

# 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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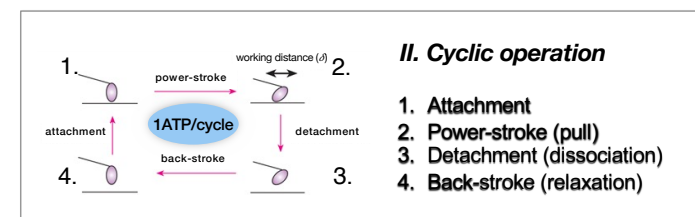
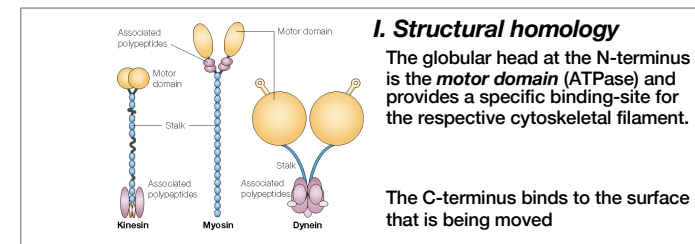
## Motor proteins

***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.

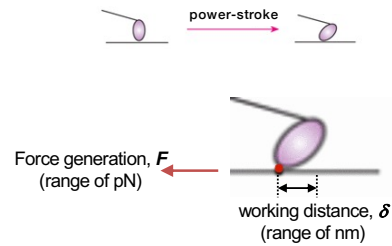
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## Common characteristics of motor proteins



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## Force generation of motor proteins



Work done by a single motor protein,  $W$

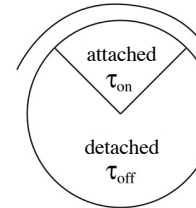
$$W = F \cdot \delta$$

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.

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

$$v_{stroke} = \frac{\delta}{\tau_{on}} \quad \tau_{on} = \frac{\delta}{v_{stroke}} \quad \tau_{total} = \frac{1}{k_{ATPase}} \quad r = \frac{\delta \cdot k_{ATPase}}{v_{stroke}}$$

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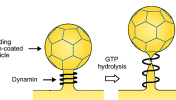
## Types of motor proteins

### 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

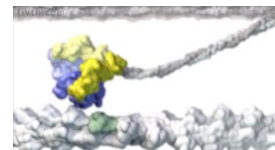
- Ribosome

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## Cytoskeleton based motors

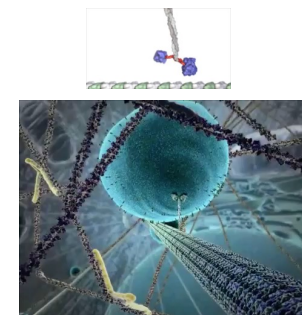
### Non-processive motor

Skeletal myosin II.  
 Moves along the actin filament



### Processive motor

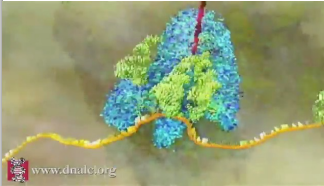
Kinesin  
 Moves along the microtubule



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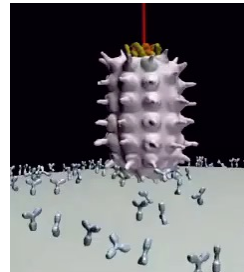
## Nucleic acid based motors

**Ribosome**  
mechanoenzyme complex



www.dnalc.org

**Virus portal motor**  
DNA „packaging“

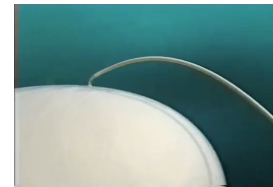
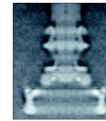


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## Rotating motors

driving force: proton gradient

**Flagellar motor**  
bacterial movement



**$F_1F_0$  ATP synthase**



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## Muscle biophysics

(mechanobiology of actin filaments and the myosin motor protein)



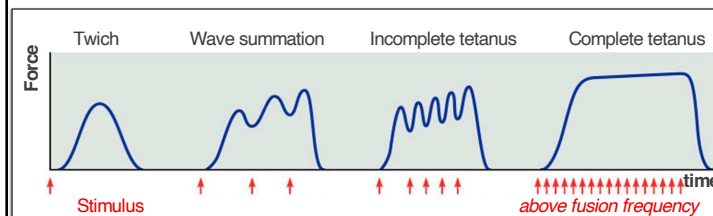
Machina Carnis

Cell and tissue specialized for movement.

