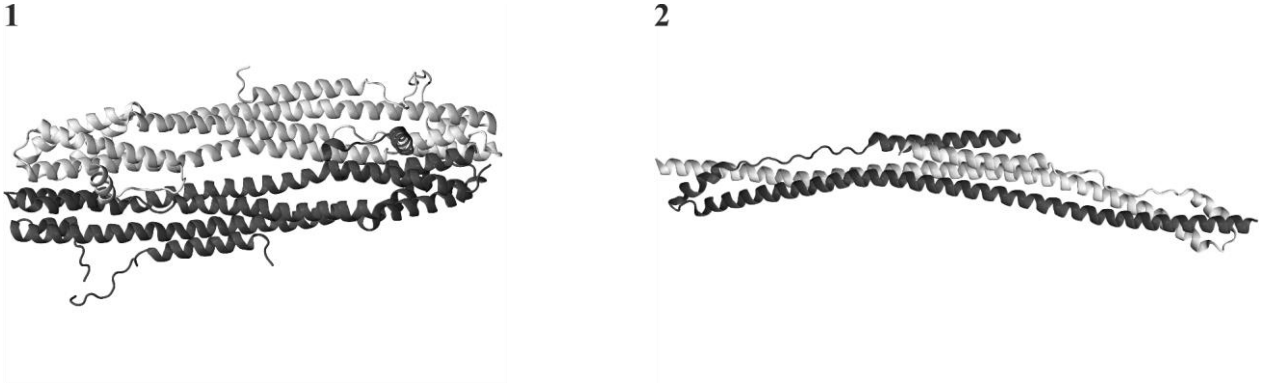
Molecular Dynamics of Viral IE1 Protein and Its Relevance for PML Interaction

Joachim D. Stump, Heinrich Sticht

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

The recently solved crystal structure of the immediate-early protein 1 of rhesus cytomegalovirus (IE1) revealed a novel protein fold with an elongated, all α-helical homodimeric topology (Figure 1). [1] Interestingly, IE1 crystallized in two slightly different dimeric forms indicating a certain degree of conformational flexibility, which was further investigated by molecular dynamics (MD) simulations.



All MD simulations were performed with AMBER/parm99SB force field in an octahedral box of explicit solvent. We simulated the two dimeric structures for 50 ns and three monomers for 100 ns, which were taken from the dimer structures.

Our results show that the interface of the asymmetric dimer is more stable indicating that IE1 has the propensity to form asymmetric protein-protein complexes probably also with other proteins. MD simulations of monomeric IE1 revealed hinge-like motions that explain the occurrence of slightly different backbone conformations of IE1 in the crystal. Interestingly, we detected a local structural similarity to the evolutionary conserved coiled-coil domain (CCD) of TRIM (tripartite motif family) proteins (Figure 2), which is also present in PML (TRIM19) a target protein of IE1. Our computational study suggests that the detected dynamics of the IE1 fold might enable a better interaction with the elongated, α-helical CCD of PML.

[1] M. Scherer, S. Klingl, et al., *PLoS Pathog.*, **2014**, *10*, 10.1371/journal.ppat.1004512