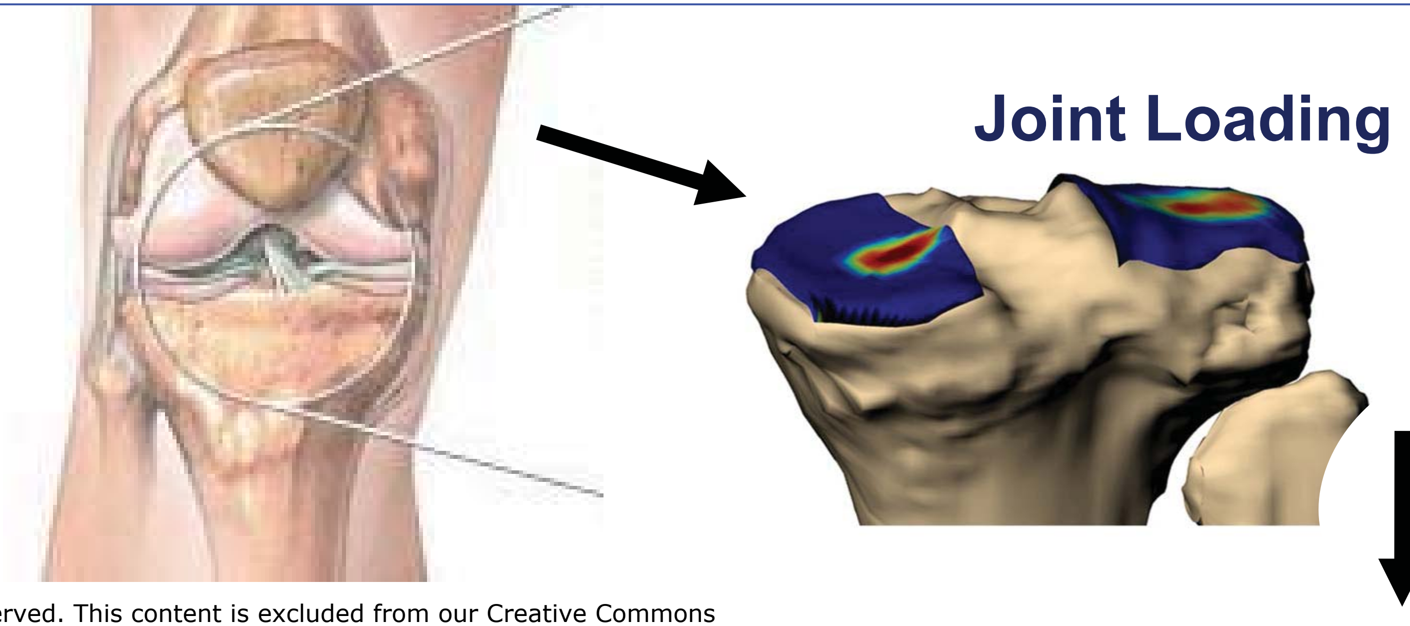
Mechanics↔Biology: Organ, Tissue, Cell, & Molecular Levels

Joint

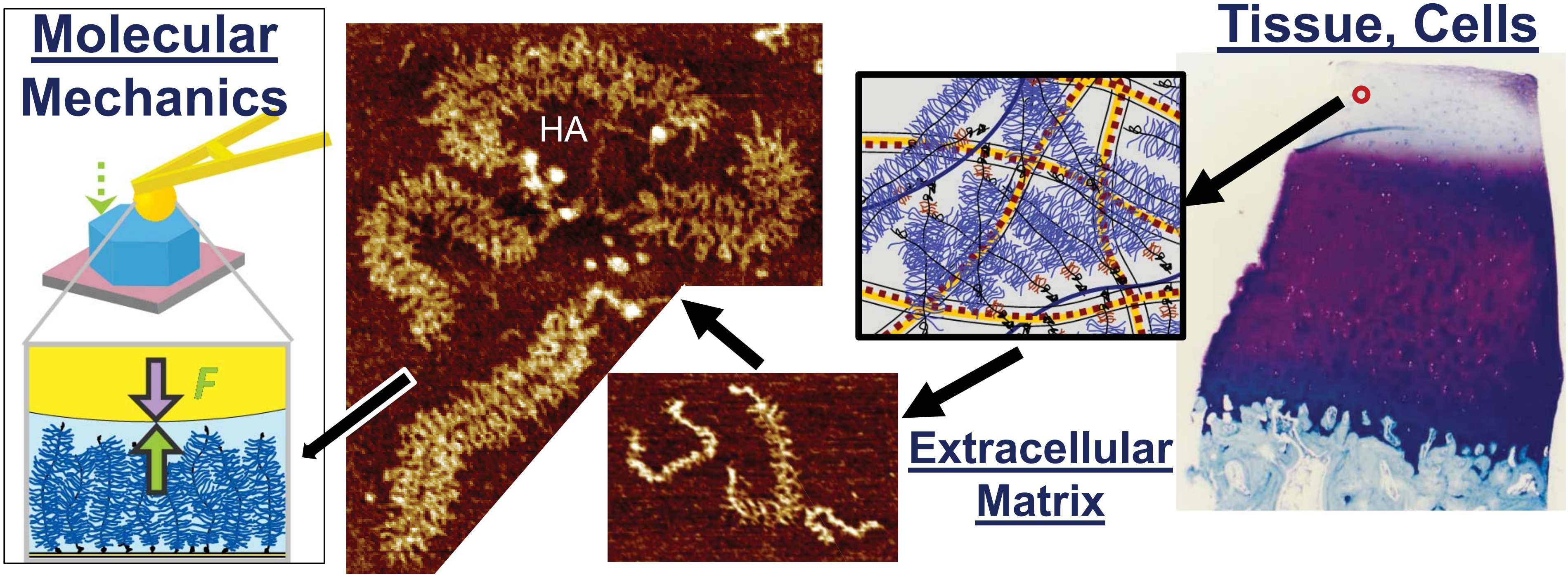
(organ)



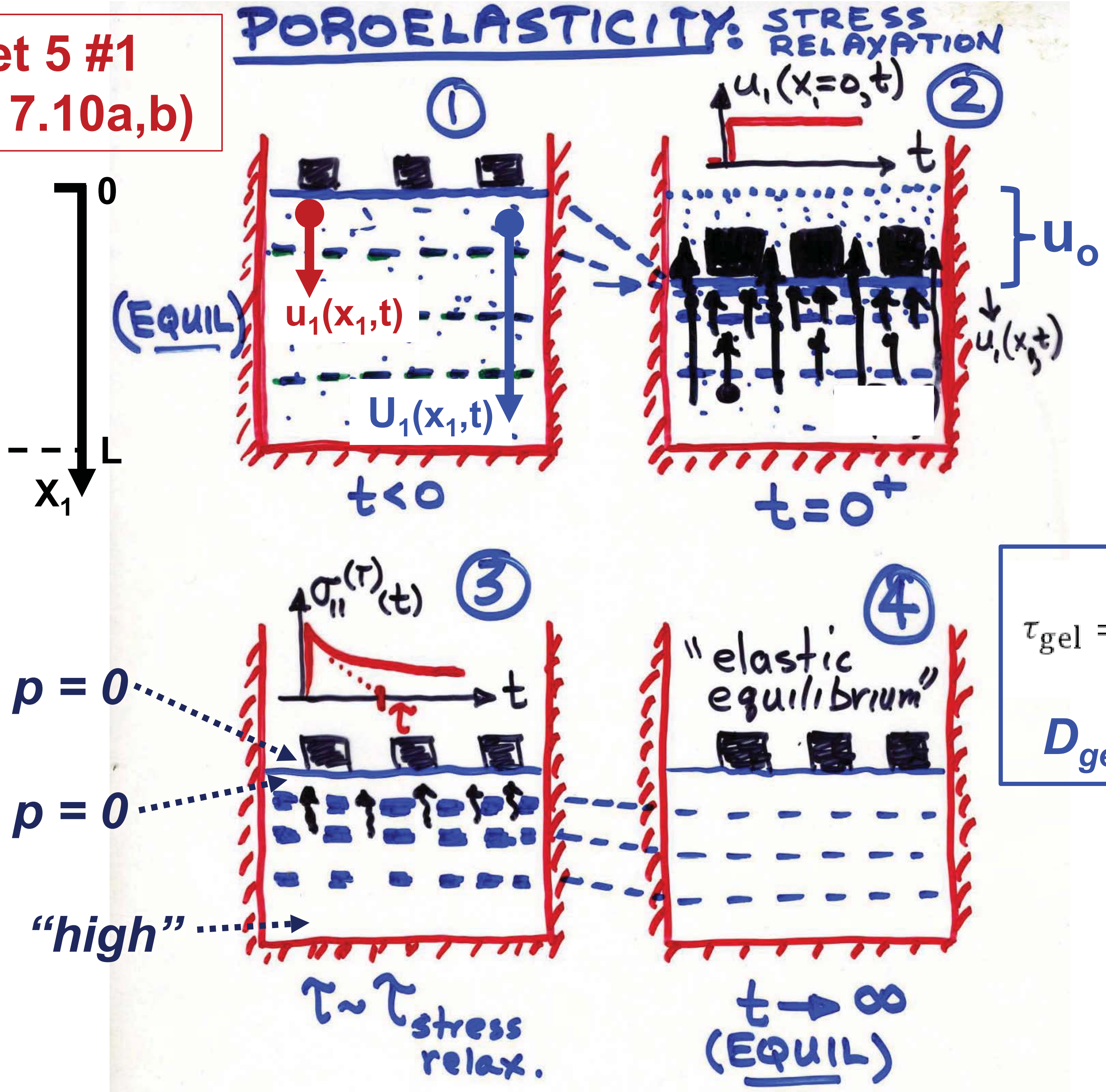
Molecular Mechanics

Tissue, Cells

Extracellular Matrix



PSet 5 #1
(Prob 7.10a,b)



p = 0

p = 0

p is "high"

$$\tau_{\text{gel}} = \frac{L^2}{\pi^2 D_{\text{gel}}}$$

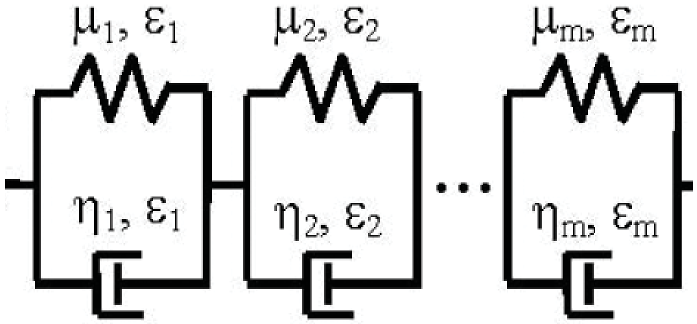
$$D_{gel} = H \cdot k$$

Questions:

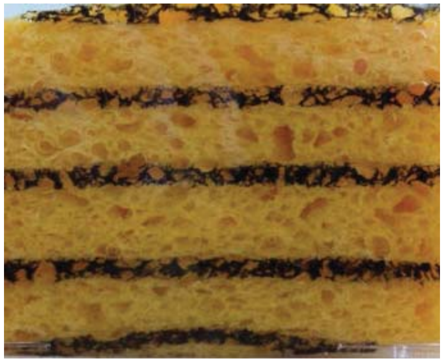
- What distinguishes solid-phase viscoelasticity..

$$\boxed{T + \alpha \frac{dT}{dt} = E_1 e + \beta \frac{de}{dt}}$$

Time Only…..



