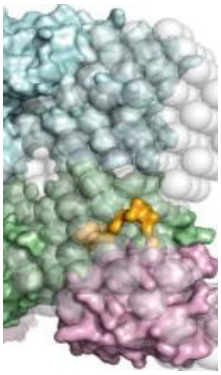
BioStructX

Newsletter No. 4
December 2014



For Life Science in Europe

Greetings from the Coordinator

Dmitri Svergun reflects on year 2014

As we approach the end of 2014, we look back at a dynamic and eventful year. Especially the second half of the year has been a flurry of activity with the Third Annual Meeting in September in Barcelona (page 2) and the submission of the 2nd periodic report at the end of October. I would personally like to thank the management team of BioStruct-X for the hard work and also to thank the consortium partners for their cooperation and support in provision of the required materials. I am glad to say that all documents have been submitted in time and we expect feedback from the Commission at the end of January 2015. Meanwhile, we continue to focus on simplifying user access provision procedures and the fulfilment of contractual obligations. Following the footsteps of the majority of BioStruct-X partners, EMBL-Hamburg as the BioStruct-X coordinating beneficiary recently decided to join the Umbrella initiative, a dedicated pan-European photon/ neutron facility user federation. The first steps in implementing the Umbrella-supported access have already taken place and BioStruct-X users will soon have the opportunity to use the Umbrella single sign on capacity. The ultimate goal will be provision of integrated access for the users among BioStruct-X facilities in close collaboration with the ESFRI initiative INSTRUCT.

Now, we are looking forward to 2015 with a number of exciting networking and training events already in the planning (page 11) for the first half of the year, and to seeing more scientific breakthroughs as the ones highlighted on pages 3-5. Finally, on behalf of the BioStruct-X management team, I would like to wish all partners and friends a happy holiday season and a successful 2015!

Contents:

BioStruct-X in numbers:

Start: September 1st 2011
Duration: 54 months
Total Budget: 9 Million Euro
Number of partners: 19
Number of installations: 44
End date: February 29th 2016

Project News

BioStruct-X enters its fourth year – Report form the Third Annual Meeting in Barcelona

The Third Annnual Meeting of the BioStruct-X project was hosted by the ALBA synchrotron facility in Barcelona, on September 29th - 30th 2014 . The two day event was structured as a series of presentations from all ten BioStruct-X work packages (WP) where the WP leaders provided yearly work progress updates.

The public part of the meeting included keynote lectures by the representatives of the BioStruct-X user community: Wojtek Rypniewski (Center for Biocrystallographic Research at the Institute of Bioorganic Chemistry of the Polish Academy of Sciences), Michael Elbaum (Weizmann Institute) and Gareth Wright (University of Liverpool) presenting scientific highlights that resulted from the use of BioStruct-X Transnational Access (TNA) support. In addition, Dave Stuart, coordinator of Instruct, outlined the cooperation between the two projects and Cecilia Blasetti, Elettra, Trieste, Italy, gave an overview of the CALIPSO project status.

Over 50 participants that attended the meeting had the opportunity to take a guided tour of the ALBA facilities and network with colleagues from across Europe.

BioStruct-X Annual Meeting Poster

BioStruct-X Annual Meeting participants taking a tour to ALBA facilities

TNA Application Deadlines

At the BioStruct-X Project Evaluation Committee (PEC) meeting that took place on October 1st 2014, the remaining TNA application deadlines until the end of the project were defined.

In 2015, there will be three application deadlines:

- **February 15th**
- **May 30th**
- **September 15th**

Dr. Mirjam Czjzek is the New Member of the BioStruct-X Project Evaluation Committee (PEC)

As of November 2014, after spending three years as SOLEIL representative in the BioStruct-X PEC, Dr. Catherine Birck was replaced by Dr. Mirjam Czjzek, head of the 'Marine glycobiology' group and scientific responsible of the platform for crystallography at the CNRS .

The BioStruct-X management would like to use this opportunity to thank Catherine for her great work, as well as for her valuable input and continuous support of the BioStruct-X project. At the same time, we welcome Mirjam and we are very much looking forward to working together towards the fulfilment of the BioStruct-X project goals.

Scientific Highlight – *Aranzazu Cruz-Adalia et al., Cell Host & Microbe, 15, p611 – 622, May 14 2014*

T Cells Kill Bacteria Captured by Transinfection from Dendritic Cells and Confer Protection in Mice

During the course of bacterial infections, antigen presenting cells (APCs), like dendritic cells (DCs) phagocytose, process, and present bacterial antigens to T lymphocytes to trigger adaptive immunity. There exist several reports showing that in vivo, bacteria can also be found inside T lymphocytes. However, T lymphocytes are refractory to direct bacterial infections, leaving the mechanisms by which bacteria invade T cells unclear.

In this recent study, Cruz – Adalia et al. showed that T cells take up bacteria from infected DCs by a process of transinfection occurring during the formation of the immunological synapse (IS) a structure formed by intimate DC/T cell contact. IS formation is the main mechanism of T cell activation and is crucial for the adaptive immune response.

