FA1-MS05-T01

Filling the missing cone: Automatic recovery of data in tilt-limited microscopy. Henning Stahlberg[a], Xiangyan Zeng[b], Daniel J. Masiel[c], Nigel Browning[c], John Spence[d], Kaoru Mitsuoka[e], and Bryant Gipson[a]
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Electron Crystallography of 2D protein crystals is a powerful tool for the determination of membrane protein structure. It is, however, dependent on the quality of the 2D crystalline arrangement, and in the past suffered from the tilt-limited data collection scheme in form of a missing cone in Fourier space, producing resolution loss in the direction perpendicular to the membrane plane. We here describe a single-particle approach to 2D crystals, employing a maximum likelihood algorithm [1]. We further describe a solution for the full recovery of the missing cone data, based on projective constraint optimization that, that for sufficiently oversampled data produces complete recovery of unmeasured data in the missing cone. We apply this method to an experimental dataset of bacteriorhodopsin and show that, in addition to producing superior results compared to traditional reconstruction methods, full, reproducible, recovery of the missing cone from noisy data is possible. Finally, we present an automatic implementation of the refinement routine as open source, freely distributed, software to be included in our 2dx software package [2] (available at http://2dx.org).

[1]. Zeng, X., Stahlberg, H., Grigorieff, B., *J. Struct. Biol.,* 2007, 160(3), 362-374. [2] Gipson, B., Zeng, X., Zhang, Z.Y., Stahlberg, H., *J. Struct. Biol*., 2007, 157, 64-72.

Keywords: missing cone, electron crystallography, membrane protein structure

FA1-MS05-T02

Small angle X-ray scattering from biological macromolecules. Alexey G. Kikhney[a], [a]*European Molecular Biology Laboratory, Hamburg Outstation, Germany*
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Small-angle X-ray scattering (SAXS) experiences a renaissance in the studies of macromolecular solutions allowing one to study the structure of native particles and to rapidly analyze structural changes in response to variations in external conditions. Novel data analysis methods [1] significantly enhanced resolution and reliability of structural models provided by the technique. Emerging automation of the experiment, data processing and interpretation make solution SAXS a streamline tool for large scale structural studies in molecular biology. The method provides low resolution macromolecular shapes *ab initio* and is readily combined with other structural and biochemical techniques in multidisciplinary studies. In particular, rapid validation of predicted or experimentally obtained high resolution models in solution, identification of biologically active oligomers and addition of missing fragments to high resolution models are possible. For macromolecular complexes, quaternary structure is analyzed by rigid body movements/rotations of individual subunits. Recent developments made it possible also to quantitatively characterize flexible macromolecular systems, including intrinsically unfolded proteins. The novel methods will be illustrated by advanced SAXS applications to solutions ob biological macromolecules.

[1] Petoukhov, M.V., Svergun, D. I., *Curr Opin Struct Biol*., 2007, 17, 562-571.

Keywords: SAXS, Biological macromolecules, Rapid characterization

FA1-MS05-T03

Electron diffractive imaging of TiO_2 nanocrystals at 70 pm resolution. C. Giannini[a], L. De Caro[a], E. Carlino[b], G. Caputo[c,d], P. D. Cozzoli[c,d]. [a]*Istituto di Cristallografia (IC-CNR) via Amendola 122/O, 70126 Bari, Italy.* [b]*TASC-INFM National Laboratory, Area Science Park - Basovizza, Bld MM SS 14, Km 163.5, 34012 Trieste, Italy.* [c]*Scuola Superiore ISUFI, Università del Salento, Distretto Tecnologico, Via per Arnesano Km 5, 73100 Lecce, Italy.* [d] *National Nanotechnology Laboratory (NNL) of CNR-INFM, Unità di Ricerca IIT, Via per Arnesano Km 5, 73100 Lecce, Italy.*
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The structure-function relationship understanding of a nanomaterial requires an accurate map of its shape, strain and surface/interface structure. Electron diffractive imaging (EDI) has recently proved to be a powerful method to image shape and internal structure of Au [1] and CdS [2] nanocrystals of few nm diameters with a spatial resolution of 80-100 pm. A synergic use of measured diffraction patterns and phase-retrieval techniques allowed to bypass the need for imaging lenses, avoiding the resolution limits associated to their aberrations. We here phase-retrieved electron diffractive HRTEM images of individual TiO_2 nanocrystals at 70 pm resolution, even exposing the specimen to a low electron dose [3]. For the first time, while retrieving the detailed crystal structure of the oxide nanomaterial, O atomic columns were visualized in the coupled EDI-HRTEM experiment without the need for any lens aberration corrector [4]. In addition, our approach allowed us to reveal subtle deviation of the nanocrystal unit cell structure from the bulk counterpart. These highlithing results demonstrate EDI-HRTEM as a unique tool to study the actual atomic structure of nanomaterials with an unprecedented level of accuracy and sensitivity to light atomic elements.
In principle, the resolution is only diffraction and dose limited (dependent on wavelength, detector aperture size and exposure time), giving to EDI-HRTEM the potential to achieve record sub-atomic resolutions and promising numerous applications in life and materials sciences.

[1] Huang, W. J. et al. Coordination-dependent surface atomic contraction in nanocrystals revealed by coherent diffraction. *Nat. Mater.*, 2008, 7, 308-313 . [2] Huang, W. J., Zuo, J. M., Jiang, B.,