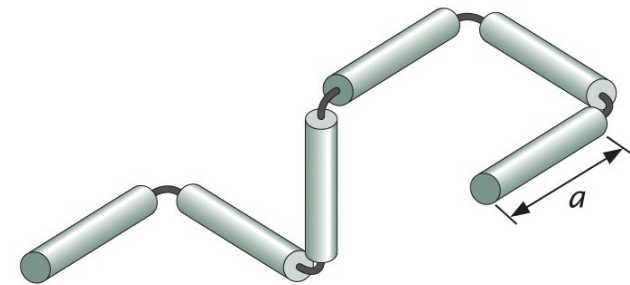
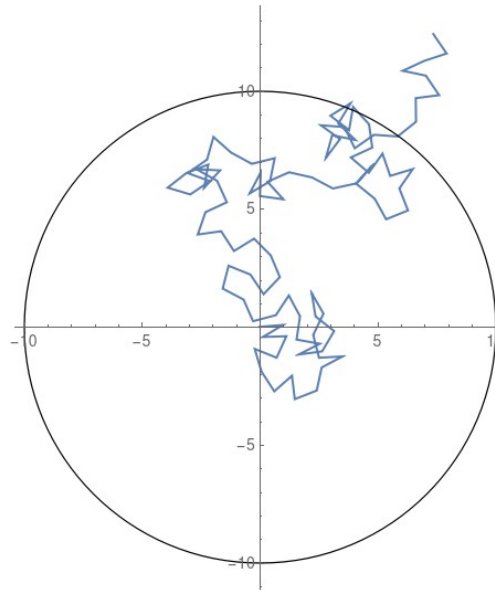


# Physics 414: Introduction to Biophysics

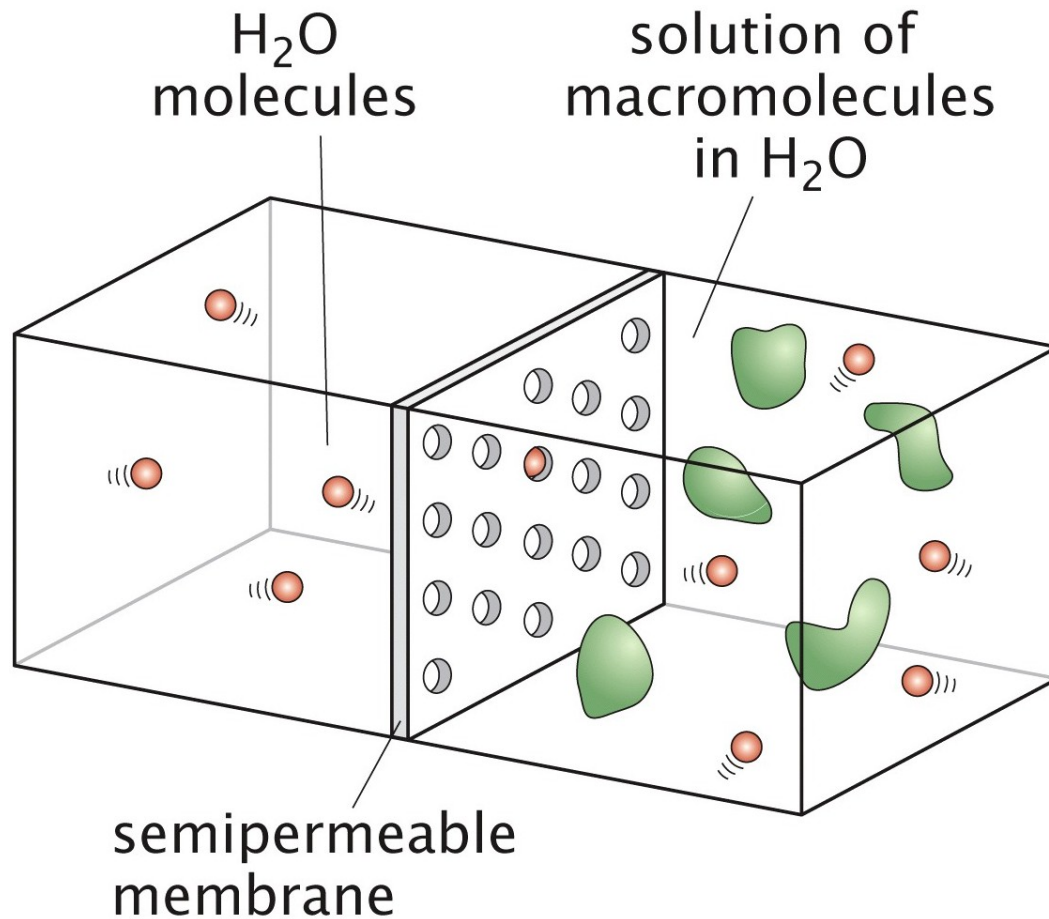
Professor Henry Greenside  
October 11, 2018



```
walk = Table[ { 0., 0. }, { length } ];  
For [ i = 2, i ≤ length, i++ ,  
  θ = RandomReal[ { 0., 2 π } ];  
  walk[[i]] = walk[[i-1]] +  
    a { Cos[θ] , Sin[θ] }  
]
```



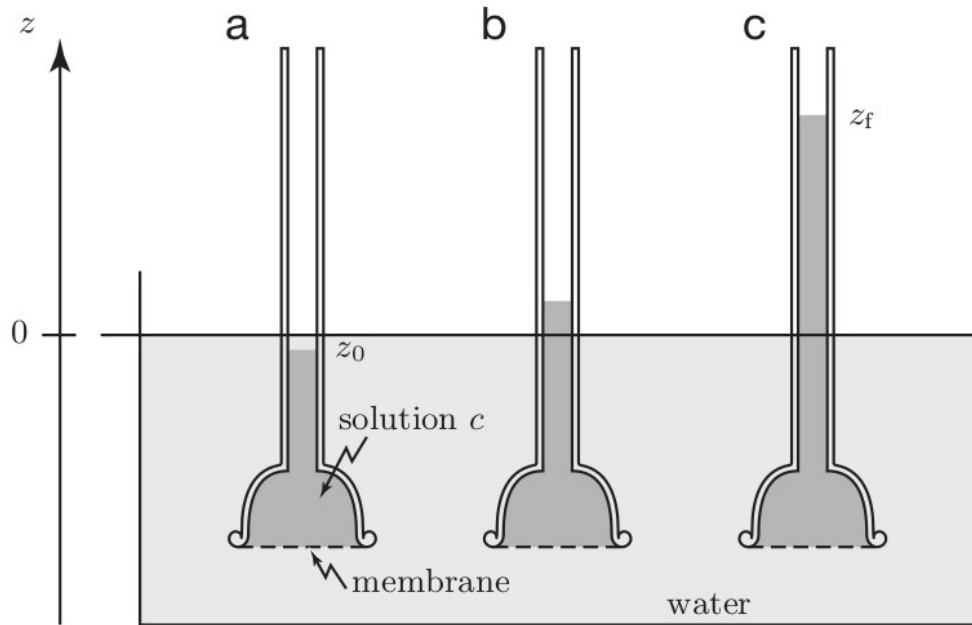
# Osmosis is a nonequilibrium phenomenon: movement of water (solvent molecules) across semipermeable membrane to region of higher solute concentration until equilibrium attained



Pure water has a higher water concentration than water “diluted” with solute molecules so chemical potential of pure water is higher than chemical potential of solution, so water will move “downhill” from higher to lower chemical potential if it can.