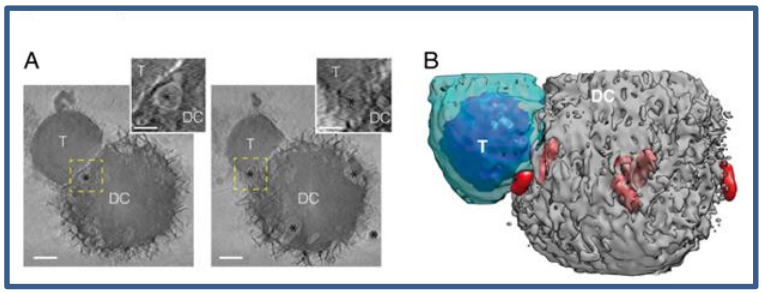


Figure 1. A) Virtual slices of a cryo soft-X-ray tomogram acquired at BESSY-II from a T-cell (T) interacting with an S. enterica-infected DC. The asterisks mark the position of Salmonella. The indicated bacteria are inside DC close to the IS (left) and outside DC and being engulfed by the T cell (right). Inset shows a detailed position of bacteria. Scale bars represent 2 micron and 1 micron in the insets. (B) Volumetric representation of the soft X-ray tomogram shown in A. Bacteria are represented in red, T-cell in cyan and DC in grey. The nucleus of the T cell is shown in blue.

Prior to transfer, bacteria localize to the IS. Strikingly, T cells efficiently eliminate the transinfecting bacteria within the first hours after infection. Transinfected T cells produced high levels of proinflammatory cytokines and were able to protect mice from bacterial challenge following adoptive transfer. Thus, T lymphocytes can capture and kill bacteria in a manner reminiscent of innate immunity. Bacterial localization at the IS was confirmed by high-resolution cryo-Soft X-ray Tomography (cryo-SXT) (Figures 1A and B).

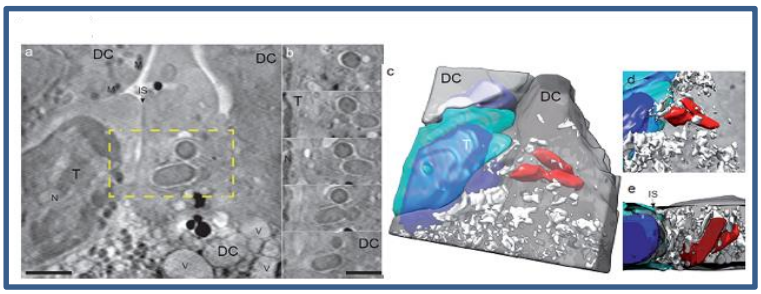


Figure 2. a) Virtual slice of a tomogram showing an infected dendritic cell (DC) exposing internal bacteria near the immune synapse (IS) with a T cell (T). N labels the nucleus position of the T cell and V some vesicles. Bacteria are visible in the dashed yellow square. b) Consecutive virtual slices every 460 nm showing the proximity of the three bacteria, in the orange square of A, to the IS with a T cell. Scale bars in a) and b) represent 2 microns. c, d and e) Volumetric representations of the tomogram in a) and b). The T cell is represented in cyan and its nucleus is shown in blue. The dendritic cells (DC) are shown in grey, the bacteria in red and the T cell in cyan (nucleus in blue). The large amount of internal vesicles in the DC is typical of dying DCs. Note that DCs are very sensitive to Salmonella infections.

Tomograms were acquired at HZB-BESSY II. Due to the size of the bacteria (larger than 1um), this high-resolution, non-standardized technology is especially useful in the studies involving bacteria-cell interactions.

Cryo-SXT is capable of imaging cellular organization and locating subcellular structures in whole, hydrated cells, thus eliminating the artefacts from embedding, dehydration, and sectioning, and allowing the in situ imaging of whole cells. In Figure 2, in a tomogram acquired at the synchrotron ALBA, we can appreciate Salmonella enterica inside infected DCs and the subcellular structures like the *Salmonella*-containing vacuole.

Scientific Highlight – Maria Lucas et al., *PNAS, August 26, 2014 vol. 111 no. 34*

Structural basis for the recruitment and activation of the Legionella phospholipase VipD by the host GTPase Rab5

A long-standing question in the field of microbial pathogenesis is how virulence factors are regulated within host cells and how their activity is specifically directed toward a particular host cell compartment. Now, *Legionella pneumophila* resolves this dilemma by tightly coupling the phospholipase A1 activity of one of its effectors, vacuolar protein sorting inhibitor protein D (VipD), to this protein's interaction with endosomal host GTPases.

The Legionella pneumophila bacteria is responsible for legionellosis, a disease that can cause pneumonia, very high fever and, in extreme cases, death. Legionella lives in stagnant water and enters our body through the airways when microscopic drops of contaminated water are inhaled.

Under normal conditions, human cells would "eat" and destroy the bacteria when it enters the body, but CIC bioGUNE, NIH and BSC have discovered that the *Legionella* bacteria releases VipD that impedes the development of the cell's "digestive system". VipD protein is activated when entering in contact with human protein Rab5, which is located in the membrane of the endosome, and boycotts its development.

