Elettra 2.0: New Structural Biology Opportunities

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AREA Science Park

Book of Abstracts

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Elettra 2.0 project and IVU beamlines

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After 27 years of successfully serving the user community, Elettra is undertaking a major upgrade towards a diffraction limited light source, called Elettra 2.0, enabling new science and the development of new technologies to the general benefit.

Due to a substantial reduction of the emittance of the stored electron beam, the new machine will be able to host in particular also in-vacuum undulators (IVU), allowing for new microfocus beamlines in the range of hard X-rays. Among these, in particular a new beamline dedicated to macromolecular crystallography (μXRD) has been designed to support the requests of structural biology community, offering high photon fluxes on a micron-sized spot, opening to a fast characterization of smaller samples and to data collection strategies of increasing complexity.

The talk will highlight some characteristics of the new machine and report design and expected features of the new beamline.

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The new MX beamline at Elettra 2.0: μXRD

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The new high brilliance microfocus μXRD beamline will be presented. μXRD aims to fullfill the needs of current XRD2 community and will open new opportunities to Elettra MX users.

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New opportunities for time resolved serial crystallography experiments at 4th generation synchrotrons

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Development and implementation of cryo-electron microscopy at the National Institute of Chemistry, Slovenia

Integrated structural biology aims to provide high-resolution structural information about biological molecules and their complexes in isolated form or in biological context based on data obtained by various experimental and theoretical methods. This helps to understand biological processes and enables drug and vaccine discovery and other applications in biotechnology. For atomic resolution approaches, X-ray crystallography has long been the gold standard, but the immense power of cryo-electron microscopy (cryo-EM) has recently contributed increasingly to the field, providing detailed structural information on many complex (biological) macromolecular systems. Recent dramatic scientific achievements have been based on the use and continuous development of high-end structural biology infrastructure, which is large both in terms of its physical size and cost. The latter could be a major disadvantage for smaller but ambitious scientific communities. In my talk, I will describe our path to establishing a cryo-EM facility at the National Institute of Chemistry, the first in Slovenia and in the region. I will describe how we combine it with other methodological approaches and show some concrete examples from our research projects. Our cryo-EM facility has been continuously active since its opening in November 2019 to answer Slovenian and foreign academic or industrial research questions and, importantly, also to train new generations of cryo-EM scientists.

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Protein production facility at Elettra: past, present and future.

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The EMBL Protein Expression and Purification Core Facility: bringing structural biology tools to the non-structural biology community

The goal of the EMBL Protein Expression and Purification Core Facility is to provide high-level services and advice regarding all aspects of protein expression, purification and characterisation.

We aim to support our users with all individual steps of the workflow, going from the choice of the expression host organism and construct design to small scale screening, expression scale-up and protein purification using a combination of chromatographic methods to protein quality control and biophysical characterisation. We are based at EMBL Heidelberg and are embedded in the local Structural and Computational Biology unit, which allows us to stay up-to-date of the latest developments in structural biology. We also work closely with our colleagues at EMBL Hamburg and EMBL Grenoble, whose laboratories are located on the German Synchrotron Research Centre (DESY) campus and the European Synchrotron Radiation Facility (ESRF) campus, respectively. Even though we cooperate frequently with the different EMBL structural biology groups and facilities across the EMBL sites, one of our core tasks is to make structural biology tools accessible to the non-structural biology community as well. We collaborate with research groups from a large variety of scientific disciplines that are typically not immediately associated with structural biology, ranging from developmental biology, neurobiology and medicine to marine biology, planetary biology and human ecosystems. We produce samples for structural characterisation by NMR, crystallisation and cryo-electron microscopy, but also for other applications such as nanobody/antibody generation and biochemical or biophysical experiments. By doing so, we hope to assist these research groups in introducing more interdisciplinary approaches into their projects as well.

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Leading a Protein Production facility for HT structural biology

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Machine Learning in Structural Biology

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We review the current progress and challenges in the field of Machine Learning for Structural Biology. We will discuss existing machine learning algorithms such as AlphaFold for structural prediction, the use of large language models for protein design, and generative models applied to protein-protein docking. The aim of the seminar will be to encourage experts from relevant communities to imagine new applications and explore potential future collaborations in the field.

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Infrastructure requirements for running high-throughput crystallographic fragment screening

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i04-1 at Diamond Light Source is a fixed wavelength, high throughput beamline, dedicated to running unattended data collection queues. We utilise the beamtime to run XChem fragment screening experiments for both industry and academic users, allowing us on average to collect 2000 samples per week. In addition to what we require from the beamline, this talk will focus on the infrastructure requirements to support high-throughput fragment screening, covering laboratory requirements, computing, staff and logistics.

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Combining visual and X-ray sample characterization information in design of macromolecular crystallography experiments

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The best thing one can do to determine the structure of a biological macromolecule at atomic resolution is to grow a large homogeneous crystal of it, then probe it with flat X-ray beam of the matching size, while rotating it using a perfect goniometer while measuring the complete reciprocal image of its electronic density with a perfect detector.

Though this ideal is not feasible in practice, it should stay the northern star of our struggle for quality. In this contribution we will address three points that have a promise of bringing us closer to the ideal.

First we will unravel the problem of achieving perfect sample alignement at arbitrary goniometer datum with mechanically imperfect goniometers.

Second we will address the problem of merging optical and x-ray sample characterization information into a coherent whole.

Third we will attempt to establish a way of optimal sampling of available diffracting volume for a more perfect measurement with beams of arbitrary size and intensity.

The talk will conclude with a discussion of the most desirable properties of a new MX beamline, with a view to the problems we will have attempted to unravel.

Session 2 Cryo-Electron Microscopy Chair: Rita De Zorzi (Università degli Studi di Trieste) / **24**

Application of cutting-edge cryo-EM methodologies to study DNA replication and repair

Cryo Electron Microscopy (cryo-EM) has revolutionized structure biology, allowing direct visualization of entire molecular machines at atomic resolution. In this talk, I will outline some of the applications of single-particle cryo-EM analysis we use in the lab to investigate the structure and function of enzymes operating in human DNA replication and repair.