Keynote Lecture

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New opportunities in structural biology with XFEL: from sources to structures

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X-ray free electron lasers (XFEL) have shown the promise of providing new opportunities in structural biology research with their extremely high peak brilliance and short pulses. It is reaching the stage where biologically important questions can be tackled using XFEL based on the "diffract-before-destroy" concept. The first part of this presentation will focus on macromolecular crystallography using XFEL with results obtained at LCLS so far and future scope. R&D efforts being pursued at SLAC/LCLS include new beam modes, (two-color beam for de novo phasing, wider bandwidth for SAXS/WAXS and spectroscopy), beam multiplexing, a dedicated new station for in-air data collection, next generation detectors, data analysis incorporating pulse-by-pulse spectrometer measurements and post refinement. These projects are being pursued in collaboration with many groups locally and globally with a goal to provide integrated facilities for cutting edge structural biology research. For example, two-color self-seeded XFEL mode is being developed for simultaneous recording of diffraction data at two energies in order to optimize the dispersive difference between the two wavelengths for phasing. Another area of collaborative effort is a development of dedicated station for in-air data collection with a variety of sample delivery schemes. The second part will discuss a possible roadmap towards atomic resolution single particle imaging using XFEL. Here, key questions are •Can XFEL single particle 3D structural analysis at atomic resolution be done? •What is the pulse characteristics required? •Can we overcome the radiation damage at soft X-ray regime? •What is the highest resolution attainable in comparison with cryoEM? A workshop at LCLS is being organized to discuss these questions in 4 areas: radiation damage, image reconstruction algorithm, beam modes and instrumentation, sample delivery and heterogeneity. The outcome of the workshop and follow-up discussions will be presented.

Keywords: XFEL, femto second macromolecular crystallography, single particle imaging