

Biopolymers:

Energy

The simplest theory for 1D structures is the Euler Bernoulli beam theory. There are three assumptions (kinetic) to consider:

- o normals remain straight (they do not bend)
- o normals remain unstretched (they keep the same length)
- o normals remain normal (they remain orthogonal to beam axis)

The total displacement of a beam

$$u^{TOT}(x, z) = u(x) - z \frac{dw}{dx}$$

axial stretch

Recall $\epsilon_{xx} = \frac{du^{TOT}}{dx} = \frac{du}{dx} - z \frac{d^2w}{dx^2}$

Since the normal remains unstretched, there are no strain components in the out of plane direction.

$$\epsilon_{xz} = \epsilon_{zz} = 0.$$

For simplicity we will drop the indices xx so $\epsilon = \epsilon_{xx}$

$$\epsilon = \frac{du}{dx} - z \frac{d^2w}{dx^2}$$

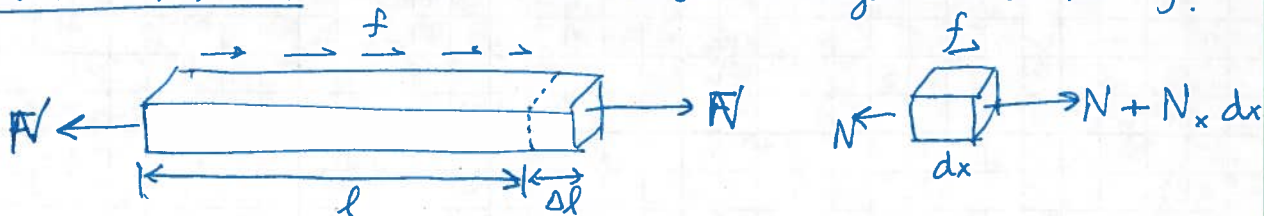
↑ independent of z-coordinate : axial deformation in the form of tension.

↙ varies linearly with thickness : transverse deformation in form of bending.

Overall deformation of beams = superposition of two basic deformation modes

- (1) axial stretching
- (2) bending.

Consider 1-D bar of initial length l subject to axial force f .



It stretches by Δl . Consider infinitesimal truss element dx

Kinematic Equation $\epsilon = \lim_{x \rightarrow 0} \frac{u}{x} = \frac{du}{dx} = u_{,x}$ $u(x)$ is displacement

~~By~~ Δl

If homogeneous. $\epsilon = \frac{\Delta l}{l}$

such that $u(x=l) = \Delta l$
 $u(x=0) = 0$

Constitutive Equation $\sigma = \sigma(\epsilon)$

If linear elastic $\sigma = E\epsilon$

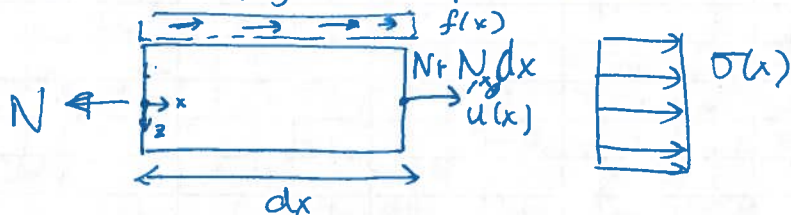
Stress Resultant

$$N = \iint \sigma dy dz$$

If homogeneous $\sigma = N/A$

Equilibrium

$\sum f = 0$ in axial direction or $N_{,x} + f = 0$



Note $\epsilon_{,x} = \frac{d\epsilon}{dx}$

$$N_{,x} + f = A\sigma_{,x} + f = EA\epsilon_{,x} + f = EAu_{,xx} + f = 0$$

Differential Eqn

$$EA \frac{d^2 u}{dx^2} + f = 0$$

If homogeneous $u = \frac{NL}{EA}$

Some numbers [CSK axial stiffness]

	r	A	E	EA
microtubule	125 nm	49 μm^2	$1.9 \times 10^9 \text{ N/m}^2$	$0.93 \times 10^{-6} \text{ N}$
IF	5.0 nm	79 μm^2	$2 \times 10^9 \text{ N/m}^2$	$0.16 \times 10^{-6} \text{ N}$
actin	3.5 nm	38 μm^2	$1.9 \times 10^9 \text{ N/m}^2$	$0.23 \times 10^{-9} \text{ N}$

