

Publication

A Structural Ensemble for the Enzyme Cyclophilin Reveals an Orchestrated Mode of Action at Atomic Resolution

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**ID** 4511676**Author(s)** Chi, Celestine N.; Vögeli, Beat; Bibow, Stefan; Strotz, Dean; Orts, Julien; Güntert, Peter; Riek, Roland**Author(s) at UniBasel** [Bibow, Stefan](#) ;**Year** 2015**Title** A Structural Ensemble for the Enzyme Cyclophilin Reveals an Orchestrated Mode of Action at Atomic Resolution**Journal** Angewandte Chemie International Edition**Volume** 54**Number** 40**Pages / Article-Number** 11657-61**Keywords** NMR spectroscopy; biophysics; enzyme mechanisms; enzymes; protein structures**Mesh terms** Biocatalysis; Cyclophilins, chemistry, metabolism; Enzyme Activation; Models, Molecular; Protein Conformation

For enzyme activity, an exact structural and motional orchestration of the active site and its surroundings is believed to be key. In order to reveal such possible phenomena at atomic resolution on the basis of experimental evidence, an experimental restraint driven two-state ensemble of the prototypical enzyme cyclophilin was determined by using a recently introduced exact NOE approach. The ensemble description reveals the presence of an open and a closed state of cyclophilin, which is indicative of large-scale correlated motion. In the open state, the catalytic site is preorganized for catalysis, thus suggesting the mechanism of action to be conformational sampling, while the ligand-binding loop appears to act through an induced fit mechanism. This finding is supported by affinity measurements of a cyclophilin designed to be more open. Overall, more than 60-70 % of the side-chain conformations of cyclophilin appear to be correlated.

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