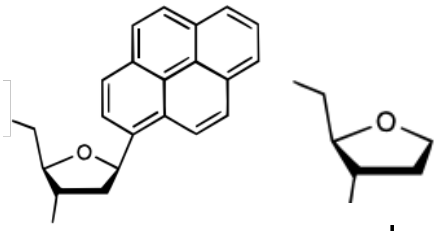
Discussion Worksheet – Winter 2026 - Week 3
Due on January 19 at 11:59pm

Please do all parts of the question your group is assigned to (i.e., group "1A" should do all parts of question 1).

Group 1:

Scientists have studied the effect of incorporating non-natural nucleosides on the Tm of DNA molecules. In particular they have used nucleotides where the base has been changed to a pyrene group (P), or nucleotides with no base (abasic = ϕ). The structure of these nucleosides is shown on the right.



P **ϕ**

The Tm of 12 base-pair long DNA duplexes containing either a normal A-T base pair, or the chemically modified nucleotides in place of the A-T base pair are indicated below:
A-T = 43.2°C A-P=38.7°C A-ϕ = 22.2°C P-ϕ = 41°C

A- Compare the stabilities of the DNAs containing either A-T or A-P and propose an explanation for the impact of the Pyrene on the stability of double-stranded DNA

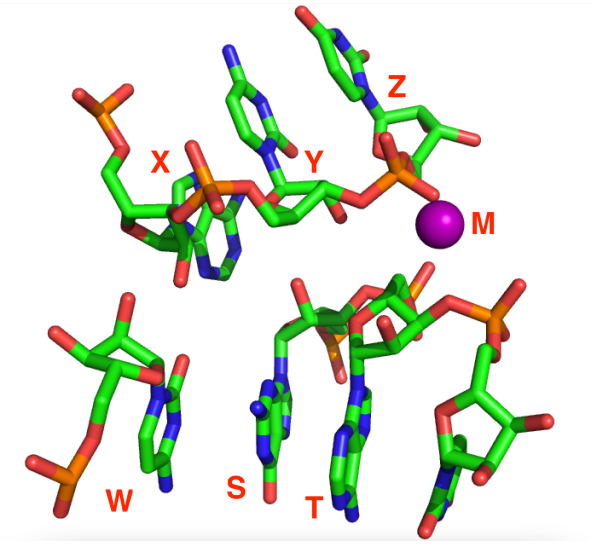
B- Compare the stabilities of the DNAs containing either A-T or A-ϕ and propose an explanation for the impact of the presence of the abasic nucleoside ϕ on the stability of double-stranded DNA

C- Compare the stabilities of the DNA containing either A-T or P-ϕ and propose an explanation for the impact of the combination of the pyrene and of the abasic nucleoside ϕ on the stability of double-stranded DNA.

D – How do these results provide experimental confirmation of the contribution of two specific type of interactions to the stability of double-stranded DNA?

Group 2:

The structure of a nucleic acid is shown on the side. M is a positively charged ion.



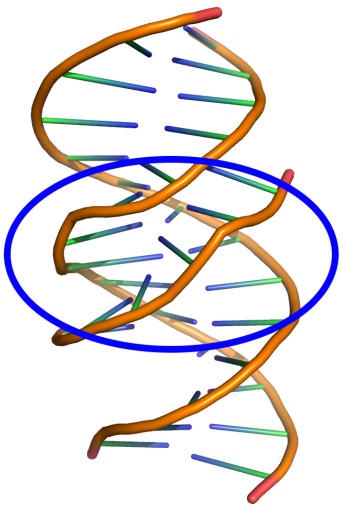
A – Describe the main potential interaction between nucleotides S and T

B – What is the primary interaction between nucleotides S and Y? There is a similar interaction between nucleotides W and X.

C – From the interactions described in part B, what structural motif can you identify in this structure? Explain your answer in one sentence.

D – What is the role of M in this structure?

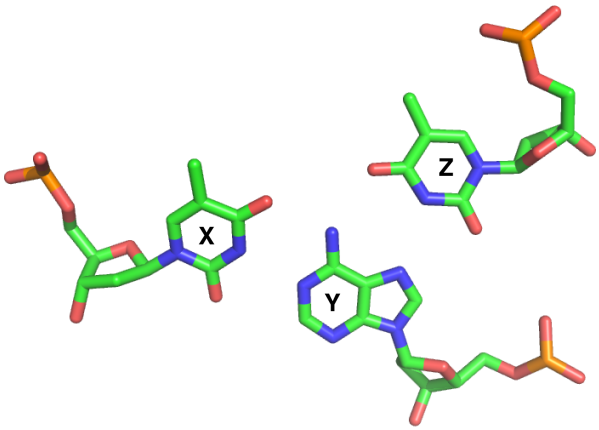
Group 3: The structure of a nucleic acid is shown on the right with a global view (top), and details of the area which is encircled in blue (middle and bottom picture).

