

Homework #7 for CCB 425/525, Spring 2017

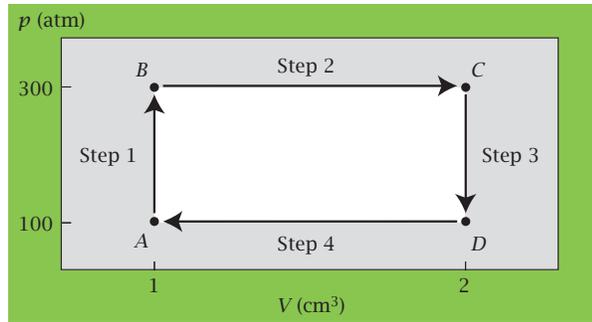
due in class, Wed. April 5

- This is a re-hash of the exam, with extra hints. Write answers that are brief but precise: none of the problems demands and complex answer. I will deduct points for answers that contains lots of redundant or irrelevant material.
 - There is no time limit, but (for this particular homework) *please do this on your own, and do not consult with anyone else.*
1. Many scientists have repeatedly hit on the idea of using simulations to estimate $\langle \exp(+\beta V) \rangle$, where V is the potential energy, and the average is over the Boltzmann distribution.
 - a) Write an expression for $\langle \exp(+\beta V) \rangle$; use the classical formula for computing averages over the Boltzmann distribution.
 - b) What is the relation of the result you got in part (a) to Q , the configuration integral?
 - c) Describe in words why this is likely to be a rather poor way to estimate Q .
 2. Starting from information like that in Table 8.1 of your text, compute the entropy $S(V, N)$ of an ideal gas with N molecules in volume V . (As originally written, this problem was too vague, and I ended up not grading it; but use the following hints to get going.) Note that for an ideal gas, U is a function just T , so that do a derivative at constant U is the same as doing a derivative at constant T .
 - a) What is the relation between U and T for an ideal gas?
 - b) Use the entropy line in Table 8.1 to relate dS to dV at constant U and N . Simplify using the equation of state, and integrate both sides.
 - c) Eq. 11.42 in your text gives the Sakur-Tetrode equation, a quantum statistical calculation of the entropy of an ideal gas. How can this equation be reconciled with the one you obtained in part (b)?
 3. An approximate equation of state for non-ideal gases is the following, first postulated by van der Waals (for one mole of molecules):

$$p = \frac{RT}{V - b} - \frac{a}{V^2} \quad (1)$$

where a and b are constants, and the other variables have their usual meanings.

- a) Suppose you reversibly compress this gas from volume $V_{initial}$ to V_{final} , at constant temperature. How much pressure-volume work is required to do this?
 - b) Modify the right-hand-side of Eq. (1) if you have n moles of molecules, keeping the left-hand side unchanged. Note that the left-hand side is an intensive variable, so each term on the right-hand-side must also have this property.
4. Consider the cycle $A \rightarrow B \rightarrow C \rightarrow D \rightarrow A$ in the following diagram:



What is the numerical amount of pressure-volume work done in this cycle? (Express your result in either cal or J). What is the numerical amount of heat produced? (Hint: consider first what the total change in U must be in going around the cycle.)

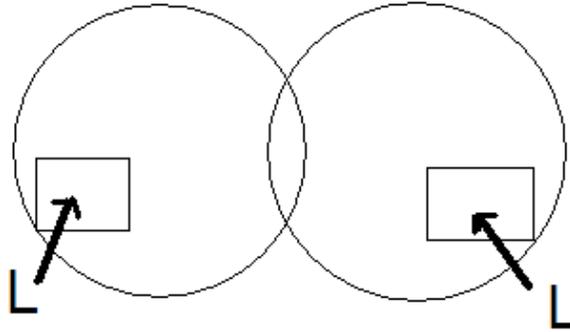
5. **Ligand binding to proteins.** Consider the situation illustrated by the following diagram, which shows a two-domain protein with ligand-bind sites in each domain (or subunit).

Call the left-hand domain α and the right-hand domain β , and let K be the association equilibrium constant for binding to subunit α , that is $K = [P_\alpha]/[P][L]$, where $[P]$ and $[L]$ are the concentrations of free (apo) protein and ligand, and $[P_\alpha]$ is the concentration of protein with a ligand bound in subunit α , with no ligand bound in subunit β . Suppose that the ligand affinity for subunit β is the same as that for subunit α , and that the affinity of a subunit is independent of whether or not a ligand is bound to the other subunit, i.e., $K = [P_{\alpha\beta}]/[P_\alpha][L]$ with the same numerical value of K as before.

- Compute the partition function in terms of the concentrations of the various species and K ; (Hint: there are four possible states, and hence four terms in the partition function.)
- Compute f , the fraction of binding sites that are occupied by the ligand in each of the four states. Then compute a weighted average this fraction, where the weights are the populations of each state. Simplify your result for the latter as much as possible.
- The Hill coefficient n_H is a measure of the cooperativity of binding. It describes the rate of change of fractional occupation vs ligand concentration at half saturation, and is defined as:

$$n_H = \left(\frac{\partial \ln[f/(1-f)]}{\partial \ln[L]} \right)_{f=1/2}$$

Determine the Hill coefficient for this problem. (Note: the notation above means: first take the derivative, then set $f = 1/2$.)



6. **Helix-coil transitions.** Suppose, in a very simple model, each residue in a polypeptide could be in either a helical configuration (“h”) or a non-helical one (“c” for “coil”). The equilibrium constant for this change is traditionally called s , so that $s = [h]/[c] \sim \exp(-\beta\Delta\epsilon)$, where $\Delta\epsilon < 0$ represents the energy of forming a helical residue relative to a coil residue. But we have to also think about the cooperativity of the transition: if one residue is helical, does that affect its neighbors likelihood of being helical?
- The simplest model model is one of complete cooperativity: either all the residues are helical, or they are all coil. For a polypeptide containing N residues, compute the partition function, and the fraction of residues that are in the helical conformation. Please express your results in terms of s and e .
 - Another simple model says that this equilibrium constant is the same everywhere, and is not dependent on the conformation of the surrounding residues. For a polypeptide containing 2 residues, compute the partition function Q , and the fraction f of residues in the helical conformation. Show your reasoning, and simplify the answer as much as you can. Repeat your analysis for $N=3$.