. A specific link tetrasaccharide is first assembled on a serine residue. In most cases it is not clear how the serine residue is selected, but it seems to be a specific local conformation of the polypeptide chain, rather than a specific linear sequence of amino acids, that is recognized. The rest of the GAG chain, consisting mainly of a repeating disaccharide unit, is then synthesized, with one sugar residue being added at a time. In *chondroitin sulfate* the disaccharide is composed of D-glucuronic acid and *N*-acetyl- D-galactosamine; in *heparan sulfate* it is D-glucosamine (or L-iduronic acid) and *N*-acetyl- D-glucosamine; in *keratan sulfate* it is D-galactose and *N*-acetyl- D-glucosamine.
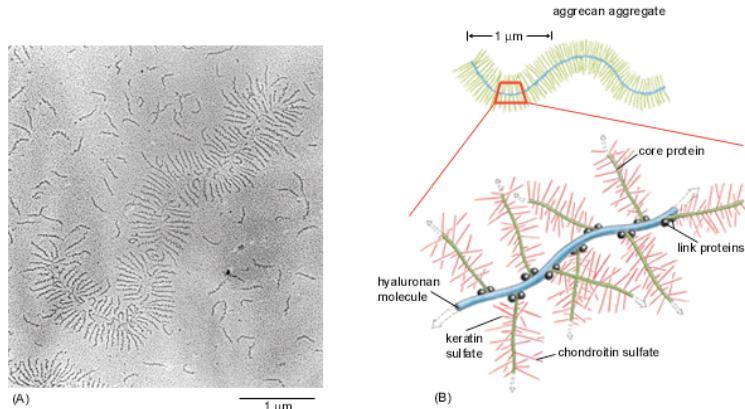

Figure 19-38. An aggrecan aggregate from fetal bovine cartilage. (A) Electron micrograph of an aggrecan aggregate shadowed with platinum. Many free aggrecan molecules are also seen. (B) Schematic drawing of the giant aggrecan aggregate shown in (A). It consists of about 100 aggrecan monomers (each like the one shown in Figure 19-37) noncovalently bound to a single hyaluronan chain through two link proteins that bind to both the core protein of the proteoglycan and to the hyaluronan chain, thereby stabilizing the aggregate; the link proteins are members of the hyaladherin family of hyaluronan-binding proteins discussed previously. The molecular weight of such a complex can be 10^8 or more, and it occupies a volume equivalent to that of a bacterium, which is about 2 x 10^{-12} cm $\underline{3}$. (A, courtesy of Lawrence Rosenberg.)

Single hyaluronic acid (HA) molecule using optical trap. Typical of the WLC models described before.

Aggrecan proteoglycans with HA core. Scale bar 1 micron

Atomic Force Microscopy of Aggrecan

50 nm

Aggrecan Chondroitin sulfate GAG Chains (Fetal Bovine)

