UK Bio-XFEL single particle imaging workshop

Rutherford Appleton Laboratory, 2nd-3rd June 2016

Objectives

The workshop brought together XFEL technique developers and expert users with the potential user community in the UK. The aims of the workshop were to:

1) Communicate the current state-of-the-art in single particle imaging with XFELs.
2) Promote the building of a XFEL single particle imaging community in the UK.
3) Determine the next steps for the community to interact with the sponsors and develop the case for a UK XFEL.

Workshop Facts & Figures

The workshop was funded by BBSRC, EPSRC, MRC, and STFC as well as a number of commercial sponsors (workshop programme and details of sponsors can be found at the end of this report). 130 delegates and speakers were registered for the workshop. These included XFEL users, structural and cell biologists, technology developers, and funding agency representatives. The meeting was opened jointly by Colin Miles (BBSRC), John Collier (Director, STFC Central Laser Facility) and Dave Stuart (Director of Life Sciences, Diamond Light Source).

There were 16 invited speakers, 7 from the UK and 9 from other countries. The workshop ended with a discussion session in which delegates were invited to give their views on the technical requirements and organisational issues affecting UK XFEL-based research, and the next steps required to promote this research and ultimately a UK XFEL.

Invited Talks

The invited talks covered a number of areas: The latest developments in XFEL technology and facilities, XFEL research highlights in single particle imaging and other areas, the organisational challenges of XFEL research across multiple institutions, and complementary techniques such as single particle cryo electron microscopy.

Although the workshop was focussed on single particle imaging, a number of both the technical and research talks also covered the area of nanocrystallography. This probably reflects the relative state of development of the two fields, with nanocrystallography being significantly more developed in terms of XFEL usage, data analysis, and interpretation. A common theme across the talks was that the main advantage of XFEL usage in structural biology was 1) the ability to collect data at room temperature, and 2) improved time resolution. An important concept was presented for the pump-probe study of enzyme dynamics using laser-induced release of their substrates. These advantages apply to crystallography (XFEL vs conventional crystallography using synchrotrons) but could also apply to single particle imaging when compared with the analogous technique of single particle cryo-electron microscopy. One talk also highlighted the value of ultrafast laser spectroscopic techniques as a way of understanding photochemical processes important in time-resolved crystallography work.

Discussion Session

The discussion session was chaired by Dr Allen Orville, Group Leader of the UK-XFEL Hub at Diamond Light Source. The hub will enable users to fully prepare for their experiments with currently operating XFELs and the European XFEL when it comes online in Hamburg in 2017. Key points emerging from the discussion were as follows:

How can the community help make the case for XFEL science?

- The community should work together to make the case, and should listen to and talk with the funding agencies and program officers.
- UK should engage with Europe as soon as possible
- Training the next generation of scientists needs to happen now, especially with respect to time-resolved data collections; prescreening at synchrotron(s) to characterize samples helps in many ways
- High-profile papers and research are critical components to everything, and there are plenty of these coming from XFELs right now
- There has been a lot of discussion about facilities; the biology community needs to express and build up its needs for the next decade.

How do we encourage the community to use existing XFEL facilities, and help those that are using them?

- Existing teams using XFELs could form nuclei for new user groups.
- It would be useful to have a source of funding to support UK teams who have been awarded XFEL beamtime (travel and other expenses). The UK-XFEL hub has a limited amount of funding available that could be used for this.
- A model might be the Australian Synchrotron Research Program (ASRP) synchrotron research programme that was run in Australia from 1992 to 2008 before the availability of the Australian synchrotron.
- A standing "training grant" could be available to support students if they get beamtime? Perhaps a supplement to an existing grant to help with data collection?
- There should be exchanges for training students and post-docs … hands on and technology transfer. XFEL Hub has some funding to help cost-share others participating in XFEL
- We could bid for a Horizon 2020 style funding scheme to support a consortium of users – science based.
- Potential formation of an XFEL Beamline Access Group (BAG)
- UK facilities can promote techniques that are relevant to XFEL activity. For example, DLS and CLF funding for a kHz time-resolved instrument (PORTO) at a DLS beamline. The work of the Dynamic Structural Sciences (DySS) group based at Harwell overlaps with XFEL activities.
- Grow community and encourage more participation around the UK; encourage them to use the proper tool for the question at hand.
- The LCLS can offer help in getting data, through collaborations.

Other relevant issues

- Multidisciplinary teams are critical and necessary, communication is critical
- The NSF-funded, US based BioXFEL is happy to cooperate and welcomes participation in data analysis, etc, potentially with data collection & their annual international conferences (each January in Puerto Rico)
- BioXFEL uses web-based interactions and lectures, live talks and feed back
- Increase and diversity of the community, speakers, leaders; how to promote this?

- A UK XFEL is some way off. Limited access also limits the horizon and the potential, but we can travel!
- Anyone interested in XFELs is encouraged to attend the DLS User Meeting (7^{th}-8^{th} September 2016). The meeting includes a large workshop focusing on electron microscopy and XFEL techniques in the physical and life sciences.

