

The Evolution of the ESRF's Structural Biology Beamlines

Structural Biologists are tackling ever more ambitious projects, for example more complex membrane proteins and larger macromolecular assemblies (Figure 1). Such systems often show considerable inter and intra crystal variation in diffraction quality. Sample evaluation prior to data collection, already widespread in Macromolecular Crystallography (Figure 2), will thus become more crucial as will data collection facilities optimised for the collection of diffraction data from crystals that are very small and/or diffract to low resolution (i.e. d_{\min} 4 – 5 Å).

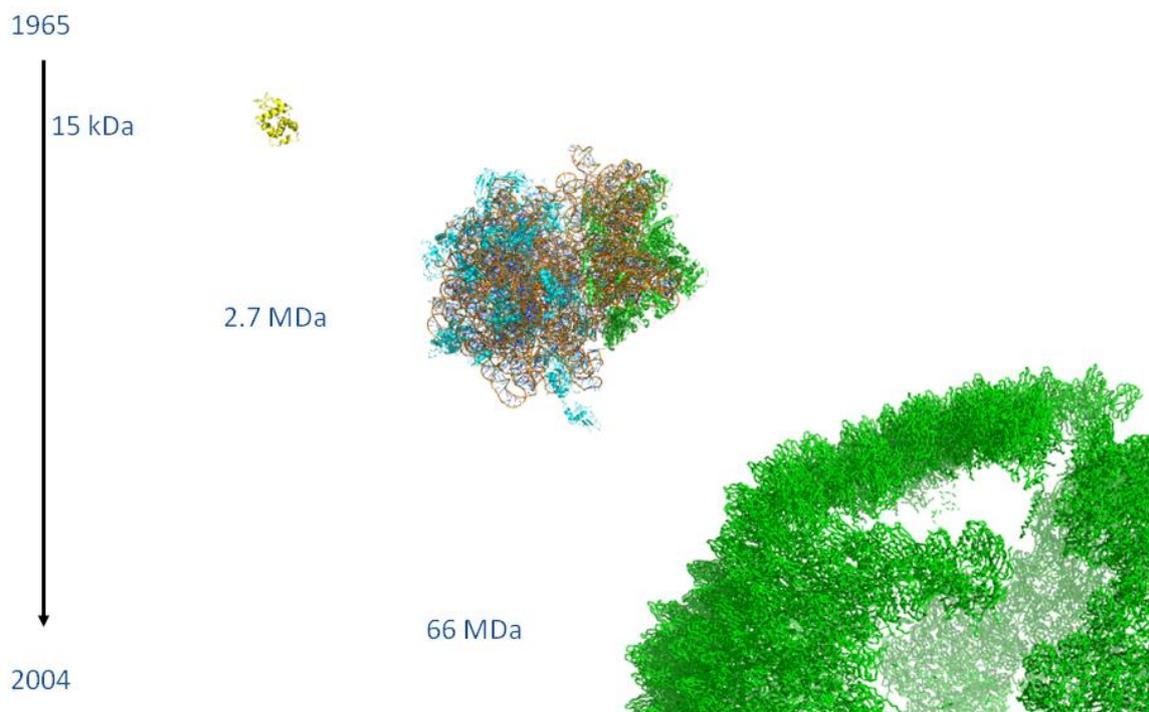


Figure 1. An illustration of the increase in the size of the complexes studied in MX since the solution of the first enzyme structure in 1965.

At the ESRF Macromolecular Crystallography (MX) is principally carried out on the beam lines ID14-1, 14-2, 14-4, ID29 and ID23-1 and ID23-2. In addition the activity of Protein Solution Scattering is undertaken on ID14-3. The presentation will discuss the comprehensive review of the needs and challenges facing this section of the ESRF's user community and the new ideas presented have been

developed following discussions undertaken with this community over the past few years.

The ESRF upgrade beamline UPBL10 (MASSIF) will be a unique resource, based on 2nd generation automation for MX experiments, designed to maximise the chances of a successful conclusion to these ambitious projects. The hub of the facility is a sample evaluation and sorting facility. The most suitable crystals from which to collect data will be distributed from this hub to the data collection facilities that also form an integral part of this proposal as well as to existing facilities on ID29 and ID23.