In the study that was recently published in the US scientific journal Proceedings of the National Academy of Sciences, a team of scientists determined the molecular structure of VipD protein, by X-ray crystallography, in complex with host cell Rab5c, providing a detailed look into the ingenious molecular mechanisms underlying the allosteric activation of a virulence factor by a host protein and its spatiotemporal regulation. Furthermore, they have proven that the blockage of both proteins is possible, which prevents activation of the VipD protein.

VipD protein is activated when entering in contact with human protein Rab5, which is located in the membrane of the endosome, and inhibits endosome maturation. This compartment, when matured, acts as the cell's "stomach". By hindering the growth of this organule, the bacteria manages to survive within the cell.

Studying *Legionella* is very interesting since it is an excellent model to assess the relationship between hosts and pathogens, due to its ability to avoid host's defences and multiply without being destroyed.

The discovery of the role of protein VipD opens a new door to the fight against Legionella, since they could explore its use as a therapeutic target. Indeed, thanks to these advances new drugs could be developed to act on this specific protein, which would allow for cells to target the bacteria.

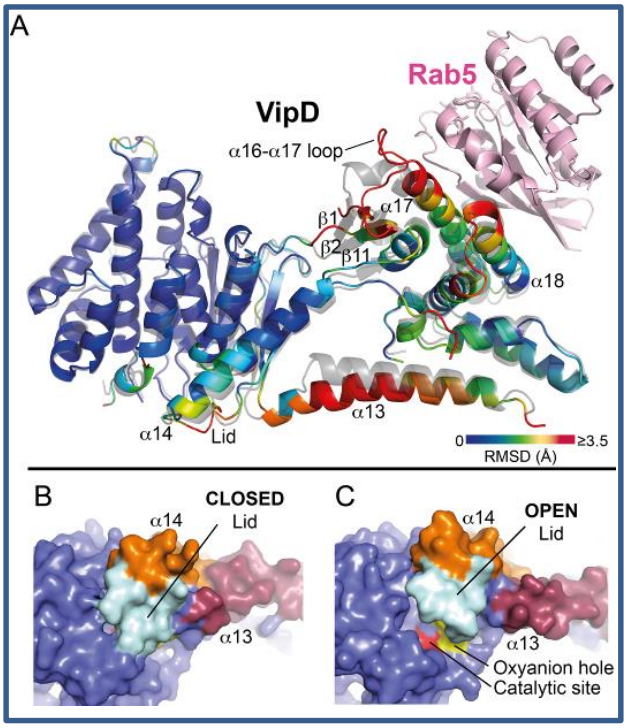


Figure 1. ***Allosteric activation of VipD through Rab5 binding.*** *(A) Structural changes in VipD upon Rab5 binding. Rab5c18-182 (colored in pink) is complexed to VipD19-564 which is colored from slate to red based on the Root Mean Square Deviation (RMSD) of C-alpha atom pairs when superimposed with the unbound form of VipD19-564 (PDB 4AKF) shown in transparent grey. The black line represents the membrane plane. (B, C) Close-up view of the catalytic site in surface representation showing the displacement of the lid upon Rab5 binding*

Scientific Highlight – Mattia Rocco et al., *J. Am. Chem. Soc.*, 2014, 136 (14), pp 5376–5384

A Comprehensive Mechanism of Fibrin Network Formation Involving Early Branching and Delayed Single- to Double-Strand Transition from Coupled Time-Resolved X-ray/Light-Scattering Detection

The formation of a fibrin network is the central event in vertebrates blood coagulation. It is also involved in several pathologies, such as thrombosis and cancer metastasis, and is of great biomedical/biotechnological relevance

The formation of afibrin network following fibrinogen enzymatic activation is the central event in blood coagulation and has important biomedical and biotechnological implications. A non-covalent polymerization reaction between macromolecular monomers, it consists basically of two complementary processes: elongation/branching generates an interconnected 3D scaffold of relatively thin fibrils, and cooperative lateral aggregation thickens them more than 10-fold.

In this study, recently published in the Journal of the Americam Chemical Society the authors studied the early stages up to the gel point by fast fibrinogen enzyme mixing experiments using simultaneous small-angle X-ray scattering and wide-angle, multi-angle light scattering detection. The coupled evolutions of the average molecular weight, size, and cross section of the solutes during the fibrils growth phase were thus recovered.