Solution has higher concentration of big molecules than pure water so the opposite should occur but the movement of big molecules to pure water is blocked by the semipermeable membrane. So water moves into the solution

Osmosis causes pressure difference  $\Delta p$  across membrane, with higher pressure on solution side



$$mg = (V \rho_m)g = (A\Delta z \rho_m)g = A\Delta p$$
$$\Rightarrow \Delta z \rho_m g = \Delta p$$

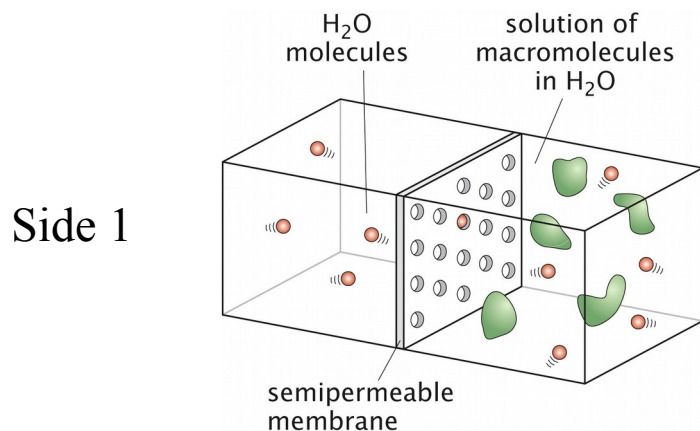
$\rho_m$  is mass density of solution  $c$

[https://youtu.be/7WX8zz\\_RlnE](https://youtu.be/7WX8zz_RlnE)

Membrane is permeable to water but impermeable to solute. Home experiment could be corn syrup inside *cellophane* membrane.

Thermodynamic equilibrium requires chemical potential  $\mu$  of water to be same on both sides of semipermeable membrane, leads to the van't Hoff equation if solutions are dilute. See Section 6.2.3 page 264-266 of PBOC2 (you do NOT need to know this derivation though)

$$p_2 - p_1 = \Delta p = (c_2 - c_1) k T$$



Side 2

$$\mu_{\text{H}_2\text{O}}(T, p) = \mu_{\text{H}_2\text{O}}^0(T, p) - \frac{N_s}{N_{\text{H}_2\text{O}}} k T$$

$$\left( \frac{\partial \mu}{\partial p} \right)_T = \frac{V}{N_S}$$

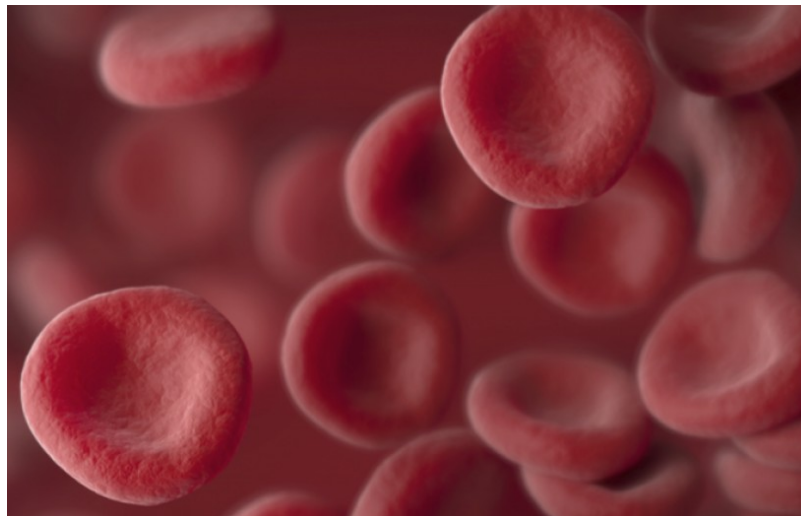
**If solutions are dilute, only number of solute molecules matters, not kind of solute molecules!** For rather deep reasons related to how ideal gas law can be derived from entropy  $S(E, V, N)$ , van't Hoff equation has same form as ideal gas law  $P = (N/V) k T = c k T$ .

# Conceptual osmosis question

It is found that when red blood cells are placed in a 1 mM solution of NaCl, the volumes of the red blood cells remain approximately constant.

If the same red blood cells are now placed in a 1 mM solution of glucose molecules, then

- 1) the red blood cells will remain the same
- 2) their volumes will increase.
- 3) their volumes will decrease.



How to understand origin of osmotic pressure via transfer of momentum is subtle but interesting, don't have time to discuss in course :(

Bernoulli's ideal-gas argument of particles colliding with and transferring momentum to wall doesn't work because, for dilute solutions, the solute particles are greatly outnumbered by solvent (water) molecules.

If you are interested, you can read a nice discussion of how the osmotic pressure arises from microscopic forces in the book "Biological Physics: Energy, Information, and Life" by Philip Nelson, see Section 7.3.1.

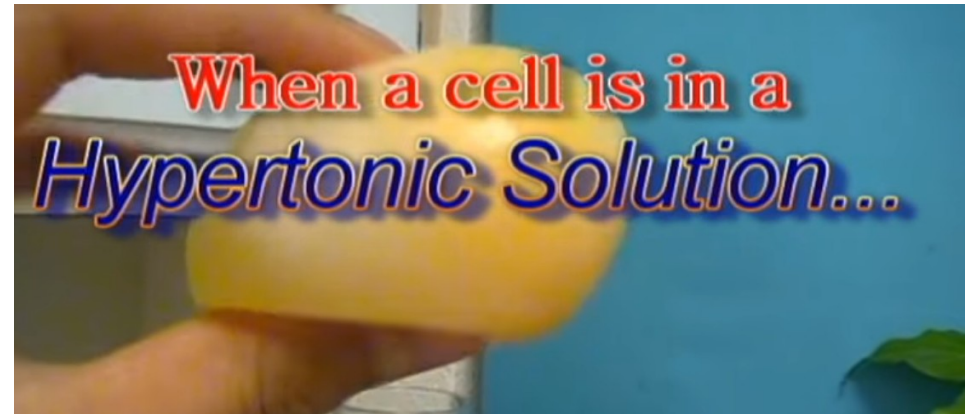
This knowledge is optional for the course, purely for your own enjoyment and satisfaction.

