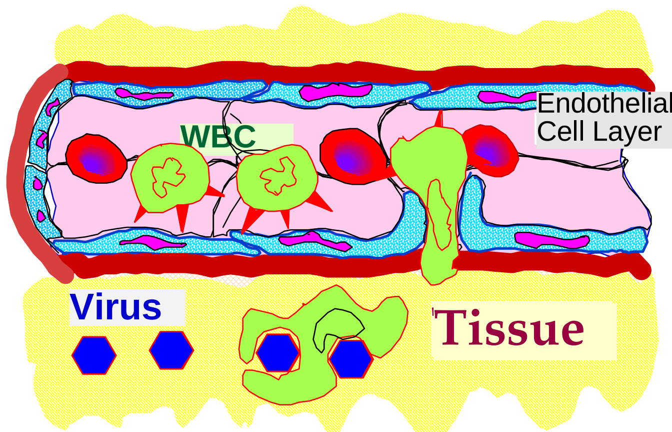
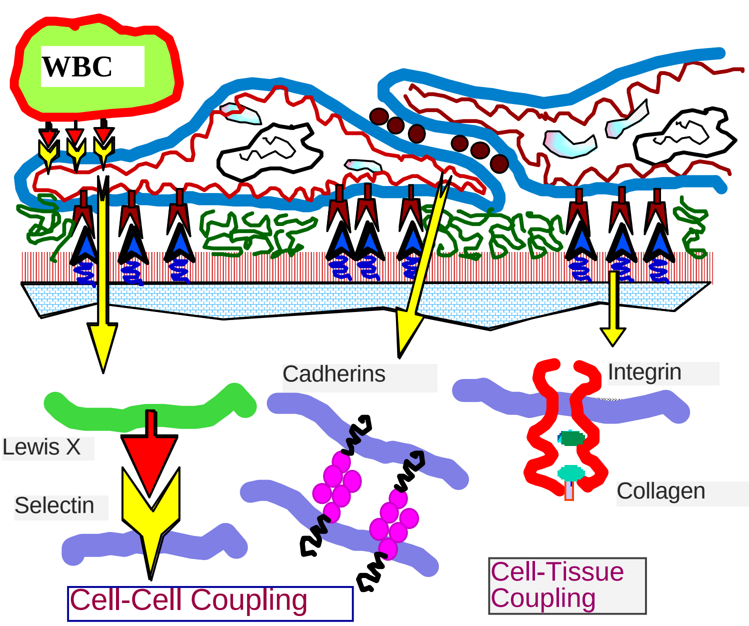
Fight of white blood cells against Intruders

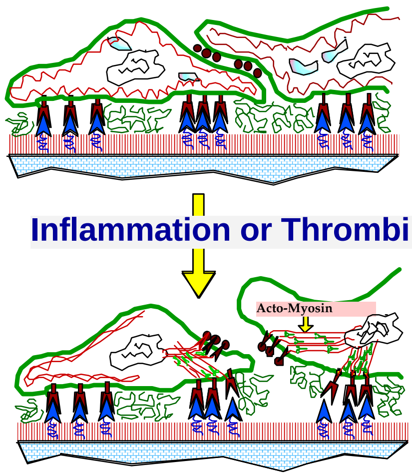
Cell Visco



Two fundamental processes involved
Cell Adhesion + Chemomechanics



Chemo-mechanical opening of Gaps



Ground State

Closed Cell Monolayer

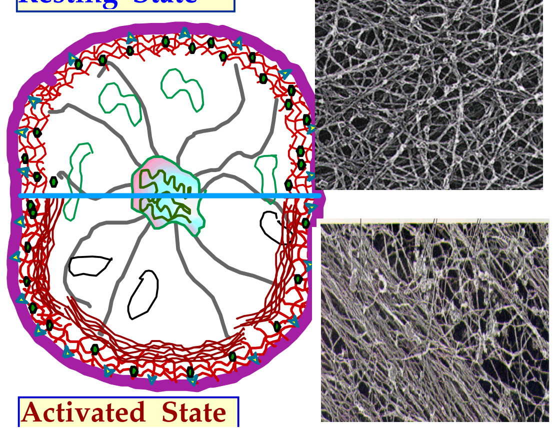
Inflammation or Thrombin

Activated State

Activation of Actin- Myosin Motor

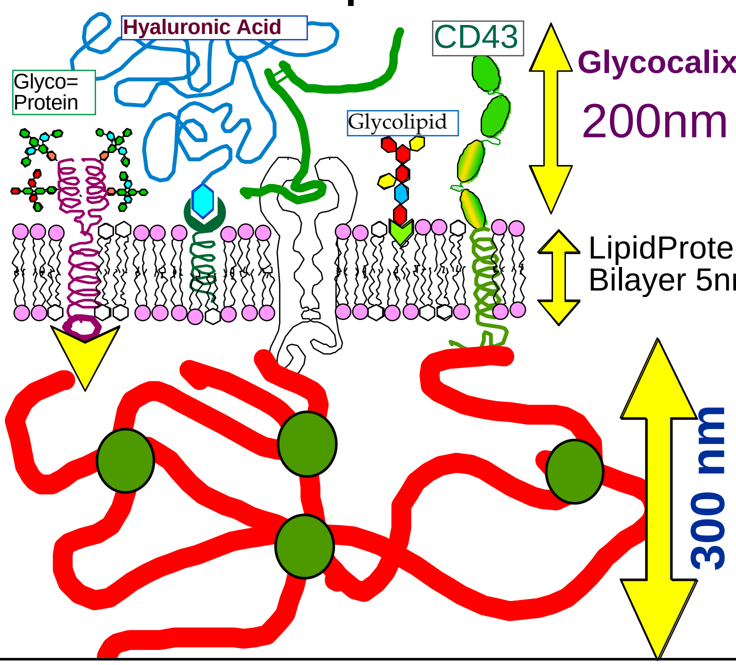
Transition from randomly organized network of actin cortex to fiber enforced network

