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PSB et al

Partnership for Structural Biology Newsletter

Scientific highlights

What fn activities have yo been p to this smmer?

Oh gosh, so many typos in the PSB newsletter you may think - all U's missing! What if an RNA sequence would miss the U's? Nonsense you may think. Exactly! No U's, no AUG, no protein.

However, this is precisely the case in the mitochondria of kinetoplastids, a group of parasitic organisms that can cause severe diseases in humans and other mammals. These parasites have a fragmented mitochondrial genome: their genes encode cryptic pre-mRNAs. To complete the mRNA, uridines (U's) have to be added or removed in a process known as RNA editing [1].

The RNA editing process requires a complex protein machinery. Among the complexes involved, the RNA editing substrate binding complex (RESC) plays a crucial role. RESC serves as a platform for bringing mRNA and guide RNAs (gRNA) together. gRNAs are small template RNAs that carry the missing sequence information. The RESC complex ensures the correct timing of all catalytic steps of the editing. RESC1 and RESC2 are key components of the large RESC complex. Both proteins have been identified to stabilize gRNAs [2]. Interestingly, RESC1 and RESC2 lack sequence homology with characterized proteins, and no RNA binding motifs have been found. For that reason, their specific role in RNA editing has been unclear and it was not obvious how they would interact with RNA.

Recently, the Kowalinski group at EMBL Grenoble made significant progress in understanding the function of RESC1 and RESC2 in RNA editing [3]. Using Cryo-EM, they successfully determined the three-dimensional structure of the RESC1-RESC2 complex. This structure revealed why RESC1 and RESC2 always form a dimer and suggested how gRNAs may be bound at two potential binding sites. Through the utilization of the PSB platform, Protein Analysis On Line (PAOL), the researchers demonstrated that only one of the subunits actually interacts with RNA. Biochemical experiments confirmed that the RNA recognition occurs through a triphosphate at the 5'-end, a characteristic and unique feature of gRNAs. Additionally, a second cryo-EM dataset was obtained, this time of the RNA-bound RESC1-RESC2 complex. This data, collected using the Titan Krios CM01 at the ESRF operated by the PSB partners, supported the notion that RESC2 is indeed the RNA-binding subunit in the complex (Figure).

Overall, this first structure of an RNA-bound RESC module, revealed that the 5'-triphosphate is a key feature of gRNAs that is recognized by RESC. Furthermore, it establishes the RESC1-RESC2 complex as 5'-end binding complex that may protect gRNAs from endonuclease cleavage, therefore stabilizing gRNAs in general. Moreover, the study opens avenues for potential therapeutic interventions targeting these crucial protein complexes to combat parasitic diseases.

L. Dolce and E. Kowalinski (EMBL)

[1] JM Shaw, JE Feagin, K Stuart, L Simpson (1988). Cell. **53**, 401–411.
[2] LK Read, J Lukes, H Hashimi (2016). Wiley Interdiscip Rev RNA. **7**, 33-51.
[3] LG Dolce, Y Nesterenko, L Walther, F Weis *et al.* (2023) Nucleic Acids Res. **51**, 4602–4612.

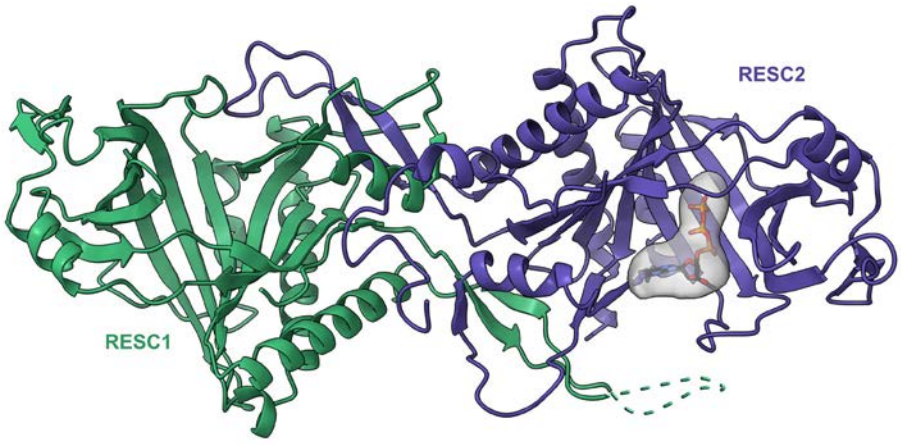


Figure: Cartoon model of RESC1–RESC2 with the 5' triphosphate (modelled as a GTP) shown as sticks and colored by heteroatom. Inside RESC2, as a grey surface, we see a density for the 5' triphosphate, generated by subtraction of the RNA-bound and unbound maps.

CONTENTS

New hope in the fight against malaria

Malaria, a mosquito-borne disease caused by *Plasmodium* parasites, poses a significant global health challenge. According to the World Health Organization (WHO), malaria caused 627,000 deaths in 2020, with the majority occurring among children under the age of five. While malaria is primarily prevalent in tropical and subtropical countries, Europe is also vulnerable to the disease due to global climate change and easy international travel.
In recent years, there has been notable progress in antimalarial therapeutics. However, the parasite is developing resistance to all existing treatments, including current first-line therapies that contain artemisinin-based combination therapies. The first-ever malaria vaccine entered the market in October 2021, but its efficacy remains relatively modest.

