ESS Science Symposium on Neutron Protein Crystallography

21-22 March 2013, Aarhus University, Aarhus, Denmark

Organising committee

Poul Nissen

Ditlev Brodersen

Søren Thirup

ESS Contact

Esko Oksanen

AARHUS UNIVERSITY

Speakers

Esko Oksanen (ESS)

Thomas Holm Rod (ESS DMSC)

Monika Budayova-Spano (IBS, Grenoble, France)

Maxime Cuypers (ILL, Grenoble, France)

Paul Adams (LBNL, Berkeley, CA, US)

Tim Grüne (University of Göttingen, Germany)

Ulf Ryde (Lund University, Sweden)

Nobuo Niimura (Ibaraki University, Japan)

Matthew Blakeley (ILL, Grenoble, France)

Derek Logan (Lund University, Sweden)

Bo Brummerstedt Iversen (Aarhus University, Denmark)

Andrey Kovalevsky (ORNL, Oak Ridge, TN, US)

Julian Chen (University of Toledo, OH, US)

Tomas Lundqvist (Astra-Zeneca, Mölndal, Sweden)

Programme

The symposium programme covered all aspects of neutron macromolecular crystallography from sample preparation and data analysis to recent results and future prospects.

The symposium started with a session about the European Spallation Source, ESS. E. Oksanen first gave a short introduction to the ESS project and then presented the proposed concept for a macromolecular diffractometer. T. Holm Rod next presented the current plans and vision for the Data Management and Support Centre (DMSC).

In the session on sample preparation, M. Budayova-Spano introduced the physical chemistry of crystal growth and presented a device for better control of crystal growth conditions. M. Cuypers then gave an overview of protein deuteration methods with examples from macromolecular crystallography and small angle neutron scattering.

The session on refinement started with a presentation of the PHENIX project by P. Adams with an emphasis on the joint neutron-X-ray refinement implemented in phenix.refine. T. Grüne presented a neutron only refinement of rubredoxin using the recently released SHELX-2013 suite. U. Ryde finally presented a methodology to combine information from quantum chemical calculations and various experimental methods (crystallography, NMR, EXAFS) with a prospect of including neutron crystallographic information.

In the next session on existing neutron sources, N. Niimura gave a historical overview of neutron macromolecular crystallography with a particular emphasis on the developments in Japan from the monochromatic BIX-3 and BIX-4 diffractometers at JRR3 to the recent time-of-flight Laue diffractometer iBIX at J-PARC including some recent results. M. Blakeley then presented the developments at the ILL from the first LADI prototype to LADI-III, also showing some recent results.

On the second day, D. Logan presented some recent neutron results on the protein galectin-3, an interesting drug-target. B. Brummerstedt Iversen then gave perspectives from the small molecule crystallography world on the accurate determination of atomic positions and modeling the scattering. In the following session on applications and future directions, A. Kovalevskiy showed some recent neutron crystallographic results on the HIV-protease and xylose isomerase, followed by a description of the available and upcoming neutron macromolecular crystallography instruments in the US. J. Chen then showed how the information from the neutron structure of di-isopropyl fluorophosphatase could be used for protein engineering, as well as some recent high-resolution work on crambin. T. Lundqvist ended the session with an overview of the use of structural biology in the pharmaceutical industry, suggesting areas where neutron crystallography could be applied.

The symposium finished with a discussion session moderated by E. Oksanen. The discussion was primed by some questions to the user community from the ESS. The preference was for a work-horse instrument for determining hydrogen positions and contrast variation crystallography was not seen as a priority. The importance of the supporting facilities was pointed out several times, particularly the ability to grow crystals on-site as crystal transport can often be problematic. For deuteration, it was suggested that establishing basic methods such as *E. coli* production will be sufficient for most projects. While developments are made in other facilities for data processing, the

existing software are far from perfect and need to be developed further. The need for flexible scheduling of beamtime was stressed by instrument scientists, as it is difficult to predict which projects will work.

Conclusions

The discussion during the sessions was lively and enthusiastic. It became clear that there is a strong scientific demand for a macromolecular diffractometer at the ESS. It was pointed out by several speakers that neutron macromolecular crystallography can provide unique information towards understanding biological systems in atomic detail, but it is always a part of a toolkit of methods that together provide insight into processes like enzyme catalysis and drug-protein interactions. While some users will be capable of producing perdeuterated proteins and large crystals on their own, there is a clear demand for deuteration and crystallization facilities. Appropriate access modes also need to be devised to guarantee timely access to beamtime before crystals degrade. A block allocation model was suggested to ensure fair peer review while allowing for flexible scheduling. Software developments for time-of-flight data processing are still needed, but efforts should be coordinated between different facilities to avoid duplication of work.