Ave. GAG length: ~36 nm

Inter-GAG spacing: 4-5 nm

(L. Ng, C. Ortiz, A. Grodzinsky)
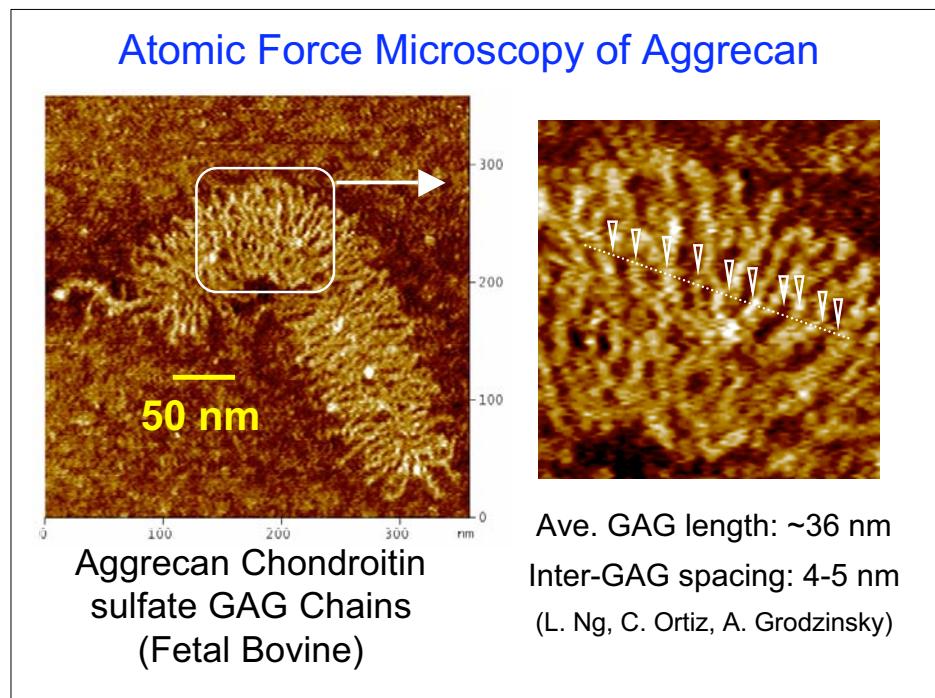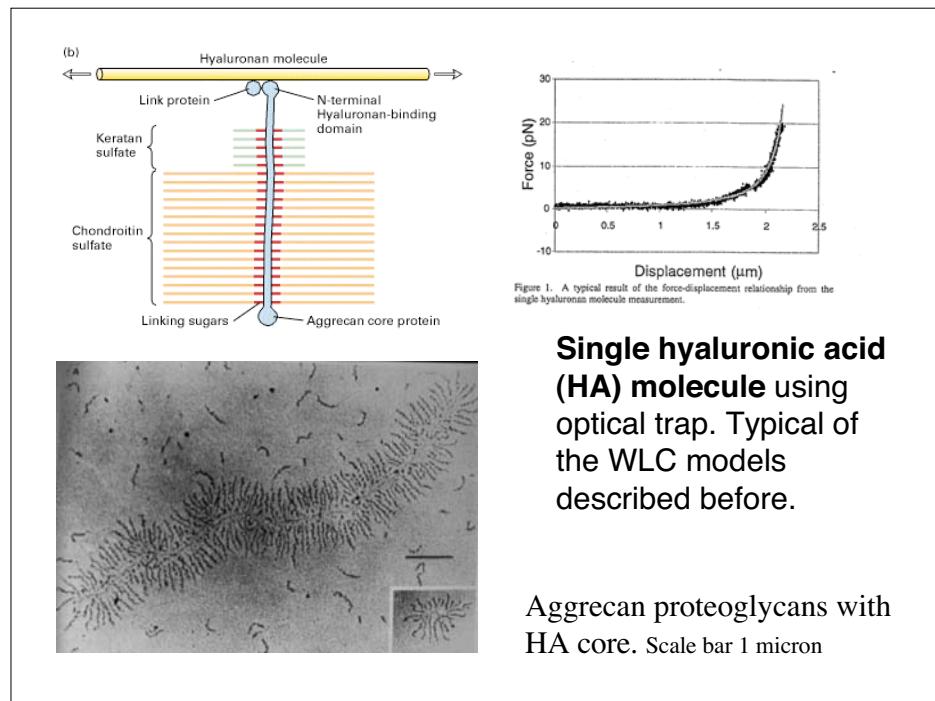
Equilibrium Modulus of Adult Bovine Articular Cartilage in Different Ionic Strengths

