

unfolded \rightleftharpoons *helix*

$$\Delta G^{\circ'} = \Delta H^{\circ'} - T\Delta S^{\circ'}$$

$$R = 0.0083 \text{ kJ} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$$

$$T = 300 \text{ K}$$

$$\Delta G^{\circ'} = -RT\ln(K)$$

$$\Delta S^{\circ'} = R\ln\left(\frac{N_{helix}}{N_{unfolded}}\right)$$

- After watching the simulation: is formation of a helix thermodynamically favorable or unfavorable?

- $\Delta H^{\circ'}$: A 12-alanine helix forms 8 backbone hydrogen bonds. If, on average, a protein hydrogen bonds contributes $-20 \text{ kJ} \cdot \text{mol}^{-1}$ to the enthalpy, what is enthalpy due to hydrogen bonds in the helical state?

- $\Delta S^{\circ'}$: A simple (and surprisingly effective) way to count possible conformations for the backbone is to count the number of rotatable bonds, and then assume that each bond can be in three possible states. The 12-alanine peptide has 24 such bonds (the $^+H_3N - C_\alpha$ and $C_\alpha - COO^-$ bonds). How many conformations are possible for a 12-alanine peptide? What is the entropy change on folding?

- $\Delta G^{\circ'}$: From these calculations, what would you predict $\Delta G_{unf \rightarrow helix}^{\circ'}$ to be?

- **Experimental $\Delta G^{o'}$:** If you make a solution of peptides made of 12 alanines at 300 K, 80% of the molecules are α -helices, 20% are unfolded. What is $\Delta G_{unf \rightarrow helix}^{o'}$? How does this number compare to your predicted $\Delta G^{o'}$?

- **Experimental $\Delta H^{o'}$:** The experimental value for $\Delta H^{o'}$ is $-41 \text{ kJ} \cdot \text{mol}^{-1}$. Assuming 8 hydrogen bonds actually form and that the hydrogen bonds are the main contribution to $\Delta H^{o'}$, what is each hydrogen bond “worth” in the helix? Why might this be different from the value we used above?

- Now you know $\Delta G^{o'}$ and $\Delta H^{o'}$. What is the contribution of entropy ($T\Delta S^{o'}$) to the free energy of helix formation? Does entropy favor or disfavor helix formation? Is it bigger or smaller than your prediction?

- What other source of entropy might be in play? What is the magnitude of this entropy term?