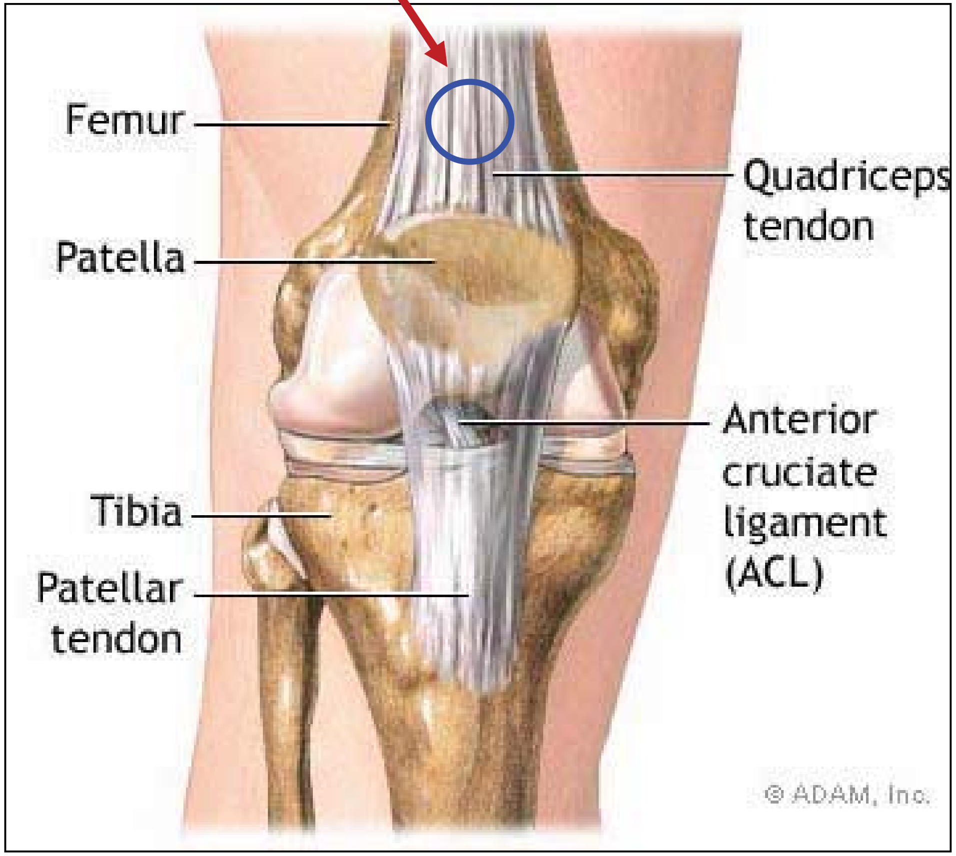
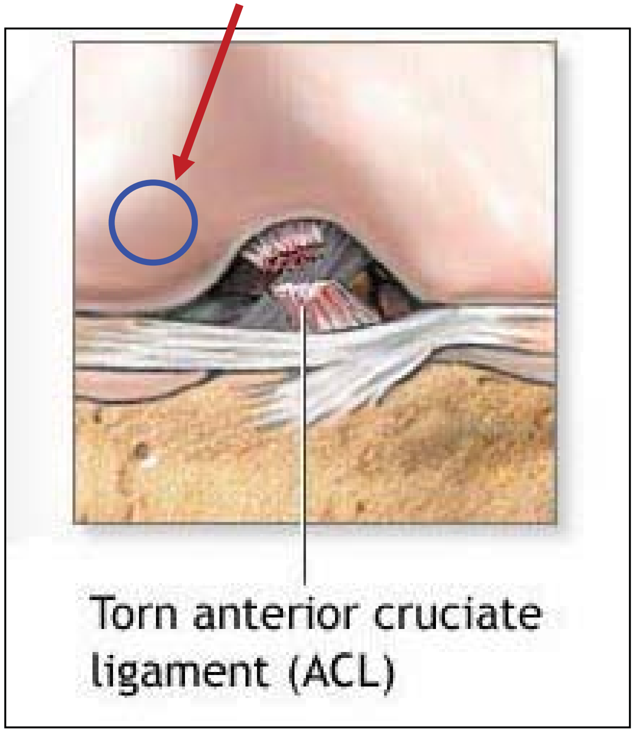
Musculoskeletal Tissues

Tension



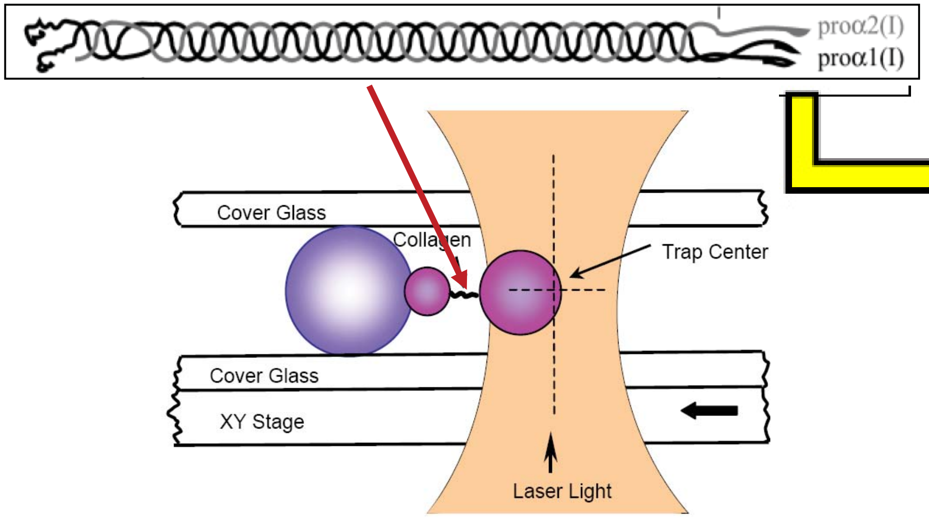
Compression & Shear

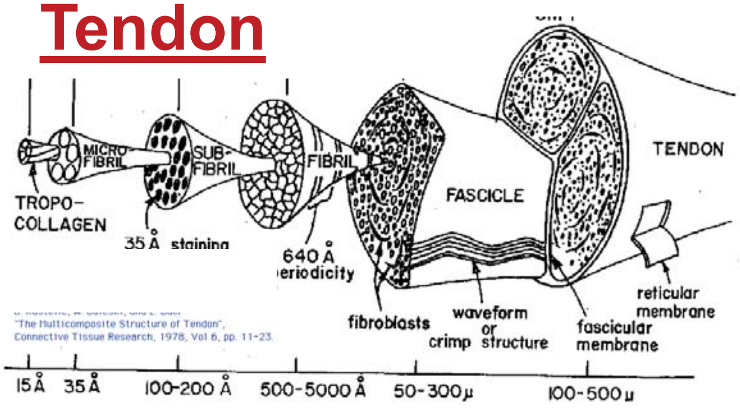


Equilibrium (Tensile) Modulus

Pro-collagen molecule →

Tendon





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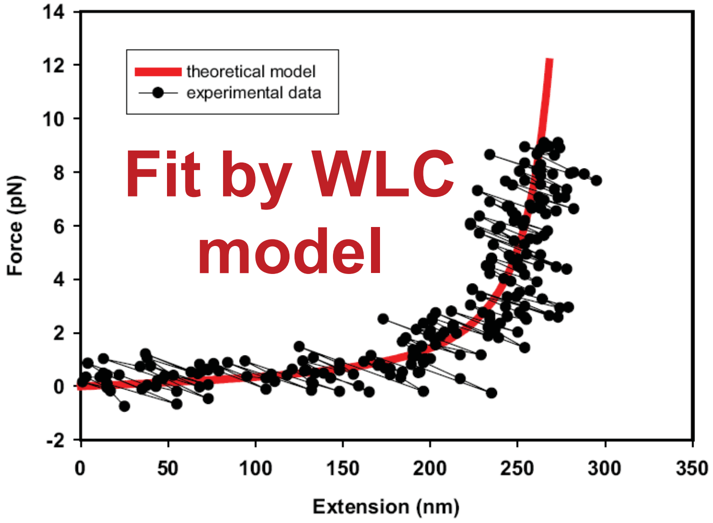
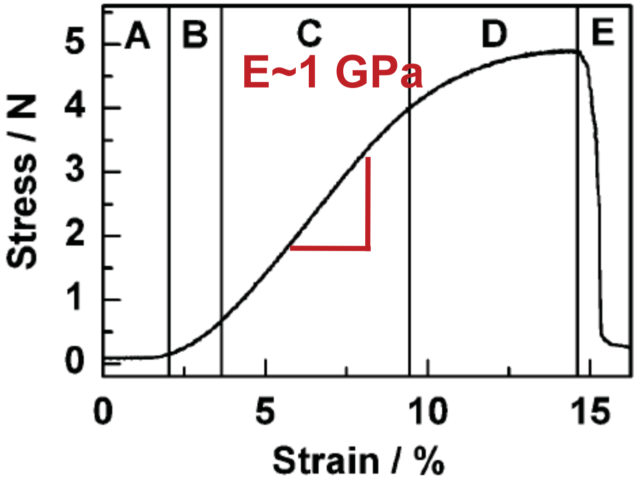
Source: Kastelic, J., A. Galeski, et al. "The Multicomposite Structure of Tendon." *Connective Tissue Research* 6, no. 1 (1978): 11-23.

Force - extension



(Sun+, J Biomechanics, 2004)

Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Sun, Yu-Long et al. "Stretching Type II Collagen with Optical Tweezers." *Journal of Biomechanics* 37, no. 11 (2004): 1665-9.