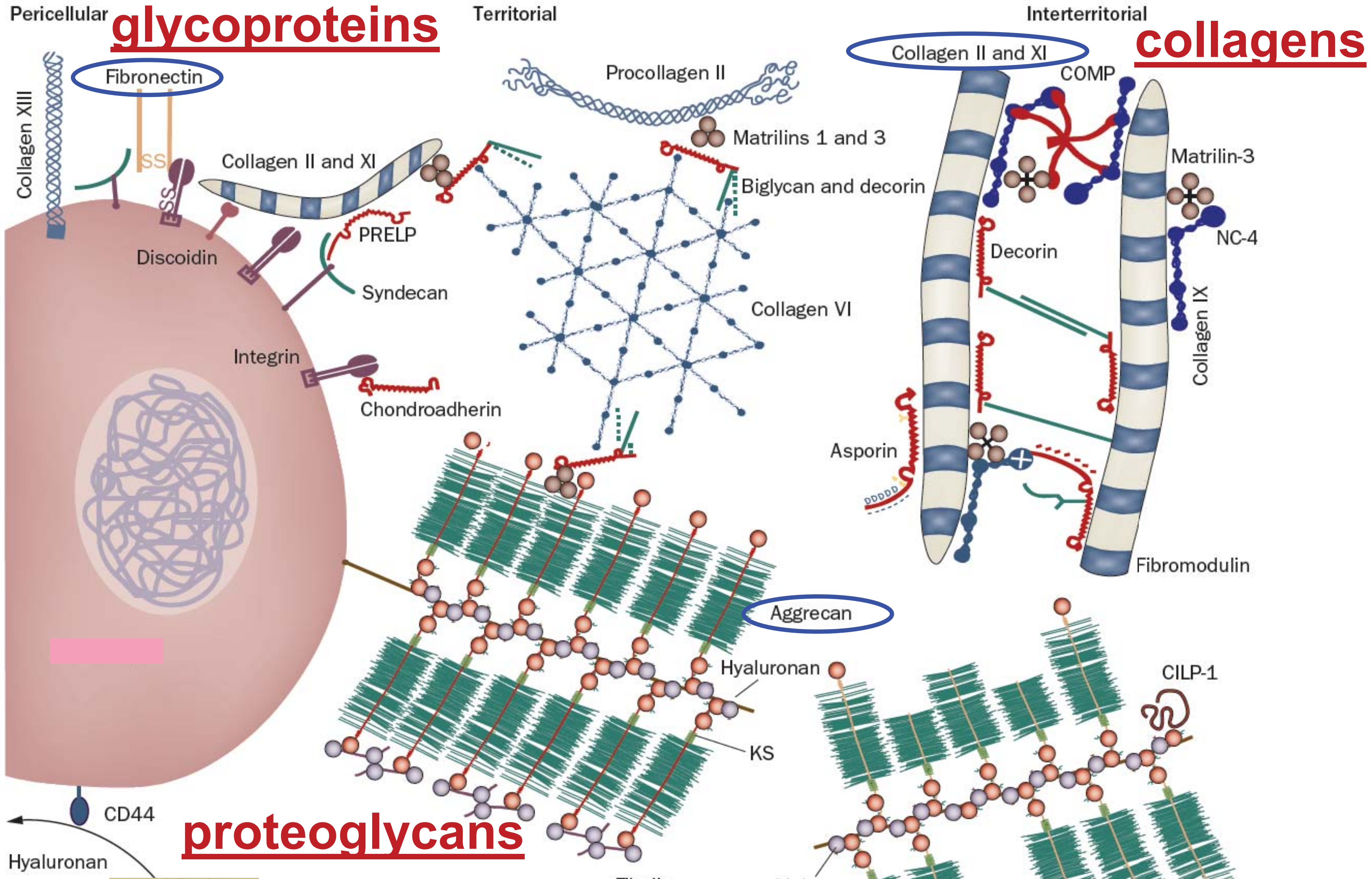
….from poroelasticity?



Space and Time

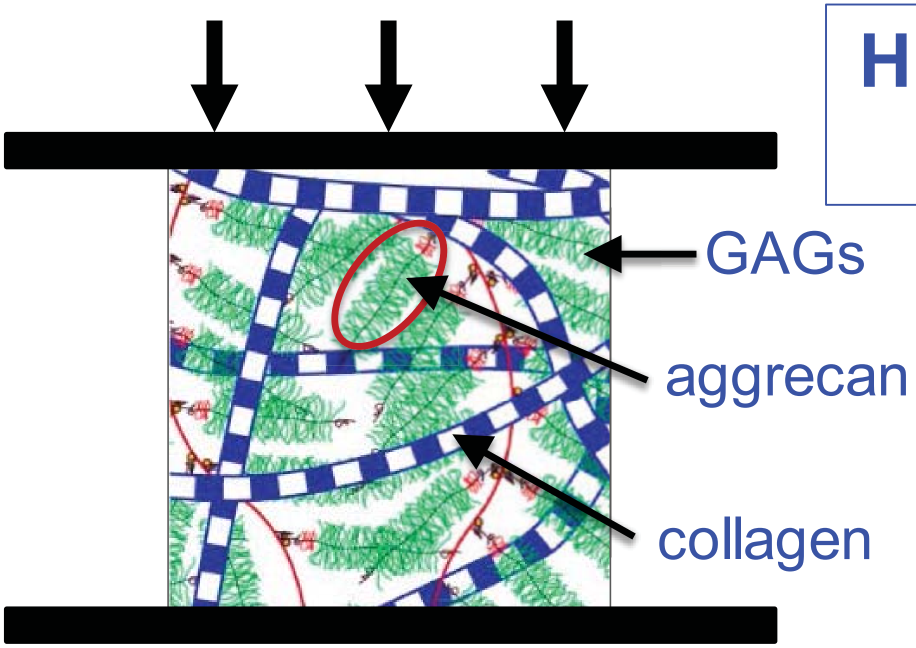
- Does poroelasticity operate at cellular and molecular scales as well as tissue scale??

Cells Synthesize 100s of Extracellular Matrix Macromolecules



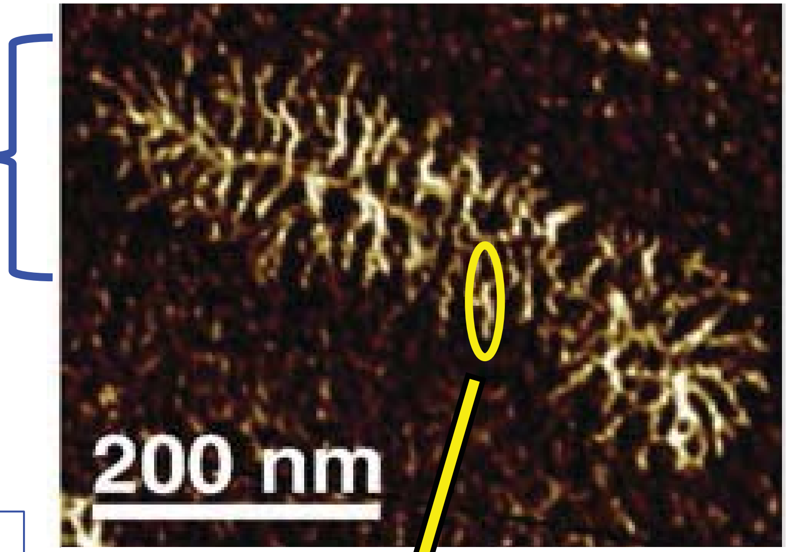
(Dick Heinegård, Nature Revs. Rheumatology 2010)

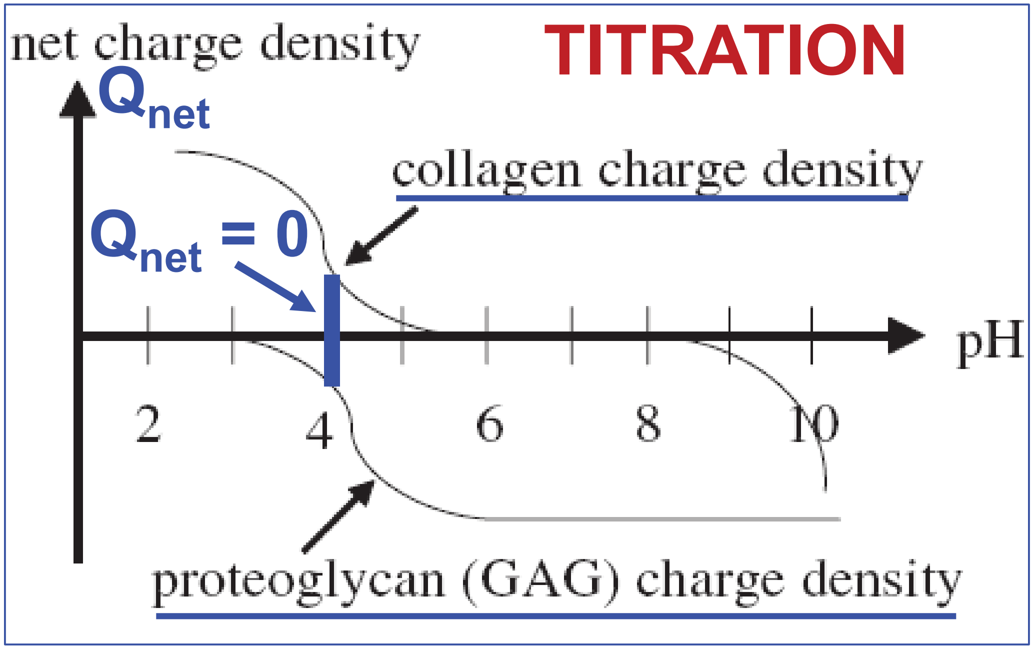
Source: Heinegård, Dick, and Tore Saxne. "The Role of the Cartilage Matrix in Osteoarthritis." *Nature Reviews Rheumatology* 7, no. 1 (2011): 50-56.

