High Resolution 3D X-ray Diffraction Microscopy and Its Potential of Imaging Single Biomolecules

Jianwie Miao, Tetsuya Ishikawa, and Keith O. Hodgson
miao@slac.stanford.edu

We report the development of X-ray diffraction microscopy based on the coherent X-ray diffraction and the oversampling phasing method. By using soft X-rays, we have carried out the first experiment in 1999 of imaging a non-crystalline specimen at 75 nm resolution. Recently, by using coherent X-rays with a wavelength of 2 Å from an undulator at SPring-8, we have experimentally determined the 2D structure of a non-crystalline specimen at 7 nm resolution and of a 2D double-layered specimen at 8 nm resolution. We have also developed an algorithm for the reconstruction of 3D images from a limited number of diffraction pattern projections without the need of interpolation. By employing this algorithm, for the first time we have experimentally determined the 3D structure of a non-crystalline specimen at 55 nm resolution from a series of 2D diffraction patterns. The 2D and 3D imaging resolution is currently limited by the exposure time and the computing power, while the ultimate resolution is limited by the X-ray wavelengths. We believe these results pave a way for the development of 3D X-ray diffraction microscopy at atomic resolution, which can image thick specimens not accessible to scanning probe microscopy and transmission electron microscopy. In combination with the planned X-ray free electron lasers having ultra-short and extremely intense pulses, this form of X-ray microscopy could be applied to image single biomolcules at atomic or near atomic resolution. Our computer simulation results have shown that a molecular diffraction pattern at 2.5 Å resolution accumulated from multiple copies of single rubisco biomolecules each generated by a femtosecond-level X-FEL pulse can be successfully phased and transformed into an accurate electron density map comparable to that obtained by more conventional methods.