01 Jan 2022

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 ΔG vs. T for such a case with two folding transitions.

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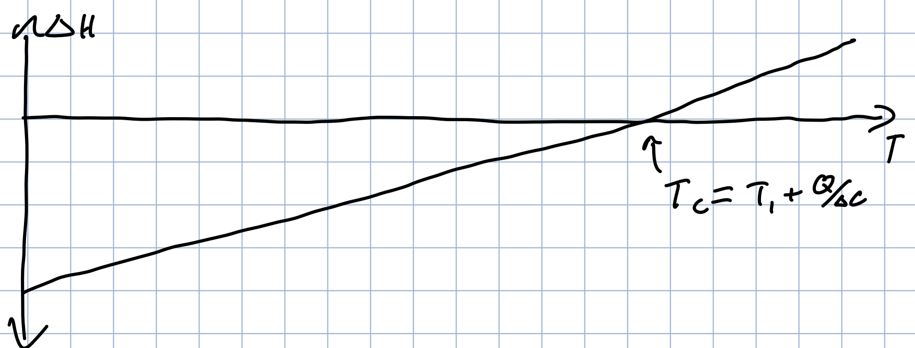
a) $dH = C\,dT \rightarrow H(T) - H(T_1) = C(T - T_1)$

$H(T) = H(T_1) + C(T - T_1)$

$$\Delta H = H^{(u)}(T) - H^{(f)}(T) = H^{(u)}(T_1) + C^{(u)}(T - T_1) - H^{(f)}(T_1) - C^{(f)}(T - T_1)$$

$$= \left(H^{(u)}(T_1) - H^{(f)}(T_1)\right) + \left(C^{(u)} - C^{(f)}\right)(T - T_1) \leftarrow C^{(u)} - C^{(f)} \equiv \Delta C,\ Q \equiv H^{(f)}(T_1) - H^{(u)}(T_1)$$

$$= \boxed{-Q + \Delta C(T - T_1)} = \Delta C\,T - (Q + \Delta C\,T_1)$$



b) $dG = -S\,dT + V\,dP = -S\,dT$

$C = T\frac{dS}{dT} \rightarrow S(T) = C\ln(T/T_0) + S(T_1)$

$dG = -(C\ln(T/T_1) + S(T_1))\,dT$

$$\int_0^G dG = G = -\int_{T_1}^{T} C\ln(T) + C\ln(T_1) + S(T_1)\,dT$$

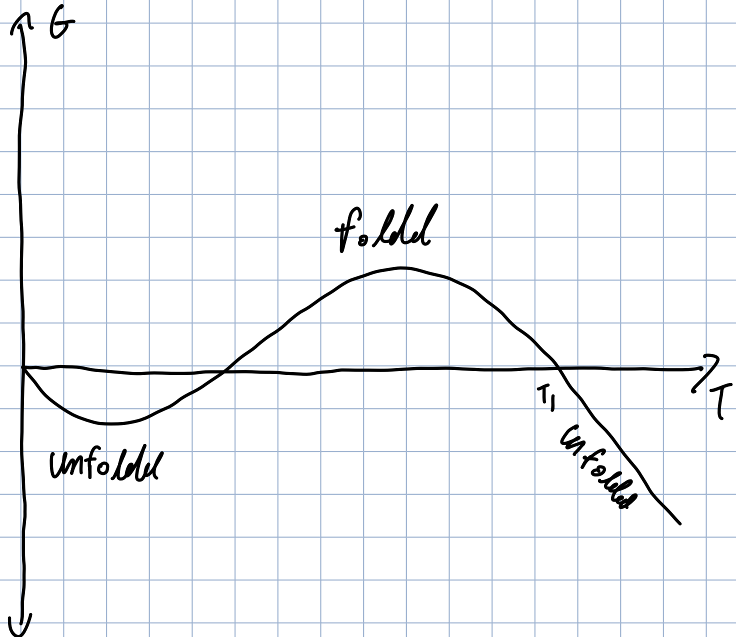
$$= -\left[C(T\ln(T) - T) + C\,T\ln T_1 + T S(T_1)\right]_{T_1}^{T}$$

$$= -\left[C(T\ln(T) - T) - C(T_1\ln(T_1) - T_1) + C\ln(T_1)(T - T_1) + S(T_1)(T - T_1)\right]$$

$$= G_0$$

$$\Delta G = G^{(u)} - G^{(f)} = \boxed{-\Delta C(T\ln(T) - T) - \Delta C\ln(T_1)(T - T_1) - \left(S^{(u)}(T_1) - S^{(f)}(T_1)\right)(T - T_1)}$$

c)



$T \approx t$

$G = -\Delta C t(\ln(t) - 1) - \Delta C \ln(T_1)(t - T_1) - (S^{(u)}(T_1) - S^{(f)}(T_1))(t - T_1)$

$\approx \Delta C T_1 \ln T_1 + T_1(S^{(u)}(T_1) - S^{(f)}(T_1)) < 0$

$\Delta C \ln T_1 < -(S^{(u)}(T_1) - S^{(f)}(T_1)) \leftarrow dQ = T dS, \; \Delta S = \Delta Q / T = S^{(f)}(T_1) - S^{(u)}(T_1)$

$\Delta C \ln T_1 < Q / T_1$

$\boxed{Q > \Delta C T_1 \ln T_1}$