Problem set 6
(Hand in by July 8)

Problem 1

Motion by diffusion.

a) Using the Einstein-Stokes relationship (also known as Einstein-Smoluchowski relation) for the diffusion coefficient D

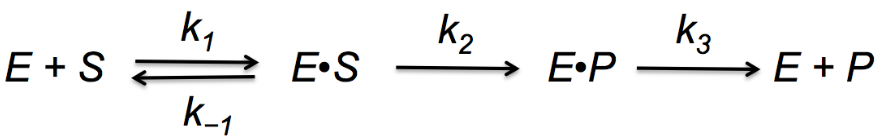
$$D = \frac{k_B T}{6\pi\psi\eta d} \tag{1}$$

where $k_B T$ is the thermal energy, η the viscosity (0.01 g cm^{-1} s^{-1} for water), d the characteristic dimension of the object, and ψ a dimensionless parameter on the order of unity that depends on the shape of the object ($\psi = 1$ for a sphere), estimate the diffusion coefficient for i) a small protein and ii) for a bacterium such as *E. coli*.

b) Roughly how far (in buffer for 3D using the RMSD distance) will i) the small protein and ii) the bacterium diffuse in 1 ms, 1 hour, and 1 year? Express your answer in μm or mm.

Problem 2

Michaelis-Menten, revisited and expanded. In class, we derived the Michaelis-Menten rate (i.e. the rate of product formation for an enzyme-catalyzed reaction under certain assumptions). We can expand the Michaelis-Menten framework discussed in class by adding an enzyme-product complex ($E\bullet P$), in addition to the enzyme-substrate complex ($E\bullet S$) considered in the standard Michaelis-Menten framework:



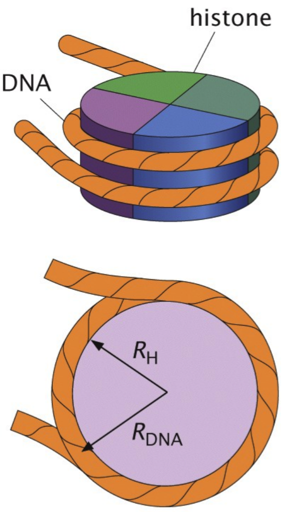
a) Using the same assumptions made in the standard Michaelis-Menten framework (constant total enzyme concentration and quasi steady-state, i.e. time derivatives for $[E\bullet S]$ and $[E\bullet P]$ are zero), derive the rate of product formation $\frac{d[P]}{dt}$ for the reaction scheme shown above.

b) What expression is now equivalent to k_2 in the standard Michaelis-Menten framework (also known as k_{cat})? What expression is now equivalent to the Michaelis-Menten constant K_M?

c) What happens to the model described above in the limiting case that $k_2 \gg k_3$? What if $k_3 \gg k_2$? What do k_{cat} and K_M reduce to? Comment (briefly) on the results. Is this what you expect and why?

Problem 3

DNA-nucleosome interactions. Nucleosomes consist of roughly 150 bp of DNA wrapped around a histone (protein) core (see schematic below). Formation of nucleosomes involves both elastic deformation of the DNA and interactions between DNA and histones. The histone octamer has a diameter of roughly 8 nm $= 2R_H$.



a) Estimate the DNA bending energy required for wrapping the DNA 1.7 turns around the histone core. Hint: you can use the expression given in Problem Set 5, Problem 3.

b) The energy required to bend the DNA is (more than) compensated for by favorable electrostatic interactions of the positively charged histones with the negatively charged DNA. As a very simply model, assume that there are 14 positive charges on the histone periphery that come into close contact (each to within 3 Å) of individual negative charges on the DNA backbone. What is the energetic contribution of these charge interactions to the nucleosome formation if you assume a dielectric constant characteristic for aqueous solution $\epsilon = 80$? How does this result change if you assume $\epsilon = 2$? What does this tell you about the local hydration environment of the DNA-histone interface?