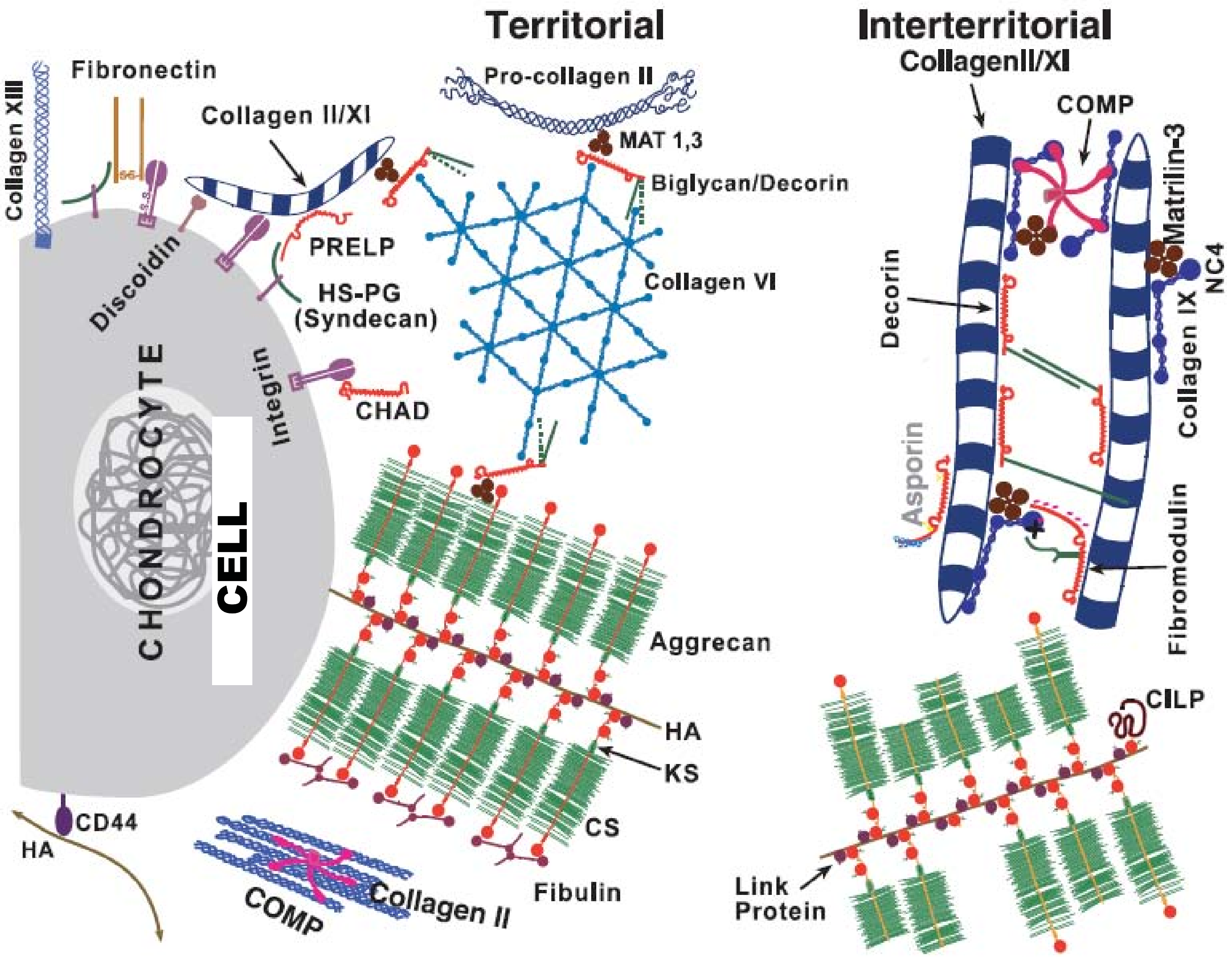


Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Gutsmann, Thomas. "Force Spectroscopy of Collagen Fibers to Investigate their Mechanical Properties and Structural Organization." *Biophysical Journal* 86, no. 5 (2004): 3186-93.

Stress vs strain curve of a rat tail tendon: (A-B) Toe - heel region, **(C) linear region**, (D) plateau, (E) rupture of the tendon.

(Gutsmann+, Biophys J, 2004)

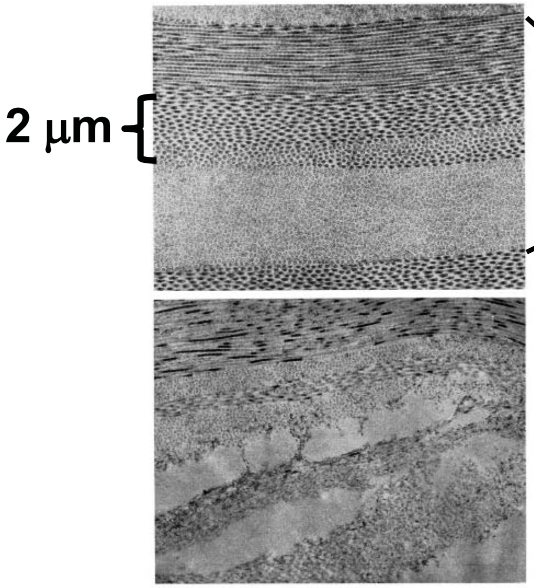
Organization and Function of Extracellular Matrix



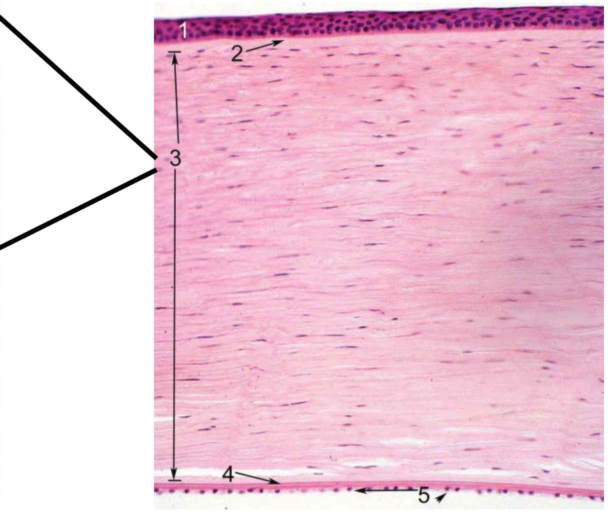
Source: Heinegård, Dick, and Tore Saxne. "The Role of the Cartilage Matrix in Osteoarthritis." *Nature Reviews Rheumatology* 7, no. 1 (2011): 50-56.

