Dimer asymmetry and protomer dynamics in enzyme catalysis

In investigating the catalytic mechanism of a bacterial homodimeric enzyme, fluoroacetate dehalogenase (FAcD), we applied freeze-trapping x-ray crystallography, nuclear magnetic resonance, and computational techniques to establish the distribution of conformational states and their interconversion rates along the reaction pathway. At high resolution, the crystal structure of apo-FAcD revealed constant asymmetry between the two subunits, which is dynamically averaged on a millisecond time scale. During catalysis, the rate of conformational exchange between subunits becomes faster, with the empty protomer exhibiting larger localized disorder and loosing bound water molecules. This release of water and the increase in dynamics compensate entropic losses generated during substrate binding and might facilitate sampling of the transition state. Computational studies suggest allosteric pathways for information exchange between subunits. The studies provide insights into how substrate-coupled allosteric modulation of structure and dynamics facilitates catalysis in a homodimeric enzyme.

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