Consider basic structural elements

<u>Element</u>	<u>Dim</u>	<u>Geometry</u>	<u>Loading</u>	<u>Deformation</u>	<u>Egn</u>
Truss	1D	straight	axial	tension	2 nd ord
Beam	1D	↓	transverse	bending	4 th
Wall	2D	flat	in plane	tension/shear	2 nd
Plate	2D	↓	transverse	bending	4 th
Membrane	3D	curved	in plane	tension/shear	2 nd
Shell	3D	↓	transverse	bending	4 th

In cell mechanics ...

- biopolymers [MT, actin, IF] are like trusses/beams.
- lipid bilayer or cell membrane is like a membrane

For now, I will skip 3D example and leave it as a worksheet.

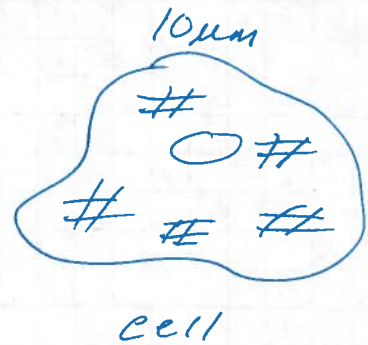
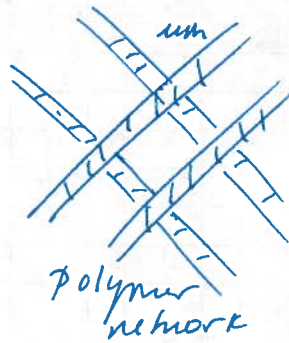
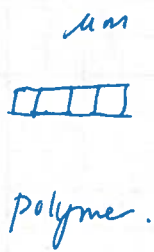
HW / Activity: We just derived CSK proteins in extension. Let's do it for torsion and bending. The worksheet will walk you through the derivation and you will fill in the table.

From these numbers, what can you say about the CSK proteins?

"CSK proteins are relatively stiff in axial tension, but flexible in torsion & bending".

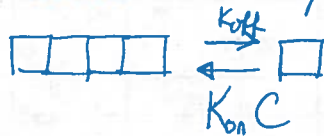
Lecture # 2: Mechanics of Cellular Polymers.

Recall, biopolymers.



In the previous worksheet, we derived some fundamental properties of actin, MT, & IF \Rightarrow CSK proteins.

Now let's understand the polymerization kinetics for an ideal polymer.



for n monomers.

and $[C]$ = free monomer concentration

$$\frac{dn}{dt} = +k_{on} C$$

monomer capture

$$\frac{dn}{dt} = -k_{off}$$

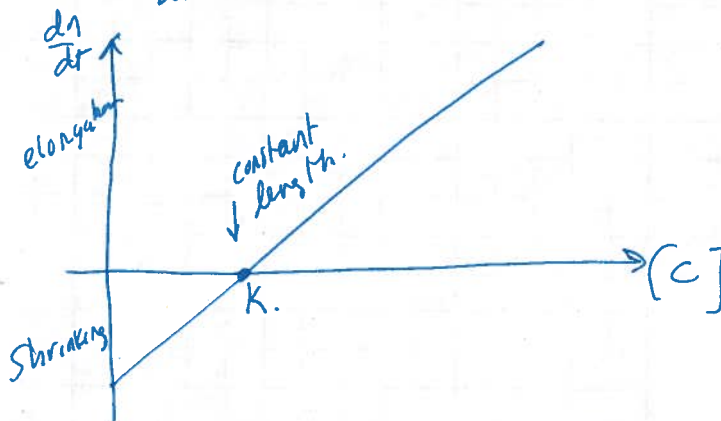
monomer release

$$\left. \begin{array}{l} \frac{dn}{dt} = +k_{on} C \\ \frac{dn}{dt} = -k_{off} \end{array} \right\} \frac{dn}{dt} = k_{on} C - k_{off}$$

