

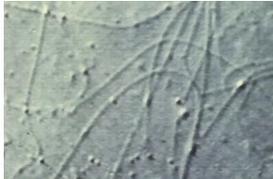
Molecular mechanisms of biological motion

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Various levels of biological motion

Molecular motion



Axoplasm

Cellular motion



crawling keratinocyte

Body motion



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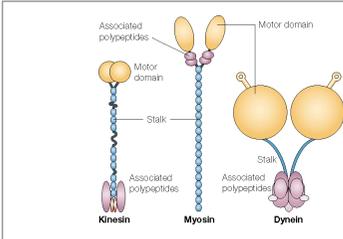
Motor proteins

Mechanoenzymes capable of converting chemical energy into mechanical work.

1. Specifically attach to a cytoskeletal filament or other biopolymer (DNA).
2. They generate force when moving along the filament.
3. They utilize energy from nucleotide cleavage for force generation.

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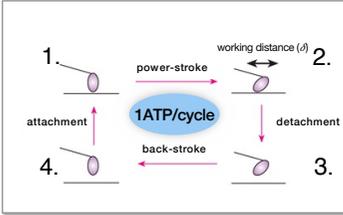
Common characteristics of motor proteins



I. Structural homology

The globular head at the N-terminus is the **motor domain** (ATPase) and provides a specific binding-site for the respective cytoskeletal filament.

The C-terminus binds to the surface that is being moved



II. Cyclic operation

1. Attachment
2. Power-stroke (pull)
3. Detachment (dissociation)
4. Back-stroke (relaxation)

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Force generation of motor proteins

Force generation, F
(range of pN)

working distance, δ
(range of nm)

Work done by a single motor protein, W

$$W = F \cdot \delta$$

range of 10^{-20} J (zeptojoule) = 10^{21} J

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Duty cycle of motor proteins

ATP hydrolysis cycle Duty ratio (r):

$$r = \frac{\tau_{on}}{\tau_{on} + \tau_{off}} = \frac{\tau_{on}}{\tau_{total}}$$

Processive motor protein: $r \sim 1$
F.e. kinesin, DNA-, RNA-polymerase.
They remain attached in most of the cycle time. They function individually.

Non-processive motor protein: $r \sim 0$
F.e. conventional myosin (skeletal muscle myosin II.) They remain detached in most of the cycle time. They function in ensembles.

$\delta = \text{working distance}$
 $v_{stroke} = \text{stroke velocity}$
 $k_{ATPase} = \text{ATPase rate}$

$$v_{stroke} = \frac{\delta}{\tau_{on}}$$

$$\tau_{on} = \frac{\delta}{v_{stroke}}$$

$$\tau_{total} = \frac{1}{k_{ATPase}}$$

$$r = \frac{\delta \cdot k_{ATPase}}{v_{stroke}}$$

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Types of motor proteins

- 1. Actin based**
 - **Myosins:** They move towards the plus end along the actin filament. (lamellipodium formation, muscle contraction)
- 2. Microtubule based**
 - **Dyneins:** Ciliary (flagellar) and cytoplasmic dyneins. They move towards the minus end along the microtubule. (axonal retrograde transport)
 - **Kinesins:** They move towards the plus end along the microtubule. (axonal anterograde transport)
 - **Dynamins:** Microtubule activated GTPase function. (pinchase)
- 3. DNA based mechanoenzymes**
 - They exert force and move along the DNS double helix. (DNA- and RNA-polymerases, viral capsid portal motor)
- 4. Rotary motors**
 - They are transmembrane mechanoenzymes that utilize the proton gradient across the membrane. F1Fo-ATP synthase, bacterial flagellar motor
- 5. Mechanoenzyme complexes**
 - Ribosome

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Cytoskeleton based motors

Non-processive motor
Skeletal myosin II.
Moves along the actin filament

Processive motor
Kinesin
Moves along the microtubule

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Basic phenomena of muscle function II.

1. Isometric contraction

The muscle does not or cannot shorten, but the tension on the muscle increases.

2. Isotonic contraction

Tension remains unchanged while the muscle's length changes.

Auxotonic contraction (simultaneous shortening and force generation)

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Basic phenomena of muscle function IV.

