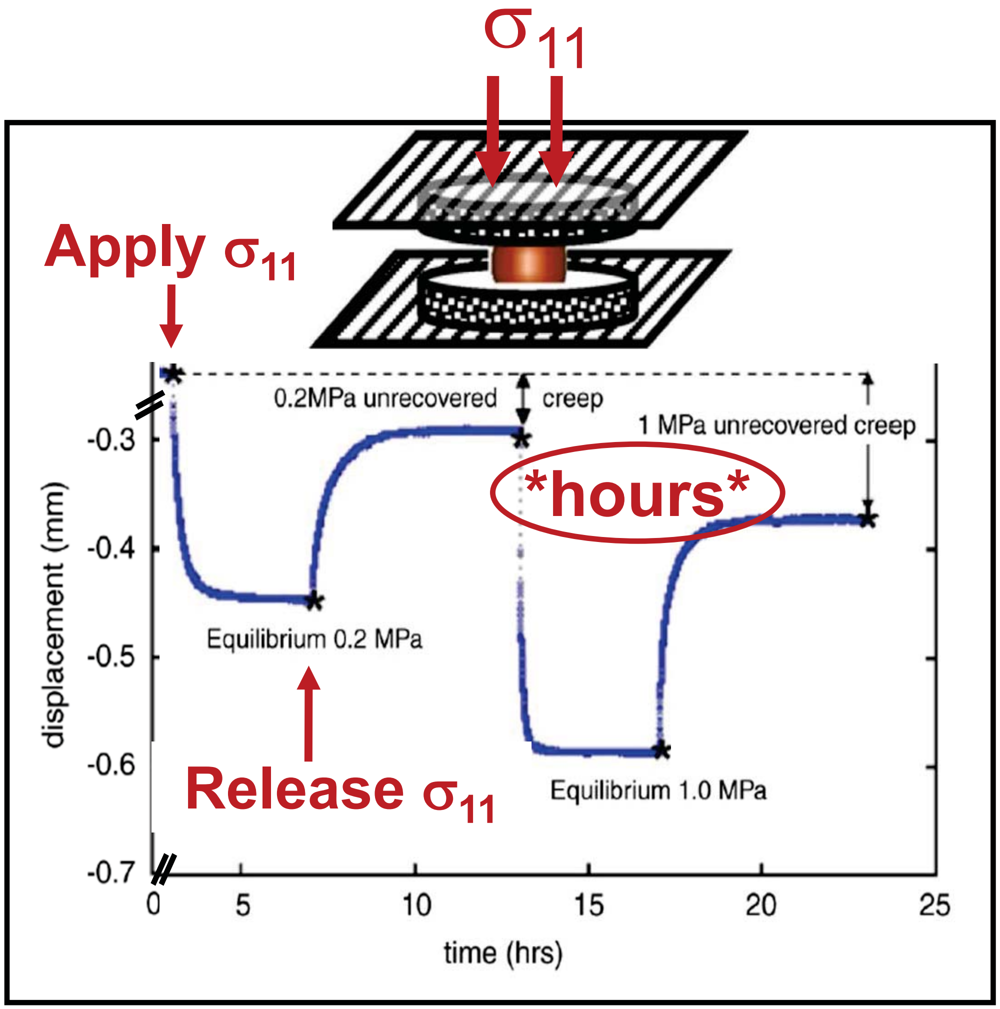
"Creep-Compression" of intervertebral disc (rat tail):

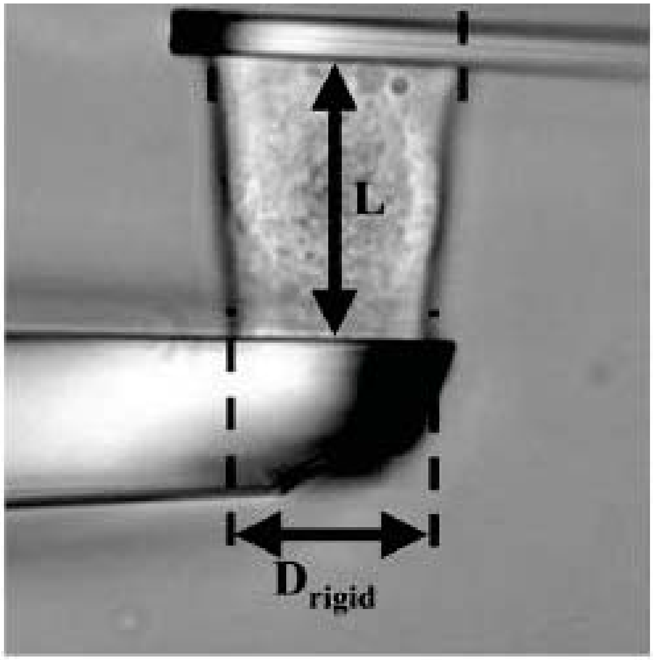
Apply step in stress (σ_{11}) and measure displacement (strain) vs time



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.

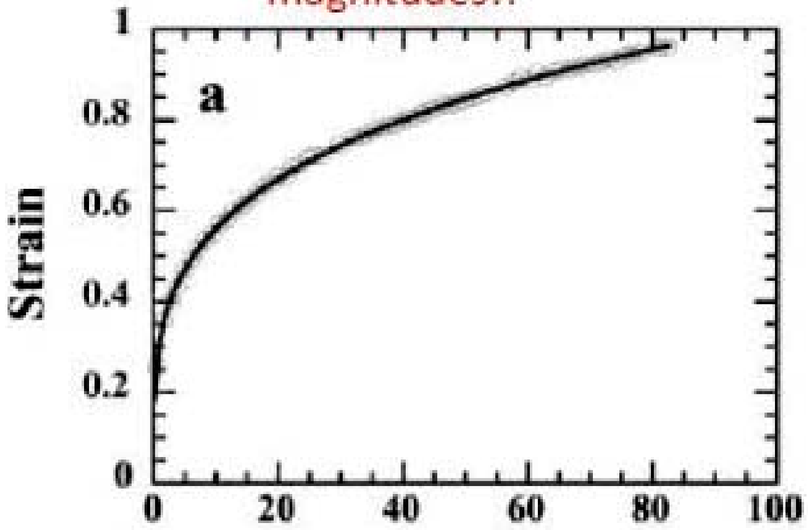
(MacLean+, J Biomechanics, 2007)

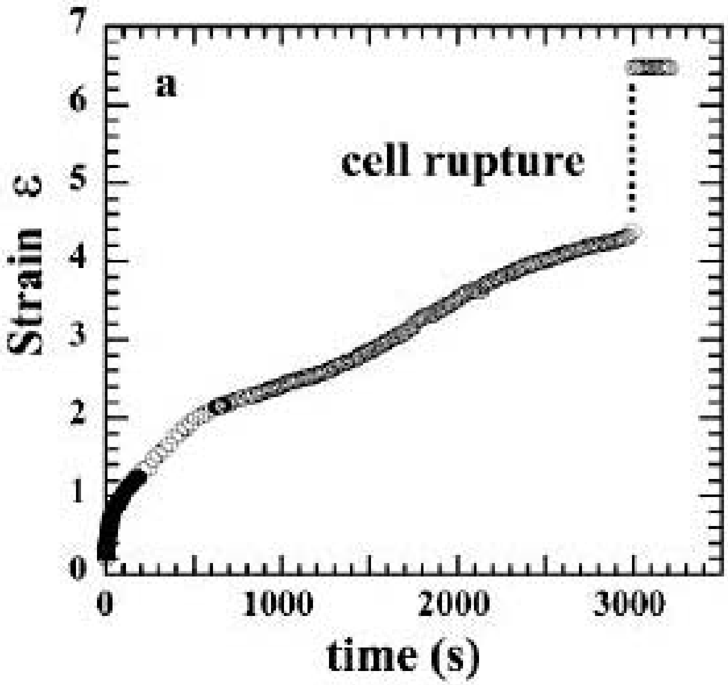
Cell stretching at constant force (creep)



Despratt et al., Biophys J., 2005

Note the strain magnitudes!!





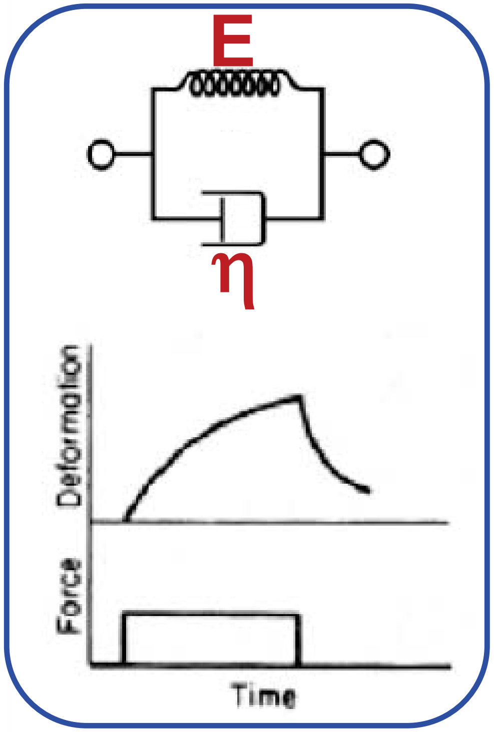
Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Desprat, Nicolas, et al. "Creep Function of a Single Living Cell." *Biophysical Journal* 88, no. 3 (2005): 2224-33.

