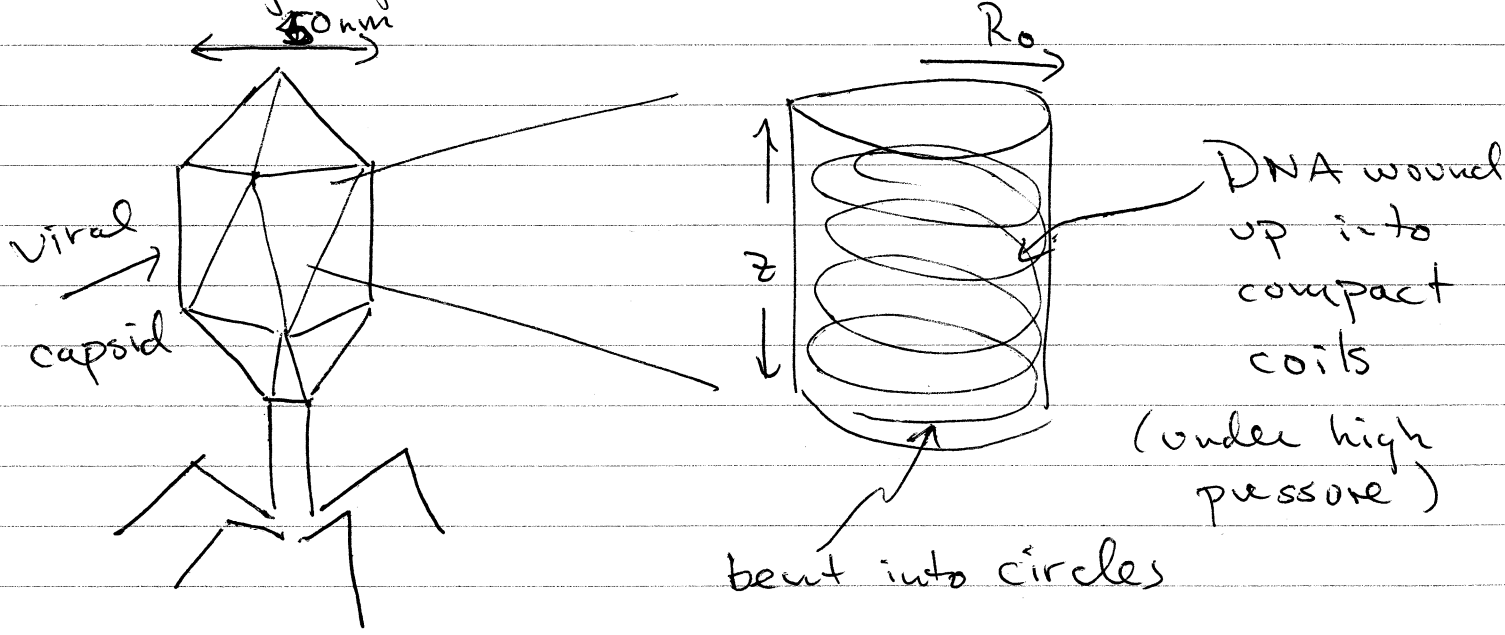


Application of Bending Energy in Biology:

We'll consider 3 cases where bending energy plays an important role

- 1) Packing of DNA into Viruses
- 2) Formation of nucleosomes
- 3) Buckling of microtubules

1) Packing of DNA in Viruses



Packing fraction:
$$\nu = \frac{V_{DNA}}{V_{capsid}}$$

for DNA, $1 \text{ bp} \approx 1 \text{ nm}^3$ so $V_{DNA} \approx N_{bp} \text{ nm}^3$