It can only pull, not push!

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## Basic phenomena of muscle function I.



A single stimulus results in a single contractile response – a muscle **twitch** (contracts and relaxes).

More frequent stimuli increases contractile force – **wave summation** - muscle is already partially contracted when next stimulus arrives and contractions are summed.

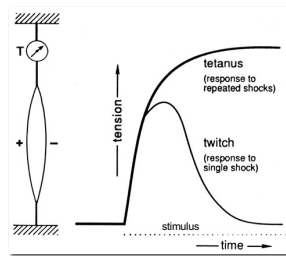
A sustained contraction that lacks even partial relaxation is known as **tetanus**.

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## Basic phenomena of muscle function II.

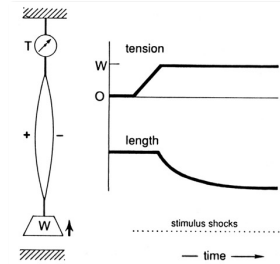
### 1. Isometric contraction

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

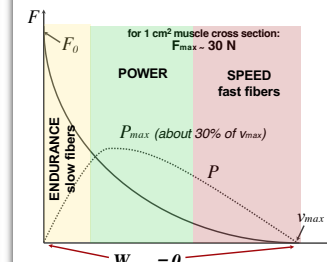
$$W = F \cdot s$$

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

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

If  $v$  = 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,

$F_0$ : maximal isometric force

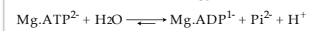
$$v_{\max} = \frac{bF_0}{a}$$

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## Energetics of muscle contraction

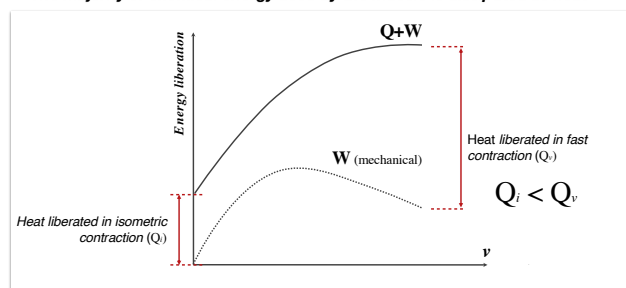
ATP hydrolysis, heat liberation

Source of energy:



**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.

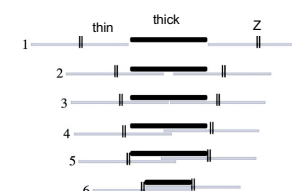
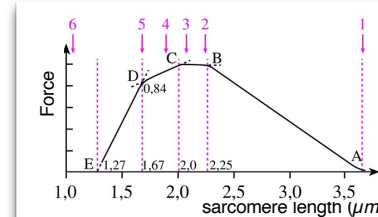
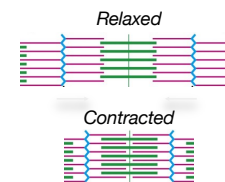
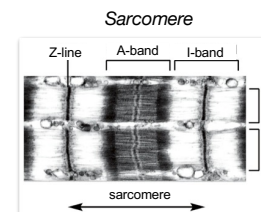
**The majority of chemical energy used by the muscle is dissipated as heat**



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## The mechanism of muscle shortening

