Medical biophysics 2.

Biomechanics
Biomolecular and tissue elasticity

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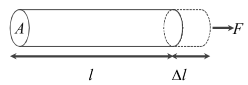
Basics of mechanics

Hookean elasticity

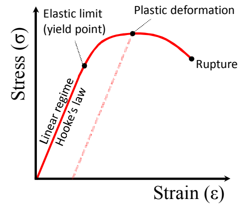


$$\frac{F}{A} = E\frac{\Delta l}{l}$$

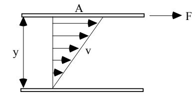
F = force
A = cross sectional area
l = rest length
Δl = extension

F/A = σ = stress (N/m² = Pa)
$\Delta l/l$ = ε = strain (dimensionless)
E= σ / ε Young's modulus (Pa)

Stress-strain diagram



Viscosity



$$\frac{F}{A} = \eta\frac{\Delta v}{\Delta y}$$

F = shear force
A = fluid surface
η =viscosity

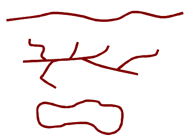
y = distance between surfaces
v = flow velocity

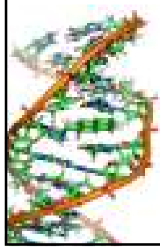
F/A = shear stress
Δv/Δy = velocity gradient (strain)

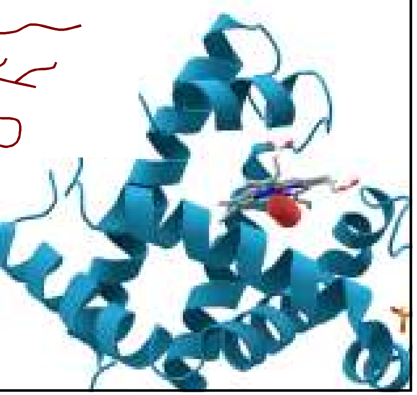
Biomolecules are polymers

Common feature: **Linear primary structure (protein, DNA)**
Strong bonds between monomers (covalent)
Weaker interactions between distant region of polymer chain

1. Linear
DNA, protein, cellulose
2. Branched
glycogen
3. Cirkular
mt DNA



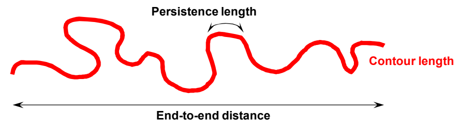




What is the shape of polymers?

AFM image of dsDNS

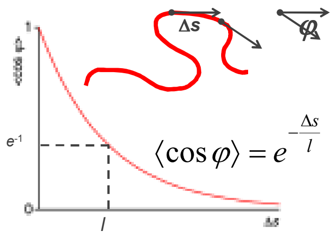
Parameters to describe the shape of a polymer



Contourlegth (L): Full lenght of the chain

End-to-end distance (R): Distance between chain termini.

Persistence length (*l*) : describe the persistence of chain orientation.

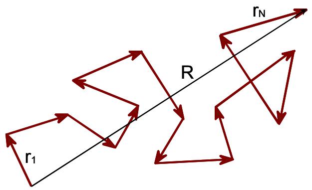


$$\langle \cos\varphi \rangle = e^{-\frac{\Delta s}{l}}$$

Shorter persistence length polymers are more flexible.

The shape of a biopolymer resembles the „random walk"

„Random" -walk



R = end-to-end distance
r_i = elementary vector

"Square root relation":

$$\langle R^2\rangle = Nl^2 = Ll$$

$\langle R^2\rangle$ = root mean squares end-to-end distance
N = number of elementary vectors
l = mean vector length (persistence length)
$Nl = L$ = contourlength

$$\langle R\rangle = \sqrt{lL}$$

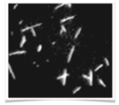
To double the average end-to-end distance of an entropic polymer, the contourlength need to be increased four times.
Shorter persistence length results in a more flexible polymer, which folds into a compact state with shorter end-to-end distance.

7.th lecture: Diffusion → $\langle x\rangle = \sqrt{2Dt}$

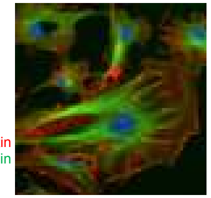
Biopolymer classification based on flexibility

l = persistence length
L = contour length

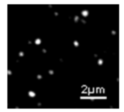
Rigid
$l >> L$



Semiflexible
$l \approx L$



Flexible
$l << L$



Are biopolymers flexible?