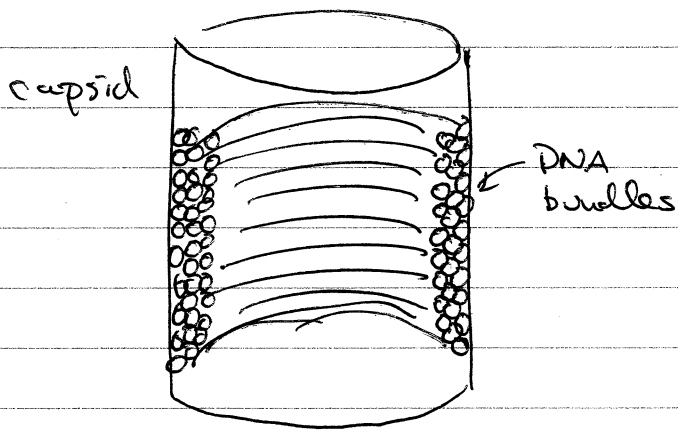
for λ -phage virus:
$$\nu_{\lambda} = \frac{(50,000) \text{ nm}^3}{\frac{4}{3} \pi (27 \text{ nm})^3} \approx 0.6!$$

For bacterial nucleoid,

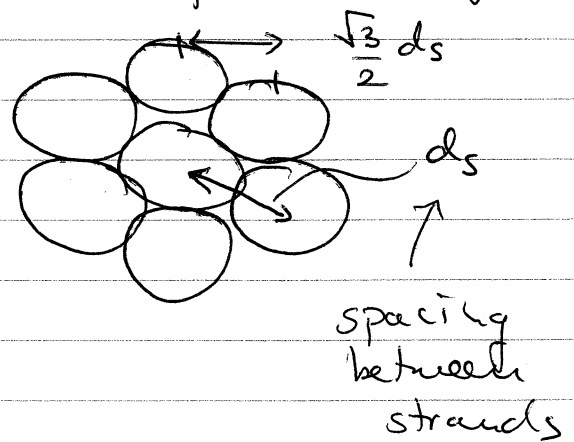
$$V_{bact} \approx \frac{(5 \times 10^6) \text{ nm}^3}{\frac{4}{3} \pi (0.25 \mu\text{m})^3} \approx 0.1$$

- So the viral DNA is packed to almost crystalline densities. How is this accomplished?

Structure of packing



- DNA is packed in a hexagonal arrangement



Scaling of d_s :

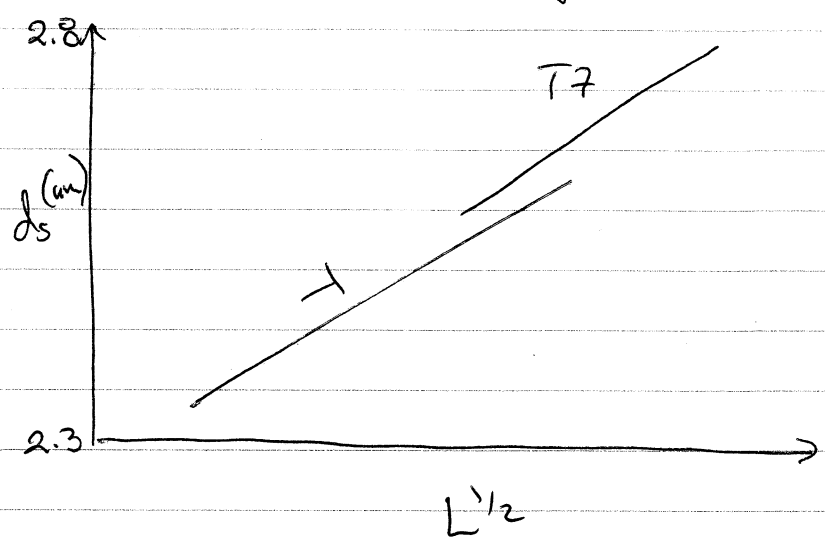
$$V_{genome} \sim L d_s^2 \quad (\text{volume of cylinder})$$

$$\approx V_{capsid}$$

so

$$d_s \approx \sqrt{\frac{V_{capsid}}{L}} \sim L^{-1/2}$$

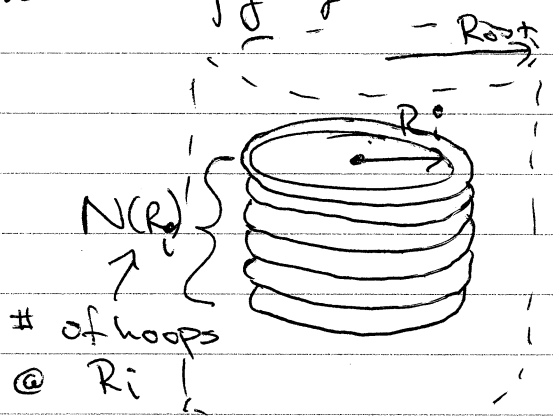
Expt confirms this scaling



from

PK Purohit et al, Biophys J 88, 851 (2005)

