Analysis of DNA structures of p53 REs

The TF p53 needs to bind to different REs in order to achieve its function as a tumor suppressor. Mutations, as well as post-translational modifications in p53 can influence the way p53 recognizes its DNA binding sites. The DNA sequence and structure, on the other side, is extremely important for the recognition of these specific Res. P53 consensus sequence is the dodecameric 5’–RRRCWWGYYY -3’ (R=purine; Y=pyrimidine; W=A/T), separated by a spacer that varies in length (0-20 bps). Here we show analysis of Bax DNA and p21, and compare DNA features between different structures.

Bax DNA

For the last available structure, the following represents the DNA analysis of Bax. In the following figure we have bax and 3kmd superimposed. From measuring distances from points in the DNA that we consider to be not as flexible (since they have to accommodate the tetramer which has specific contacts with the G bases), we can see that DNA is largely deformed in the middle part, where the tetramer does not interact with the DNA the complex has to accommodate an extra bp. The red lines represent the largest distances observed between the G7-G37 (from the consensus CWWG)
Bax - Minor Groove width and Electrostatics
If we also analyze other DNA structures, we see that p21 (3TS8) has also a very wide minor groove in the same region, showing that this type of deformation is not specific to the existence of a spacer (extra base pair) that needs to be accommodated.

**Analysis of DNA parameters of p21: crystal structure, individual models from MC**

For the p21 RE, we analyzed all the pdb structures that had the smallest rmsds when compared to the DEER. Looking at different DNA parameters, even if there are DNA deformations in the model that best fits to the DEER, we expect to see the same pattern of deformation in the other structures. Another step that still needs to be done is the superposition of the different sites, and the measurement of distances between points that are being used by Peter’s group. In order to see if the energy of these complexes is favorable, the energy of the snapshot and the average of accumulated energy are still need to be analyzed. For example, the model that best fits into their measurement (76.pdb) has energy and average accumulated energy of -288.485 -276.863 respectively; The following plots show minor groove, buckle, propel and roll for p21 models with varying rmsds (from 0.763763 – 1.10519). The black line is equivalent to the same DNA parameter for the DNA structure of the complex p53-p21RE