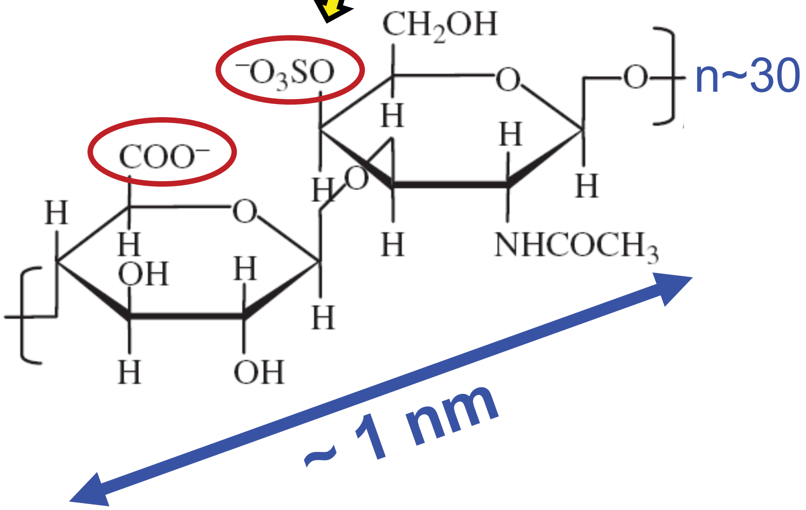


H,k = f(pH, Ionic strength)

[PSet 4, Prob 1]







The Amino-acid Composition and Titration Curve of Collagen

Biochem J

By JOANE H. BOWES and R. H. KENTEN
The British Leather Manufacturers' Research Association, London, S.E. 1

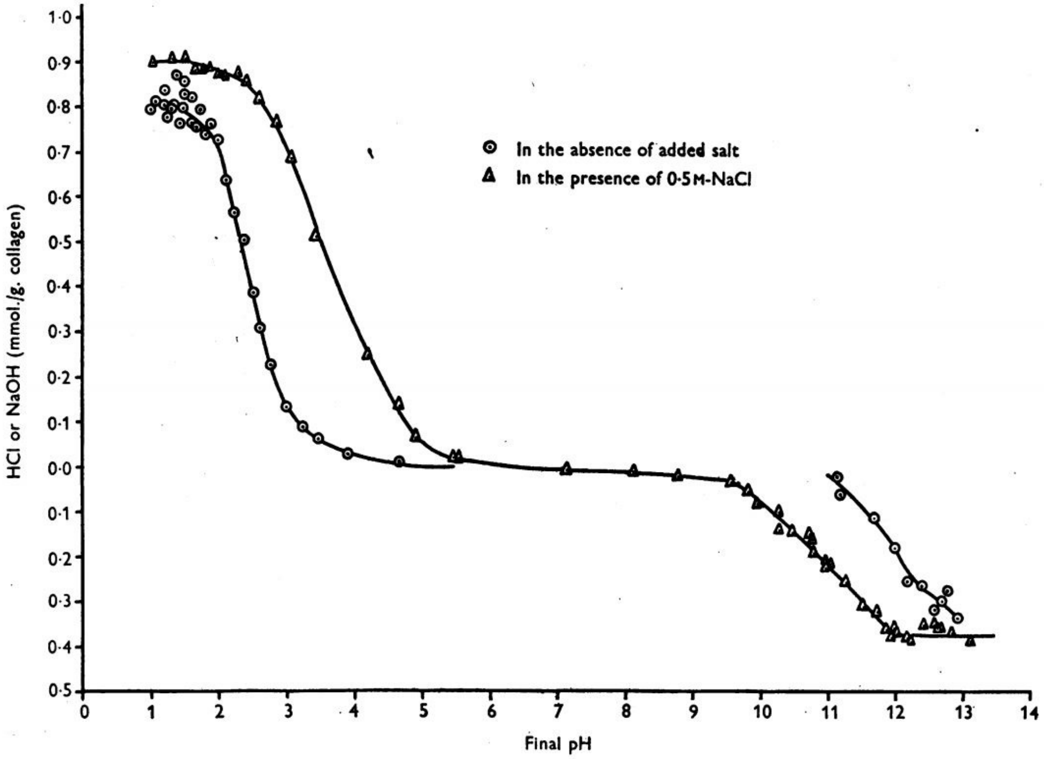
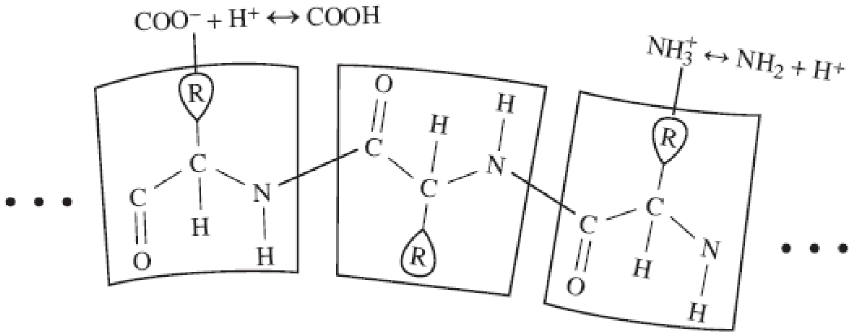
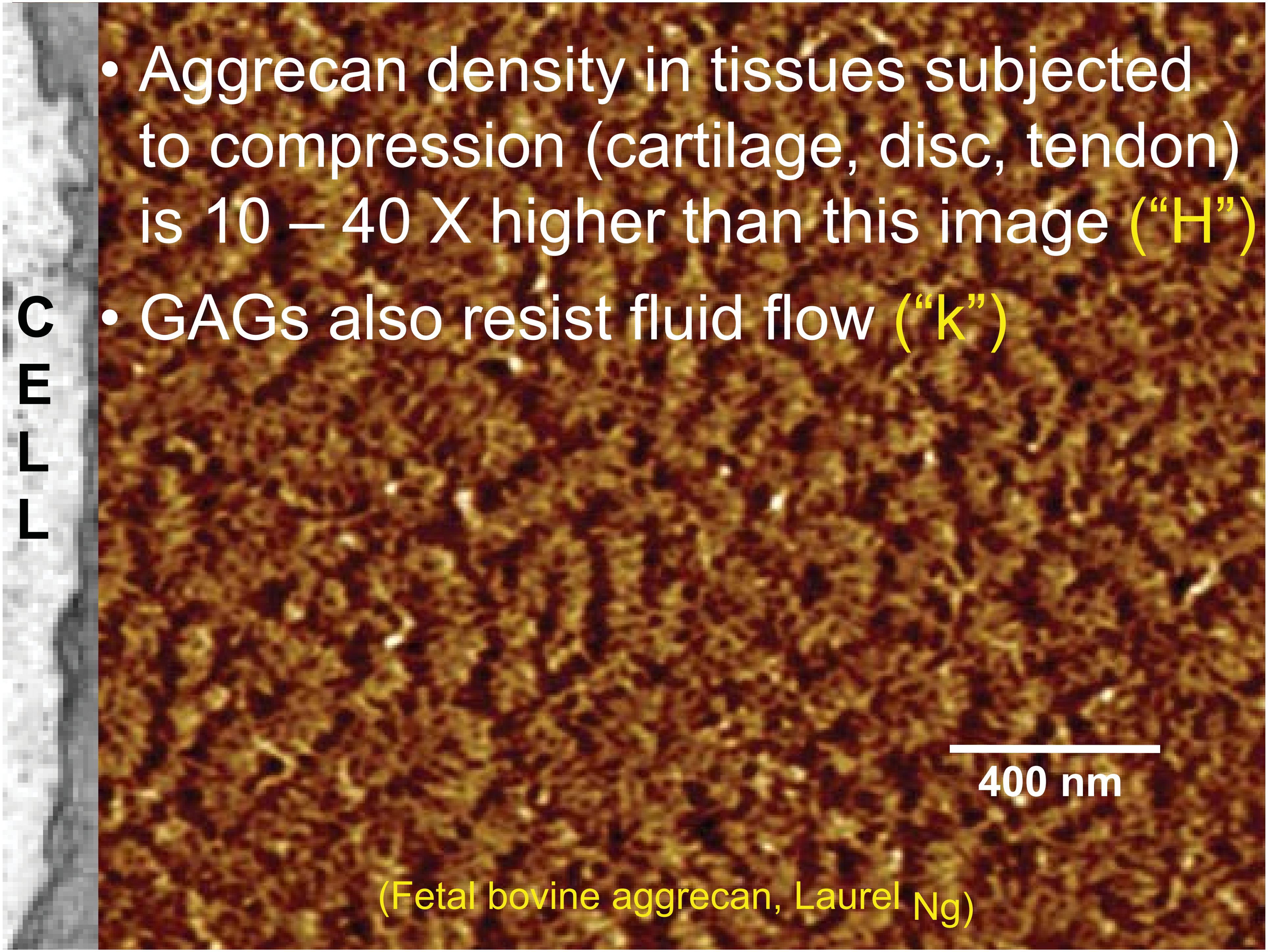


Fig. 2. Titration curves of collagen with and without sodium chloride.

Source: Bowes, Joane H., and R. H. Kenten. "The Amino-acid Composition and Titration Curve of Collagen." *%LRFKHPLFDO -RXUQDO* 43, no. 3 (1948): 358.