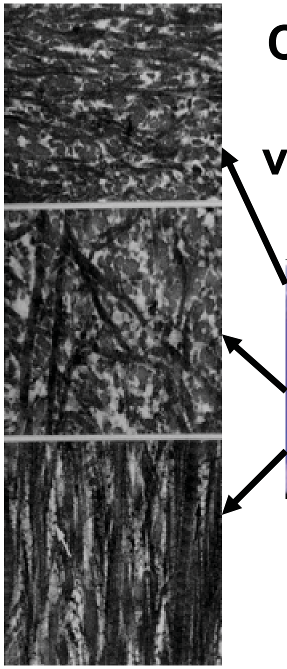
Dick Heinegård Int. J. Exp Pathol, 2009

Cornea collagen architecture

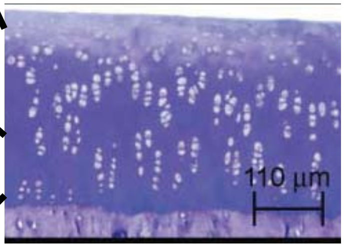


Human Cornea

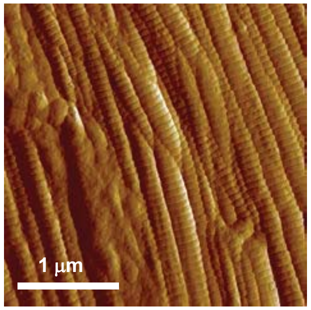


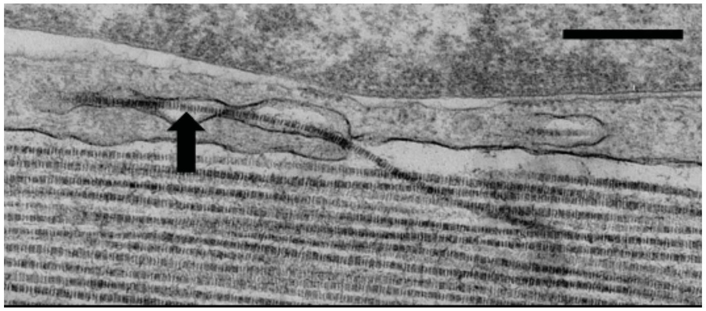


Collagen (type II) architecture varies with depth in cartilage



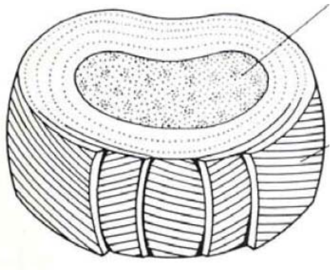
Type I collagen imaged by AFM

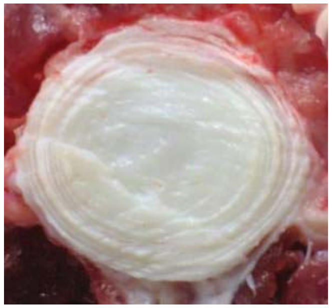




Tendon collagen fibrils (~28 nm) secreted and organized by tendon fibroblast

Collagen architecture of the disc

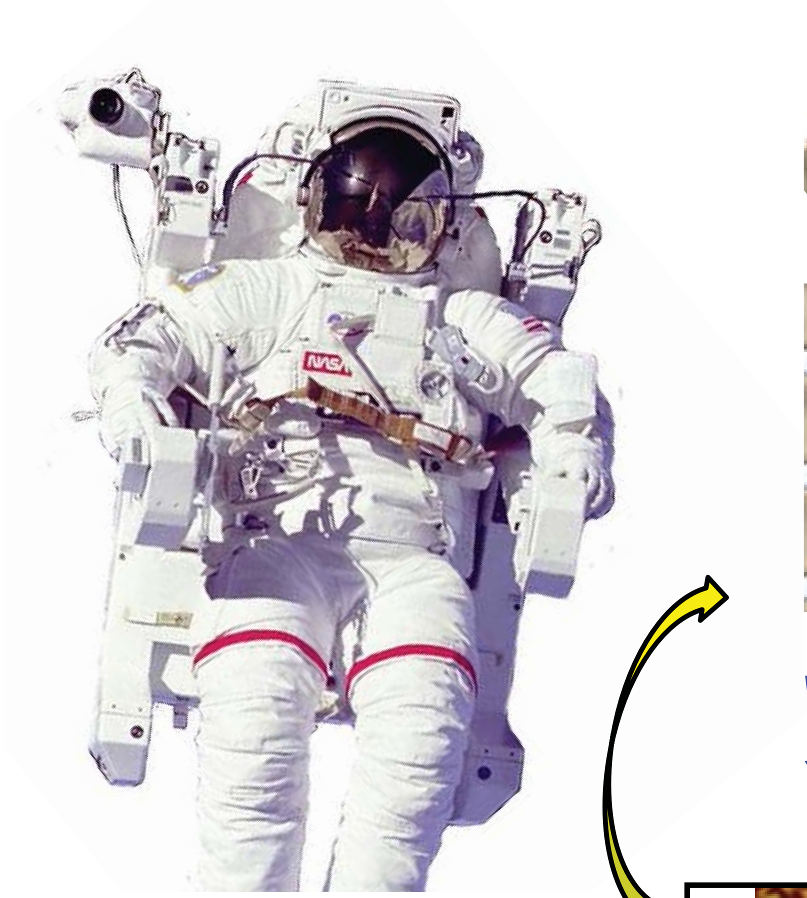


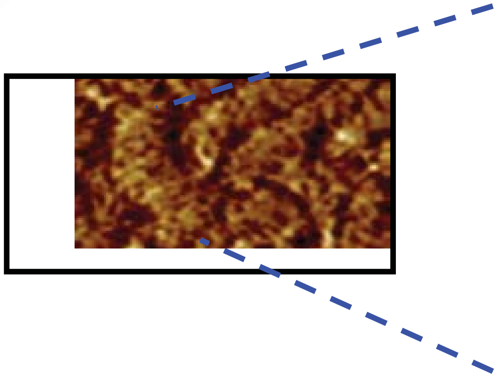


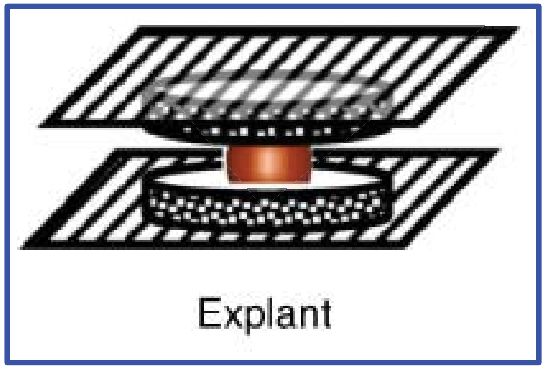
Human intervertebral disc

Astronauts gain $\simeq$ 2 in height during space flight: <u>swelling of the intervertebral discs under 0-gravity</u>:

"swelling pressure" of highly charged aggrecan !!







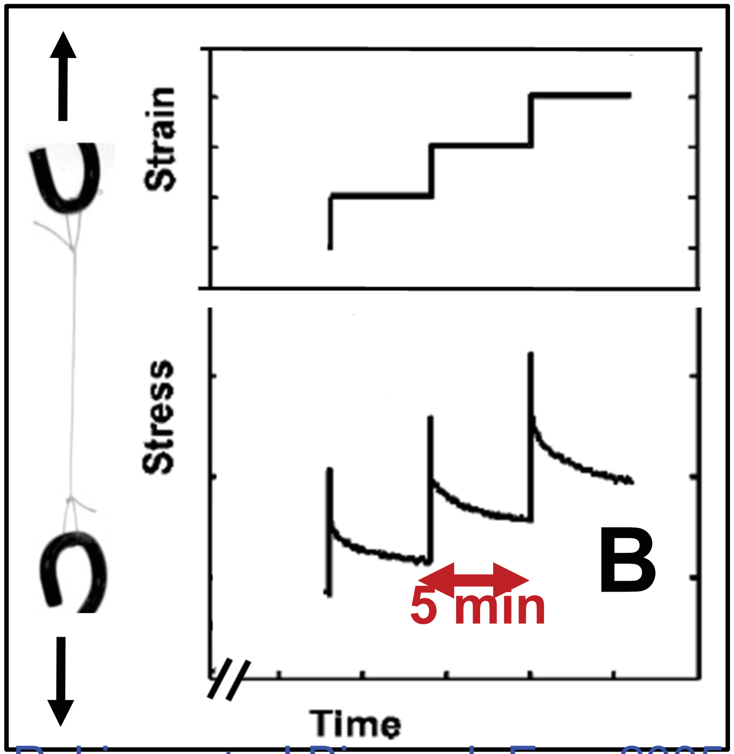
<u>Disc</u>

Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: MacLean, Jeffrey J., et al. "Role of Endplates in Contributing to Compression Behaviors of Motion Segments and Intervertebral Discs." *Journal of Biomechanics* 40, no. 1 (2007): 55-63.

Stress Relaxation: is $\tau = (\eta/E)$ the same for molecules, fibrils, fibers, tendon-tissue???

Apply constant strain (ε_{11}) and measure stress vs time

Mouse tendon fascicle



Robinson+, J Biomech Eng, 2005

Tendon Hierarchy

Tissue

Molecule

Fibril

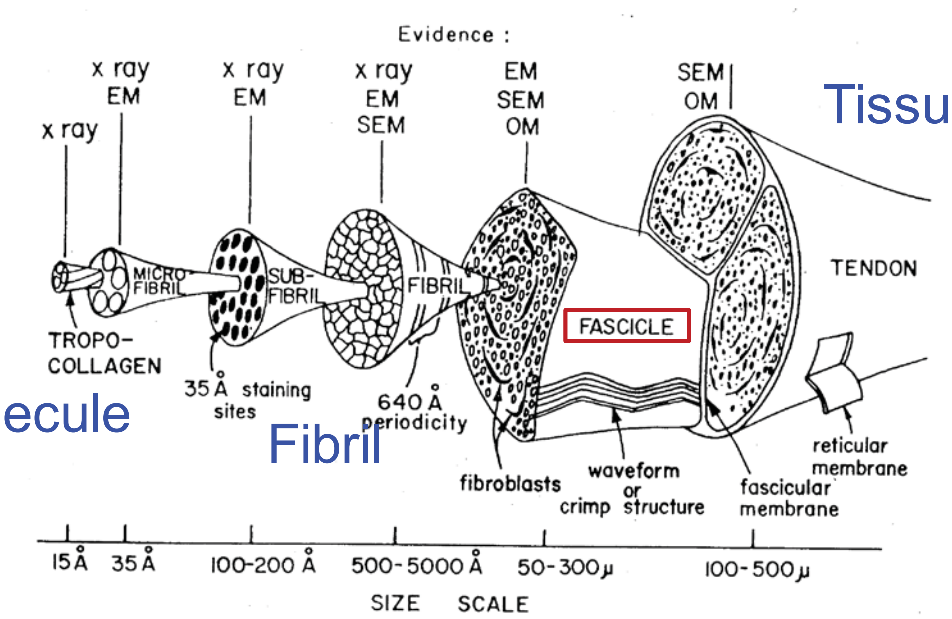


Figure 7.3:6 Hierarchy of structure of a tendon according to Kastelic et al. (1978). Reproduced by permission. Evidences are gathered from X ray, electron microscopy (EM), scanning electron microscopy (SEM), and optical microscopy (OM).

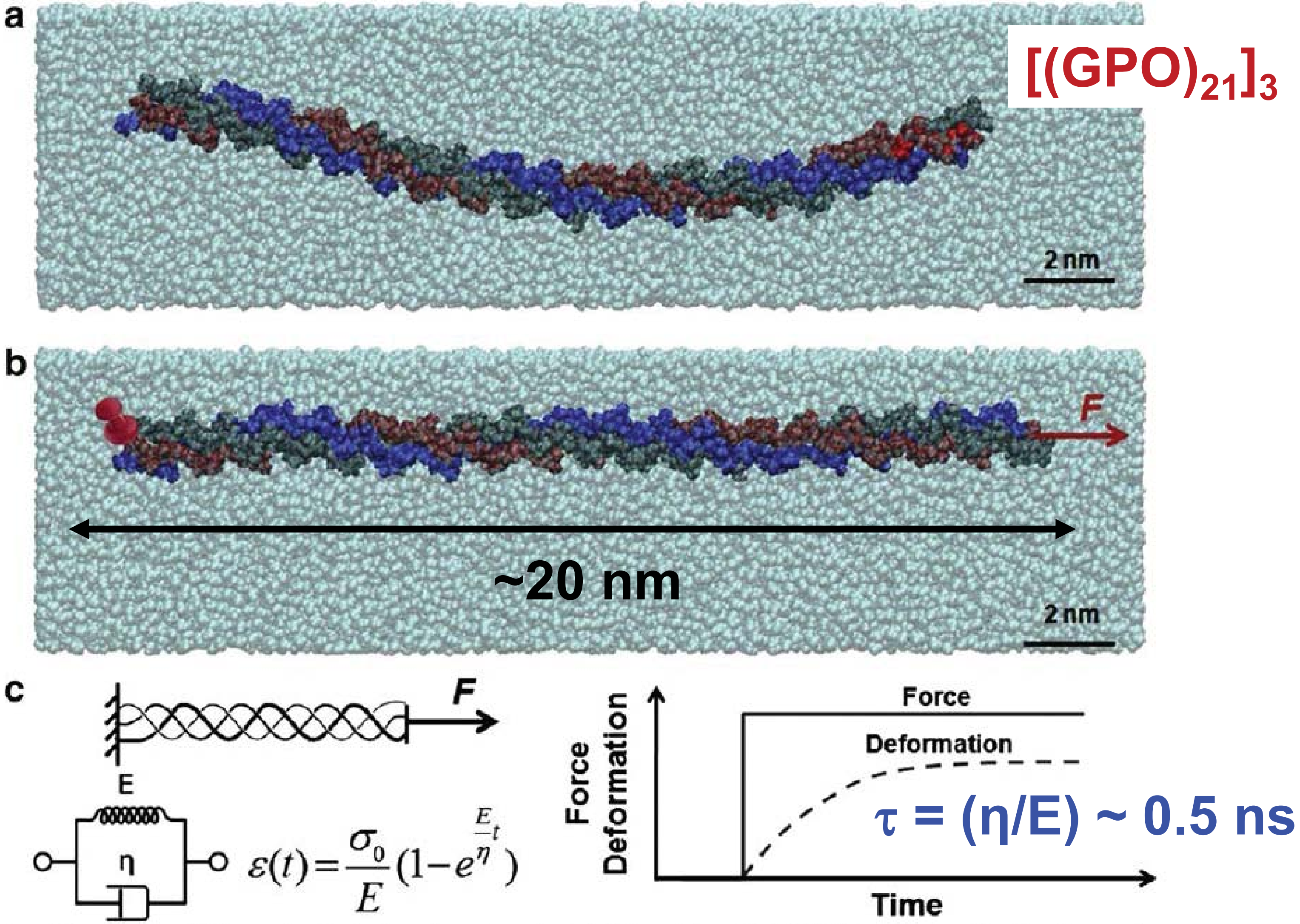
(Y.C. Fung)

Source: Kastelic, J., A. Galeski, and E. Baer. "The Multicomposite Structure of Tendon." *&RQQHFWLYH 7LVVXH 5HVHDUFK* 6, no. 1 (1978): 11-23.