Resting State



Activated State

The composite Shell

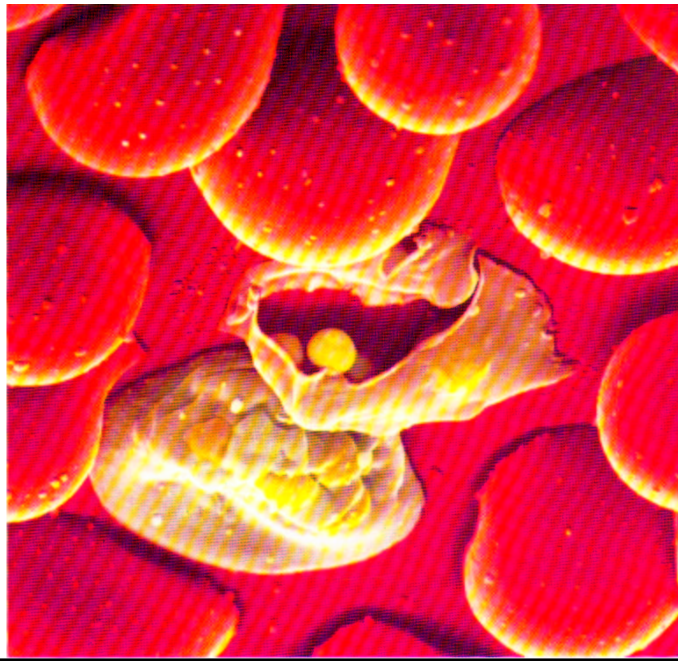


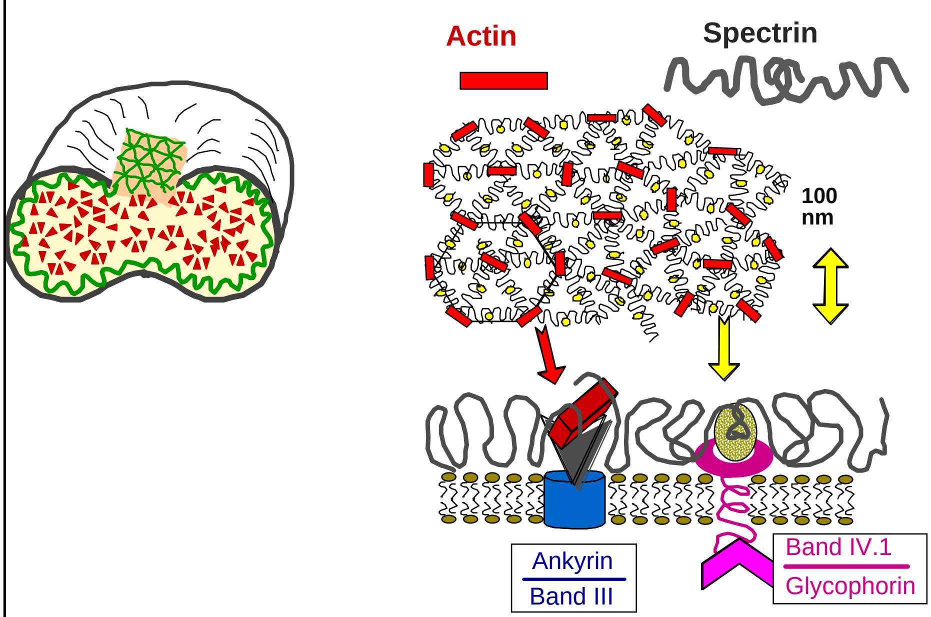
Can we ever understand such complex systems on the basis of physics ?

Does nature make use of physical principles to control such multi-component systems ?

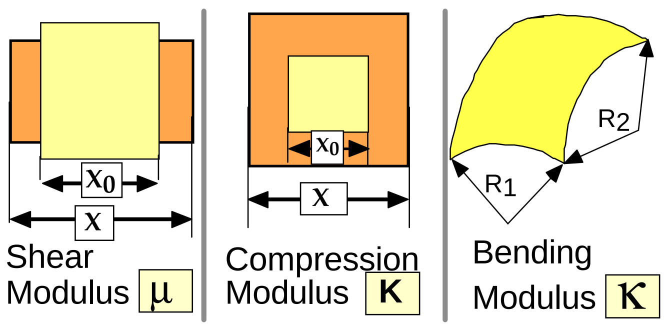
A possible Answer

Hierarchical Design and Principles of Viscoelasticity




Actin
Spectrin
100 nm
Ankyrin
Band III
Band IV.1
Glycophorin

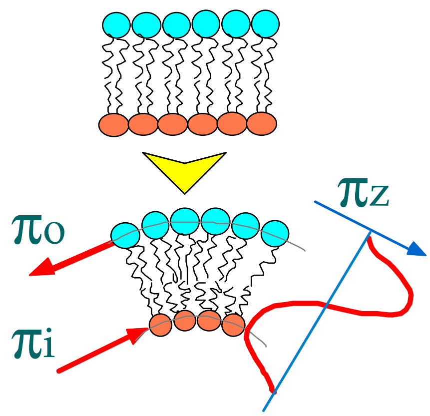
Erythrocytes are ideal visco-elastic bodies



Unique Combination of Elastic Moduli

Material	Shear [dyne/cm]	Bending [erg]	Compression [dynes/cm]
Polyethylene	$3 * 10^{+2}$	$2 * 10^{-10}$	$5 * 10^{+3}$
Erythrocyte	$6 * 10^{-3}$	$5 * 10^{-13}$	$1 * 10^{+3}$

Bending energy Concept (Helfrich 1972)