- Aggrecan density in tissues subjected to compression (cartilage, disc, tendon) is 10 – 40 X higher than this image ("H")
- GAGs also resist fluid flow ("k")

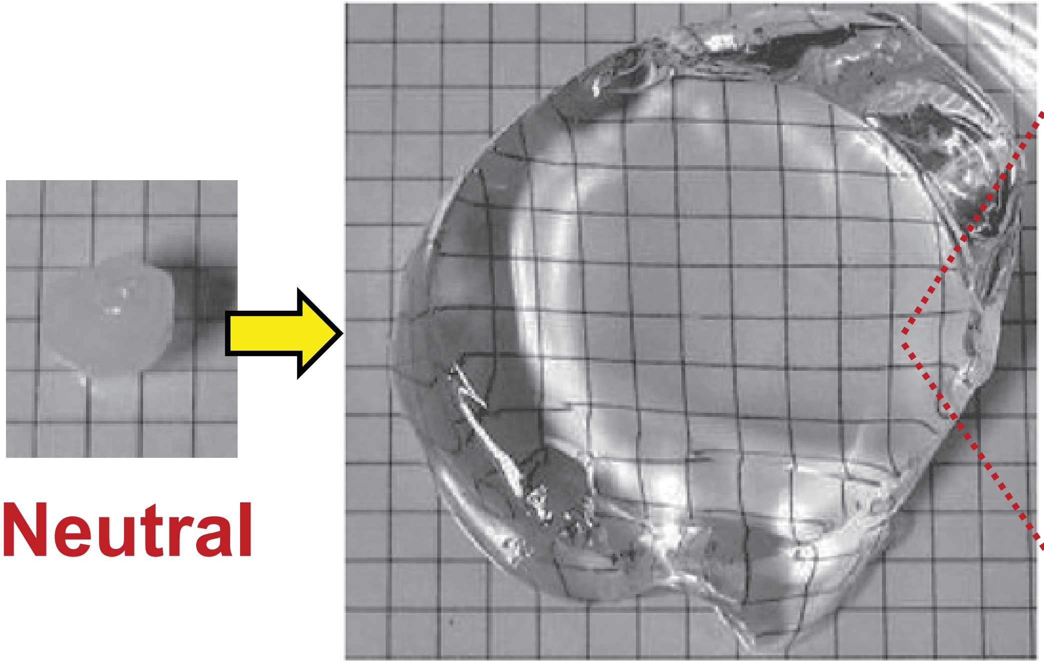


(Fetal bovine aggrecan, Laurel Ng)

Courtesy Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Ng, Laurel, et al. "Individual Cartilage Aggrecan Macromolecules and their Constituent Glycosaminoglycans Visualized via Atomic Force Microscopy." *Journal of Structural Biology* 143 (2003): 242-57.

Swelling (“H”) & Fluid Flow (“k”) in "Bio-Porous Media”: Molecular Networks & Gels

Polyelectrolyte Gels Swell: Electrostatic Forces **(“H”)**

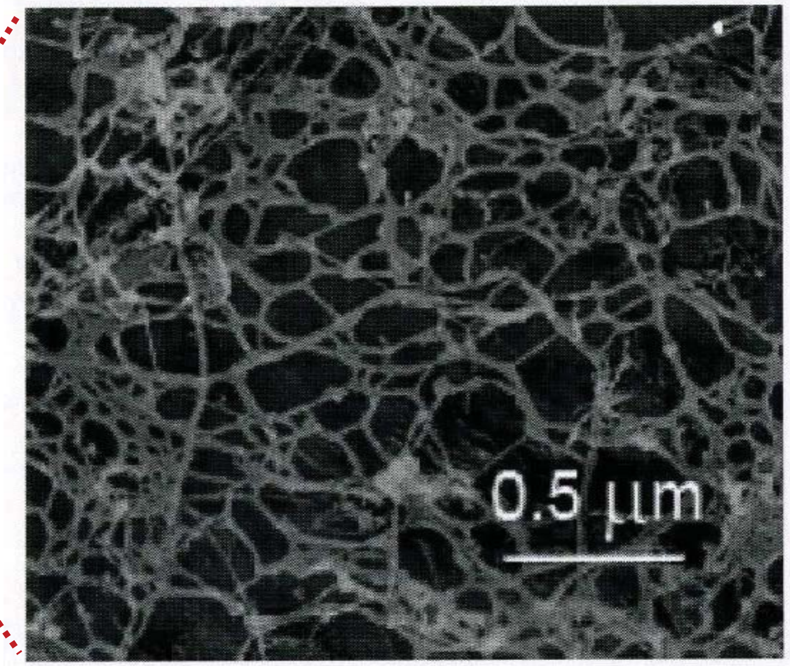


Neutral

Charged

Courtesy of Macmillan Publishers Limited. Used with permission.
Source: Ono, Toshikazu, et al. "Lipophilic Polyelectrolyte Gels as Super-absorbent Polymers for Nonpolar Organic Solvents." *Nature Materials* 6, no. 6 (2007): 429-33.

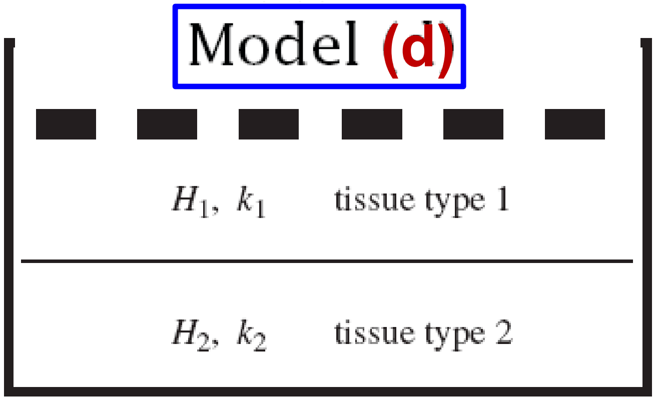
Network resists fluid flow (“k”)



Problem 7.11 and Figure 7.34 removed due to copyright restrictions. See the problem in the textbook.
Source: Grodzinsky, Alan. *Field, Forces and Flows in Biological Systems*. Garland Science, 2011.

Problem 7.11 and Figure 7.34 removed due to copyright restrictions. See the problem in the textbook.
Source: Grodzinsky, Alan. *Field, Forces and Flows in Biological Systems*. Garland Science, 2011.

Two-Layer Poroelastic Model



Problem 7.11 and Figure 7.34 removed due to copyright restrictions. See the problem in the textbook.
Source: Grodzinsky, Alan. *Field, Forces and Flows in Biological Systems*. Garland Science, 2011.

PSet 5
Prob 3

Motivated by:
Malaviya
J Orthop Res, 2000

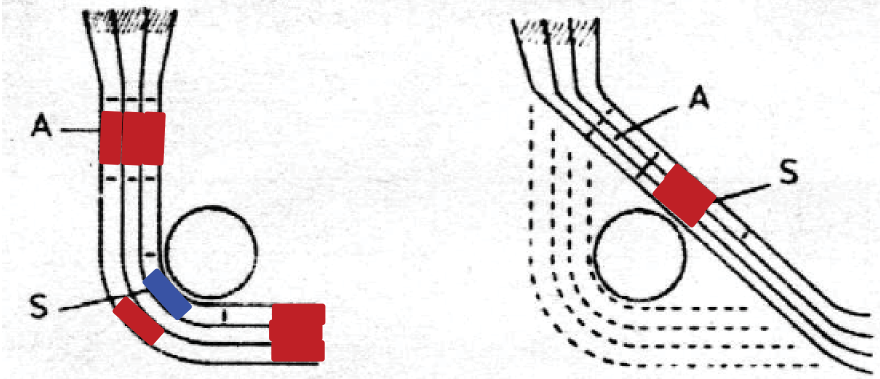
(Connective Tiss. Res, **1979**)

THE INFLUENCE OF MECHANICAL FORCES ON THE GLYCOSAMINOGLYCAN CONTENT OF THE RABBIT FLEXOR DIGITORUM PROFUNDUS TENDON

GERALD C. GILLARD, HELEN C. REILLY, PAUL G. BELL-BOOTH
and MICHAEL H. FLINT

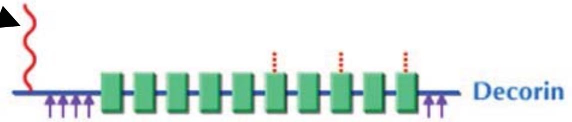
Department of Surgery, School of Medicine, University of Auckland,
Private Bag, Auckland 1, New Zealand

- The physical forces acting on the flexor digitorum profundus tendon of the rabbit were altered by anterior translocation of the tendon. The glycosaminoglycan (GAG) content was determined in regions of the tendon previously under tension or previously subjected to pressure.
- The original pressure bearing region showed a rapid loss of total GAG. This was mainly due to a loss of chondroitin sulfate component, and eventually the region showed a GAG composition similar to that of normal tension transmitting tendon. Replacement of the translocated tendon to its normal position resulted in a slow replacement of the GAG, particularly chondroitin sulfate
- → Later when tension was restored to the translocated tendon, the content of these two GAG decreased to normal values while the high overall GAG concentration was maintained by increased amounts of dermatan sulfate.



Chondroitin sulfate ≡ Aggrecan

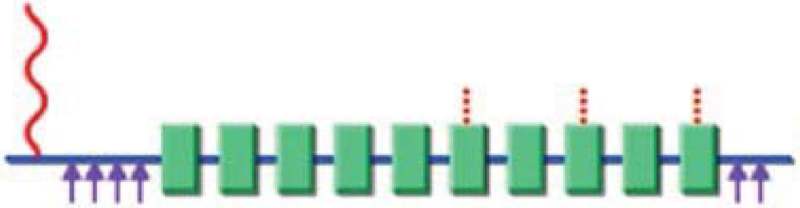
Dermatan sulfate ≡ decorin (“SLRPs”)



Source: Gillard, Gerald C., et al. "The Influence of Mechanical Forces on the Glycosaminoglycan Content of the Rabbit Flexor Digitorum Profundus Tendon." *Connective Tissue Research* 7, no. 1 (1979): 37-46.

