Biology 5357

Chemistry & Physics of Biomolecules

Examination #2

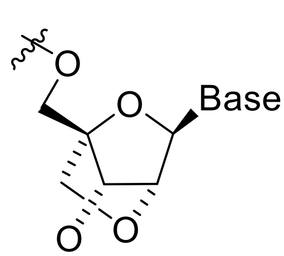
Nucleic Acids Module

November 3, 2017

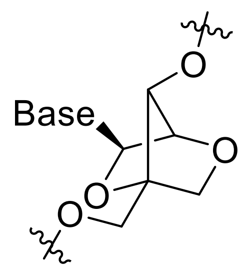
Name: ________________________________

Question 1. (8 points) Draw a Watson-Crick A-T base pair as well as the sugar phosphate backbone with the glycosyl bonds in the conformation found in B DNA. Also indicate what would be the major and minor groove sides of the base pairs in a B DNA duplex. Show where metal ions might interact strongly with this base pair in B DNA and explain why.

Question 2. (10 points; A-E, 2 pts each) In an effort to better understand and control the conformation and thermodynamics of nucleic acid duplex formation, chemists have developed "locked nucleic acids" or LNAs shown below as a structural drawing, and as a 3D perspective drawing.



LNA



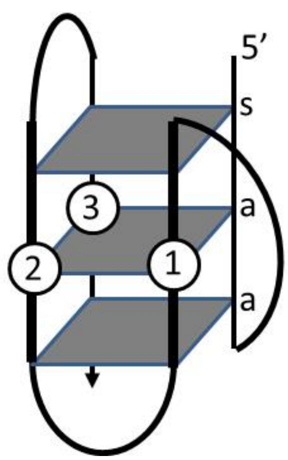
(A) Why is the term "locked" being used?

(B) What conformation is the sugar ring portion of the molecule in? Be specific using $C_{X'}$-endo/exo nomenclature for twist or envelope conformations.

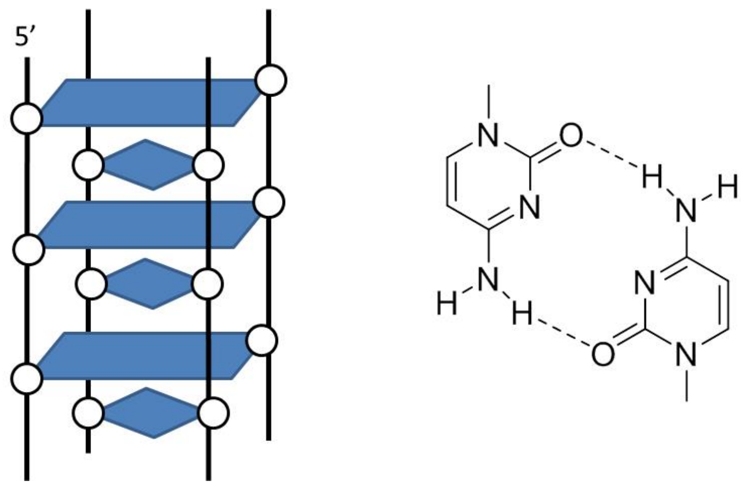
(C) What nucleic acid duplex conformation adopts this type of sugar conformation, if any?

(D) It has been found that the thermodynamic stability of DNA duplexes increases when nucleotides are replaced with LNAs. How might you explain this based on what you know about what contributes to the thermodynamic stability of DNA duplexes.

(E) Into which of the positions shown in the following G-quadruplex would you introduce LNAs to stabilize the structure? Why?



Question 3. (10 points; A = 6 pts, B = 4 pts) Consider the folding of the strand complementary to the GGGTTA strand of human telomeric DNA which forms the intercalated structural motif shown, where each parallelogram represents a C-C base pair and each circle represents the sugar phosphate unit of the C.



(A) Based on the geometry of the base pair shown propose a folded structure for four repeats of TAACCC, *i.e.*, connect the individual strands with TAA loops in a way that would accommodate the C-C pairs in which both C's are in *anti* glycosyl conformations.

(B) This motif structure is facilitated at lower pH. Explain. [Hint: What will happen to the base pair shown at low pH, and how might this affect the stability of the base pair ?]