Stress relaxation

Creep

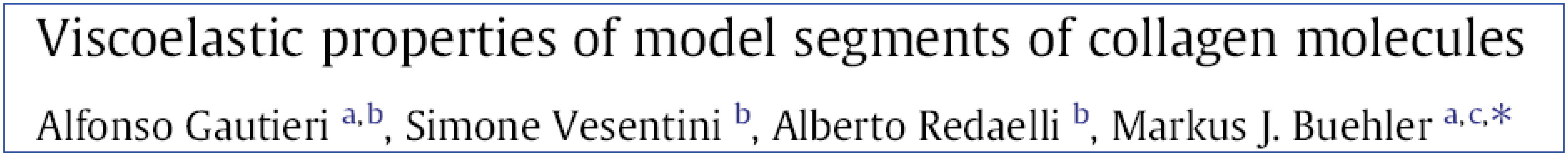
Model

Voigt Model



“Spring-Dashpot” models: first used by polymer physicists to model time-dependent viscoelastic behavior of rubber and synthetic solid polymer networks……more recently applied to biomechanics of tissues/cells

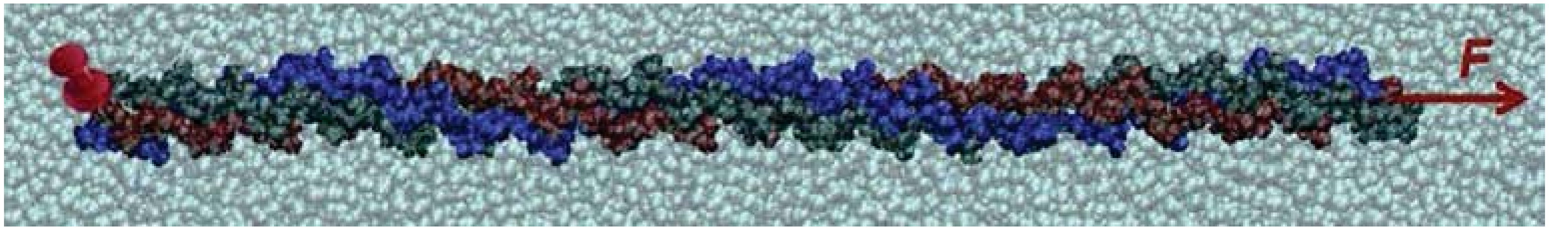
Matrix Biology, March 2012, 31:141-9



Viscoelastic properties of model segments of collagen molecules

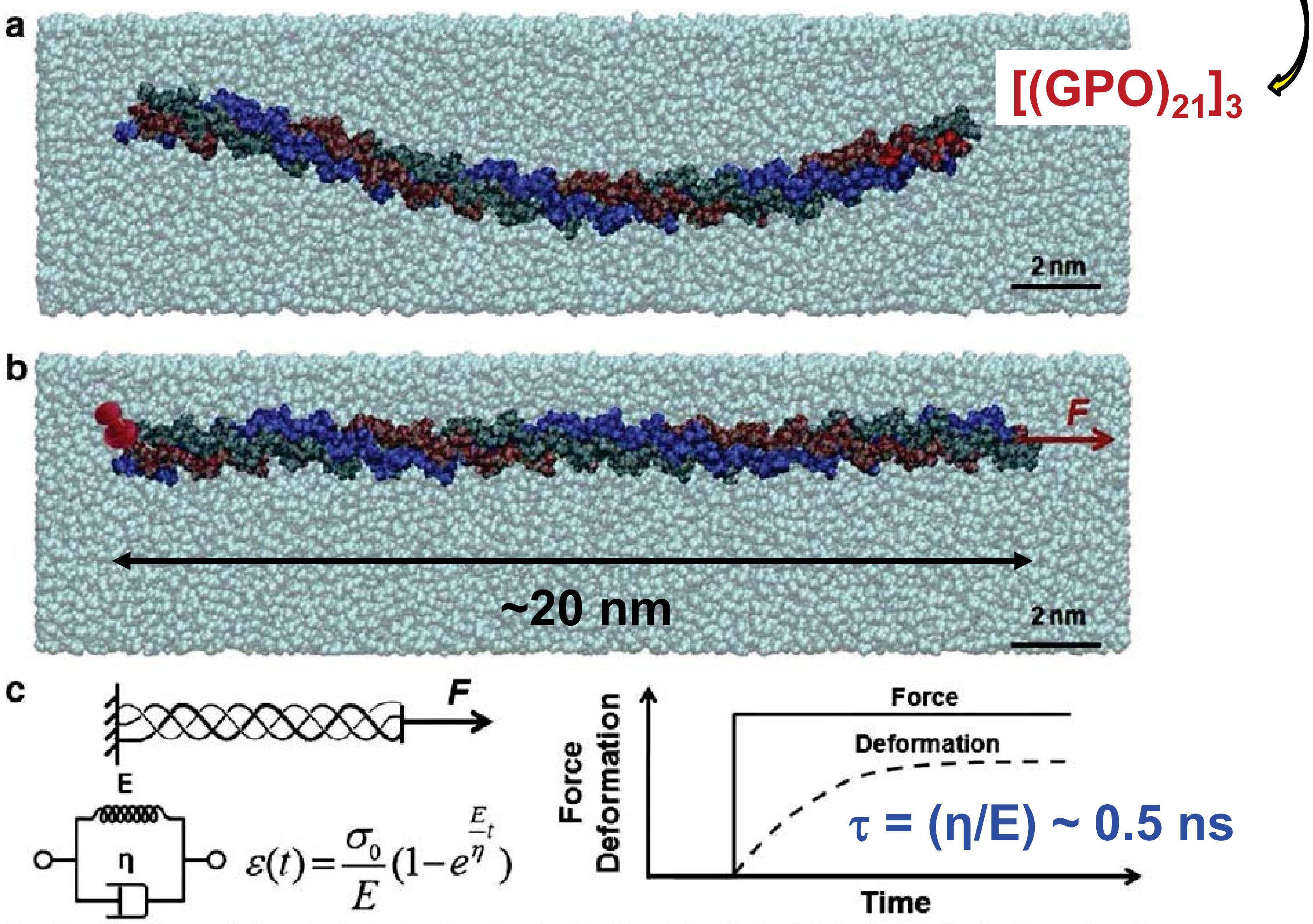
Alfonso Gautieri [a,b], Simone Vesentini [b], Alberto Redaelli [b], Markus J. Buehler [a,c,*]

- **Although extensive studies of viscoelastic properties have been pursued at the macroscopic (fiber/tissue) level, fewer investigations have been performed at the smaller scales, including collagen molecules and fibrils.**
- Here, using atomistic modeling, we perform **“in silico” creep tests** of a collagen-like peptide…..



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.

"In silico" creep test of a segment of a collagen molecule



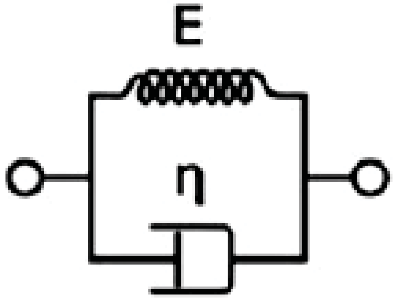
$[(GPO)_{21}]_3$

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

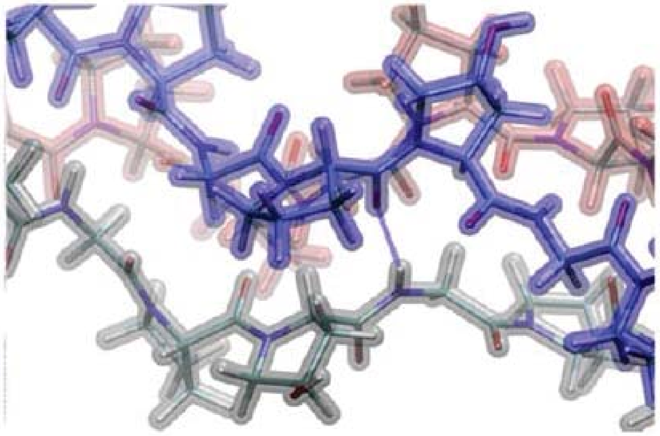
Fig. 1. Snapshots of the collagen peptide in water box. Panel a shows the conformation of the full atomistic model of a $[(GPO)_{21}]_3$ collagen peptide solvated in water box and equilibrated for 30 ns. After equilibration the molecule is subjected to virtual creep tests: one end of the collagen peptide 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.

