DYNAMICS IN LARGE PROTEIN ASSEMBLIES

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Studies of protein dynamics in large assemblies, and of the constituent components before assembly, is of great interest for understanding biological mechanisms at the atomic level. In this presentation, I will show recent data from our research, combining solid-state NMR, solution-state NMR, MD simulations and a host of other techniques to shed light onto two biological questions. In the first part I will provide insight into a 500 kDa large enzyme, the TET aminopeptidase. By combining magic-angle-spinning NMR with a host of biophysical methods we show that a highly flexible loop, which is even undetected in crystal structures, is a key functional element. Its dynamics allows substrate passage, and a conserved motif within this loop plays an important role in substrate stabilisation. In the second part, we focus on a very different type of assembly: the encounter of a chaperone with its client protein. We demonstrate that such chaperone-client complexes are characterized by extensive dynamics, and that these dynamics are the key for chaperone function. Subtle changes in the sequence of the chaperone can greatly impact the binding of client proteins, and thereby confer specificity to chaperone