Biophysics of Cells and Single Molecules: Problem set for weeks 36-37, 2023

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1 Problem 1: Cell polymers with $\xi_p << L_c$

The virus λ-bacteriophage infects bacteria like E. coli. It consists of a protein capsule carrying the viral DNA as well as a machinery to infect the bacterial cell. The λ-bacteriophage DNA has the length of $\sim 10^5$ base pairs (bp) each of length $0.34nm/bp$ and a persistence length, $\xi_p = 53nm$.

1. **Calculate the contour length L_c.**

   Since the length of each base pair is $0.34nm$ and the λ-bacteriophage has approximately 10^5 base pairs, the length is roughly

   $$L_c = (0.34nm)(10^5) = \boxed{3.4 \times 10^4 nm,}$$

   which is much larger than the persistence length $\xi_p = 53nm$.

2. **If the DNA has the diameter, $d = 2nm$, what is the minimum capsule volume in which it can be packed?**

   If it is packed perfectly, without letting any empty spaces (which of course isn't the case, but that would give us a minimum), the volume in which it can be packed is that of the DNA itself. Since it has a diameter of $d = 2nm$, the radius is $r = 1nm$, and therefore, considering the DNA as a cylinder, the volume is:

   $$V = \pi r^2 L_c = \pi (1nm)^2 (3.4 \times 10^4 nm) \simeq \boxed{1.068 \times 10^5 nm^3.}$$

   Imagine that the virus $\lambda-$ bacteriophage infects a bacterial cell.

3. **Find the root-mean-squared end-to-end distance, $\sqrt{\langle r_{ee}^2 \rangle}$, for this piece of DNA.**

In the bacteria, the DNA becomes a random chain. Then, since $L_c >> \xi_p$, we can use equation 3.33 of the book, $\langle r_{ee}^2 \rangle \simeq 2\xi_p L_c$ to conclude that:

$$\begin{aligned}\sqrt{\langle r_{ee}^2 \rangle} &\simeq \sqrt{2\xi_p L_c} \\ &= \sqrt{2(53nm)(3.4 \times 10^4 nm)} \\ &= \boxed{1898nm}\end{aligned}$$

4. **Compare to the dimensions of a bacterial cell, e.g., E. coli.**

The E. coli is approximately between $1\mu m$ and $2\mu m$ long. Since the result for $\sqrt{\langle r_{ee}^2 \rangle}$ is almost $2\mu m$, the DNA will occupy pretty much the whole bacteria from end to end.

Now imagine that the same piece of DNA has been extracted form the bacterial cell and transferred to an optical tweezers setup. Here the DNA is pulled from each end to extension: $x \to L_c$

5. **Plot the force $F(x)$ vs. x, using the Gaussian approximation and the simplified worm-like chain model (eq. 3.58):**

$$F(x) = \frac{k_B T}{\xi_p} \left(\frac{1}{4(1 - x/L_c)^2} - \frac{1}{4} + x/L_c \right)$$

As seen in the text, the Gaussian approximation gives rise to a spring constant of $k_{sp} = \frac{3k_B T}{2\xi_p L_c}$ and the force is $F = k_{sp}x$, which is:

$$F(x) = \frac{3k_B T}{2\xi_p L_c} x.$$

Then, we can plot this function and the worm-like chain model and compare the resulting graphs:

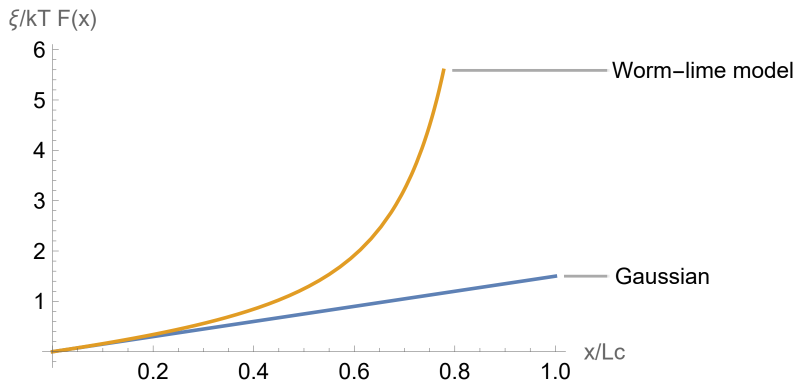

Figure 1: Plots of the two graphs.

