

## 3D X-ray microscopy by phasing diffraction patterns: prospects and limitations

M. R. Howells<sup>1</sup>, H. Chapman<sup>2</sup>, R. M. Glaeser<sup>1</sup>, S. Hau-Riege<sup>2</sup>, H. He<sup>1</sup>, J. Kirz<sup>1,3</sup>, S. Marchesini<sup>1</sup>, H. A. Padmore<sup>1</sup>, J. C. H. Spence<sup>4,1</sup>, U. Weierstall<sup>4</sup>.

<sup>1</sup>Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA.

<sup>2</sup>Lawrence Livermore National Laboratory, Livermore, CA 94550, USA.

<sup>3</sup>State University of New York, Stony Brook, NY 11794, USA.

<sup>4</sup>Arizona State University, Tempe, AZ 85287, USA.

Corresponding author: [mrhowells@lbl.gov](mailto:mrhowells@lbl.gov)

This presentation addresses the questions of what performance can we expect from a 3D diffraction microscope and what will set the limits. In particular we make a quantitative calculation of the dose required for imaging at any given resolution and statistical accuracy with a model sample consisting of protein against a background of water. We derive the dose needed for 3D imaging by use of the dose-fractionation theorem of Hergel and Hoppe and determine that for 3D imaging, the dose scales inversely as the fourth power of the resolution. Thus far the calculation has made no reference to the amount of dose that the sample can tolerate. The critical dose for destruction of features of a given size in a protein sample has been fairly widely investigated by various interested communities (spot-fading experiments etc) and we have assembled a body of information from the literature of both x-ray and electron imaging. When the dose required for imaging a feature according to the Rose criterion and the critical dose for destruction of features is displayed on a common plot of the dose against feature-size, one can see that imaging life science samples with a resolution of about 10 nm should be possible. For the more radiation-resistant samples investigated in material science research, significantly better resolution of about 2-4 nm is expected. Another requirement for these experiments to be useful is that the exposure time should be not more than a few hours for a complete tilt series. We address this question in a similar way to the dose and find that (a) the required coherent flux also scales with the inverse fourth power of the resolution and (b) the exposure times are reasonable even for present-day synchrotron sources provided that optimally chosen undulators and optical systems achieving their design performance are used.

### Acknowledgements

This work was supported by the Director, Office of Energy Research, Office of Basic Energy Sciences, Material Sciences Division of the U. S. Department of Energy, under Contract No. DE-AC03-76SF00098.