1. Work and Power

$$W = F \cdot s$$

$$P = \frac{W}{t} = \frac{F \cdot s}{t} = F \cdot v$$

If the shortening velocity is zero, the force is maximal: maximal isometric force (F_0)

If $v = \text{maximum}$, then $F = 0$

2. Force - velocity diagram

Hill equation:

$$(F + a)(v + b) = (F_0 + a)b$$

F: force, v: shortening velocity
a and b: constants,
F₀: maximal isometric force

$$v_{\max} = \frac{bF_0}{a}$$

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Energetics of muscle contraction

ATP hydrolysis, heat liberation

Source of energy:

$$\text{Mg} \cdot \text{ATP}^{2-} + \text{H}_2\text{O} \longrightarrow \text{Mg} \cdot \text{ADP}^{1-} + \text{P}_i^{2-} + \text{H}^+$$

Fenn effect: The liberation of heat increases when the muscle is doing work during shortening. The amount of heat liberated increases with increasing speed of contraction.

The majority of chemical energy used by the muscle is dissipated as heat

$Q_i < Q_f$

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The mechanism of muscle shortening

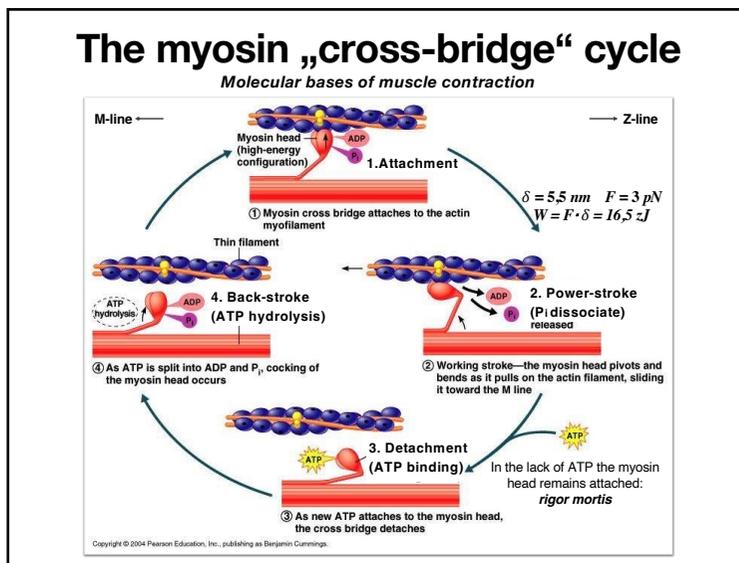
Phenomenological mechanism: sliding filament model

Sarcomere

Relaxed

Contracted

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Medical Biophysics II.

Biomechanics

Biomolecular and tissue mechanics

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Physical bases of biomechanics

Stress

$$\sigma = \frac{F}{A_0} \quad \left[\frac{\text{N}}{\text{m}^2} = \text{Pa} \right]$$

Strain (deformation)

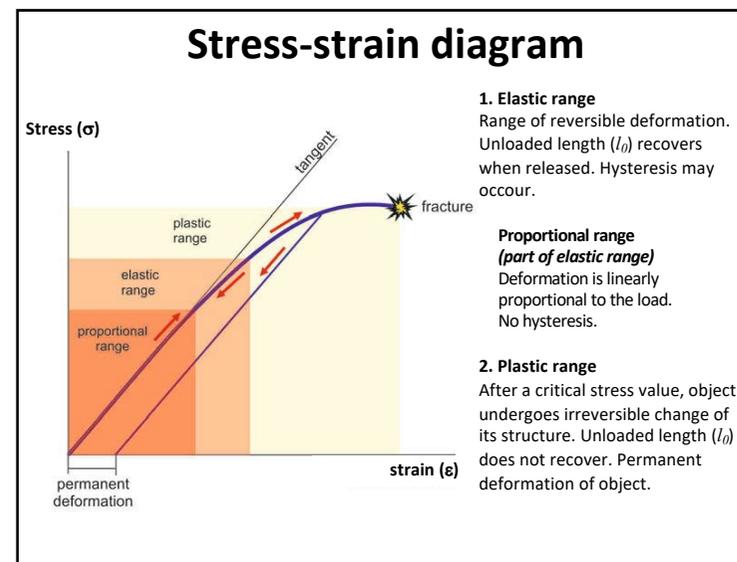
$$\varepsilon = \frac{\Delta l}{l_0} \quad \left[\frac{\text{m}}{\text{m}} \right] \text{ no dimension}$$