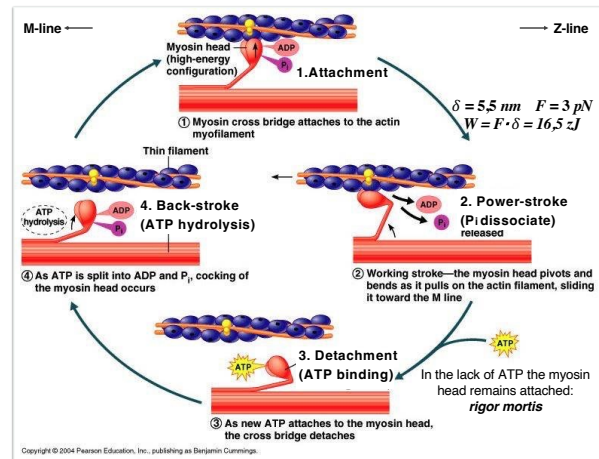
Phenomenological mechanism: sliding filament model



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## The myosin „cross-bridge“ cycle

Molecular bases of muscle contraction



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## Biomechanics

### Biomolecular and tissue mechanics

Medical Biophysics II.

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## Physical bases of biomechanics

Stress

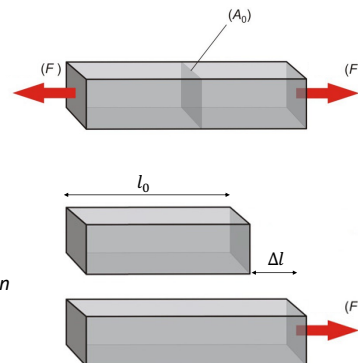
$$\sigma = \frac{F}{A_0} \quad \left[ \frac{N}{m^2} = Pa \right]$$

Strain (deformation)

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

Strain is proportional to stress!

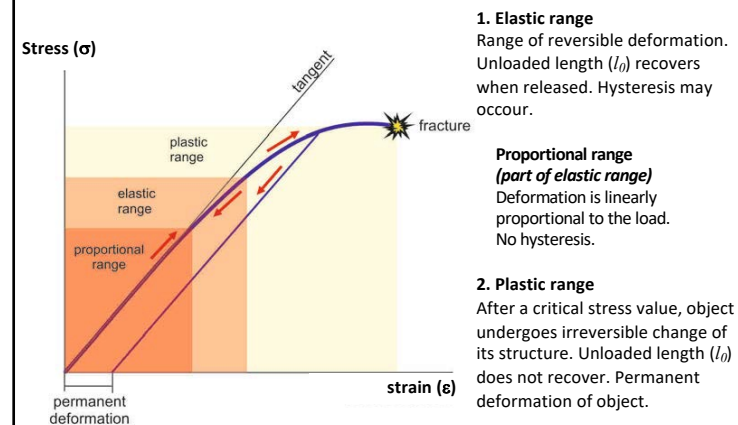
$$\sigma \sim \varepsilon$$



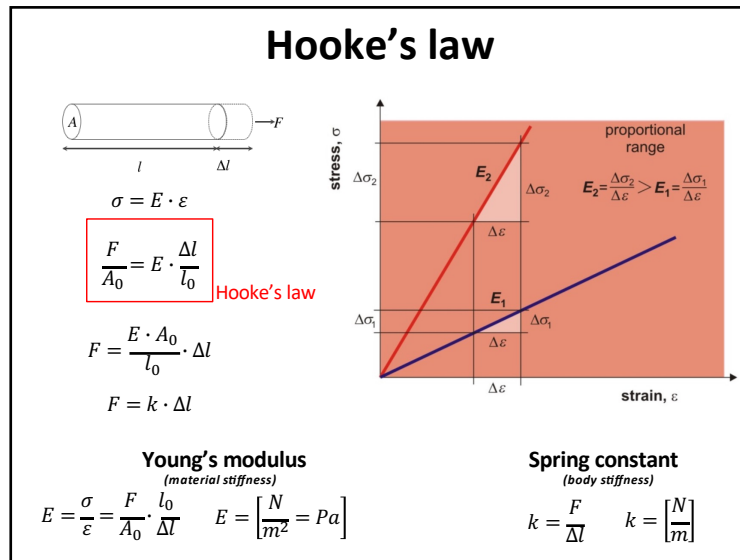
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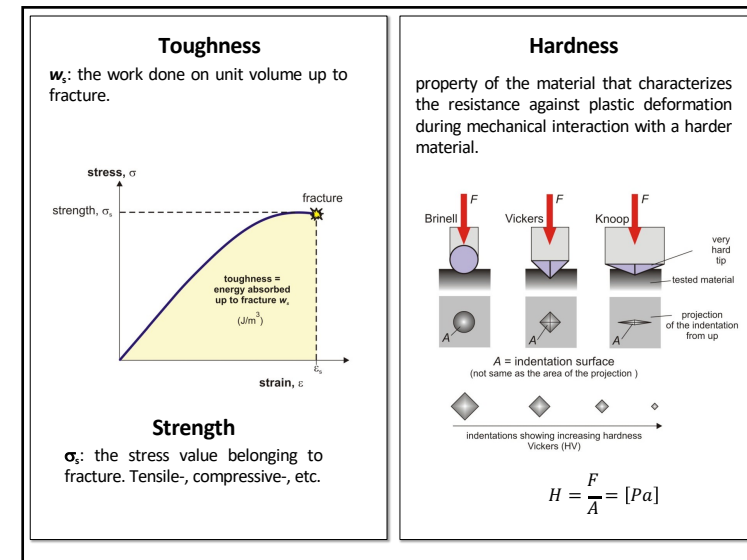
## Stress-strain diagram