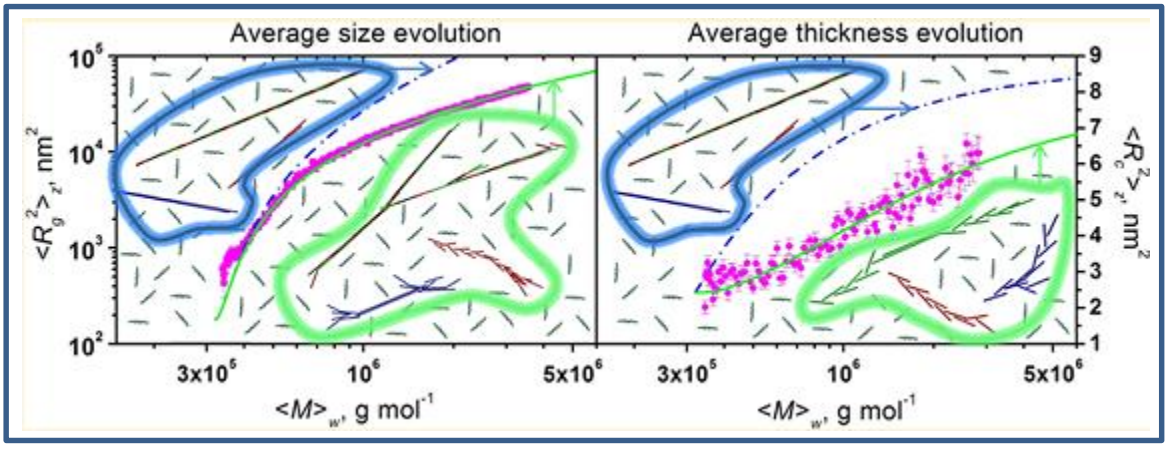


Figure 1. The coupled evolutions of the average molecular weight, size, and cross section of the solutes during the fibrils growth phase

They revealed that extended structures, thinner than those predicted by the classic halfstaggered, double-stranded mechanism, must quickly form. Following extensive modeling, they propose an initial phase in which single-bonded “Y-ladder” polymers rapidly elongate before undergoing a delayed transition to the double-strandedfibrils. Consistent with the data, this alternative mechanism can intrinsically generate frequent, random branching points in each growingfibril. The model predicts that, as a consequence, some branches in these expanding“lumps”eventually interconnect, forming the pervasive 3D network. While still growing, other branches will then undergo a Ca2+/length-dependent cooperative collapse on the resulting network scaffolding filaments, explaining their sudden thickening, low final density, and basic mechanical properties.

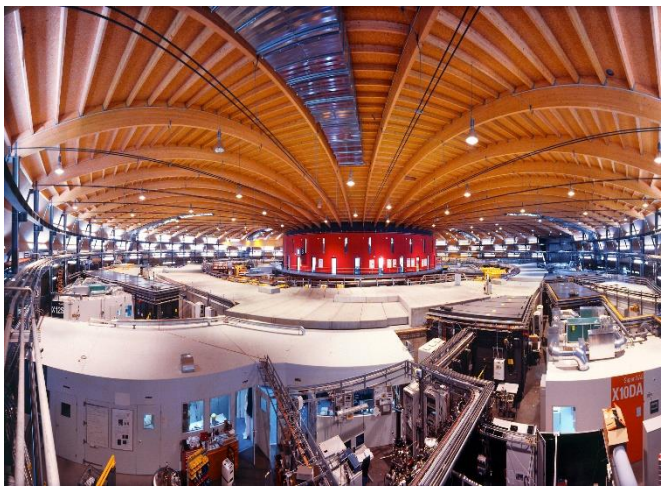
Experimental SAXS data for this study were collected at SWING beamline at SOLEIL.

Centre Feature – Swiss Light Source at PSI, Switzerland

The Paul Scherrer Institut (PSI) is the largest research centre for natural and engineering sciences within Switzerland, with research activities concentrated on three main subject areas: Matter and Material, Energy and Environment, and Health. The PSI develops, constructs and operates complex large-scale research facilities. Among them are the Swiss Light Source (SLS), one of the most advanced synchrotron radiation sources worldwide, and the X-ray laser SwissFEL coming on-line in 2016.

Every year, more than 2000 scientists from Switzerland and other countries travel to PSI in order to perform experiments at our unique facilities.

The PSI contributes in the BioStruct-X project through the Macromolecular Crystallography (MX) group at the SLS, who operates two high-performance undulator beamlines as well as a state-of-the-art superbend magnet beamline, and is involved in the development of advanced beamline instrumentation and crystallographic methods, as well as various structural biology projects (http://www.psi.ch/macromolecular-crystallography/).



View from the inside of the Swiss Light Source

Features of the macromolecular beamlines at the SLS

Beamline	PXI (X06SA)	PXII (X10SA)	PXIII (X06DA)
Source	U19	U19	2.9T Superbend
Energy range	6.0 – 17.5 keV	6.5 – 20.0 keV	5.5 – 17.5 keV
Flux, phs/s (12.4 keV, focused beam)	2×10^{12}	2×10^{12}	5×10^{11}
Beamsize, μm^2 (with apertures, slits)	10 × 3 <-> 100 × 100 (2 × 2)	50 × 10 30 × 10, 20 × 10, 10 × 10	80 × 45
Goniometer	Micro-diffractometer		Multi-axis PRIGo
Detector	PILATUS 6M FAST	PILATUS 6M FAST	PILATUS 2M FAST
Data collection time	2 – 3 minutes		
Sample changer	IRELEC CATS		

X06SA-PXI (http:/www.psi.ch/sls/pxiii), in operation since 2001, has built his success on state-of-the-art optical design consisting of a double-crystal monochromator with sagittal focussing and vertical focussing mirrors. In 2007, it was the first beamline to feature a PILATUS 6M pixel array detector (also developed at PSI) and developed fine-f slicing data collection. A two-stage microfocus upgrade was initiated in 2014 with the aim of offering tunable focus down to 1 × 1 mm^2 without sacrifice on photon flux. In 2015, an EIGER 12M detector will be installed.

