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Diffraction Microscopy a New Tool for Structural Biologists. Andrew A. Stewart¹, Enju Lima¹, Huijie Miao¹, Xiaojing Haung¹, David Shapiro³, Pierre Thibault², Veit Elser², Chris Jacobsen¹, Janos Kirz³, David Sayre¹, ¹Dept. of Physics and Astronomy, Stony Brook Univ., Stony Brook, NY 11794, ²Dept. of Physics, Cornell Univ., Ithaca, NY, 14853, ³Advanced Light Source, Lawrence Berkeley National Laboratory, Berkeley, CA 94720.

The Emerging technique of diffraction microscopy opens up the possibility of studying macromolecular assemblies within a cell and has the potential to become a powerful tool for structural biology. Unlike crystallography the technique does not require multiple copies of an object to be built into a crystal, only one copy of the object is needed, thus allowing structural biology to access information about objects which were until now the exclusive domain of electron microscopy. The advantage of this new technique is that it has the ability to study larger objects such as whole cells without sectioning. In principle, resolution in diffraction microscopy is only limited by radiation damage, to about 10nm resolution. The technique has many parallels with crystallography. The sample is inserted into a X-ray beam, the far field diffraction pattern is recorded, and the recorded diffraction intensities need to be phased to produce an image.

A 2-D image of a freeze dried yeast cell has already been reconstructed¹. We will present the latest advances towards 2-D frozen hydrated specimens and 3-D reconstruction of cells. We will discuss the limitations and benefits of this new technique, and implications they for structural biology, with particular respect to complexes and macromolecular assemblies within cells, and cell structure.

¹ Shapiro et al. Proceedings of the National Academies of Sciences, Vol 102 No. 43, 15343 - 15346