Massachusetts Institute of Technology - Spring 2003
BEH.410 / 2.798J / 6.524J / 10.539J
Molecular, Cellular & Tissue Biomechanics

Review sheet for midterm quiz (April 9, 2003)

1 – Molecular Biomechanics

Length, Time & Forces in Biology

Thermal energy scale $E_{th} \sim k_B T \approx 4.\ 10^{-21}$ J (and $RT = N_A\, k_B T \approx 2.5$ kJ.mol^{-1}) at 298°K
Thermal force scale $F_{th} \sim E_{th} / L_{th} \approx 4.\ 10^{-21} / 10^{-9} = 4$ pN
Orders of magnitude in biology

Brownian motion in d dimensions $< \underline{r} . \underline{r} > = 2d$ D t with D ~ $k_B T/\xi$
ξ drag coefficient defined by $\underline{F_d} = -\xi \underline{v}$ (Stokes law for spheres: $\xi = 6\pi\mu a$)

Langevin equation (very difficult to solve but good for dynamics)

$$m\frac{d^2\underline{r}(t)}{dt^2} = -\xi\frac{d\underline{r}(t)}{dt} + \underline{f}(t) + \underline{G}(t)$$

Stochastic model for $\underline{f}$ and equipartition theorem yield

$$\langle \underline{r}.\underline{r} \rangle = \frac{2k_\mathbf{B}T}{\xi}\underline{\underline{\delta}}\left\{t + \frac{m}{\xi}\left[\exp\left(-\frac{\xi}{m}t\right) - 1\right]\right\}$$

Limiting cases

$$\begin{cases} t << \dfrac{m}{\xi} \Rightarrow \langle \underline{r}.\underline{r} \rangle = \dfrac{k_\mathbf{B}T}{m}\underline{\underline{\delta}} \cdot t^2 \rightarrow \textit{ballistic} \\ t >> \dfrac{m}{\xi} \Rightarrow \langle \underline{r}.\underline{r} \rangle = \dfrac{2k_\mathbf{B}T}{\xi}\underline{\underline{\delta}} \cdot t \rightarrow \textit{diffusive} \end{cases}$$

General Thermodynamics & Statistical Mechanics

Fondamental energy equation

$$dU = TdS - pdV + \underline{F}_{rev}.d\underline{r}$$

Helmholtz free energy

$$dA = d(U - TS) = -pdV + \underline{F}_{rev}.d\underline{r} - Sdt \Rightarrow \left(\frac{\partial A}{\partial \underline{r}}\right)_{T,V} = \underline{F}_{rev}$$

2 postulates

- ergodic: Time average = ensemble average
- Gibbs: All microstates with same N, V, U are equally probable

Entropy

$$S = k_\mathbf{B}\ln W = -k_\mathbf{B}\sum_{i=1}^{t} p_i \ln p_i$$

Boltzmann distribution

$$p_i = \frac{\exp\left(\dfrac{-U_i + \underline{f}.\underline{r}_i}{k_\mathbf{B}T}\right)}{Q'}$$

Partition function

$$Q' = \sum_i \exp\left(\frac{-U_i + \underline{f}.\underline{r}_i}{k_\mathbf{B}T}\right)$$

Thermodynamic system (T, V, N, $\underline{f}_{rev}$), equilibrium for minimized $A' = A - \underline{f}_{rev}.\underline{r}$
Also enthalpy $H = U + pV$, and Gibbs free energy $G = H - TS$

For one macrostate

$$A = -k_B T \ln Q$$

Forces tilt energy profiles and change distribution

$$\frac{p_1}{p_2} = \frac{Q_1}{Q_2} = \exp\left(-\frac{A_1 - A_2}{k_B T}\right)\exp\left(\frac{\underline{f}.(\underline{r}_1 - \underline{r}_2)}{k_B T}\right)$$

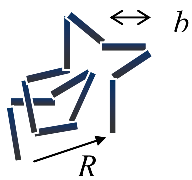
Polymer Chain Model & Entropic Elasticity

Freely-jointed chain model
(polymers are coiled at equilibrium)

$$\underline{R} = \sum_{i=1}^{N} \underline{b}_i, \langle \underline{R} \rangle = 0, \sqrt{\langle \underline{R}.\underline{R} \rangle} = \sqrt{N} b$$

Probability distribution for $\underline{R}$ in d dimensions

$$p(x, y, z, N) \approx p_{Gaussian} = \left(\frac{d}{2\pi N b^2} \right)^{d/2} \exp\left(\frac{-dR^2}{2Nb^2} \right)$$



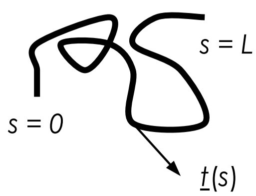
In 3D

$$\langle \underline{f} \rangle = -T \left(\frac{\partial S}{\partial \underline{R}} \right)_{T,V} = -k_B T \frac{\partial}{\partial \underline{R}} \left(\ln p(\underline{R}) \right) = \frac{3 k_B T}{b} \cdot \frac{\underline{R}}{L}$$

$$\langle \underline{r} \rangle = Nb \left[\coth\left(\frac{fb}{k_B T} \right) - \frac{k_B T}{fb} \right] \frac{\underline{f}}{f}$$