Hypothesis:

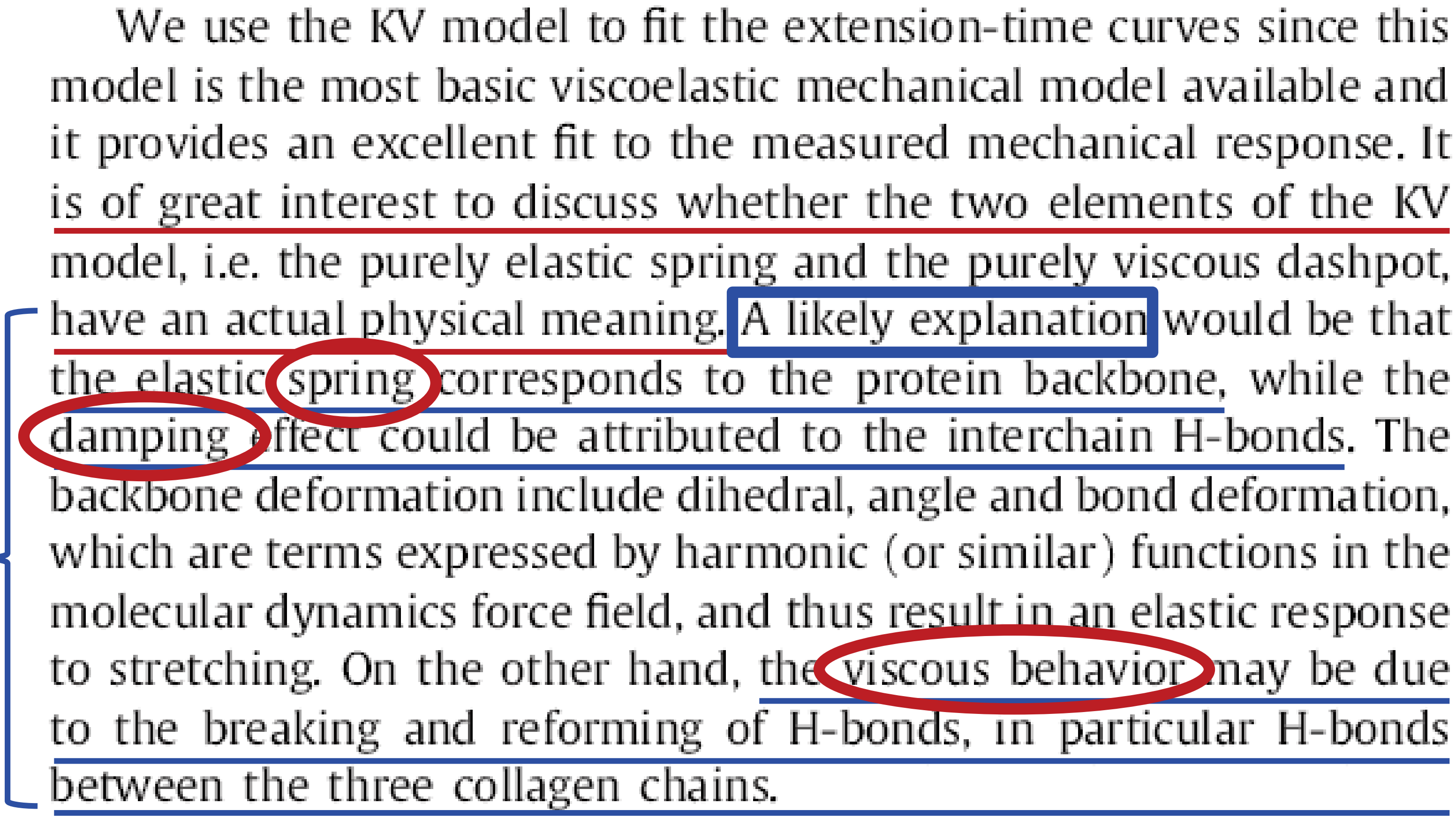


$$\varepsilon(t)=\frac{\sigma_0}{E}(1-e^{-\frac{E}{\eta}t})$$



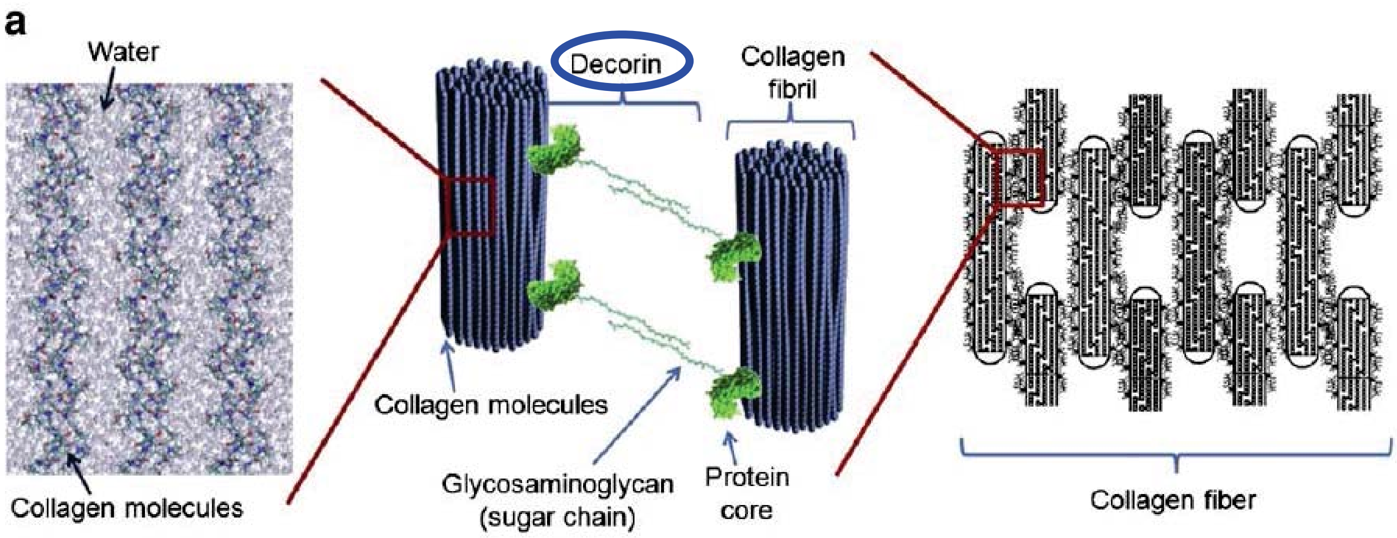
$\tau = (\eta/E) \sim 0.5$ ns

Source: Vesentini, Simone, et al. "Nanomechanics of Collagen Microfibrils." *Muscles, Ligaments and Tendons Journal* 3, no. 1 (2013): 23.

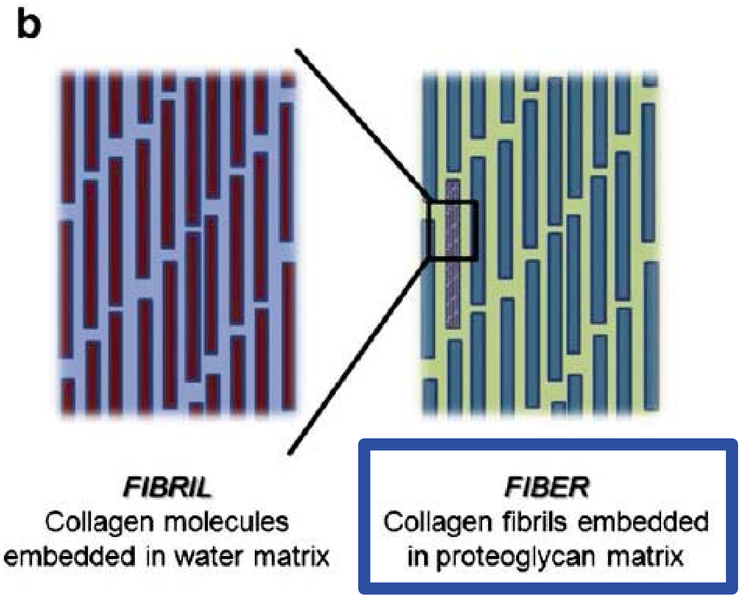


We use the KV model to fit the extension-time curves since this model is the most basic viscoelastic mechanical model available and it provides an excellent fit to the measured mechanical response. It is of great interest to discuss whether the two elements of the KV model, i.e. the purely elastic spring and the purely viscous dashpot, have an actual physical meaning. A likely explanation would be that the elastic spring corresponds to the protein backbone, while the damping effect could be attributed to the interchain H-bonds. The backbone deformation include dihedral, angle and bond deformation, which are terms expressed by harmonic (or similar) functions in the molecular dynamics force field, and thus result in an elastic response to stretching. On the other hand, the viscous behavior may be due to the breaking and reforming of H-bonds, in particular H-bonds between the three collagen chains.

Molecular Level



τ = (η/E) can be <u>minutes at Tissue Level</u>



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.

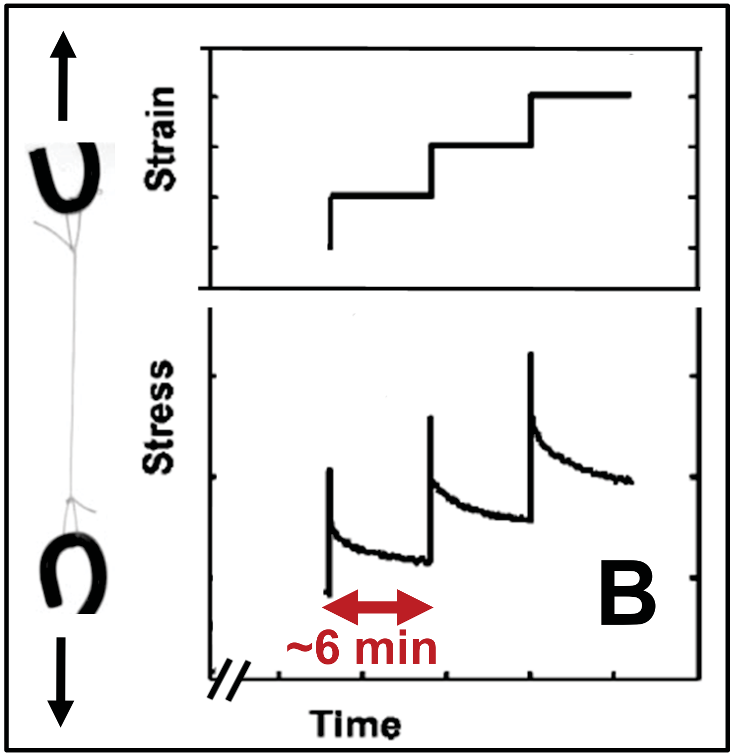
- ......the viscous behavior of fibrils and fibers involves additional mechanisms, such as molecular sliding between collagen molecules within the fibril……and collagen fiber uncramping…..