What is the condition for polymer to remain at constant length?

$$n = \text{constant} \text{ so } \frac{dn}{dt} = 0.$$

$$\frac{dn}{dt} = 0 = k_{on} C - k_{off} \Rightarrow C_{crit} = \frac{k_{off}}{k_{on}} = K$$



In idealized model, k_{off} & k_{on} govern polymerization dynamics

Units: k_{on} [$1/\mu\text{M}\cdot\text{s}$]
 k_{off} [$1/\text{s}$]

C [μM]

Thermal fluctuations

Imagine a small particle floating in fluid. This particle will undergo Brownian Motion — random movements as it is randomly pushed around by the molecules around it. This motion is dependent on temperature: $\uparrow T$, \uparrow motion.

In the case of polymers, random molecular forces cause them to "wiggle," aka thermal fluctuations.

Thus as $\uparrow T$, \uparrow wiggles. Why?

The conformation of the polymer is determined by its free energy — or rather ~~energy~~ minimization of their free energy.

Recall free energy

$$\Psi = W - TS$$

\uparrow strain energy \uparrow temp. entropy

Thus to minimize Ψ either
 $\downarrow W$ or $\uparrow S$

Entropy [S]

What is entropy? Typically, definitions you hear relate it to the degree of disorder.

Mathematically

$$S = k_B \ln \Omega$$

\uparrow # of microstates

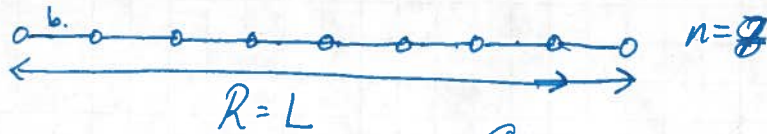
$$k_B = 1.38 \times 10^{-23} \text{ J/K} \quad \text{Boltzmann Constant}$$

Wait! What do you mean by microstates?

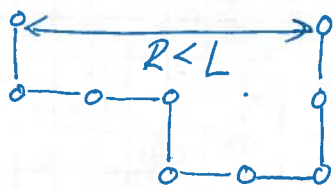
Consider a polymer. It has n rigid links of size b .

These links are connected to each other by freely rotating hinges. The links can be oriented horizontally or vertically so 2D.

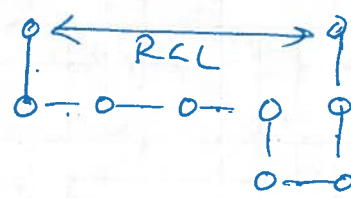
①



②



③



We can define two lengths:

④ Contour length $L =$ size of polymer if completely stretched out
 $L = nb$

⑤ End to End length R

$\rightarrow R < L$ in the examples above and most cases.

Different microstates Ω ~~are~~ polymer configurations
 \downarrow
 Macroscopic quantity of interest = R .

For case 1: there is only one polymer conformation where
 $R=L$ so $\Omega(R=L) = 1$

For case 2 & 3: there are multiple conformations where
 $R < L$ so $\Omega(R < L) > 1$

Recall

$\propto \ln \Omega$ so $\uparrow \Omega \Rightarrow \uparrow S$

thus an unstretched polymer has more entropy.

To decrease free energy, the polymer wants to $\uparrow S$ so
 it wants to remain unstretched or globular.

Energy $|W|$

Consider the same polymer models as before, but now imagine the links are attached by rotational springs. Now, the polymer wants to remain straight because bending takes more work.