Source: Robinson, Paul S. et al. "Influence of Decorin and Biglycan on Mechanical Properties of Multiple Tendons in Knockout Mice." *Journal of Biomechanical Engineering* 127, no. 1 (2005): 181-5.

“In silico” creep test of a segment of a collagen molecule

(Gautieri, Matrix Biology, 2012)



$[(GPO)_{21}]_3$

~20 nm

$\tau = (\eta/E) \sim 0.5$ ns

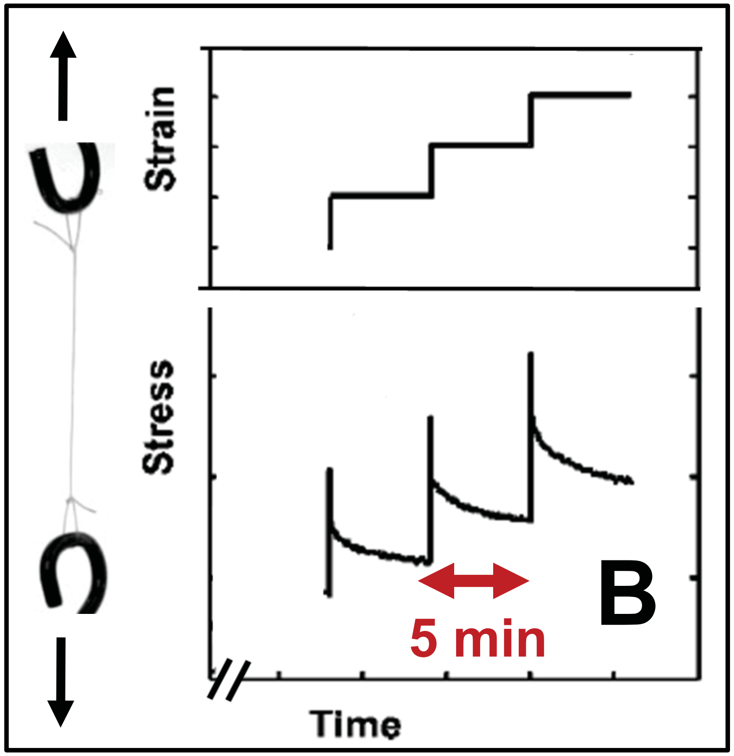
Fig. 1. Snapshots of the collagen peptide in water box. Panel a shows the conformation of the full atomistic model of a $[(GPO)_{21}]_3$ collagen peptide solvated in water box and equilibrated for 30 ns. After equilibration the molecule is subjected to virtual creep tests: one end of the collagen peptide is held fixed, whereas the other end is pulled with constant force (from 300 pN to 3000 pN) until end-to-end distance reaches equilibrium (Panel b). Panel c shows a schematic of the creep test; a constant force is applied instantaneously to the molecule and its response (deformation over time) is monitored. The mechanical response of collagen molecule is modeled using a KV model, from which molecular Young's modulus (E) and viscosity (η) are calculated.

Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Gautieri, Alfonso et al. "Viscoelastic Properties of Model Segments of Collagen Molecules." *Matrix Biology* 31, no. 2 (2012): 141-9.

Stress Relaxation: is τ = (η/E) the same for molecules, fibrils, fibers, tendon-tissue???

Apply constant strain (ε_{11}) and measure stress vs time

Mouse tendon fascicle



Robinson+, J Biomech Eng, 2005

Source: Robinson, Paul S. et al. "Influence of Decorin and Biglycan on Mechanical Properties of Multiple Tendons in Knockout Mice." *Journal of Biomechanical Engineering* 127, no. 1 (2005): 181-5.

$\tau \sim 0.5$ **ns**

$\tau \sim 5$ **min**

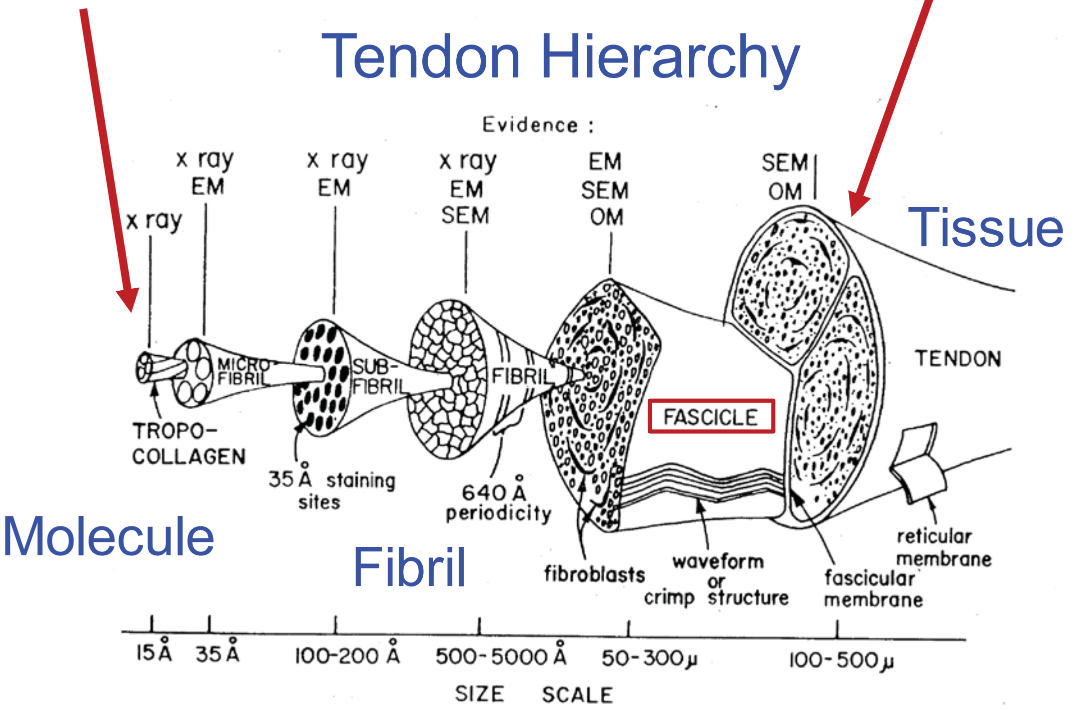
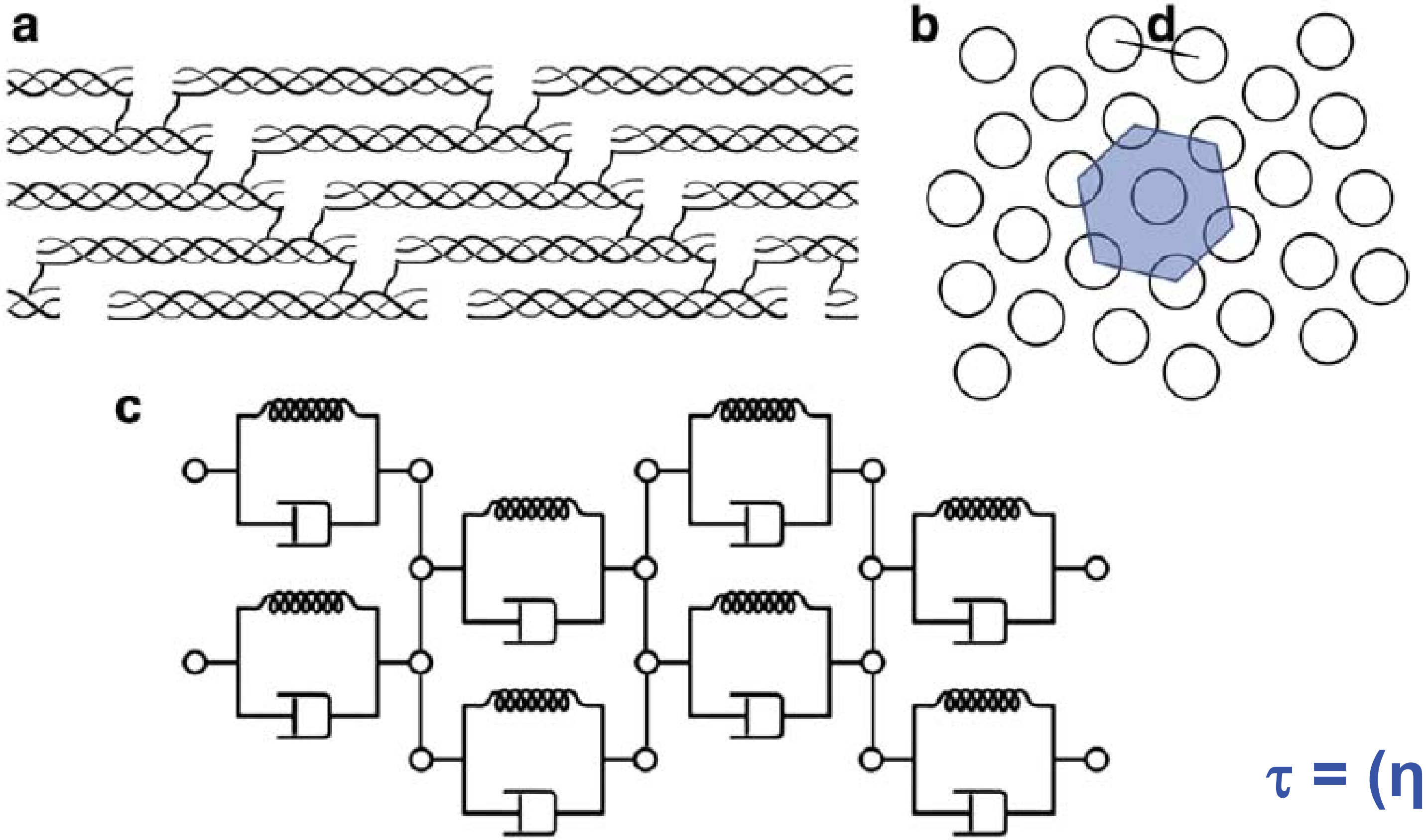


Figure 7.3:6 Hierarchy of structure of a tendon according to Kastelic et al. (1978). Reproduced by permission. Evidences are gathered from X ray, electron microscopy (EM), scanning electron microscopy (SEM), and optical microscopy (OM). (Y.C. Fung)

