State-of-the-art: status of the European Synchrotron

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The European Synchrotron (ESRF) is a user facility producing intense X-ray beams in the hard X-ray range. The ESRF is funded by 21 countries, most European, with the latest affiliates being South Africa in 2013 and the Russian Federation in 2014. Over a period of 21 years, the ESRF has established itself as the world’s most intense source of synchrotron-generated light and has been at the forefront of scientific research, providing unrivalled opportunities for an international community of scientists in the exploration of materials and living matter in a very wide variety of fields: material physics, chemistry, archaeology and cultural heritage, structural biology and medical applications, environmental sciences, information science and nanotechnologies. Each year, the 43 highly-specialised beamlines accommodate around 6500 academic and industrial researchers who either travel to Grenoble to carry out their research or send in their samples for remote access experiments or data collection services. In 2015, a total of 1,653 public experiment sessions took place, resulting in 6,409 user visits, and 14,160 shifts of 8 hours were delivered.

For academic research, access to the beamlines is gained through a peer reviewed proposal system with two proposal rounds per year, in March and September. In 2015, 1937 proposals were received of which 46.5\% were accepted. The publication of results from academic research is necessary. For proprietary research, applications are assisted by a dedicated office and beam time or data collection services are charged for. In this case, the research is confidential and there is no obligation to publish.

The facility has just completed its 168 m\(\text{€}\) Phase I Upgrade Programme (2009-2015), with the creation of 19 new experimental stations, a new 8,000 sq m experimental hall and the upgrade and renewal of the majority of equipment. Compared to pre-Upgrade Programme operation, in 2015, there have been increased numbers for experiments and user visits although less beamtime was delivered as two beamlines remained closed and two beamlines are still being upgraded. Of these beamlines, the new materials chemistry and materials engineering beamline, ID15A, is being eagerly awaited by it future users as it received 87 proposals, the highest number of all the beamlines, in the March 2016 round.

While Phase I focussed on the beamlines, the next evolution of the facility will focus on the X-ray source. New concepts for accelerators have emerged in recent years [1], leading to the possibility of building a new generation of storage rings with an increase in brilliance of two orders of magnitude. Key areas of research would benefit from such a project, including coherent diffraction imaging and microscopy in the mesoscopic scale, spectroscopy with nanometre spatial resolution, and time-resolved studies in the millisecond to sub-nanosecond scale. The ESRF has been one of the leaders in the development of these new concepts and, in 2015, launched the second development phase of the Upgrade Programme: the ESRF Extremely Brilliant Source Programme, or ESRF-EBS. This new programme is centred on the construction of a new storage ring that will adopt an all-new hybrid multi-bend achromat lattice design with an equilibrium emittance of about 135 pm\(\cdot\)rad [2], which, after taking into account radiation damping by the insertion devices, should deliver a final horizontal emittance of about 100 pm rad – at least a factor of 10 better than any other synchrotron source of similar energy constructed or presently under construction and a factor 40 better than the present ESRF double-bend achromat lattice.

Picture 1. Layout of the existing (above) and the new hybrid multi-bend achromat lattice (below). The new lattice is expected to deliver X-ray beams to the ESRF beamlines with approximately 100 times increase in brilliance and coherence.

Advances in accelerator control technology and better magnet materials have made such a design feasible. An associated benefit through the use of permanent magnets in place of many electromagnets will be a reduction in the electricity consumption of the new storage ring. The ESRF-EBS project is now well underway and already 90\% of the design work for the components has been completed and prototypes for key components have already been tested.
An exceptional shutdown period in 2019 is planned for the construction of the new storage ring. To exploit this major enhancement of the X-ray source, the project is accompanied by an ambitious scientific instrumentation programme, construction of new beamlines and enhanced computing facilities.

The ESRF-EBS represents an investment of 150 M€ over the period 2015-2022. It has been recognised as one of the “landmarks” by the European Strategy Forum on Research Infrastructures (ESFRI), highlighting its scientific excellence, pan-European relevance, socio-economic impact and innovation.

Major steps have already been made in preparation for the new storage ring. Very recently, top-up operation has been tested over a period of four weeks. Top-up provides users with better beam stability, low vertical emittance in all filling modes (with correspondingly higher brilliance and resolution) and a nearly constant beam current.

**Figure 2.** Top-up operation in 16-bunch mode. This snapshot of the control room synopsis screen shows the 20-minute injection periods and a low vertical emittance of 6.5 pm rad.

As a hard X-ray source, the majority of the ESRF’s beamlines are currently optimised for X-rays between 5 and 30 keV. An extended range is provided by one soft X-ray beamline reaching down to 0.3 keV and eight high-energy beamlines with upper limits between 60 and 750 keV. One of these high-energy beamlines is ID31, a beamline for interfaces and materials processing, that opened to users in November 2015. Users appreciate the high photon flux (a gain by a factor of 10 over beamline ID15A that it replaces) in the high-energy range and the new detector, a Pilatus 2M, with frame-rates up to 250 Hz. The beamline is currently focusable to the micrometre level and its exceptional flux makes following processes inside reaction vessels or energy storage devices feasible.

**Figure 3.** ID31 experimental hut during construction of the beamline. Credit ESRF/P. Jayet.

Users at this beamline recently set a record for the highest quantity of data collected in one experiment: 100 Tb in just over 1 week, despite using the detector at only 60 Hz. The ESRF-EBS project will further enhance this a beamline by a further increase in brilliance and a reduction in size of the beam which will provide far greater precision when probing buried interfaces.