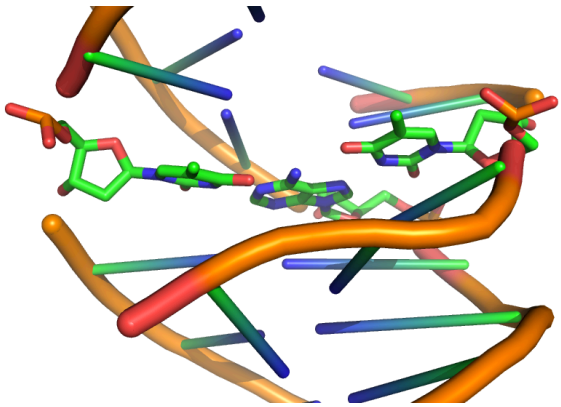


A – What type of structure is formed by this nucleic acid? Explain your answer.

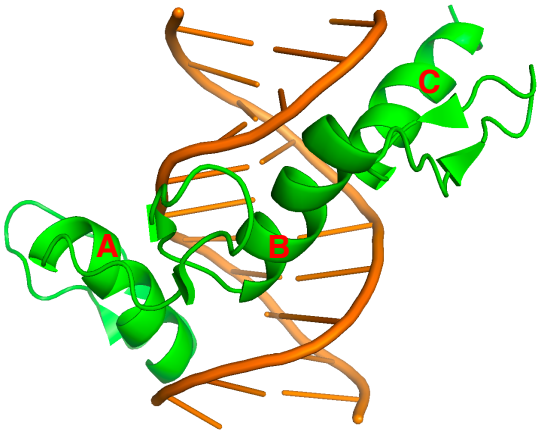
B – From the picture at the bottom, explain what interactions exist between nucleotides X, Y and Z. Specify the type of interactions and atoms involved.

C – A similar structure involving a viral RNA has been studied in class. Explain below two major differences between the structure shown here and the structure studied in class.



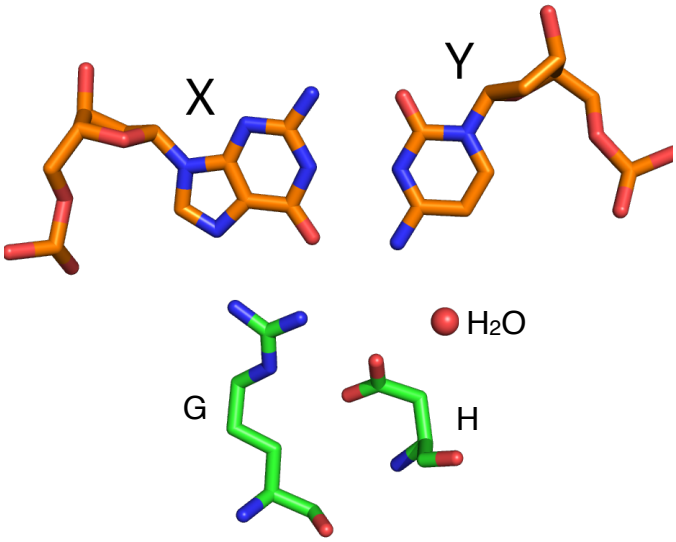


Group 4:
Scientists determined the structure of a sequence-specific DNA binding protein (shown in green) to better understand how it recognizes its target DNA (orange). The protein is comprised of three alpha-helical domains, which are labeled A-C on the upper image.



A. Which groove of the DNA is this protein predominantly engaging to identify its target sequence? List three structural features that led you to this conclusion.

B. An atomic view of domain B interacting with its target DNA sequence is shown in the lower image. How does residue G of the protein interact with base X of the DNA? Mark all hydrogen bond donors (as D) and acceptors (as A), draw any hydrogens, and explain in one sentence.



C. In the lower image, how does residue H of the protein interact with base Y of the DNA? Mark all hydrogen bond donors/acceptors, draw any hydrogens, and explain your answer in one sentence (hint: think about the properties of water)

D: Do the interactions shown in the lower image likely contribute to the affinity or specificity of the protein for its target DNA sequence? Explain your answer in one sentence.