Influence of Decorin and Biglycan on Mechanical Properties of Multiple Tendons in Knockout Mice

"Stress Relaxation"

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

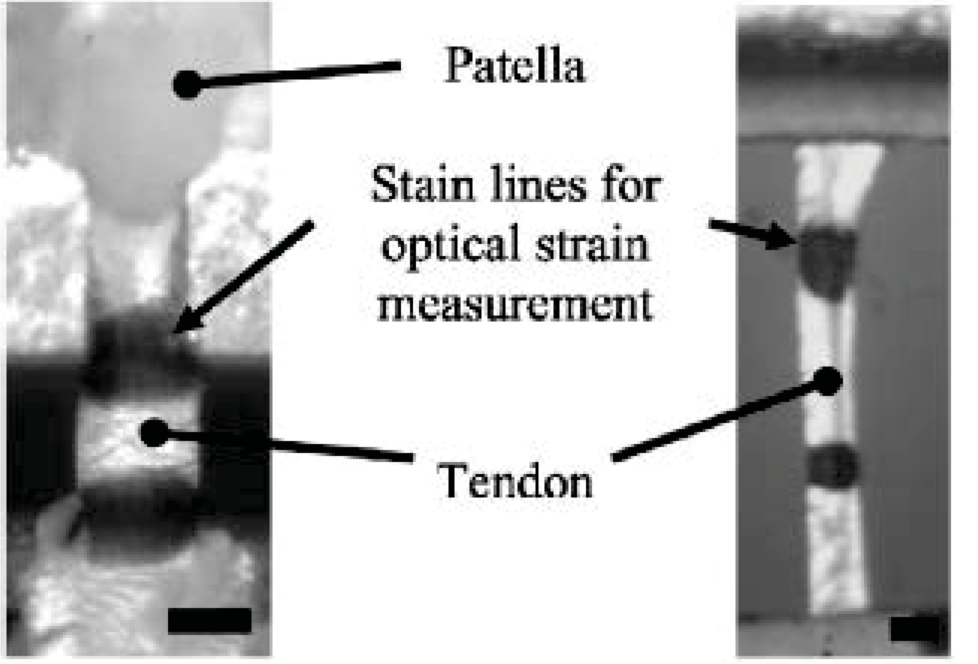
Mouse tendon fascicle



Robinson+, J Biomech Eng, 2005

decorin k/o
Modulus ↓

Biglycan k/o
Modulus ↑



Patellar (left) and flexor digitorum longus (right)

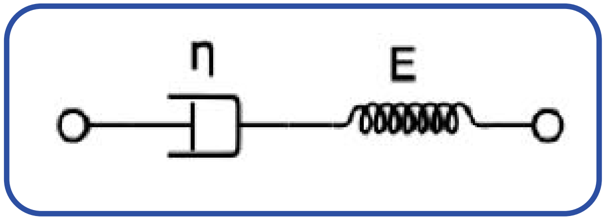
Source: Robinson, Paul S. et al. "Influence of Decorin and Biglycan on Mechanical Properties of Multiple Tendons in Knockout Mice." *Journal of Biomechanical Engineering* 127, no. 1 (2005): 181-5.

Model

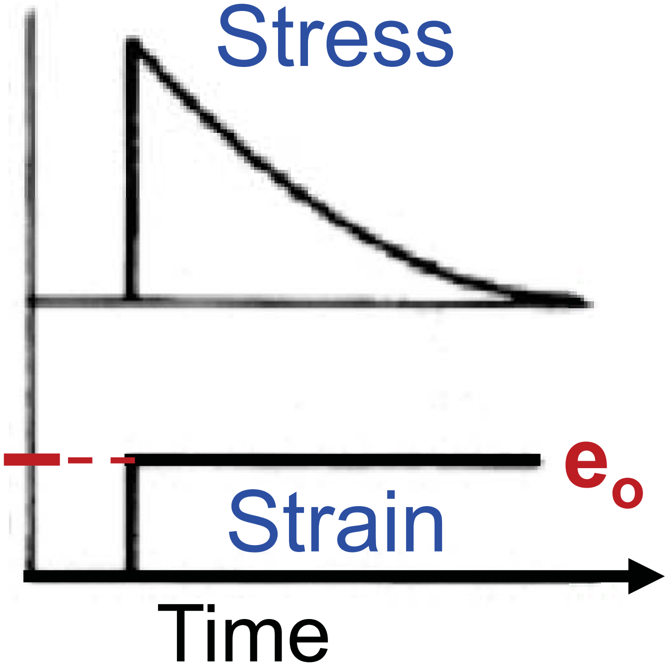
Creep

Stress relaxation

Maxwell Model



$\tau = (\eta/E)$



(Measure)

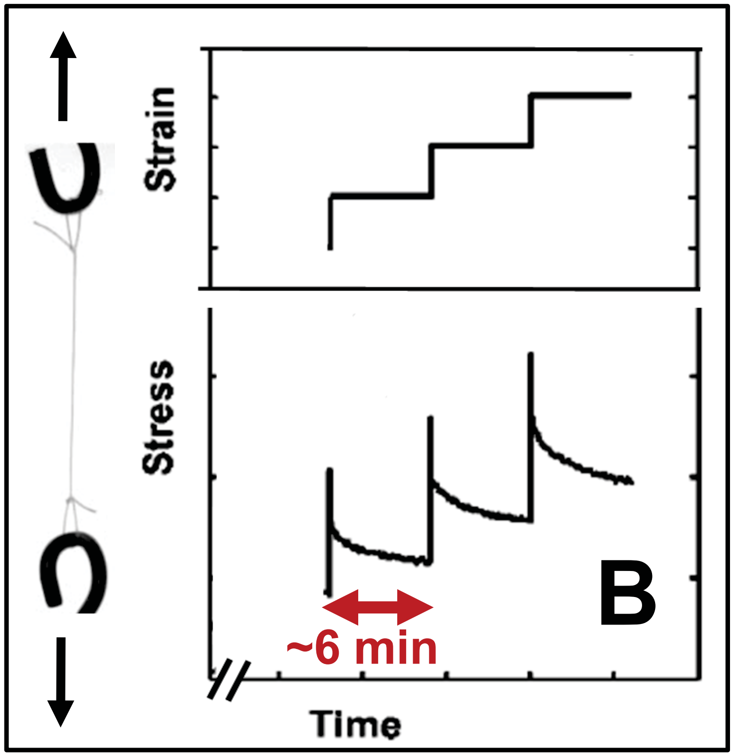
(Applied step)

Influence of Decorin and Biglycan on Mechanical Properties of Multiple Tendons in Knockout Mice

"Stress Relaxation"

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

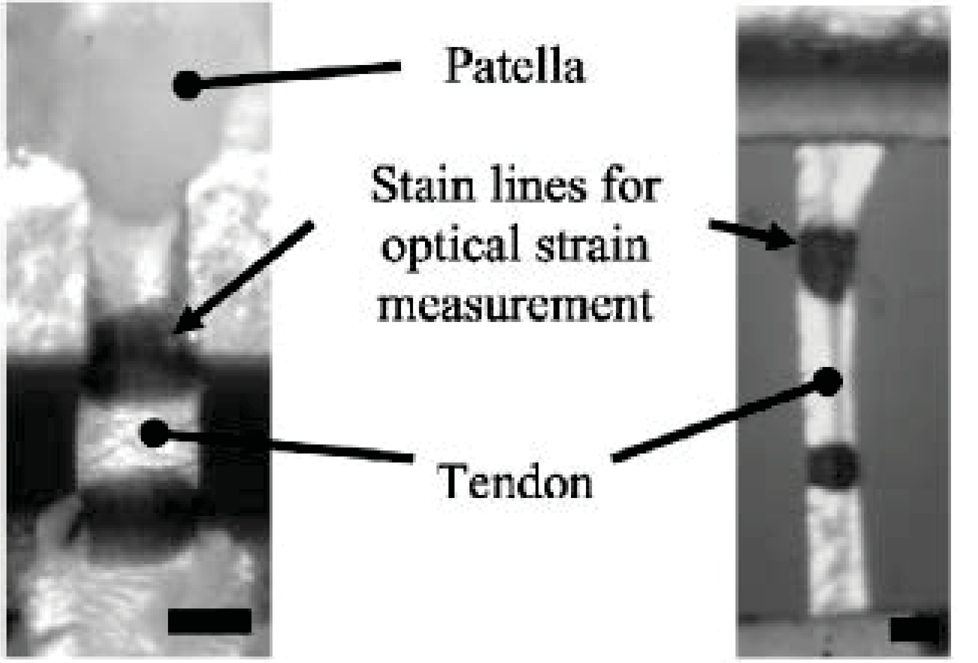
Mouse tendon fascicle



Robinson+, J Biomech Eng, 2005

decorin k/o
Modulus

Biglycan k/o
Modulus ↑



Patellar (left) and flexor digitorum longus (right)

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.

Question:

How to "fix" Voigt and Maxwell models...

