Physics of adherent cells, Part 1

Force & movement are central to the behaviour of biological systems.

Animal cells are very sensitive to environmental cues

Differentiation of stem cells can be guided by the mechanical or adhesive properties of the substrate

→ exciting regenerative medicine
→ fundamentally not well understood

Physics : ×  How can the cell know the properties of the surroundings?

- × actively generate a force
- × transmit force to surroundings
- × sense response

× Soft matter
- liquid crystals
- colloidal dispersions
- emulsions
- fluid membranes
- gels

"Soft" interaction energies $\sim kT$ ⇒ sensitive to thermal fluctuations

Biology : × active remodelling controlled by
- genetics
- signalling networks

⇒ active matter

Cytoskeleton (CSK)
- f-actin
- microtubules
- intermediate filaments

Extracellular matrix
- gel-like network
- fibrous proteins
  - × collagen
  - × fibronectin

— adhesive contacts

Cell response to mechanical perturbations

Short timescale (s): elastic (passive)
Long —"— (min →): active reorganization of CSK

Stress & strain $\underset{F/A}{\sigma} = E \underset{L/L_0}{\varepsilon}$ E - Youngs modulus, stiffness / rigidity (spring constant)

$[\sigma] = [E] = Pa$

typical $E \sim 10\,kPa$

length scale of deformation ~ membrane thickness $l \sim 10\,nm$ macromolecule

⇒ Strain energy $\sigma \cdot l^3 \sim 10\,nm \cdot 10^{-16} \cdot 10^{4} N \sim 10\,nm\,pN$
$kT = 4.1\,nm\,pN$
≈ Thermal noise

In addition: "biological noise"

For example force generation of × molecular motors
× actin polymerization

Soft matter

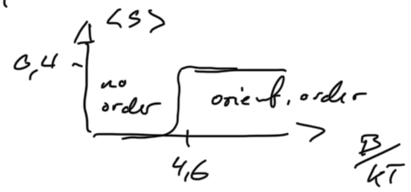
<u>Liquid crystals</u>
- They move around like fluid
- They can align

No direction ⇒ order parameter is even function of angle

$$S_i = \frac{1}{2}\left(3\cos_i^2 - 1\right)$$

Energy of element $U_i = B \langle S \rangle S_i$ $\langle S \rangle$ is mean orient.
B interaction coeff

$$\langle S \rangle = \frac{1}{Z} \int d\Omega \, S_i \, e^{-U_i/kT}$$



<u>Polymers</u> single polymers DNA, actin, proteins, microtub.

Flexible: No energy penalty for bending ⇒ purely entropic
· random walk  $R^2 \propto N$ — number of monomers (MSD ∝ t)

(synthetic polymers)

Semiflexible

Actin, DNA ... bend on longer length scales L
50 nm

$\Rightarrow$ Energy $\propto$ curvature^2 $\quad H_b = \frac{K}{2}\int ds \left(\frac{\partial^2 R}{\partial s^2}\right)^2$ $\quad$ s - distance

$L \sim \sqrt{R}$

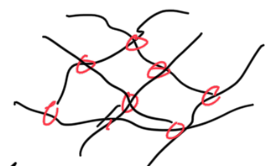
Persistence length $\quad \xi \sim \frac{K}{kT}$ $\quad$ K - bending modulus

$l < \xi$: stiff, rod like

$l > \xi$ $\quad$ excluded volume RW: $R \sim N^{3/5}$ $\quad$ (not $N^{1/2}$)

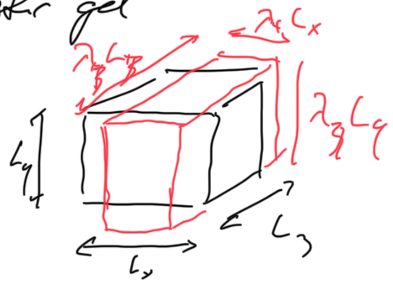
Polymer gels

Actin & microtubules crosslink in CSK



Timescale $t <$ tens of sec
crosslinks are rigid $\Rightarrow$ elastic gel

Flexible polymers (RW, entropic)



$$\varepsilon_i = \lambda_i - 1 \quad (i = x, y, z)$$

incompressible : $\lambda_x \cdot \lambda_y \cdot \lambda_z = 1$

Free energy $\quad F \propto \frac{kT}{2}\left(\lambda_x^2 + \lambda_y^2 + \lambda_z^2 - 3\right)$

small ε $\quad \sigma \propto \rho kT \cdot \varepsilon$ $\qquad$ ($P \propto \overset{N/V}{\rho} kT$

large ε $\quad$ nonlinear $\qquad$ $\Delta P \propto \rho kT(\Delta V + \dots)$)