6. **Speculate on the difference in these two models**

As we can see in the graph, the Gaussian model predicts a linear growth of the force as we stretch the DNA, while the worm-like chain shows that the force diverges as we approach $x = L_c$. The worm-like model makes more sense in this aspect, since the maximum length we could possibly have is $x = L_c$ (when the DNA is completely stretched) and any more than that is impossible if the chain segments are individually inextensible, so we would expect the force to diverge at that point.

However, for small extensions (around $x/L_c < 0.2$), both models are similar and give as a result a linear relation between $F(x)$ and x with a slope of $\dfrac{3k_BT}{2\xi_p L_c}$. In this situation, the Gaussian model is therefore a very good approximation.

2 Problem 2: Cell polymers with $L_c << \xi_p$

Now consider the eukaryotic cell S. pombe - also called fission yeast - with microtubules growing from nucleosomes on the nuclear membrane towards the cell poles. The microtubules in the cell extend $L_c = 5\mu m$ with the persistence length $\xi_p = 5mm$.

1. **Find the root-mean-squared end-to-end distance, $\sqrt{\langle r_{ee}^2 \rangle}$, for one of these microtubules.**

   Since in this case $L_c << \xi_p$, intuitively, the microtubule is pretty much straight and therefore the end to end distance is simply the whole length L_c of the microtubule. That is,

   $$\boxed{\sqrt{\langle r_{ee}^2 \rangle} = L_c.}$$

   Alternatively, this can also be found following equation 3.32 of the book, which says that

   $$\langle r_{ee}^2 \rangle = 2\xi_p L_c - 2\xi_p^2[1 - \exp(-L_c/\xi_p)].$$

   Then, given that $\xi_p >> L_c$, the exponent $-L_c/\xi_p$ is very small and therefore using the Taylor expansion up to the quadratic term, we have: $\exp(-L_c/\xi_p) \simeq 1 - \dfrac{L_c}{\xi_p} + \dfrac{1}{2}\dfrac{L_c^2}{\xi_p^2}$. Consequently, the expression reduces to

   $$\begin{aligned}\langle r_{ee}^2 \rangle &= 2\xi_p L_c - 2\xi_p^2 \left[1 - \left(1 - \frac{L_c}{\xi_p} + \frac{1}{2}\frac{L_c^2}{\xi_p^2}\right)\right] \\ &= 2\xi_p L_c - 2\xi_p^2 \frac{L_c}{\xi_p} + \xi_p^2 \frac{L_c^2}{\xi_p^2} \\ &= L_c^2.\end{aligned}$$

   Which implies that $\sqrt{\langle r_{ee}^2 \rangle} = L_c$.

2. **When this dynamic polymer reaches the cell pole it buckles. Calculate the force, F_B.**

   As seen in equation 3.69, the buckling force is equal to:

   $$F_B = \pi^2 \kappa_f / L_c^2.$$

   We already know L_c and to calculate κ_f we may use the definition of the persistence length, which is

   $$\xi_p = \frac{\kappa_f}{k_B T} \quad \Rightarrow \quad \kappa_f = \xi_p k_B T.$$

Then, substituting on the equation for the buckling force, we conclude that:

$$F_B = \frac{\pi^2 \xi_p k_B T}{L_c^2}. \tag{1}$$

We substitute the values of $\xi_p = 5 \times 10^{-3} m, L_c = 5 \times 10^{-6}$ and we approximate $k_B T = 4pNnm$. Doing so, the numerical result is:

$$F_B = \frac{\pi^2 (5 \times 10^{-3} m)(4 \times 10^{-12} N \times 10^{-9} m)}{(5 \times 10^{-6} m)^2} = \boxed{7.9 \times 10^{-12} N}$$

In S. pombe the microtubules bundle to raise the compression load they can withstand before they buckle. It has been found that the resulting flexural rigidity, κ_N , relates to the number of microtubules in the bundle, N, and the flexural rigidity of a single microtubules, κ_f like:

$$\kappa_N = N^\alpha \kappa_f,$$

where $\alpha \in \{1 : 3\}$ depending on cross-linking between microtubules.