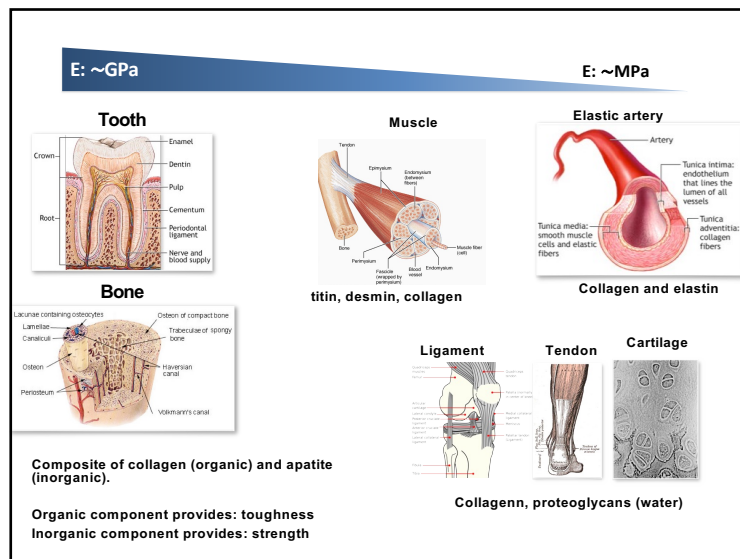
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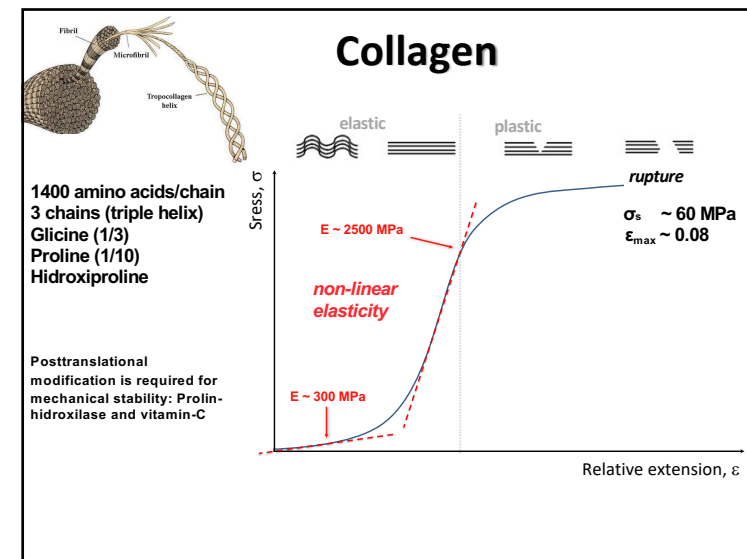
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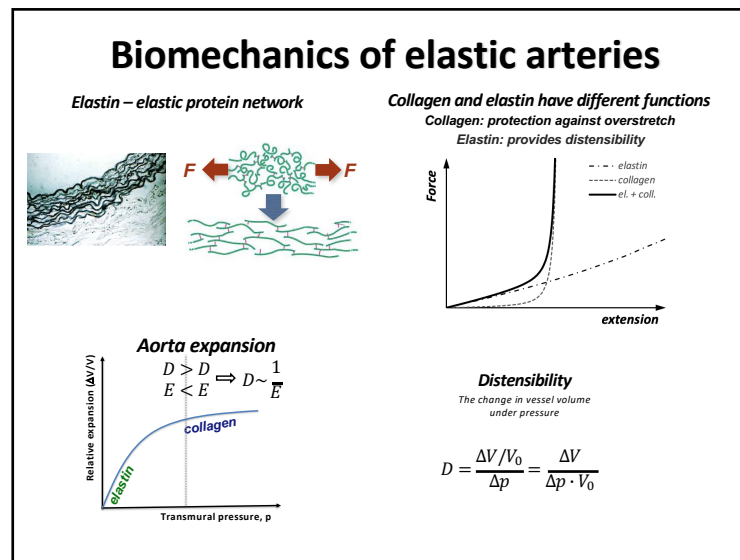
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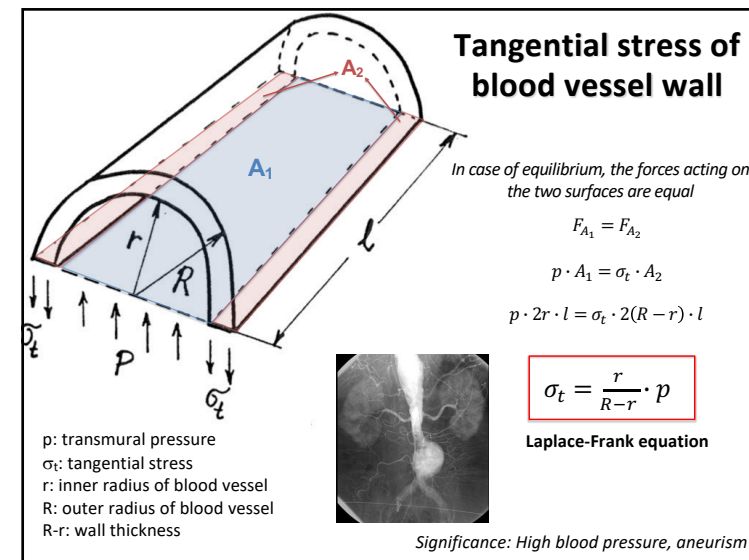