Semiflexible polymers

small $\varepsilon \propto \frac{\sigma}{\xi}$ $\quad$, large nonlinear

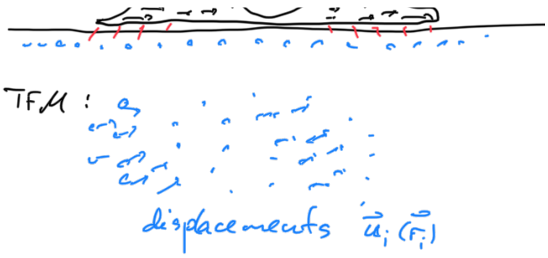
Longer time-scales : Polymer networks continuously remodel
$\Rightarrow$ crosslinks disappear
$\Rightarrow$ creep / flow

Elasticity

smooth displacement field $\quad \vec{u}(\vec{r})$

strain tensor :

$$u_{ij}(\vec r) = \frac{1}{2}\left(\frac{\partial u_i(\vec r)}{\partial r_j} + \frac{\partial u_j}{\partial r_i}\right) + NL$$



Free energy per unit volume

$$f_e = \frac{K}{2}\left(\sum_i u_{ii}\right)^2 + \mu \sum_{ij}\left(u_{ij} - \frac{1}{3}\delta_{ij}\sum_l u_{ll}\right)^2$$

Youngs modulus : $E = \frac{9K\mu}{3K+\mu}$

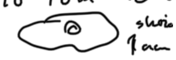
Poissons ratio $\nu = \frac{3K-2\mu}{6K+2\mu}$ tissue : $\nu = \frac{1}{3} \to \frac{1}{2}$

Incompressible materials $\frac{K}{\mu} \to \infty$, $\boxed{\nu = \frac{1}{2}}$

$$\sigma_{ij} = \frac{\partial f_e}{\partial u_{ij}} , \quad f_e = \frac{1}{2}\sum_{ij}\sigma_{ij}u_{ij}$$

local Force density: $f_i(\vec r) = -\sum_j \frac{\partial \sigma_{ij}}{\partial r_j} = -\frac{E}{1+\nu}\left[\sum_j \frac{\partial u_{ij}^2}{\partial r_j} + \frac{\nu}{1-2\nu}\frac{\partial u_{ll}}{\partial r_i}\right]$

water
Bulk modulus
$K = 2\,\mathrm{GPa}$
$= -V\frac{dP}{dV}$
$\varepsilon_V = \frac{dV}{V} = -\frac{dP}{K}$
$\frac{1\,\mathrm{atm}}{K} = 10^{-4} = 0.0$
$10^{-4} \cdot 10^{-5}\,\mathrm{m} = 10^{-9}$



Adhesion on surfaces

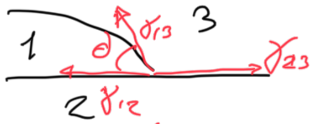
Vesicles

only surface energy | surf energy + solid elast. | surf en. bending energy | surf. en. bend + stretch energy

Young-Laplace equation $\Delta p = -\gamma H = -\gamma\left(\frac{1}{R_1} + \frac{1}{R_2}\right)$ → mean curvature

Surface energy $\gamma = \frac{W}{\Delta A}$ $\left(= \frac{F}{2L} = \text{surface tension}\right)$

Youngs law : $\cos\theta = \frac{\gamma_{23} - \gamma_{12}}{\gamma_{13}}$



Elastic deformation counteracts adhesion energy gain W:

contact radius a: $a^3 = \frac{9\pi(1-\nu^2)}{2E}R^2 W$ JKR theory

Bending energy $U_b = 2\kappa \int H^2 dA$ κ - bending rigidity

Biological bilipid membranes : $\kappa = 20 kT$

Stretching + bending => buckling , crumpling ...

No buckling in cells, but shape is modified