

Poster Presentation

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Impact of crystal packing on coiled-coil flexibility.

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The structural characterization of various constructs of the Measles virus (MeV) Phosphoprotein (P) multimerization domain (PMD) has brought to light significant discrepancies in the quaternary structure due to both crystal constraints and the flexible nature of this coiled-coil. Indeed, despite a conserved tetrameric parallel coiled-coil core, structural comparison unveiled significant deformations in the C-terminal extremities that even led to the partial unfolding of the coiled-coil. These deformations were induced by intermolecular interactions within the crystal, as well as by the crystallization condition. These deformations also suggest that PMD has the ability to adapt to external mechanical constraints. Using a combination of biophysical methods (size-exclusion chromatography, circular dichroism and small angle X-ray scattering), we assessed the differential flexibility of the C-terminal region of the MeV PMD in solution. Taken together, these results show that crystal packing can be used to “freeze” in a certain state, parts of proteins known to be in a dynamic folding-unfolding equilibrium. They also bring awareness that conclusions about function and mechanism based on analysis of a single crystal structure of a known dynamic protein can be easily biased, and they challenge to some extent the assumption that coiled-coil structures can be reliably predicted from the amino acid sequence.

Keywords: crystal packing constrain, flexibility, viral protein