Problem Set 3 - Proteins

Introduction to Bioengineering

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Problem 1

Use the browser protein structure viewer available on RCSB.ORG or download a software to view PDB structure files:

- http://spdbv.vital-it.ch/
- http://www.bernstein-plus-sons.com/software/rasmol/
- http://www.pymol.org/
- http://www.ks.uiuc.edu/Research/vmd/

Then download the following structures from the PDB (www.rcsb.org):

- Zif268-DNA (1AAY or 1ZAA)
- MAX - DNA (1AN2)
- TAL (3UGM, 3V6T)

Problem 1.1: Show a picture of the three transcription factors.

Problem 1.2: Measure the width of the major and minor groove of DNA. Provide an image indicating where you measured with a line. Provide a short but detailed description of how you decided to measure the width and explain and justify why you chose to measure the width that way.

Problem 1.3: Choose your favorite of the 3 structures and display a detailed view of the DNA - transcription factor binding interface and clearly indicate one non-specific and one specific interaction between the TF and DNA. Specific interactions are contacts between the protein and the nucleobases of DNA, whereas non-specific interactions are contacts between the protein and the phosphate backbone of DNA. (Hint: using the slab view feature will help to display only the parts you are interested in)

Answer 1.2: Specific and non-specific interactions are shown at the end of the problem set (Figure 1, Figure 2).

Problem 2

Problem 2.1: Why is the α-helix the dominant secondary structure used by transcription factors?

Answer 2.1: The α-helix is of comparable size to the major groove of DNA. It thus physically can fit into the major groove of DNA to make base specific and non-specific contacts. Furthermore, the amino-acid side chains are positioned well to make these contacts.

Problem 2.2: Do you expect transcription factors to bind equally well to A-DNA? Explain why or why not.

Answer 2.2: No, transcription factors are not expected to bind equally well to A-DNA. The major groove of A-form DNA is much narrower then the major groove of B-form DNA, thus α helixes would not be able to make the same contacts as with B-form DNA. Since A-form DNA only occurs in non-physiological conditions, no transcription factors could have evolved to bind A-form DNA. (Z-DNA on the other can form under physiological conditions and it is thus possible that transcription factors could have evolved that bind specifically to Z-DNA, but it is again unlikely that one transcription will be able to bind both B-DNA and Z-DNA).

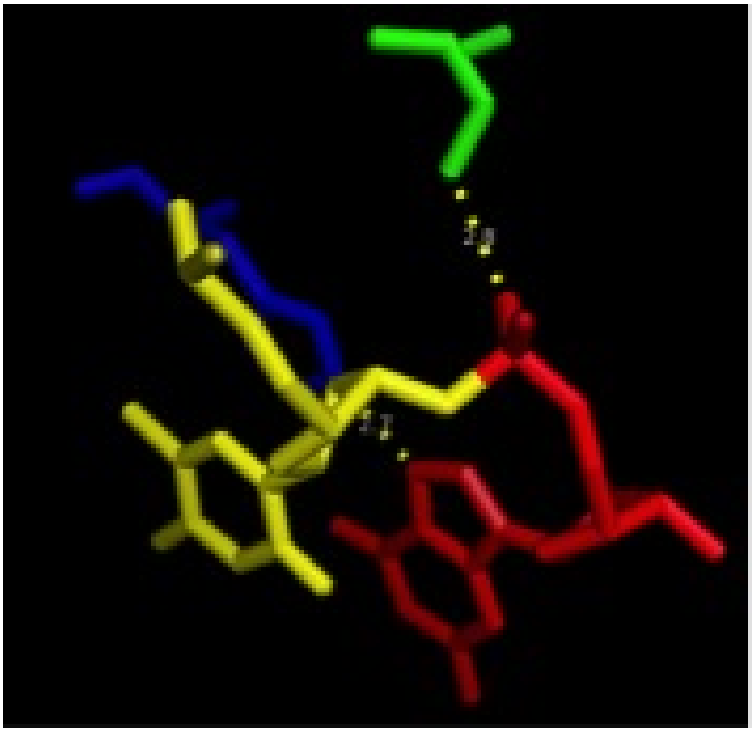

Figure 1: Non-specific protein-DNA contact: The OH group of the serine (green) forms a hydrogen bond with the phosphate group of the DNA backbone (red).

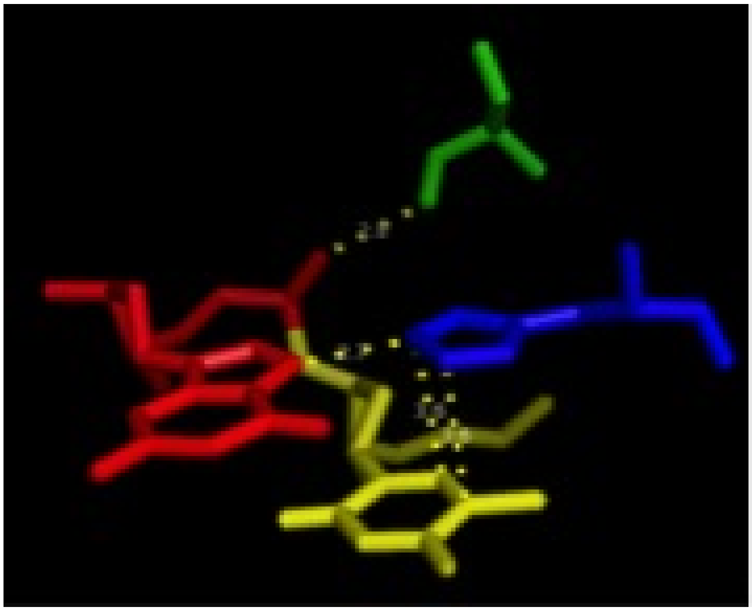

Figure 2: Specific protein-DNA contact: N3 of histidine (blue) hydrogen bonds with N7 of guanine (red). The aromatic ring of histidine also stacks parallel to thymine (yellow), forming a stabilizing π-π interaction.