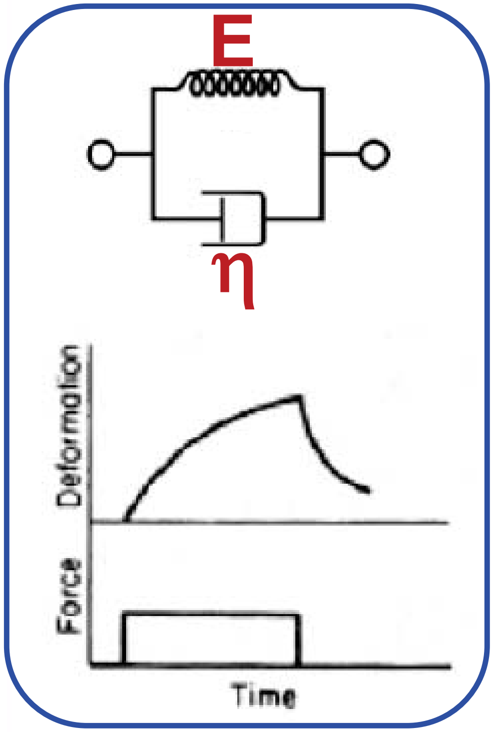
- Tissues stress-relax to a finite strain
- Tissue-creep involves an initial elastic like jump in stress

Stress relaxation

Creep

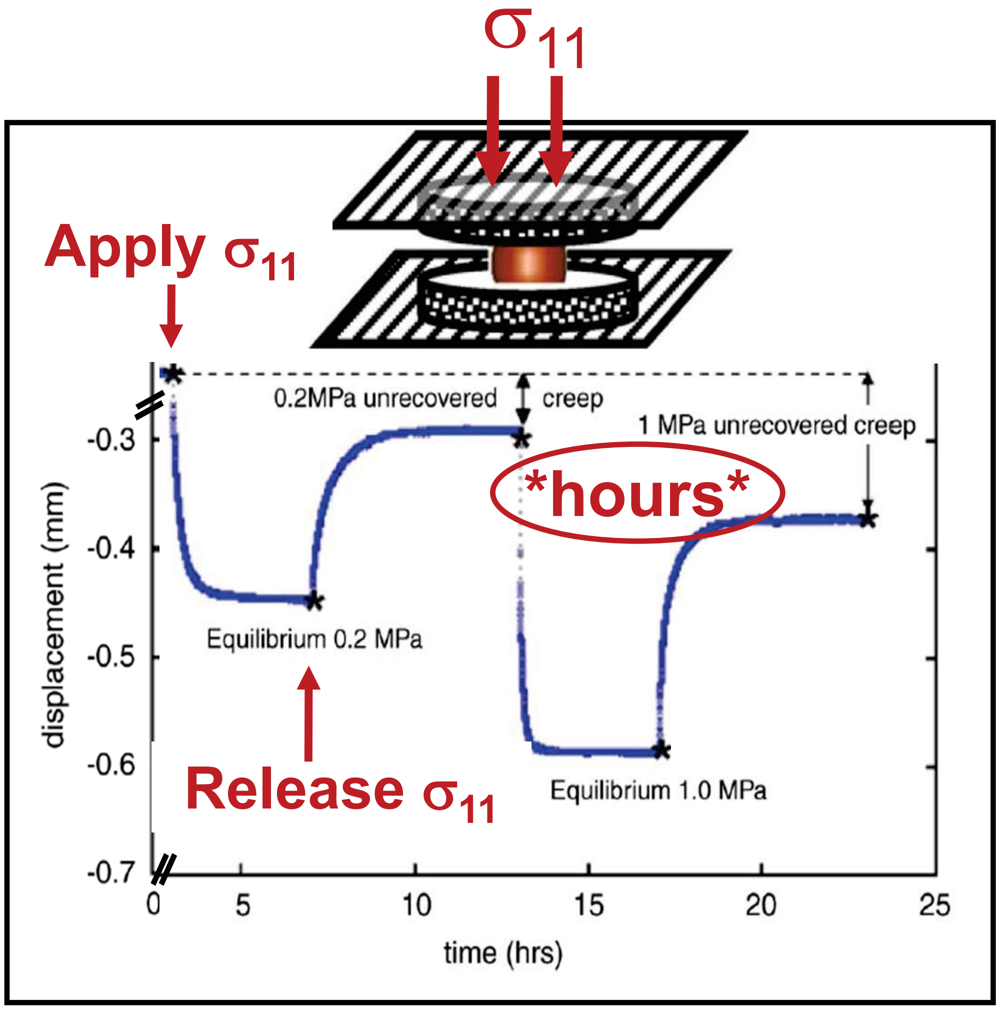
Model

Voigt Model



“Creep-Compression” of intervertebral disc (rat tail):

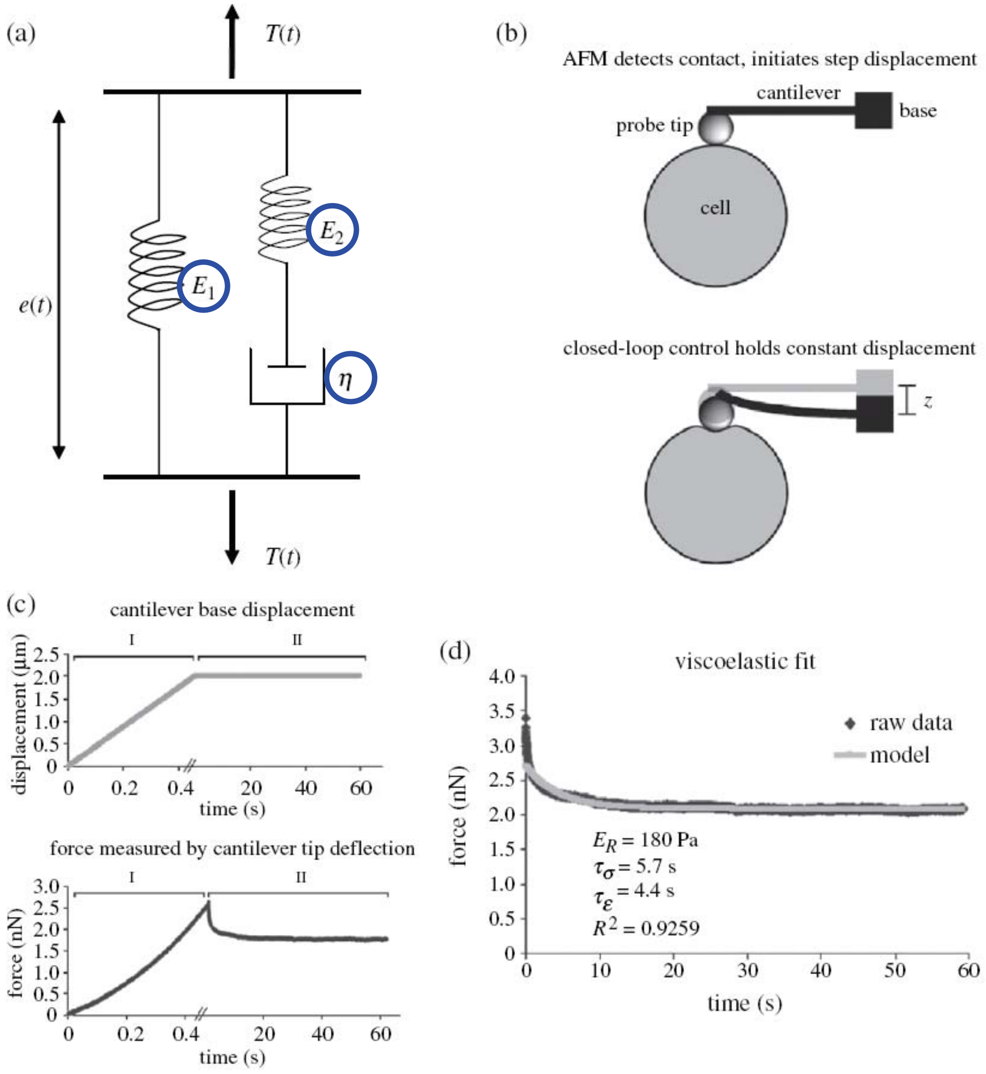
Apply step in stress (σ_{11}) and measure displacement (strain) vs time



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.

(MacLean+, J Biomechanics, 2007)

PSet 4: P2 (text prob 7.9 parts a,b)



(a)

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

Show that this form is correct, and find the algebraic expressions for α and β in terms of the element values E_1, E_2, and η.

(b) Based on the form of (7.73), find expressions for the stress relaxation time constant τ_e (the relaxation time at constant strain) and the creep time constant τ_c (the relaxation time under constant load) in terms of E_1, E_2, and η.

(c) In Figure 7.32(d), the stress relaxation data of Figure 7.32(c) (region II of the "force" curve) are compared with the predictions of the three-element model of Figure 7.32(a) by obtaining best fit values of the three model parameters. Describe qualitatively how you would change the model in an attempt to improve the fit to the data even further at very early times (i.e., within the first 2 s) on the time scale of Figure 7.32(d). In the frequency domain, this would correspond to testing frequencies above about 1 Hz in part (d) below.