Gradient of Tension π

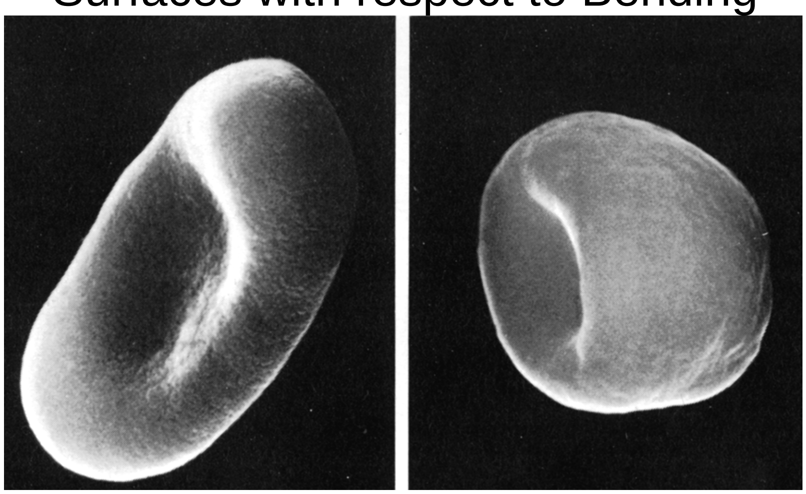
Bending Moment

$M = \int z\,\pi(z)\,dz$

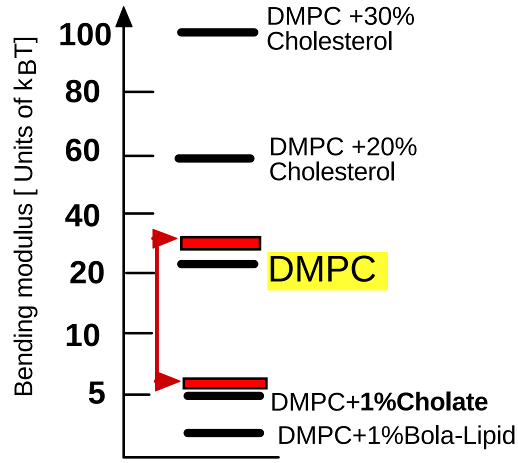
Bending Energy (Hooks Law)

$W_{ela} = 1/2 \oint \left(\kappa \Delta u^2 + \gamma \nabla u^2 - C_0\right) dO$

Cell Shapes areMinimum Surfaces with respect to Bending



Selection Membrane Bending Moduli



Non-classical Feature :
Undulation-induced Entropy-Elasticity

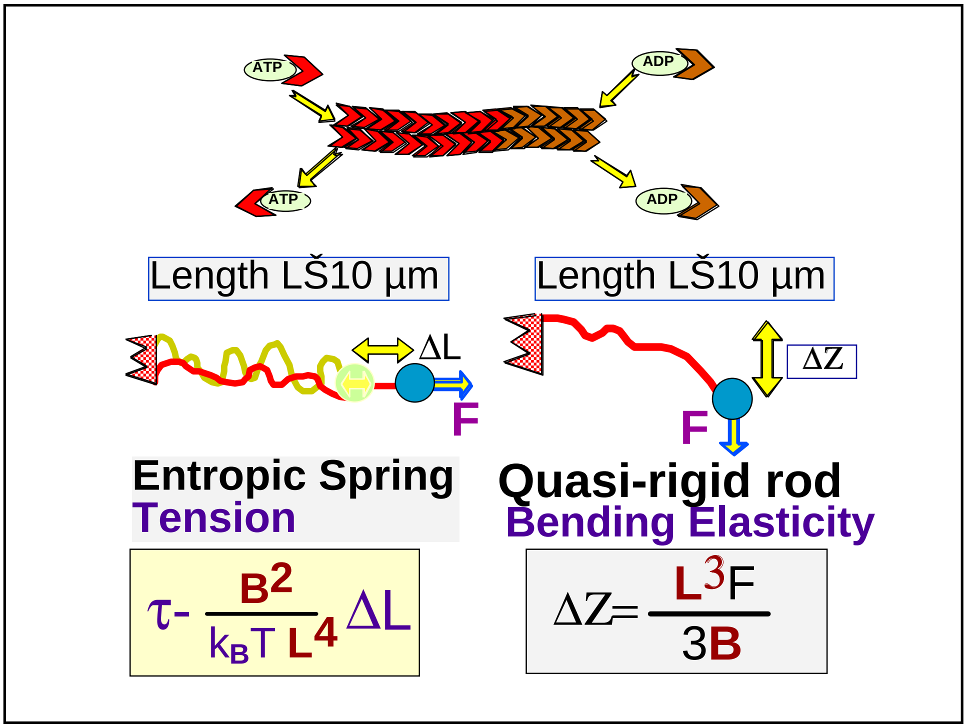
$$u(\mathbf{r},t) = \sum_q u_q(t) \exp\{\mathbf{qr}\}$$