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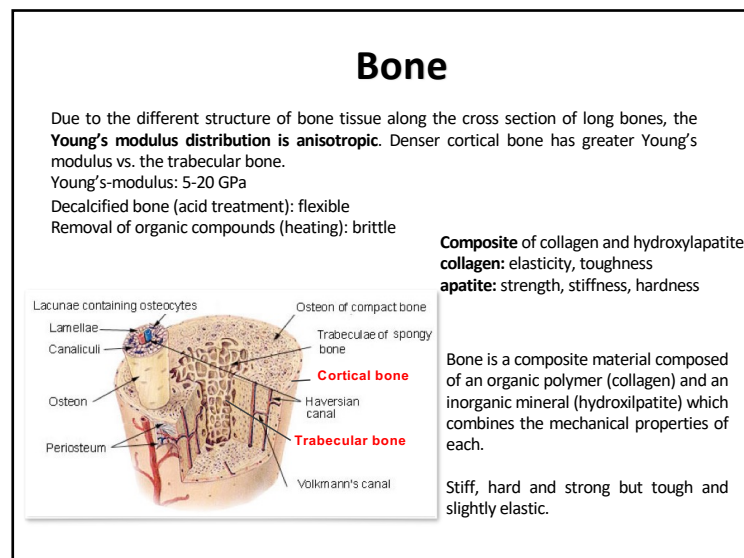
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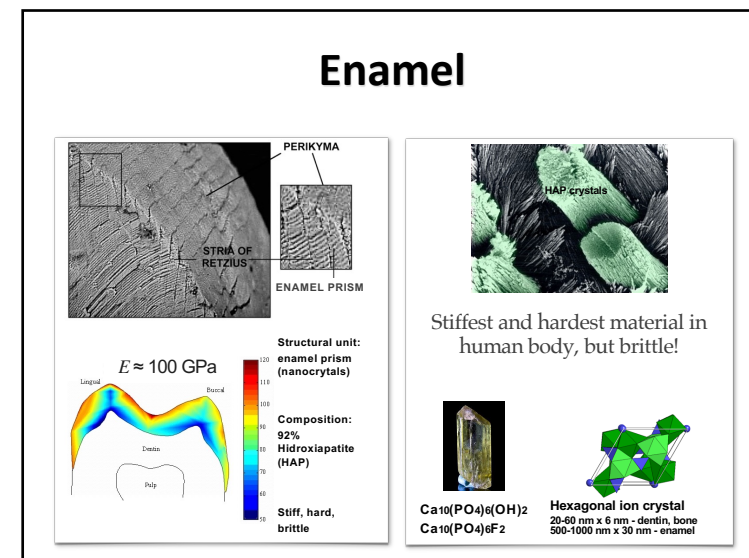
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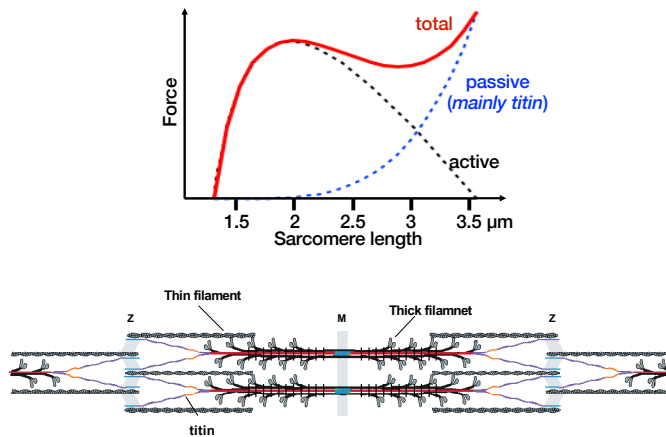
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## Titin: the elastic filament of the sarcomere