There was also some discussion on technical requirements and challenges, summarised in the table below:

	Single Particle Imaging	Serial Femtosecond Crystallography
Sample preparation & delivery	Homogenous (proteins, viruses …) Heterogeneous (cells, tissues), Fixed targets (R-T and cryo)	Crystal slurries (nm - µm), Jets, extruders, microfluidics,… Fixed targets (cryo & RT), On-demand injector methods … Time-resolved methods
Data processing	Background subtraction 3D-reconstruction Shrink-wrap algorithms (boundary of samples)	CrystFEL, cctbx.xfel, ccpxfel Real-time feedback (quality & quantity) Complementary methods (spec.) Time-resolved methods / meta data
Outstanding issues	Sample delivery methods Detectors Cryo –vs– room temp Growth of the community	Managing complex datasets and meta data (e.g SFX ± Spec.) Sample consumption Detectors, dynamic range, speed T-R reaction mixing for membrane proteins Measuring function in X'tals Pulsed injector speed at Eu.XFEL Growth of the community

UK Bio-XFEL single particle imaging workshop
Pickavance Theatre – RAL
2nd and 3rd of June 2016
Organisers - Ian Robinson (UCL) and Mohammed Yusuf (STFC/UCL),
Stan Botchway (STFC) and Dave Clarke (STFC)
Funders - BBSRC, STFC, MRC and EPSRC

2nd of June 2016

08:45-09:45	Registration & Tea and Coffee (Main RAL reception and Diamond Atrium)
	Welcome and opening speeches
10:00-10:10	Colin Miles (BBSRC, UK)
10:10-10:20	John Collier (STFC, UK)
10:20-10:30	Dave Stuart (Diamond Light Source**,** Oxford University, UK)
	Session 1 Chair – Ian Robinson (UCL-RCaH, UK)
10:30-11:00	**Riccardo Bartolini (Diamond Light Source, UK)** Possible options for a UK X-ray FEL facility
11:00-11:30	**Allen Orville (Diamond Light Source, UK)** Dynamic structural biology: awakened and enabled by new sources and complementary methods
11:30-12:00	Group photo (outside Research Complex at Harwell-R92 building)
12:00-13:00	Lunch (Diamond Atrium)
	Session 2 Chair – Ian Robinson (UCL-RCaH, UK)
13:00-13:30	**Sébastien Boutet (SLAC, USA)** The SPI Initiative at LCLS
13:30-14:00	**Thomas Earnest (**Shanghai Institute of Applied Physics, China) The Shanghai X-FEL Projects: Current Status and Future Directions
14:00- 14:30	**Helen Saibil (Birkbeck, UK)** Single particle cryo EM of macromolecular machines
14:30-14:50	Tea and Coffee break (Diamond Atrium)
	Session 3 Chair – Stan Botchway (STFC, UK)
14:50-15:20	**Changyong Song (POSTECH, Korea)** XFEL single-shot imaging of specimens on fixed targets
15:20-15:50	**Ian Robinson (UCL-RCaH, UK)** Towards Chromosome Imaging at SACLA
15:50-16:20	**Yoshinori Nishino (Hokkaido University, Japan)** Controlled environment nano-imaging free from radiation damage by X-ray laser diffraction
18:00	Evening Dinner at Cosener's House, Abingdon (Meet at Diamond entrance for coach, return coach to RAL, 22:15)

3rd of June 2016

08:30-09:30	Registration (RAL Reception and Diamond Atrium) Tea and Coffee (Diamond Atrium)
	Session 4 Chair - Dave Clarke (STFC, UK)
9:30-10:00	**Eaton E. Lattman** (**Hauptman-Woodward Institute, USA)** Synergies Created by the BioXFEL Organizational Structure
10:00-10:30	**John Spence (Arizona State University, USA)** Single-particle hit rates and the ASU compact XFEL
10:30-11:00	**Anton Barty (Desy, Germany)** Molecular imaging using free electron lasers
11:00-11:20	Tea and Coffee break (Diamond Atrium)
	Session 5 Chair – Mohammed Yusuf (UCL-RCaH, UK)
11:20-11:50	**Masayoshi Nakasako (Keio University, Japan)** Structural analyses of cellular organelles and cells by cryogenic coherent X-ray diffraction imaging at SACLA
11:50-12:20	**Amane Kobayashi (Keio University, Japan)** Diffraction apparatus for fast data collection following the repetition rate of 30 Hz at SACLA
12:20-13:20	Lunch (Diamond Atrium)
	Session 6 Chair – Allen Orville (Diamond Light Source, UK)
13:20-13:50	**Isabel de-Moraes (Diamond MX, UK)** The use of XFEL in Membrane Protein Structural Biology
13:50-14:20	**Samar Hasnain (University of Liverpool, UK)** Serial Crystallography and diffractive imaging results using SR and XFEL
14:20-14:50	**Jasper van Thor (Imperial College London, UK)** Femtosecond time resolved X-ray crystallography of biological photoisomerisation and coherence
14:50-15:10	Tea and Coffee break (Diamond Atrium)
	Session Chair – Allen Orville (Diamond Light Source, UK)
15:10-16.00	**Open discussion on SPI XFEL**
16:00	Close of Workshop

Other Sponsors - TAAB Laboratories Equipment Ltd, Silson Ltd, Diamond Light Source Ltd, Hamamatsu Photonics UK Ltd, 3dmagination Ltd, Kurt J Lesker Company Ltd, Oxford Cryosystems Ltd, Linkam Scientific Instruments Ltd