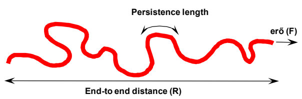
Yes, but Hooke's law is not valid! Non-linear elasticity.

Entropic elasticity

Thermal energy (k_BT) excites bending movements in the chain

The chain's disorder (entropy) increases

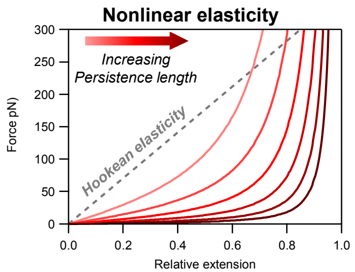
The chain shortens



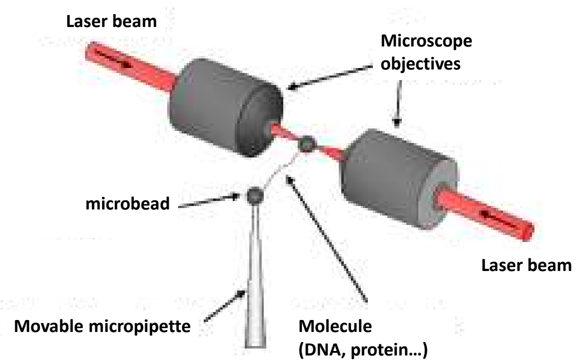
Force is needed to stretch an entropic chain

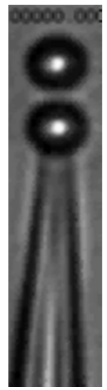
$$F \sim \frac{k_BT}{l}\cdot\frac{R}{L} + \left(\frac{R}{L}\right)^{a}$$

F = force
l = **persistence length**
k_B = Boltzmann constant
T = absolute temperature
L = contour length
R = end-to-end distance
R/L = relative extension



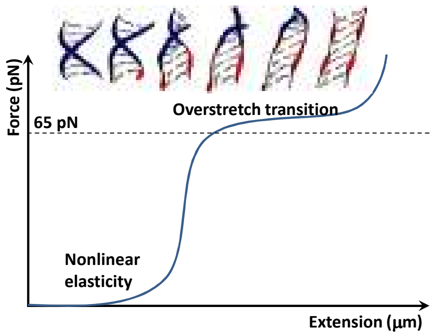
How to stretch single molecules?
Optical tweezers



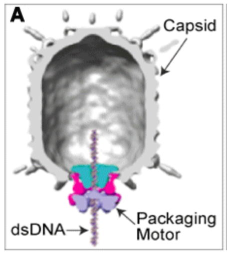


http://glass.phys.uniroma1.it/dileonardo/Applet.php?applet=TrapForcesApplet

Stretching dsDNA with optical tweezers

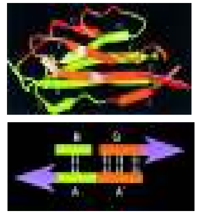


DNA packaging of bacteriophage



F = 55 pN

Unfolding of globular protein with force



Bases of mechanical stability:

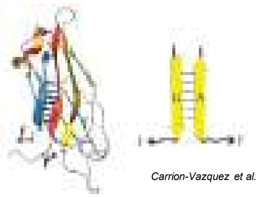
H-bridges between the first and last ß-strands of the domain

Tertiary structure determines the mechanical stability of a protein

H-bridges perpendicular to the force: High stability, unfolding forces above 200 pN

Carrion-Vazquez et al. 2000

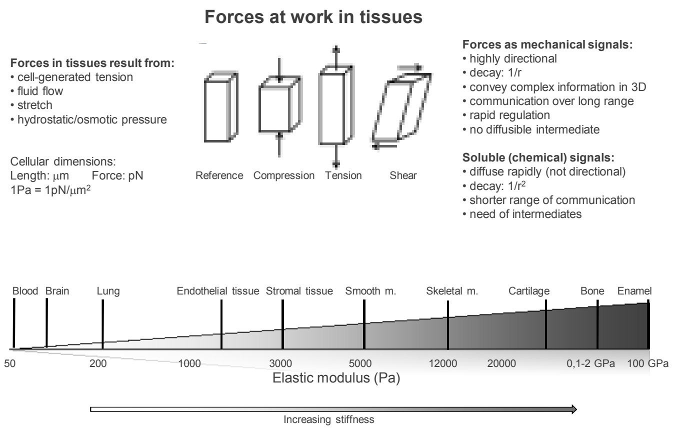
H-bridges parallel to the force: low stability, unfolding forces under 100 pN