Eisenberg and Grodzinsky
J Orthop Res 3:148 1985

Electrostatic: GAG
other
TISSUE

Shear Modulus

Compression

Load Cell

Torque Cell

NaCl

Platen

TISSUE

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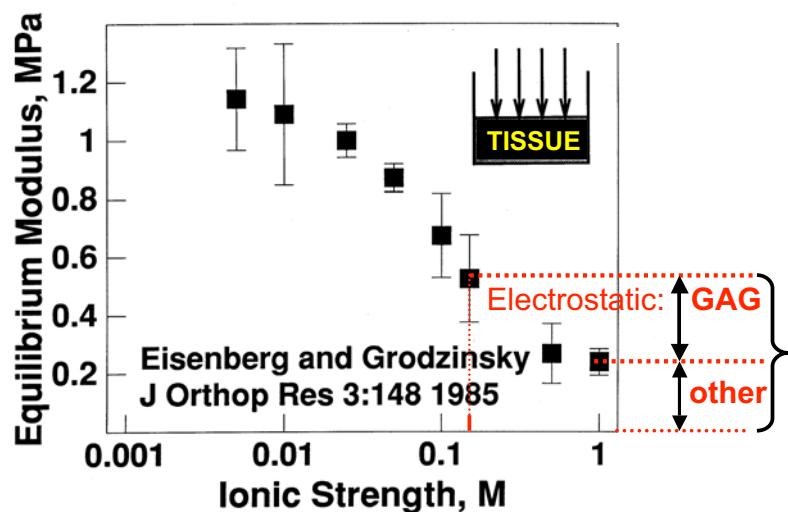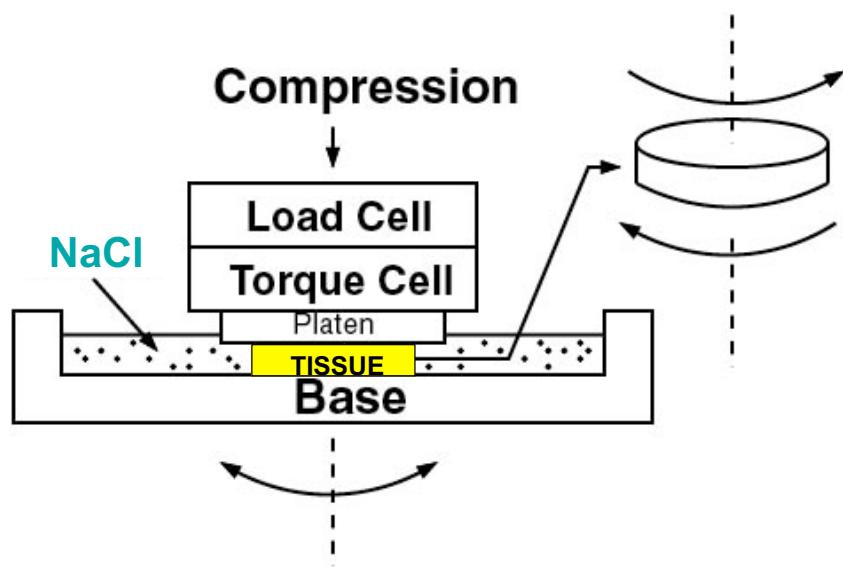
Shear Modulus: (Dynamic @ 0.5Hz, 0.8% strain)

(B) (Mean ± S.D, n=3-6)
Dynamic G
Equilibrium G

Equilibrium G, MPa

Dynamic G Magnitude, MPa

(C) (Mean ± S.D, n=4, f=0.5Hz, γ=0.8%)
Dynamic Phase

Dynamic G Phase Angle (degree)

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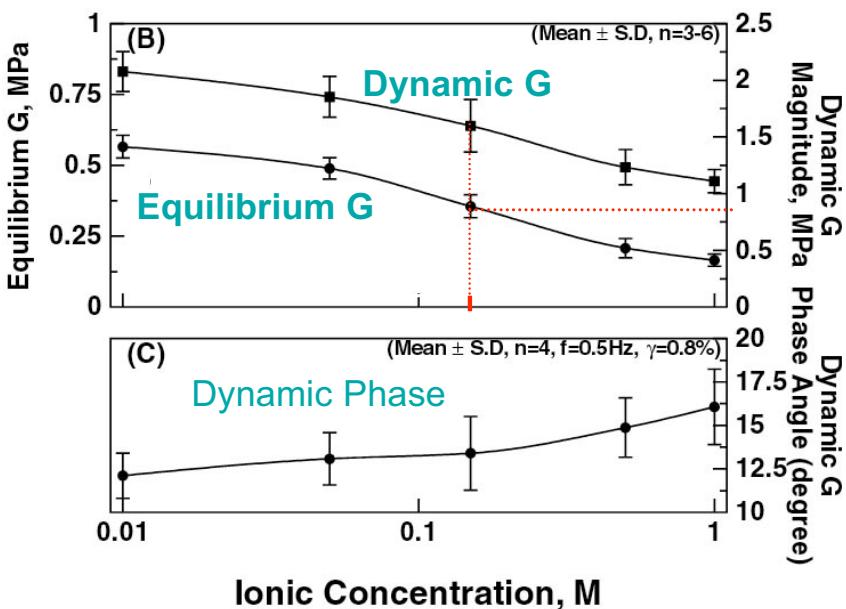
Like charge repulsion accounts for a large fraction (~50%) of the stiffness in tissues with high GAG content.