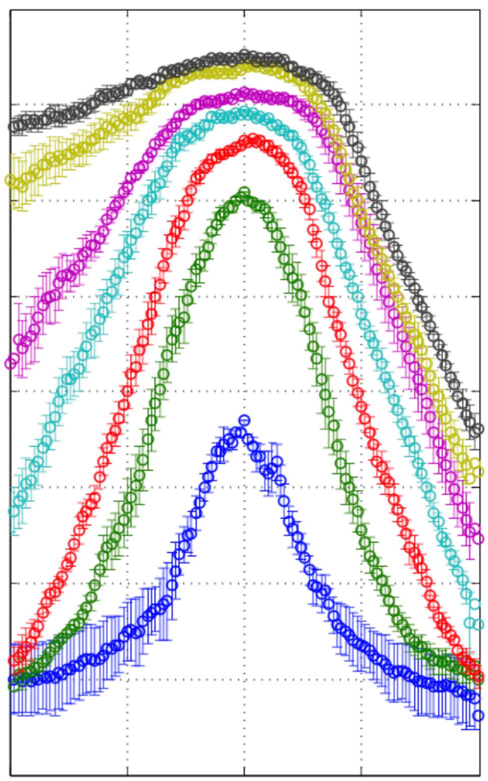
Question 4. (6 points) The equation below describes the polymer behavior of DNA under tension. $\boldsymbol{k_B}$ is the Boltzmann constant. What are the other six parameters in the equation ($\boldsymbol{x}$, $\boldsymbol{L_0}$, $\boldsymbol{T}$, $\boldsymbol{F}$, $\boldsymbol{P}$ *and* $\boldsymbol{K_0}$) ?

$$x = L_0\left(1 - \frac{1}{2}\left(\frac{k_B T}{FP}\right)^{1/2} + \frac{F}{K_0}\right)$$

Question 5. (4 points) Describe, using the concepts of entropy and enthalpy, what happens as you use increasing amounts of force (starting from zero force) to stretch a dsDNA molecule.

Question 6. (4 points) Is DNA perfectly straight over its persistence length? Why or why not?

Question 7. (6 points) The below shows rotation-extension curves for dsDNA obtained with the magnetic tweezers under different conditions (different colors). Label the axis of the plot. Provide an explanation for what parameter or parameters may be being varied in the experiment and include a physical description of why changes in this parameter leads to differently shaped curves using the concepts of linking number, twist, and writhe.



Question 8. (10 points; A = 6 pts, B = 4 pts) Two useful quantities to describe the conformations of proteins and DNA are the end-to-end distance and the radius of gyration.

(A) Provide a concise description of these two important quantities using words and/or equations.

End-to-End Distance:

Radius of Gyration:

(B) For an ideal chain, an important relationship connects the mean square end-to-end distance with the mean square radius of gyration. Which one is larger? What is the conversion factor?

Question 9. (12 points; A-C = 4 pts each)

(A) Scaling exponents, commonly designated by the Greek letter ν, are an important concept in polymer physics. Indicate three different scaling exponents that describe the dependence of the root-mean-squared radius of gyration versus the polymer length (expressed in numbers of monomers N). For each scaling exponent assign the corresponding quality of the solvent and describe the average shape adopted by the polymer when all the configurations are aligned in the same direction.

ν	**Solvent Quality**	**Shape**

(B) Write the scaling equation for the radius of gyration versus the number of monomers N:

$$\left\langle R_g^2 \right\rangle^{1/2} \propto \boxed{}$$

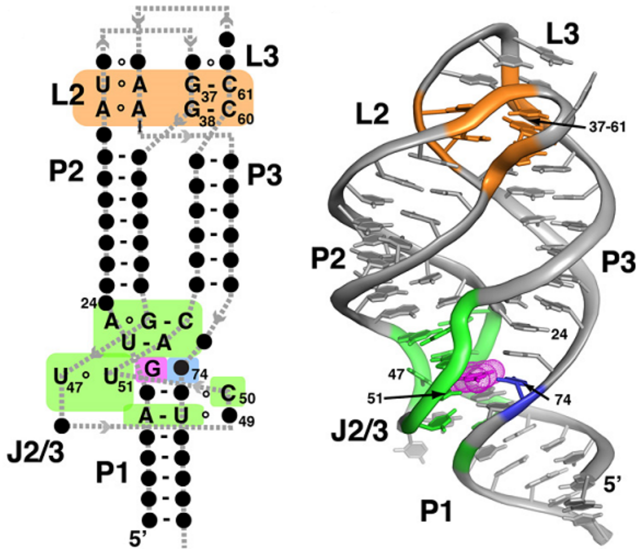
(C) The disordered tails of two proteins have identical repeated sequences. One tail is 60 amino acids long, whereas the other is 120 long. The measured radius of gyration for the tails are indicated as R_g^{60} and R_g^{120}. Using the measured numbers can you estimate the scaling exponent and the solvent quality.

	R_g^{60} (nm)	**R_g^{120} (nm)**	ν	**Solvent Quality**
6M Urea	4.30	6.5		
50 mM NaP	1.40	1.76		

Question 10. (6 points) Describe the probability distribution for the end-to-end vector and for the end-to-end scalar distance of an ideal chain. Which one of the two is centered at zero? Why? Discuss the difference between the two distributions.

Question 11. (8 points) What do imino protons in NMR experiments tell you about the structure and stability of an RNA duplex? Explain, and provide structural examples to illustrate your answer.

Question 12. (16 points; A-B = 8 pts each) Shown below is the purine riboswitch aptomer, in this case with bound Guanosine.



(A) Identify what differences you might expect between this RNA aptamer and a DNA molecule of the same sequence.

(B) How would you experimentally demonstrate those differences? Illustrate any experimental results if needed for clarity.