

Problem Set 2

(Due Sept 9th)

- Consider these two polynucleotides: AAGCGT GCACTG
 - Draw each molecule in the 2' deoxy form (DNA).
 - What is the sequence of the complementary strand? Write this in the 5' → 3' direction.
 - Draw the first base pair in each case. You can use 'X' in place of the deoxyribose.
 - Which oligonucleotide will anneal more favorably (higher T_m) with its complement? Why?
 - If Adenine were added to the 2nd strand by DNA Polymerase, where would it go? Why?
- What is meant by cooperative folding/unfolding with respect to DNA structure?
- Describe all intermolecular forces that contribute to DNA structure.
- cGMP(3'-5' cyclic guanosine monophosphate) is generated from GTP. Propose a mechanism by which this could happen. What is the product? Do you expect this to be energetically favorable? Why?
- We have seen that base pairing occurs between keto tautomers of the nucleotides. However, base pairing could potentially occur between enol-enol or enol-keto forms of the nucleotides as well. Determine if enol tautomers of the nucleotides have base pairing potential. Assume that at least two hydrogen bonds must be present to create a stable base pair.
- Describe the distinct characteristics of A-DNA, B-DNA and Z-DNA.
- Draw each of the nucleotide monophosphates. Identify the Watson-Crick, Hoogsteen, and sugar faces. Explain why the H-bonding pattern of each of these faces is important.
- Summarize the factors that dictate DNA stability. Include stabilizing forces as well as structural arguments (torsion angles, etc.).
- Hydrogen bonding patterns are important for DNA to obey Chargaff's Rule but do not play a very important role when considering the stability of dsDNA. Justify both of these statements.
- Why is supercoiling necessary? What contributes to stress in a supercoiled DNA molecule and how is that stress relieved (so how is the Linking Number decreased)?
- Use Chimera to view the 3D structures of A-form (pdbID 1VJ4) and B-form (pdbID 1BNA) DNA. I recommend turning off nucleic acid objects (Actions → Atoms/Bonds → Nucleic Acid Objects → Off) and hiding the ribbon form. **For this question, please create a word document that contains images supporting the answers to each question.** Please do not waste paper and print this unless you really want to; email it instead.
 - In both structures, determine the distance between adjacent phosphorus atoms. You can use the Distance tool under Structure Analysis. Select the two atoms and then 'create'. For each structure, do this for P-P distances and average them.
 - Turn each molecule so that you're looking down the helical axis. What difference do you observe?
 - Zoom in on one of the deoxyribose units (if you select an atom, you can set it as your focus Actions → focus). Orient the sugar so that 4 of the atoms are roughly in the same plane. Which atom appears to be puckered out of the plane of the ring?

12. Using the tools you learned in Biochemistry Lab this week:
- a. Determine the nucleotide and amino acid sequence for glucokinase from *Escherichia coli* (strain K-12 sub-strain W3310). I recommend searching NCBI using the 'gene' option instead of 'nucleotide'. Make sure to list the nucleotide sequence from 5'→3' with the start codon at the 5' end.
 - b. From the gene page, you can quickly determine what genes are genetic neighbors (upstream and downstream of glucokinase in the genomic context window).
 - c. From the gene page, follow the KEGG link under "Links to other resources". This is on the right side of your screen. What metabolic Pathways are glucokinase involved in? List the top two.
 - d. What amino acids are involved in nucleotide binding? List these in this format: Tyr4, meaning the tyrosine at the 4th position.
 - e. What conserved domains are present in this protein?
 - f. Run a Blast search on the amino acid sequence. Are there any homologues in *Yersinia pestis* (the cause of the Bubonic Plague)?
 - i. If yes, determine the % Identity and % Similarity (positives) between these two proteins.
 - ii. List the amino acid sequence of this protein.