BME 42-620 Engineering Molecular Cell Biology

Lecture 13:

Mechanical Properties of Cytoskeletal Polymers

Modeling Biochemical Reactions (I)

Course Administration Notes

- Third reading assignment posted online.

  → Presentation schedule

- Problem set 1 graded and returned today.

  MEAN = 104; STD = 18; MIN = 65; MAX = 139

- Lectures to choose from (http://www.ibioseminars.org)

  1) Julie Theriot, *Cell Organization & Cell Motility*
  2) Ron Vale, *Cytoskeletal Motor Proteins*
  3) Jennifer Lippincott-Schwartz, *Breakthroughs in Intracellular Fluorescent Imaging*

A one-page summary report is due Oct-18 in class.

Outline

- Review: problem set 1
- Mechanical properties of cytoskeletal filaments
- Fundamentals of chemical reaction modeling

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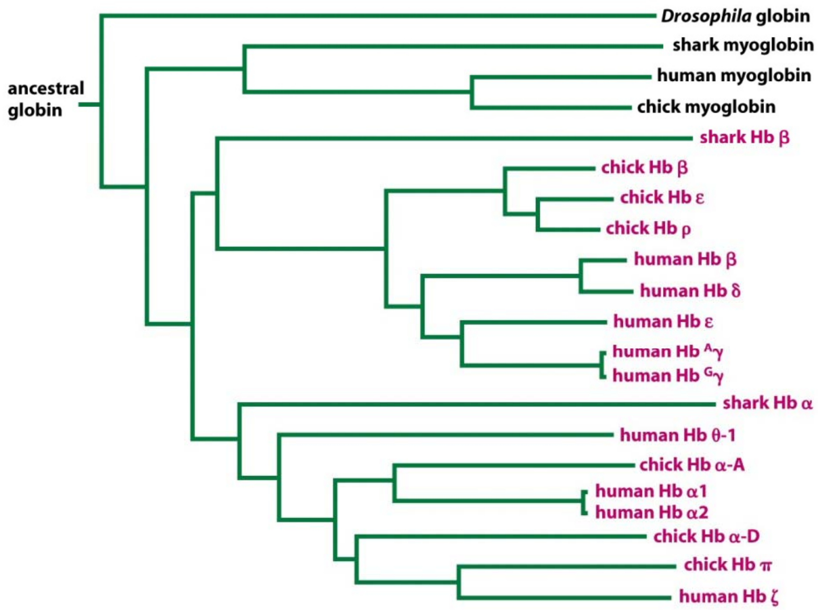
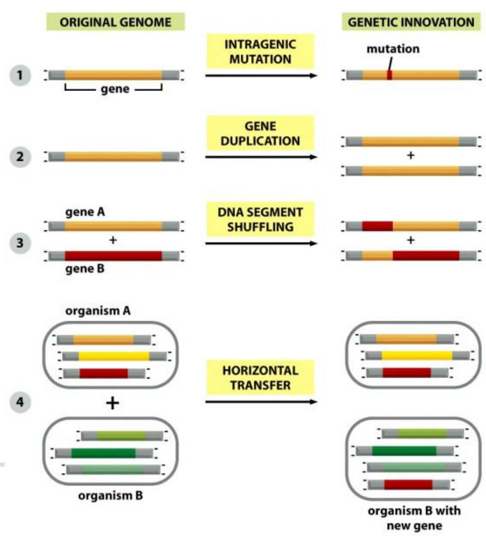
Problem Set 1 (I)

- 1-1



- 1-2



Problem Set 1 (II)

- 1-3
- 1-5
  - → Protein analysis
  - → DNA sequence analysis
  - → Genetic code

Table 1–1 Some Genomes That Have Been Completely Sequenced

SPECIES	SPECIAL FEATURES	HABITAT	GENOME SIZE (1000s OF NUCLEOTIDE PAIRS PER HAPLOID GENOME)	ESTIMATED NUMBER OF GENES CODING FOR PROTEINS
BACTERIA				
Mycoplasma genitalium	has one of the smallest of all known cell genomes	human genital tract	580	468
Synechocystis sp.	photosynthetic, oxygen-generating (cyanobacterium)	lakes and streams	3573	3168
Escherichia coli	laboratory favorite	human gut	4639	4289
Helicobacter pylori	causes stomach ulcers and predisposes to stomach cancer	human stomach	1667	1590
Bacillus anthracis	causes anthrax	soil	5227	5634
Aquifex aeolicus	lithotrophic; lives at high temperatures	hydrothermal vents	1551	1544
Streptomyces coelicolor	source of antibiotics; giant genome	soil	8667	7825
Treponema pallidum	spirochete; causes syphilis	human tissues	1138	1041
Rickettsia prowazekii	bacterium most closely related to mitochondria; causes typhus	lice and humans (intracellular parasite)	1111	834
Thermotoga maritima	organotrophic; lives at very high temperatures	hydrothermal vents	1860	1877

Genome size and gene number vary between strains of a single species, especially for bacteria and archaea. The table shows data for particular strains that have been sequenced. For eucaryotes, many genes can give rise to several alternative variant proteins, so that the total number of proteins specified by the genome is substantially greater than the number of genes.