Strain is proportional to stress!

$$\sigma \sim \varepsilon$$

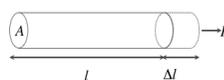
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Hooke's law



$$\sigma = E \cdot \varepsilon$$

$$\frac{F}{A_0} = E \cdot \frac{\Delta l}{l_0}$$

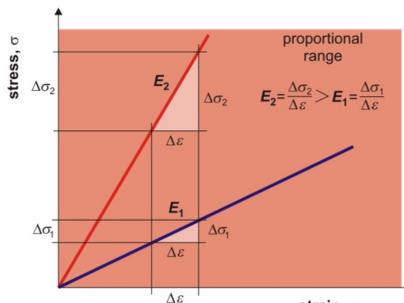
Hooke's law

$$F = \frac{E \cdot A_0}{l_0} \cdot \Delta l$$

$$F = k \cdot \Delta l$$

Young's modulus
(material stiffness)

$$E = \frac{\sigma}{\varepsilon} = \frac{F}{A_0} \cdot \frac{l_0}{\Delta l} \quad E = \left[\frac{N}{m^2} = Pa \right]$$



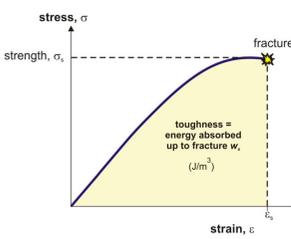
Spring constant
(body stiffness)

$$k = \frac{F}{\Delta l} \quad k = \left[\frac{N}{m} \right]$$

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Toughness

w_f : the work done on unit volume up to fracture.

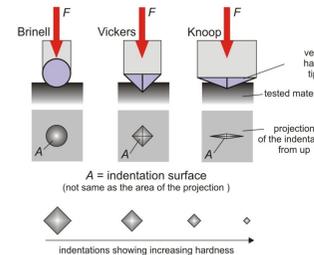


Strength

σ_f : the stress value belonging to fracture. Tensile-, compressive-, etc.

Hardness

property of the material that characterizes the resistance against plastic deformation during mechanical interaction with a harder material.



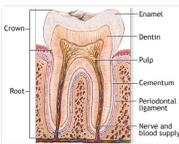
$H = \frac{F}{A} = [Pa]$

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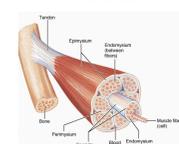
E: ~GPa

E: ~MPa

Tooth

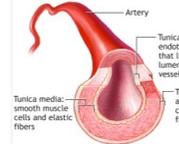


Muscle



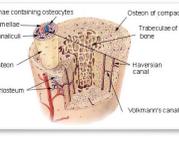
titin, desmin, collagen

Elastic artery



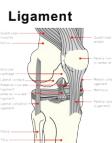
Collagen and elastin

Bone

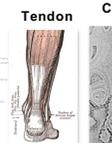


Composite of collagen (organic) and apatite (inorganic).
Organic component provides: toughness
Inorganic component provides: strength

Ligament



Tendon

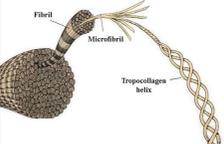


Cartilage



Collagen, proteoglycans (water)

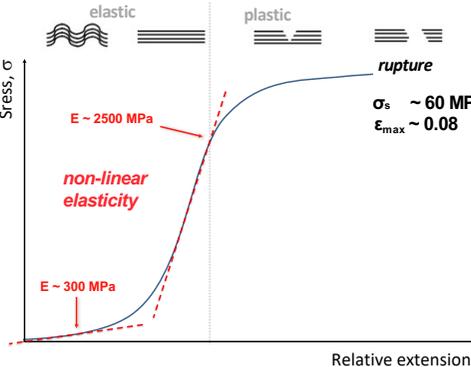
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Collagen

1400 amino acids/chain
3 chains (triple helix)
Glicine (1/3)
Proline (1/10)
Hydroxiproline

Posttranslational modification is required for mechanical stability: Prolin-hydroxylase and vitamin-C

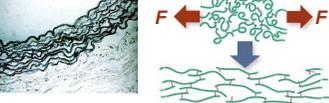


Relative extension, ε

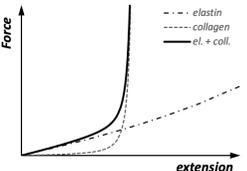
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Biomechanics of elastic arteries

