Date: Thursday, November 9

Instructions: You may utilize notes and problem set solutions (both your solutions and the posted solutions). You may not, however, discuss the problems with others.

Problem 1:	/	12
Problem 2:	/	15
Problem 3:	/	16
Problem 4:	/	30
Problem 5:	/	27
Total:	/	100

Equations you may find useful:

$$1 = \int_{-\infty}^{\infty} dx \; \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left(-\frac{(x-\mu)^2}{2\sigma^2}\right)$$

$$\mu = \int_{-\infty}^{\infty} dx \; \frac{x}{\sqrt{2\pi\sigma^2}} \exp\left(-\frac{(x-\mu)^2}{2\sigma^2}\right)$$

$$\sigma^2 = \int_{-\infty}^{\infty} dx \; \frac{(x-\mu)^2}{\sqrt{2\pi\sigma^2}} \exp\left(-\frac{(x-\mu)^2}{2\sigma^2}\right)$$

$$P(\nu) = \frac{e^{-\beta E(\nu)}}{Q(\beta)} \quad \text{[Canonical]}$$

$$S = k_{\mathrm{B}} \ln \Omega$$

$$-\beta A = \ln Q \quad \text{[Canonical]}$$

$$\beta = \frac{1}{k_{\mathrm{B}}T} = \frac{1}{k_{\mathrm{B}}} \left(\frac{\partial S}{\partial E}\right)_{N,V}$$

$$C_V = \left(\frac{\partial \langle E \rangle}{\partial T}\right)_{N,V}$$

$$Q(\beta) = \sum_{\nu} e^{-\beta E(\nu)} \quad \text{[Canonical]}$$

$$\ln n! \approx n \ln n - n$$

$$_M C_N = \frac{M!}{N!(M-N)!}$$

1. **System size scaling. [12 pts.]**

2. **Protein-ligand binding. [15 pts.]** The pharmaceutical industry routinely wrestles with the challenge of identifying small molecules which can act as drugs by binding to disease-related proteins. For decades they have used computers to help screen through candidates of potential drugs. A common approach to such screens, known as docking, is summarized in the following picture:
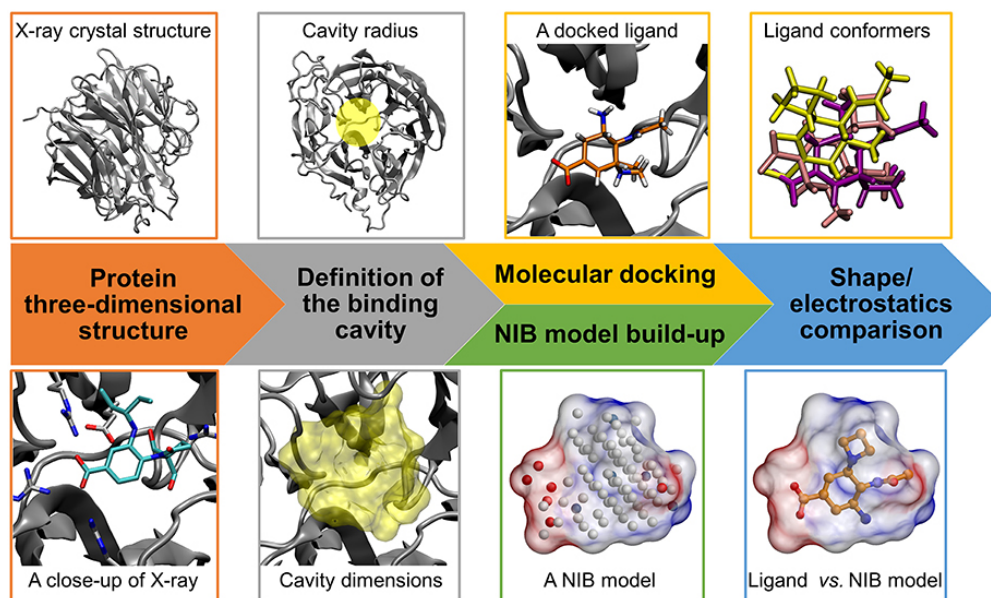

Briefly, the idea is to take the structure of a frozen protein from a crystal, understand the shape and charge distribution around some binding pocket (cavity), then computationally try to fit different ligands into that pocket. The picture refers to that last step as "shape/electrostatics comparison".

You can perhaps imagine that powerful quantum chemistry techniques like density functional theory could be used to compute the energy for the protein configuration in the presence of the ligand, and you could seek ligands which minimize that energy. That approach makes me a little uncomfortable because it has "integrated out" all of the solvent degrees of freedom. My stat mech upbringing makes me worried that ignoring the solvent could cause problems.

3. **Fluctuating energy and particles. [16 pts., 2 pt. each]**

4. **Heat capacity. [32 pts.]** The heat capacity per mole of a diatomic gas, HD, is plotted below in terms of the gas constant $R = N_A k_B$, with N_A being Avogadro's number.
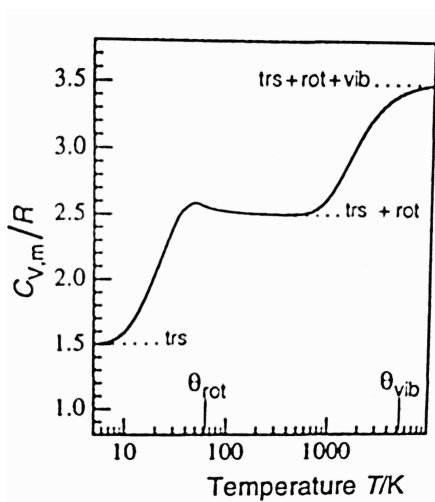
Based on the labels and your chemical intuition, you see that as you move to higher temperatures you "unlock" higher energy states. At low temperatures the molecules have translational motion but are stuck in the ground rotational and vibrational states. At a high enough energy, the rotational excitations start to become relevant, and at a still higher temperature the vibrations also influence the heat capacity.

Todd tries to claim that the HD heat capacity should be simple to understand—the heat capacity should go up the more microstates you unlock. You point out to him that the behavior around $T = \theta_{\text{rot}}$ seems to contradict his simplistic explanation.

5. **Hard Spheres. [27 pts.]** This year's Nobel Prize in Chemistry was awarded for quantum size effects, including in colloidal nanoparticles. While much of the interest in those colloidal nanoparticles has focused on their optical properties, it is also been interesting to consider how multiple colloids interact with each other. As roughly spherical crystals, you might reasonably approximate a nanoparticle as if it is just a "hard sphere". Like billiard balls, such a model would express (a) that is is impossible for two nanoparticles to overlap each other and (b) that two nanoparticles separated by a gap do not exert forces on each other. Mathematically, one would express these facts with the pair potential:

$$V(r) = \begin{cases} \infty, & r < \sigma \\ 0, & r > \sigma, \end{cases}$$

where r is the distance separating the center of the two spheres and σ is the diameter of the spheres. Models of hard spheres are most natural in two dimensions (hard disks) or three dimensions (hard spheres), though sometimes they're even considered in higher dimensions. In this problem, we will discuss an important statistical mechanical consideration for how two nanoparticles can interact in two-dimensional space.