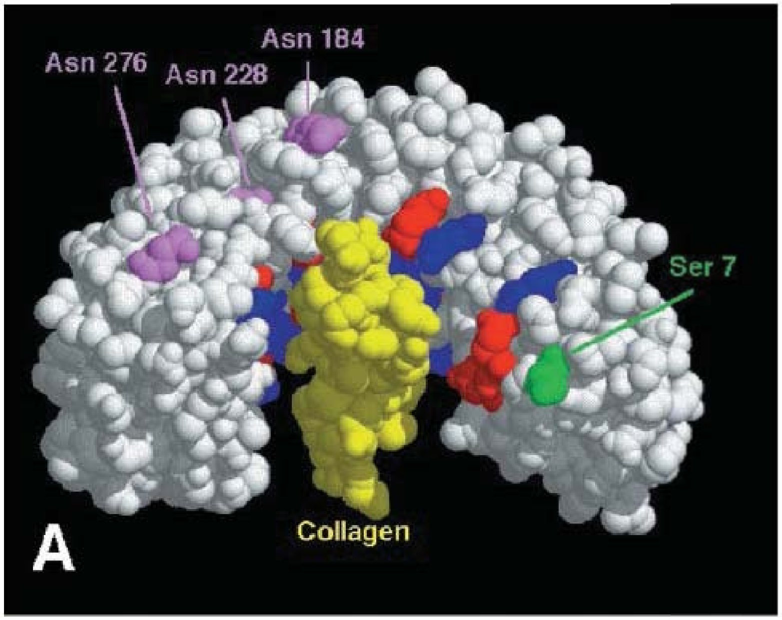
PROTEOGLYCAN SUPERFAMILY

- **ECM molecules with (1) Core protein, and (2) Glycosaminoglycan (GAG) chains**
- **“Sub-families” of extracellular PGs:**
  - Large Aggregating (Aggrecan)
  - Small Leucine-Rich PG (SLRPs)

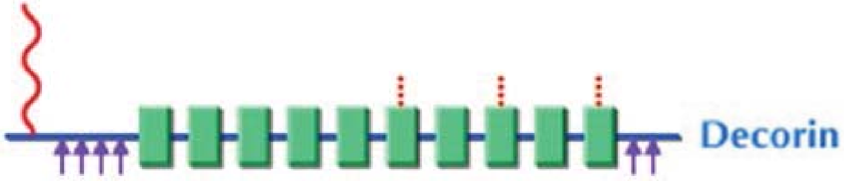


(Decorin)

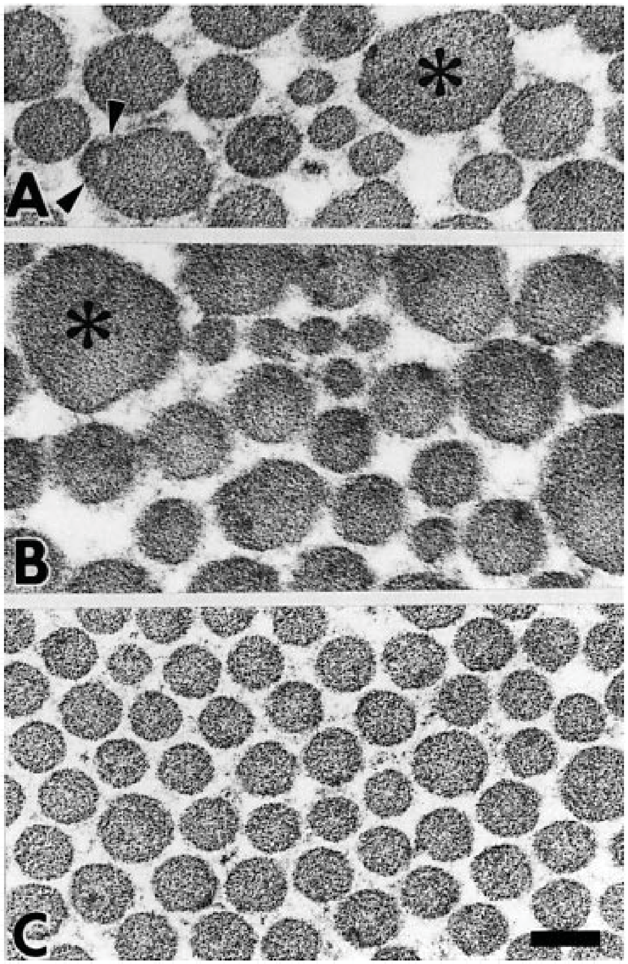
Decorin & Tendon Collagen Fibrillogenesis



Source: Iozzo, Renato V. "The Biology of the Small Leucine-rich Proteoglycans Functional Network of Interactive Proteins." -RXUQDO RI %LRORJLFDO &KHPLVWU\ 274, no. 27 (1999): 18843-6.



Example of Small-Leucine-Rich Proteoglycans



SKIN
decorin
KO

decorin
KO

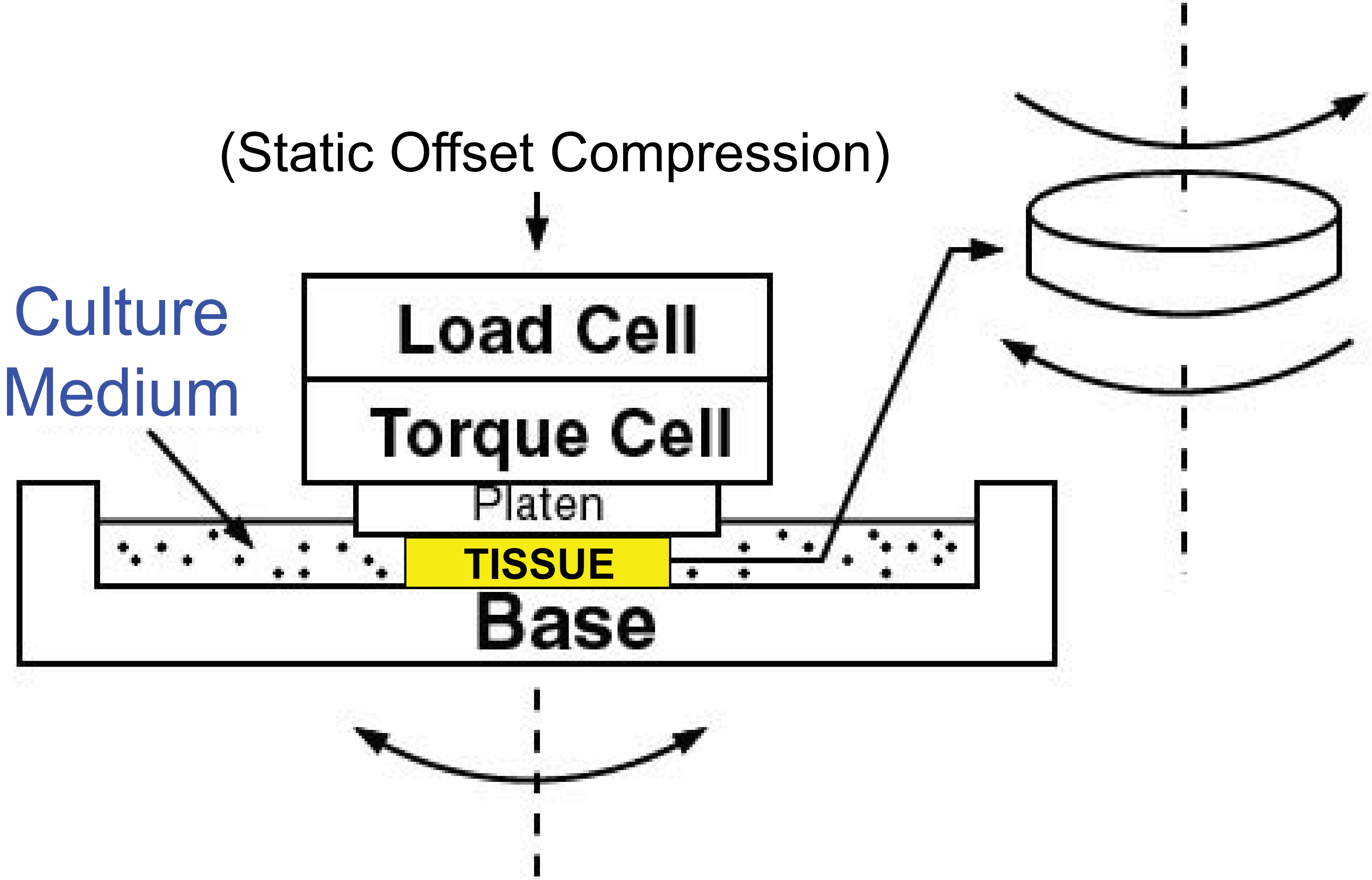
Normal
(WT)

Figure 4 Ultrastructural appearance of dermal collagen from the skin of decorin null (*A* and *B*) and wild-type (*C*) mice. Notice the larger and irregular cross-sectional profiles in the decorin null collagen fibers (*asterisks*) with evidence of lateral fusion (*A*, *arrowheads*). Bar: 90 nm.

Source: Iozzo, Renato V. "Matrix Proteoglycans: From Molecular Design to Cellular Function." $QQXDO 5HYLHZ RI %LRFKHPLVWU\ 67, no. 1 (1998): 609-52.

(Iozzo +, Normal and decorin null mice, J Biol Chem 1999)