Elastin – elastic protein network

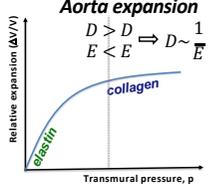


Collagen and elastin have different functions
 Collagen: protection against overstretch
 Elastin: provides distensibility



Aorta expansion

$$D > D \Rightarrow D \sim \frac{1}{E}$$

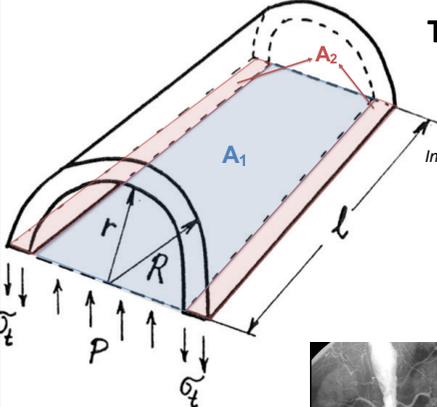
$$E < E \Rightarrow D \sim \frac{1}{E}$$


Distensibility
 The change in vessel volume under pressure

$$D = \frac{\Delta V/V_0}{\Delta p} = \frac{\Delta V}{\Delta p \cdot V_0}$$

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Tangential stress of blood vessel wall



In case of equilibrium, the forces acting on the two surfaces are equal

$$F_{A_1} = F_{A_2}$$

$$p \cdot A_1 = \sigma_t \cdot A_2$$

$$p \cdot 2r \cdot l = \sigma_t \cdot 2(R - r) \cdot l$$

$$\sigma_t = \frac{r}{R-r} \cdot p$$

Laplace-Frank equation

p: transmural pressure
 σ_t : tangential stress
 r: inner radius of blood vessel
 R: outer radius of blood vessel
 R-r: wall thickness

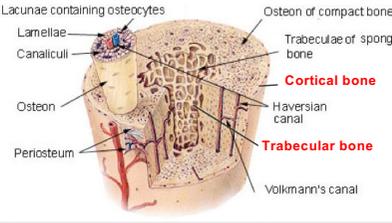


Significance: High blood pressure, aneurism

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Bone

Due to the different structure of bone tissue along the cross section of long bones, the **Young's modulus distribution is anisotropic**. Denser cortical bone has greater Young's modulus vs. the trabecular bone.
 Young's-modulus: 5-20 GPa
 Decalcified bone (acid treatment): flexible
 Removal of organic compounds (heating): brittle



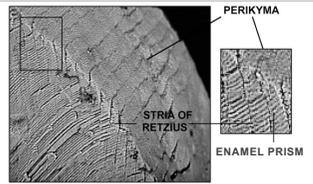
Composite of collagen and hydroxylapatite
collagen: elasticity, toughness
apatite: strength, stiffness, hardness

Bone is a composite material composed of an organic polymer (collagen) and an inorganic mineral (hydroxylapatite) which combines the mechanical properties of each.

Stiff, hard and strong but tough and slightly elastic.

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Enamel



Structural unit: enamel prism (nanocrystals)

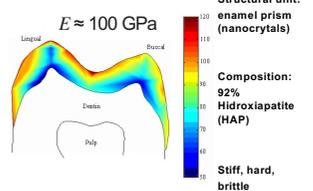
Composition: 92% Hydroxylapatite (HAP)

Stiff, hard, brittle

Stiffest and hardest material in human body, but brittle!