(Darling+, 2006, OA&C)

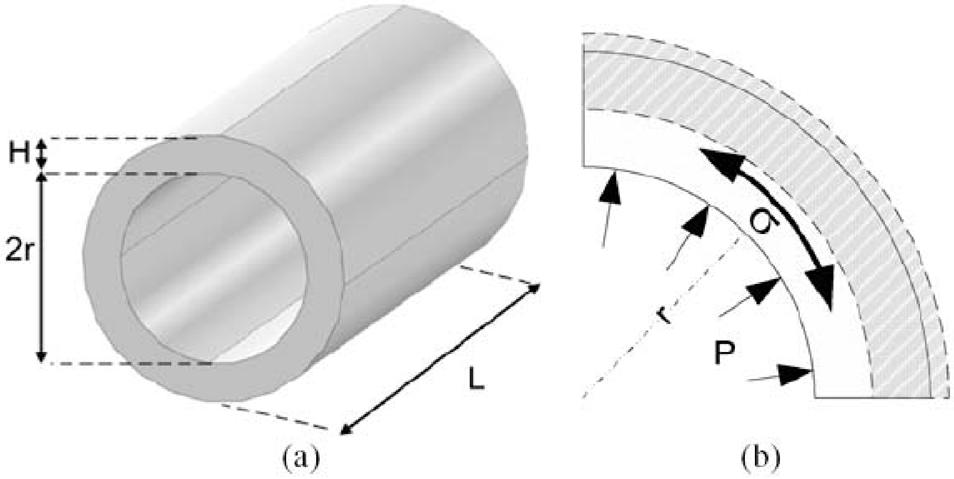
Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Darling, E. M. et al. "Viscoelastic Properties of Zonal Articular Chondrocytes Measured by Atomic Force Microscopy." *Osteoarthritis and Cartilage* 14, no. 6 (2006): 571-9.

Estimation of the viscoelastic properties of vessel walls using a computational model and Doppler ultrasound

Simone Balocco[1,2,3,4,5], **Olivier Basset**[4], **Guy Courbebaisse**[4], **Enrico Boni**[5], **Alejandro F Frangi**[2,3,6], **Piero Tortoli**[5] and **Christian Cachard**[4]

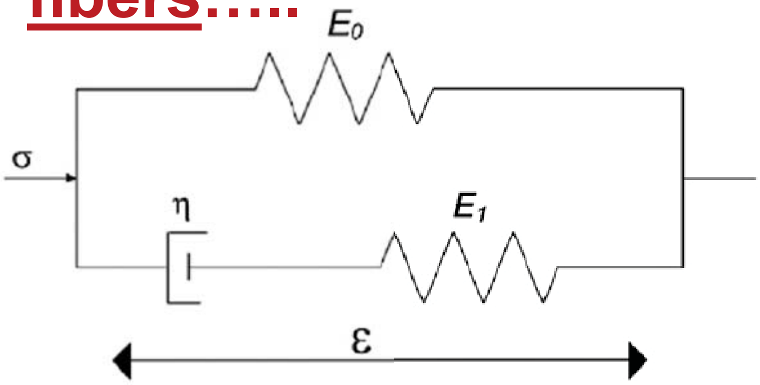
Physics in Med and Biol, 2010

Tissues containing elastin and collagen fibers…..



(a) (b)

Figure 1. Isometric view of the vessel geometry (a) and scheme illustrating the mechanical interactions between blood pressure and tissue (b). The dashed region indicates the dilatation and thinning of the vessel wall under the application of pressure *P*.



Source: Balocco, Simone, et al. "Estimation of the Viscoelastic Properties of Vessel Walls using a Computational Model and Doppler Ultrasound." *Physics in Medicine and Biology* 55, no. 12 (2010): 3557.

Human arteries affected by atherosclerosis are characterized by altered wall viscoelastic properties. The possibility of noninvasively assessing arterial viscoelasticity *in vivo would significantly contribute to the early diagnosis* and prevention of this disease.

PSet 4: P2 (text prob 7.9 parts **c**)

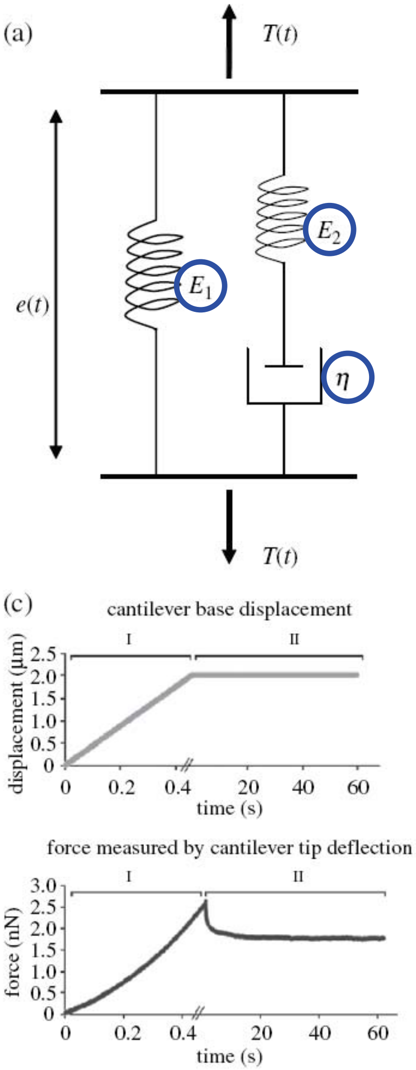
(a)

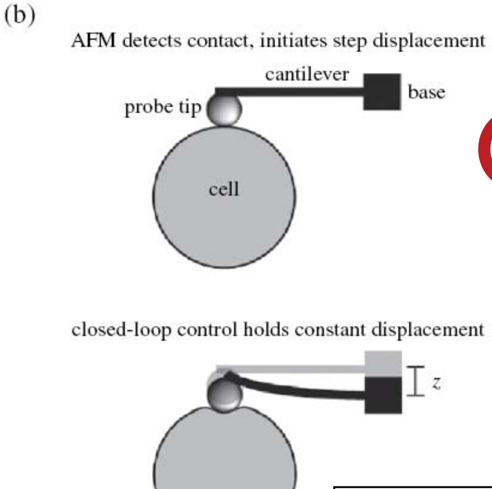
$$T + \alpha \frac{dT}{dt} = E_1 e + \beta \frac{de}{dt} \qquad (7.73)$$

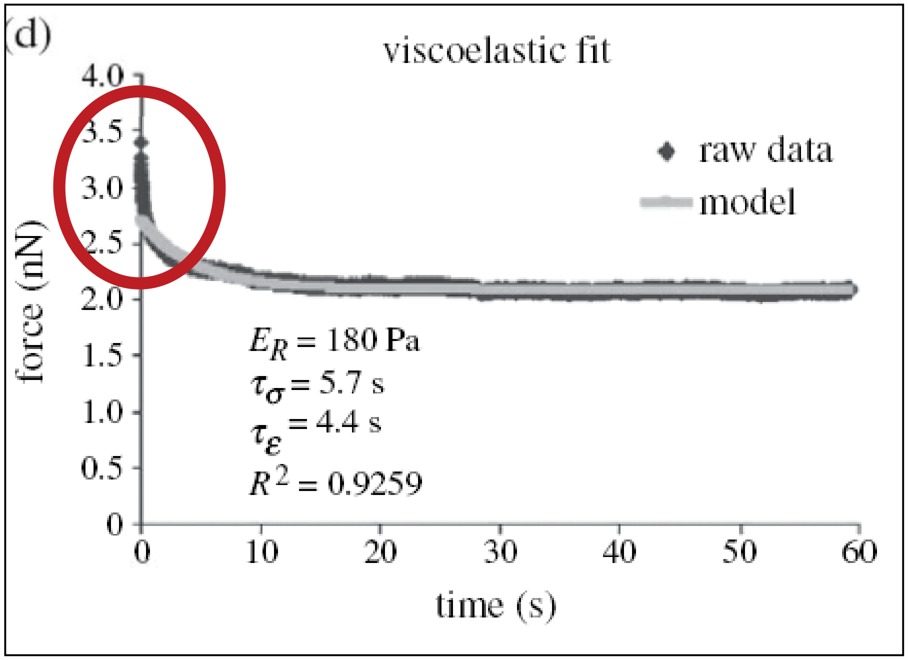
Show that this form is correct, and find the algebraic expressions for α and β in terms of the element values E_1, E_2, and η.

(**b**) Based on the form of (7.73), find expressions for the stress relaxation time constant τ_e (the relaxation time at constant strain) and the creep time constant τ_c (the relaxation time under constant load) in terms of E_1, E_2, and η.

(**c**) In Figure 7.32(d), the stress relaxation data of Figure 7.32(c) (region II of the "force" curve) are compared with the predictions of the three-element model of Figure 7.32(a) by obtaining best fit values of the three model parameters. Describe qualitatively how you would change the model in an attempt to improve the fit to the data even further at very early times (i.e., within the first 2 s) on the time scale of Figure 7.32(d). In the frequency domain, this would correspond to testing frequencies above about 1 Hz in part (d) below.







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." *Osteoarthritis and Cartilage* 14, no. 6 (2006): 571-9.

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]

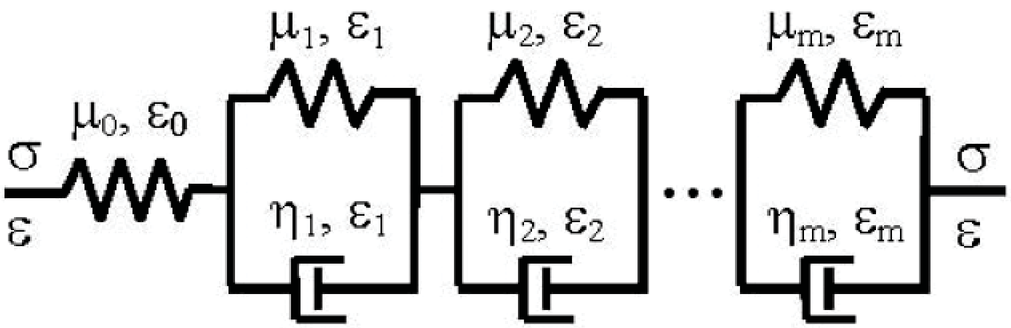


Fig. 3.
A generalized Maxwell viscoelastic model (a linear spring in serial with *m* Voigt elements).

