The DNA Binding Lab - Investigating how molecules interact with DNA

Background

Molecules bind to specific shapes and sequences in DNA. Some molecules bind to the narrow grooves in DNA, others fit into the wider, major grooves. This ability to recognize three-dimensional shapes helps proteins identify specific DNA sequences and determine where to start copying DNA or making RNA. This specificity is also important for the action of certain drugs. Some anti-cancer drugs, for example, bind specifically inside the narrow grooves

Materials

1. Touch the question mark icon in Molecule World to open the information section.
2. Touch "View Structure Collections" to access Digital World Biology structure collections.
3. Choose the DNA Binding Lab collection.
4. Touch "DNA_Binding_Lab.mwc" to select this collection.
5. Choose "open in Molecule World" to download and open the collection in Molecule World.

Skills

Before starting, it may be helpful to practice the following skills:

1. Use the options in the visualization menu to change the drawing and coloring styles.
2. Use the palette icon to see a color key
3. Touch the Sequence button to open and close the sequence viewer.
4. Touch the names of different chains or the letters to select or deselect DNA or protein chains or individual residues.
5. Use the Show/Hide menu to hide or show the complete amino acid side chains or the bases for nucleotides.

Learning Objectives:

1. Identify key features of DNA structure.
2. Explore examples of molecules that bind to specific shapes in DNA.
3. Practice working with DNA models to discover how proteins and chemicals like drugs bind to DNA shapes.

Part I. Learn about DNA structure

1. Open the structure of double-stranded DNA with hydrogens.
2. Change the drawing style to Ball & Stick. Each ball represents an atom and each stick, a covalent bond.
3. Change the drawing style to Space Fill. This style shows the approximate size of the electron cloud for each atom.

4. Change the coloring style to Element. The Element coloring style uses color to identify each type of atom.
5. Touch the palette icon to open a color key. Use the color key to identify the elements in DNA.
6. The atoms are drawn with different sizes because the chemical elements are different sizes. Which type of element is the smallest?
7. In double-stranded DNA, nucleotide residues are joined together in single strands. Together, the two strands form a double helical shape with the phosphate backbone on the outside.

   Major groove: the major groove is the indented region where the backbones from the DNA strands are farthest apart.

   Minor groove: the minor groove is the indented region where the phosphate backones are closest together.

8. Notice where each element is found in the DNA structure.
9. Change the coloring style to Charge to determine whether DNA has a positive, negative, or neutral charge. Use the color key to find out.
10. Change the coloring style to Hydrophobicity and use the color key to determine if DNA is hydrophobic or hydrophilic?
11. Use the Molecule coloring style to determine the number of distinct single-stranded molecules in double-stranded DNA.
12. Change the coloring style to Residue coloring style to see each type of base in a different color.
13. Use the color key to see which colors are letters are used to represent the different bases.
14. Change to the Tube drawing mode to make the bases easier to see.
15. The number of bases is used to describe the length of a DNA strand. How long is each strand of DNA in the example?

Part II. Look at molecules that bind to specific shapes in DNA.

1. Open the structure of double-stranded DNA with hydrogens.
1. Find the major and minor grooves. These are distinct shapes in a DNA helix. It may help to change the drawing style to spacefill.
2. Open the example structure with protein bound in the major DNA groove.
3. Try different combinations of drawing and coloring styles to see which methods make it easiest to see where the protein is bound. Also try using the Secondary View towards to the bottom of the menu. This view emphasizes the secondary structure elements in proteins.
4. What happens when you color this structure by molecule? What part of the structure is DNA? What part is protein?
5. What happens when you color the example protein structure by element? Are the elements the same in both protein and DNA?

6. What happens when you color this structure by residue? Are the residues the same in both protein and DNA?
7. Try other coloring modes to see differences between proteins and DNA.
8. Open the example structure with a chemical bound in the minor DNA groove.
9. This example shows two molecules bound to the minor groove.
10. What happens when you color the minor groove example by element? Are all the elements in the chemicals the same as the elements in the DNA?
11. What happens when you color this structure by residue? Does the other example structure contain residues?
12. Which drawing and coloring styles work best to show binding to the minor groove and confirm that the drug is not protein? You might find it helpful to look at the sequence as well.

Part III. Practice working with the unknown DNA structures to discover how proteins and drugs bind to specific shapes in DNA.

1. Record the name of your unknown.
2. Try different visualization methods to find the combination that works best to help you distinguish between the DNA and the substance binding to the DNA.
3. Use different visualization methods to determine if the unknown substance binds mostly to the major groove, the minor groove, or both.
4. Use different visualization methods to determine if the unknown substance is protein or if it's something else.
5. Use the camera icon to save images for evidence to support your decisions.
6. What evidence makes you think that a protein or drug binds mostly to the major groove, minor groove, or both?
7. What characteristics tell you that a substance is a protein or if it's something else?