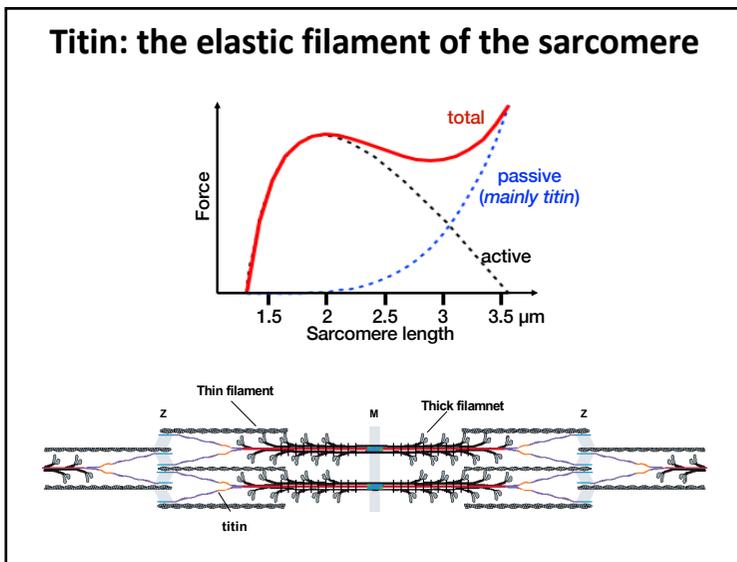


Hexagonal ion crystal
 20-60 nm x 6 nm - dentin, bone
 500-1000 nm x 30 nm - enamel