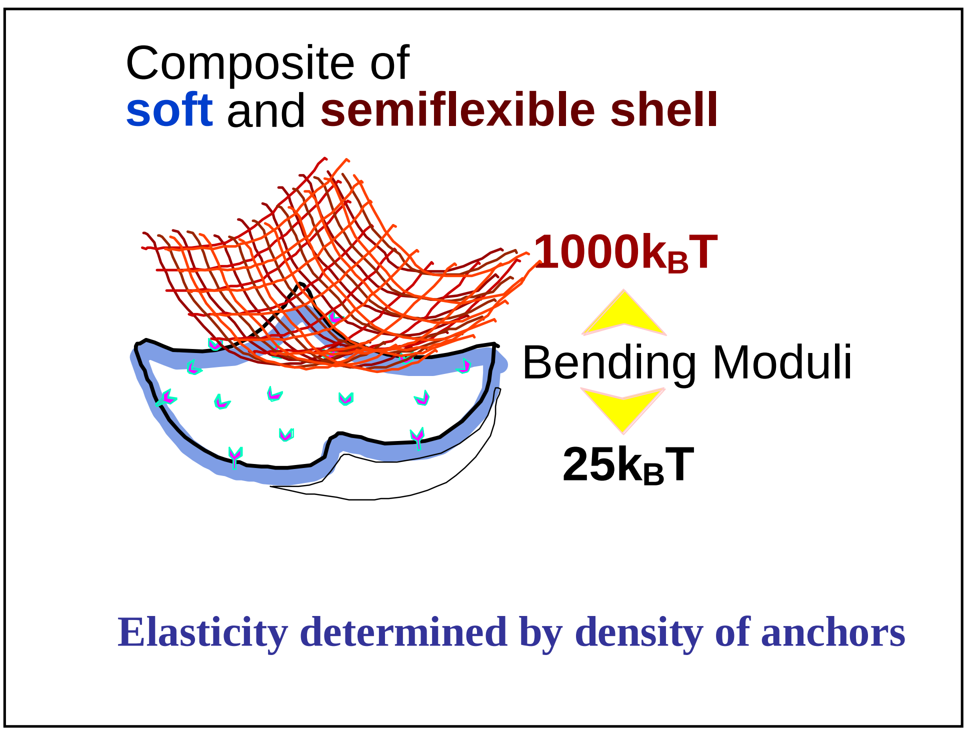
Roughness

$$\langle u^2 \rangle = \frac{k_B T}{K_c} R^2$$

K_c: 20 $k_B T$

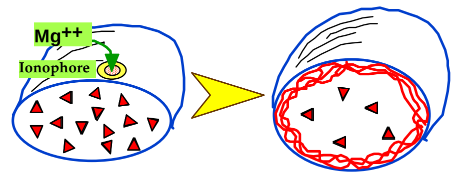
R-1µm → u- 40nm

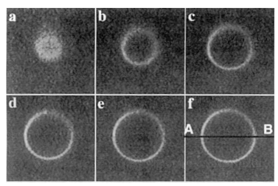

ATP
ADP
ATP
ADP
Length LŠ10 µm
Length LŠ10 µm
ΔL
F
ΔZ
F
Entropic Spring
Tension
Quasi-rigid rod
Bending Elasticity
τ- B2 / kBT L4 ΔL
ΔZ= L3F / 3B


Composite of
soft and semiflexible shell
1000kBT
Bending Moduli
25kBT
Elasticity determined by density of anchors

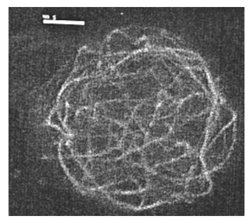
Self assembled Actin network in giant vesicles