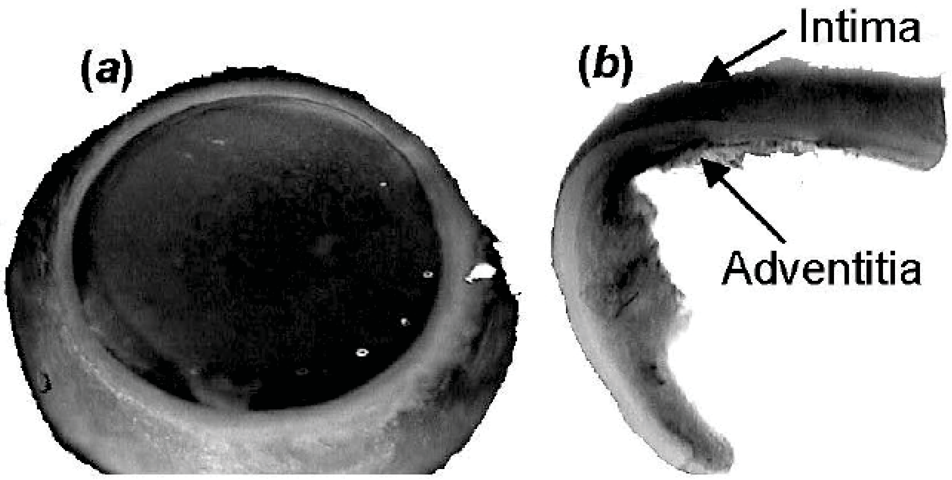


Fig. 2.
Photographs of a porcine coronary artery at the (*a*) loaded state with hardened elastomer in the lumen and (*b*) zero-stress state where opening angle is larger than 180°.

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.

Tendon Hierarchy

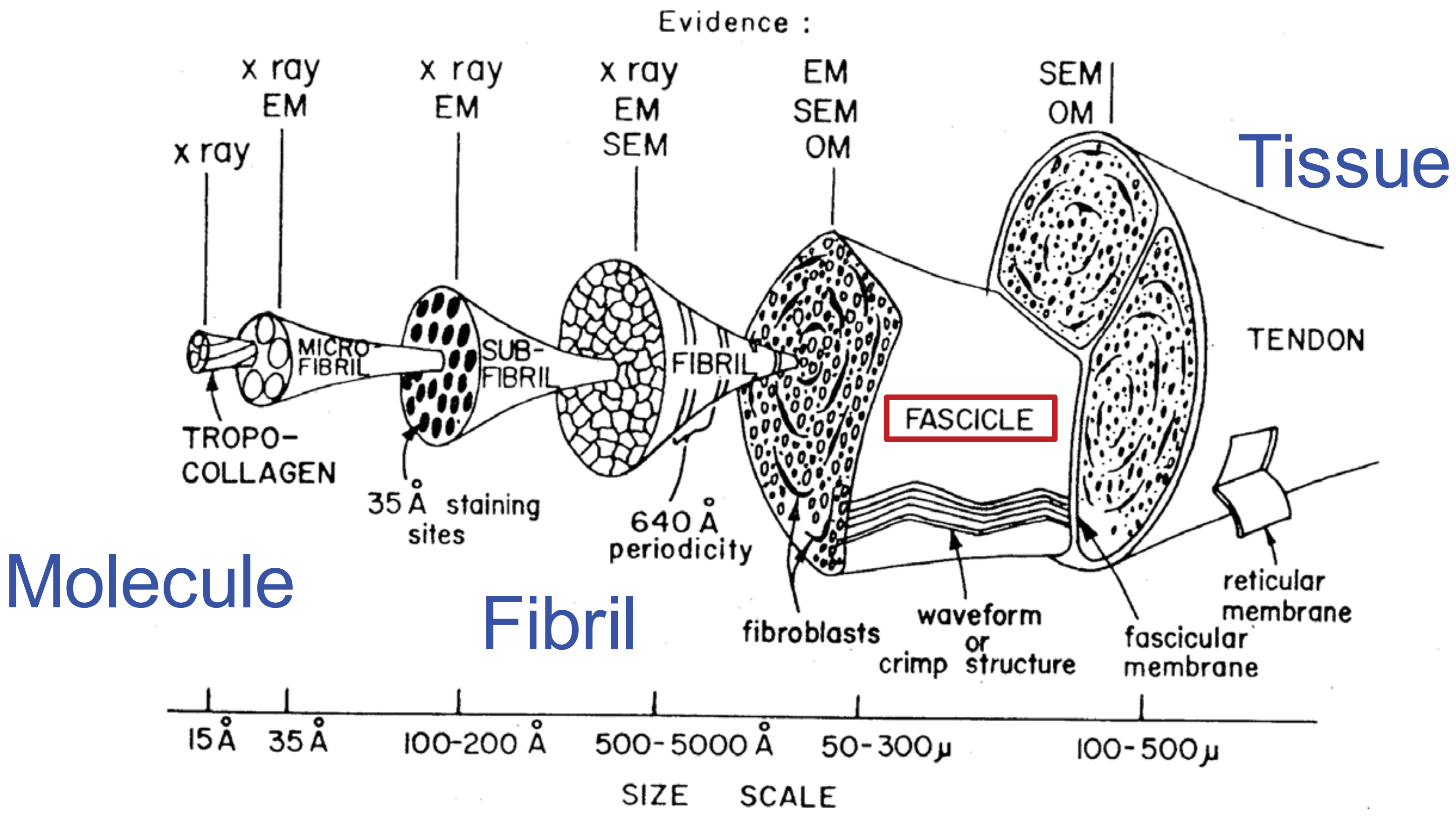
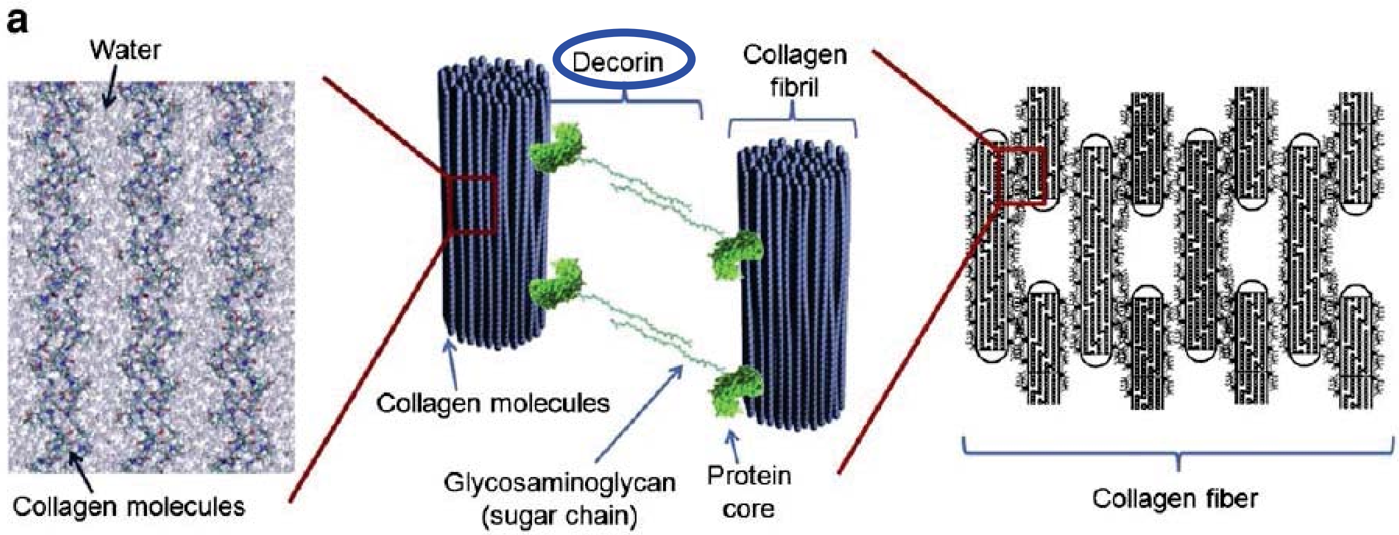
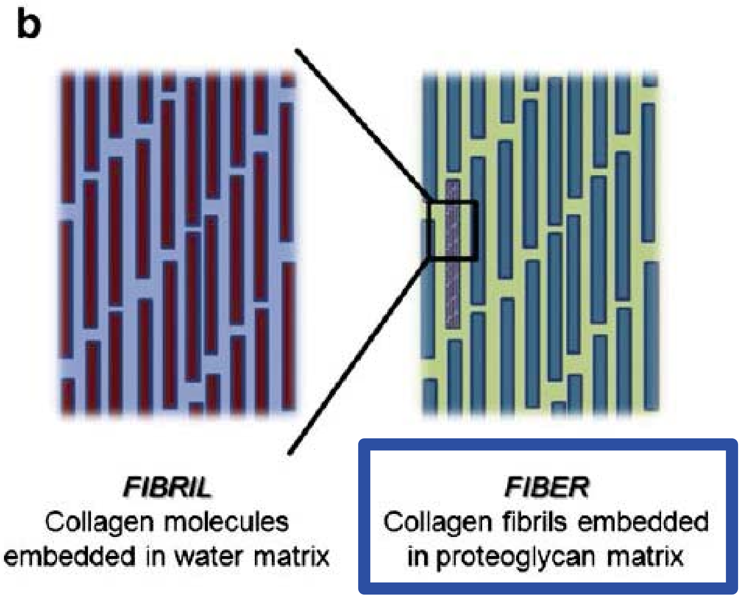


Figure 7.3:6 Hierarchy of structure of a tendon according to Kastelic et al. (1978). Reproduced by permission. Evidences are gathered from X ray, electron microscopy (EM), scanning electron microscopy (SEM), and optical microscopy (OM). (Y.C. Fung)

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



$\tau = (\eta/E) = 0.5\ \underline{\text{ns}}$



$\tau = \underline{\text{minutes}}$

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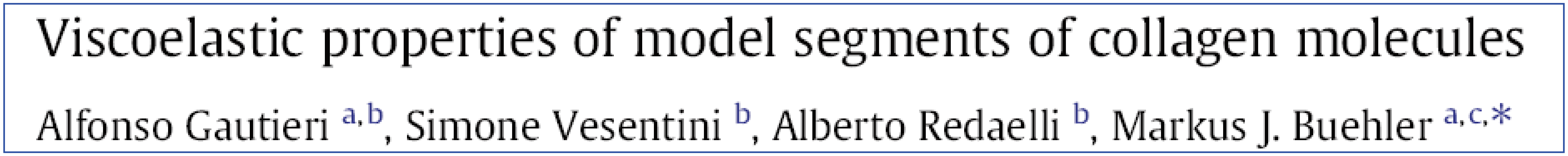
Source: Gautieri, Alfonso, et al. "Viscoelastic Properties of Model Segments of Collagen Molecules." *Matrix Biology* 31, no. 2 (2012): 141-9.

