MX Frontiers at the One Micron Scale: Workshop Makes Case for Micro-Beams

Macromolecular crystallographic (MX) structure determination at synchrotron radiation sources has the potential to advance significantly through use of x-ray beams of one micron or smaller cross-sections. Recently, the MX Frontiers at the One Micron Scale Workshop explored structural biology scientific opportunities made possible through the use of micro-beams, and anticipated technical challenges for developers of MX beam lines at NSLS-II. Over 100 attendees participated in the workshop, which included a day-and-a-half of lectures, discussions, and a semi-formal poster session on July 23-24 at Brookhaven National Laboratory.

The workshop was particularly relevant given the development of the NSLS-II, a brilliant new synchrotron facility under construction at BNL. As he welcomed participants, ***Wayne Hendrickson*** (Columbia U), the recently appointed Associate Project Director for Life Sciences at NSLS-II, highlighted the facility's design features and new capabilities. Regarding the future at NSLS-II, Hendrickson predicted that "what we think of as difficult today will become routine by 2015."

David Eisenberg (UCLA) then illustrated Hendrickson's assertions as he spoke about his adventures in microcrystallography of biological specimens, which have led to stunning breakthroughs in structure determination of proteins in the amyloid state from crystals that are 10,000 times smaller than conventional samples. Eisenberg revealed that it was the scientific problem of Alzheimer's and other amyloid-related diseases that first sparked his interest in micro-diffraction and he expects further developments to enable him to probe even smaller granules in vivo.

He was followed by ***Gebhard Schertler*** (MRC) who spoke about the structure of G protein coupled receptors and shared his work studying the structures of rhodopsin and beta adrenergic receptors, all membrane proteins yielding small variable crystallites. He highlighted the crucial role microcrystallography played in his work, requiring extensive experimentation in close collaboration with beamline scientists "on equal terms."

Tiny beams also drive the development and use of new crystallographic methods, such as that of serial crystallography pursued by ***John Spence*** (Arizona State U). After summarizing the state of microdroplet delivery, he addressed the problem of solving protein structures from molecular aggregates containing only a few unit cells. However, serial crystallography assumes mastery of powder diffraction analysis, a technique then reviewed by ***Irene Margiolaki*** (ESRF). In a lucid talk, she highlighted the experimental and analytical methods that now yield high resolution structures of modest size proteins, such as the SH3 domain of ponsin.

In the afternoon of the first workshop day, talks given by ***Colin Nave*** (DLS), ***Robert Fischetti*** (APS), ***James Holton*** (ALS) and ***Elspeth Garman*** (Oxford U) addressed radiation damage issues and their potential mitigation using micro-beams.

In his after-dinner talk, ***Christian Riekel*** (ESRF) traced the origins of micro-diffraction at ESRF's ID13 to small-angle scattering and documented its multi-disciplinary evolution. However, crystallography dominated his program as he demonstrated remarkable results ranging from work with chromatin to spider silk, to inorganic dusts, and eventually to Eisenberg's amyloid proteins. In a bold outlook, he touched on the many optical techniques and innovative instruments that now propel micro-diffraction towards the nano-scale, a development that will require exhaustive experimental studies as well as strong, renewed collaborations between scientists in the field.

Talks continued on the second day of the workshop addressing optics and instrumentation issues, including integrated beamlines, related to micro-beams. ***Clemens Schulze-Briese*** (SLS), ***Sean McSweeney*** (ESRF), ***Gwyndaf Evans*** (DLS), ***Masaki Yamamoto*** (SPring-8), ***Kenneth Evans-Lutterodt*** (BNL) and ***Antonio Lanzirotti*** (U. Chicago) presented these new challenges.

The workshop concluded with a final discussion that considered the key question of whether or not a solid case had been made in favor of micro-beams. Participants debated the matter with enthusiasm throughout, deliberating about the appropriateness of the one micron scale, the role of submicron beams, and the usefulness of beamlines with flexible capabilities. Ultimately, the sum of lectures and discussions clearly illustrated that tiny beams will enable new science, particularly so if the beam is of sub-micron size. At this scale, structural work will be characterized by experimentation rather than routine measurements and involve many pursuits in life sciences such as MX, SAXS, and fiber diffraction, potentially borrowing from electron microscopy as well.

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of Basic Energy Sciences, Brookhaven Science Associates, BNL Biology Department, NIH National Center for Research Resources, and the National Institute of General Medical Sciences. It was also supported commercially by FMB-Oxford Ltd, Bruker ASC, and Area Detector Systems Corporation, and organized by ***Dieter Schneider, Marc Allaire,*** and ***Lonny Berman*** with the great support of ***Gretchen Cisco*** and her NSLS team.

Please refer to the workshop website for further information.

www.nsls.bnl.gov/newsroom/events/workshops/2009/mx/

Marc Allaire

ACA 2009 - Workshop on Incommensurate Crystal Structures

Based on the great interest expressed at the session on incommensurate and modulated structures (organized by Lee Daniels) at the 2008 ACA meeting, a two-day workshop on In was held Friday and Saturday 24-25 July in Toronto, and attended by ~40 crystallographers. Because the Jana2006 program package is by far the most commonly used to solve and refine incommensurate structures, we invited ***Václav Petříček, Michal Dušek,*** and ***Juan Manuel Perez-Matao*** to lead the workshop. They periodically offer a three-day Jana workshop in Europe, and felt that it was impossible to do justice to the topic in only one day, hence the unusual two-day ACA workshop.

Students were required to download and install Jana2006 (***www-xray.fzu.cz/jana***) on their own computers before the workshop. The software was packed with a demo version of Diamond for visualization, as well as data for the examples used in the workshop and a detailed "cookbook" of instructions. The software installation and configuration went remarkably smoothly, and we could get to work rapidly. Students were expected to have worked through two simple examples – $(NH_3CH_2CH_2NH_3)ZnCl_6$ and *bis*[N-(2-benzylidenepropylidene)phenyl]ether – before the workshop. These examples covered the mechanics of the program and data file handling, determination of symmetry, solving the structures using charge flipping, editing of atomic parameters, refinement, assigning hydrogens, finding the pseudo-merohedral twinning matrix from group-subgroup transformations, and creating a CIF for publication.

The workshop began by considering single crystal data on the disordered structure of $[Cu(CH_3NHCH_2CH_2NH_2)_2][Pt(CN)_4]$, followed by an introduction to modulated structures. For the rest of the day, we worked on the simple (3+1)d modulated structure of YPO_3 using single crystal data.

The second day began with an introduction to aperiodic crystals and superspace symmetry, followed by solving the modulated structure of $KSmMo_2O_8$ using synchrotron powder data. A lecture on incommensurate tools to investigate families of commensurate compounds was followed by work on the commensurately modulated structure of ephedrine.

The workshop was intense, and we learned a lot. As always, the challenge is to keep in practice once we get home. The charge flipping program Superflip incorporated into Jana2006 was especially impressive at solving structures.

Jim Kaduk - Olivier Gourdon