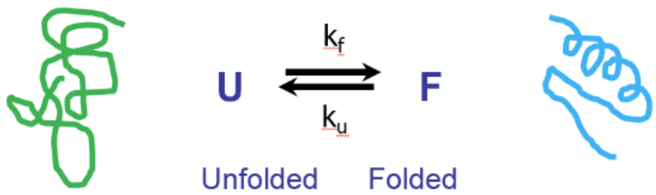
18.2: Two-State Thermodynamics

Here we describe the basic thermodynamics of two-state systems, which are commonly used for processes such as protein folding, binding, and DNA hybridization. Working with the example of protein folding analyzed through the temperature-dependent folded protein content.

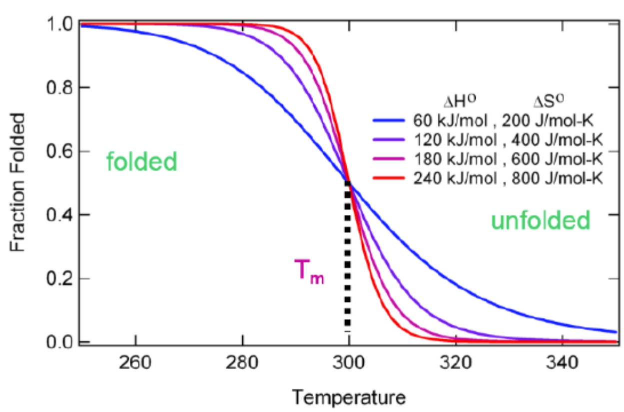


$$K = \frac{k_f}{k_u} = \frac{[F]}{[U]} = \frac{\phi_F}{1-\phi_F}$$

where φ_F is the fraction of protein that is folded, and the fraction that is unfolded is $(1-\varphi_F)$.

$$\phi_F = \frac{K}{K+1}$$
$$K = e^{-\Delta G^0/RT}$$
$$\phi_F = \frac{1}{1+e^{-\Delta G^0/RT}} = \frac{1}{1+e^{\Delta H^0/RT}e^{-\Delta S^0/R}}$$

Define the melting temperature T_m as the temperature at which φ_F= 0.5. Then at T_m, $\Delta G^0 = 0 \text{or} T_m = \Delta H^0/\Delta S^0$. Characteristic melting curves for T_m= 300 K are below:



We can analyze the slope of curve at T_m using a van't Hoff analysis:

$$\frac{d\phi_F}{dT} = \frac{d\phi_F}{dK}\cdot\frac{dK}{dT} = \frac{d\phi_F}{dK}\cdot K\frac{d\ln K}{dT}$$
$$\frac{d\ln K}{dT} = \frac{\Delta H^0}{RT^2}$$
$$\frac{d\phi_F}{dK} = K^{-2}(1+K)^{-2}$$
$$\left(\frac{d\phi_F}{dT}\right)_{T=T_m} = \frac{\Delta H^0}{4RT_m^2} \quad \text{since } K=1 \text{ at } T_m$$

This analysis assumes that there is no temperature dependence to ΔH, although we know well that it does from our earlier discussion of hydrophobicity. A more realistic two-state model will allow for a change in heat capacity between the U and F states that describes the temperature dependence of the enthalpy and entropy.

$$\Delta G^0(T) = \Delta H^0(T_m) - T\Delta S^0(T_m) + \Delta C_p\left[T - T_m - T\ln\frac{T}{T_m}\right]$$