IF we bend the polymer, this work becomes stored in springs as energy.

$$\begin{array}{l}
 R=L \quad \rightarrow \quad W=0 \\
 R<L \quad \rightarrow \quad W>0
 \end{array}
 \left. \vphantom{\begin{array}{l} R=L \\ R<L \end{array}} \right\} \begin{array}{l} \text{To } \downarrow \psi \\ \text{polymer wants to be} \\ \text{stretched, energetically.} \end{array}$$

Then now consider temperature

low T , W dominates so polymers straighter.
 high T , S dominates so polymer wigglier

Now, there is a quantity that stems out of this discussion:

Persistence Length! [Derive in HW]

Written as either A or L_p or ξ_p

N.B. $\frac{EI}{k_B T}$ stiffer filaments are straighter.

$$A = \frac{EI}{k_B T} = \frac{\text{bending rigidity}}{\text{thermal energy}} = \frac{\text{energetic cost}}{\text{entropic cost}}$$

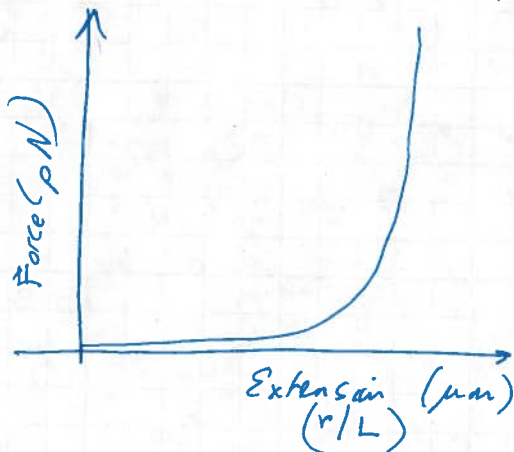
<u>Biopolymers</u>	<u>Configuration</u>	<u>A [nm]</u>
specklin	double stranded filament	10-20
DNA	double helix	51-55
F-actin	filament	$10-20 \cdot 10^3$
Microtubule.	13 protofilaments	$1-6 \cdot 10^6$

Thus, the goal now is to actually model this.

From a pure mechanics point of view, when we think elasticity we think $F = kx$ or Hooke's Law.

→ Essentially a linear increase of force with length.

However with biopolymers like DNA, you get a plot like



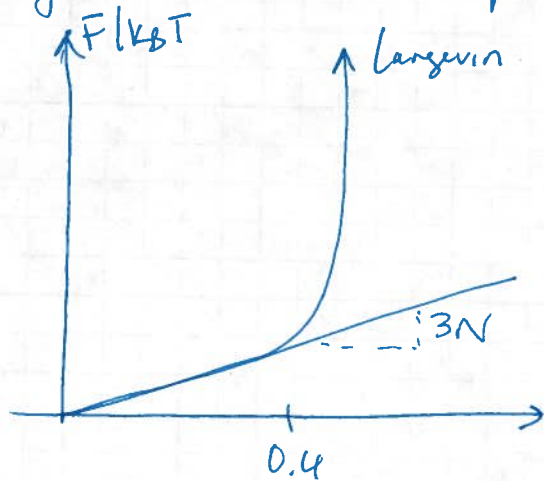
Nonlinearity occurs for $\frac{r}{L} < 0.2$

Why does this happen?

~~There are two models we can discuss.~~

First, I want to introduce Langevin model. I will not discuss this in class but it helps explain this phenomenon mathematically. You will see mention of this in the reading.

Consider a plot



Gaussian model acts as a linear entropic spring

$$k_{\text{Gauss}} = \frac{3k_B T N}{L^2}$$

[This comes from $\psi = \frac{1}{2} k_{\text{spring}} u^2$
 so $\frac{\partial^2 \psi}{\partial u^2} = k_{\text{spring}}$]

Clearly, ^{polymer} systems are nonlinear so a Gaussian model will not suffice

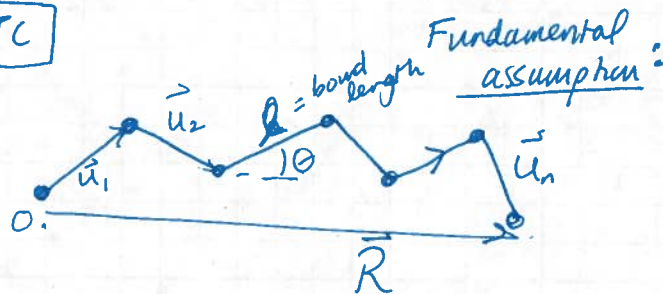
1. Freely Jointed Chain Model (FJC)

→ polymer modeled w/ rigid segments connected by freely rotating hinges

2. Wormlike chain model (WLC)

→ polymers modeled as continuous space curves rather than discrete segments.