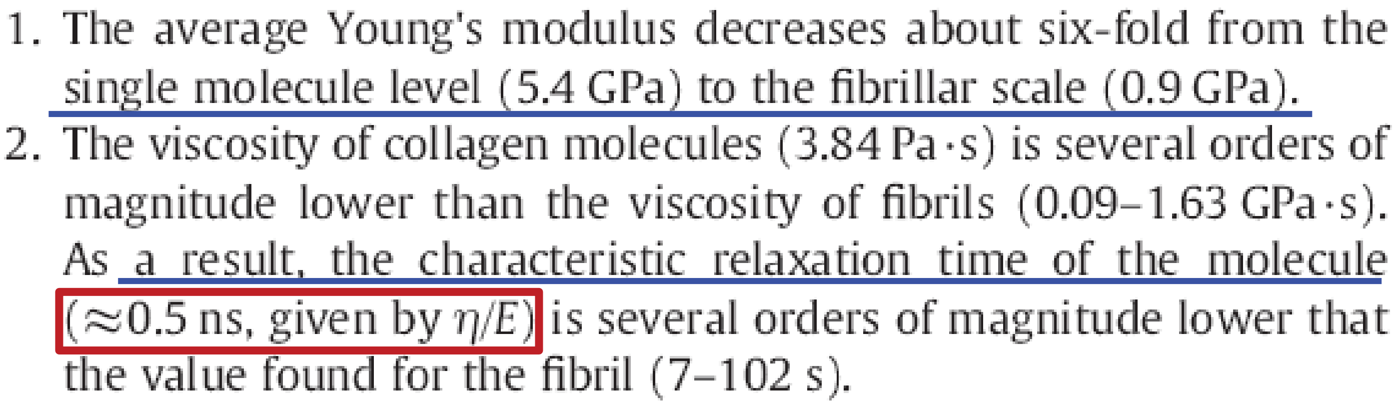
Source: Kastelic, J., A. Galeski, and E. Baer. "The Multicomposite Structure of Tendon." *&RQQHFWLYH 7LVVXH 5HVHDUFK* 6, no. 1 (1978): 11-23.

Need More Elements ? (e.g., Fibril → Fiber → Tissue)



$\tau = (\eta/E)$

Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Gautieri, Alfonso et al. "Viscoelastic Properties of Model Segments of Collagen Molecules." *Matrix Biology* 31, no. 2 (2012): 141-9.



1. The average Young's modulus decreases about six-fold from the single molecule level (5.4 GPa) to the fibrillar scale (0.9 GPa).
2. The viscosity of collagen molecules (3.84 Pa·s) is several orders of magnitude lower than the viscosity of fibrils (0.09–1.63 GPa·s). As a result, the characteristic relaxation time of the molecule ($\approx$0.5 ns, given by η/E) is several orders of magnitude lower that the value found for the fibril (7–102 s).

A Generalized Maxwell Model for Creep Behavior of Artery Opening Angle

J Biomech Eng, 2008

W. Zhang[1], **X. Guo**[1], and **G. S. Kassab**[1,2,3]

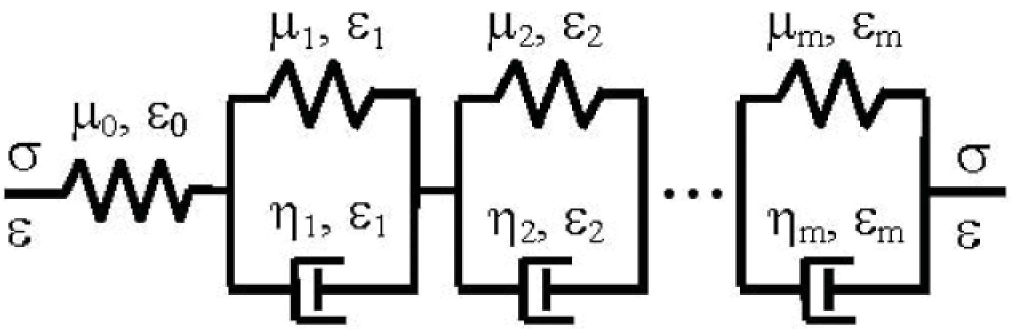


Fig. 3.
A generalized Maxwell viscoelastic model (a linear spring in serial with *m* Voigt elements).

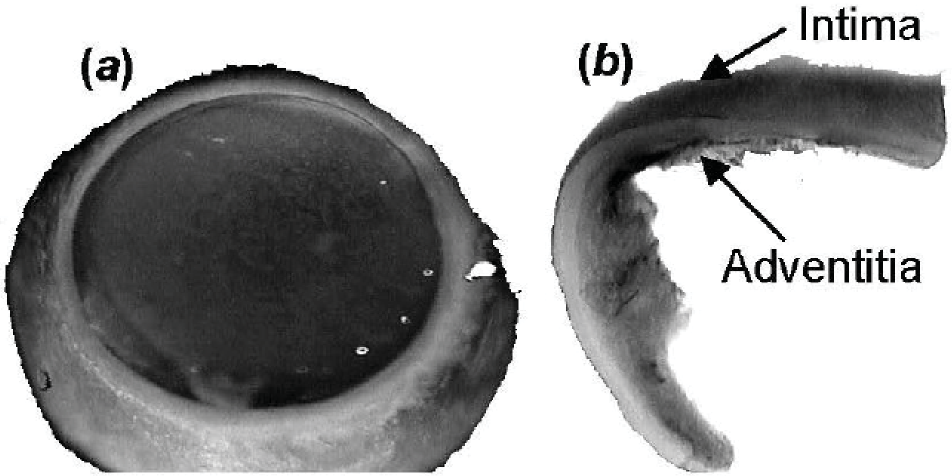
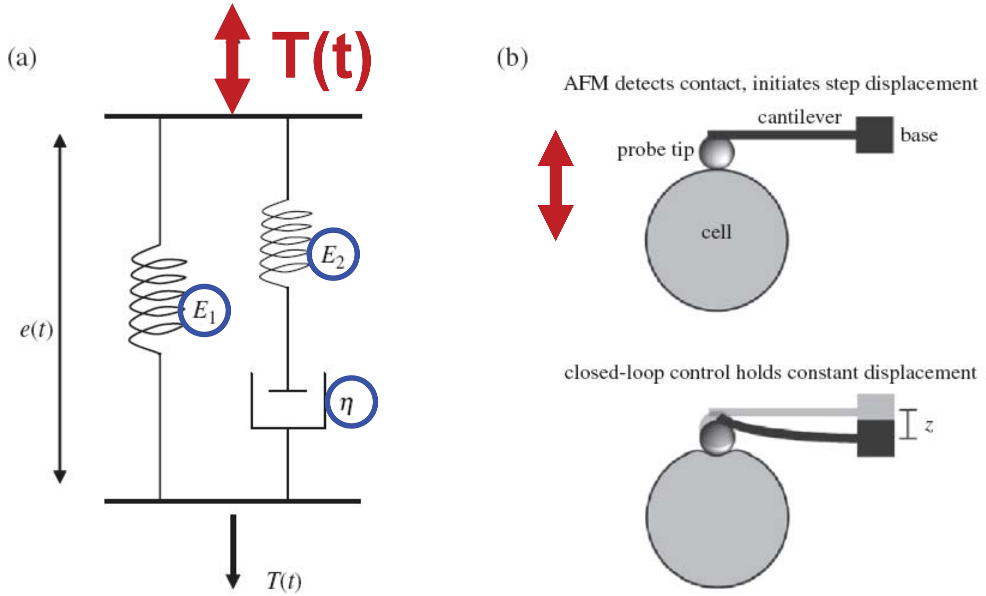


Fig. 2.
Photographs of a porcine coronary artery at the (*a*) loaded state with hardened elastomer in the lumen and (*b*) zero-stress state where opening angle is larger than 180°.

Source: Zhang, W., et al. "A Generalized Maxwell Model for Creep Behavior of Artery Opening Angle." *Journal of Biomechanical Engineering* 130, no. 5 (2008): 054502.

PSet 4: P2 (text P7.9 part c)

Time-varying loading

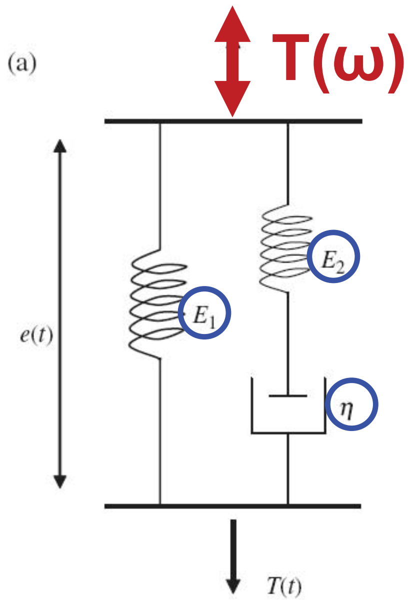


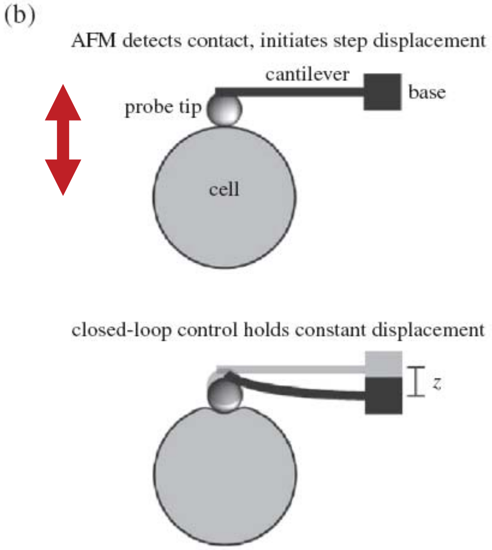
$$T + \alpha \frac{dT}{dt} = E_1 e + \beta \frac{de}{dt} \qquad (7.73)$$

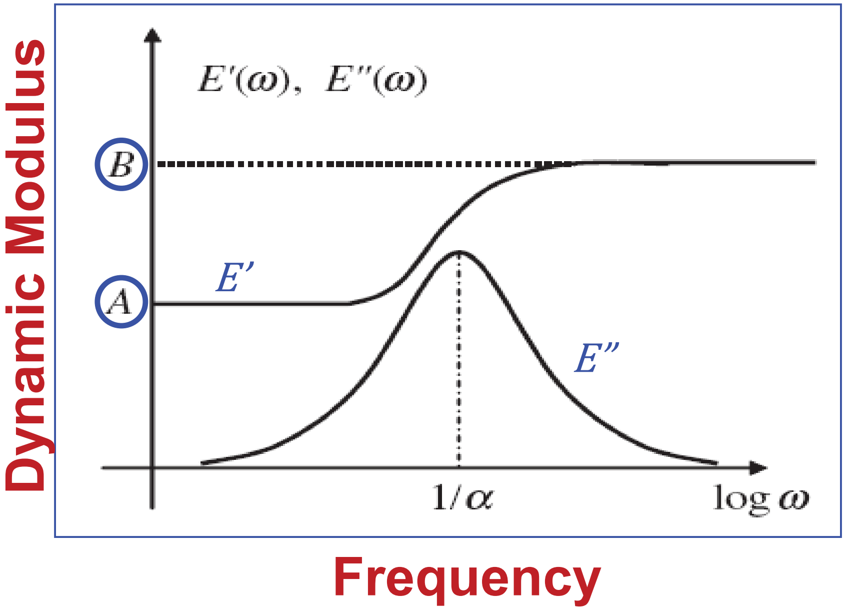
Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission. Source: Lee, BoBae et al. "Dynamic Mechanical Properties of the Tissue-engineered Matrix Associated with Individual Chondrocytes." *Journal of Biomechanics* 43, no. 3 (2010): 469-76.