# Egg Osmosis (Hypertonic vs. Hypotonic Solution)

<https://www.youtube.com/watch?v=SSS3EtKAzYc>

Experiment, Day 1:

Placing Eggs in a  
Hypotonic and  
Hypertonic Solution



Search YouTube also for “dialysis tubing”

# Is osmotic pressure significant for a biological cell?

Typically 30% of eukaryotic cell's volume (volume fraction  $\phi$ ) occupied by globular proteins of radius  $R \approx 10$  nm. (Think hemoglobin inside red blood cell.) Then

$$0.3 = c \times \frac{4\pi}{3} (10^{-8} \text{ nm})^3 \Rightarrow c \approx 7 \times 10^{22} \frac{\text{molecules}}{\text{m}^3} \approx 0.12 \text{ mM}. \quad (1)$$

If cell placed in pure water and other stuff in cell ignored (e.g.,  $\approx 100$  mM of ions),

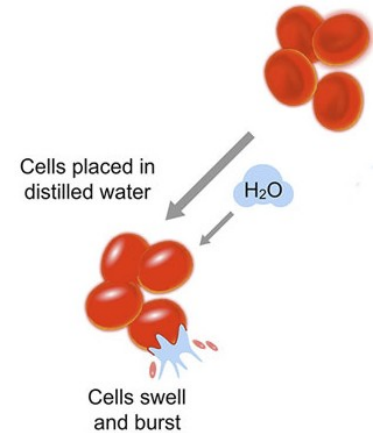
$$\Delta p = ckT \approx (7 \times 10^{22}) kT \approx 300 \text{ Pa} \ll 1 \text{ atm} \approx 10^5 \text{ Pa} \quad (2)$$

Osmotic pressure from fewer large molecules is tiny compared to atmospheric pressure but need to look at what pressure means in terms of cellular parameters. If cell has radius  $R \approx 10 \mu\text{m}$ , Young-Laplace law gives

$$\Delta p = \frac{2\sigma}{R} \Rightarrow \sigma = \frac{R\Delta p}{2} \approx 2 \times 10^{-3} \text{ J/m}^2. \quad (3)$$

This exceeds  $\sigma$  for eukaryotic cell bilipid membranes so bang, cell explodes.

Several evolutionary choices: pump water out, pump small molecules out, or build strong wall to prevent membrane from expanding (plants, bacteria).



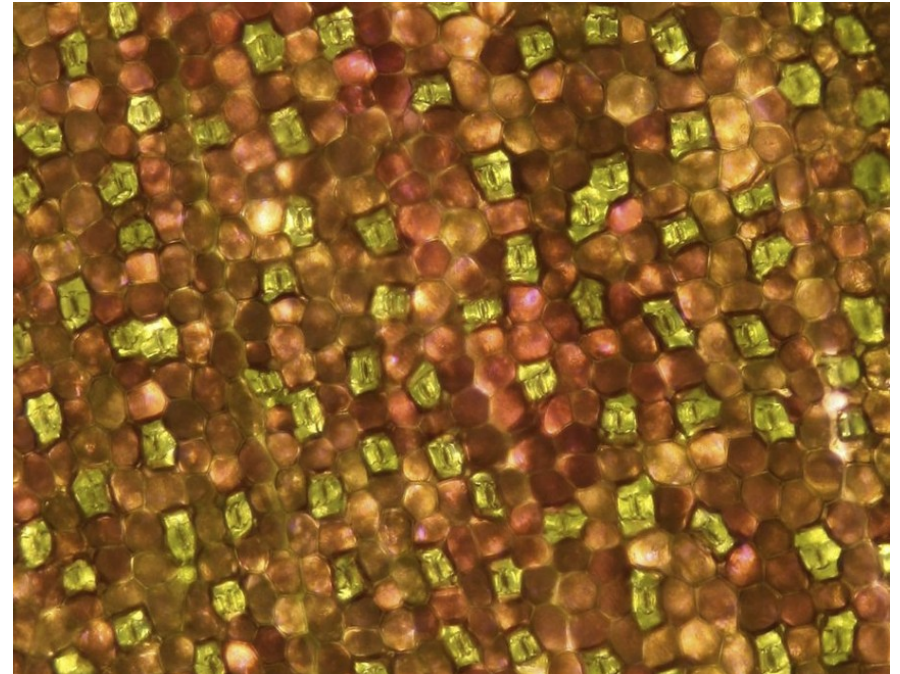


# Consequences, applications of osmosis

- 1) Cell shape and volume (how to kill a slug with salt...)
- 2) Photosynthesis by plants (stomata), roots extracting water
- 3) Cholera: bacterial-induced release of water into the small intestine
- 4) Reverse osmosis: desalination of seawater by pushing sea water through semi-permeable membrane with high pressure.



Stomata of a plant leaf (singular “stoma”)  
open and close via osmotic pressure  
<https://en.wikipedia.org/wiki/Stoma>



~60  $\mu\text{m}$

Stoma controls local intake and release of gases related  
to photosynthesis

# Venus Fly Trap (North and South Carolina) and Electroosmosis



<https://youtu.be/Hzk1bM2vVFU>  
“True Facts : Carnivorous Plants

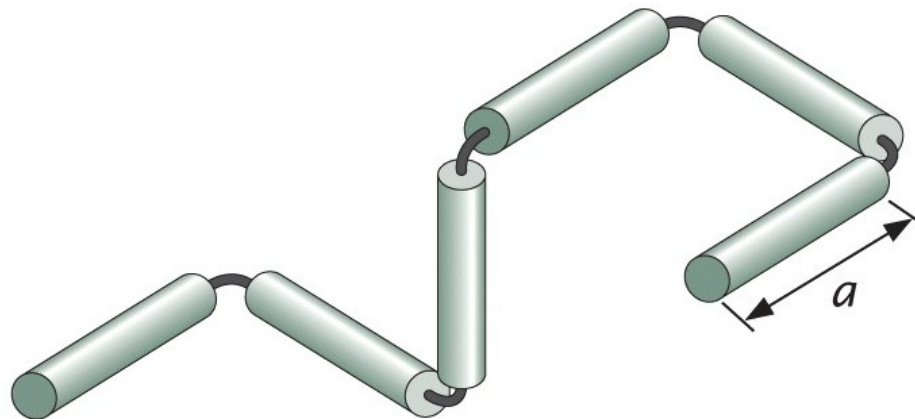
Class discussion: Are wrinkled fingers after bath/swim due to osmosis?



# Chapter 8: Random Walks and the Structure of Macromolecules

Claim: many polymers and biomolecules act in solution at room temperature as if they consist of approximately equal-size rigid links connected by frictionless joints that can rotate in any direction: the “**freely jointed chain model**” or **FJC model**.

When this is true, can use mathematics of so-called random walks to describe and deduce some of their properties such as average size, average distance between free ends, force-extension curve



Effective length of rigid segment is called the “Kuhn length”  $a$

# Applications of random-walk model of polymers

- 1) Size, volume of random-walk polymer
- 2) Tethering of ligand to increase local concentration of ligand
- 3) Loop formation: probability of one end of random-walk polymer meeting other end to close up and form a loop
- 4) Deduce structure of DNA inside nucleus, how affected by pinning of DNA to nuclear membrane, existence of chromatin domains.