Carrion-Vazquez et al. 2000

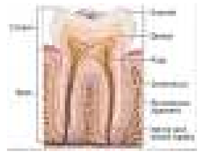
600 seconds brake

Biomechanics at the cellular level



Hard tissues

Tooth tissues

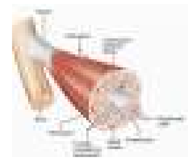


Bone

Major components:
collagen (organic),
apatite (inorganic)

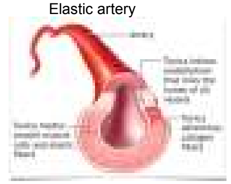
Soft tissues

Skeletal muscle



Passive mechanics: titin, desmin
Active mechanics: actin, myosin

Elastic artery



collagen, elastin

Ligament

Tendon

Cartilage

Collagen, proteoglicans (water)

Flashback: What did you learn about ultrasound propagation….?

What is the speed of sound in different tissues?

Acoustic properties of various tissues are determined by their flexibility

	E (GPa)	κ (GPa^{-1})	c_{sound} (m/s)
Bone	18	0.05	3600
Muscle	7x10^{-5}	0.38	1568

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

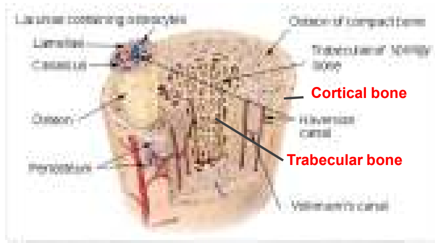
$$\kappa = \frac{-\Delta V/V}{\Delta p}$$

strain (numerator), stress (denominator), compressibility (κ)

Greater Young's modulus, faster sound speed

Bone

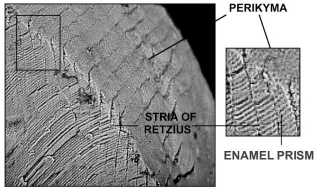
Due to the different structure of bone tissue along the cross section of long bones, the **Young's modulus distribution is anisotropic**. Denser cortical bone has greater Young's modulus vs. the trabecular bone..
Young's-modulus: 5-20 GPa
Decalcified bone (acid treatment): flexible
Removal of organic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

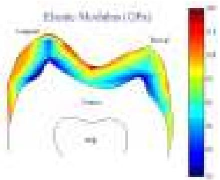


Calculation:

Bone has a Young's modulus of about 18 GPa. Under compression, it can withstand a stress of about 1.60x10^{8} Pa before breaking. Assume that a femur (thigh-bone) is 46 cm long, and calculate the amount of compression this bone can withstand before breaking.

Tooth enamel



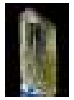


Structural unit: enamel prism (rod)

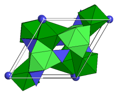
Composition: 92% Hydroxy-apatite (HAP)

Stiff, hard, brittle

The hardest material in human body

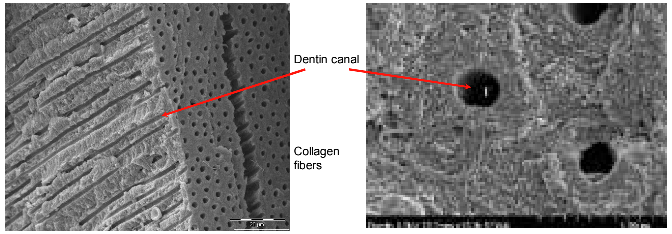


$Ca_{10}(PO_4)_6(OH)_2$
$Ca_{10}(PO_4)_6F_2$



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

Dentin



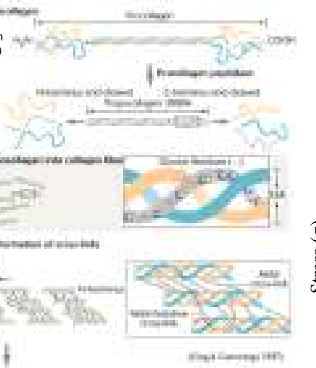
Composition: 35% organic material (collagen) + water, 65% hydroxy-apatite

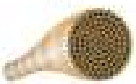
Structure: collagen matrix with attached hydroxy-apatite crystals

Biomechanics: moderately hard, very strong and tough and flexible

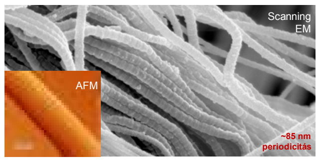
Collagen

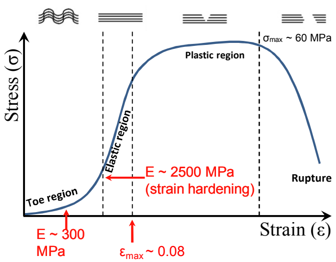
1400 residues/chain
3 chains (tiple helix)
Glycine (1/3)
Proline (1/10)
Hydroxyproline
Hydroxylysin





Posttranslational modification is necessary for tropocollagen polymerization
Hydroxylation of lysin and prolin residues requires vitamin-C as cofactor!