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ARCHAEA				
Methanococcus jannaschii	lithotrophic, anaerobic, methane-producing	hydrothermal vents	1664	1750
Archaeoglobus fulgidus	lithotrophic or organotrophic, anaerobic, sulfate-reducing	hydrothermal vents	2178	2493
Nanoarchaeum equitans	smallest known archaean; anaerobic; parasitic on another, larger archaean	hydrothermal and volcanic hot vents	491	552
EUCARYOTES				
Saccharomyces cerevisiae (budding yeast)	minimal model eucaryote	grape skins, beer	12,069	~6300
Arabidopsis thaliana (Thale cress)	model organism for flowering plants	soil and air	~142,000	~26,000
Caenorhabditis elegans (nematode worm)	simple animal with perfectly predictable development	soil	~97,000	~20,000
Drosophila melanogaster (fruit fly)	key to the genetics of animal development	rotting fruit	~137,000	~14,000
Homo sapiens (human)	most intensively studied mammal	houses	~3,200,000	~24,000

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Problem Set 1 (III)

- 1-7 (A, B, E) ((A, B), E) (A, (B, E)) ((A, E), B)

Table 2–1 Covalent and Noncovalent Chemical Bonds

BOND TYPE	LENGTH (nm)	STRENGTH (kcal/mole) IN VACUUM	IN WATER
Covalent	0.15	90	90
Noncovalent: ionic*	0.25	80	3
hydrogen	0.30	4	1
van der Waals attraction (per atom)	0.35	0.1	0.1

*An ionic bond is an electrostatic attraction between two fully charged atoms.

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Polymer Mechanics (I)

- Rationale: characterizing mechanical properties of individual filaments as a starting point for understanding mechanical properties of cells, tissues, and organs.

- Polymer mechanics is an established research field.
  - A classic treatment: M. Doi & S.F. Edwards, *The theory of polymer dynamics*, Oxford University Press, 1986.

- Investigating the mechanics of biopolymers in cells is a very active research field.

Polymer Mechanics (II)

- We will take an approach of simplification and approximation here.
- Theory of elasticity holds at the scale of single filaments.
- Cytoskeleton polymers are modeled as thin and slender beams.

