BME 42-620 Engineering Molecular Cell Biology

Lecture 14:

Review: Polymer Mechanics

Modeling Biochemical Reactions (I)

Project Assignment 02

Review: Project Assignment 01

Outline

- Review: polymer mechanics; Problem set 02
- Modeling biochemical reactions
- Project assignment 02
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Basic Mechanical Properties of Cytoskeletal Filaments

- Bending rigidity
- Viscous drag coefficient
- Buckling force
- Persistence length

Buckling Force

- Euler's force: buckling force on both ends

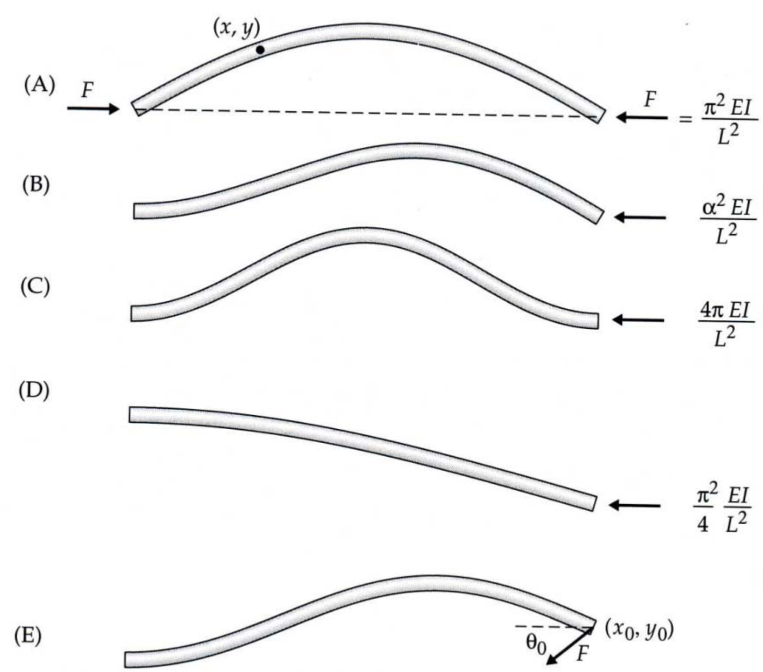
$$F_c = \pi^2 \frac{EI}{L^2}$$

- Example: microtubule buckling force

EI=30 $\times 10^{-24}$ N·m^2. L = 10 μm

Fc=6.1pN

$$F_c = \alpha^2 \frac{EI}{L^2}$$



Persistence Length (I)

- Persistence length is defined as the characteristic distance determined in

$$\left\langle cos\left[\theta(s)-\theta(0)\right]\right\rangle = exp\left(-\frac{s}{2L_p}\right)$$

- Persistence length is proportional to the bending rigidity and inversely proportional to thermal energy.

$$L_p = \frac{EI}{kT}$$

Persistence Length (II)

- Persistence length of cellular filaments

  - Actin: 15 μm
  - Microtubule: 6 mm
  - Keratin intermediate filament: ~ 1 μm

  - Coiled coil: 100-200 nm
  - DNA: 50 nm

Cytoskeletal Filaments *in vivo*

- Cytoskeletal filaments

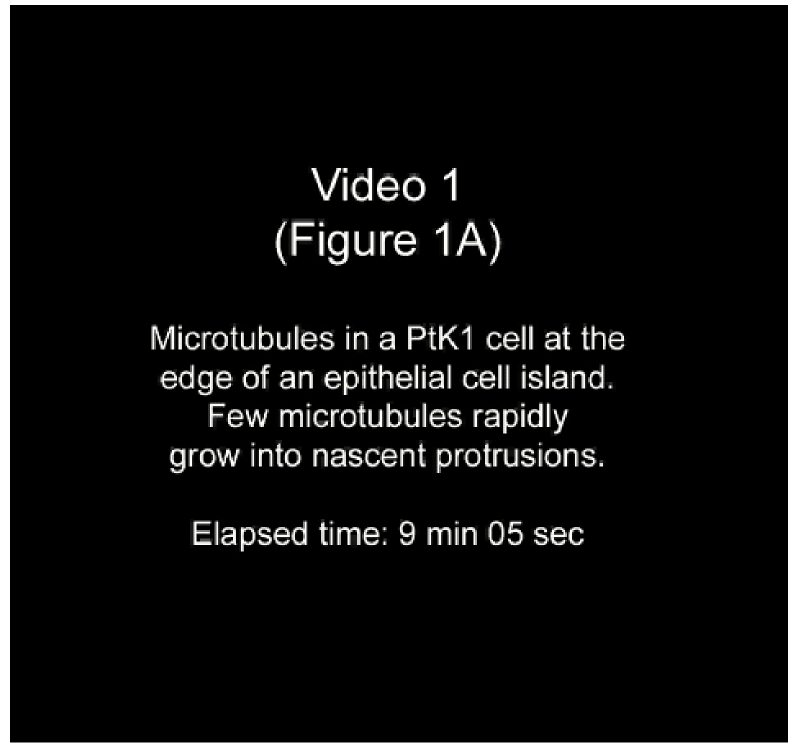
  - Highly dynamic *in vivo*.

  - Function in networks.

  - Function under tight regulation.

  - Crosstalk between different filaments.

- Current research focuses on understanding polymer mechanics in vivo.