These effects can be eliminated either by shielding (importance of Debye length -- BE.430!) with counter-ions or neutralization by changing pH.
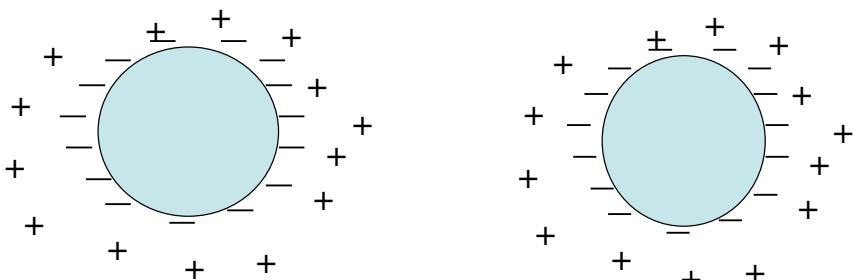
Table 19-3. Some Common Proteoglycans

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
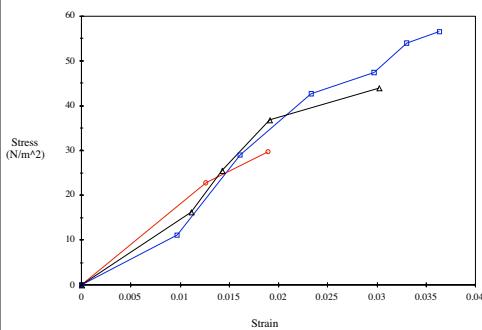
Leon, et al., 1998
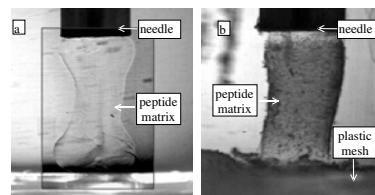
Linear behavior up to fracture

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)
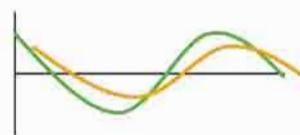
Behavior Pre- and Post-Gelation

1%wt KFE12

100 µM KCl
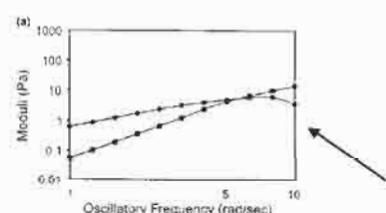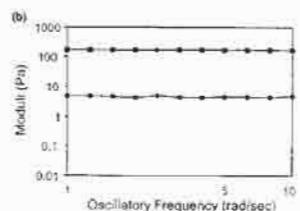
1000 µM KCl

● Storage Modulus (G')
■ Loss Modulus (G'')

Fig. 2. Primary data for gel formation of 1 wt% KFE12 equilibrated with (a) 0.1mM NaCl and (b) 1.0mM NaCl. The storage modulus (squares), G', and loss modulus (circles), G'', are plotted against oscillatory frequency on log-log scales.