3. **Calculate F_B in the limit of weak cross linking, $\alpha = 1$ and $N = 10$ as above.**

Since $\kappa_N = N^\alpha \kappa_f = 10^1 \kappa_f = 10 \kappa_f$ and F_B depends linearly on κ_f, the result will just be 10 times bigger than for the previous question. Therefore:

$$F_B = 7.9 \times 10^{-11} N.$$

4. **Each of these microtubules has an outer radius, $R = 14nm$, and the inner radius, $R_i = 11.5nm$. Now imagine that you constructed a single solid polymer with the same cross-sectional area, A, and length as the bundle and calculate the buckling force.**

The buckling force we are looking for is calculated with equation 1 of this document:

$$F_B = \frac{\pi^2 \kappa_f}{L_c^2} = \frac{\pi^2 IY}{L_c^2},$$

with $L_c = 5\mu m$. To use the equation, we need to find I and Y for this single solid polymer.

We can calculate the ratio between the buckling force for the single solid polymer and the buckling force for a microtubule:

$$\frac{F_{B,S}}{F_{B,MT}} = \frac{\frac{\pi^2 I_S Y_S}{L_{c,S}^2}}{\frac{\pi^2 I_{MT} Y_{MT}}{L_{c,MT}^2}}.$$

Given that they both have the same lengths and assuming that they have the same Young modulus, we get that:

$$\frac{F_{B,S}}{F_{B,MT}} = \frac{I_S}{I_{MT}}.$$

According to equation 3.12 of the book, the moment of inertia of a solid cylinder with radius R_s is $\pi R_s^4/4$. On the other hand, the moment of inertia of a hollow cylinder is $\pi(R^4 - R_i^4)$. Then:

$$\frac{F_{B,S}}{F_{B,MT}} = \frac{R_s^4}{R^4 - R_i^4}.$$

Now we are only missing the radius of the solid cylinder. To calculate it, we can use that the area of each microtubule is $A = \pi(R^2 - R_i^2) = \pi(14^2 - 11.5^2) = 200nm^2$. On the other hand, the area of the solid cylinder is $A = \pi R_s^2 \Rightarrow R_s = \sqrt{A/\pi} = 7.98nm$. Substituting in the equation, we get:

$$\frac{F_{B,S}}{F_{B,MT}} = \frac{R_s^4}{R^4 - R_i^4} = \frac{(7.98)^4}{14^4 - 11.5^4} = \boxed{0.176}$$

Therefore, the buckling force for the solid cylinder is around 6 times smaller than that of a microtubule.

5. **Speculate on the structural advantage of bundles of hollow microtubules.**

From the previous excercise, we can see that a solid cylinder has a buckling force much smaller than a hollow cylinder with the same area and length. Therefore, given an amount of material to build a rod, creating a hollow cylinder gives a better resistance to buckling forces.

Furthermore, bundling many microtubules is also advantagues, since the flexual rigidity of N microtubules grows as $N^\alpha \kappa_f$ with $\alpha \in \{1:3\}$. Therefore, when the exponent α is bigger than 1, the buckling force is larger than what we would get by just adding the buckling forces of each microtubule in the bundle. That is, having the microtubules together in a bundle increases their buckling force as compared to the total buckling force if they were separated.

3 Problem 3: Two-dimensional network with six-fold connectivity

The shear modulus of a spring network with six-fold connectivity is given by $\mu = \sqrt{3}k_{sp}/4$, where k_{sp} is the force constant of the springs. To establish this consider the deformation of a network plaquette, whose native shape is that of an equilateral triangle. The sides of the plaquette are the springs, the corners are the six-fold vertices. Under deformation the top vertex of the triangle is moved by an amoung δ in the $x-$direction.