Worm-like chain model
Total internal energy from bending

$$U_{tot} = \int_{chain} \frac{E_{arc}}{L_{arc}} = \int_{chain} \frac{\kappa_f}{2} \cdot \frac{1}{R_c^2} = \frac{YI}{2} \int_{s=0}^{s=L} \left(\frac{\partial \underline{t}}{\partial s} \right)^2 ds$$



$$\langle \underline{t}(s) \cdot \underline{t}(s + \Delta s) \rangle = \exp\left(\frac{-\Delta s \cdot k_B T}{\kappa_f} \right)$$

Persistence length

$$\lambda_p = \frac{b}{2} = \frac{\kappa_f}{k_B T}$$

Coil size

$$\langle R^2 \rangle = 2\lambda_p \left[\frac{L}{\lambda_p} + \exp\left(\frac{-L}{\lambda_p} \right) - 1 \right]$$

Interpolation of force/elongation

$$f_z \approx \frac{k_B T}{\lambda_p} \left[4 \left(1 - \frac{\langle z \rangle}{L} \right)^{-2} + \frac{\langle z \rangle}{L} - \frac{1}{4} \right]$$

Filament Polymerization & Forces

$$\frac{dn}{dt} = k_{on}[M] - k_{off}$$

At equilibrium

$$K_{eq} = \frac{k_{on}}{k_{off}} = K_{eq}^0 \exp\left(\frac{f \cdot \Delta x}{k_B T} \right) = \exp\left(\frac{\Delta G^0}{k_B T} \right) \left(\frac{f \cdot \Delta x}{k_B T} \right)$$

Lower dissociation constant if pulling ($f > 0$)

$$K = \frac{k_{off}}{k_{on}} = \frac{1}{K_{eq}} = \left[M^c(f) \right] = \left[M^c \right]^0 \exp\left(\frac{-f \cdot \delta}{k_B T} \right)$$

Equilibrium force: Depending on monomer reserve [M], system can push or pull

$$f^{eq} = -f = -\frac{k_B T}{\delta} \ln\left(\frac{\left[M^c(f) \right]}{\left[M^c \right]^0} \right)$$

Eyring & Kramers rate theories (see reading “Chapter 5 – Howard”)
Reaction-limited & diffusion-limited polymerization (see reading “Chapter 10 – Howard”)
Brownian ratchet for kinesin-microtubule & myosin-actin

Dimensional analysis

2 – Tissue Biomechanics

Linear Elasticity

Concepts of linear elasticity, isotropic or anistotropic materials, homogeneous materials
Methods for measuring elastic properties: extension, shear, confined or unconfined compression

Generalized Hooke's law (continuum, homogeneous, linearly elastic, isotropic)

$$\sigma_{ij} = C_{ijkl}\varepsilon_{kl} = \lambda\delta_{ij}\varepsilon_{kk} + 2G\varepsilon_{ij}$$

$$\varepsilon_{ij} = \frac{1}{2}\left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i}\right) = \frac{1+\nu}{E}\sigma_{ij} - \frac{\nu}{E}\delta_{ij}\sigma_{kk}$$

$$\lambda = \frac{\nu E}{(1+\nu)(1-2\nu)} \qquad G = \frac{E}{2(1+\nu)} \qquad H = 2G + \lambda \qquad K = \lambda + \frac{2}{3}G = \frac{E}{3(1-2\nu)} = \frac{\sigma_{kk}}{3\varepsilon_{kk}}$$

Force balance relation in differential form

$$\rho\frac{Dv_i}{Dt} = \rho\left(\frac{\partial v_i}{\partial t} + v_j\frac{\partial v_i}{\partial x_j}\right) = f_i + b_i = \frac{\partial \sigma_{ij}}{\partial x_j} + b_i$$

For Hookean solid → Navier-Stokes

$$\rho\frac{\partial^2 u_i}{\partial t^2} = G\frac{\partial^2 u_i}{\partial x_i x_j} + (\lambda + G)\frac{\partial}{\partial x_i}\left(\frac{\partial u_j}{\partial x_j}\right) + b_i$$

Neglecting inertia & body forces

$$\frac{\partial \sigma_{ij}}{\partial x_j} = 0$$

Strain energy density
scales as $U_0 \sim G\varepsilon^2$ or $U_0 \sim \sigma^2 / G$

$$U_0 = \frac{dU}{d\forall} = \frac{1}{2}\left[\lambda(\varepsilon_{kk})^2 + 2G\varepsilon_{kk}^2 + 4G\left(\varepsilon_{12}^2 + \varepsilon_{23}^2 + \varepsilon_{13}^2\right)\right]$$

$$U_0 = \frac{1}{2E}\sigma_{kk}^2 - \frac{\nu}{E}\left(\sigma_{11}\sigma_{22} - \sigma_{22}\sigma_{33} - \sigma_{11}\sigma_{33}\right) + \frac{1}{2G}\left(\sigma_{12}^2 + \sigma_{23}^2 + \sigma_{13}^2\right)$$

For bending of a rod

$$U = \frac{1}{2}M\theta = \int_\forall \frac{\sigma_{11}^{\ 2}}{2E}d\forall = \int_\forall \frac{1}{2E}\left(\frac{Mx_2}{I}\right)^2 dx_1 dA = \frac{M^2 L}{2EI}$$

and because $\theta = L / R_C$

$$M = \frac{\kappa_f}{R_C} = \frac{EI}{R_C}$$

Composition & Structure of Biological Materials

<u>Extracellular Matrix</u>

- Collagen (stiff)
- Proteoglycans (compressive, glycosaminoglycan charge repulsion)
- Elastin (elastic, compliant, random)
- Adhesion proteins

Other examples in handouts