Therefore, there is a need to explore new therapeutic approaches. An international collaboration of scientists, including Dihia Moussaoui from the ESRF and Institut Curie in France, the University of Vermont in the USA, and Imperial College in the United Kingdom, conducted research on a large molecular complex known as the glideosome, which plays a critical role in the movement of the *Plasmodium falciparum (Pf)* parasite.
The study revealed that the motor component (PfMyosin) within this glideosome complex, specifically *Pf* myosin A (PfMyoA), is an essential protein for the parasite's life cycle [1, 2, 3]. Without PfMyoA, the parasite cannot move within its host or infect human cells. Myosins belong to a large class of molecular motors that generate force and movement using ATP, the energy currency in living organisms. Importantly, PfMyoA is specific to malaria parasites and sufficiently distinct from human myosins, making it a potential target for antimalarial drugs.

Building upon these findings, the research team focused on a promising inhibitor called KNX-002, which specifically

binds to PfMyoA. They conducted studies on living malaria parasites and obtained highly promising results: in the presence of KNX-002, the parasites were unable to invade human red blood cells. The inhibitor was subsequently crystallized in complex with PfMyoA, and the high-resolution structure was determined using the structural biology beamline ID30B at the ESRF, the data were collected with Christoph Mueller Dieckmann, the beamline responsible. The atomic level structure revealed how KNX-002 interacts near the ATP binding pocket of PfMyoA (Figure), thereby blocking its ability to generate force. This breakthrough lays the foundation for the development of a new class of antimalarial treatments [1].

D. Moussaoui, C. Mueller-Dieckmann (ESRF)

[1] D. Moussaoui, C. Mueller Dieckmann *et al.* (2023). Nature Commun., **14**, 3463.
[2] D. Moussaoui *et al.* (2020). eLife, **9**, 60581.
[3] J. Robert-Paganin , D. Moussaoui *et al.* (2019). Nature Commun., **10**, 3286 .

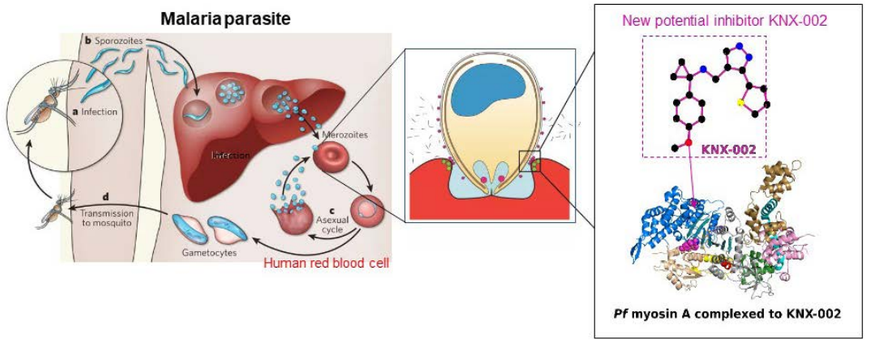


Figure: KNX-002, the first inhibitor of Plasmodium molecular motor. Malaria is caused by *Apicomplexan* parasites of the genus Plasmodium. The life cycle of Plasmodium is complex, and the symptoms (headaches, anemia) are due to the phases of asexual reproduction during which the merozoite stages infect blood cells. The infection relies on a specific molecular motor called Myosin A. We described the effect of a small molecule capable of inhibiting the activity of Myosin A: KNX-002.

Understanding the production of the colibactin genotoxin in *E. coli*

The continuous development of novel antibiotics is crucial in the actual context of bacterial resistance to classical antibacterial molecules. We are focusing our research on natural molecules production from the Polyketide/Non-Ribosomal Peptide synthase (NRPS/PKS) family of enzymes that are often used by microorganisms to synthesize antibiotics or antifungal molecules for interspecies competitiveness [1]. In particular we are interested in the *pks* operon present in *E. coli* that is responsible for the biosynthesis of the colibactin genotoxin involved in the development of colorectal cancers. The *pks* operon is composed of 19 genes and amongst them, 8 belong to the NRPS and PKS family, acting as an assembly line in order to synthesize the new natural colibactin product. Interestingly, due to their similar mode of action, these PKS and NRPS modules can associate on the same polypeptide in order to produce highly diverse hybrid products.

In this study, we have deciphered the three-dimensional architecture of a key component of the colibactin biosynthesis machinery, the NRPS/PKS hybrid ClbK protein by biophysical and structural methods including small angle X-ray scattering (SAXS) and X-ray crystallography (Figure) [2]. First, we solved the structure of the PKS module of ClbK by X-ray crystallography using the ESRF beamline ID30A-1. The structure reveals several adaptations compared to pure PKS modules that are associated to its hybrid nature. Next, we used the SEC-MALLS PSB platform located at the IBS in order to determine the oligomerization state of full-length ClbK. Surprisingly, we could identify two different sites of dimerization, one on the PKS module and one on the NRPS module. Finally, we used the ESRF beamline BM29 for SAXS measurements on full-length ClbK in order to obtain the first complete picture of a PKS/NRPS hybrid protein.