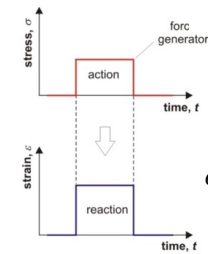
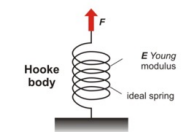


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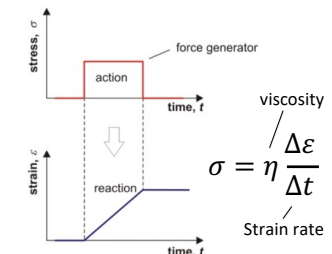
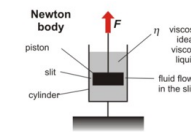
## Viscoelasticity

(mechanical model)

### Elastic body



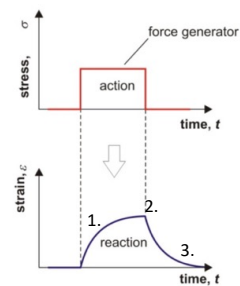
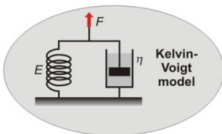
### Viscous body



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## Viscoelasticity

(mechanical model)



Viscoelasticity means the co-appearance of viscous and elastic behavior.

model: parallel connection of spring and dashpot (Kelvin-Voigt model)