# Numerical exploration of random walks

## Mathematica notebook random-walks.nb

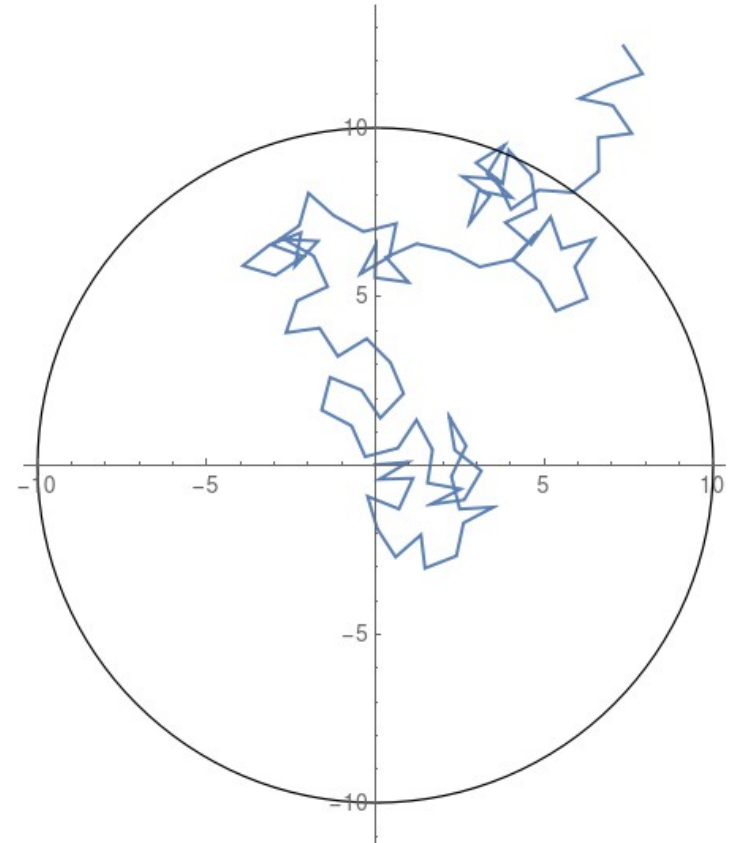
```
a = 1; (* constant step size *)
length = 100; (* number of steps in walk *)

walk = Table[
  {0., 0.},
  {i, 1, length}
];

For[i = 2, i ≤ length, i++,
  θ = RandomReal[{0., 2π}];
  walk[[i]] = walk[[i - 1]] + a {Cos[θ], Sin[θ]};
];

g1 = ListLinePlot[walk];
g2 = Graphics[Circle[{0., 0.}, Sqrt[length a]]];

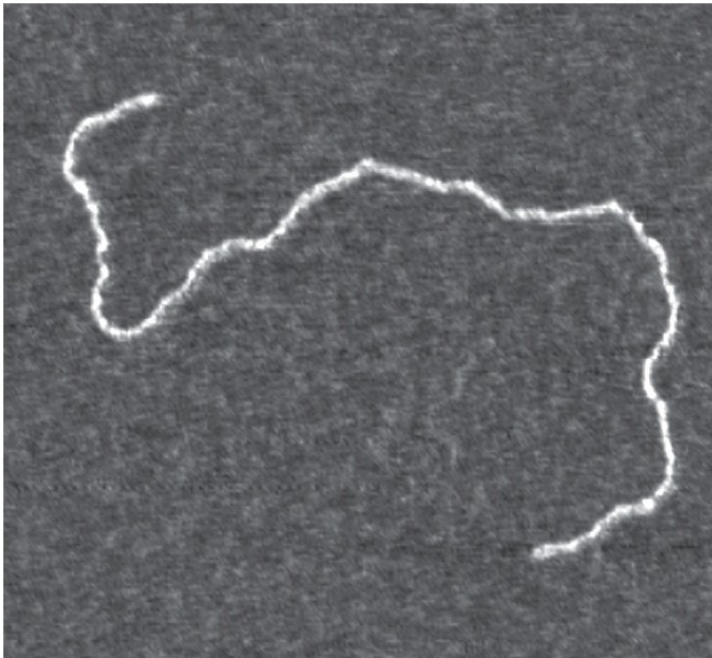
Show[
  g1, g2,
  AspectRatio → Equal,
  PlotRange → All
]
```



<http://webhome.phy.duke.edu/~hsg/414/files/mma-and-matlab/random-walks.nb>

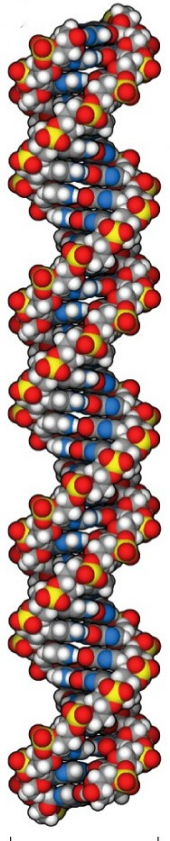
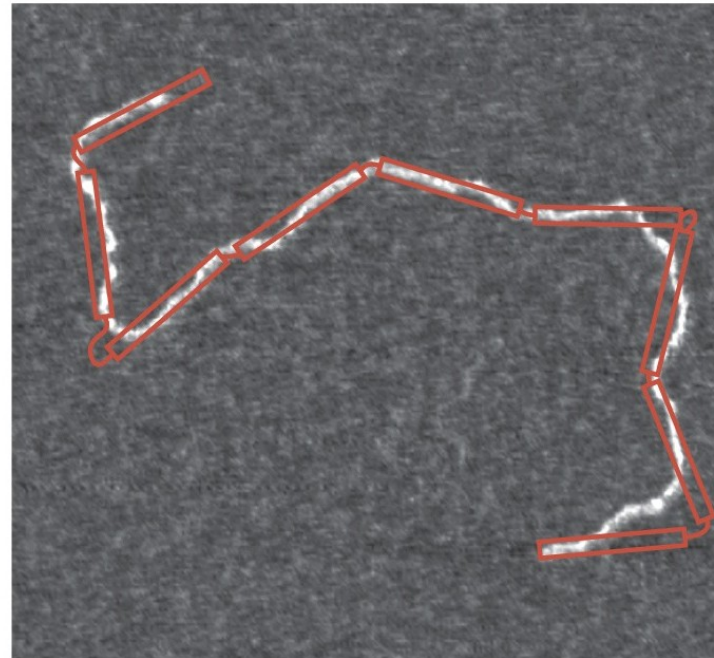
**Experimental example:  
Atomic Force Microscopic (AFM) images  
DNA writhing on a flat mica surface  
See Fig 8.2 p. 313 PBOC2**

(A)



100 nm

(B)



2 nm



# Nonequilibrium shaken chain spontaneously contracts to “blob” because of multiplicity (entropy)



YouTube video of beaded chain (not a molecule!) being shaken vertically

<https://youtu.be/zC0fS-g15m0>

“KNOT: Unknotting of a beaded chain #5”

# At the blackboard: why root-mean-square distance from origin of random walk goes as $\text{Sqrt}[\text{number of steps}]$ (You need to understand this derivation!)

