The Advanced Photon Source

The Future is Pink for Molecular Movies

For many years, investigators who decipher the mysteries of protein structure have sought a way to move from the static environment of protein crystals to a more dynamic method for determining the structures of proteins in action. Protein conformational changes have been approximated by taking "snapshots" of protein crystals with and without different substrates or inhibitors and then comparing the two structures. But what if it was possible to capture many snapshots of different small crystals in random orientations at different time points and piece together the data to see time-resolved changes? This could provide data about a protein's structure and its movement through possible conformations, creating a series of images that could be turned into a kind of movie. The research team in this study, from Arizona State University, Argonne National Laboratory, The University of Chicago, and the University of Southern California hypothesized that combining polychromatic photon beams from third-generation synchrotron sources, with the latest high-viscosity injection technology to deliver thousands of nano- or microcrystals to the beam could generate a complete dataset in a shorter time with a smaller sample volume, providing time-resolved data without damaging radiation exposures (Fig. 1).

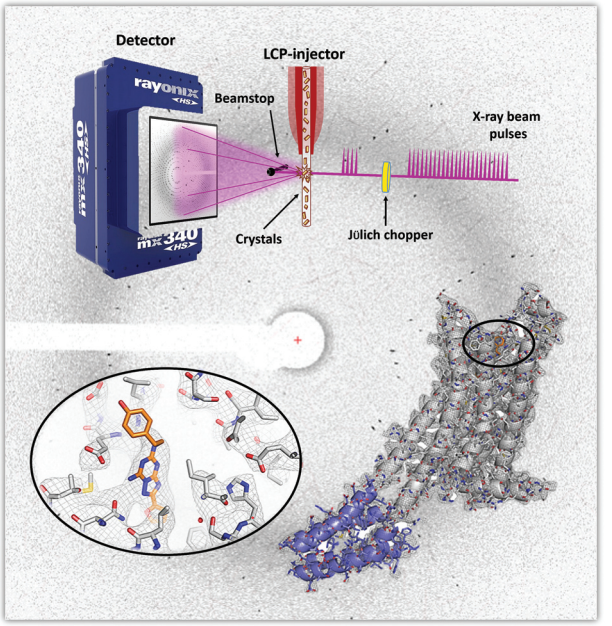

Fig. 1. Experimental set-up for data collection from pink-beam radiation with high viscosity sample injection at BioCARS 14-ID-B (Top) and quality of the electron-density map of the A2AAR structure with difference electron density map shown as inset (bottom).

Now, the first proof-of-concept experiments using high viscosity sample injection combined with pink-beam serial crystallography (SX), carried out at the U.S. Department of Energy's Advanced Photon Source (APS). Pink-beam radiation is utilized for these experiments because it provides a higher photon flux (100 times higher than monochromatic beams) that allows detection of much shorter time scales than standard synchrotron beams.

To test their hypothesis, the team chose two proteins for which structures have already been determined: an enzyme, proteinase K (PK), and a G-protein coupled receptor, the human A2A adenosine receptor (A2AAR). They were able to solve the structure of PK with the new method at 1.8-Å resolution using the BioCARS 14-ID-B X-ray beamline at the APS. The structure for A2AAR was a bit more complicated because the crystals were very small (~5 µm) and only weak and sparse diffraction data of low resolution were observed under the data collection conditions used for PK. Therefore, the team increased the consecutive pulses of pink-beam radiation to 24 (from 4 for PK, 3.5-µs total exposure) and obtained data that enabled them to resolve the structure at 4.2 Å

With this positive proof-of-concept experiment for the use of pink-beam radiation with high viscosity injection of the sample, the researchers believe that molecular movies may soon be coming to a theater near you.

— Sandy Field

See: Jose M. Martin-Garcia[1], Lan Zhu[1], Derek Mendez[1], Ming-Yue Lee[1], Eugene Chun[1], Chufeng Li[1], Hao Hu[1], Ganesh Subramanian[1], David Kissick[2], Craig Ogata[2], Robert Henning[3], Andrii Ishchenko[4], Zachary Dobson[1], Shangji Zhang[1], Uwe Weierstall[1], John C. H. Spence[1], Petra Fromme[1], Nadia A. Zatsepin[1], Robert F. Fischetti[2], Vadim Cherezov[4]*, and Wei Liu[1]**, "High-viscosity injector-based pink-beam serial crystallography of microcrystals at a synchrotron radiation source," IUCrJ **6**, 412 (2019).
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Author affiliations: [1]Arizona State University, [2]Argonne National Laboratory, [3]The University of Chicago, [4]University of Southern California
Correspondence: * cherezov@usc.edu, ** w.liu@asu.edu

Call for APS General-User Proposals

The Advanced Photon Source is open to experimenters who can benefit from the facility's high-brightness hard x-ray beams.
General-user proposals for beam time during Run 2020-2 are due by Friday, February 28, 2020.
Information on access to beam time at the APS is at http://www.aps.anl.gov/Users/apply_for_beamtime.html or contact Dr. Dennis Mills, DMM@aps.anl.gov, 630/252-5680.

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Bldg. 401/Rm A4113
Argonne National Laboratory
9700 S. Cass Ave.
Argonne, IL 60439 USA
aps.anl.gov
apsinfo@aps.anl.gov