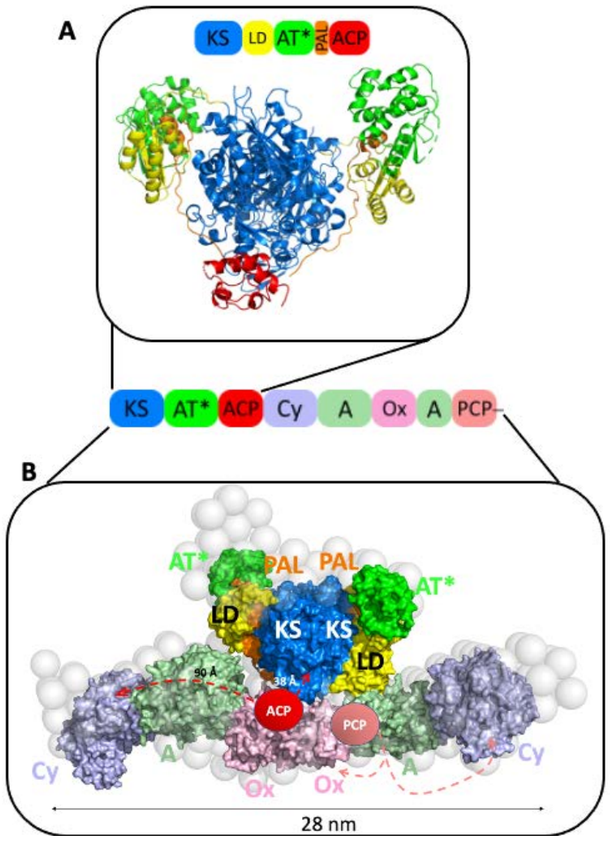


Figure: Multi-scale structural characterization of (A) the PKS module of ClbK by X-ray crystallography and (B) full-length ClbK by small-angle X-ray scattering.

This first structural characterization of a PKS/NRPS hybrid enzyme from the colibactin assembly line will pave the way for a better comprehension of this very complex enzymatic pathway leading to the production of a genotoxin. In addition, this structural information will be helpful for the biosynthesis of new molecules by biochemical engineering. Indeed, NRPS and PKS enzymes synthesize very diverse metabolites and many efforts have been made this past decade to rationally engineer NRPS/PKS assembly lines. For now, this engineering has focused on pure NRPS or PKS systems; however, the combination of the two, as nature does, could generate highly diverse metabolites with many applications. Future engineering on hybrid megaenzymes could thus benefit from this work.

P. Macheboeuf (IBS)

[1] S. Bonhomme, A. Dessen, P. Macheboeuf (2021) Open Biol. **11**, 200386.
[2] S. Bonhomme, C. Contreras-Martel, A. Dessen, P. Macheboeuf (2023) Structure **31**, 700-712.e4.

An F-box cofactor acts by forming a transcriptional complex with a master regulator transcription factor during flower development

In plants, the formation of flowers is a major developmental transition that requires a deep genetic reprogramming. At this step, many flower-specific genes must be activated to produce the different floral organs. Genetic studies in the model plant *Arabidopsis thaliana* allowed the identification of several key regulators of flower development. One of them is LEAFY (LFY), a transcription factor (TF) discovered more than 30 years ago. This unique TF is of paramount importance in flower development as it activates most of the genes required for flower production. Given its importance, LFY was extensively studied over the past years; most of its target genes are known and its DNA-binding properties are described *in vivo* and *in vitro*. It is also well established that LFY's activity is very adjustable and that several cofactors finely tune its transcriptional activity.

The best-described LFY cofactor is UNUSUAL FLORAL ORGANS (UFO). LFY and UFO act together in a synergistic way, in particular to activate genes required for petal and stamen development. However, the molecular mechanism underlying this synergy was unknown, and it was not clear why LFY requires UFO for some gene activations but not for others. The role of UFO in transcription regulation was also very intriguing as UFO belongs to the F-box protein family, a family of proteins usually involved in the ubiquitination and the degradation of their targets.

In this work, we dissected the molecular basis of the LFY-UFO synergy [1]. First, we established that LFY requires UFO to activate some promoters but not others, revealing that DNA sequences dictate whether the two proteins act together or not. To explain these results, we then performed *in vitro* genomic assays and we found that LFY and UFO form a transcriptional complex that binds a new DNA motif that LFY cannot bind on its own. We called this new motif, jointly bound by the two proteins, the LFY-UFO Binding Site (LUBS). We identified LUBS in the regulatory sequences of several LFY-UFO target genes and we confirmed that these sites are necessary for their activation.

A closer examination of the LUBS motif showed that it comprises a canonical LFY Binding Site (the previously-described DNA motif bound by LFY alone) but also a specific signature that we called the UFO Recruiting Motif (URM). To better understand the position of each protein in the complex, we reconstituted in vitro an LFY-UFO complex bound to an LUBS site and we characterized it using cryo-EM (Figure). We found that UFO binds both LFY and DNA at the URM, thus explaining its role as a cofactor.

Our study demonstrates how UFO modulates the activity of the master regulator LFY by redirecting it to new sites. The mechanism we uncovered is also a very unique case where an F-box protein acts through its ability to bind DNA. Finally, as the existence of LFY-UFO complexes was demonstrated in many other plant species, our results will help to understand how flowers are formed in many plant species, including crops.

P. Rieu (CEA-IRIG, LPCV)

[1] P. Rieu, L. Turchi, L., E. Thévenon, E. Zarkadas *et al.* (2023) Nat. Plants **9**, 315-329.

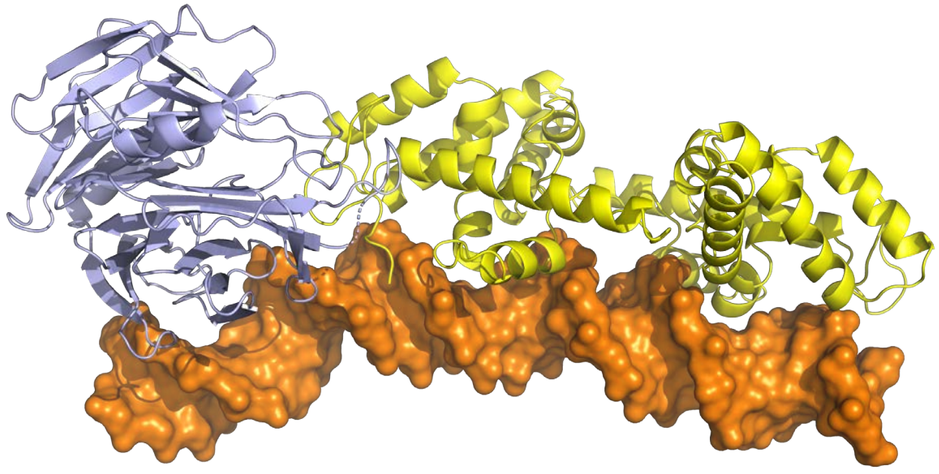


Figure: The *Arabidopsis* transcription factor LFY forms a transcriptional complex with its cofactor UFO on a new DNA motif. The LFY DNA-Binding Domain (DBD) dimer is shown in yellow and UFO in light blue. The LUBS DNA is colored in orange.

