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## Fixed Target 2D and 3D Protein Crystallography at XFELs

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Over the last years, serial femtosecond nanocrystallography (SFX) has been demonstrated successfully in a number of experiments at LCLS and SACLA. Most SFX applications to date have used three-dimensional (3D) nano- or microcrystals and have utilized a liquid jet based sample introduction approach. That approach typically requires large amounts of sample and is not conducive to measuring two-dimensional (2D) protein crystals. 2D crystallography of membrane proteins has been developed originally for cryo electron microscopy and is an avenue for obtaining structural information on membrane proteins that do not easily form 3D crystals necessary for traditional x-ray crystallography. Here we describe a fixed target approach for 2D and 3D crystallography at XFELs that allows x-ray diffraction measurements on samples supported by thin substrates at room temperature. We present first promising results from experiments at LCLS that included 2D crystal samples of the membrane protein bacteriorhodopsin and 3D microcrystal samples of REP24, a soluble protein. We discuss strategies for reducing amounts of sample required and increasing speed of data acquisition further to render this approach a viable alternative to the liquid jet based sample introduction approaches. The fixed target approach is expected to open up new opportunities for time-resolved SFX on samples that are not abundant and/or require the sample to be flat.

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