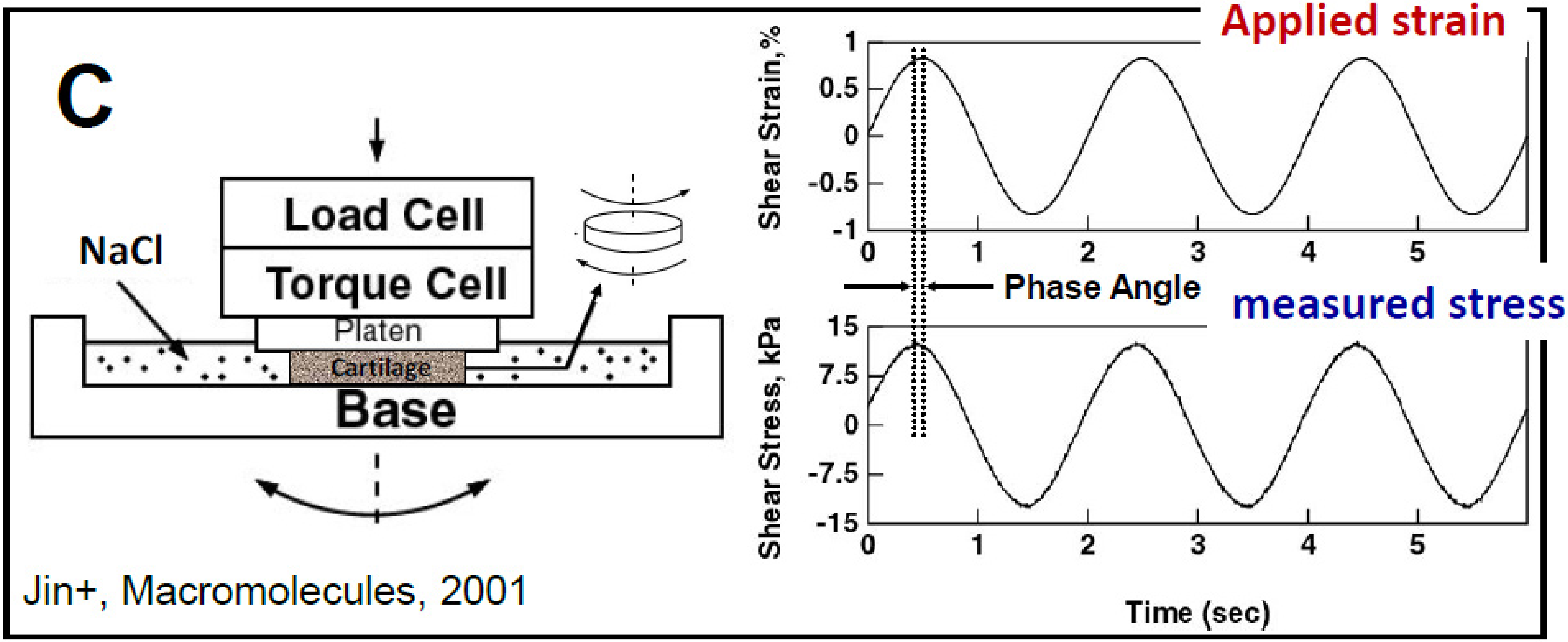
Dynamic Torsional Shear



Source: Jin, Moonsoo, and Alan J. Grodzinsky. "Effect of Electrostatic Interactions between Glycosaminoglycans on the Shear Stiffness of Cartilage: A Molecular Model and Experiments." *Macromolecules* 34, no. 23 (2001): 8330-39.

“Dynamic Torsional Shear”

Apply sinusoidal shear strain (0.8% amplitude at 0.5 Hz) and measure sinusoidal stress amplitude & phase

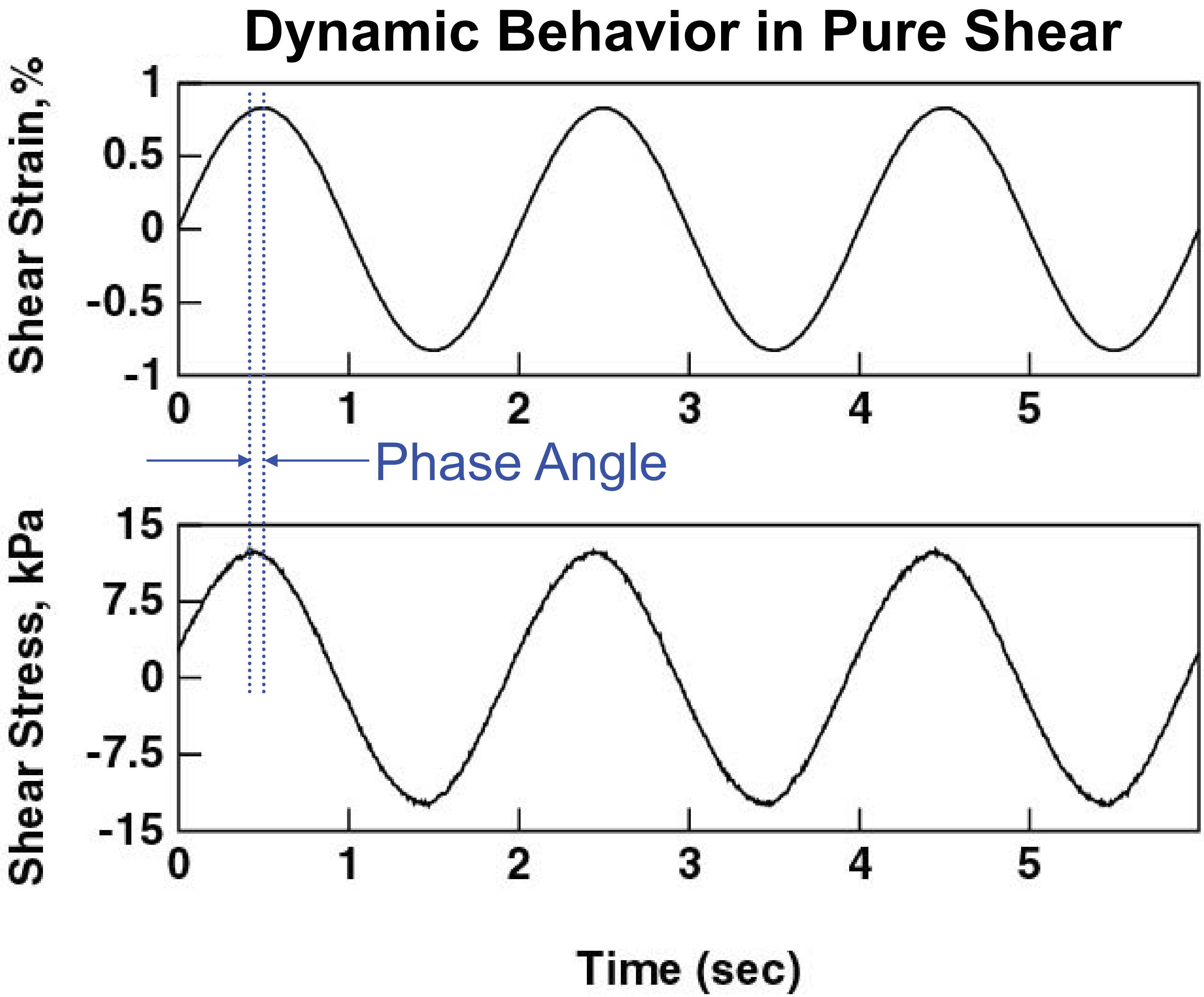


Jin+, Macromolecules, 2001

Source: Jin, Moonsoo, and Alan J. Grodzinsky. "Effect of Electrostatic Interactions between Glycosaminoglycans on the Shear Stiffness of Cartilage: A Molecular Model and Experiments." *Macromolecules* 34, no. 23 (2001): 8330-39.

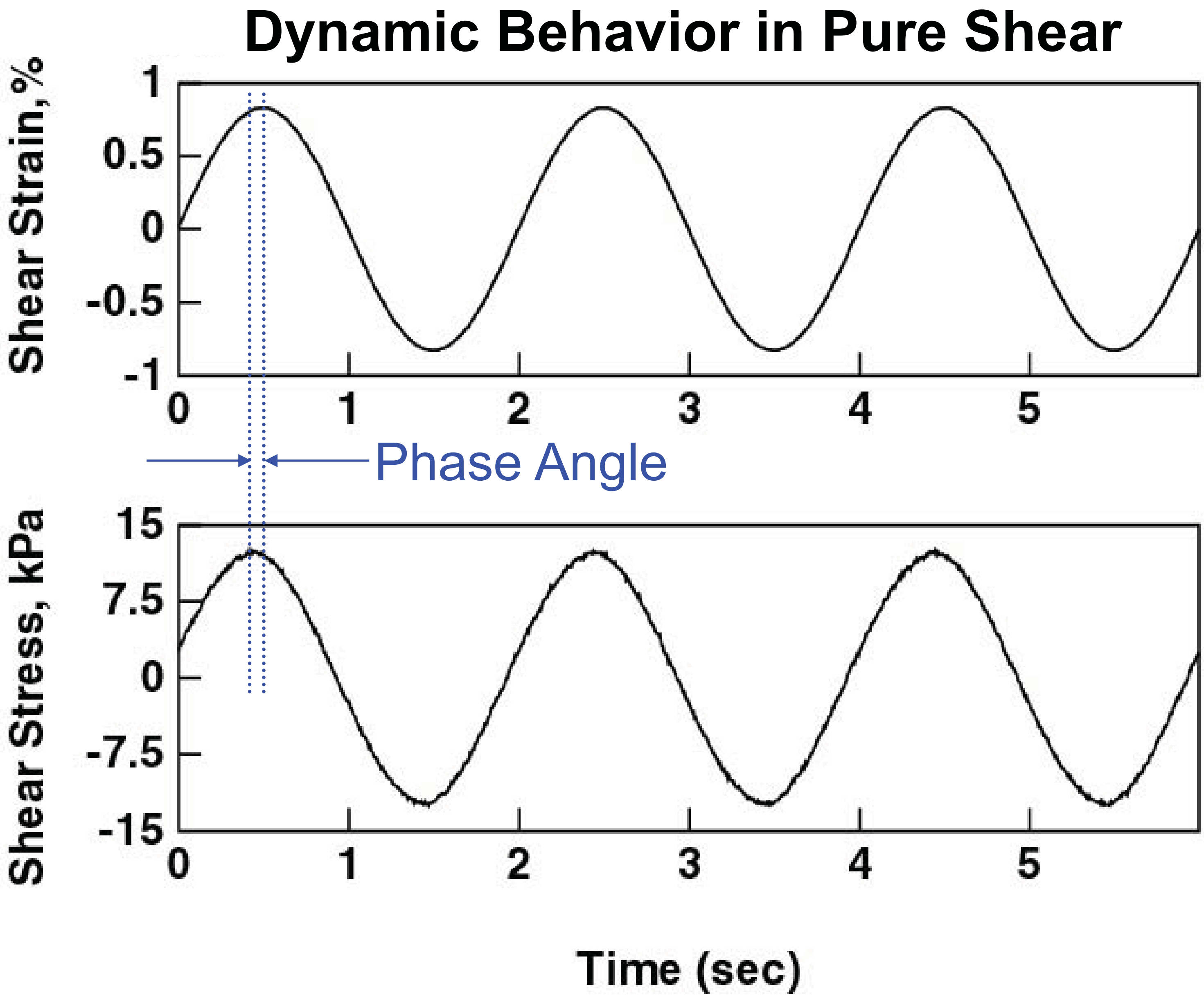
Is Phase Delay due to
Viscoelastic -OR- Poroelastic behavior?

Non-zero phase angle → Viscoelastic? Poroelastic? both??