X10SA-PXII (http:/www.psi.ch/sls/pxii) is the second undulator beamline for macromolecular crystallography, jointly funded by the Max Planck Society (MPG) and the pharmaceutical companies Novartis and Hoffmann-La Roche in 2014. Based on beamline X06SA-PXI design, it was recently upgraded with an in-house developed diffractometer integrating beam shaping devices down to a beam size of 10 × 15 mm^2 and featuring fast scanning capabilities essential for membrane protein crystallography.

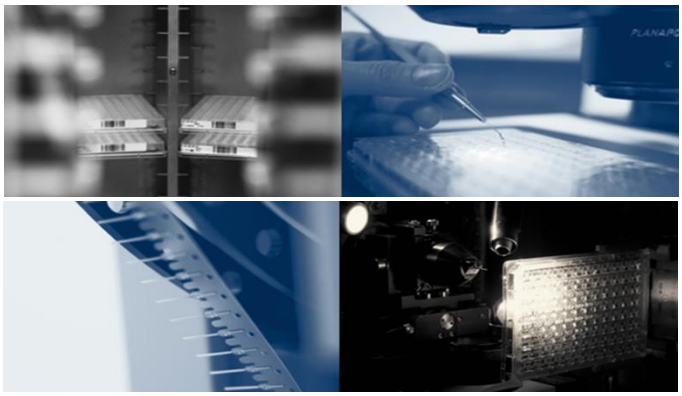
The superbend magnet beamline **X06DA-PXIII** (http:/www.psi.ch/sls/pxiii), funded by a partnership between the PSI and Swiss and international pharmaceutical companies (Novartis, Actelion, Boehringer Ingelheim, Proteros and Mitsubishi Tanabe), is in operation since 2008. The diffractometer is equipped with an in-house developed high-precision PRIGo multi-axis goniometer particularly well suited for experimental phasing data collection. The beamline is complemented with an integrated crystallization facility (open to external users) with automated *in situ* X-ray diffraction screening capability (directly in the crystallization plate).

For more information about MX beamlines at SLS –PSI see http://www.biostructx.eu/content/psi-mx-beamlines

Protein production and crystallization platforms at PSI

Within BioStruct-X project, the PSI offers supported access for European users with interest in eukaryotic membrane protein expression and/or crystallizationto at the state-of-the-art Protein Production (PP) Platform and Macromolecular Crystallisation Facility.

The **PSI Protein Production Platform (P4)** of the Biology and Chemistry Department (BIO) is a research facility specialized in recombinant protein production, with state-of-the-art equipment and a team of highly skilled and dedicated professionals with extensive experience in protein expression and purification. The principal aim of P4 is to support research groups at the Laboratory of Biomolecular Research (LBR) and to produce high-quality protein for high-resolution structure determination by X-ray crystallography with a particular focus on membrane proteins and cytoskeletal proteins. Furthermore, P4 collaborates with research groups in Switzerland and world-wide and also offers recombinant protein production on a fee-for-service basis.



The top left figure shows plates stored inside the Rockimager 1000 plate hotel. The top right figure shows crystals being crushed to make a seed stock. Bottom left is a close up of the tips used by the Mosquito LCP to dispense crystallisation drops and the bottom right figure shows a crystal plate being screened with in-situ x-ray screening at beamline X06DA at the SLS.

Together with the PSI Crystallization Facility, P4 represents the “gene-to-structure” pipeline designed to cover all steps from cloning to rapid mutant generation, biophysical and functional studies, as well as X-ray data collection at the SLS and high-resolution structure determination.

We aim to provide the best possible advice on construct design, expression systems and vectors for each project to warrant optimal results. A range of molecular services including construct design, cloning gene of interest into expression vector, site-directed mutagenesis, specialised expression vectors and vector development are available. We offer recombinant protein production in bacterial, insect and mammalian cells. P4 uses ÄKTA chromatography systems for the routine purification of recombinant proteins (typically IMAC followed by gel filtration), to obtain optimal protein purification results. Results are routinely analysed by Western blotting and mass spectrometry. Biophysical techniques such as multi angle light scattering, analytical ultracentrifugation (instrument equipped with fluorescence option), circular dichroism and isothermal titration calorimetry are available for state-of-the-art protein characterization.

The **Macromolecular Crystallisation Facility** at the PSI is maintained by the SLS and the BIO department. The facility is situated at the X06DA beamline. We work with scientists from the BIO department, the SLS, the SwissFEL, and elsewhere, to produce and to optimise macromolecular micro- and nano-crystals for x-ray diffraction experiments at the forefront of structural biology.

