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Femtosecond-to-Millisecond Structural Biology using Synchrotrons and X-ray Lasers

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Providing detailed experimental insights into how proteins change over time and to relate these structural changes to biological function remains one of the major challenges in structural biology. Next generation X-ray sources including diffraction-limited synchrotrons and X-ray Free Electron Lasers offer exciting new opportunities to study protein dynamics by time-resolved pump-probe crystallography.
In the last few years, my group has demonstrated the use of high-viscosity injectors to increase sample efficiency in time-resolved measurements[1]. This allowed us and our collaborators to assemble over 40 structural snapshots of the light-driven proton pump bacteriorhodopsin. In a wide temporal window, we cover the light-induced isomerization of retinal within the first few hundred femtoseconds[2], the following proton release steps within microseconds[3] and the proton uptake reaction in the early milliseconds[4]. Together this provides the most complete molecular view of a membrane pump in action and acts as a template how to approach studies on proteins with increasing complexity. As a first step in this direction, we and our collaborators concluded piloting time-resolved crystallographic measurements at the Swiss Light Source and the Swiss X-ray Free Electron Laser to resolved the structural changes within light-driven sodium pumping[5] and chloride pumping rhodopsins[7]. In our latest work we aimed at increasing the number of proteins that can be studied using pump-probe techniques through the use of synthetic photoaffinity switches[6]. The overarching goal is to map the structural dynamics of protein-ligand interactions in a series of proteins used in optogenetics and photopharmacology.

References:

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No

Primary author: STANDFUSS, Jörg (Laboratory of Biomolecular Research, Paul Scherrer Institute, Switzerland)

Presenter: STANDFUSS, Jörg (Laboratory of Biomolecular Research, Paul Scherrer Institute, Switzerland)

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