Basic Mechanical Properties of Cytoskeletal Filaments

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

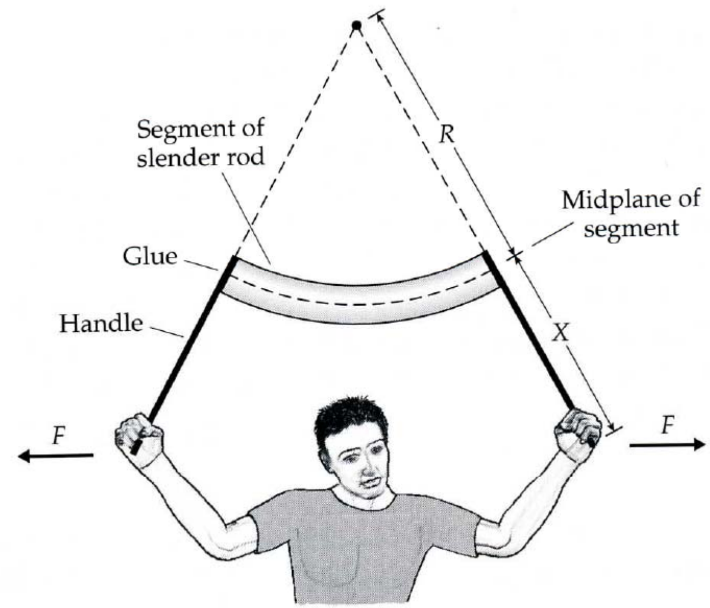
Bending Rigidity

- Basic equation

$$M = EI\frac{1}{R}$$

R: Radius of curvature
M: Torque; bending moment

E: Young's modulus
I: second moment of inertia
EI: bending (flexural) rigidity

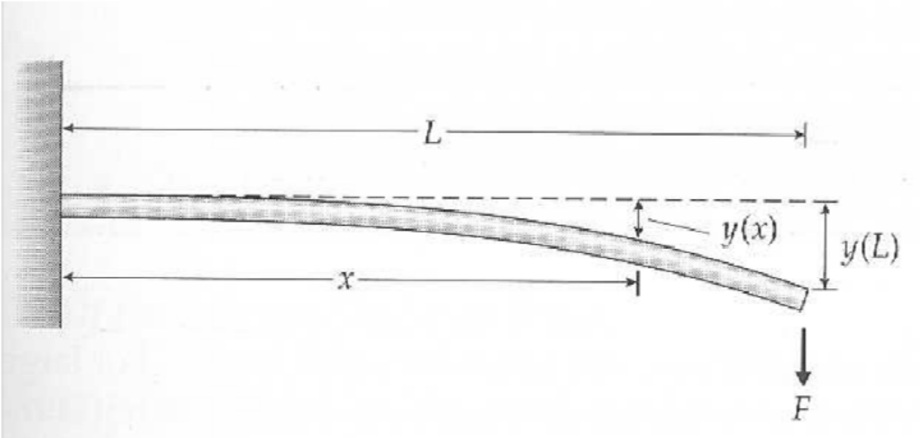


- Bending rigidity of cytoskeletal filaments is generally independent of bending direction since cytoskeletal filaments have approximately circular or helical symmetry.

Cantilever Beam Under Small-Angle Bending

- Beam deflection

$$\frac{d^2y}{dx^2} = \frac{M(x)}{EI}$$



- Cantilever beam

$$\frac{d^2y}{dx^2} = \frac{F(L-x)}{EI} \qquad y(x) = \frac{F}{EI}\left(\frac{Lx^2}{2} - \frac{x^3}{6}\right)$$

- Spring constant

$$y(L) = \frac{FL^3}{3EI} \qquad k = \frac{F}{y(L)} = \frac{3EI}{L^3}$$

Mechanics of Materials, 7th ed., J. M. Gere & B. J. Goodno, 2008

Examples: cantilever beam models

- Glass cantilever beam

  $r = 0.25\mu m$, $L = 100\ \mu m$
  $E=70$ GPa, $I=(\pi/4)r^4=3\times10^{-27}$

  $k=0.64$ pN/nm

$$1\text{Pa}=1\frac{\text{N}}{\text{m}^2}=1\frac{\text{kg}}{\text{m}\cdot\text{s}^2}$$

- Microtubule

  $EI=30\times10^{-24} N\cdot m^2$. $L = 10\ \mu m$
  $k = 0.00009$ pN/nm

- Coiled coil

  $EI=400\times10^{-30} N\cdot m^2$. $L = 8$ nm
  $k = 2.34$ pN/nm

Drag Coefficient

- Viscous drag on slender rods

- Example: drag on a sperm

  Head: length 5.8 μm, width 3.1 μm, viscosity 1mPa·s (assuming water)

  Head drag coefficient = 0.0547 pN/ (μm·sec) [use the sphere model, r =2.9]

Table 6.2 Drag coefficients in an unbounded solution

Parameter	Direction	Cylinder ($L>>r$)	Ellipsoid ($b>>a$)	Sphere
$\gamma_{\parallel}$	→	$\frac{2\pi\eta L}{\ln(L/2r)-0.20}$	$\frac{4\pi\eta b}{\ln(2b/a)-0.5}$	$6\pi\eta r$
$\gamma_{\perp}$	↑	$\frac{4\pi\eta L}{\ln(L/2r)+0.84}$	$\frac{8\pi\eta b}{\ln(2b/a)+0.5}$	$6\pi\eta r$
γ_r		$\frac{\frac{1}{3}\pi\eta L^3}{\ln(L/2r)-0.66}$	$\frac{\frac{8}{3}\pi\eta b^3}{\ln(2b/a)-0.5}$	$8\pi\eta r^3$
γ_a		$4\pi\eta r^2 L$	$\frac{16}{3}\pi\eta a^2 b$	$8\pi\eta r^3$