Energy of bent DNA in capsid:



capsid radius

DNA bent into $N(R_i)$ hoops of radius R_i

so $E_{bend} = \sum_{R_i} E_{hoop}(R_i) \cdot N(R_i)$

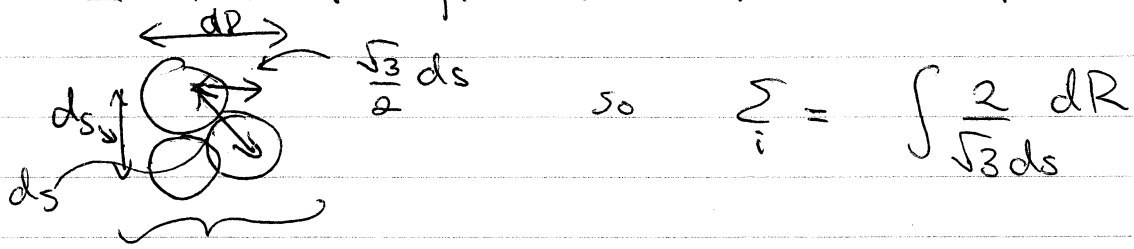
now

$$E_{hoop}(R_i) = \frac{\sum_p h_p T (2\pi R_i)}{2 R_i^2} = \frac{\pi \sum_p h_p T}{R_i}$$

so

$$E_{bend} = \pi \sum_p h_p T \sum_{R_i} \frac{N(R_i)}{R_i}$$

Convert Σ into integral over radius via



of hoops in dR
 $= \frac{dR}{\left(\frac{\sqrt{3} ds}{2}\right)}$

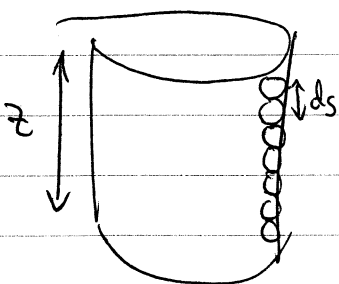
so

$$E_{\text{bend}} = \frac{2\pi \frac{2}{\sqrt{3} ds} k_B T}{\sqrt{3} ds} \int_R^{R_{\text{out}}} \frac{N(R')}{R'} dR' \quad (1)$$

- This gives the bending energy as a function of R , the extent of the DNA that has been packed into the capsid.
- Would rather express it in terms of L , the length of DNA inside the capsid.

$$L = \frac{2}{\sqrt{3} ds} \int_R^{R_{\text{out}}} 2\pi R' N(R') dR$$

• Consider a cylindrical capsid



so $N(R) = \frac{z}{ds}$ (indep of R)

So Eqn (1) gives

$$E_{\text{bend}}(R) = \frac{2\pi \frac{9}{2} k_B T z}{\sqrt{3} d_s^2} \ln\left(\frac{R_{\text{out}}}{R}\right)$$