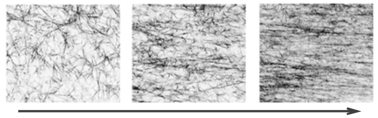


Moderately elastic and tough, but soft

Collagen responses to force

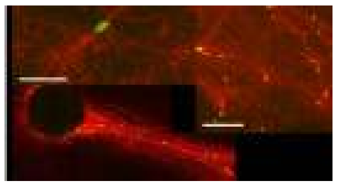
(forces in the extracellular matrix)

Stretched collagen gel



Individual fibers in a stretched collagen matrix align to the direction of stress. The structural alignment of the extracellular matrix depends on the stress.

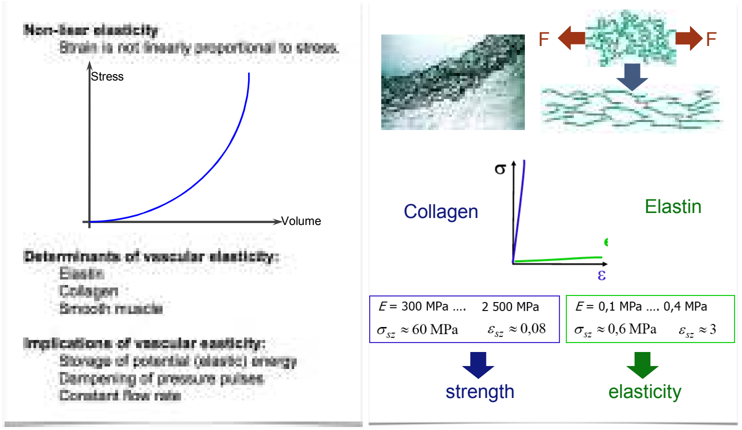
Cells in collagen matrix



Green: nucleus
Red: collagen fibers

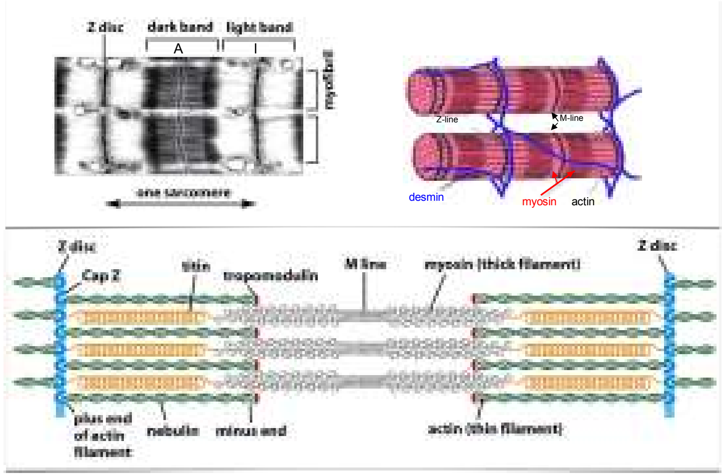
The presence of cells in a collagen network induces stress variations and modifies the network texture in its vicinity.

