$$\Delta G^{\circ\prime} = \Delta H^{\circ\prime} - T\Delta S^{\circ\prime}$$

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

$$T = 300\ K$$

$$\Delta G^{\circ\prime} = -RTln(K)$$

$$unfolded \rightleftarrows helix$$

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

  ↳ IT HAPPENED SPONTANEOUSLY.

- A 12-alanine helix forms 8 backbone hydrogen bonds. If, on average, backbone hydrogen bonds are $-20\ kJ \cdot mol^{-1}$, what is enthalpy due to hydrogen bonds in the helical state?

  $-20 \times 8 = -160$ kJ/mol

- 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?

  3^{24}

- With the robot, the entropy change for $out \rightleftarrows in$ was given by:

  $$\Delta S \equiv Rln\left(\frac{A_{in}}{A_{out}}\right)$$

  where A is area. Given this, can you figure out a way to estimate the entropy change to $unfolded \rightleftarrows helix$?

  $-0.22 = R\ln\left(\frac{1}{3^{24}}\right)$ ← FOLDED / UNFOLDED

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

  $\Delta G = \Delta H - T\Delta S$

  $-160 - 300(-0.22) = -94$ kJ/mol

- If you make a solution of 12-alanine peptides at 300 K, 80% of the molecules are α-helices, 20% are unfolded. What is $\Delta G^{\circ\prime}_{unf \rightarrow helix}$? How does this number compare to your predicted $\Delta G^{\circ\prime}$?

$\theta = \frac{F}{F+U} = 0.8$

$(F+U)\theta = F$

$\theta F + \theta U = F$

$\theta U = F - F\theta$

$\theta U = F(1-\theta)$

$\frac{\theta}{1-\theta} = \frac{F}{U}$

$\frac{0.8}{0.2} = \frac{F}{U} = 4$

$-RT\ln\left(\frac{F}{U}\right) =$

$-0.0083 \cdot 300 \cdot \ln(4)$

$= -7.5$ kJ/mol

-3.5 kJ/mol ←

Using a technique called Differential Scanning Calorimetry, one can measure $\Delta H^{\circ\prime}$ for helix formation. The experimental value for $\Delta H^{\circ\prime}$ is $-41\ kJ \cdot mol^{-1}$. Assuming 8 hydrogen bonds actually form, what is each hydrogen bond "worth" in the helix? Why might this be different from the value we used above? LESS FAVORABLE.

$-41/8 = -5.1$ kJ/mol. COMPETITION WITH H_2O

- What is the contribution of entropy ($T\Delta S^{\circ\prime}$) to the free energy of helix formation? Does entropy favor or disfavor helix formation? Is it bigger or smaller than your prediction?

$-3.5 = -41 - T\Delta S$

$-3.5 - -41 = 37.5 = T\Delta S$

$\Delta S = 37.5/300 = 0.125$

ENTROPY CHANGE LESS THAN EXPECTED (0.22)

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

HYDROPHOBIC EFFECT.

$\Delta S_{OBS} = \Delta S_{HELIX} + \Delta S_{HPHOBE}$

$-0.125 = -0.22 + \Delta S_{HPHOBE}$

$-0.125 - -0.22 = 0.095$ kJ/mol K $= \Delta S_{HPHOBE}$