I gave more general vector version of argument on page 314 of PBOC2 of why the root-mean-square (rms) distance from the origin after taking  $N$  successive random steps of equal length  $a$  is  $\text{Sqrt}[N]$ . Key point is to take “ensemble average”  $\langle \dots \rangle$  of the distance squared, which means to average over all possible random walks starting from the origin and taking the same number of steps. Outline of algebra is following:

$\mathbf{X}_N$  = location of random walker after  $N$  random steps of length  $a$

$$= \Delta \mathbf{X}_1 + \Delta \mathbf{X}_2 + \dots + \Delta \mathbf{X}_N = \sum_{i=1}^N \Delta \mathbf{X}_i \quad \Rightarrow$$

$$\langle R^2 \rangle = \langle \mathbf{X}_N \cdot \mathbf{X}_N \rangle = \left\langle \left( \sum_{i=1}^N \Delta \mathbf{X}_i \right) \cdot \left( \sum_{j=1}^N \Delta \mathbf{X}_j \right) \right\rangle$$

$$= \sum_{i=1}^N \langle \Delta \mathbf{X}_i^2 \rangle + 2 \sum_{i < j} \langle \Delta \mathbf{X}_i \cdot \Delta \mathbf{X}_j \rangle$$

$$= Na^2 + 2a^2 \sum_{i < j} \langle \cos(\theta_{ij}) \rangle \quad \text{since } \mathbf{a} \cdot \mathbf{b} = ab \cos(\theta)$$

$$= Na^2, \quad \text{since } \forall i, j, \langle \cos(\theta_{ij}) \rangle = 0.$$

## Why does $\langle \cos(\theta_{ij}) \rangle = 0$ ?

Why does the ensemble average  $\langle \cos(\theta_{ij}) \rangle = 0$ , where  $\theta_{ij}$  is the angle between the  $i$ th and  $j$ th vector steps,  $\Delta \mathbf{X}_i$  and  $\Delta \mathbf{X}_j$ ?

Without giving a careful proof, the gist is that if we choose two vectors of identical length with random directions in dimension 2 or 3, the angle  $\theta_{ij}$  between those vectors must itself vary randomly in the interval  $[0, 2\pi)$  and so  $\cos(\theta_{ij})$  must take on all possible values in the range  $[-1, 1]$  of cosine with equal likelihood, both positive and negative, and so the average of  $\cos(\theta_{ij})$  over many identical random walks (always starting at origin,  $N$  steps, all steps of same length) will involve adding many numbers that are equally positive and negative and so add up to zero.

It is perhaps easier to see this in two dimensions, for which

$$\begin{aligned}\Delta \mathbf{X}_i \cdot \Delta \mathbf{X}_j &= [a (\cos(\theta_i), \sin(\theta_i))] \cdot [a (\cos(\theta_j), \sin(\theta_j))] \\ &= a^2 (\cos(\theta_i) \cos(\theta_j) + \sin(\theta_i) \sin(\theta_j)) \\ &= a^2 \cos(\theta_i - \theta_j).\end{aligned}$$

So in 2D,  $\theta_{ij} = \theta_i - \theta_j$  is the difference in angles that give the directions for the  $i$ th and  $j$ th steps. If the  $\theta_i$  are being chosen randomly from a uniform distribution on the interval  $[0, 2\pi]$ ,  $\theta_i - \theta_j$  is a uniformly distributed random number on the interval  $[-2\pi, 2\pi]$  which spans two periods of  $\cos(\theta)$ , so any average over all of its values must be zero.

# Kuhn length versus persistence length $\xi_p$

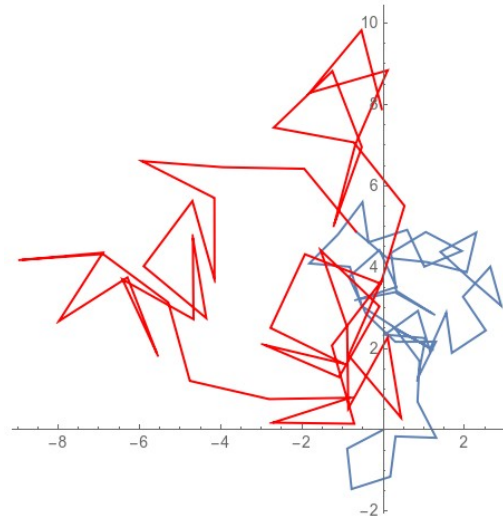
## Pages 319-321 of PBOC2

Will discuss after the midterm exam when we get to Chapter 10 on beams, involves technical details not important for the midterm. For now, just realize that experimental measurements like Fig 8.5 on page 319 yield a persistence length and a calculation (page 320 PBOC2) relates the Kuhn length of a random-walk polymer to the persistence length by:

$$a = 2\xi_p$$

So logic is that IF a polymer is described by a random walk with equal Kuhn lengths, THEN the Kuhn length is related to the persistence length by this simple relation. However, there are cases where the two lengths are not simply related; knowing the persistence length does not automatically give the Kuhn length without further information.

# At the board: let's figure out what happens if we attach one random-walk polymer (blue) to the end of a second random-walk polymer (red)?



$M=50$  steps with  $a=1$  followed by  $N=50$  steps with  $b=2$ .

Consider random-walk polymer consisting of  $M$  identical monomers of Kuhn length  $a$ . One end of this monomer is attached to a glass bead that is held in a fixed position by an optical tweezer. The free end of this polymer is attached to a second random-walk polymer of  $N$  identical monomers of Kuhn length  $b$ . Let  $\mathbf{X}_{\text{end}}$  be the location of the free end of the second polymer.

1) What is the mean or average location:  $\langle \mathbf{X}_{\text{end}} \rangle$ ?