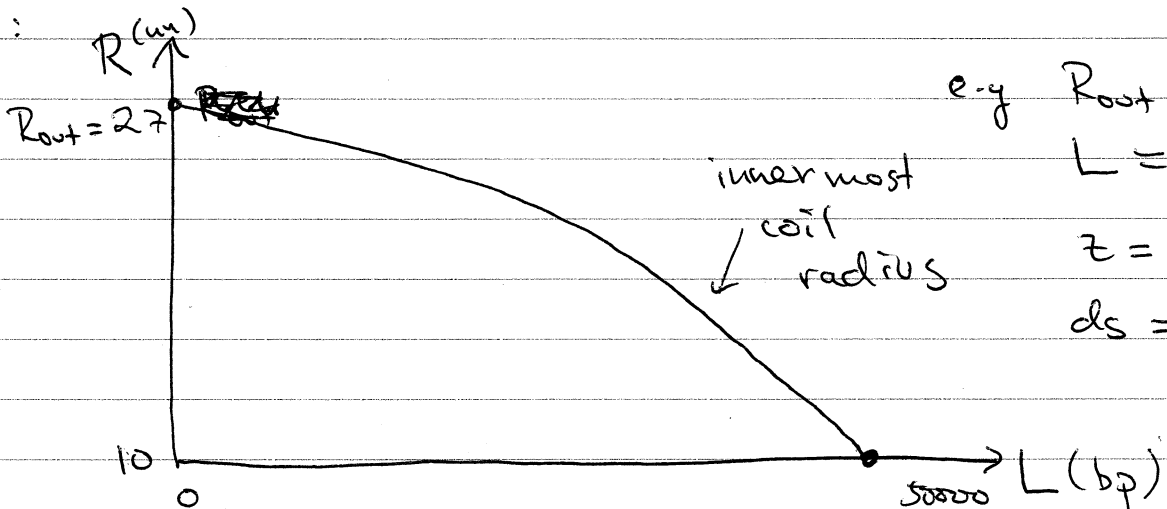
and

$$L(R) = \frac{2\pi z}{\sqrt{3} d_s^2} (R_{\text{out}}^2 - R^2)$$

or

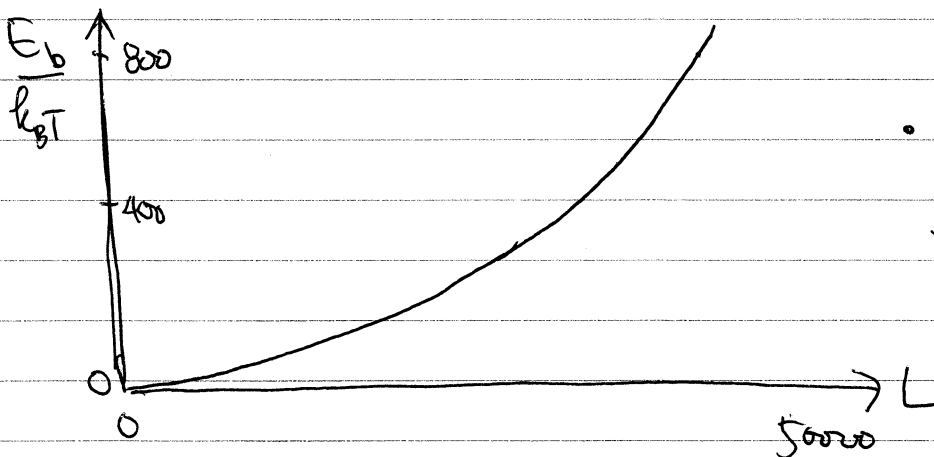
$$R = R_{\text{out}} \sqrt{1 - (\sqrt{3} d_s^2 L) / (2\pi z R_{\text{out}}^2)}$$

Graphs:



so

$$E_{\text{bend}} = -\pi \frac{9}{2} \frac{k_B T z}{\sqrt{3} d_s^2} \ln\left(1 - \frac{\sqrt{3} d_s^2 L}{2\pi z R_{\text{out}}^2}\right)$$



• So elastic energy increases as more DNA gets put into virus

This generates a force:

$$f = - \frac{dE_{\text{bend}}}{dL} = - \frac{\left(\frac{3}{2} p k_B T / 2 R_{\text{out}}^2 \right)}{1 - \sqrt{3} d_s^2 L / 2 \pi z R_{\text{out}}^2}$$

- This is not the only energy; the DNA has -ve charge and so the strands repel each other. So there's a competition between E_{bend} & E_{charge}