PSet 4: P3 (text P7.9 part d)

Sinusoidal loading versus Frequency







Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Lee, BoBae et al. "Dynamic Mechanical Properties of the Tissue-engineered Matrix Associated with Individual Chondrocytes." -RXUQDO RI %LRPHFKDQLFV 43, no. 3 (2010): 469-76.

$$\boxed{\hat{E}(\omega) \equiv \frac{\hat{T}(\omega)}{e_0}}$$

Read p. 258, Example 7.4.4

"….we can convert from the time domain to the frequency domain using $\boxed{d/dt \rightarrow j\omega}$ and replacing *T(t)* with $\hat{T}(\omega)$ and *e(t)* with $\hat{e}(\omega)$…."

$$\boxed{T(t) = \mathrm{Re}\left[\hat{T}(\omega)e^{j\omega t}\right]}$$

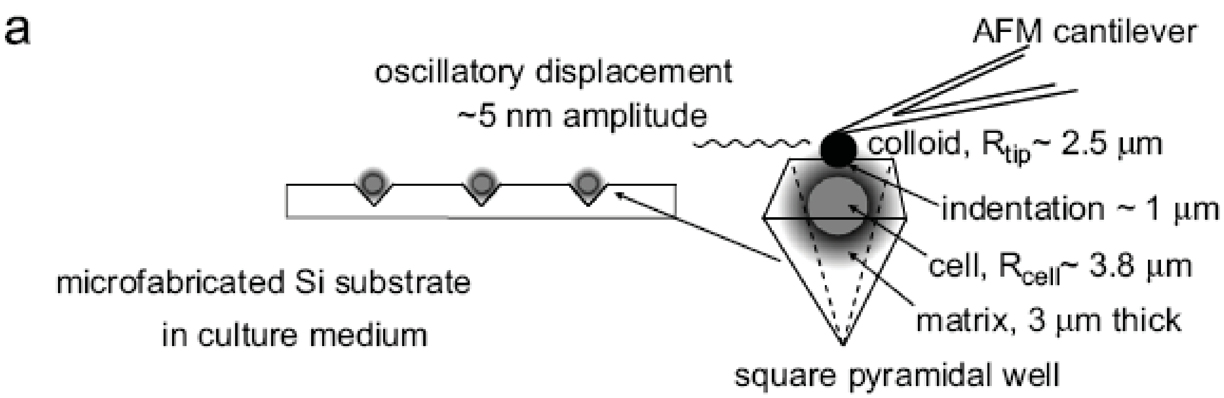
(d) Based on the differential equation (7.73), derive an expression for the complex modulus that describes the frequency behavior of the three-element model of Figure 7.32(a) having the form

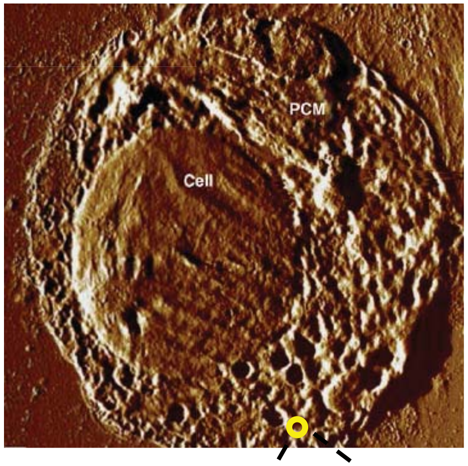
$$\hat{E}(\omega) = E'(\omega) + jE''(\omega)$$

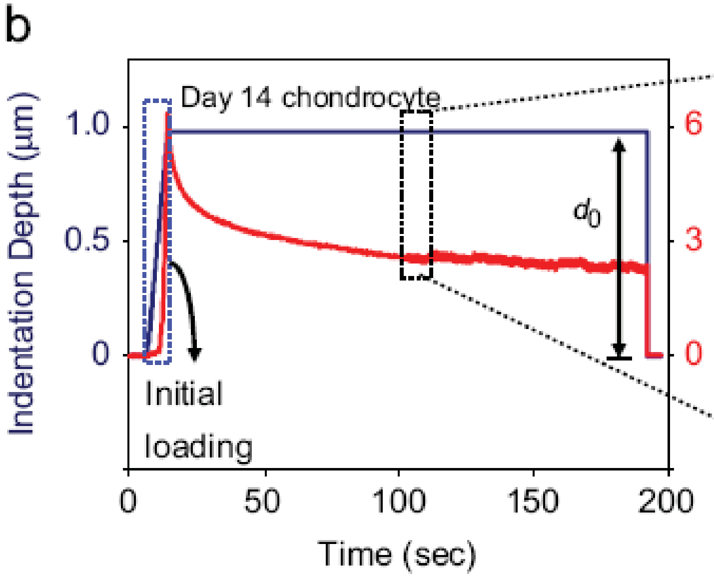
Show that $E'(\omega)$ and $E''(\omega)$ have the frequency dependences shown qualitatively in Figure 7.33 by reasoning the low- and high-frequency limits. Find the constants A and B in terms of the element values E_1 and E_2 based on physical (and/or mathematical) arguments.

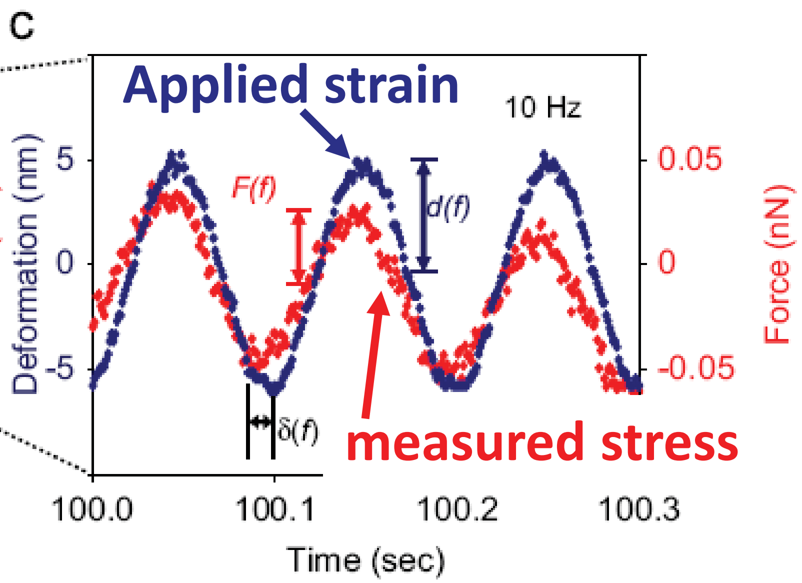
(BoBae Lee+ Biophys J, 2010)

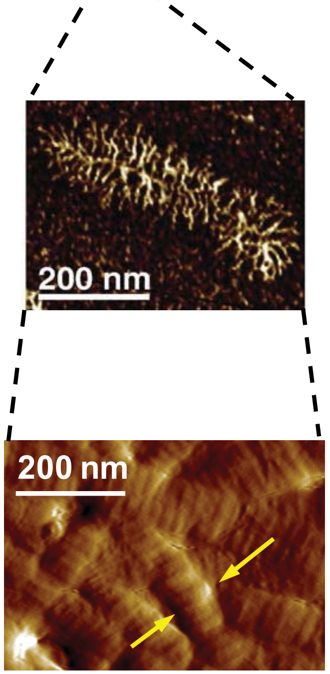
Dynamic mechanical analysis of newly synthesized chondrocyte pericellular matrix (for tissue engineering)







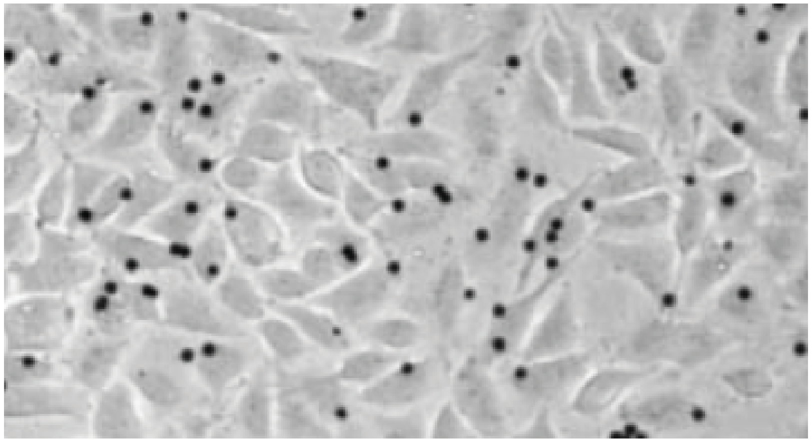




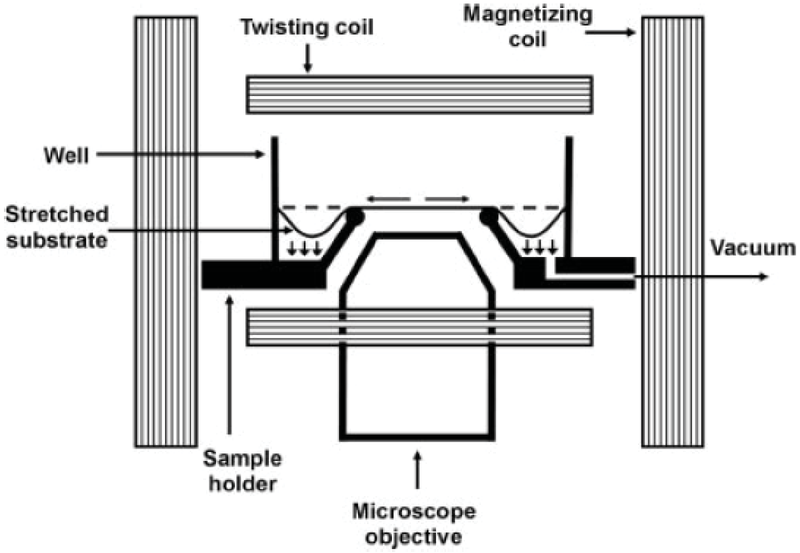
Viscoelasticity of human alveolar epithelial cells subjected to stretch