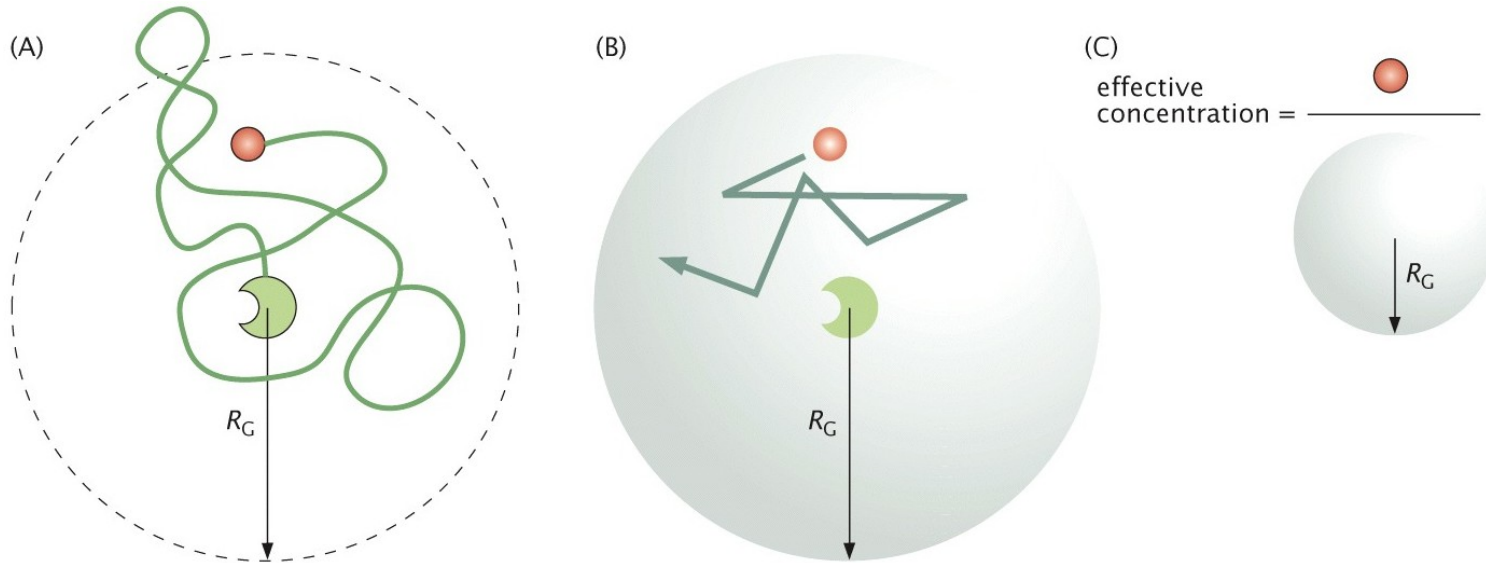
2) What is the variance of the location of the end:  $\langle (\mathbf{X}_{\text{end}} - \langle \mathbf{X}_{\text{end}} \rangle) \cdot (\mathbf{X}_{\text{end}} - \langle \mathbf{X}_{\text{end}} \rangle) \rangle$ ?

Answer to (1):  $\langle \mathbf{X}_{\text{end}} \rangle = \mathbf{0} = (0, 0, 0)$

Answer to (2): the mean-square-distance is  $Ma^2 + Nb^2$ .

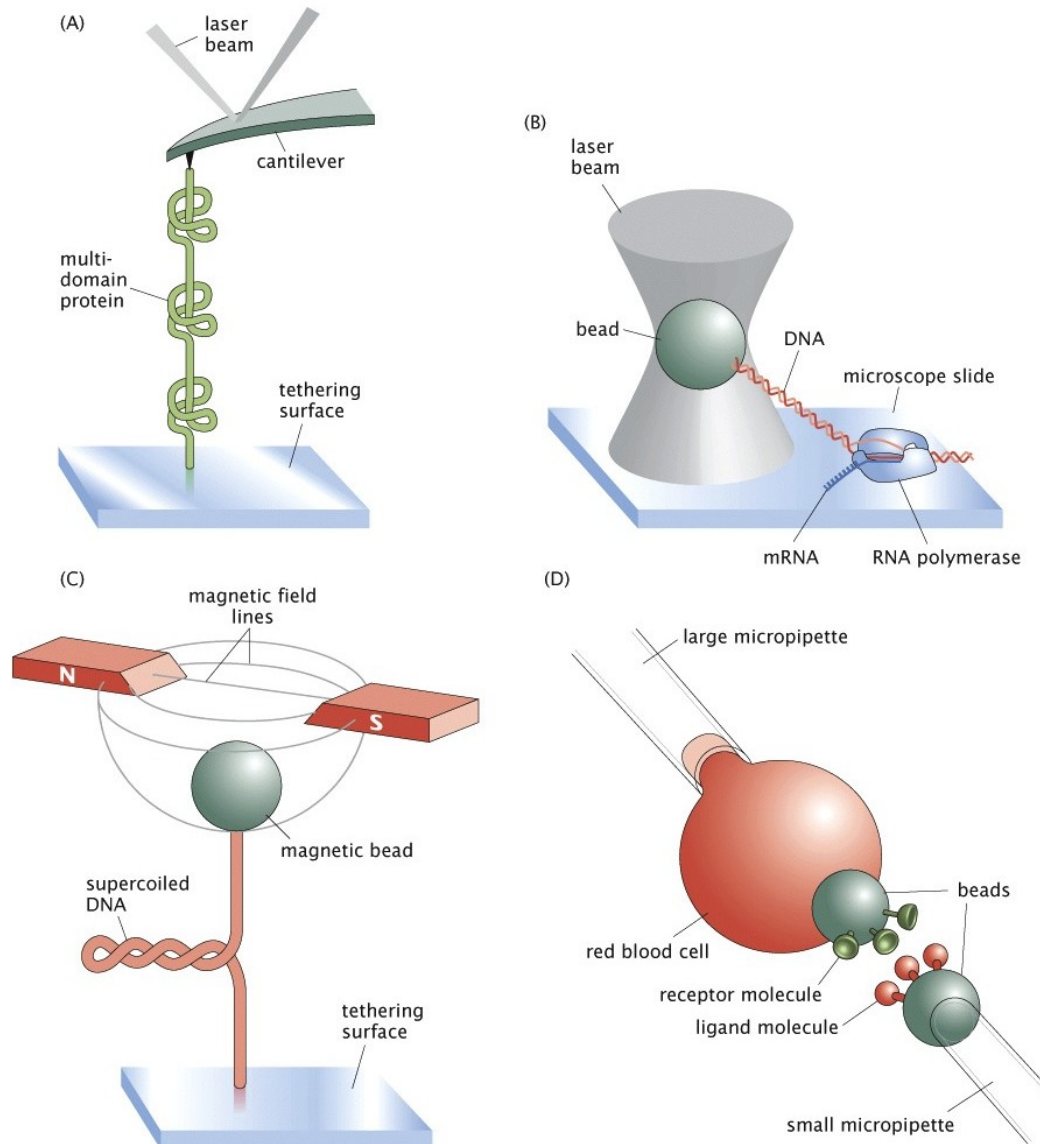
# Tethering of ligand with random-walk polymer can increase local ligand concentration