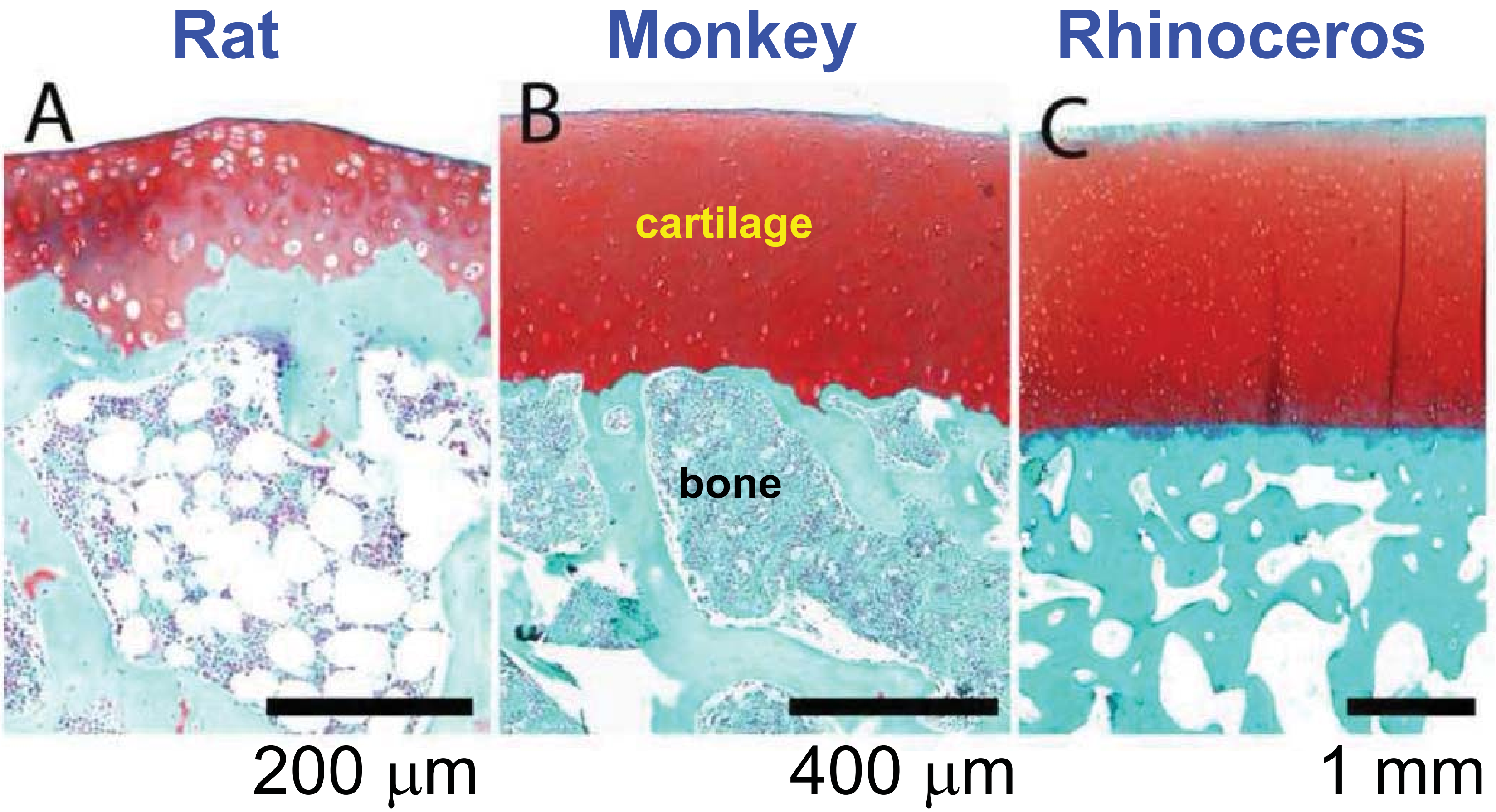
Source: Jin, Moonsoo, and Alan J. Grodzinsky. "Effect of Electrostatic Interactions between Glycosaminoglycans on the Shear Stiffness of Cartilage: A Molecular Model and Experiments." *Macromolecules* 34, no. 23 (2001): 8330-39.

Non-zero phase angle → Isolates Viscoelasticity of ECM (or gel, or molecular network)!!!



Source: Jin, Moonsoo, and Alan J. Grodzinsky. "Effect of Electrostatic Interactions between Glycosaminoglycans on the Shear Stiffness of Cartilage: A Molecular Model and Experiments." *Macromolecules* 34, no. 23 (2001): 8330-39.

Compression

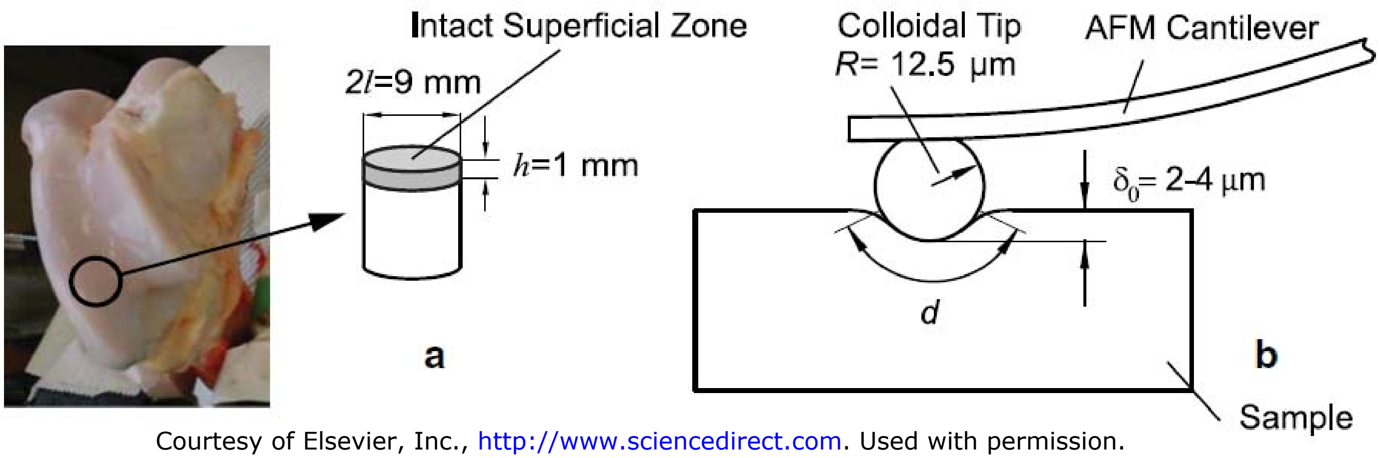


Courtesy of the authors. Used with permission.
Source: Malda, Jos, et al. "Of Mice, Men and Elephants: The Relation between Articular Cartilage Thickness and Body Mass." *30R6 RQH* 8, no. 2 (2013): e57683.

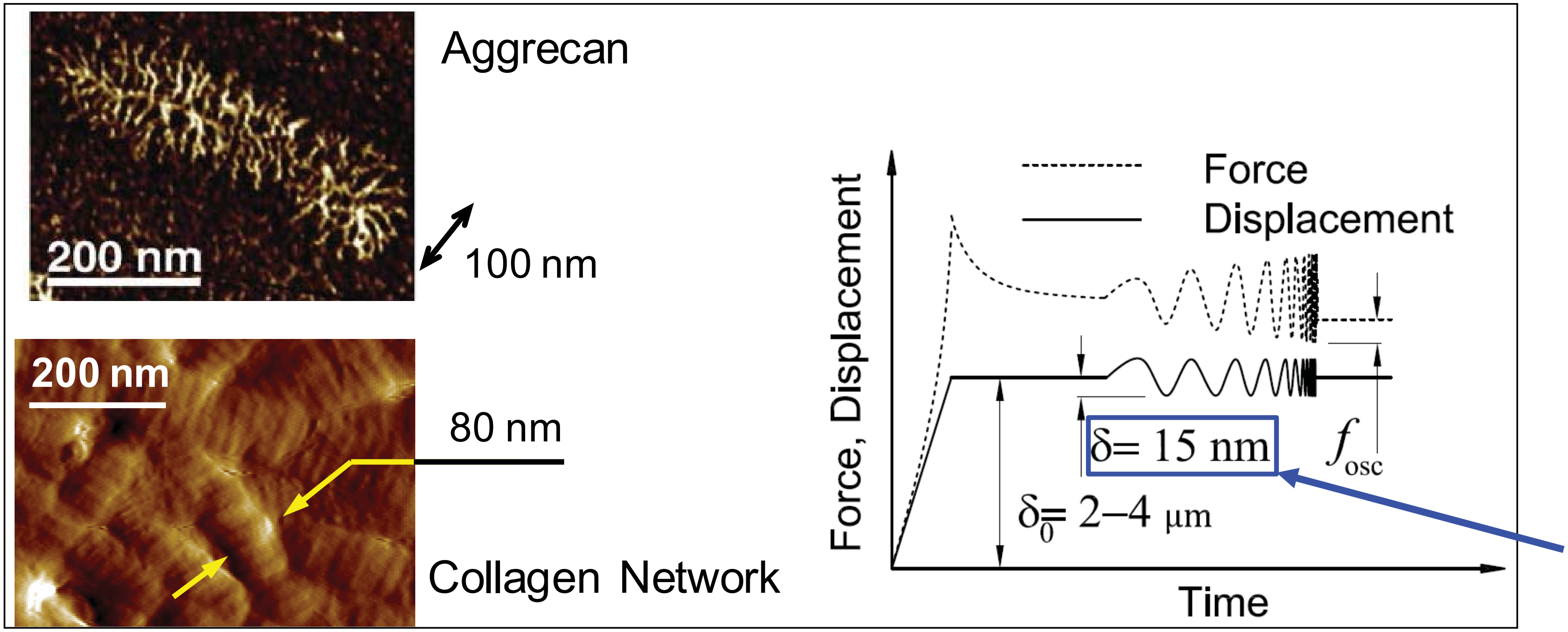
"Safranin-O" (red) stains Glycosaminoglycans (of Proteoglycans)

Tissue-Level Nanomechanics

Hadi Tavakoli Nia,
Biophysical J, 2011, 2013

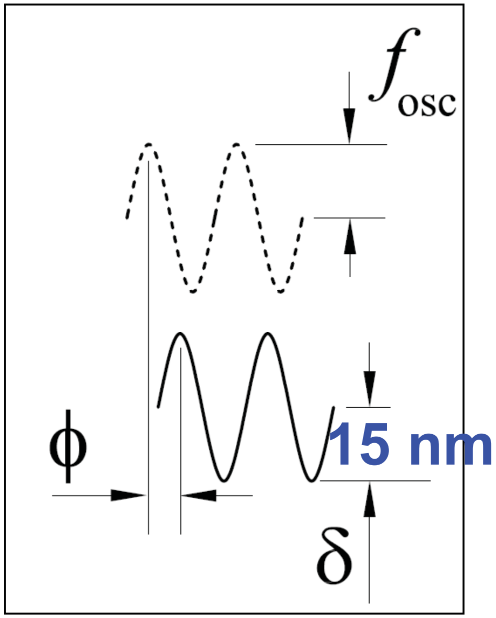


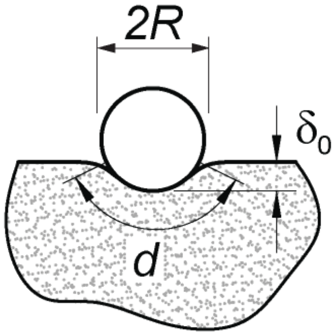
Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Nia, Hadi Tavakoli, et al. "Poroelasticity of Cartilage at the Nanoscale."
Biophysical Journal 101, no. 9 (2011): 2304-13.