1. **Find the new lengths of the springs forming the left-hand and right-hand sides of the plaquette under the deformation. [define the equilibrium spring length to be s_0 and work to lowest order in δ].**

   The situation described is that pictured in the following figure:

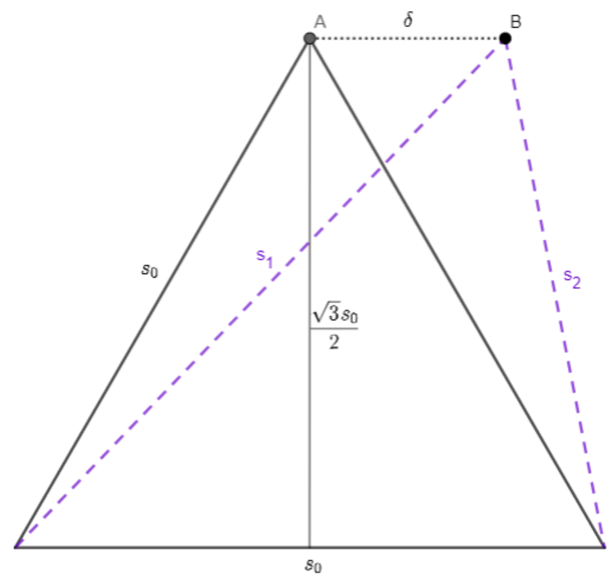

Figure 2: Deformation of an equilateral triangle. The original triangle is shown in black, while the deformed one is shown in purple and has sides of lengths s_0, s_1, s_2. The vertical line is the height of the original triangle, which is $\frac{\sqrt{3}s_0}{2}$.

To calculate the length of s_1, we can notice that the vertical length it transverses is $\frac{\sqrt{3}s_0}{2}$ (because it reaches the same height as the height of the triangle). On the other hand, the horizontal length it transverses is $\frac{s_0}{2} + \delta$, since point A is at $\frac{s_0}{2}$, while point B is a length δ to the right. Therefore,, we conclude that:

$$s_1 = \sqrt{\frac{3s_0^2}{4} + \left(\frac{s_0}{2} + \delta\right)^2} = \sqrt{\frac{3}{4}s_0^2 + \frac{1}{4}s_0^2 + s_0\delta + \delta^2} \simeq \sqrt{s_0^2 + s_0\delta}.$$

In the last step we discarded δ^2 for being too small. We can simplify further as follows:

$$\begin{aligned} s_1 &= \sqrt{s_0^2(1+\delta/s_0)} \\ &= s_0\sqrt{1+\delta/s_0} \\ &\simeq s_0\left(1+\frac{\delta}{2s_0}\right) \\ &= \boxed{s_0+\frac{\delta}{2},} \end{aligned}$$

where before the last step, we used the Taylor expansion $f(\delta) = \sqrt{1+\delta/s_0} = f(0) + \left.\frac{\partial f}{\partial \delta}\right|_{\delta=0} \delta + O(\delta^2) \simeq 1 + \frac{\delta}{2s_0}$.

The case for s_2 is analogous, but now the horizontal displacement is $\frac{s_0}{2} - \delta$. Therefore, we get the same result but with a sign change:

$$\boxed{s_2 \simeq s_0 - \frac{\delta}{2}.}$$

2. **Find the energy density associated with the deformation in terms of spring characteristics (k_{sp}, s_0 and δ)**

   Since the energy of each spring follows Hooke's law, $V = \frac{1}{2}k_{sp}(s-s_0)^2$, the total energy is:

$$\begin{aligned} V &= \frac{1}{2}k_{sp}(s_0-s_0)^2 + \frac{1}{2}k_{sp}(s_1-s_0)^2 + \frac{1}{2}k_{sp}(s_2-s_0)^2 \\ &= \frac{1}{2}k_{sp}\left(\frac{\delta}{2}\right)^2 + \frac{1}{2}k_{sp}\left(-\frac{\delta}{2}\right)^2 \\ &= \frac{k_{sp}\delta^2}{4}. \end{aligned}$$

   However, each spring is shared between two triangles, so to consider only the energy of one, we have to divide by two: $V = \frac{k_{sp}\delta^2}{8}$.

