**Problem 6.1** (Connections between free energy and entropy, 25 pts)**.**
Consider a system whose microstates are described by the Boltzmann distribution, that is the probability of realizing microstate $i$ is

$$P_i = \frac{e^{-\beta E_i}}{Z}, \tag{6.1}$$

where $\beta = 1/k_B T$ and

$$Z = \sum_i e^{-\beta E_i} \tag{6.2}$$

is the partition function. Given the probability mass function above, that the free energy, often called the Helmholtz free energy, is $F = -k_B T \ln Z$, and the result we derived in lecture, $S = k_B \beta \langle E \rangle + k_B \ln Z$, show the following results.

a)  Show that the expectation value of the energy, $\langle E \rangle$, is

$$\langle E \rangle = -\frac{\partial \ln Z}{\partial \beta} = \frac{\partial \beta F}{\partial \beta}. \tag{6.3}$$

b)  Show that $F = \langle E \rangle - TS$.

c)  Show that $S = -\partial F/\partial T$.

As we discussed in lecture, taken together these results show that the free energy is a Legendre transform of the energy. *Hint*: It is up to you, but I found in all cases that it is easier to start with the right hand sides of the above equations and verify that they equal the left.

**Problem 6.2** (Grouping microstates, 10 pts)**.**
As a motivating example for this problem, consider a biomolecule that can be in a helical or coiled state. However, there are several microstates corresponding to the helical state. For example, there are many configurations of the molecule due to bond vibrations that are still classified as helical. Similarly, there are several other microstates corresponding to the coiled state.

Now let us generalize. Imagine we have a set of microstates for a system and we can put each microstate into a specific group. We will refer to these groups as macrostates. In the motivating example, we have two macrostates, helical and coiled. We will index the macrostates with $i$ and the microstates within each macrostate with

$j$ such that the energy of microstate $j$ in macrostate $i$ is $E_{ij}$ and the partition function for the system is

$$Z = \sum_i \sum_j e^{-\beta E_{ij}}. \tag{6.4}$$

Show that the probability of the system being in macrostate $i$ is

$$p_i = \frac{e^{-\beta F_i}}{Z}, \tag{6.5}$$

where $F_i$ is the free energy of macrostate $i$. That is, $F_i$ is the free energy of a system that consists only of microstates in macrostate $i$.

**Problem 6.3** (Bounds on susceptibilities, 25 pts).

a) Prove that the isothermal compressibility $\kappa_T$ is positive for a thermodynamically stable system with a constant number of particles.

b) We showed in lecture that thermodynamic stability requires that $C_p > 0$. Show that in addition to $C_p > 0$ and $\kappa_T > 0$, thermodynamic stability requires that

$$\frac{\kappa_T C_p}{VT} - \alpha^2 < 0, \tag{6.6}$$

for a system with a constant number of particles, where $\alpha$ is the thermal expansivity. This means that while $\alpha$ can be positive or negative (or zero), it is nonetheless constrained in the values it may take.

As a reminder,

$$C_p = T \left( \frac{\partial S}{\partial T} \right)_p, \tag{6.7}$$

$$\kappa_T = -\frac{1}{V} \left( \frac{\partial V}{\partial p} \right)_T, \tag{6.8}$$

$$\alpha = \frac{1}{V} \left( \frac{\partial V}{\partial T} \right)_p. \tag{6.9}$$

**Problem 6.4** (Phase transitions in regular solutions, 40 pts).
In the last couple of decades, **membraneless organelles** have been an important

2

research topic in cell biology. (See, for example, this review.) Membraneless organelles are typically liquid droplets that are enriched in one or more molecule compared to the surroundings. As such, many of these membraneless organelles form by liquid-liquid phase separation. In such a separation, a liquid mixture, like the cytoplasm, is well-mixed in its components, but conditions change to induce *de*mixing, and the components of the mixture separate.

To understand the physics behind liquid-liquid phase separation, we will use a simple model referred to as a **regular solution**. We will build up to it, though, starting first with an **ideal solution**.

