Physics Circle Question Set

January 25, 2025

1 Modeling Polymers

A polymer can be modeled as a single chain-linked molecule, where the path of the molecule in space follows a ‘random walk’. For example, we can model DNA as a three-dimensional string of N units, in which each unit is joined to the next by a flexible joint, whose orientation fluctuates at random. The random walk model intrinsically assumes polymers to be loose structures. Let us consider what we mean by this:

(a) What assumptions have we made about the likelihood distribution of the location of polymer units with respect to one another? How would

  - the interactions between polymer units (e.g., attractive, repulsive) and
  - their physical size

  affect the measured polymer size?

(a) Look up what is meant by a self-avoiding random walk and comment on its relevance to experimental measurements of DNA sizes and protein sizes. What are some examples of molecules that are bigger and smaller than would be predicted by our random walk model, and why?

(a) The persistence length of a polymer describes its bending stiffness. Below the persistence length, a polymer behaves like a stiff rod. Polymers that are much longer than their persistence length can be described by a random walk. The persistence length of DNA is 50 nm and the persistence length of RNA is 2 nm. Why is this? How would this affect the random walk of the molecule? How would this affect how DNA and RNA behave inside of a cell?

2 DNA Stretching with Optical Tweezers

A single DNA molecule is attached to a microscopic bead and stretched using optical tweezers. The force exerted by the optical tweezers follows Hooke's Law at small extensions:

$$F = kx$$

where:

- F is the applied force (in pN),
- k is the trap stiffness (in pN/μm),
- x is the displacement of the bead from the trap center (in μm).

At room temperature ($T = 298$ K), the persistence length of double-stranded DNA is approximately $L_p = 50$ nm, and its contour length per base pair is 0.34 nm. The force-extension relationship for DNA can be described using the Worm-Like Chain model (more accurate than the random walk model, look up the derivation if you're interested):

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

where:

- k_B is Boltzmann's constant (1.38×10^{-23} J/K),
- T is temperature in Kelvin,
- L is the total contour length of the DNA (in μm),
- x is the extension of the DNA (in μm).

(a) Suppose a $60,000$ base pair DNA molecule is stretched to 60% of its contour length.

1. Calculate the contour length L of this DNA molecule.
2. Using the WLC model, calculate the force required to stretch the DNA to 60% of L.

(a) The optical trap has a stiffness of $k = 0.2$ pN/μm.

1. Determine how far the bead must be displaced from the trap center to generate the force found in Part A.

(a) For very high forces ($F > 10$ pN), the DNA behaves almost like an inextensible rod, and the WLC model simplifies to:

$$F = \frac{k_B T}{L_p}\frac{1}{4(1 - x/L)^2}$$

Calculate the required force to stretch the DNA to 99% of its contour length using this approximation.

These questions were inspired from a problem set written by Dr. Sabrina Leslie.

3 Solutions

3.1 Modeling Polymers

1. We have assumed that polymer units can be completely overlaid over one another, which is not physically possible as the units take up space. Polymer units with like charges would repel each other, and bulky polymer units would have restricted motion, both of which would contribute to the polymer being stiffer and the average end-to-end distance being longer than the random walk model predicts.

2. A self-avoiding random walk will not visit the same point more than once – the polymer cannot go back on itself. This is relevant as DNA is negatively charged and therefore self-avoiding. Proteins are made of amino acids, some of which are larger molecules that cause steric hindrance and self-avoidance. DNA would be larger than predicted by a random walk. A protein with opposite charges or hydrophobic/hydrophilic interactions could be inclined to fold in on itself and therefore be smaller than predicted by the random walk.

3. DNA is double stranded and therefore much stiffer than single-stranded RNA. Each 'step' of a random walk, or polymer unit, would be much longer for DNA than for RNA. DNA is much more difficult to package into a small space than RNA, which is evident during mitosis when all the DNA inside a cell must be packaged into chromosomes, which takes significant energy input. DNA is also much more stable inside the cell.

3.2 Stretching DNA with Optical Tweezers

1. (a) $L = 60,000 \times 0.34 \times 10^{-9} = 20.4\ \mu$m.
   (b) $x = 0.6 \times L = 12.24\ \mu$m. Plugging into the WLC equation gives $F = 0.157$ pN.

2. Using $F = kx$, solve for x:

$$x = \frac{F}{k} = \frac{0.157}{0.2} = 0.786\ \mu m.$$

3. For $x = 0.99L$:

$$F = \frac{k_B T}{L_p} \frac{1}{4(1-0.99)^2}$$

Substituting values gives $F = 205.62$ pN - much more force is required!