Spring: ideal elastic (Hooke) body

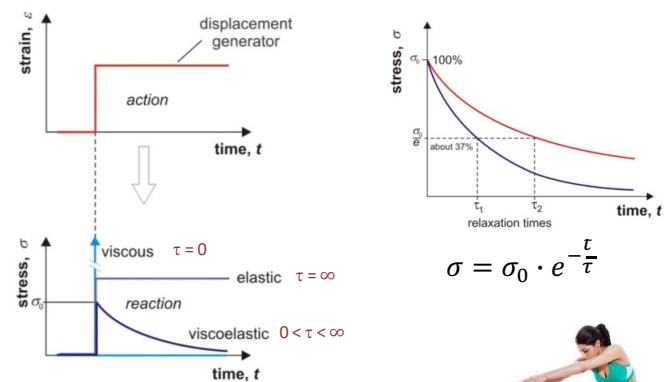
Dashpot: ideal viscous (Newton) body

1. Upon stretch, the extension of the spring is slowed down by the dashpot.
2. Extension stops when the elastic spring force equals the external force.
3. When the external force is quenched, the contraction of the spring is slowed down by the dashpot.

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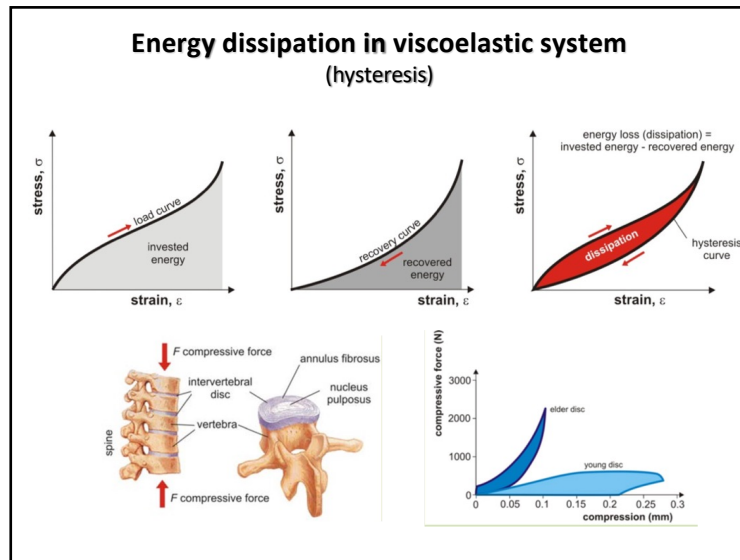
## Stress-relaxation in viscoelastic system

Decrease in stress while strain remains constant

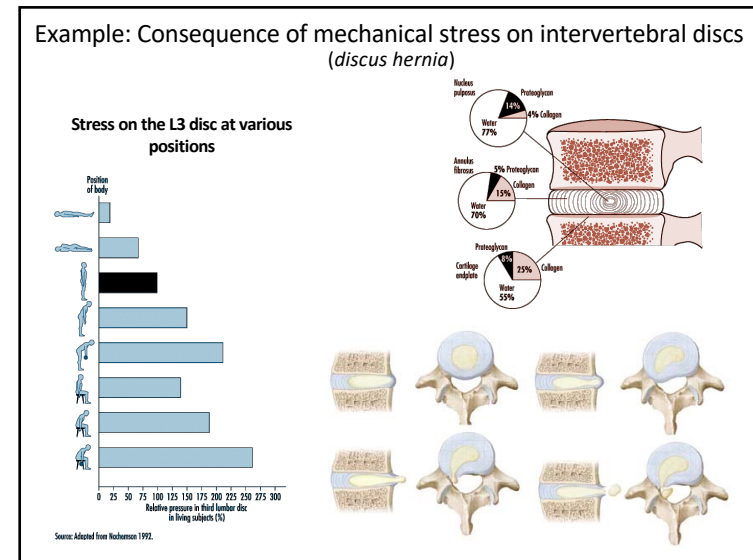


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### Flashback: What did you learn about US propagation....?

#### In wich types of tissue does sound propagate faster?

The acoustic properties of each tissue are characterized by their stiffness

|               | $E$ (GPa)          | $K$ (GPa <sup>-1</sup> ) | $c_{sound}$ (m/s) |
|---------------|--------------------|--------------------------|-------------------|
| Cortical bone | 18                 | 0.05                     | 3600              |
| Muscle        | $7 \times 10^{-5}$ | 0.38                     | 1568              |

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

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

compressibility

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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