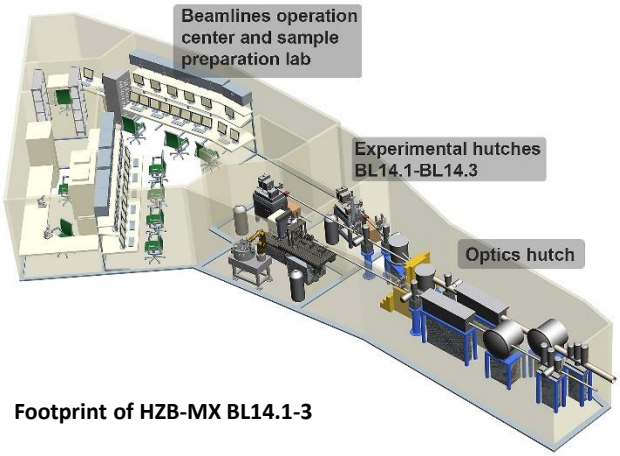
The facility is equipped for robotic crystallization screening by sitting-drop vapour diffusion or lipidic cubic phase using two TTP Labtech Mosquito LCP robots situated at 4 and 20°C. We have a Formulatrix Rockimager 1000 plate hotel situated at 20°C with UV imaging capabilities and a Formulatix Rockimager 182 plate hotel situated at 4°C. We are also equipped to optimize, mount and test crystals grown in those experiments. We offer different modes of access for different users: we can set up experiments for users who provide macromolecular material, we can provide training in robotic crystallisation screening and imaging for new users who will make regular use of the facility, and we can provide experimental advice to more experienced scientists.

For more information about PP and crystallization platforms at PSI see http://www.biostructx.eu/content/psi-protein-production-and-htx

Centre Feature – Helmholtz-Zentrum Berlin für Materialien und Energie (HZB), Germany

HZB operates two large-scale facilities for basic science research: the neutron source BER II at its Wannsee campus and the synchrotron radiation source BESSY II at its Adlershof campus. BESSY II is a third generation electron storage ring operated at a ring energy of 1.7 GeV. It is a dedicated light source for the production of vacuum ultraviolet (UV) and soft X-rays. Despite its medium electron energy, BESSY II is also able to produce hard X-rays and a number of hard X-ray beamlines are successfully operated at BESSY II. BESSY II produces synchrotron radiation for a total of 46 beamlines and a user community of more than 2500 users per annum.

Within the BioStruct-X project transnational access to the European user community is provided by the three macromolecular crystallography (MX) beamlines BL14.1-3 and the soft X-ray microscopy beamline U41-TXM.



Footprint of HZB-MX BL14.1-3

Aerial view of the BESSY II synchrotron

The X-ray source for the three MX-beamlines is a 7 T-wavelength shifter, which was built and installed within the low-beta section 14 of the BESSY II ring by the Budker Institute (Novosibirsk, Russia).

Beamlines **BL14.1** and **BL14.2** are operated at photon energies between 5 and 16 keV, which **BL14.3** is a fixed-energy side station operated at an energy of 13.8 keV. The three MX beamlines have been differentially instrumented to support experimental techniques. BL14.1 features an MD2-microdiffractometer, a PILATUS 6M-detector and a CATS sample changer. It can be used for fast data collection, to analyze large sample ensembles and is capable to support very small crystals down to 10 µm smallest dimension. BL14.2 consists of a MARdtb goniometer and a 225mm Rayonix CCD-detector. In early 2015 the beamline will be upgrade with a nano-diffractometer, a PILATUS 2M-detector and an automated sample changer with a large capacity dewar.

The beamline produces a high quality long-wavelength beam at high intensity and is capable of the collection of large scattering angles of diffracted X-rays by its very short detector to sample distance of down to 50 mm. Hence, it can be used for long wavelength phasing applications like sulphur- and phosphorus-SAD as well as atomic resolution data collections. BL14.3 also has a MARdtb goniometer and 225mm Rayonix CCD-detector. It is currently operated as a general test beamline for the optimization of the diffraction properties of crystals with biophysical methods such as the controlled dehydration of crystals using the HC1c device. In addition to the beamlines, users have access to an S1-BioLab and a crystallization facility.

For more information about MX beamlines at HZB see
http://www.biostructx.eu/content/hzb-mx-beamlines?instTab=tech

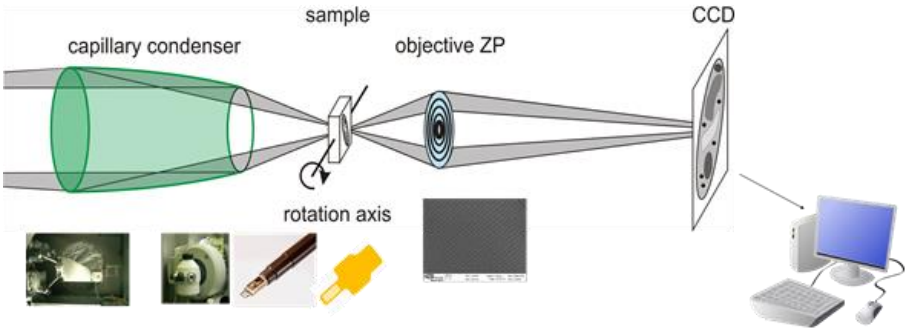
Centre Feature – Helmholtz-Zentrum Berlin für Materialien und Energie (HZB), Germany

With over 1300 PDB depositions and over 200 new depositions per annum, the HZB-MX beamlines are currently Germany's most productive facilities for MX.