   To get the energy density, we should divide by the are of the triangle, which is $\frac{1}{2}s_0\frac{\sqrt{3}s_0}{2} = \frac{\sqrt{3}s_0^2}{2}$. Therefore, the energy density is:

$$F = \frac{V}{A} = \frac{k_{sp}\delta^2/4}{\sqrt{3}s_0^2/2} = \boxed{\frac{k_{sp}\delta^2}{2\sqrt{3}s_0^2}}$$

3. **Show that the energy density in the strain representation is given by $\Delta F = (2\mu/3)(\delta/s_0)^2$.**

As we saw in class, the energy density associated with deformations of a six-fold network in $2D$ is

$$\Delta F = (K_A/2)(u_{xx} + u_{yy})^2 + \mu[(u_{xx} - u_{yy})^2/2 + 2u_{xy}^2]. \tag{2}$$

To calculate the components u_{ij}, we may start by finding the displacement vector $\mathbf{u}(x, y)$, defined as $\mathbf{x}' - \mathbf{x}$.

First of all, referring back to figure 2, we may notice that the displacement is only dependent on y, since points at the same value of y are all displaced to the right by the same amount. Secondly, the only part of $\mathbf{u} = (u_x, u_y)$ different from zero is u_x, since there is no displacement on the vertical direction.

Finally, we can see that the displacement at $y = 0$ is equal to 0 (because the base of the triangle does not move), while at $y = \dfrac{\sqrt{3}s_0}{2}$ the displacement is $(\delta, 0)$. With these observations, and imposing u_x to be a linear function of y, we conclude that:

$$\mathbf{u} = \left(\frac{2\delta}{\sqrt{3}s_0}y, 0\right),$$

which is the only function $\mathbf{u}(x, y)$ that satisfies the observations mentioned above.

Therefore, we can now calculate the tensor elements

$$u_{ij} \equiv \frac{1}{2}\left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i}\right),$$

by using that $u_x = \dfrac{2\delta}{\sqrt{3}s_0}y$ and $u_y = 0$.

Clearly, $u_{xx} = u_{yy} = 0$, since u_x does not depend on x and u_y does not depend on y. This also makes sense, since there is no compression or expansion. On the other hand:

$$\begin{aligned} u_{xy} &= \frac{1}{2}\left(\frac{\partial u_x}{\partial y} + \frac{\partial u_y}{\partial x}\right) \\ &= \frac{1}{2}\left(\frac{2\delta}{\sqrt{3}s_0} + 0\right) \\ &= \frac{\delta}{\sqrt{3}s_0} \end{aligned}$$

Then, substituting into equation 2, we have that:

$$\begin{aligned} \Delta F &= (K_A/2)(u_{xx} + u_{yy})^2 + \mu[(u_{xx} - u_{yy})^2/2 + 2u_{xy}^2] \\ &= \mu\left[2\left(\frac{\delta}{\sqrt{3}s_0}\right)^2\right] \\ &= \frac{2\mu}{3}\left(\frac{\delta}{s_0}\right)^2. \end{aligned}$$

4. **Equate your answers from parts** (2) **and** (3) **to obtain the shear modulus.**

   When we equate both answers, we get:

$$\frac{k_{sp}\delta^2}{2\sqrt{3}s_0^2} = \frac{2\mu}{3}\left(\frac{\delta}{s_0}\right)^2.$$

   From which we conclude that

$$\frac{k_{sp}}{2\sqrt{3}} = \frac{2\mu}{3}$$

$$\Rightarrow \boxed{\mu = \frac{\sqrt{3}k_{sp}}{4}}$$

4 Problem 4: Three dimensional network with cubic symmetry

Consider a network of springs connected in the shape of a cube, such that the springs are forced to lie at right angles to one another. Each spring has the same unstretched length s_0 and force constant k_{sp}.

1. **By minimizing the enthalpy per vertex H_V of the network under pressure ($H = E + PV$), find the spring legth s_p at pressure P, and show that $s_p = s_0(1 - Ps_0/k_{sp})$ at small P (where $P > 0$ is compression).**

   To calculate the energy per vertex, we need to know how many springs are there per every vertex. To do it, first notice that each cubic cell has 8 vertices and 12 springs. However, each vertex is shared by 8 cubic cells, so that actually each cubic cell has $8/8 = 1$ vertex. On the other hand, the springs are shared by 4 cubes, so that each cubic cell has $12/4 = 3$ springs. Therefore, for every vertex, there are 3 springs.

