MXIS-2016, Part 2

Practical course on in-plate crystallography and in situ diffraction
30 November – 2 December 2016
IBS, EMBL & ESRF (Grenoble)

Wednesday 30 November (IBS, Grenoble)

10:00AM-11:00AM:	"Introduction to protein crystallography", Dominique Housset, IBS (IBS, seminar room)
11:00AM-11:30AM:	Coffee break (IBS, main lobby)
11:30AM-12:30AM:	"Crystallographic fragment-screening at the HZB-MX beamlines in Berlin", Manfred Weiss, BESSY, Germany (IBS, seminar room)
12:30AM-12:45PM:	Introduction to MXIS, Jean-Luc Ferrer, IBS, Grenoble (IBS, seminar room)
12:45AM-02:00PM:	Lunch (ESRF canteen)
02:00PM-03:00PM:	"Diffract before Disturbance: *In-situ* X-ray Screening at the Swiss Light Source", May Marsh, SLS, Swizerland (IBS, seminar room)
03:00PM-04:00PM:	"Integrated pipelines for ligand screening through macromolecular crystallography", Jose A. Marquez, EMBL, Grenoble (IBS, seminar room)
04:00PM-04:30PM:	Coffee break (IBS, main lobby)
04:30PM-05:30PM:	"In situ crystal screening on ID30B at the ESRF", Andrew McCarthy, ESRF, Grenoble (IBS, seminar room)
05:30PM-06:30PM:	"Robot based in situ diffraction on FIP-BM30A: from crystal to ligand screening", Jean-Luc Ferrer, IBS, Grenoble (IBS, seminar room)
08:00PM:	Dinner

Thursday 1 December (ESRF, Grenoble)

08:30AM-10:30AM:	In situ data collection on FIP-BM30A and ID30B (Practical Session 1)
10:30AM-11:00AM:	Coffee break (ESRF, room 03-1-07)
11:00AM-01:00PM:	In situ data collection on FIP-BM30A and ID30B (Practical Session 2)
01:00PM-02:00PM:	Lunch (ESRF canteen)
02:00PM-04:00PM:	In situ data collection on FIP-BM30A and ID30B (Practical Session 3)
04:00PM-04:30PM:	Coffee break (ESRF, room 03-1-07)
04:30AM-06:30PM:	In situ data collection on FIP-BM30A and ID30B (Practical Session 4)
07:00PM:	Dinner (ESRF canteen)

Friday 2 December

09:00AM-10:30AM:	Visit of IBS / EMBL / ESRF (IBS, main lobby)
11:00AM-01:00PM:	In situ data collection on FIP-BM30A and ID30B (Practical Session 5, ESRF)

MXIS 2016
Invited speakers from BESSY and SLS synchrotrons

Crystallographic fragment-screening at the HZB-MX beamlines in Berlin

Dr. Manfred Weiss
BESSY, Germany

Wednesday 30 November, 11:30AM, IBS Seminar room

Fragment screening is a widely spread approach to identify compounds, which are able to bind to protein targets. Typically, binding fragments are identified by a cascade of biophysical methods and then further analyzed structurally by X-ray crystallography. Recently, however, this pre-screening cascade has been put on the spot and evidence is accumulating that X-ray crystallography should indeed be used as the primary screening method. In the talk, I will discuss a large fragment-screening study (361 compounds vs. the protease endothiapepsin), as well as some results using a new small, affordable and versatile compound library, which we have recently assembled at the HZB and which is available to the HZB-MX beamline users. Further, I will show the MX-facilites at the HZB, including a new X-ray crystallography beam line dedicated to fragment screening experiments, which is currently being completed at the BESSY II synchrotron. Finally, in order to facilitate high-throughput crystallography I will also show an example for the efficient identification of fragment hits.

Diffract before Disturbance: *In-situ* X-ray Screening at the Swiss Light Source

May Marsh
Swiss Light Source at the Paul Scherrer Institut, Switzerland

Wednesday 30 November, 2:00PM, IBS Seminar room

The beamline X06DA at the SLS has a fully automated setup that allows the testing of the X-ray diffraction characteristics of crystals directly within the crystallization plate. This enables rapid feedback on crystal quality without disturbance of the crystal by mounting and freezing. The beamline setup allows for quick switching between *in-situ* and standard crystal mounting modes, encouraging *ad-hoc* use of the technique during any beamline shift.

This presentation will focus on the ways that *in-situ* X-ray screening can help practically with the crystal optimisation process. The technique allows crystal hits to be screened quickly and non-invasively. Macromolecular crystals can readily be distinguished from unwanted salt crystals, and the best-diffracting crystals identify the best crystallisation conditions for further optimisation. Thus the optimisation process can undergo rapid diffraction-guided iterations that are better targeted to producing the high-quality diffraction needed for structure determination.

In addition this presentation will cover the use of the *in-meso in-situ* serial crystallography (IMISX) method. The current LCP (in meso) protocol uses glass sandwich crystallization plates, which are challenging to harvest crystals from and are impractical for *in-situ* X-ray diffraction measurements. The IMISX method combines the many advantages of glass plates with high throughput *in-situ* serial data collection capabilities. This method has recently been developed in a collaboration between the SLS MX group and Martin Caffrey's group from Trinity College Dublin.