Biomechanics of elastic arteries

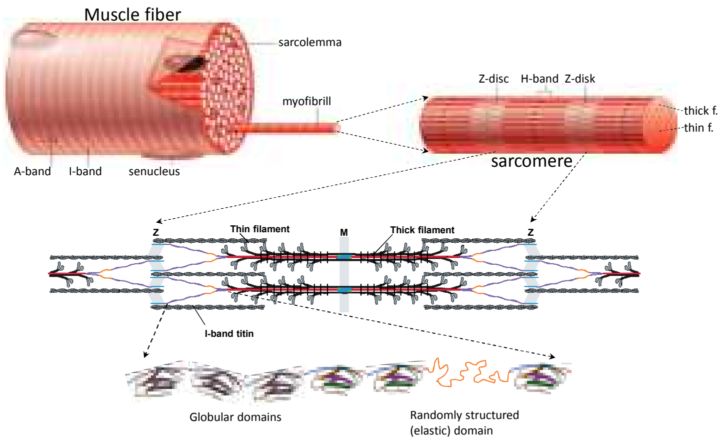


Sarcomere

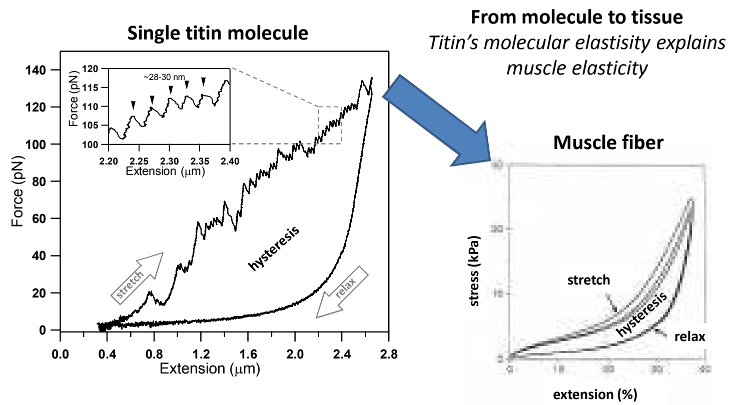
structural unit of sceletal muscle



Titin: elastic filament of the sarcomere

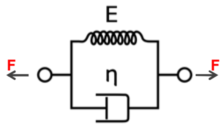


Titin is the main determinant of muscle elasticity



Visco-elasticity

(mechanical model)



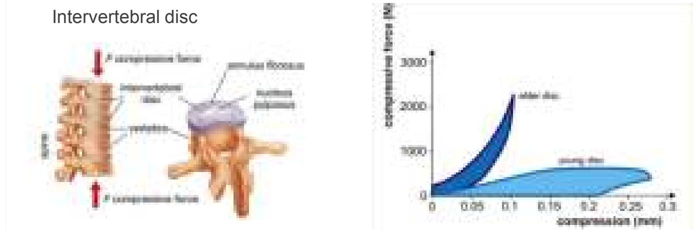
model: parallel connection of a spring and a dashpot (Kelvin-body)

Spring: ideally elastic (Hooke) body
Dashpot: ideally viscous (Newton) body

Visco-elasticity

(examples)

Intervertebral disc

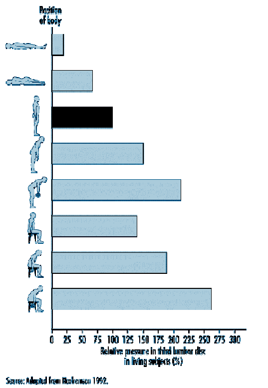


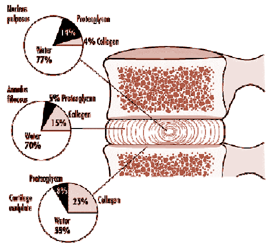
Periodontal ligament

Running shoe

Example I: Consequences of increased mechanical stress on intervertebral discs (*discus hernia*)

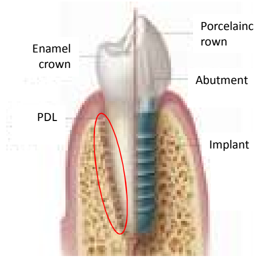
Relative sress on L3 intervertebral disc at various positions

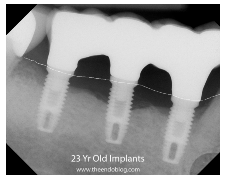




Example II: Implants vs nastural tooth

PDL makes the difference!





Absence of PDL result in :

- **loss of masticatory force perception**
- **loss of visco-elastic (damper) effect**
- **loss of force sensory mechanisms**
- **No implant movement**

Implant is in direct contact with bone tissue

⬇

Increased compressive stress

⬇

Bone loss (0.2 mm / year)
Loss of gingival height

Implants ⟺ Root Canal Treatment

Calculations

To stretch a relaxed biceps muscle 3 cm requires a force of 25 N. To do the same stretch of a contracted muscle at its maximal tension requires a force of 500 N. Find the Young's modulus for both relaxed and tense muscle tissue. Assume the biceps is a uniform cylinder of length 20 cm and diameter 6 cm. (59 kPa, 1.18 MPa)

Collagen fiber is stressed with 12 N force. The cross-sectional area of the fiber is 3 mm^2, its coefficient of elasticity is 500 MPa. Give the percentage of relative extension. (0.8 %)

The length of an elastic thread used in orthodontics is 6 cm, its cross-sectional area is
1 mm^2, its coefficient of elasticity is 5 MPa. We extend the thread with 40 %. How large is the retracting force and what is the amount of elastic energy stored in the thread? (F = 2 N, E = 24 mJ)