   Then, since the energy of a spring is $\frac{1}{2}k_{sp}(s - s_0)^2$, the energy per vertex is $E_V = \frac{3}{2}k_{sp}(s - s_0)^2$. On the other hand, the volume per vertex is simply the volume of a cube, s^3. This is because we showed that there is one vertex per cube after accounting for sharing of vertices. Therefore, the enthalpy is:

$$\begin{aligned} H &= E_V + PV \\ &= \frac{3}{2}k_{sp}(s - s_0)^2 + Ps^3. \end{aligned}$$

   To find the point where the entropy reaches a maximum, we set the derivative equal to zero:

$$\begin{aligned} &3k_{sp}(s_p - s_0) + 3Ps_p^2 = 0 \\ &\Rightarrow Ps_p^2 + k_{sp}s_p - k_{sp}s_0 = 0 \end{aligned}$$

   Then, solving this quadratic equation, we obtain:

$$\begin{aligned} s_p &= \frac{-k_{sp} + \sqrt{k_{sp}^2 + 4Pk_{sp}s_0}}{2P} \\ &= \frac{-k_{sp} + \sqrt{k_{sp}^2\left(1 + \frac{4Ps_0}{k_{sp}}\right)}}{2P} \\ &= \frac{-k_{sp} + k_{sp}\sqrt{1 + \frac{4Ps_0}{k_{sp}}}}{2P} \\ &= \frac{-k_{sp} + k_{sp}\left(1 + \frac{2Ps_0}{k_{sp}} - \frac{2s_0^2}{k_{sp}^2}P^2\right)}{2P}, \end{aligned}$$

where the last step was done using the Taylor series $f(\epsilon) = \sqrt{1+\epsilon} = f(0) + \left.\frac{\partial f}{\partial \epsilon}\right|_{\epsilon=0} \epsilon + \frac{1}{2}\left.\frac{\partial^2 f}{\partial \epsilon^2}\right|_{\epsilon=0} \epsilon^2 + O(\epsilon^3) \simeq 1 + \frac{\epsilon}{2} - \frac{\epsilon^2}{8}$ with $\epsilon = \frac{4Ps_0}{k_{sp}}$, which is sufficiently small since we assume that P is small. We can simplify further:

$$
\begin{aligned}
s_p &= \frac{2Ps_0 - \frac{2s_0^2}{k_{sp}}P^2}{2P} \\
&= \boxed{s_0 - \frac{s_0^2}{k_{sp}}P}.
\end{aligned}
$$

2. **Using $V = s_p^3$ of a single cube, determine the compression modulus K_V at $P = 0$ from your results in part (1).**

Following the last result, we have that $s_p = s_0 - \frac{s_0^2}{k_{sp}}P$, which implies that $P = \frac{k_{sp}}{s_0} - \frac{k_{sp}s_p}{s_0^2}$. Then, using that $V = s_p^3$, we have that:

$$
P = \frac{k_{sp}}{s_0} - \frac{k_{sp}\sqrt[3]{V}}{s_0^2}
$$

Now we can use the definition of K_V, which is:

$$
\begin{aligned}
K_V &= -V\frac{\partial P}{\partial V} \\
&= -V\frac{\partial}{\partial V}\left(\frac{k_{sp}}{s_0} - \frac{k_{sp}\sqrt[3]{V}}{s_0^2}\right) \\
&= -V\left(-\frac{k_{sp}}{3s_0^2}V^{-2/3}\right) \\
&= \frac{k_{sp}V^{1/3}}{3s_0^2}.
\end{aligned}
$$

Then, substituting back $V = s_p^3$, we conclude that:

$$
\boxed{K_V = \frac{k_{sp}s_p}{3s_0^2}}
$$

When $P = 0$, the result from part 1 implies that $s_p = s_0(1 - Ps_0/k_{sp}) = s_0$, so that

$$K_V = \frac{k_{sp}s_p}{3s_0^2} = \frac{k_{sp}s_0}{3s_0^2} = \boxed{\frac{k_{sp}}{3s_0}}$$