Measuring network elasticity

Two principal techniques:
- micromechanical manipulation: a cell or extracted network is subject to a known stress and the response of the cell is observed by optical microscopy or another imaging method
- thermal fluctuations in a system's geometry; these fluctuations are inversely proportional to the stiffness of the system

**Human erythrocyte**
- apply suction to a flaccid cell

![Video image of aspiration](image1)

![Computer simulation](image2)

- length of the aspirated segment $L$ is related to the applied pressure $P$
  \[ P = \left( \frac{\mu}{R_p} \right) \left( \frac{2L}{R_p} - 1 \right) + \ln\left(\frac{2L}{R_p}\right) \]
  \[ \mu = 2D \text{ shear modulus} \]
  \[ R_p = \text{pipette radius} \sim 1/2 \text{ micron} \]
- experiments typically yield $\mu \sim 6-9 \times 10^{-6} \text{ J/m}^2$ for human erythrocytes
  $\mu \sim 10^{-5} \text{ J/m}^2$ for most mammalian red cells (no nucleus)
  $\mu \sim 10^{-4} \text{ J/m}^2$ for nucleated cells (Waugh and Evans)
- deforming a cell with optical tweezers gives $\mu = 2.5\pm0.4 \times 10^{-6} \text{ J/m}^2$ (Hénon et al.)
- thermal fluctuations of red cell shape gives $\mu < 10^{-5} \text{ J/m}^2$ (Peterson, Strey, and Sackmann)

Just how small is this? For a material of thickness $t$
\[ K_v \sim K_s/t. \]

For the red cell cytoskeleton, $K_s \sim 2\mu \sim 10^{-5} \text{ J/m}^2$ and $t \sim 40 \text{ nm}$, so
\[ K_v \sim 10^{-5}/4 \times 10^{-8} = 250 \text{ J/m}^3. \]
Compare this with an ideal gas at STP, where $K_v = P = 10^5 \text{ J/m}^3$: this cytoskeleton is very soft.

**Auditory outer hair cell**

- cell is about 78 $\mu$m long and 10 $\mu$m wide

Videomicrograph of an auditory outer hair cell from a guinea pig (Sit *et al.*)

- assuming the cortex is isotropic, $\mu = 1.5\pm0.3 \times 10^{-2} \text{ J/m}^2$ (Sit *et al.*), which is 1000 times the red cell modulus
- $Y \sim 1 \times 10^7 \text{ J/m}^3$ for principal filaments, $Y = 3 \times 10^6 \text{ J/m}^3$ for cross-links (Tolomeo, Steele, and Holley); $10^{-2}$ of what we quoted for polymers
- $\mu \sim 2-4 \times 10^{-3} \text{ J/m}^2$ for inhomogeneous networks in fibroblasts (Bausch *et al.*)

**Bacteria**

STM image of a bacterial sheath over a 0.3 $\mu$m gap in a Ga-As substrate (Xu *et al.*)

- sheath of the bacterium *Methanospirillum hungatei* has $Y \sim 2-4 \times 10^{10} \text{ J/m}^3$
- bulk Young's modulus of Gram-positive bacterium *Bacillus subtilis* (Thwaites and Surana)
  - $Y = 1.3\pm0.3 \times 10^{10} \text{ J/m}^2$ for a dry cell wall
  - $Y \sim 3 \times 10^7 \text{ J/m}^3$ for a wet cell wall

**Interpretation of measurements**

- entropic springs have an effective spring constant $k_{sp} = 3k_B T / <r_{ee}^2>$
- area per vertex $A_v$ of an equilateral triangle $A_v \sim \sqrt{3} <r_{ee}^2>/2$
$$k_{sp} \sim 3\sqrt{3} \, k_B T / 2 A_v$$

- 2D density of chains $\rho = 3/A_v$ (three chains per vertex)
  $$k_{sp} = (\sqrt{3} / 2) \, \rho k_B T$$

- six-fold spring network has $\mu = \sqrt{3} \, k_{sp}/4$ at low temperature
  $$\mu = (3/8) \, \rho k_B T$$

- factor of 3/8 isn't too meaningful, so we use
  $$\mu \sim \rho k_B T$$

spread erythrocyte cytoskeleton
(Liu, Derick, and Palek, 1987)

simulated cytoskeleton
(Boal, 1994)

Applications

- human erythrocyte has a spectrin tetramer density of $\rho \sim 800 \, \mu m^{-2}$
  $$\mu \sim \rho k_B T \sim 800 \times 10^{12} \, (m^2) \cdot 4 \times 10^{-21} \, (J) \sim 3 \times 10^{-6} \, J/m^2$$
  (within a factor of two or so of experiment)

- micropipette aspiration finds $K_A/\mu \sim 2$ (Discher, Mohandas and Evans, 1994)
  6-fold spring networks obey $K_A/\mu = 2$

- cortical lattice of outer hair cells has two chains per 25 x 65 nm rectangular plaquette,

- corresponding density is $\rho \sim 1.2 \times 10^{15} \, m^{-2}$
  $$\mu \sim \rho k_B T \sim 1.2 \times 10^{15} \, (m^2) \cdot 4 \times 10^{-21} \, (J) \sim 5 \times 10^{-6} \, J/m^2$$

- measured $\mu$ is three orders of magnitude larger (Sit et al., 1997)!
  $$\mu \sim \rho k_B T$$

- shear resistance is probably energetic, not entropic; reflects the stiffness of the network filaments