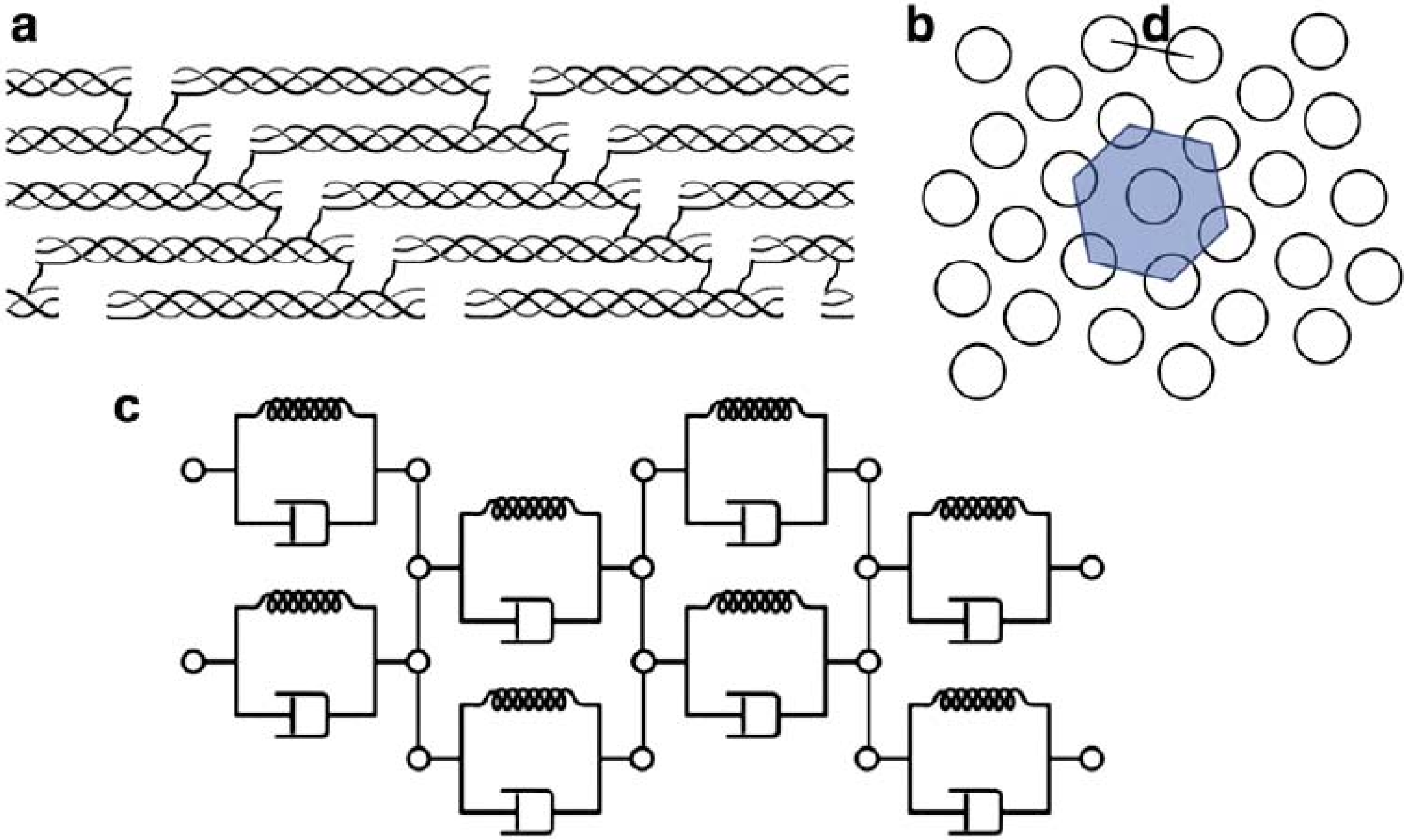
- ......the viscous behavior of fibrils and fibers involves additional mechanisms, such as <u>molecular sliding between collagen molecules within the fibril….and uncramping of collagen fiber</u>



Viscoelastic properties of model segments of collagen molecules

Alfonso Gautieri [a,b], Simone Vesentini [b], Alberto Redaelli [b], Markus J. Buehler [a,c,*]

Type I Collagen Molecule → <u>Fibril</u> → Fiber → Tissue



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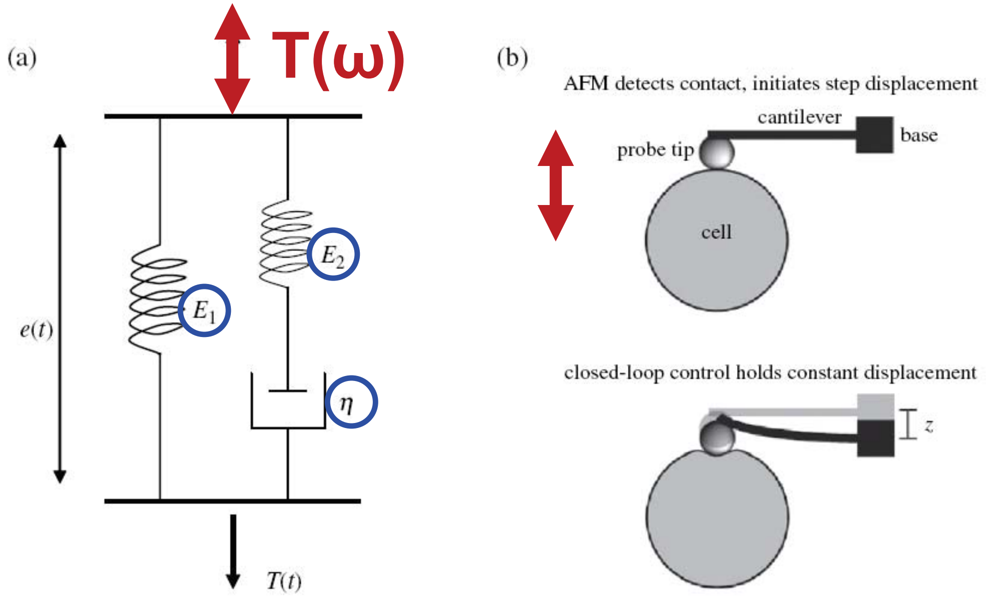
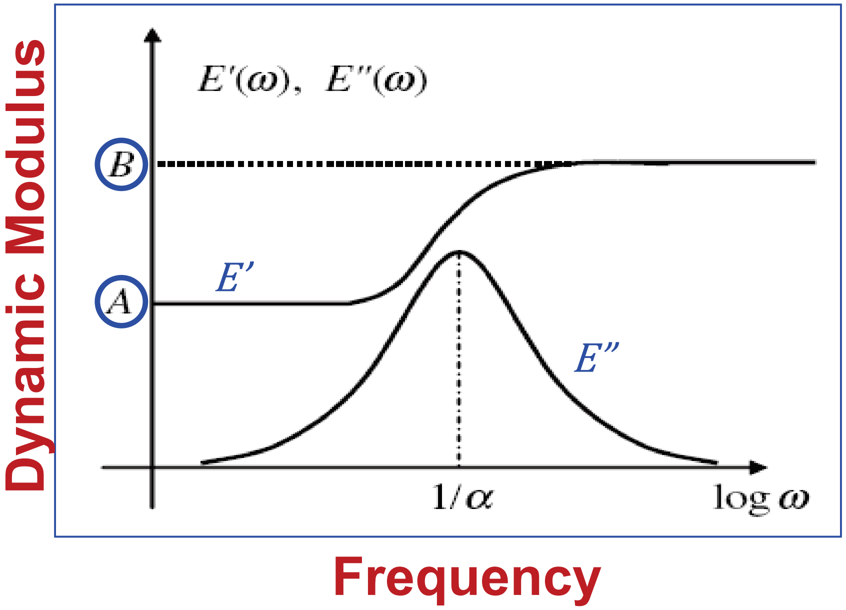
Source: Gautieri, Alfonso, et al. "Viscoelastic Properties of Model Segments of Collagen Molecules." *Matrix Biology* 31, no. 2 (2012): 141-9.

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

Sinusoidal loading versus Frequency





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

(**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.

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