UniSysCat - Colloquium

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Start Time: Wednesday, October 13, 2021 05:00 pm

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Online Colloquium

Structural Dynamics of complex molecular systems: Watching an enzyme at work using time-resolved serial crystallography

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Experimental approaches start to provide detailed molecular movies of chemical and biochemical processes, with time-resolutions from femtoseconds onwards in combination with high local resolution up to full atomic resolution. Among the methods driving these studies of structure-dynamics relationships are time-resolved crystallography with X-Rays and electrons, as well as multidimensional infrared spectroscopy (2D-IR).

I will review highlights from a recent time-resolved serial crystallography (TR-SX) experiment, which resolved the full catalytic reaction in an enzyme with full atomic detail in real-time [1,2]. We were able to follow the entire reaction cycle of the enzyme fluoroacetate dehalogenase, and captured 18 time points from 30 milliseconds to 30 seconds during the non-reversible turnover.The experimental details reveal four catalytic turnovers and show the entire reaction mechanism, including the formation of the covalent intermediate and reveal the allosteric mechanism leading to the previously observed half-the-sites reactivity. Surprisingly, local water structure both on the protein surface and at the dimer interface shows a strong asymmetry between the subunits, revealing a “molecular phone wire” of water molecules, which seem to transmit the allosteric signal.

Methods development that enabled these serial crystallography experiments will further benefit other pump-probe type experiments, like transient IR and 2D-IR spectroscopy, enabling full multiscale experiments to follow protein dynamics from femtoseconds to seconds.

[1] Schulz, Mehrabi, Müller-Werkmeister, et al. Nat. Methods, Vol. 15, pp. 907-904(11) (2018)
[2] P.Mehrabi, et al. Science 365 (6458), 1167-1170, (2019).

Prof. Dr. Holger Dobbek

Organizer