Developing advanced models of biological membranes composed of natural glycerophospholipids

Cellular membranes are complex systems composed of several glycerophospholipid (GPL) species, that are characterized by a polar head bound to a distinct structural backbone that is further linked to a tail composed of various acyl chains. This, therefore, allows for the generation of a plethora of combinatorial chemical possibilities. Due to the high level of complexity, their investigation often relies on simpler model systems built from fewer synthetic GPL species. In order, to be able to recreate a more biologically relevant cell membrane, GPL molecules extracted from eukaryotic cells can be a valuable resource to produce more advanced models of biological membranes. In addition, the ability to deuterate GPL molecules adds a powerful dimension to investigate biomimetic membrane models by employing neutron scattering techniques. Currently, such studies are hampered by the low availability of several biologically relevant deuterated species in their unsaturated form. This limitation could be overcome by extracting and separating GPL molecules from microbial cells that are adapted to deuterated conditions.

After several years of efforts, we have recently attained success in isolating deuterated GPL class mixtures from total lipid extracts after producing them biologically in *Pichia pastoris* in the D-lab facility at ILL. This was achieved by employing high-performance liquid chromatography coupled to an evaporative light scattering detector (HPLC-ELSD) (see Figure). Molecular compositional analysis of these natural polar mixtures as shown by gas chromatography (GC), showed that biodeuteration led to an alteration in the relative abundances of fatty acyl chains. Given these differences, for a recent study, we utilized these mixtures to create bilayer model membrane systems comprising either phosphatidylcholine/phosphatidylserine or phosphatidylcholine/phosphatidylglycerol [80:20 w/w], both in their hydrogenated ('H') and deuterated ('D') variants. Thereafter, substantial efforts at the Partnership for Soft and Condensed Matter (PSCM) and Partnership for Structural Biology (PSB) have been deployed to well-characterize these model membranes by various physico-chemical and neutron scattering techniques thus allowing us to increase our understanding of systems resulting from them. Detailed characterization was carried out on lipid bilayers both on solid substrates and as vesicles in solution. The supported lipid bilayers were characterized by quartz crystal microbalance with dissipation monitoring (QCM-D) and neutron reflectometry (NR), whereas the vesicles by small-angle X-ray (SAXS) and small-angle neutron scattering (SANS). In our latest publication, we show that despite a small difference in the acyl chain composition, the 'H' and 'D' mixtures produced bilayers with very comparable structures, thus making them valuable to design experiments involving selective deuteration with techniques such as nuclear magnetic resonance spectroscopy, neutron scattering or infrared spectroscopy [1]. All these developments enable researchers to mimic natural bilayers thus helping pursue neutron scattering investigations.

K. C. Batchu (ILL) and G. Corucci (Imperial College London)

[1] G. Corucci, K.C. Batchu, *et al.* (2023). J. Colloid Interface Sci, **645**, 870-881.

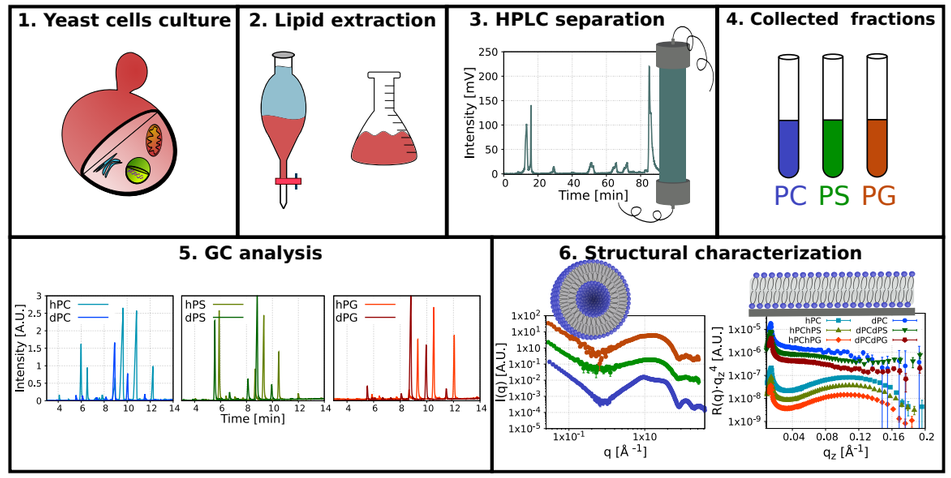


Figure: Pipeline depicting steps undertaken to extract and purify glycerophospholipid (GPL) mixtures and characterization of membrane bilayer systems composed of these mixtures.

