Functional dynamics in a half-megadalton large enzyme complex from solid-state NMR, functional assays and MD simulations

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Protein complexes of hundreds of kilodaltons size are the main actors in many cellular processes. Understanding their functional mechanisms in detail requires studying their structures and characterizing how they dynamically sample a range of different conformations.

Here we show how an integrated approach using magic-angle spinning NMR spectroscopy, cryo-electron microscopy, MD simulations and functional assays can provide a comprehensive picture of the structure and functionally important dynamics of a ~half-megadalton large aminopeptidase enzyme.

We show how MAS NMR provides direct insight into functionally important dynamics of this enzyme: we reveal an allosteric network that couples active sites and substrate entry pores, and a key role of a highly flexible loop for the enzyme function.