Gelation at 6 < pH < 10

Activation barrier is due to like charge repulsion.
Therefore, gelation occurs when KFE12 has net zero charge
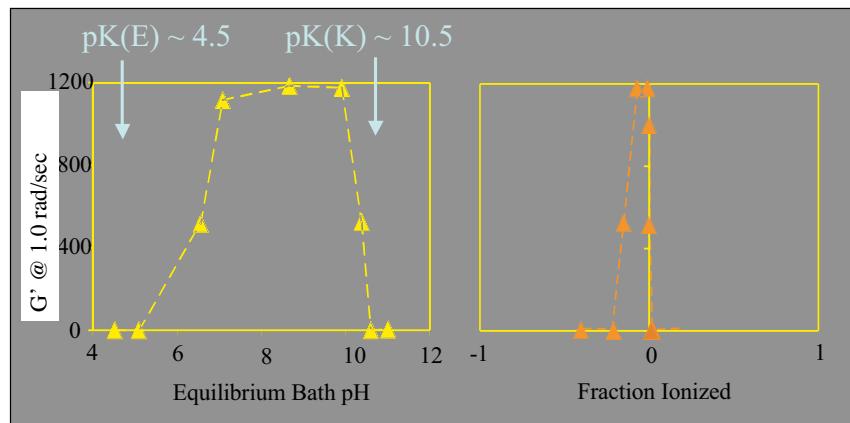
ADHESION PROTEINS
- a) fibronectin
    - i) principal adhesion protein of connective tissues
    - ii) fibronectin is a dimeric glycoprotein
    - iii) fibronectin interacts with other molecules
- b) laminin
    - i) found in basal laminae
    - ii) form mesh-like polymers
    - iii) has various binding 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
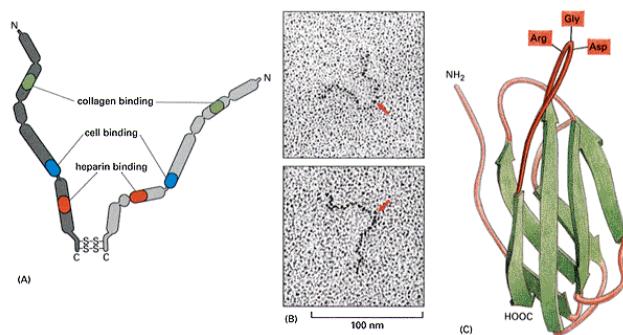
Figure 19-51. The structure of a fibronectin dimer. As shown schematically in (A), the two polypeptide chains are similar but generally not identical (being made from the same gene but from differently spliced mRNAs). They are joined by two disulfide bonds near the carboxyl terminus. Each chain is almost 2500 amino acid residues long and is folded into five or six rodlike domains connected by flexible polypeptide segments. Individual domains are specialized for binding to a particular molecule or to a cell, as indicated for three of the domains. For simplicity, not all of the known binding sites are shown (there are other cell-binding sites, for example). (B) Electron micrographs of individual molecules shadowed with platinum; *arrows* mark the carboxyl termini. (C) The three-dimensional structure of a type III fibronectin repeat, as determined by nuclear magnetic resonance studies. It is the main type of repeating module in fibronectin and is also found in many other proteins. The Arg-Gly-Asp (RGD) sequence shown is part of the major cell-binding site (shown in *blue* in [A]) that we discuss in the text. (B, from J. Engel et al., *J. Mol. Biol.* 150:97-120, 1981. Academic Press Inc. [London] Ltd.; C, adapted from A.L. Main, T.S. Harvey, M. Baron, J. Boyd, and I.D. Campbell, *Cell* 71:671-678, 1992. © Cell Press.)
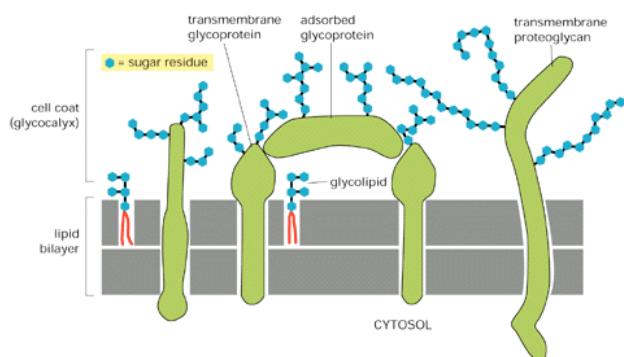
Figure 10-41. Simplified diagram of the cell coat (glycocalyx). The cell coat is made up of the oligosaccharide side chains of glycolipids and integral membrane glycoproteins and the polysaccharide chains on integral membrane proteoglycans. In addition, adsorbed glycoproteins and adsorbed proteoglycans (not shown) contribute to the glycocalyx in many cells. Note that all of the carbohydrate is on the noncytoplasmic surface of the membrane.