Overview of the experimental hutch of BL14.1

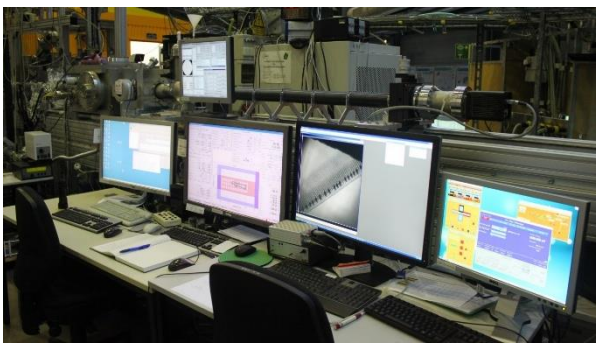
The **full-field Trans-mission X-ray Microscope (TXM)** is installed on an undulator beamline **(U41-TXM)** at HZB. It is operated between energies of 250 eV and 1300 eV and features a CompuStage-goniometer and a thinned backside-illuminated CCD detector from Roper Scientific. World-leading resolutions better than 30 nm have already been achieved for biological specimens and the resolution is being improved towards 10 nm via the development of new and improved zone plates.

Other developments include sample changing facilities, exploitation of different contrast methods and the correlation of the images with those from light and electron microscopy. Due to its leading capabilities this instrument attracts users throughout Europe and beyond and is approximately 2 times oversubscribed. Most of the time on the instrument is now devoted to biological applications.



X-ray optical setup of the full-field TXM with tomography stage for flat sample holders

U41-TXM also provides facilities for cryogenic preparation of cells, acquisition of high resolution tomograms at cryo-temperatures and data processing and analysis software for producing and examining tomographic reconstructions from the data. Together with the available fluorescence light microscope the simultaneous recording of fluorescence, bright field and DIC images of cryogenic samples, e.g. cells, inside the TXM is possible. The two complementary imaging modalities thus support correlative studies.



The X-ray microscope at the U41-TXM beamline

For more information about XI microscopy beamline at HZB see http://www.biostructx.eu/content/hzb-x-ray-imaging-beamline

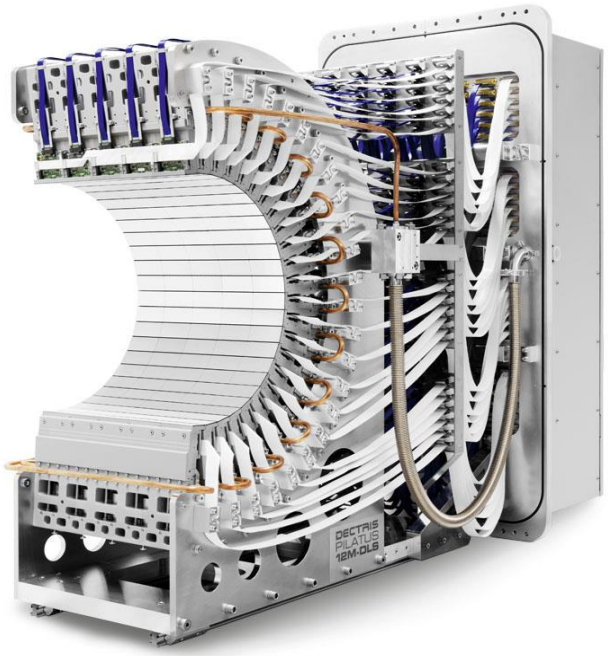
Partner Feature – DECTRIS Ltd., Switzerland

DECTRIS was the first company to provide Hybrid Photon Counting (HPC) detectors for synchrotron research and continues to be technology leader in X-ray detection. PILATUS detectors have set new standards for acquisition speed and data quality in crystallography and SAXS that many synchrotron beamlines and users benefit from. As a partner, DECTRIS contributes its expertise in detector specific corrections and data collection strategies to Work Package 6 of BioStruct-X.

Structural biologists can benefit from the advantages of DECTRIS HPC detectors at more than thirty crystallography and SAXS beamlines around the world, many of these accessible through BioStruct-X. Just recently, for instance, DECTRIS detectors helped Stephen Cusack and his team to achieve a major breakthrough with the determination of the structure of influenza A polymerase: “The high-intensity X-ray beamlines at the ESRF, equipped with state-of-the-art DECTRIS detectors, were crucial for getting high quality crystallographic data from the weakly diffracting and radiation sensitive crystals of the large polymerase complex,” says Cusack. “We couldn’t have got the data at such a good resolution without them”.

In addition to the popular and widely used standard detector models such as the PILATUS 6M, DECTRIS also designs and builds specific solutions that are tailored to the requirements of individual beamlines. A highlight of these specific solutions is the PILATUS 12M-DLS build for the I23 beamline of Diamond Light Source. This detector and beamline are optimized for long X-ray wavelengths and provide an ideal instrument for native SAD phasing and locating ions.

PILATUS HPC detectors



DECTRIS is a partner of BioStruct-X WP6 that aims at providing structural biologists easy methods and tools for the analysis of complex diffraction data using both synchrotrons and free electron lasers. The software enables full exploitation of the potential of HPC detectors in fine-phi slicing and further improves data quality by using crystallographic knowledge for more accurate detector corrections. DECTRIS contributes algorithms and data for accurate detector specific corrections to the newly developed software.