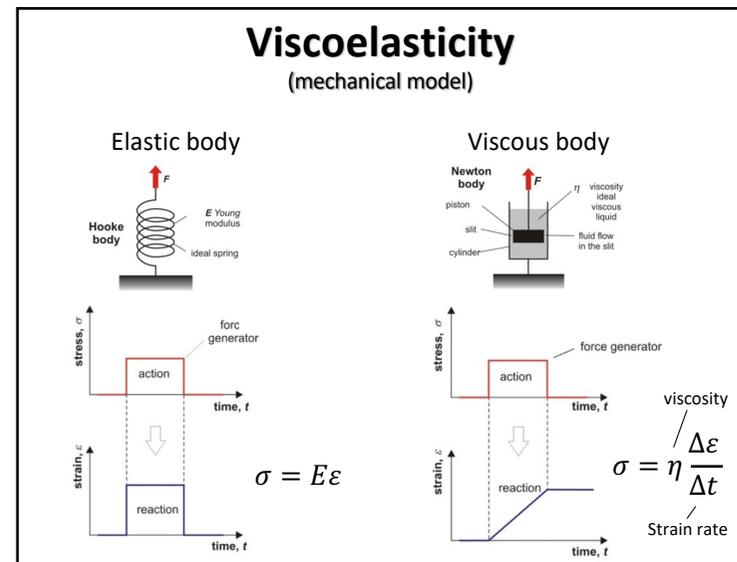


$E \approx 100 \text{ GPa}$

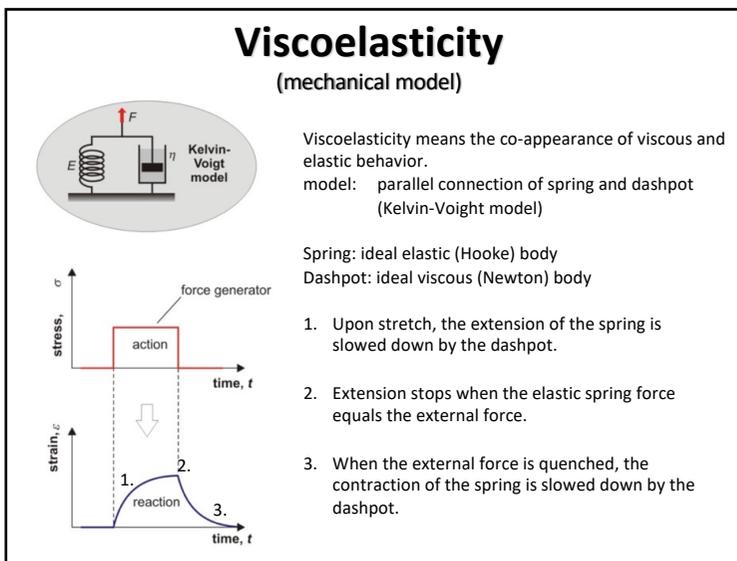
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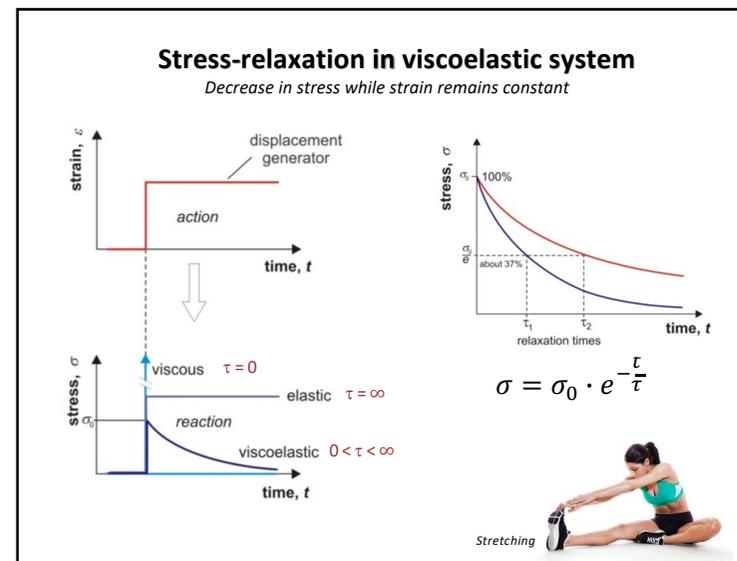
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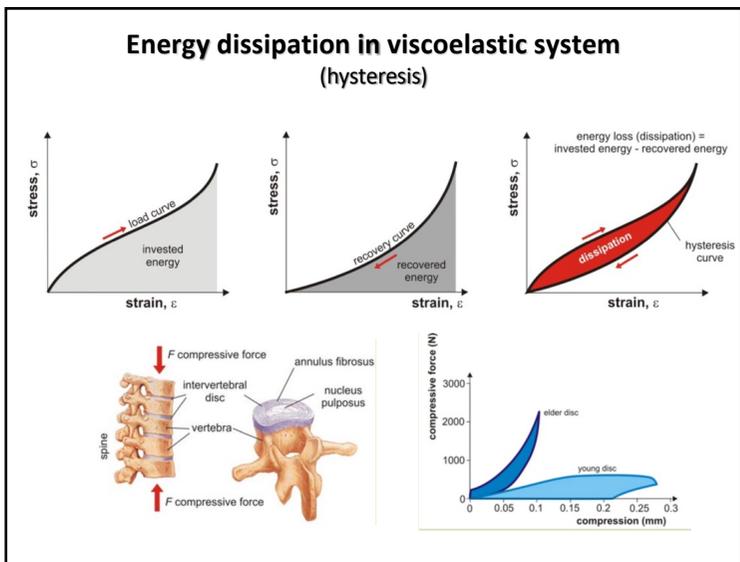
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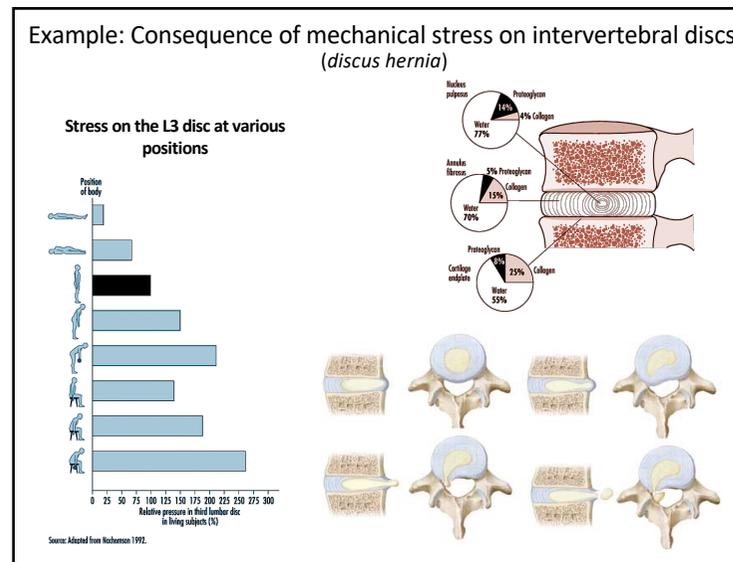
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Flashback: What did you learn about US propagation....?

In wich types of tissue does sound propagate faster?

The acoustic properties of each tissue are characterized by their stiffness

	E (GPa)	\mathcal{K} (GPa ⁻¹)	c_{sound} (m/s)
Cortical bone	18	0.05	3600
Muscle	7×10^{-5}	0.38	1568

$$c_{sound} = \frac{1}{\sqrt{\rho \cdot \kappa}}$$

$\kappa = \frac{-\Delta V/V}{\Delta p}$

compressibility

Volumetric strain

stress

Greater Young-modulus, faster propagation speed

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Diagnostic application: sonoelastography

Achilles examination

Lymph node

Transient elastography (measurement of liver stiffness based on pulse-echo principle)

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