News from the platforms

TR-*ic*OS: a new instrument for microsecond time-resolved *in crystallo* UV-vis absorption spectroscopy at the *ic*OS Lab

Photoactive protein dynamics is being studied in the crystalline state at synchrotron sources for timescales ranging from microseconds to minutes. *In crystallo* optical spectroscopy (*ic*OS) can be used to complement time-resolved (TR) X-ray crystallography experiments: to estimate the optimal number of photons needed to trigger a given photoreaction, to detect potential artefacts resulting from the crystalline state and to identify the most relevant time points. A dedicated laboratory, named the *ic*OS Lab [1], has been jointly developed over the years by the IBS and the ESRF to record optical spectroscopy data from protein crystals. We have recently developed there the dedicated TR-*ic*OS setup for time-resolved spectroscopic experiments using a pump-probe scheme with a time resolution of a few microseconds. It is composed of a tunable nanosecond laser as pump, a xenon flashlamp as probe and an optomechanical setup focusing light onto crystals (Figures A and B). Slurries of (micro) crystals are placed in-between two layers of UV-visible light transparent films of COC polymer (Figure C). The instrument was commissioned using crystals of the membrane proton pump bacteriorhodopsin, whose photocycle could be monitored between 3 microseconds and 600 milliseconds (Figure D). The TR-*ic*OS setup will help assist diffraction measurements on the newly built serial crystallography beamline ID29 in its TR operation mode.

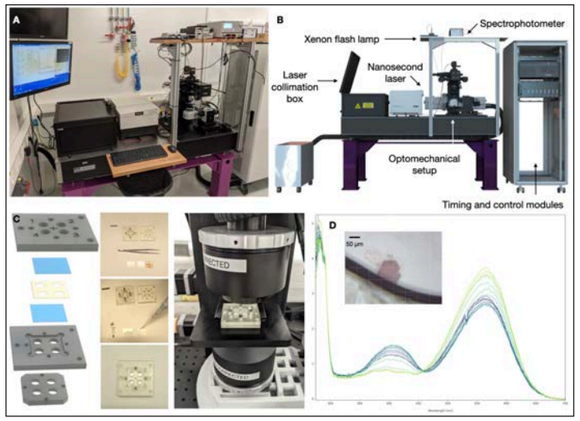


Figure: A. Photo, and **B**. Schematic representation of the TR-*ic*OS setup. **C**. Principle of the crystalline sample holder. **D**. Series of UV-vis absorption spectra obtained on a bacteriorhodopsin crystal with delays ranging from 3 µs and 600 ms after 532 nm laser excitation.

S. Engilberge (IBS) and A. Royant (IBS/ESRF)

[1] D. von Stetten, T. Giraud, P. Carpentier, F. Sever *et al.* (2015). Acta Crystallogr. D**71**, 15-26.

New OMNISEC at the ISBG Biophysics Platform

An OMNISEC instrument (MALVERN) has been installed on the biophysics platform. Funded by the EMBL, the new OMNISEC is replacing the SEC-MALLS. The instrument combines size exclusion chromatography and multiple detectors (static light scattering at two angles, UV, refractive index and viscometer) to access molecular weight, hydrodynamic radius, oligomerisation, aggregation and the homogeneity of your biological samples. The platform provides various columns for your analysis (Superose 6 10/300 increase, Superdex 200 10/300 increase, Superdex 75 10/300 increase and Superdex 30 10/300 increase). The instrument has been installed in CIBB room 001.

The new OMNISEC instrument at the biophysics platform of the ISBG.

The platform offers a service for OMNISEC analyses: all analysis requests must be accompanied by an application form (download here: https://www.isbg.fr/biophysics-characterisation/sec-malls/?lang=en). The form is completed in consultation with platform staff in order to assess feasibility and define the best strategy for conducting the study, before validation by signature by both parties. Platform staff will perform the experiment and will provide training in data analysis. The first data analysis session will be held in September 2023. More information can be found on our website. You can also contact Aline Le Roy (aline.le-roy@ibs.fr) or Caroline Mas (caroline.mas@ibs.fr).

C. Mas (ISBG)

20 YEARS 2002-2022

A Brief history of the PSB

2022 marked the 20th Anniversary of the Partnership for Structural Biology (PSB) that has grown from a long history of collaboration between research institutes located on the European Photon and Neutron (EPN) campus in Grenoble. In early 1977, the Institut Laue-Langevin (ILL) and the European Molecular Biology Laboratory (EMBL) concluded an agreement on scientific co-operation in the field of biological research, which led to the construction of a joint ILL/EMBL building in support of biological work at ILL. In 1992, the EMBL and the European Synchrotron Radiation Facility (ESRF) signed a memorandum of understanding (MoU) concerning the optimisation and use of the ESRF for molecular biological research through beamline design and construction, as well as a collaborative use of the various facilities.

Signing ceremony of the MoU to establish the PSB. From left to right: Colin Carlile (ILL), William G. Sterling (ESRF), Fotis C. Kafatos (EMBL), André Syrota (CEA), Bernard Pau (CNRS), and Yannick Vallée (UJF).

In the same spirit, the PSB was established on 15 November 2002 by a MoU involving four partners, the EMBL, the ESRF, the ILL and the Institut de Biologie Structurale (IBS). The aim of this partnership was to benefit from each other's expertise and resources, and to establish a unique multi-disciplinary environment for integrated structural biology, creating a European Centre of Excellence for the study of challenging problems, notably in human health.