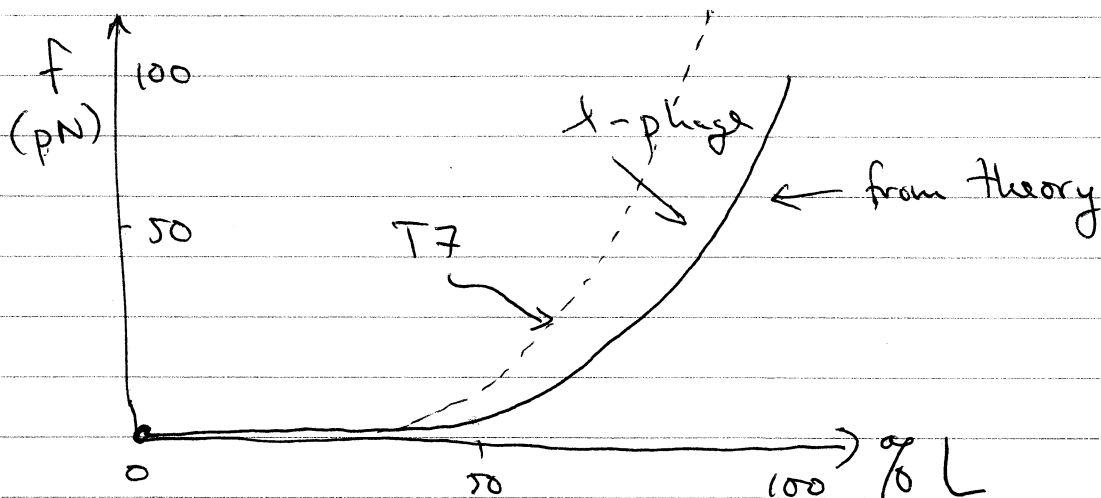
- E_{bend} wants d_s small so that most of the DNA can get packed with large R

But

E_{charge} wants d_s large so that the strands are far apart

- This competition leads to an optimal $d_s(L)$ that minimizes $E_{\text{tot}}(L) = E_{\text{bend}}(L) + E_{\text{charge}}(L)$

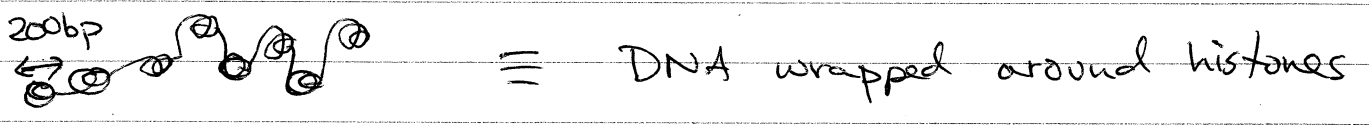
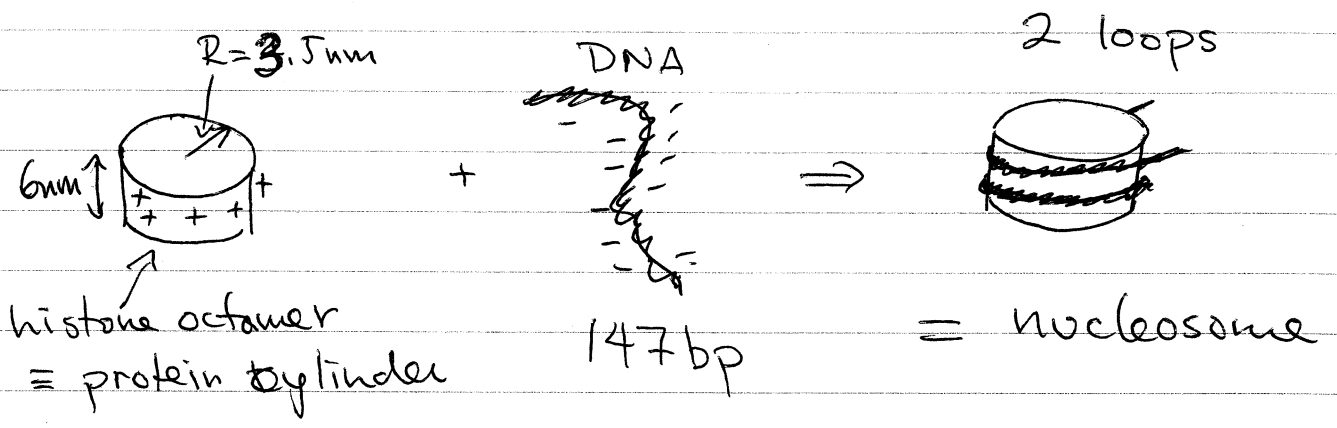
- The total force, $f = -dE_{\text{tot}}/dL$ using optimal $d_s(L)$