Laurent
Limozin





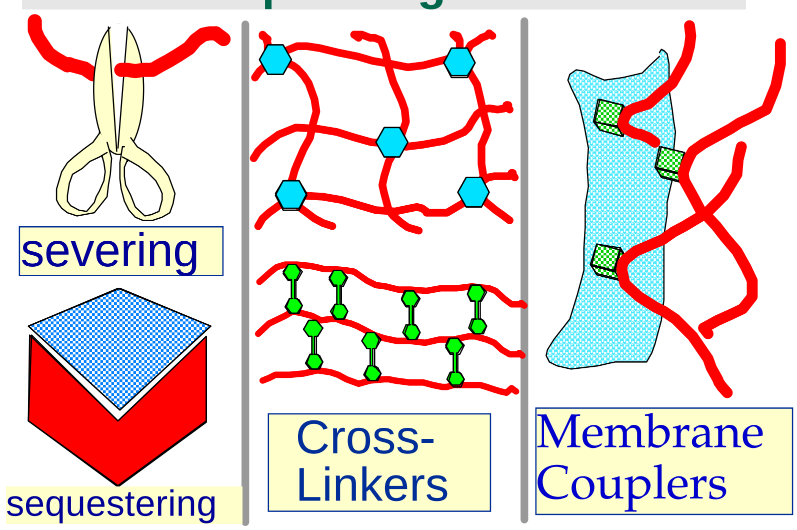
Entangled network



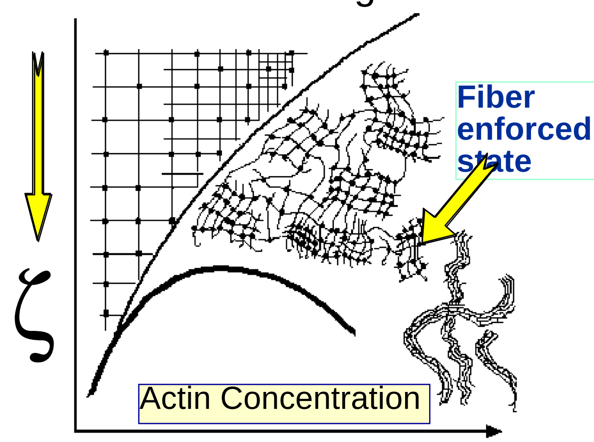
Actin/α-Actinin

How to make smart networks

Actin Manipulating Proteins



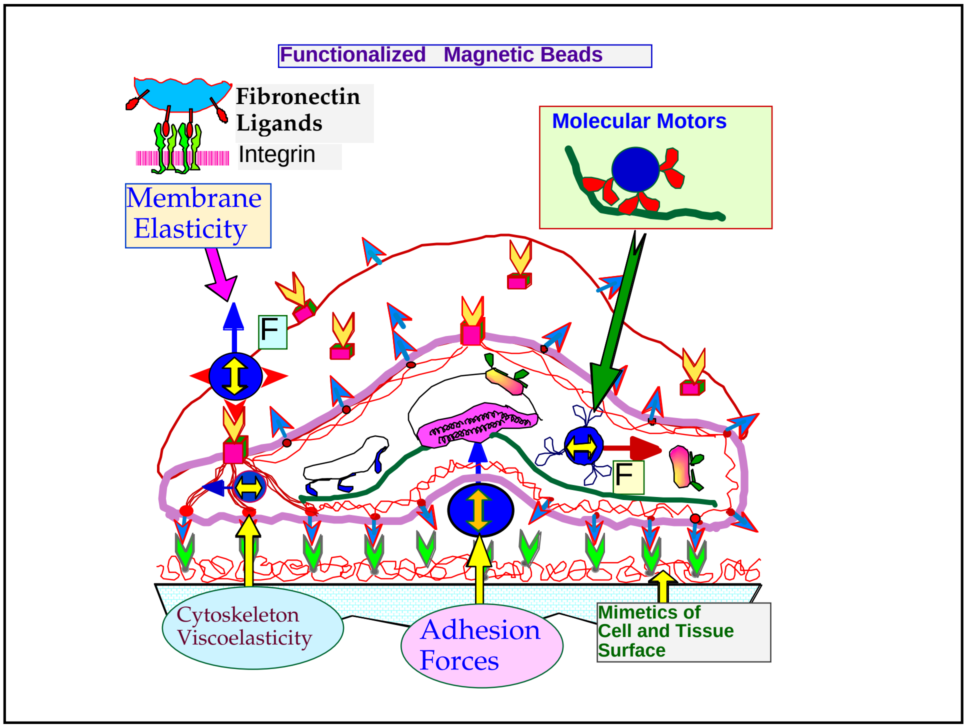
Universal Phase Diagram of Actin -Gel

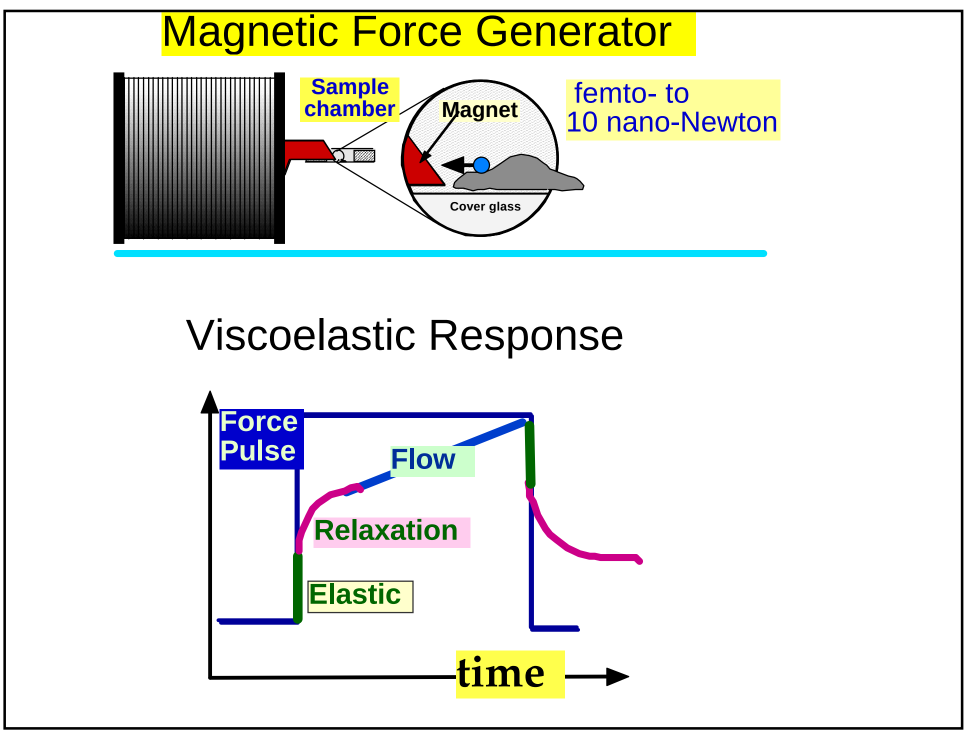


Example a-Actinin

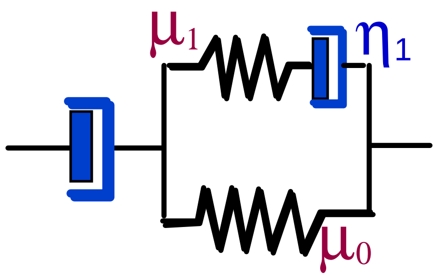
Bundle Formation during Cell Activation
as Transition of Hetero-Gel ???

Microrheometry of Cells


Functionalized Magnetic Beads
Fibronectin
Ligands
Integrin
Molecular Motors
Membrane
Elasticity
F
F
Cytoskeleton
Viscoelasticity
Adhesion
Forces
Mimetics of
Cell and Tissue
Surface


Magnetic Force Generator
Sample
chamber
Magnet
Cover glass
femto- to
10 nano-Newton
Viscoelastic Response
Force
Pulse
Flow
Relaxation
Elastic
time