For **FJC**



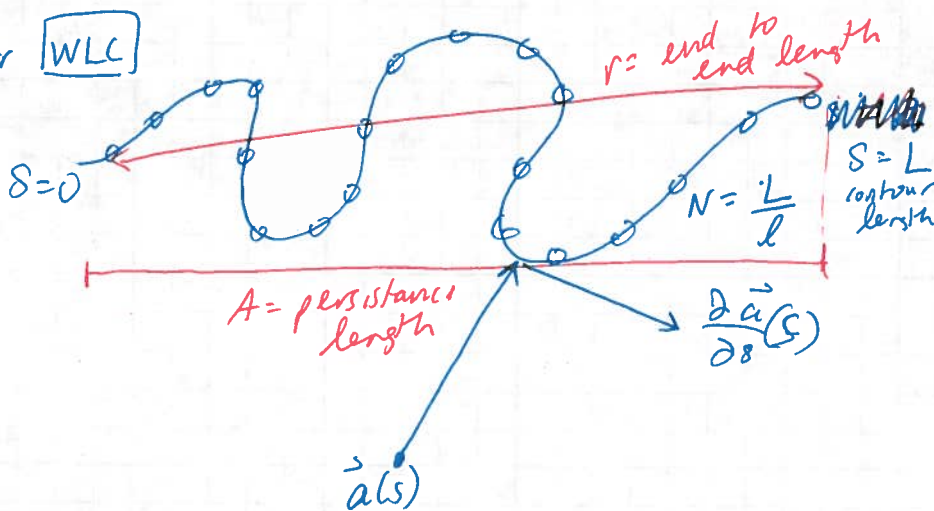
two neighboring bonds are completely uncorrelated so the overall chain configuration seems random.

→ The polymer can only have disorder at joints between segments.

→ can model as a 3D random walk.

→ This only considers entropic contribution.

For **WLC**



This is now a correlated chain that takes into account both entropic & energetic contribution

Persistence length is a measure of the initial chain stiffness.

$l \leq A \leq L$
bond length contour length

$A = l$ → uncorrelated chain

$A = L$ → elastic beam.

Persistence length has 3 classifications

$A \ll L$ flexible

$A \approx L$ semi-flexible

$A \gg L$ stiff.

What are the models mathematically?

$$\text{FJC} \quad \left\langle \frac{z}{L_{\text{TOT}}} \right\rangle = \coth \left(\frac{f_b}{k_B T} \right) - \frac{k_B T}{f_b}$$

For low limit stretching ... $k_B T \gg f_b$

$$\coth(x) \approx 1/x + \frac{1}{3}x - \frac{1}{45}x^3 + \dots$$

$$\left\langle \frac{z}{L_{\text{TOT}}} \right\rangle = \left[\frac{k_B T}{f_b} + \frac{1}{3} \frac{f_b}{k_B T} \right] - \frac{k_B T}{f_b}$$

Hooke's Law • $f_b = 3 k_B T \left(\frac{z}{L_{\text{TOT}}} \right)$

Typically

$$L_{\text{TOT}} = N b$$

$$b = \text{Kuhn length}$$

$$b = \frac{1}{2} l_p \quad \text{or} \quad \frac{1}{2} A$$

For high limit force ... $k_B T \ll f_b$

$$\coth(x) = 1 + e^{-2x} \quad \text{so as } x \rightarrow \infty$$

$$\coth(x) \rightarrow 1$$

$$\left\langle \frac{z}{L_{\text{TOT}}} \right\rangle = 1 - \frac{k_B T}{f_b}$$

WLC

$$f = \frac{k_B T}{L_p} \left(\frac{1}{4 \left(1 - \frac{z}{L_{\text{TOT}}}\right)^2} - \frac{1}{4} + \frac{z}{L} \right)$$

$z =$ extension length

$L =$ contour length