- Predict T7 can exert a stronger force than λ

2) Formation of nucleosomes

- DNA in eukaryotes gets packaged into nucleosomes



- How many histones for a genome of size 3×10^9 bp

$$N_{\text{hist}} = \frac{3 \times 10^9 \text{ bp}}{200 \text{ bp/histone}} \approx 10^7 \text{ histones}$$

- Histone is +vely charged & DNA is -vely charged
 ⇒ attractive interaction

BoI DNA is very bent! Loops with $R \sim 4.5 \text{ nm}$ which is much smaller than the persistence length $\xi_p = 50 \text{ nm}$

The free energy of nucleosome formation is

$$F_{tot} = F_{band} + F_{charge}$$

Now,

$$F_{band} = 2 \left(\pi \frac{\sum_p \frac{1}{R} k_B T \right) \approx 70 k_B T \text{ for } R=4.5$$

2 loops

E_{charge} is an adhesive interaction.

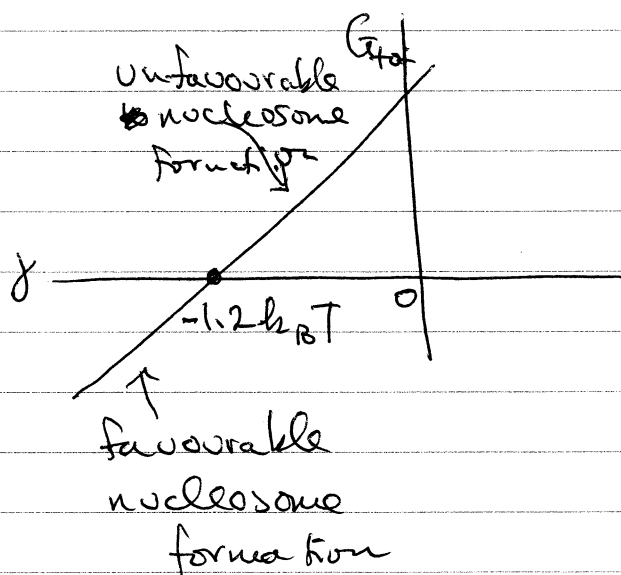
$$F_{charge} = 2(\gamma L) = 2(2\pi R)\gamma$$

where $\gamma \equiv$ adhesive energy per length

and $\gamma < 0$

So $G_{tot} = 70 k_B T + 56 \gamma$

For small γ , $G > 0$ & loop will not form

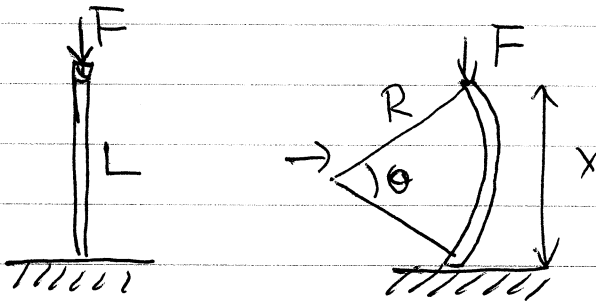


for $\gamma < -1.2 k_B T / \text{nm}$
then nucleosome formation is possible.

- ~~for $\gamma > -1.2 k_B T / \text{nm}$ then nucleosome formation is not possible.~~
- N.B. Σ_p depends on sequence

B) Beam buckling:

• Consider pushing on a beam with force F , at what force will the beam buckle?