The legendary structural biology cluster of four beamlines, ID14, has been replaced by MASSIF (Massively Automated Sample Selection Integrated Facility) comprising 3 end stations and ID30B [3]. MASSIF–1, beamline ID30A-1, was the first of the new beamlines to enter user operation, starting in July 2014. This beamline is the world’s first fully-automated facility. It comprises robotic sample handling and positioning and an expert system to control data collection. The performance of this beamline has recently been reviewed [4]: 9872 crystals were analysed automatically during 2015. These crystals typically came from projects involving a large amount of screening to find the one crystal out of many that diffracts sufficiently or where large numbers of repetitive data collections are required, such as fragment screening campaigns. The benefits of a fully automated beamline are:

- Optimal use of beamtime by collecting data both day and night.
- Eliminates human error: automatic centring of crystals using X-rays is more accurate than a human operator relying on visible light.
- Optimised data collection strategies taking into account the crystal size and diffraction quality produce higher-quality data than equivalent human operated beamlines through a reduction in radiation damage.

**Figure 4.** Data quality comparison for data sets automatically processed on MASSIF-1 and the ESRF human-operated beamlines in 2015: Plot of signal to noise ratios $<I/\sigma(I)>$ vs number of crystals. Credit [4].

The software workflows developed for MASSIF–1 have been deployed to the other ESRF structural biology beamlines and can be run by users. Currently, the X-ray centring routine is the most frequently used.

Beamline ID30B is a variable-focus, tuneable-energy beamline. It features FlexHCD, a new generation of high-throughput sample changer robot developed at the EMBL (European Molecular Biology Laboratory). FlexHCD accepts samples in either EMBL/ESRF pucks or Unipucks and it can even manipulate crystallisation trays for *in situ* screening and data collection. FlexHCD will become the standard sample changer, soon to be installed at other ESRF structural biology beamlines.
Serial millisecond crystallography (SMX) has recently been tested at the microfocus beamline, ID13 [5]. Using lipid cubic phases as the delivery medium, this experiment aimed to reproduce an experiment typically carried out at XFEL (X-ray free-electron laser) sources but with millisecond timing, and so bridging the gap between the traditional protein crystallography experiments at synchrotron sources and the serial femtosecond crystallography experiments of XFELs. At room temperature, a stream of many thousands of bacteriorhodopsin microcrystals (less than a mg) were delivered using a microfluidics system such that exposure time to each crystal was between 10 and 50 μs. Merging the data from 5700 frames for structure solution culminated in a 2.4 Å resolution structure that was comparable to one obtained through a conventional cryocooled crystallography experiment on a single crystal. Some minor radiation damage was evident, which could be avoided in future.

MeshAndCollect [6] is another approach to synchrotron serial crystallography. It involves automatic identification of many cryocooled crystals mounted on the same sample holder. The crystals are ranked, partial datasets collected, and hierarchical cluster analysis is used to provide the best combination. This method holds promise for difficult to crystallise proteins such as membrane proteins grown in lipidic mesophase and is available for users.

The ESRF-EBS will provide a smaller and more intense X-ray beam which will enhance SMX, permitting faster timescales and creating opportunities for room-temperature kinetics studies, e.g. via laser excitation.

At the microtomography beamline, ID19, experiments have explored time-resolved diffraction imaging exploiting the temporal structure of the X-ray beam [7]. In single-bunch beam mode with 10 mA in the single bunch, a 140 ps X-ray flash is produced at a frequency of 355 kHz, corresponding to 2.81 μs, which is long enough to allow separation of individual flashes by a commercial CMOS-based camera. Making use of the coherence properties of the beamline, crack propagation was tracked in a piece of glass breaking from the impact of an accelerated bolt. In a more recent experiment, direct transmission and diffraction X-ray imaging were combined to follow crack propagation and strain in real time [8]. The resulting movie of crack propagation in a silicon wafer with a 1.28 μs frame rate revealed that the crack propagates in fits and starts.

For X-ray diffraction topography, the gain in photon flux density envisaged for the ESRF-EBS would allow significant improvement in the spatio-temporal resolution and should make accessible more details of the dynamics around the propagating crack tip.

Focussing again on time resolution but this time for soft matter, users of the new Time-resolved USAXS/SAXS/WAXS Beamline, ID02, have discovered how sleeping muscles economise energy, resulting in a novel dual-filament concept for the regulation of contraction in skeletal muscle [9].

**Figure 6.** Time series recording crack propagation in a glass plate initiated by an accelerated bolt. Credit [7].

X-ray diffraction patterns were recorded from single muscle cells on a millisecond timescale while they were stimulated electrically. It was discovered that the majority of myosin proteins, which effectuate muscle contraction, remained in the resting state until a high stress causes a conformational change that activates them. The very high brilliance and X-ray collimation of this new beamline made these challenging experiments possible.

**Figure 7.** X-ray diffraction pattern from a resting muscle fibre. Credit: E. Brunello, [9].

Looking back over the last 21 years, since the start of user operation in 1994, the ESRF’s users and staff have published a record 26,958 refereed publications in top scientific journals and four Nobel prizes have been awarded to laureates using the ESRF for their work. In 2010, for the first time ever, more than 1000 protein structures were deposited in a single year in the worldwide Protein Data Bank (PDB) from data collection at the ESRF [10], the total to date reaching 11,918 structures and accounting for over 40% of the European facility deposits [11].

The outlook for the next 20 years is that the users should be even more productive following the ESRF - EBS. The higher brilliance of the X-ray beams, faster detectors, increased automation and suitably-dimensioned data infrastructure will all contribute to making experiments faster. While the smaller X-ray
source will permit a transition from the micrometre scale towards the nanometre scale for beamlines that privileges a small beam size. Furthermore, a significant increase in the coherence of the source holds promise for new experiments that have yet to be imagined.