Data collection trends at the ESRF MX beamlines (see link below) show clearly that automation has led to a fundamental change in the way that MX data are collected. With the introduction of the automatic sample changer (SC3) in 2005, a dramatic increase in the number of samples that were tested for diffraction quality before any full data collections were carried out was observed. Automation has had a spectacular effect on the scientific output of the ESRF MX beamlines. Over the past seven years there has been a more than three-fold increase in the number of structures elucidated using data collected at the ESRF. Although the output has increased - MX beamlines now produce over a quarter of the publications from the ESRF - this has not been at the cost of quality. The scientific impact of the experiments remains extraordinarily high, with around 20% of publications appearing in journals with an Impact Factor greater than 10. **Automation of synchrotron beamlines thus not only increases scientific output but it also maintains the high-level impact of the science performed.**

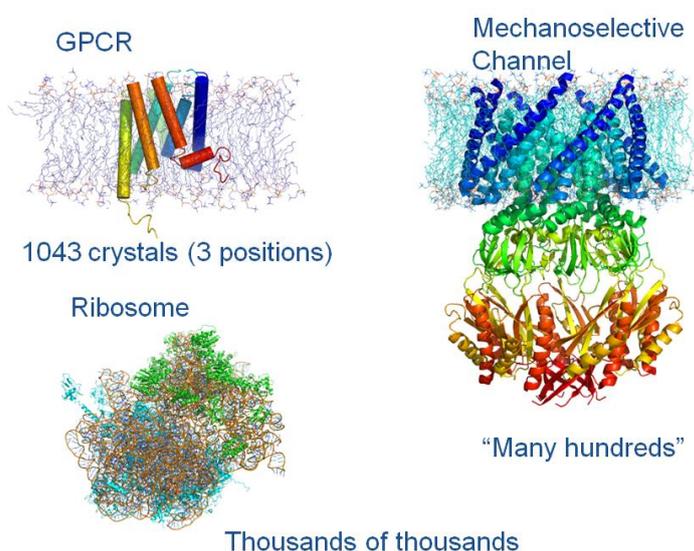


Figure 2. Recent projects that required significant numbers of samples to be evaluated in order to collect the data set needed to solve the structure.

In essence, UPBL10 will provide an upgraded set of beamlines regenerating ID14 A&B on ID30. The

project consists of a suite of beamlines. Three end-stations will provide facilities for different types of sample evaluation: testing the diffraction resolution limit, locating the best part of a crystal on which to perform data collection, detecting the presence of anomalous scatterers, screening for bound inhibitors and ligands, screening in crystallisation plates - integrating and building on the developments made with [DNA](#) and [EDNA](#). **The screening stations directly address a fundamental problem in modern Structural Biology – that of inter and intra sample variability** and will have different beam sizes (two stations with 80 μm beam diameter and one microbeam station with a beam-size of 10-20 μm in diameter).

The plans envisaged for the medium term upgrade of ID29 are complementary to those proposed in the CDRs for UPBL10 and ID23. In particular, by developing multi-wavelength micro-beam experiments new possibilities and experimental challenges will be revealed. In a parallel development, the growing interest in exploiting the weak anomalous signal from sulphur, phosphorous and other light elements in macromolecular structure determination will be supported by enhancing the flux available at relatively long wavelengths (2- 3 \AA).

The ID23 beamlines are the most recent constituents of the MX group portfolio. For this beamline two upgrade projects will dovetail with the other projects proposed. Signal-to-noise will remain one of the most important experimental parameters to optimise and, with this in mind, we suggest for ID23-1 a mechanism for providing variable beam shape with smooth spatial distribution. As with the proposal for ID30 the intention is to allow matching of X-ray beam to crystal size for optimised data collection. The microfocus beamline ID23-2 will be enhanced (by building on existing ESRF developments) in the provision of $\sim 1 \mu\text{m}$ X-ray beams for MX. This evolution will continue the significant success enjoyed by marrying automation with micron dimension X-ray beams.

The proposals for the evolution of MX constitute a symbiotic system whereby the gains for the Science are greater than the individual contributions. As an ensemble the MX upgrade proposals build upon the ESRF's world leading place in automation for macromolecular crystallography, this leading position will be enhanced by the combination of "next generation automation" with the capacity to tailor the X-ray beam properties to the experimental demands. This enhancement will be possible because the planning for the MX Group's proposals has considered the beamlines as components of a successful portfolio rather than treating each beamline individually. The inter-relationship is demonstrated in Figure 4 where the complementary properties of the beamlines proposed are clear. "outsourcing" sample evaluation to MASSIF will mean the availability of more beam-time (*i.e.* longer-term access) on the new data collection stations (*i.e.* ID23, ID29, ID30-4) and will thus allow experimenters to get the best data possible from the best samples identified by MASSIF.