Mechanical Equivalent Model



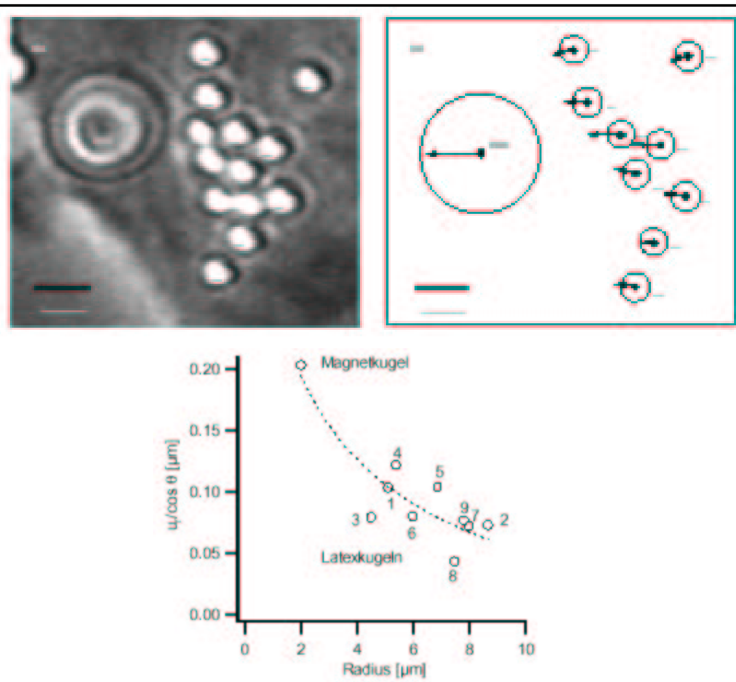
Elastic Moduli

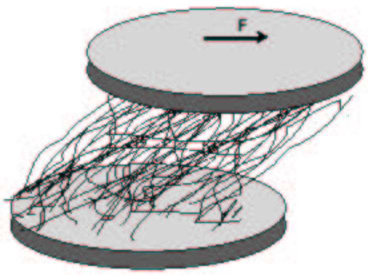
Viscosity

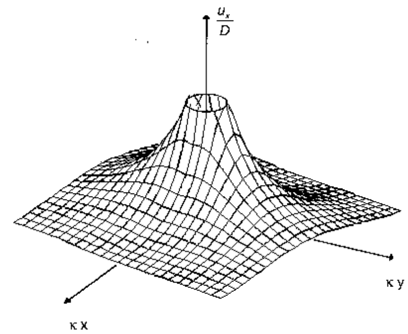
Active Forces

Theory of Elastic Shells

Membrane Viscoelastic Moduli





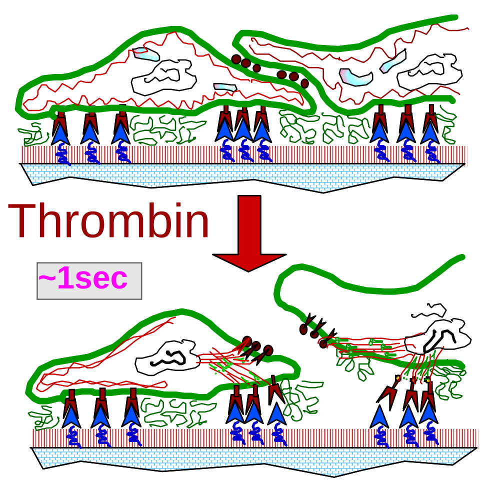


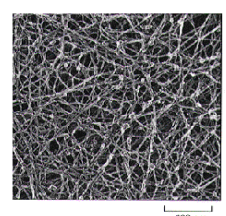
$$\Delta\vec{u} + \frac{1+\sigma}{1-\sigma}\vec{\nabla}\vec{\nabla}\vec{u} - \kappa^2\vec{u} = \frac{\vec{F}\delta(\vec{r})}{\mu^*}$$

