Questions:  
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I. Polyelectrolyte Theory (Manning 1969, C&S Chapter 22)

A. What are the simplifying assumptions made by Manning (JCP, 1969) regarding the condensation of counter-ions by polyions? (Choose Three)

B. When would these assumptions be invalid?

C. What is the relationship between the Bjerrum length and the thermal energy of charged particles? What type of limit does it place on the structure of any charged polymer in the absence of counter-ion?

D. What is the Bjerrum length of a polyanion (monovalent) in ethanol at 25°C? (ε ~ 24)

E. In Manning theory, the charge density parameter $\xi$ is defined by the equation:

$$\xi = \frac{e^2}{\varepsilon kTb}$$

where $\xi$ is the charge density parameter, $e$ is the charge of an electron, $\varepsilon$ is the solvent dielectric, $k$ is Boltzmann’s constant, $T$ is the temperature in Kelvin, and $b = L/P$ where $L$ is the length of the polyelectrolyte chain and $P$ is the number of charged groups. If $\xi > 1$, what does this tell us about the condensation of counter-ions? What if $\xi \leq 1$?

E. $\theta_n$ represents the fraction of counter-ions condensed per phosphate and is related to $\xi$ by the equation:

$$\theta_n = \frac{(1 - 1/N\xi)}{N}$$

where $N$ is the valence of the counter-ion. The distance between phosphates in dsDNA is 1.7Å and for ssDNA it is 3.4 Å. Calculate $\xi$ for dsDNA and for ssDNA. What is the partial negative charge/phosphate for ssDNA? For dsDNA?

II. Ionic Strength and Nucleic Acid Stability (C&S Chapter 22)

A. Given the following simple equilibria governing the melting of a single strand DNA hairpin:

$$M_n:D \leftrightarrow M_n:S + \Delta nM$$
Where \( M_n \) represents the amount of counter-ion bound to the duplex, \( D \), and \( M_n' \) represents the amount of counter-ion bound to the single strand. The \( \Delta n \) term is a measure of the stoichiometric release/consumption of counter-ions upon formation of the single strand. \( M \) is simply the concentration of the counter-ion \( M \) in solution. What is the expression for the equilibrium constant for helix formation \( K_h \) in terms of \([M]\) and \( \Delta n \)?

B. How does \( K_h \) change with increasing ionic strength? Sketch a graph of \( \ln K_h \) vs. \( \ln [M] \) and label the slope.

C. What is the relationship between the value of the slope in part C and the charge density parameters, \( \xi_{ss}, \xi_{ds} \)?

D. Describe the two opposing energetic effects of monovalent cations on the equilibrium between ssDNA and duplex DNA. Which

E. Which of these effects predominates at low ionic strength, leading to duplex melting?

F. Is the effect of ionic strength on duplex stability dependent on the base composition of the duplex? Explain (1 sentence)

III. Hydrophobic Effect (Baldwin, 1989)

Link: [www.its.caltech.edu/~bch176/Baldwin1986.pdf](http://www.its.caltech.edu/~bch176/Baldwin1986.pdf)

A. Describe the experiment by which Baldwin calculates the standard state entropy of transfer (\( \Delta S^0_{\text{transfer}} \)) of aqueous hydrocarbon solutions. How are the entropy and enthalpy of transfer calculated? What is the significance of \( \Delta S^0_{\text{transfer}} \) and \( T_s \) in the context of the hydrophobic effect?

B. Baldwin calculates the temperature at which \( \Delta S^0_{\text{transfer}} = 0 \). A similar calculation can be performed to obtain the temperature at which \( \Delta H^0_{\text{transfer}} = 0 \). What physical property of hydrocarbon:water solutions is associated with this value? In the context of the hydrophobic effect, \( \Delta H^0_{\text{transfer}} \) corresponds to \( \Delta H^0_{\text{hyd}} \). Based on the data for hen lysozyme unfolding (Table 3), what is the contribution of \( \Delta H^0_{\text{hyd}} \) to the observed change in enthalpy of folding (\( \Delta H^0_{\text{obs}} \)) at low temperatures? At high temperatures? How might this be related to the problem of protein folding?

C. Baldwin posits that the observed entropy of protein folding (\( \Delta S^0_{\text{Obs}} \)) is related to the entropy of hydrophobic burial (\( \Delta S^{\text{Hyd}} \)) by:

\[
\Delta S^0_{\text{Obs}} = \Delta S^{\text{Hyd}} + \Delta S^{\text{Res}}.
\]
What factor(s) contribute to \( \Delta S^{\text{Res}} \)? Based on the data for hen lysozyme unfolding Table 3), what is the relative contribution of \( \Delta S^{\text{Res}} \) to the observed entropy of protein folding at low temperatures? At high temperatures? How can \( \Delta S^{\text{Res}} \) be obtained from values of \( \Delta S^{\text{Obs}} \)?

D. Based on the hydrocarbon model, explain why different proteins could have an intersection near 110 °C in the plot of specific entropy of unfolding against temperature. What are the major limitations of the hydrocarbon model?