**Problem Set #2, Structure and thermodynamics of protein-DNA complexes**

Please submit your answer before Thursday, November 14, 2024, 14:15 hour per e-mail to karsten.rippe@bioquant.uni-heidelberg.de and include [BPC2024] in the subject line.

**1**. Specific and unspecific interactions between proteins and the DNA double helix are mediated between various types of amino acid side chains with the DNA double helix:

a) Give an example of specific interactions between an amino acid side chain and a guanine residue in the DNA and another example of a specific interaction with adenine. What type of protein secondary structure will facilitate these interactions, and where on the DNA helix do they occur?

b) List the amino acids frequently found to mediate unspecific binding of the protein to the sugar-phosphate backbone of the DNA. Which type of non-covalent interaction forces are involved?

c) What could be differences in the biological functions of DNA-binding proteins that make some proteins strongly distort the DNA upon specific binding while others hardly affect the DNA conformation?

**2.** Examine the nucleosome crystal structure for which the pdb coordinates are given in the file “nucleosome.pdb” with a molecular viewer (see below for different viewers).

a) Evaluate interactions of the histone octamer protein core with the DNA. Do they occur mostly with DNA bases or with the sugar-phosphate backbone of the DNA? At which periodicity (expressed in the number of base pairs) are interactions between DNA and protein core present?

b) How long is the DNA fragment wrapped around the histone octamer protein core? Give the sequence of the 5 base pairs where the interaction starts and the 5 base pairs where it ends.

c) Does the histone octamer contain protein regions that are unfolded, and if so, where are they located?

*Molecular visualization programs*: UCSF chimera (macOS), https://www.cgl.ucsf.edu/chimerax/; VMD, http://www.ks.uiuc.edu/Research/vmd; pymol (trial version), https://pymol.org

*Nucleosome structure pdb coordinates can be found on the lecture web page*.

**3.** The free energy ∆G of protein binding to DNA involves favorable and unfavorable entropy terms.

a) Describe three different contributions to the entropy change that occurs if a protein binds to DNA.

b) Explain which of these entropic changes drive binding and which would favor dissociation of the complex.

c) Which entropy term could significantly differ between a specific and unspecific protein-DNA complex and favor specific binding?