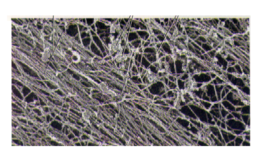
K=screening length ≈1-5µm

Elastcity a local quantity

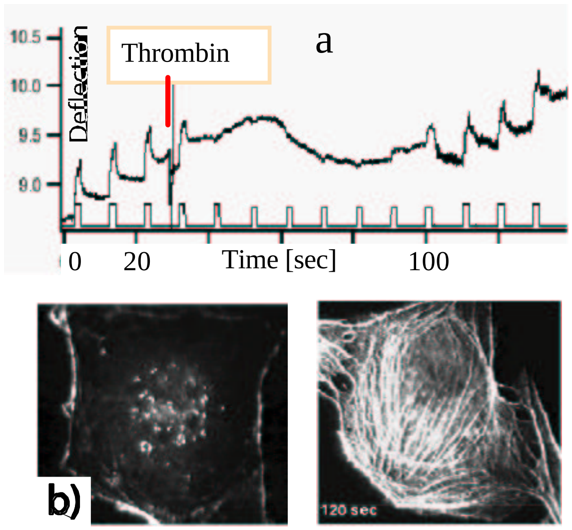
Reconsider Activation of Cells





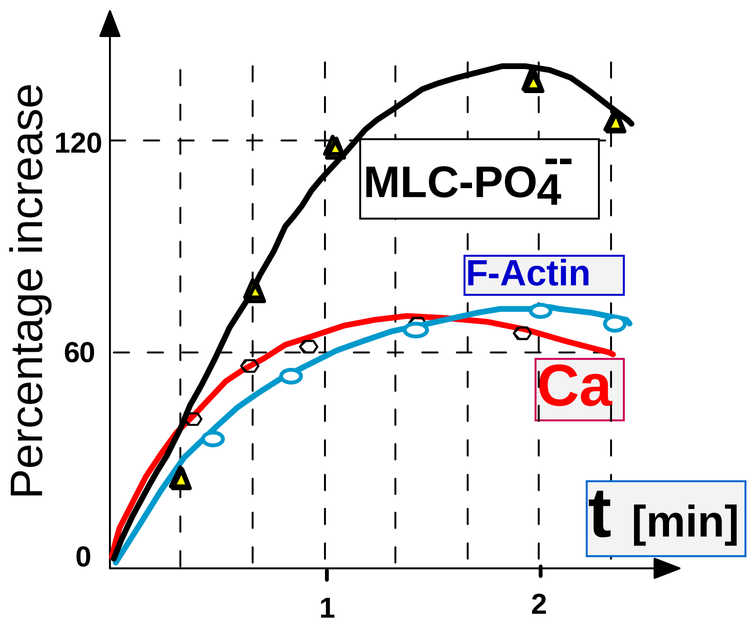


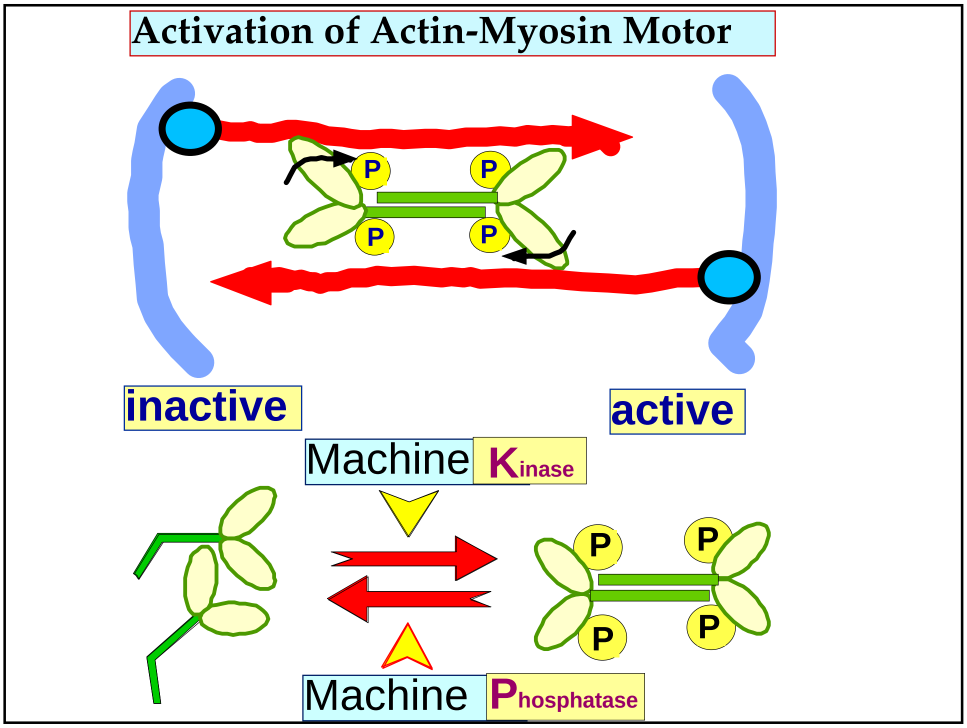
Real Time analysis by microrheometry



Spontaneous Fiber Formation

Thrombin induced reorganisations



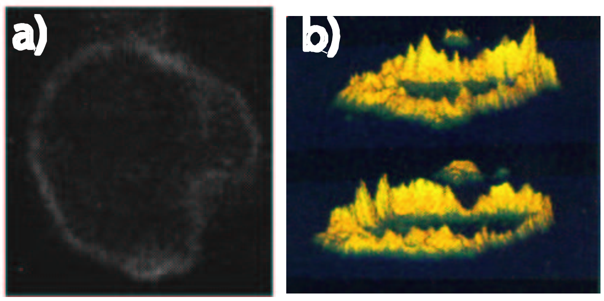


Viscoplasticity of Cells

Essential for intracellular trafficking

Cells as Viscoplastic Bodies

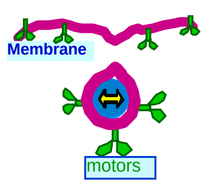
Dictyostelia

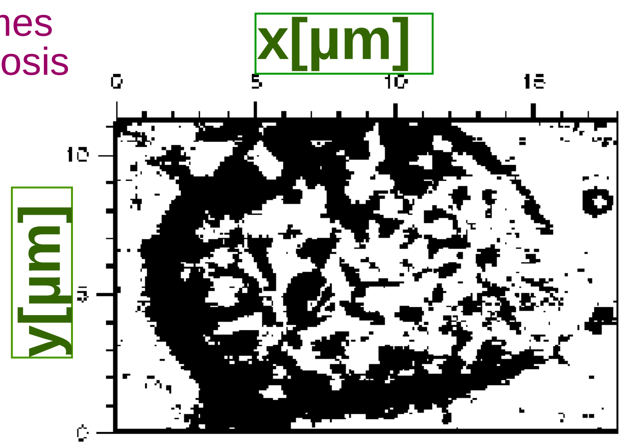


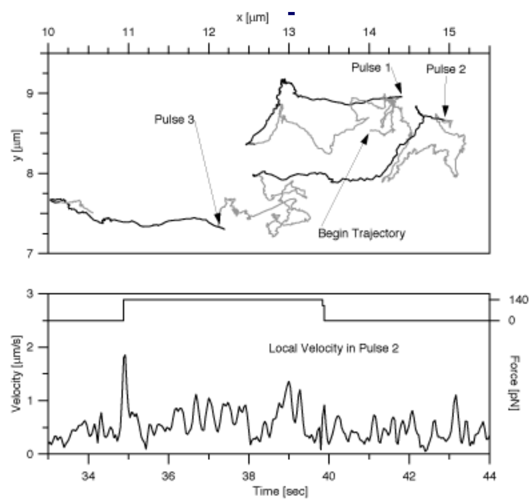
Actomyosin

Shell

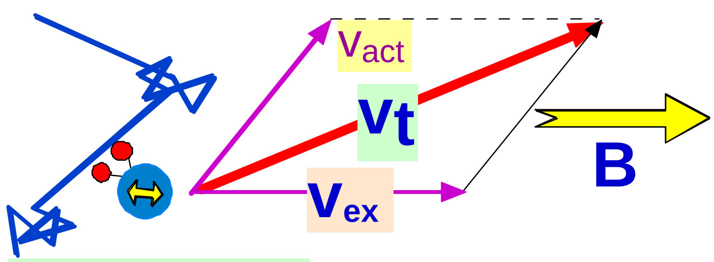
Magnetosomes
by Phagocytosis







Local Measurement of Force