• bending energy:

$$E_b = \frac{\int p k_B T}{2} \frac{L}{R^2}$$

• work:

$$E_w = -F(L-x)$$

so

$$E_{tot} = \frac{\int p k_B T}{2} \frac{L}{R^2} - F(L-x)$$

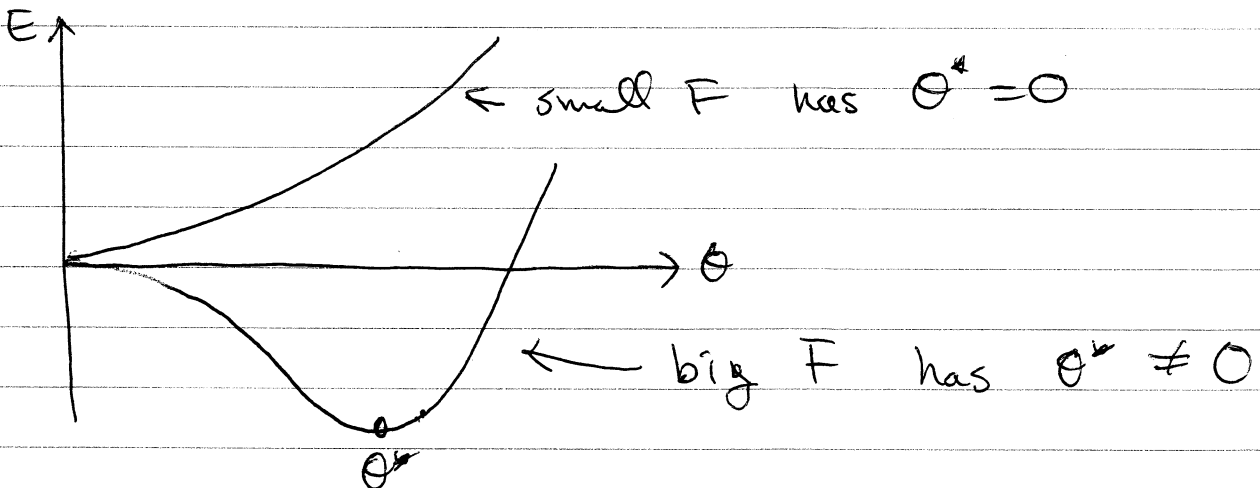
where

$$x = 2R \sin \frac{\theta}{2} \quad \& \quad R = \frac{L}{\theta}$$

so

$$\frac{E_{tot}}{k_B T}(\theta) = \frac{\int p}{L} \frac{\theta^2}{2} - \frac{FL}{k_B T} \left(1 - \frac{2}{\theta} \sin \frac{\theta}{2} \right)$$

• What θ^* minimizes E_{tot} @ a given F ?



• What is the critical force when beam buckles?

- near the critical force $\theta \approx 0$, so expand $\sin \frac{\theta}{2}$

$$\rightarrow \frac{E_{tot}}{k_B T} \approx \frac{\frac{3}{2} \theta^2}{L^2} - \frac{FL}{k_B T} \frac{\theta^2}{(24)}$$

$$\left[\sin x = x - \frac{x^3}{3!} + \dots \right]$$

so when $F < F_{crit} \Rightarrow E < 0$ & $\theta = 0$ solution

where $F_{crit} = 12 \frac{k_B T \frac{3}{2} p}{L^2} \sim L^{-2}$

• for $F > F_{crit}$, beam will buckle

N.B. Larger beams will buckle more easily
~~For DNA~~

• dsDNA : $\frac{3}{2} p = 50 \text{ nm}$, $k_B T = 4.1 \text{ pN} \cdot \text{nm}$; $L = 50 \text{ nm}$

$\rightarrow F_{crit} = 50 \text{ pN}$ to make it buckle

• microtubule : $\frac{3}{2} p = 7.3 \times 10^6 \text{ nm}$, $k_B T = 4.1 \text{ pN} \cdot \text{nm}$; $L = 20 \text{ } \mu\text{m}$

$\rightarrow F_{crit} = \underline{\underline{0.9 \text{ pN}}}$