The NSF BioXFEL Science and Technology Center (STC) is a new consortium of six research campuses devoted to the application of x-ray free-electron lasers (XFELs) to structural biology. Over the last four years a variety of approaches have been made to the observation of protein structure and dynamics for various classes of proteins. The Linac Coherent Light source at SLAC, the first hard-Xray EXFEL, provides intense coherent hard X-ray pulses at 120 Hz which vaporize protein when focussed to a sub-micron beam. Atomic-resolution Bragg diffraction patterns are nevertheless obtained using 50 fs pulses prior to the onset of significant damage, in this "diffract-then-destroy" mode, which outruns radiation damage. This use of short pulses instead of freezing samples to reduce radiation damage therefore opens the way to the study of protein dynamics at room temperature in a native environment. I'll review the work of several groups using a range of approaches to different types of sample, including the following: 1. Differences between the frozen sychrotron structure of GPCR proteins and the RT XFEL structure [1]. 2. Pump-probe dynamic structures in Photosynthesis [2]. 3. XFEL study of 2D protein crystals [3]. 4. Prospects for improved resolution in XFEL imaging from single particles such as viruses, where patterns can be obtained from a single virus. 5. New ideas - the Lipid Cubic Phase injector (which allows protein nanocrystals to be studied also at sychrotrons) [4], prospects for fast Laue diffraction using coherent attosecond X-ray lasers, ab-initio phasing [5], the use of angular correlation functions for analysis of fast solution scattering, and two-color opportunites for serial femtosecond crystallography (SFX). See [6] for a recent review of the field. 1. W.Liu et al Science 342, 1521 (2013) 2. A.Aquila et al Optics Express 20, 2706 (2012) 3. M.Frank et al IUCrJ (2014) In press. 4. U.Weierstall et al Nature Comms. (2014) In press. 5. J. Spence et al Optics Express 19, 2866 (2011). 6. J. Spence et al Rep. Prog. Phys. 75, 102601 (2012).

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