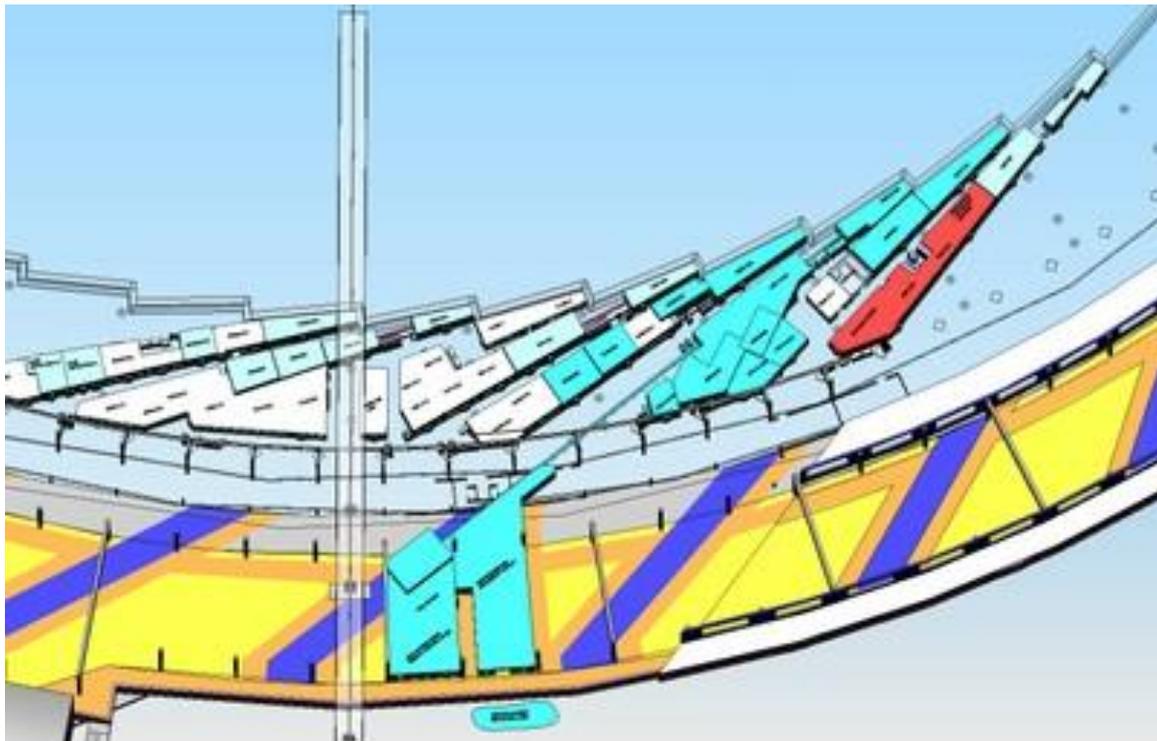


Figure 3. The proposed layout of UPBL10. The hutches of the MASSIF sample evaluation stations are located within the current experimental hall (light blue), the MAD station and sample handling and sorting facility are located in the new experimental hall (EX2) and the new bioSAXS beamline, BM29, is shown in the current experimental hall (red).

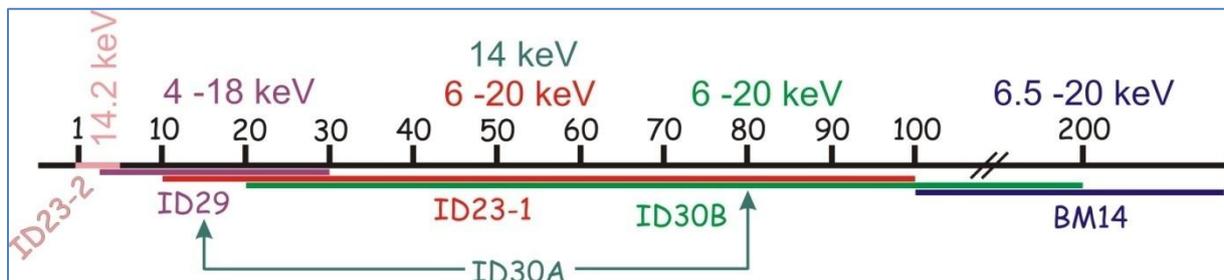


Figure 4: Colour coded representation of the spatial dimensions and energy spectra of the focused X-ray beams achievable within the upgraded MX beamline portfolio.

Links.

Structural Biology Group : <http://www.esrf.fr/UsersAndScience/Experiments/MX>

Data Collection Trends: <http://www.esrf.fr/UsersAndScience/Experiments/MX/data-collection-statistics>.

DNA: <http://www.dna.ac.uk/>

EDNA: <http://www.edna-site.org/>