We consider a mixture of two components, A and B. The mole fraction of A is $x_A = n_A/N$, where $n_A$ is the number of A molecules and $n_B$ is the total number of B molecules with $N = n_A + n_B$. The mole fraction of B is similarly defined as $x_B$ with $x_B = 1 - x_A$. For notational convenience later on, we will take $x \equiv x_A$ with $x_B = 1 - x$.

a) Imagine separating the space of the solution into little boxes, where each box contains either an A molecule or a B molecules. In an ideal solution, the molecules have no interactions with each other at all. So, every configuration of the A and B molecules in the boxes has the same energy. Write down an expression for the partition function $Z(T, n_A, n_B)$.

b) Compute the free energy, $F(T, n_A, n_B)$. Write it as a function only of $N$ and $x$ so that you can compute the per-lattice site free energy $f(T, x) = F(T, n_A, n_B)/N$. In doing the calculation, assume that $n_A$ and $n_B$ are big enough that **Stirling's approximation** ($\ln a! \approx a \ln a - a$) applies to all factorials.

c) Sketch a plot of $f(T, x)$ as a function of $x$ for a given $T$. Further, prove the $f(T, x)$ is a strictly convex function of $x$ for a given $T$.

d) In a regular solution, molecules interact with one another when they come into contact. When two A molecules are proximal, the energy of interaction is $E_{AA}$. Similarly with two B molecules are proximal, the energy of interaction is $E_{BB}$. And when an A and a B molecule are proximal, the energy of interaction is $E_{AB}$. Thus, the energy of a given configuration of the solution is

$$E_{config} = \sum_{ij} \left[ E_{BB}(1 - m_i)(1 - m_j) + E_{AA}m_i m_j + E_{AB}m_i(1 - m_j) + E_{AB}(1 - m_i)m_j \right],$$

(6.10)

where $m_i = 1$ if site $i$ on the lattice is occupied by an A molecule and $m_i = 0$ if site $i$ is occupied by a B molecule. The sum is the nonredundant sum over nearest neighbors. We define $\gamma$ to be the coordination number of the lattice. That is, $\gamma$ is the number of nearest-neighbor sites any given site on the

lattice has. Thus, there are $N\gamma/2$ total terms in the sum $\sum_{ij}$. Show that the configuration energy may be written as

$$E_{\text{config}} = \frac{N\gamma}{2}E_{\text{BB}} + \frac{\gamma}{2}(E_{\text{AA}} - E_{\text{BB}})\sum_i m_i + (2E_{\text{AB}} - E_{\text{BB}} - E_{\text{AA}})\sum_{ij} m_i(1 - m_j).$$
$$(6.11)$$

e) Computing the partition function, and therefore also the free energy, for this $E_{\text{config}}$ is pretty monstrous, since

$$Z = \sum_{\text{all configs}} e^{\beta E_{\text{config}}}. \tag{6.12}$$

We will not attempt this. Rather, we will take a **mean field** approach in which we make the approximation that every lattice site has the same probability of being inhabited by an A molecule (and therefore also the same probability of being inhabited by a B molecule) independently of its neighbors. That is, we take

$$\sum_i m_i \approx n_{\text{A}}, \tag{6.13}$$

$$\sum_{ij} m_i(1 - m_j) \approx \gamma \frac{n_{\text{A}}n_{\text{B}}}{N}. \tag{6.14}$$

Explain how the two above approximate equations follow from the mean field approximation. Henceforth, we will be applying this mean field approximation.

f) Write down an expression for the partition function, $Z(T, n_{\text{A}}, n_{\text{B}})$. When you write it, define $\chi = \gamma(2E_{\text{AB}} - E_{\text{BB}} - E_{\text{AA}})$ as an interaction parameter.

g) Write down an expression for the per-lattice site free energy, $f(T, x)$, again employing Stirling's approximation.

h) Prove that above a critical temperature, $T_c$, the free energy is strictly convex and that below $T_c$ the free energy loses convexity for $\chi > 0$.

i) Plot $f(T, x)$ versus $x$ for various values of $T$, demonstrating the loss of convexity.

j) What does the analysis you just did say about how we might get two phases, one rich in A and one rich in B, if we start with a solution with equal numbers of A and B molecules? Specifically, what must be true of $\chi$?