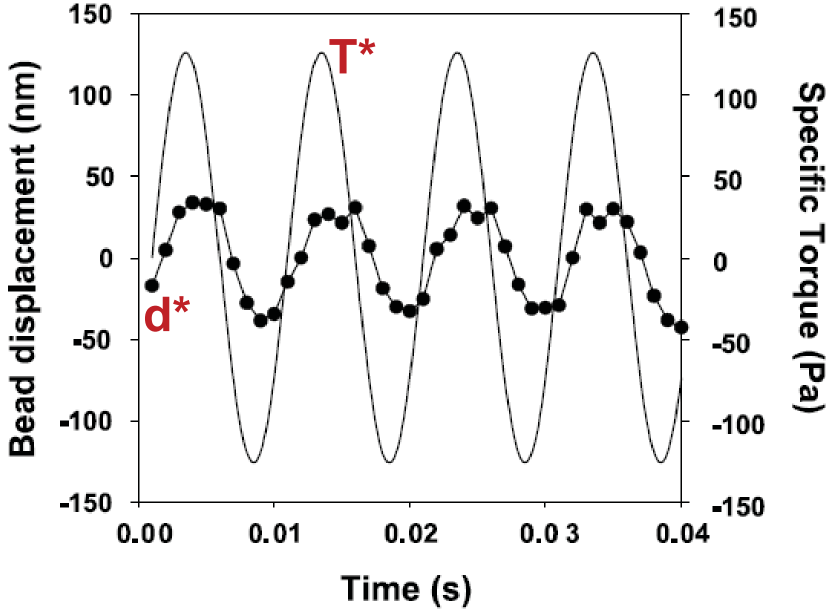
Amer J Physiol, 2004

Xavier Trepat,[1] Mireia Grabulosa,[1] Ferranda Puig,[1]
Geoffrey N. Maksym,[2] Daniel Navajas,[1] and Ramon Farré[1]



Magnetic Twisting Cytometry





Median displacement d* of 51 beads tracked in response to 120-Pa Torque T* at 1 Hz

"Complex Modulus"

$$G^*(\omega) = G'(\omega) + jG''(\omega) = \frac{T^*(\omega)}{d^*(\omega)}$$

$$T^* = \left(\frac{[(\text{bead magnetic moment}) \bullet (\text{B-field})]}{[\text{bead volume}]} \right)$$

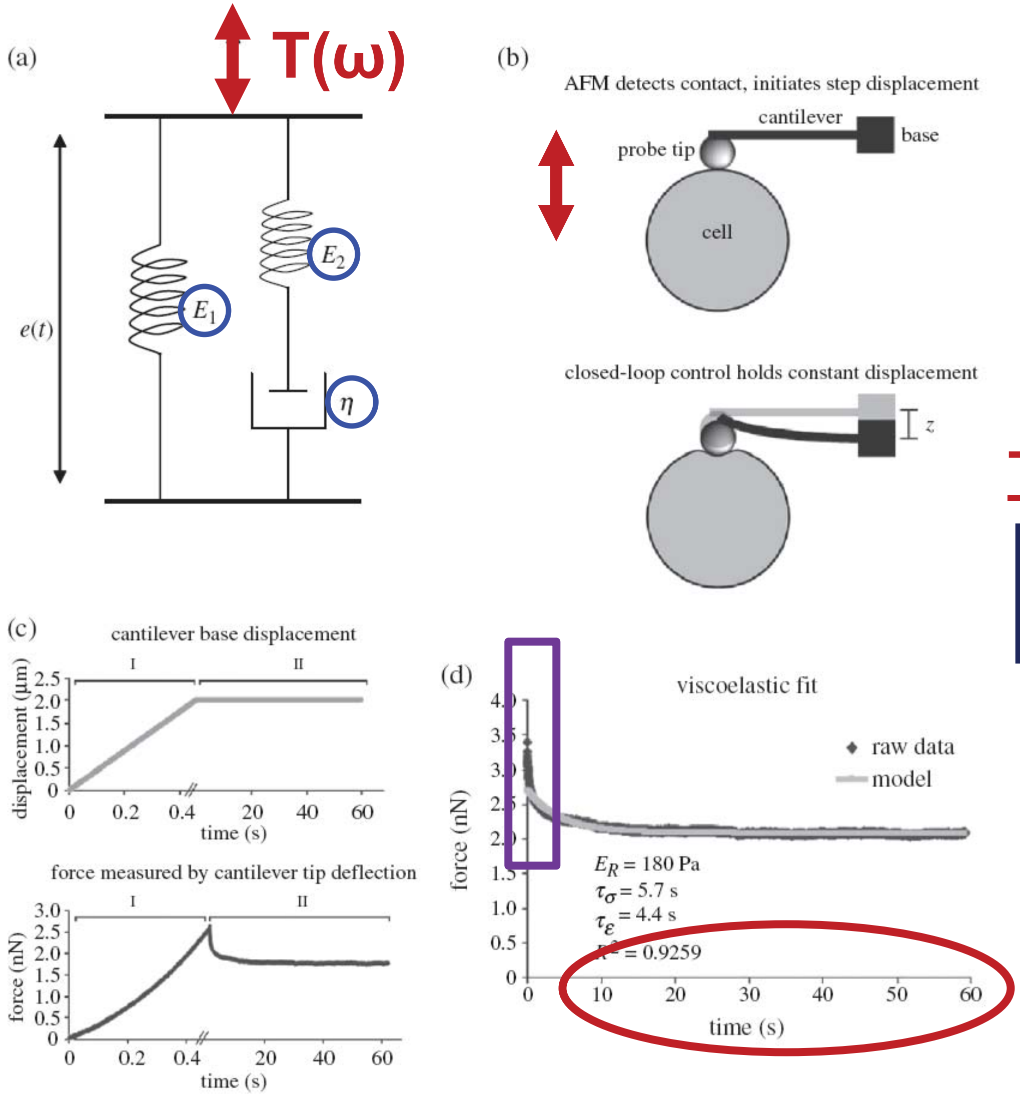
Source: Trepat, Xavier, et al. "Viscoelasticity of Human Alveolar Epithelial Cells Subjected to Stretch." *$PHULFDQ -RXUQDO RI 3K\VLRORJ\ /XQJ &HOOXODU DQG 0ROHFXODU Psychology* 287, no. 5 (2004): L1025-034.

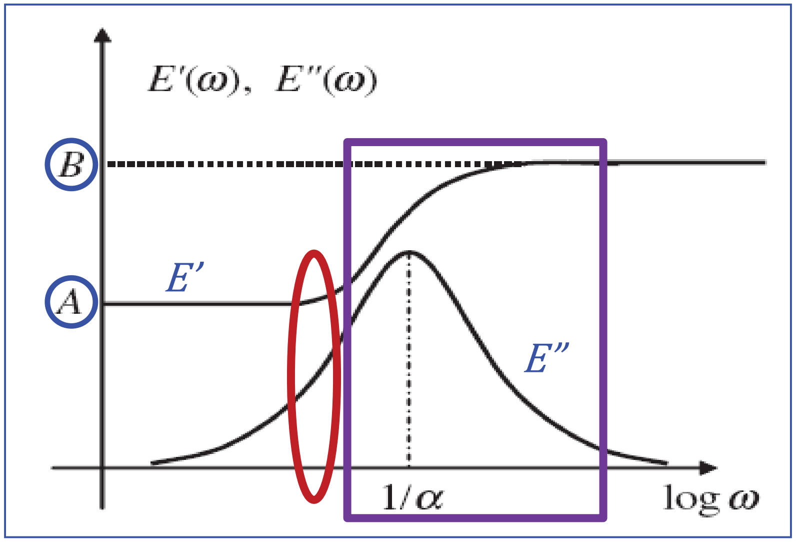
Questions:

- What **mechanism(s)** are responsible for time / frequency dependence:

Poroelasticity v. “solid-phase” viscoelasticity?

- Does poroelasticity operate at cellular and molecular scales as well as tissue scale??





Time Domain: creep; stress relax.

$$T + \alpha \frac{dT}{dt} = E_1 e + \beta \frac{de}{dt} \qquad (7.73)$$

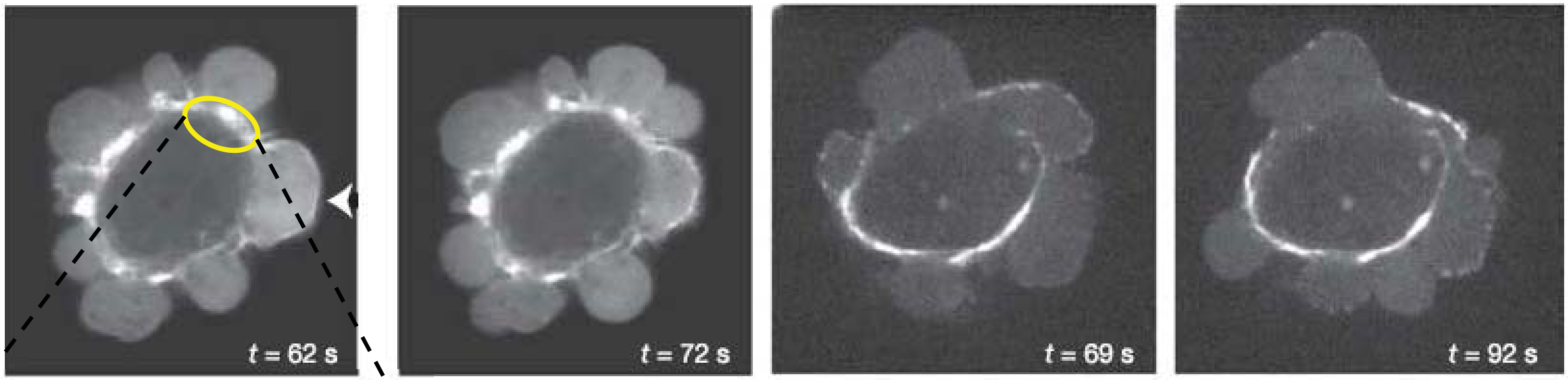
Note: spring-dashpot models involve time (freq), but not space!!