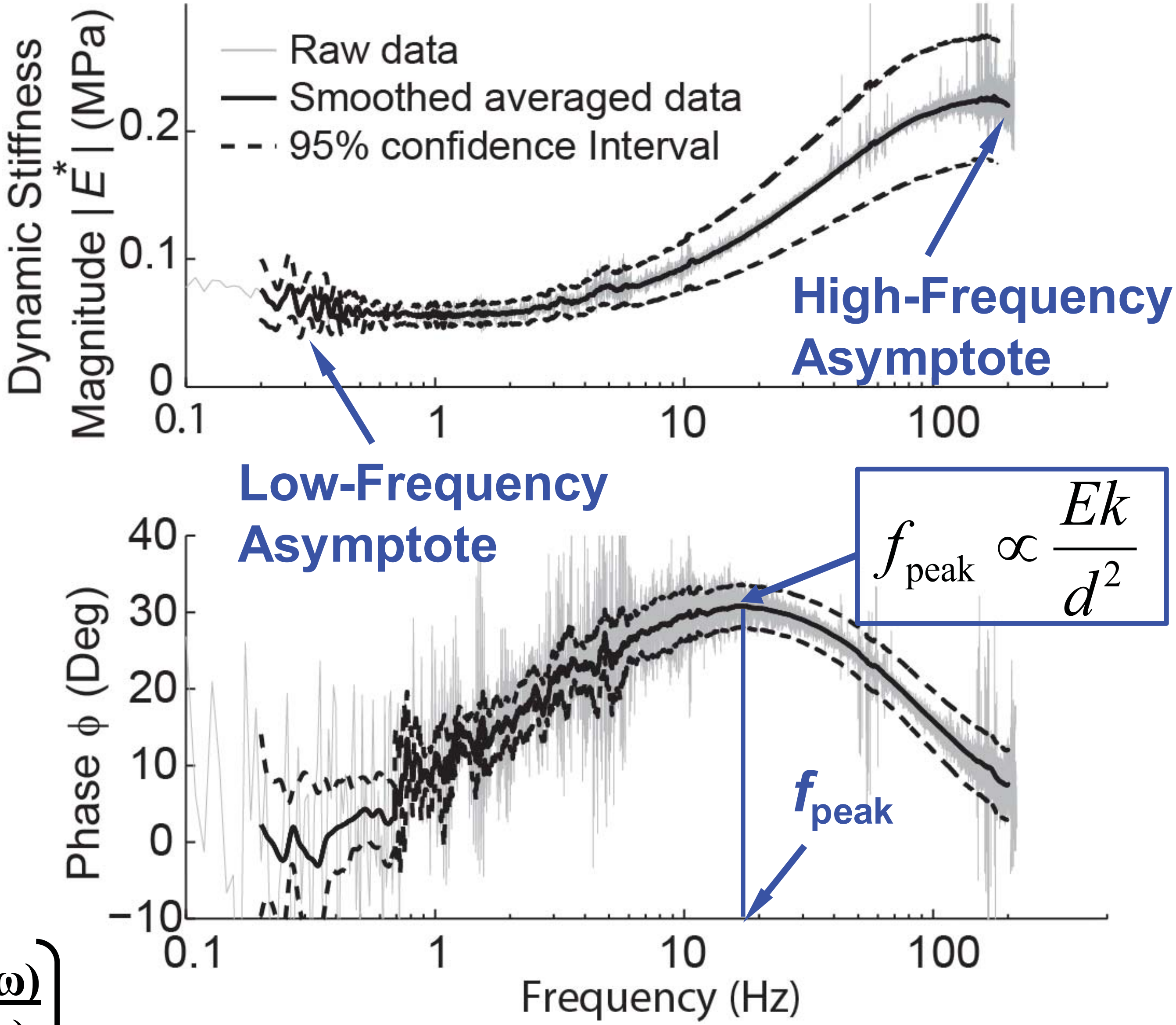
Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Nia, Hadi Tavakoli, et al. "High-bandwidth AFM-based Rheology Reveals that Cartilage is Most Sensitive to High Loading Rates at Early Stages of Impairment."
Biophysical Journal 104, no. 7 (2013): 1529-37.

Tissue-Level Nanomechanics: dominated by poroelasticity





$$\tan\phi = \left(\frac{E''(\omega)}{E'(\omega)}\right)$$



High-Frequency Asymptote

Low-Frequency Asymptote

$$f_{\text{peak}} \propto \frac{Ek}{d^2}$$

f_{peak}

Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Nia, Hadi Tavakoli, et al. "Poroelasticity of Cartilage at the Nanoscale." *Biophysical Journal* 101, no. 9 (2011): 2304-13.

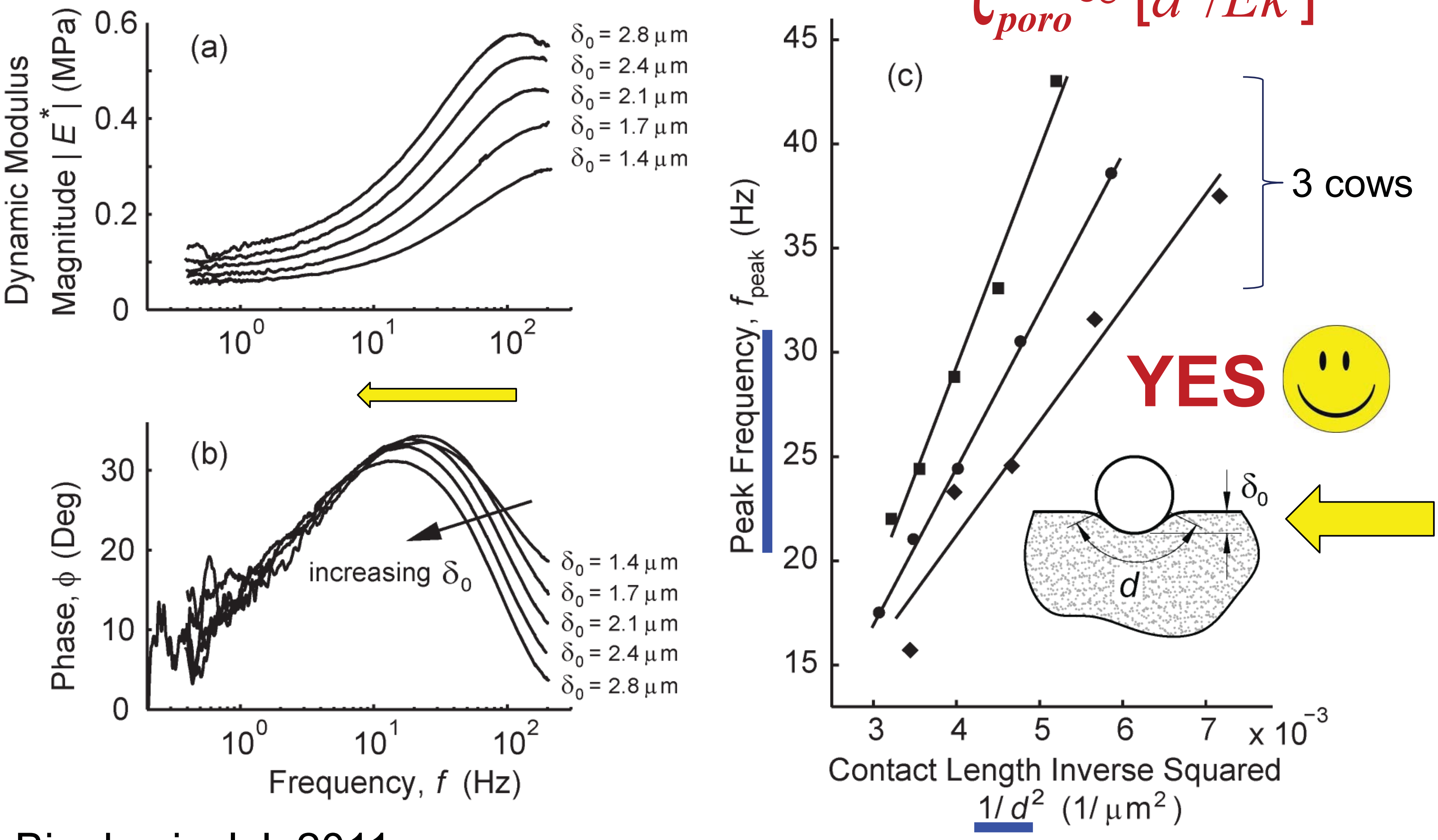
Problem removed due to copyright restrictions. See the problem in the textbook.
Source: Grodzinsky, Alan. *Field, Forces and Flows in Biological Systems*. Garland Science, 2011.

Is this tissue Poroelastic ??

Test f_{peak} vs. d^2

$$f_{\mathrm{peak}} \propto [Ek/d^2]$$

$$\tau_{poro} \propto [d^2/Ek]$$



Nia, Biophysical J, 2011

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Source: Nia, Hadi Tavakoli, et al. "Poroelasticity of Cartilage at the Nanoscale." *Biophysical Journal* 101, no. 9 (2011): 2304-13.

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