

### 3. Protein folding

The thermodynamics of protein folding plays an essential role in biology.

This problem is all at one atmosphere of pressure: Consider a large protein that folds at temperature  $T_1$ , so for  $T > T_1$  it is unfolded at equilibrium, while for a range of temperature  $T$  with  $T < T_1$  it is folded at equilibrium in to a compact form and thus “hides” some hydrophobic parts of the long protein molecule from the surrounding water. Assume the folded ( $f$ ) state of the protein has a temperature-independent specific heat  $C^{(f)}$  and that its thermal expansion is negligible so  $C_P^{(f)} = C_V^{(f)}$ . Assume the same is true for the unfolded ( $u$ ) state, so  $C_P^{(u)} = C_V^{(u)} = C^{(u)}$  is also temperature-independent. The latent heat released on unfolding at temperature  $T_1$  is  $Q > 0$ . The unfolded state has the larger specific heat:  $\Delta C = C^{(u)} - C^{(f)} > 0$ .

(a) What is the enthalpy ( $H = E + PV$ ) difference,  $\Delta H = H^{(u)} - H^{(f)}$ , between the unfolded and folded states as a function of  $T$ ? Sketch a plot of this function, assuming the above assumptions.

(b) What is the Gibbs free energy ( $G = H - TS$ ) difference,  $\Delta G = G^{(u)} - G^{(f)}$ , between the unfolded and folded states as a function of  $T$ ?

(c) What conditions on the parameters mean that this protein will unfold also at some low temperatures, given all the above assumptions? Sketch  $\Delta G$  vs.  $T$  for such a case with two folding transitions.