Homework 9
March 24, 2025
Polymer Physics

You might be familiar with proteins as enzymes in the native folded (or collapsed) state which is often described as a lock-and-key structure. For Eukaryotes, such as human cells, natively folded proteins account for about 70% of the proteins. 30% are unfolded or partially folded. These intrinsically disordered proteins (IDPs) may have domains of folding but are largely unfolded. IDPs are highly sensitive to the environment and are important in the control of function in biological response to environmental conditions and in the expression of normal cellular activities. These are thought to be the control mechanisms by which cells respond to the environment, why two identical twins brought up in different locations differ. Waszkiewicz R, Michaś A, Białobrzewski MK, Klepka BP, Cieplak-Rotowska MK, Staszałek Z, Cichocki B, Lisicki M, Szymczak P, Niedzwiecka A, *Hydrodynamic Radii of Intrinsically Disordered Proteins: Fast Prediction by Minimum Dissipation Approximation and Experimental Validation* J. Phys. Chem. Lett. **15** 5024–5033 (2024) present a new method to calculate the hydrodynamic radius of IDPs which can be used to determine, for example, changes in functionality with environmental conditions.

a) What is an IDP and why are they important? What is "epigenetics" and how is it related to intrinsically disordered proteins. Lookup "2w0o" in the protein data bank and in UniProtKB, Figure 2, and explain what you find. Can this be done for an IDP? How or why not?
b) The Kirkwood formula, equation 2, is a harmonic mean. Explain briefly how this formula is arrived at. How does this calculation compare with the calculation of the radius of gyration (an arithmetic mean)? For a rod chain of five beads separated by 1 unit distance what is R_g and what is R_H? What about a cube of four beads? How does R_g/R_H compare for these two objects.
c) What is the difference between the short-time and long-time diffusion coefficient for a polymer? Explain the minimum dissipation approximation (MDA). What is the advantage of the MDA over the Kirkwood-Reisman approach? What is the difference between a diffusion center and the center of mass?
d) What is the difference between the Rouse model, the Zimm model and the the globule-linker model (GLM)? How is the GLM an improvement over the Rouse and Zimm models?
e) Waszkiewicz notes that all methods for determination of the hydrodynamic radius have certain problems. Explain how each measurement works and the associated problems with size exclusion chromatography (SEC), dynamic light scattering (DLS), pulsed field gradient NMR (PFG) and analytic ultracentrifugation (AUC) with reference to figure S8 in the supplemental file which compares Waszkiewicz's calculated R_H and these measurements.