The first Scientific Advisory Board (SAB) review took place in January 2006 and coincided with the inauguration of the Carl-Ivar Brändén building (CIBB), which houses research teams from all PSB partners and several technical platforms. The CIBB is centrally located on the EPN campus and its construction was funded by the PSB partners and the Université Joseph Fourier (UJF). The building was initially shared with the Institut de Virologie Moléculaire et Structurale (IVMS) which, in 2007, transformed into a "Unité Mixte Internationale" (UMI): the EMBL-UJF-CNRS International Unit of Virus Host Cell Interactions (UVHCI). As an associate member of the PSB, the UVHCI offered the PSB a direct link to Grenoble's University Hospital and, thanks to its expertise in virology and cellular biology, enabled the building of bridges between structural biology and medical subjects. This association lasted until 1st January 2016, when the French groups of the UVHCI joined the IBS (while remaining in the CIBB). In October 2013, the IBS moved onto the EPN campus into a larger purpose-designed building that has allowed the institute to host new teams, and to further enhance the synergy of the PSB.

13 January 2006 – CIBB Inauguration

Since its creation, the PSB has dedicated large efforts and manpower to the development of its platforms in order to provide the local and external scientific community with state of the art tools and cutting edge technologies. The PSB platforms have grown impressively both in number and complexity from the six that were installed at the outset, to 17 or so that we have today (see list here: https://www.psb-grenoble.eu/spip.php?rubrique4), including the Titan Krios cryo-electron microscope at ESRF, which is run as a beamline (CM01), and whose operation is carried out by a team comprising members of all partner institutes, providing an excellent example of a PSB collaboration benefitting a wide range of international users.

Today the PSB is a mature organisation involving over 300 structural biologists, including 45 postdocs and 75 PhD students. The research carried out within the PSB is broad and diverse, but several strong and clearly identifiable research themes have nevertheless emerged, such as: host-pathogen interactions; membrane proteins; fundamental cellular processes (e.g. transcriptional regulation); extremophiles, and among all the publications produced by PSB scientists every year, close to 15% have multi-partner authorship involving at least two of the PSB partners.

In view of the success of the PSB over the years, on 1st January 2021 the partners haved renewed their engagement in the Partnership by extending their Collaboration Agreement for a further five-year period.

The CIBB building named after Carl-Ivar Brändén (1934-2004), who was a visionary in structural biology. After developing structural biology in Uppsala, Sweden, he joined the ESRF as Director of Research between 1992 and 1997. During this period he played a pivotal role in stimulating structural biology research activities in Grenoble.

20 YEARS 2002-2022

Short reflections on 20th anniversary of the PSB

Stephen Cusack (EMBL Grenoble)

How were you involved in the beginning of the PSB?

As Head of EMBL Grenoble, I was involved in the early discussions leading to the founding of the PSB and almost everthing that happened thereafter until my retirement from EMBL at the end of 2022. The PSB was a new millennium project inspired by the ambition and promise of two major advances occurring in the year 2000: the publication of the first high-resolution crystal structures of fundamentally important, multi-subunit biological complexes, the ribosome (Steitz lab) and RNA polymerase II (Kornberg lab) and, secondly, the completion of the first survey of the entire human genome (announced by Bill Clinton in June 2000, but published in 2001) predicting around 25000 genes. The former showed that structural biology was capable of giving atomic level mechanistic insight into the functioning of large multi-subunit molecular machines, whilst the latter led to the humbling realisation that we knew nothing about most human proteins. More parochially, in 1999 EMBL and ESRF were contacted by Robert Cooke (GlaxoWelcome), who was trying to set up the nascent Structural Genomics Corporation (a pharma industry initiative to do large-scale structure determination on proteins of human health interest) with a view to our engagement in the project as a production centre. The realisation that we were not set up to do integrated large-scale structure determination from gene to structure inspired the vision of setting up on the EPN Campus a 'Centre of Excellence for Structural Biology' with a focus on high throughput methods of structure determination applied to problems related to human health. In a remarkably short time, EMBL, ESRF and ILL management (and slightly later, the IBS and Grenoble University Joseph Fourier) signed up to this project, endorsing joint plans to establish advanced protein production methods (e.g. ESPRIT and EEF), a deuteration facility (D-lab), high-throughput crystallisation (now HTX), a new, dual endstation protein crystallography beamline (ID23) and construction of a new shared building to act as the PSB focus (the CIBB, opened in 2005, and incorporating the new UJF-EMBL-CNRS Unit of Virus Host Cell Interactions (UVHCI)). Even the European Comission took note by awarding us a 'Construction of a new infrastructure' grant (2004-2007), which I co-ordinated, to establish the 'CISB' (Centre for Integrated Structural Biology).

How has the PSB contributed to the science in your institute?

The PSB has underpinned most of the research done at EMBL, fluidifying access to essential structural biology techniques not available at EMBL itself (NMR, mass-spectroscopy, biophysics, X-rays), as well as promoting inter-institutional collaborations. Speaking for myself, my multi-disciplinary reaearch on influenza polymerase (initially in collaboration with Rob Ruigrok's group), especially in the phase leading up to the first structure of the complete polymerase, requiring for example ESPRIT, EEF, biophysics, NMR, X-ray crystallography that I don't think could have been done anywhere else.

What is the best achievement of the PSB in your opinion?

The beauty of the PSB was that, by enhancing the quality, efficiency and ease of access to advanced structural biology infrastructure, and regularly upgrading these facilities as instituional budgets permitted, it enhanced the visibility and attractiveness of the Campus for both external users and on site scientists, all of whom could benefit from the PSB's 'uniquely comprehensive palette of structural biology techniques'. It is not unusual that papers are published that make use of technologies at multiple PSB institutes. On another level, the PSB through its various animations, training and outreach activities has contributed to creating a sense of identity amongst structural biologists on the EPN Campus. Perhaps the single most significant action was that all four institutes, taking stock of the cryo-EM resolution revolution, contributed to setting up and running the Krios CM01 at the ESRF from 2017. This maintained the site as an advanced center for not only X-ray and neutron technologies but also electron cryo-microscopy.

