# Crystallography in Motion: New Sample Delivery for Time-Resolved Serial Crystallography at Diamond and XFELs

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Serial crystallography is gaining popularity, particularly for studying dynamic events in biology. Time-resolved serial crystallography (tr-SSX) is a powerful technique for determining the structures of reactive intermediates at atomic resolution, effectively creating a "molecular reaction movie." Depending on the enzyme turnover rate, slower reactions can be investigated using synchrotron sources, while faster reactive intermediates require X-ray Free Electron Laser (XFEL) sources.

To support scientists in the macromolecular crystallography (MX) community studying dynamic structural biology, the XFEL-Hub at Diamond is developing techniques for time-resolved experiments at both synchrotron and XFEL facilities. Our strategy involves offering various sample delivery modes through our "dynamic structural biology" BAG at Diamond Light Source. We are now capable of collecting time-resolved serial MX datasets at synchrotron sources and preliminary data for serial femtosecond crystallography (SFX) for XFEL beamtime proposals. At both Diamond and PAL-XFEL, we routinely perform time-resolved experiments by mixing crystal slurry with substrate/inhibitor using fixed targets [1] and piezoelectric picolitre injectors, similar to the T-REXX setup [2]. Additionally, we are adapting a sample delivery system initially developed at LCLS for Diamond, enabling time-resolved pump-probe and mixing experiments combined with X-ray emission spectroscopy (XES) [3-7]. Complementary XES data will provide valuable information about redox and spin states of metal atom (such as Fe, Cu, Ni, Mn…) bound to the protein. We are planning to offer this new sample delivery system to our user community in 2026 at Diamond Light Source with the possibility to install it at Cristallina endstation at SwissFEL.

Our goal is to make time-resolved studies more accessible by transferring appropriate technology between XFEL, synchrotron, and cryo-EM facilities.

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