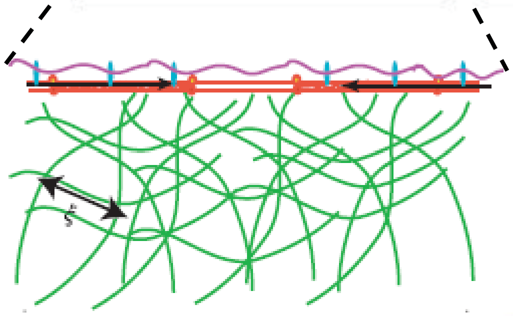
Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Darling, E. M. et al. "Viscoelastic Properties of Zonal Articular Chondrocytes Measured by Atomic Force Microscopy." *2VWHRDUWKULWLV DQG &DUWLODJH* 14, no. 6 (2006): 571-9.

Non-equilibration of hydrostatic pressure in blebbing cells

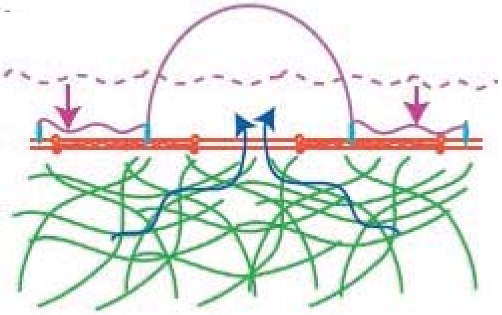
(Nature, 2005)

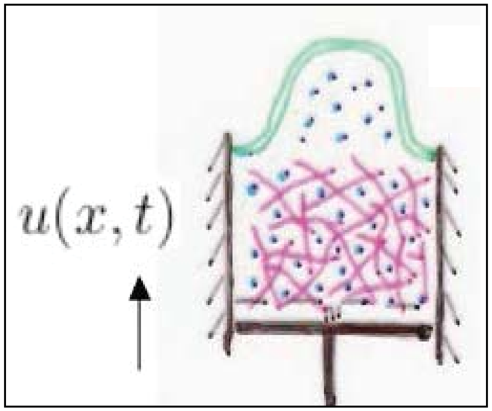
Guillaume T. Charras[1], Justin C. Yarrow[1], Mike A. Horton[2], L. Mahadevan[1,3,4] & T. J. Mitchison[1]





Cytoskeletal contraction





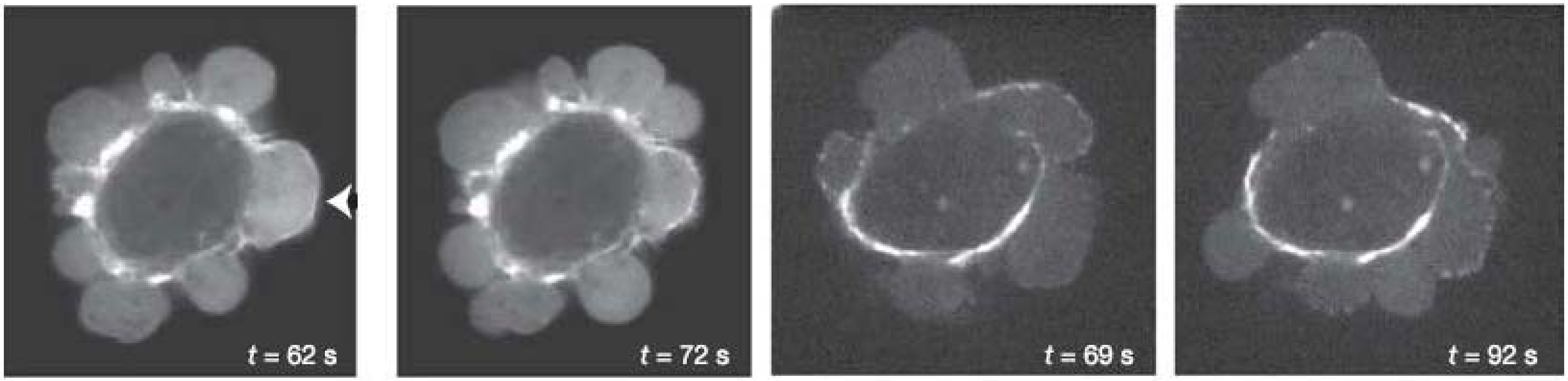
$$\frac{\partial u}{\partial t} = \frac{Ek}{\phi}\frac{\partial^2 u}{\partial x^2}$$

diffusion eqn:

“D” = “E•k”

(Text: P 7.13)

Courtesy of Macmillan Publishers Limited. Used with permission.
Source: Charras, Guillaume T., et al. "Non-equilibration of Hydrostatic Pressure in Blebbing Cells." *Nature* 435, no. 7040 (2005): 365-9.



Courtesy of Macmillan Publishers Limited. Used with permission.
Source: Charras, Guillaume T., et al. "Non-equilibration of Hydrostatic Pressure in Blebbing Cells." *Nature* 435, no. 7040 (2005): 365-9.

Current models of the cytoplasm cannot account for spatio-temporal variations in hydrostatic pressure. **We propose a new description of the cytoplasm based on poroelasticity**. We consider cytoplasm to be composed of a porous, actively contractile, elastic network (cytoskeletal filaments, organelles, ribosomes), infiltrated with an interstitial fluid (…water, ions, soluble proteins), **similar to a fluid-filled sponge**. Contraction of the acto-myosin cortex creates a compressive stress on the cytoskeletal network, leading to localized increase in hydrostatic pressure & … cytosol flow out of the network;… the resulting pressure can lead to membrane detachment and bleb inflation

Non-equilibration of hydrostatic pressure in blebbing cells

(Nature, 2005)

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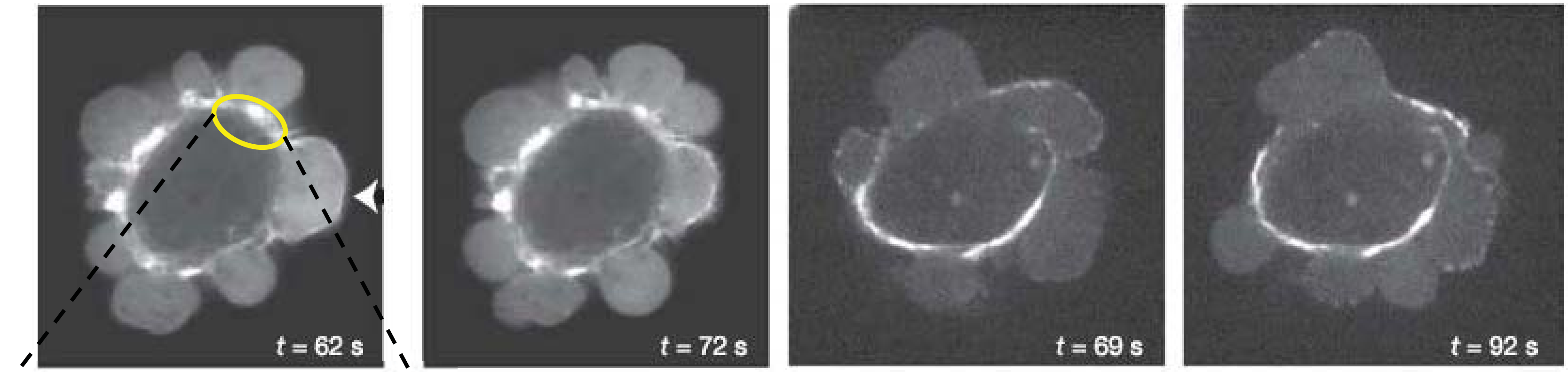
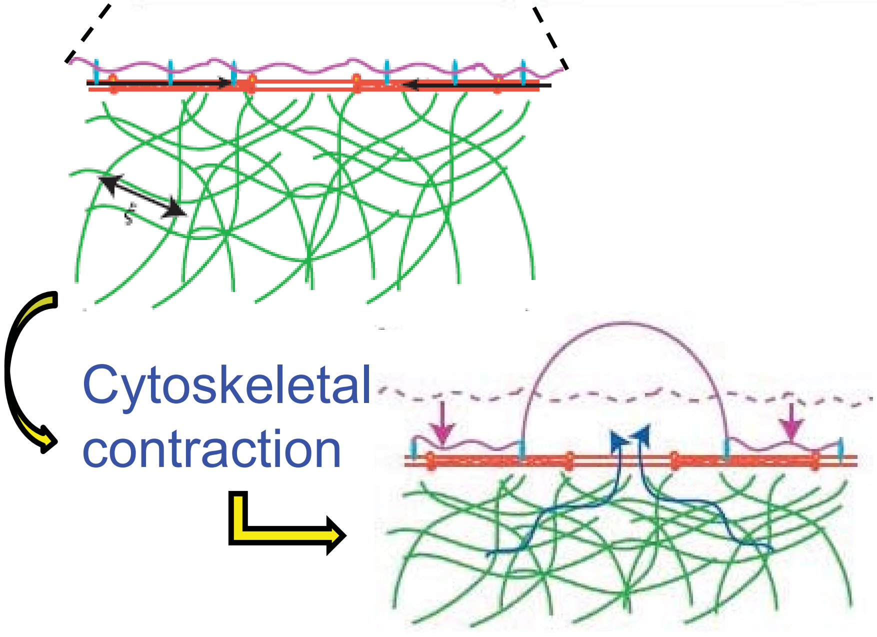
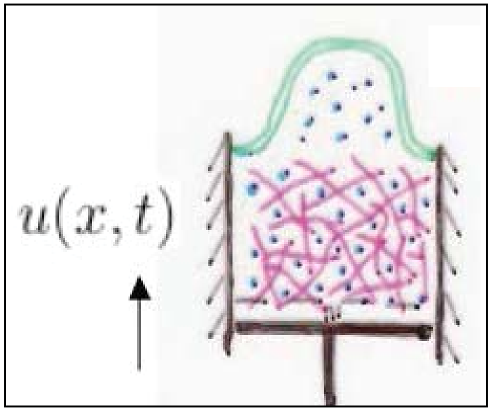




Cytoskeletal contraction



$$\frac{\partial u}{\partial t} = \frac{Ek}{\phi}\frac{\partial^2 u}{\partial x^2}$$

diffusion eqn:
"D" = "E•k"

(Text: P 7.13)

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Source: Charras, Guillaume T., et al. "Non-equilibration of Hydrostatic Pressure in Blebbing Cells." *Nature* 435, no. 7040 (2005): 365-9.

20.310J / 3.053J / 6.024J / 2.797J Molecular, Cellular, and Tissue Biomechanics
Spring 2015