Prof. Rob Ruigrok (Université Grenoble Alpes)

How were you involved in the beginning of the PSB?

Around 1996, and after working at the EMBL since 1988, I was looking to start a larger initiative to study viruses. After discussing this possibility with many people it was Michel van der Rest and Emmanuel Drouet who really championed the cause with me.
After many meetings with representatives at the state, regional and local level we finally managed to secure a significant amount of funding in the CPER (contrat de plan État-Région) for a new building to host these activities. Around the same time there was an urgent need from the ILL, ESRF and EMBL for additional laboratory space so in the end it really made sense to combine resources for the common scientific good. Roland Douce, the IBS director at the time, and Pierre Berard from the Université Joseph Fourier (UJF - now Université Grenoble Alpes) were really supportive. In 2003 I joined the Université to lead their contribution to the creation of new Unit of Virus Host Cell Interactions (UVHCI), a Unite Mixte International (UMI 3265 UJF-EMBL-CNRS) in 2007 that I co-directed with Stephen Cusack (EMBL). This was situated in the new CIBB building and the opening of several scientific positions at the UJF and CNRS. The unit was dissolved in 2015 and integrated with the IBS when they moved onto the EPN campus.

How has the PSB contributed to the science in your institute?

The creation of the PSB and CIBB enabled the recruitment of several talented research scientists, including Winfried Weissenhorn, Wim Burmeister, Guy Schoen, and Thibaut Crepin, to name just a few. This provided a critical mass of researchers that enabled the UVHCI to attract substantial external funding to tackle fundamental questions in influenza, rabies, measles and Epstein-Barr viral biology. It was an exciting time with weekly scientific meetings in viral biology and even though I contemplated positions elsewhere none of them could really provide the range of platforms and techniques available within the PSB.

What is the best achievement of the PSB in your opinion?

A key feature of the PSB was the establishment of many diverse platforms, which is still quite unique in the world and one of its major strengths. For example the ESPRIT platform run by Darren Hart (EMBL) allowed us to identify the first structured domains of Influenza polymerase and the Eukaryotic Expression Facility established by Imre Berger (EMBL) enabled recombinant Influenza polymerase hetero trimers to be produced for biochemical and structural studies. This common pooling of resources ensures they are accessible to everyone and really complements the diverse structural biology techniques
(X-ray, neutrons, NMR and Cryo-EM) available on the EPN campus. With EU funding (FLUPOL and FLUPHARM) and PSB platform support the UVHCI was able to answer fundamental questions on the Influenza polymerase, which is probably the best collective achievement so far. Now it's time for the newer PSB groups to identify a new and exciting scientific challenge, whatever that may be.

Ed Mitchell (ESRF)

How were you involved in the beginning of the PSB?

I was asked to join in the PSB build-up from about 2003 as a kind of project manager and then general manager once the PSB existed on the ground. Lots of work with the admin people in contracts, Jo Sedita for the buildings work, Pierre Métais for setting up lab services. Exciting times with the new building, new people working together from the PSB partners.

How has the PSB contributed to the science in your institute?

Structural biology is special. Sample preparation is somehow the ultimate bottleneck. The PSB allowed ESRF a step function improvement in sample preparation for in-house and collaborative research, which is important for attracting scientific staff to the ESRF, and also providing facilities for the users.

What is the best achievement of the PSB in your opinion?

Inspiring other similar centres to be created. Now the PSB needs to look to what it wants to be, must be, in 2030; how to better serve science, our user communities and drive solutions to real challenges that the world faces by drawing on and drawing together the extraordinary technologies and brains which make up the PSB.

Prof. Eva Pebay-Peyroula (Université Grenoble Alpes)

How were you involved in the beginning of the PSB?

I was representing IBS in the PSB steering committee from 2002 as a deputy director of IBS, then from 2004 to 2014 as the IBS director.

How has the PSB contributed to the science in your institute?

It is more difficult to give precise scientific examples. But more generally, thanks to the synergy between the partners, structural biology in Grenoble became visible by French authorities and institutions and this was essential to get the funds to build IBS2. IBS was thus inserted into a European environment. All this contributed to attract scientists, to favor collaborations and obtain external grants..

What is the best achievement of the PSB in your opinion?

Setting up common platforms is the most important achievement. We have now on site an ensemble of technics that are remarkable. Among the instruments, the development of cryo-EM was the most impressive. The strong support by the PSB scientific advisory board was certainly instrumental to push the requests for microscopes.

Trevor Forsyth (LINXS Institute of Advanced Neutron and X-ray Science, Lund, Sweden)

How were you involved in the beginning of the PSB?

I was involved in the development of the PSB from its inception, initially through the involvement of a platform for biological deuteration (D-Lab) in the early 2000s, and subsequently as the Head of ILL's Life Sciences Group, located in the top floor of the Carl Ivar Bränden Building (CIBB). The strongest impression I had upon arrival at ILL in 1999 was that the single most important aspect of neutron scattering for the study of biological systems – the use of isotope labelling (in particular deuterium labelling) – was massively underexploited. With management backing from Colin Carlile and Christian Vettier (ILL Directors of the day), we secured major grant funding from the UK research councils (EPSRC) for the creation of a deuteration facility. This formed the basis of ILL's Life Sciences group which matured to fulfil key service roles as well as a thriving in-house research programme and strong connectivity to the international user base. These capabilities, and the close connectivity that developed with the other PSB platforms in CIBB and elsewhere have had a crucial impact for ILL-driven science ever since.

How has the PSB contributed to the science in your institute?

