New Opportunities for Structural Biology Research at LCLS and SSRL

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Femtosecond crystallography (FX) is an emerging method that expands the structural information accessible from very small or very radiation sensitive macromolecular crystals. Utilizing extremely bright, short-time-scale X-ray pulses produced by an X-ray free electron laser (XFEL), this method exploits a 'diffraction before destruction' phenomenon where a still diffraction image is produced by a single X-ray pulse before significant radiation induced electronic and atomic rearrangements occur within the crystal. FX confronts a major challenge impeding progress in structural enzymology by providing a means to determine catalytically accurate structures of acutely radiation sensitive metalloenzymes which may be significantly photo-reduced during a single X-ray exposure at the synchrotron, even at very small doses.

A goniometer-based experimental setup for FX experimentation is available to general users at the new Macromolecular Femtosecond Crystallography (MFX) instrument of the LCLS XFEL. LCLS-MFX began experiments on July 1, 2016. This instrument is based on developments at SSRL and LCLS-XPP to provide an efficient framework to carry out goniometer-based FX experiments using automated strategies tailored to handle a variety of sample requirements, crystal sizes and experimental goals. Various sample delivery and data acquisition systems are currently being implemented including injectors and in-situ spectroscopic monitoring. Also supported is a new sample delivery device developed by SSRL-SMB, the Sample-Extractor that uses a mesh to mount crystals directly from a vial of mother liquor. These developments coupled with improvements in data processing algorithms make it possible to derive high resolution crystal structures using only 100 to 1000 still diffraction images. The MFX project and recent results using radiation sensitive crystals in limited supply and a variety of crystal delivery methods for serial diffraction data collection will be described.

New methods originally developed for serial diffraction experiments at an XFEL, are proving valuable at synchrotron sources to study protein dynamics. Recent results using the MESH injector at the SSRL undulator micro-focus station BL12-2 will be described. Building on experiences at BL12-2, a next-generation undulator microfocus beam line, BL12-1, which will provide a preeminent capability for serial diffraction in the US, is under development. BL12-1 will be outfitted with a broad bandpass capability which will provide exceptional brightness, smaller microbeams and a high number of reflections when rastering crystals on the fly or using crystal injectors. It will be equipped with a high speed EIGER PAD detector and a high speed multi-axis goniometer, enabling new approaches for data collection and phasing. Similarities in instrumentation, existing and new sample delivery systems, and software environments will form the foundation of a synergistic relationship between the SSRL BL12-1 and the new MFX instrument at LCLS, through a Gateway approach.