Buckling Force

- Euler's force: buckling force on both ends

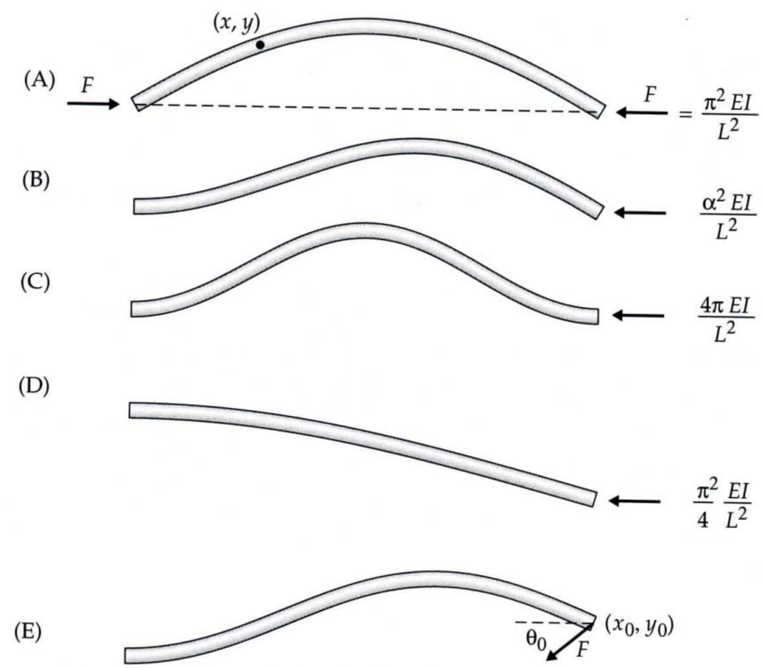
$$F_c = \pi^2 \frac{EI}{L^2}$$

- Example: microtubule buckling force

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

  $Fc = 6.1pN$

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



Persistence Length (I)

- Persistence length is defined as the characteristic distance defined in

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

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

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

Persistence Length (II)

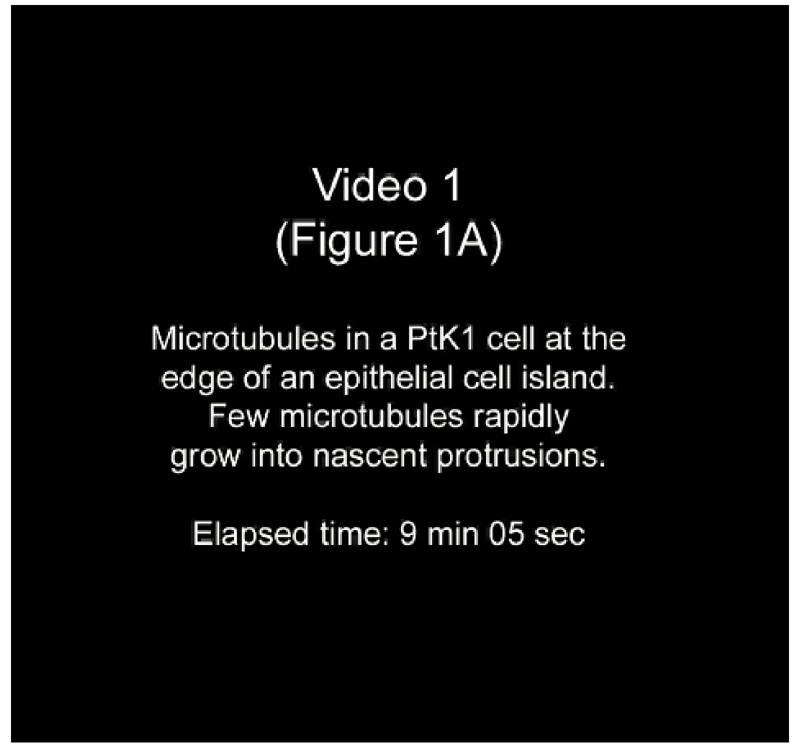
- Persistence length of cellular filaments

  - 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.



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

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Modeling First Order Reactions (I)

- First order reactions involves one reactant (A).

$$A \rightarrow P$$

- Two examples
  → Protein conformation change
  → Disassociation of a molecular complex

- Reaction rate model

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

Modeling First Order Reactions (II)

- Determination of equilibrium state

$$A \underset{K_-}{\overset{K_+}{\rightleftharpoons}} P$$

- Reaction rate model

$$R_- = \frac{d[A]}{dt} = -\frac{d[P]}{dt} = k_-[P]$$

$$k_+[A_{eq}] = k_-[P_{eq}]$$

$$k_{eq} = \frac{P_{eq}}{A_{eq}} = \frac{k_+}{k_-}$$

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

$$R_+ = \frac{d[P]}{dt} = k_+ [A][B]$$

$$R_- = k_- [AB]$$

$$k_{eq} = \frac{k_+}{k_-} = \frac{[AB]}{[A][B]}$$

Questions ?

Calculation of Diffusion Coefficient

- Einstein-Smoluchowski Relation

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

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

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
- η=0.8904mPa·s$=0.8904\times10^{-3}\times10^{-12}$N·μm^{-2}·s
- r= 500nm=0.5μm
- D=0.5 μm^2/s