T. Wittmann et al, *J. Cell Biol.*, 161:845, 2003.

Calculation of Diffusion Coefficient

- Einstein-Smoluchowski Relation

$$v_d = \frac{1}{2} a\tau = \frac{1}{2} \frac{F_x}{m} \tau \qquad f = \frac{F_x}{v_d} = \frac{2m}{\tau} = \frac{2m\frac{\delta^2}{\tau^2}}{\frac{\delta^2}{\tau}} = \frac{m v_x^2}{D} = \frac{kT}{D}$$

$$D = \frac{kT}{f}$$

f: viscous drag coefficient

- Stokes' relation: the viscous drag coefficient of a sphere moving in an unbounded fluid

$$f = 6\pi\eta r$$

η: viscousity
r: radius

An example of D calculation

- Calculation of diffusion coefficient

$$D = \frac{kT}{6\pi\eta r}$$

- $k=1.381\times10^{-23}$J/k$=1.381\times10^{-17}$ N·μm/k
- T = 273.15 + 25
- $\eta=0.8904$mPa·s$=0.8904\times10^{-3}\times10^{-12}$N·μm^{-2}·s
- r= 500nm=0.5μm
- D=0.5 μm^2/s

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Overview

- In general, there are two approaches
  - Classical approach
  - Contemporary approach

- The classical approach describes the steady state of biochemical reactions.

- Contemporary approach can also describes the dynamics of biochemical reactions.

Modeling First Order Reactions (I)

- First order reactions involves one reactant (*R*).

$$R \rightarrow P$$

- Two examples

→ Protein conformation change

→ Disassociation of a molecular complex

Modeling First Order Reactions (II)

- Forward reaction model

$$Forward: \frac{d[P]}{dt} = -\frac{d[R]}{dt} = k_+[R]$$

- Backward reaction model

$$Backward: \frac{d[R]}{dt} = -\frac{d[P]}{dt} = k_-[P]$$

- Putting together

$$\frac{d[R]}{dt} = -k_+[R] + k_-[P]$$

$$\frac{d[P]}{dt} = k_+[R] - k_-[P]$$

Modeling First Order Reactions (III)

- Determination of equilibrium state

$$R \underset{k_-}{\overset{k_+}{\rightleftharpoons}} P$$

$$k_+ \left[R_{eq} \right] = k_- \left[P_{eq} \right]$$

$$K_{eq} = \frac{\left[P_{eq} \right]}{\left[R_{eq} \right]} = \frac{k_+}{k_-}$$

Classic Approach to Determine 1st Order Rate Constant

- First order rate constant can be measured from reaction half-time.

$$\frac{d[R]}{dt} = -k_+[R]$$

$$[R]_t = [R]_0 e^{-k_+ t}$$

$$\frac{1}{2}[R]_0 = [R]_0 e^{-k_+ t_{1/2}}$$

$$k_+ t_{1/2} = ln2 = 0.6931$$

Modeling Second Order Reactions (I)

- Second order reactions involves two reactants (A,B).

- A second order molecular binding reaction

$$A + B \rightleftarrows [AB]$$

- Reaction rate model

$$Forward: \quad \frac{d[P]}{dt} = k_+[A][B]$$

$$Backward: \quad \frac{d[A]}{dt} = \frac{d[B]}{dt} = k_-[AB]$$

$$K_{eq} = \frac{k_+}{k_-} = \frac{[AB_{eq}]}{[A_{eq}][B_{eq}]}$$

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Basic Concept of Single Particle Simulation

- Initialization: Set the original position x(0)

- Update: calculate the displacement at each time point

  $$x(1) = x(0) + \Delta x(0)$$
  $$x(2) = x(1) + \Delta x(1)$$
  …

- MATLAB function for linear regression: *robustfit*

Numerical Solution of PDE (I)

- Basic elements of a PDE
  - The equation that the unknown function of multiple variables satisfies

  - Initial condition: initial spatial profile of the function

  - Boundary condition: boundary constraints

- Example

$$\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2} \qquad -\frac{L}{2} \le x \le \frac{L}{2} \qquad 0 \le t \le \infty$$

$$\text{B.C.} \quad \left.\frac{\partial C}{\partial x}\right|_{x=-\frac{L}{2}} = \left.\frac{\partial C}{\partial x}\right|_{x=\frac{L}{2}} = 0$$

$$\text{I.C.} \quad \left.C(x,t)\right|_{t=0} = C(x,0) = \Phi(x)$$

Numerical Solution of PDE (II)

- Numerical solution of PDE

$$\left.\frac{\partial^2 C}{\partial x^2}\right|_{x=j\cdot\Delta x;t=n\cdot\Delta t} \approx \frac{1}{(\Delta x)^2}\left\{c_{j+1}^n - 2c_j^n + c_{j-1}^n\right\} = \frac{1}{\Delta x}\left\{\frac{c_{j+1}^n - c_j^n}{\Delta x} - \frac{c_j^n - c_{j-1}^n}{\Delta x}\right\}$$

- Outline of the program

```
for  j = 1 : M
        c(j, 1) = …      % this needs to be set according to initial condition;
end
for  n = 1 : N
        for  j = 2 : (M – 1)
                c(j, n+1) = c(j,n) + D * deltaT / deltaX / deltaX * (c(j+1, n) …
                                -2 * c(j, n) + c(j – 1, n));
        end
        c(1, n+1) = c(2, n+1);
        c(M, n+1) = c(M-1, n+1);
end
```

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