DECTRIS®

The PILATUS 12-DLS will help protein crystallographers to exploit long wavelength X-rays at I23 beamline of Diamond Light Source. The detector is an outstanding example for DECTRIS’ excellence in developing and building state-of-the-art HPC detectors.

www.dectris.com

Networking News

The aim of the networking work package (**WP10**) is to foster a culture of cooperation between the BioStruct-X participants and the scientific communities that benefit from the research infrastructures. Key tasks are to promote the dissemination of good practices, promote the clustering of and coordinated actions between related projects, coordinate with international related initiatives, support the deployment of global and sustainable approaches in the field, and to support training for new users.

In April 2014, two workshops funded by BioStruct-X within the scope of **task 10.4.1** took place. A workshop ***"Strategic pipeline planning: from sample preparation to 3D structure determination with bio SAXS and other biophysical techniques"*** was held at the National Hellenic Research Foundation (NHRF) in Athens, April 5th -10th 2014. The workshop targeted mainly PhD students and post-doctoral scientists and provided training on creating a roadmap towards determining the 3D structure of a macromolecular target with emphasis on BioSAXS as a method of choice to characterize the structure of a single protein and protein complexes in solution coupled with X-ray crystallography, NMR spectroscopy, and electron microscopy.

The ***8th International Workshop on X-ray Radiation Damage to Biological Crystalline Samples (RD8)*** took place in Hamburg, April 10th – 12th 2014 and consisted of 25 invited presentations covering recent results, practical understanding and new challenges to the field of radiation damage.

After a short summer break, the seventh course on ***Fundamentals of Modern Methods of Biocrystallography - BioCrys2014,*** addressing the fundamental theoretical concepts of Crystallography took place in the BioStruct-X TID centre ITQB in Oeiras, Portugal on 20th – 27th September 2014. The course was primarily aiming at PhD students and early stage researchers working in crystallography. The 36 participants attended formal introductory lectures to the high-throughput methods used in crystallography research that were followed up by practicals and tutorials addressing studies of membrane proteins and the use of free electron lasers in macromolecular Crystallography.

Upcoming Events

1st March – 1st April 2015
HERCULES School, Grenoble, France

23rd – 24th March 2015
Cryo 3D X-ray imaging of the cell – satellite workshop of the International meeting of the German Society of Cell Biology (DGZ 2015), Cologne, Germany

18th – 22nd May 2015
BioStruct-X TID centre OULU - Practical X-ray course on methods in protein crystallography, Oulu, Finland

19th May 2015
Second BioStruct-X / Instruct workshop on "Passed experiences and future challenges in providing access to the Structural Biology community" , Florence, Italy

20th – 22nd May 2015
Instruct Biennial Meeting, Florence, Italy

15th – 17th June 2015
BioStruct-X Industry Workshop, EMBL Hamburg/DESY, Hamburg, Germany

ITQB, Portugal, September 2014

NHRF, Greece, April 2014

EMBL HH, Germany, April 2014

News and reports of all networking events can be found on the BioStruct-X webpages under **www.biostruct-x.eu/content/networking**

Project Announcements

BioStruct-X installations that are no longer operational or have allocated all available units

- **The station I911-5 at MAX Lab** is permanently closed for user access
- **Elettra** experienced severe delays in the construction and the commissioning of the **XRD2 beamline** and will thus not be able to provide access on that beamline within BioStruct-X.
- **ESPRIT platform at EMBL Grenoble** has allocated all available BioStruct-X units and is now closed. BioStruct-X will no longer accept applications for this platform.

PETRA III at DESY back in operations in April 2015

The civil construction of the PETRA III extensions with the new experimental halls in the North and East is proceeding as planned and the restart of the user operation at the existing beamlines P11-P14 is planned from April 27th 2015.

Publications acknowledging BioStruct-X support

Please note that BioStruct-X support needs to be acknowledged by the following statement: *"The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under BioStruct-X (grant agreement N°283570)."* For the list of publications acknowledging BioStruct-X support, please visit the BioStruct-X website: http://www.biostructx.eu/content/publications.

User group questionnaire

One of the aims of the European Community Research Infrastructures Action is to provide scientists from anywhere within the Community with easy access to Europe's major research infrastructures. To enable the Commission to evaluate the Research Infrastructures Action, to monitor the individual grant agreements, and to improve the services provided to the scientific community, each Group Leader of a user-project supported under an EC Research Infrastructure BioStruct-X grant agreement is requested to complete the present "User Group Questionnaire". The questionnaire must be submitted once by each user group and can be found following the link below.
http://cordis.europa.eu/fp7/capacities/questionnaire_en.html

How to apply for Access

Interested researchers are invited to visit the BioStruct-X website (www.biostruct-x.eu) where they will find all relevant information about the participating facilities and platforms as well as information about the application process. Proposal submission is done entirely online. Submitted proposals will be evaluated by the Project Evaluation Committee (PEC).

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SEVENTH FRAMEWORK PROGRAMME

instruct Integrating Biology

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