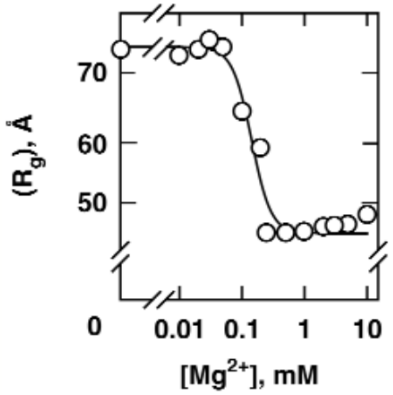
Problem set 5
(Discussion on June 10)

Problem 1

Mg^{2+} induced RNA folding. Russell *et al.* (*Nature Structural Biology*, 2000) have measured the radius of gyration R_g of the *Tetrahymena* ribozyme (a functional RNA) by SAXS under different Mg^{2+} concentrations (circles in the figure below).



a) Why does the R_g decrease with increasing salt concentration? Why is the transition sharp, i.e. happens at a relatively narrow salt concentration?

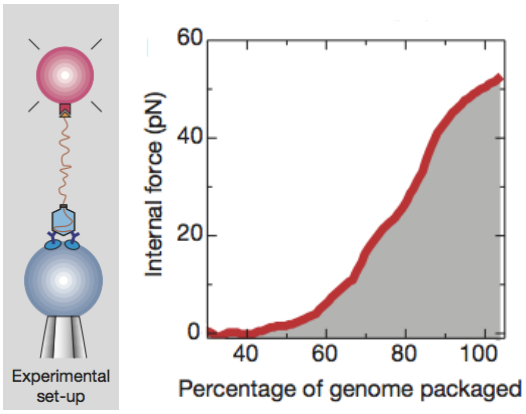
b) The authors have fit their data with the Hill model (black line in the figure) and determined the Hill coefficient to be $n = 2.8$. What does this tell you about the interaction of the *Tetrahymena* ribozyme and Mg^{2+}?

c) While the Hill model provides a reasonable fit to the data, it has some shortcomings. What are limitations of the Hill model? Why is the Hill model problematic in particular in the context of ions binding to RNA?

Problem 2

Packing viral DNA. A viral capsid is a shell of proteins surrounding the nucleic acid genome of a virus. The bacteriophage Φ29 (a virus that infects bacteria) has a double-stranded DNA genome approximately 20,000 base pairs long, which is tightly packed into a spherical capsid of radius $R = 20$ nm.

a) Estimate the electrostatic energy that needs to be overcome to pack the Φ29 genome inside the capsid. Consider that the phage is in aqueous solution, but neglect the effect of counterions. Hint: What is the total charge of the DNA genome? You can approximate the charge of the DNA packed capsid as uniformly spread over the sphere of radius R.



b) The DNA is packed into the Φ29 capsid by a powerful molecular motor that can generate forces up to ≈ 60 pN (Smith et al., *Nature*, 2001). Bustamante and coworkers have used an optical tweezers system (see figure above) to measure the forces generated by the packing motor to pack the DNA genome inside the capsid (shown above on the right). Estimate the work done by the packing motor from the fact that the DNA genome is 20,000 bp long (Hint: how many nm is the genome?) and from the data shown below on the right. You can approximate the force vs. genome packed relationship as simply linear.

c) Compare the energies estimated in part a) and b). What does this tell you about the likely role of counterions?

Problem 3

Estimates of molecular forces. In this problem, we will carry out some very simple estimates of the forces required to break interactions in biomolecular systems. A simple estimate of the force F required to break a certain interaction can be obtained by considering the characteristic energy E and the typical length scale Δx over which it acts: $E = F \cdot \Delta x$.

a) Estimate the forces required to break covalent bonds. A C-O bond has a binding energy of 84 kcal/mol; a S-S bond has an energy of 51 kcal/mol (data from `https://www.ncbi.nlm.nih.gov/books/NBK21595/`). You can assume that the bonds break over a characteristic distance of ≈ 1 Å.

b) Biological interactions are often mediated by non-covalent bonds. Non-covalent interactions tend to be weaker and longer ranged than covalent bonds. Obtain a rough estimate of the energies and rupture forces of non-covalent interactions, by assuming that they act over distances of ≈ 1 nm and taking into account that they are much weaker than covalent interactions but still stronger than forces due to thermal fluctuations. Hint: the thermal energy at room temperature is $k_B T \approx$ 4 pN·nm.