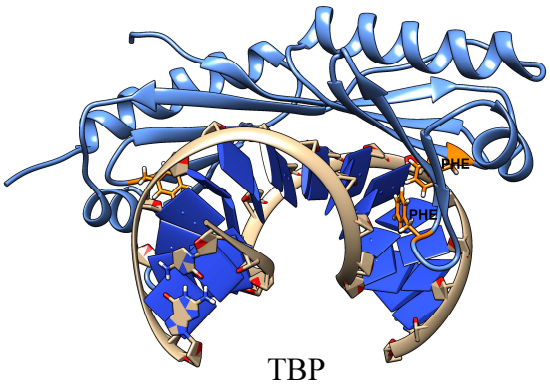
Effects of Protein Side Chain Intercalation in DNA Binding

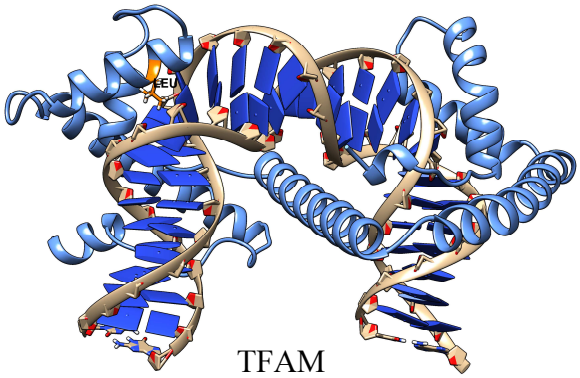
Achim Sandmann, Heinrich Sticht

Bioinformatik, Institut für Biochemie, Friedrich Alexander Universität Erlangen-Nürnberg

Fahrstraße 17, 91058 Erlangen



TBP



TFAM

Several crucial functions including binding site recognition by shape readout, alignment of DNA-bound proteins with respect to each other, and compacting DNA to fit it into small compartments rely on deformation of DNA by DNA-binding proteins. One common way of strong DNA deformation is a localized kink between two successive base pairs, which is mainly visible in the roll angle.

We conducted a search of the Protein Data Bank to find structures of protein-DNA complexes with kinked DNA. One widespread mechanism of inducing kinks is the intercalation of amino acid side chains between DNA base pairs; however, there exist also systems, which achieve kinking without intercalation. By comparing the different X-ray structures of various protein-DNA complexes, we found that intercalated systems show narrow roll angle distributions while systems in which DNA is bent without intercalation show broad roll angle distributions.

Using MD simulations, we investigated the effect of intercalation by comparing WT-proteins and mutants with alanines in place of the intercalating residues. We used CcpA, Cren7, Sac7d, Sox-4, TBP and TFAM as model systems. For Sac7d we found that if two residues intercalate, mutation of one to alanine made no difference. Upon mutation of all intercalating residues, the roll angle decreased, but did not completely vanish. These findings agree with previous mutational experiments [1]. The preliminary data of the simulations for the remaining systems suggest that the properties of these systems are affected by intercalation in a similar fashion. We also compared systems with different DNA sequences and found that, while intercalating wt-protein-DNA complexes showed no sequence dependent roll angles, some of the non-intercalating mutants did bend different DNA sequences to varying degrees.

[1] Chen, C.Y., et al., *Nucleic Acids Res*, **2005**, *33*, 430-438.