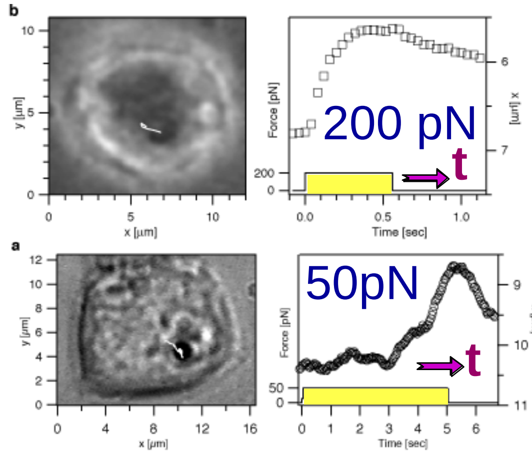
$V_{ex} = \eta_{loc} F_{ex}$

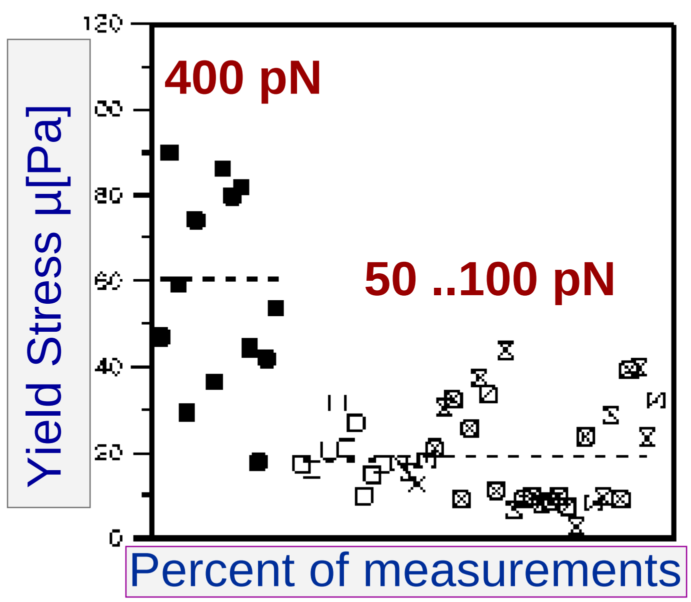
Yields η_{loc}

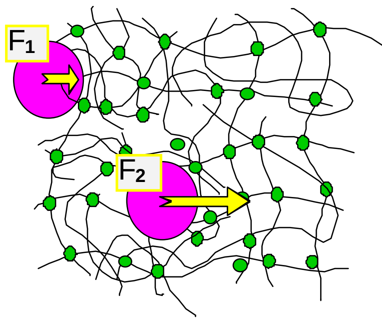
$$F_{act} = \frac{V_{act}}{\eta_{loc}}$$

Forces generated by Kinesin/Microtubuli in Dictiostelia ≈30 picoNewton

Force dependent viscoelastic response







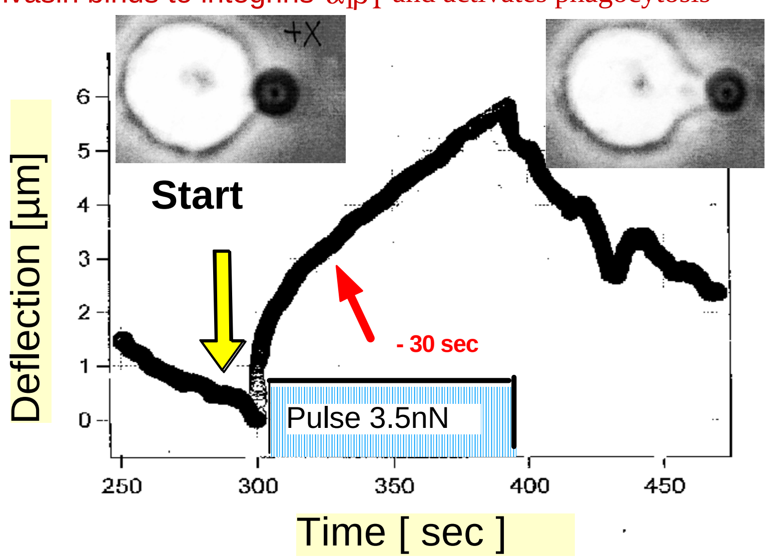
Weak forces induce statistical bond breakage

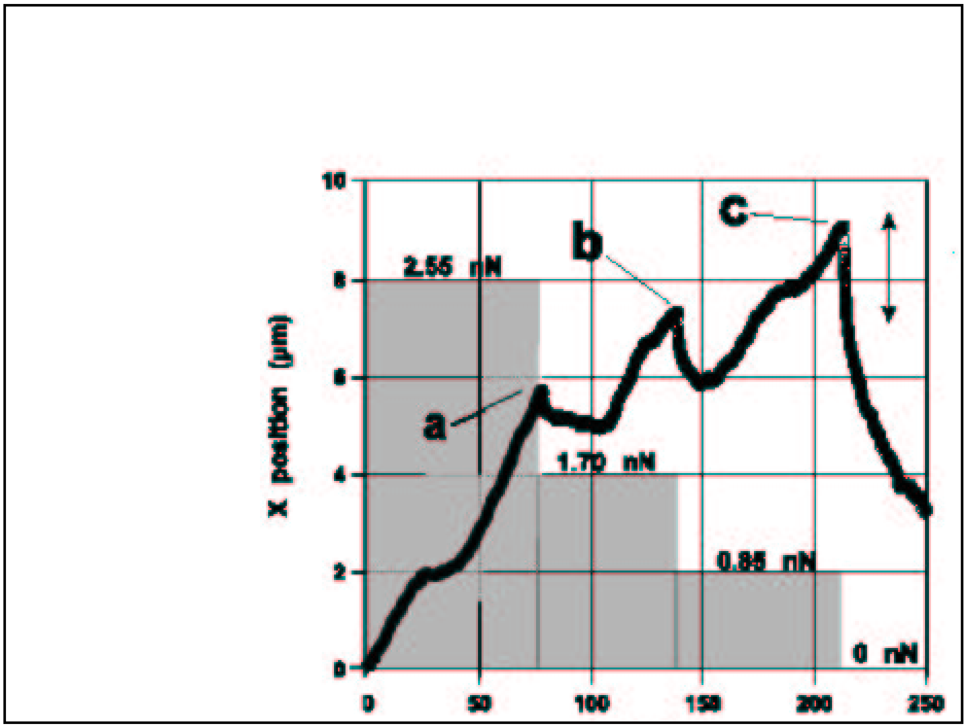
$$\mu(t,\sigma)=\mu_{O(t)} \exp\left\{\frac{\Delta G - \xi^2\sigma}{k_B T}\right\}$$

Cells as adaptive viscoelastic bodies

Laurent Vonna

Invasin binds to integrins $\alpha_i\beta_1$ and activates phagocytosis




10
8
6
4
2
0
X position (µm)
2.55 nN
1.70 nN
0.85 nN
0 nN
a
b
c
0
50
100
150
200
250