See Section 19.4.2, Fig 19.61, page 884 of PBOC2

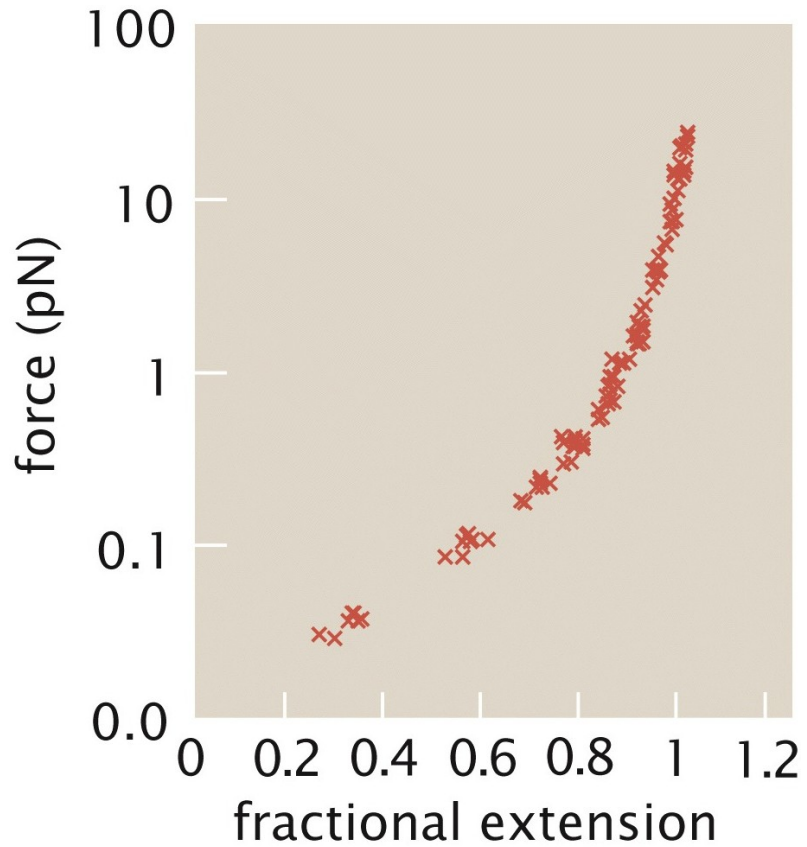


$$c_{\text{effective}} = \frac{1}{\frac{4\pi}{3} R_G^3} = \frac{1}{\frac{4\pi}{3} (Na^2)^{3/2}}$$

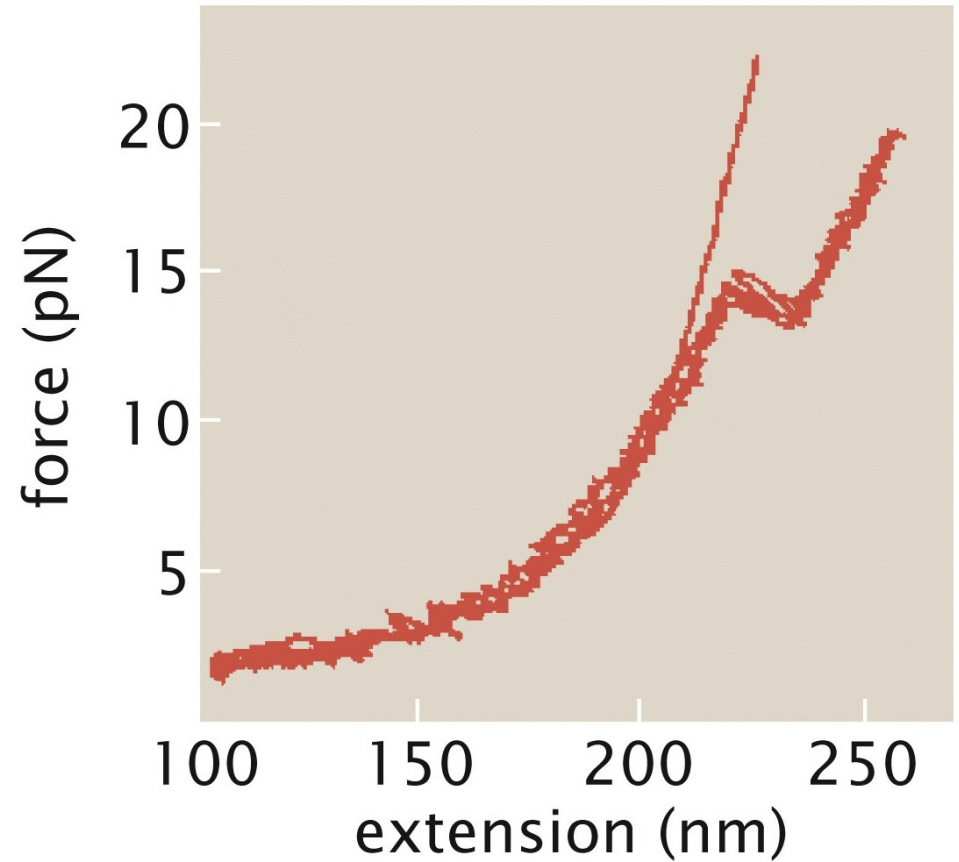
# Single-molecule force-extension curves: “Force spectroscopy” Fig 8.21 page 338 PBOC2



# Different macromolecules have different force-extension profiles



ds DNA



RNA



# At blackboard: low-force linear regime of force-extension curve using freely-jointed chain model and partition function

$$F = -kT \ln Z_N, \quad Z_N = Z_1^N$$

$$\langle L \rangle = - \left( \frac{\partial F}{\partial f} \right) = -NkT \frac{\partial \ln(Z_1)}{\partial f}$$

$$Z_1(1d) = e^{\beta f a} + e^{-\beta f a}, \quad Z_1(3d\text{-lattice}) = 4 + e^{\beta f a} + e^{-\beta f a}$$

$$Z_1(3d\text{-continuous}) = \int_0^{2\pi} d\phi \int_0^\pi d\theta \exp \left[ \frac{f a \cos(\theta)}{kT} \right] \sin(\theta)$$

