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Course 565/665 Lecture Number ______ Date 4/7/03

Lecturer Cavagnero Note Taker Lena Ho

Protein Stability

Native $\rightleftharpoons$ Unfolded

(low energy) (Higher energy)

G : here refered to as ΔG_{NU} ← difference between N and U states

C_p : ΔC_{pNU} ; S : ΔS_{NU} ; H : ΔH_{NU}

From gas phase, $\mu = \mu_0 + kT \ln P$

Multiplying by N $G = G^o + RT \ln P$

For a process, $\Delta G = \Delta G^o + RT \ln \dfrac{P_U}{P_N}$

$$\Delta G = \Delta G^o + RT \ln K_{p\,NU}$$

Extrapolating to solution phase (ideal, no mutual interactions among particles)

$K_{p\,NU} \Rightarrow K_{NU} = \dfrac{a_U}{a_N} \overset{*}{=} \dfrac{[U]}{[N]}$ activity coefficient

activities : $a = \gamma$ [concentration]

*Since solution is ideal, $\gamma = 1$

$$\boxed{\Delta G = \Delta G^o + RT \ln K_{NU}}$$

At equilibrium : $\Delta G = 0$

At T_m, $[N] = [U]$, $K_{NU} = 1$: $\Delta G = 0 = \Delta G^o_m + RT \cancelto{0}{\ln 1}$

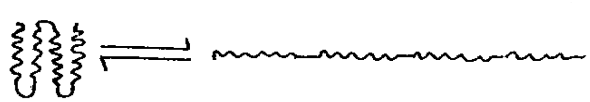
$\therefore \Delta G^o_m = \Delta G = \Delta H^o_m - T_m \Delta S^o_m = 0$

$\Delta G^o = G^o_{final} - G^o_{initial} = G^o_U - G^o_N$ $\Rightarrow$ $\underline{\Delta H^o_m = T_m \Delta S^o_m}$

$$\boxed{\Delta G = \Delta H^o_m \left(1 - \frac{T}{T_m}\right) + C_p \left(T - T_m - \ln \frac{T}{T_m}\right)}$$

- Governs stability of all 2-state processes in nature where H(T), S(T), ΔC_p is not T-dependent and C_p = constant

Myoglobin



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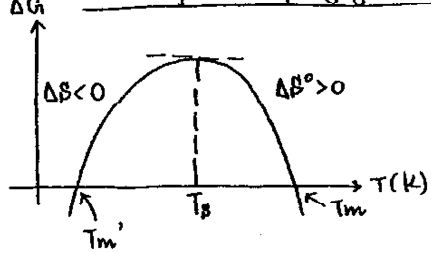
Stability Curve of Myoglobin



Tm = Melting temperature [U] = [N]

Tm' = [U] = [N]
= cold unfolding Temperature

Tm' is often not observed because it is so low that protein solution freezes before the transition can occur.

$\left(\frac{\partial \Delta G^\circ}{\partial T}\right)_p = -\Delta S^\circ \Rightarrow$ slope of the curve (Myoglobin Tm' = −7°C)

T_s : $\Delta S^\circ = 0$ (close to room temperature for many proteins)

- As we unfold the protein from Ts — Tm, $\Delta S^\circ > 0$ since the multiplicity of states increase
- Below Ts, $\Delta S^\circ < 0$ since [U] < [N], so it seems that the unfolded state has less freedom than the native state.

$$\left(\frac{\partial \Delta S^\circ}{\partial T}\right)_p = -\frac{\Delta C_p}{T} = \left(\frac{\partial^2 \Delta G^\circ}{\partial T^2}\right)_p$$ Curvature (2nd derivative)

From Ts → Tm, Negative Curvature $\therefore \Delta C_p > 0$