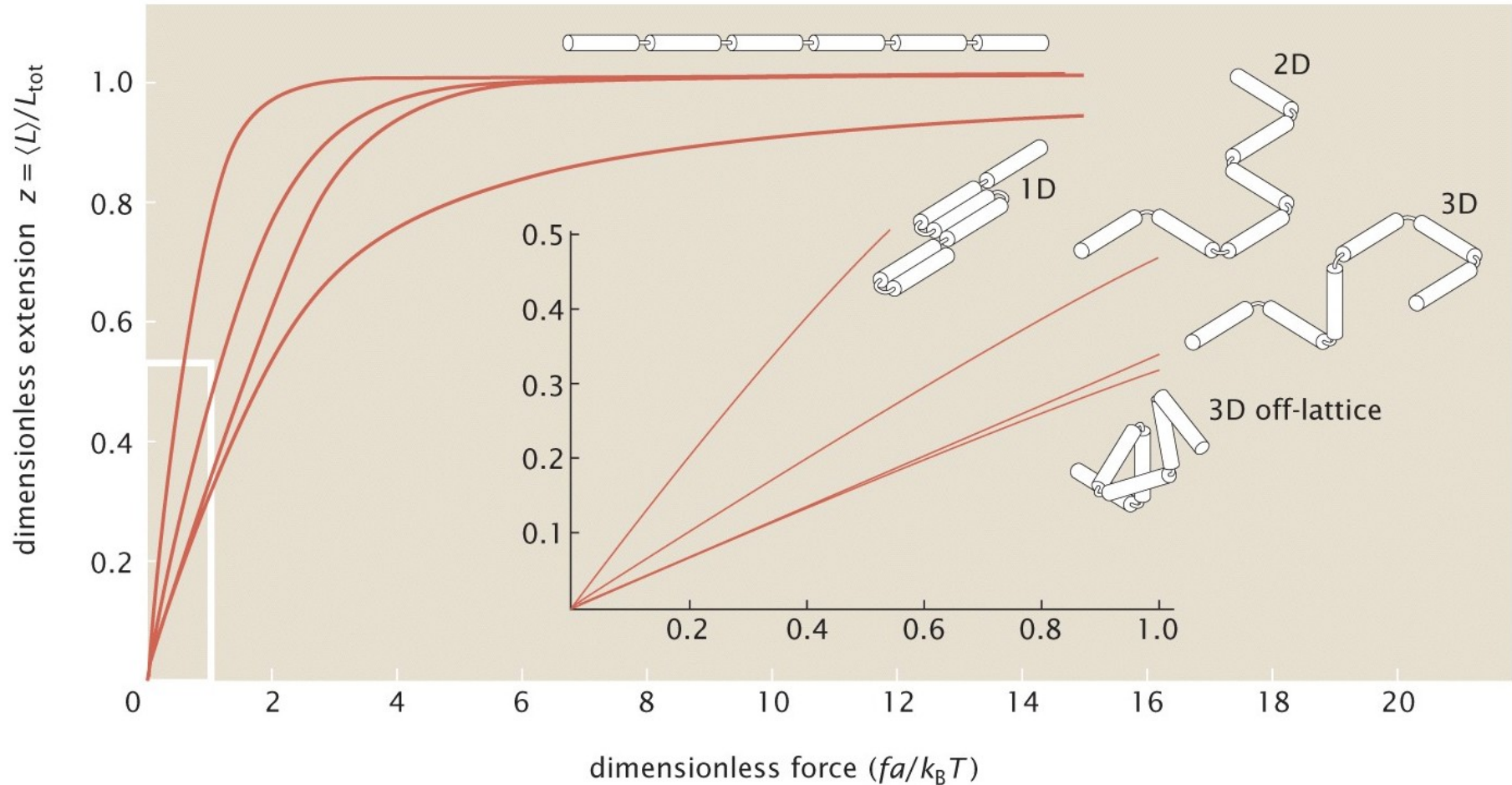
$$\langle L \rangle_{1d} = N a \tanh \left( \frac{f a}{kT} \right)$$

$$\langle L \rangle_{3d\text{-lattice}} = N a \frac{\sinh(\beta f a)}{2 + \cosh(\beta f a)}$$

$$\langle L \rangle_{3d\text{-cont}} = N a \left[ \coth \left( \frac{f a}{kT} \right) - \frac{kT}{f a} \right]$$

For 3D continuous independent links, get Langevin function  $L(x) = \coth(x) - 1/x$  that shows up in using statistical mechanics to calculate polarization or magnetization of gas of independent electric or magnetic dipoles aligning in external uniform field at finite temperature  $T$ .

# Freely-jointed chain model predictions of force-extension curves



# PBOC2 uses entropy to derive linear (“Hookean”) regime of force-extension curve using 1d freely-jointed chain but better, easier to use Boltzmann distribution

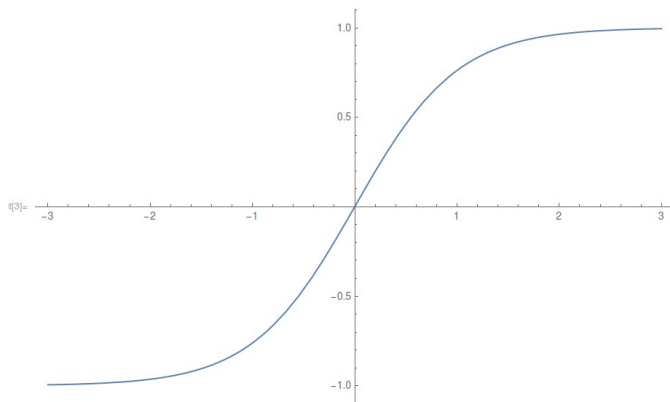
$$G(n_R) \approx -2fa n_R + kT [n_R \ln(n_R) + (N - n_R) \ln(N - n_R)] \Rightarrow$$

$$\frac{\partial G}{\partial n_R} = -2fa + kT \ln n_R - kT \ln(N - n_r) = 0 \Rightarrow$$

$$\frac{n_R}{n_L} = \exp \left[ \frac{2fa}{kT} \right] \Rightarrow$$

$$z = \frac{\langle L \rangle}{L_{\text{tot}}} = \frac{n_R - n_L}{n_R + n_L} = \tanh \left( \frac{fa}{kT} \right)$$

Plot[ Tanh[x], {x, -3, 3} ]



Although using entropy leads to a more detailed longer argument, it makes more clear why a random-walk polymer or rubber acts like a spring: the entropy is greatest when the polymer is not too long (fully extended) nor not too compact. At finite temperature, when entropy matters, there is a finite equilibrium size (of order  $R_G$ ) and it takes a force to make the molecule deviate from its state of greatest multiplicity (largest entropy).

**All these expressions for  $\langle L \rangle$  predict linear “Hookean” regime with spring constant  $k$  that is proportional to  $T$**

$$f = -k\langle L \rangle, \quad k = \frac{3kT}{L_{\text{tot}}a}$$

Compare some order-of-magnitudes:

For  $\lambda$ -phage ssDNA,

$$L_{\text{tot}} \approx 20 \mu\text{m}, \quad a \approx 1.5 \text{ nm}, \quad k = \frac{3kT}{aL_{\text{tot}}} \approx 200 \frac{\text{fN}}{\mu\text{m}}.$$

For commercial steel spring

$$k \approx 10^4 \text{ N/m} \approx 10^{13} \text{ fN}/\mu\text{m}.$$

For chemical bond in diatomic molecule like HCl,

$$k \approx 10^3 \text{ N/m} \approx 10^{12} \text{ fN}/\mu\text{m}.$$

So DNA is weak spring compared to some familiar springs.

**Temperature dependence of spring constant explains why rubber contracts upon being warmed, and why random-walk polymers become more compact with increased  $T$**

$$f = -k\langle L \rangle, \quad k = \frac{3kT}{L_{\text{tot}}a}$$

See the YouTube videos “Rubber band shrinks when heated”,  
<https://www.youtube.com/watch?v=eB4B2xZI77A>

and “Rubber band heat engine”  
<https://www.youtube.com/watch?v=dBXL93984cQ>

# One-minute End-of-class Question