The PSB had very special importance to ILL – in fact it could be argued that it helped stop declining usage of neutrons for the study of biological systems. This occurred mainly through the enhanced access to deuterium labelling given that without this capability, the use of neutrons offered relatively little beyond what could be done with X-rays. However major impact also derived from the fact that neutron methods are at their very best when combined with other methods – notably X-rays, NMR, cryo-EM, mass spectrometry, etc. The PSB provided an amazing array of technology platforms that were easily accessible to ILL-driven science, as well as a strong collaborative ethos across the campus.

What is the best achievement of the PSB in your opinion?

It is possibly unwise to single out any one particular achievement given that the PSB had such a broad impact. Crystallographic, small-angle scattering, reflection, and spectroscopic studies have all benefitted from step changes in capability and as reflected by successive external reviews of the PSB, there have been some dazzling high-profile publications and a huge effect on the quality of science arising from ILL instrumentation. The PSB has played a pivotal role in the development of what is now widely known as *Integrative Structural Biology*. It also provided an outstanding resource for training of placement students, PhD students, and postdoctoral researchers – providing very tangible impact on ILL's research reputation as well on the creation of the next generation of researchers.

EVENTS

PSB SAB review and twentieth anniversary celebration

The PSB Science Advisory Board (SAB) review took place on 30 and 31 May 2023. The SAB is composed of eight internationally renowned scientists (current composition: Robert Gilbert, Oxford U., UK; Birthe Kragelund, U. Copenhagen, DK; Sandra Macedo-Ribeiro, IBMC, PT; Andrea Mattevi, DBB, IT; Guillermo Montoya, U. Copenhagen, DK; Lori Passmore, MRC-LMB Cambridge, UK; Jeremy C. Smith, U. of Tennessee/ORNL, USA; and Henning Stahlberg (Chair), EPFL, CH), who visit the EPN campus every 3-4 years to critically evaluate the functioning and organisation of the partnership, and give advice to maintain the high quality and standard of the PSB science and services. On day 1 of the review, an overview of the PSB activities and actions was presented to the SAB, and the heads and science directors of EMBL, ESRF, IBS and ILL, who then presented their respective institutes and described their relation and interactions with the PSB. Latest developments of platforms were also presented, and in particular of cryo-EM on the EPN campus with the collaboration on CM01, and the construction of the future CM02. The SAB then visited several of the plaforms and instruments in the four institutes, and had the opportunity to interact with the people in charge of these facilities, which enabled the panel to better understand how things work in practice. In the evening, the SAB had dinner with the PSB Steering Committee and Science Board to continue the discussion informally.

Excitement was in the air in the morning of Day 2 (31st May), as the SAB members gathered with over 110 participants in the IBS seminar room for the celebration of the PSB twentieth Anniversary. Eva Pebay-Peyroula, former IBS director, opened the day and described the route that led to the creation of the PSB and how structural biology has evolved since the early 2000s, pointing out how different scientific projects have benefitted from the PSB collaboration. The great science performed in the PSB today was then showcased through its young scientists. Lindsay McGregor (ESRF) described her work to understand the root causes of Alzheimer's disease, Victor Armijo Gomez (EMBL) presented the latest developments in the EMBL Instrumentation Team to automate cryo-EM/ET and X-ray nano-imaging sample preparation, Lukáš Gajdoš (ILL) explained his studies of protein-carbohydrate interactions using neutron diffraction, and Rebekka Wild (IBS) illustrated how the polymerisation mechanism of heparan sulphate chains can be revealed thanks to 3D structures. The quality and diversity of the research projects performed within the PSB were also further highlighted through flash presentations by eight PhD students from all four Partners. The closing talk was given by Stephen Cusack, former head of EMBL Grenoble, who further described the history and the milestones in the evolution of the partnership, and detailed reasons for success of the PSB, thanks to 'a great environment for great science'. He then concluded his talk by describing the future 'big' challenges to be faced, and discussed strategies for the future developments of the PSB to maintain a leading role in Europe for Structural Biology. The morning session then ended with a large cocktail lunch buffet during which all the participants in the audience could continue to discuss and interact in a lively and informal setting.

In the afternoon, the SAB met with a panel of PhD students and postdocs, to discuss their views and experience in the PSB. The SAB panel then had concluding discussions with the PSB Science Board and Steering Committee, and a closed working session to prepare their written report which final version was sent a few weeks later. The feedback of the SAB was overall very positive, and among other comments stated that “the initial mission of the PSB, to efficiently determine and make publicly available structures of biologically relevant proteins, using the combined possibilities of the four institutes, has been extremely successful”, and that “the PSB has been a major player in the highest-resolution and dynamic (time-resolved) structural analysis of macromolecules. The PSB works and has seen two amazingly successful decades of operation!”

In the evening of 31 May the twentieth anniversary celebration then continued, as dozens of participants gathered in the EPN Chalet to share a lively and friendly moment with refreshments, a great barbecue, and delicious cakes!

F. Bernaudat (PSB)

Photos: M. André, F. Bernaudat, J. Devos, V. Guerard, S. Monfront & A. Stanescu

PSB Symposium "Dynamics in Structural Biology"

© M. Duding

The fourth edition of the PSB biennial Symposium focused on " Dynamics in Structural Biology" (www.esrf.fr/psbsympo-sium2023), and took place on 6th and 7th July 2023. The aim of this meeting was to illustrate how big biological questions can be resolved in structural biology through the application of interdisciplinary methodological approaches (including, but not limited to, cryo electron microscopy and tomography, NMR and EPR spectroscopy, X-ray serial crystallography at synchrotrons and XFELs, super resolution microscopy, MD simulations, atomic-force microscopy, and neutron and X-ray scattering methods), enhancing our understanding of the dynamic behaviour of macromolecules.

The meeting gathered close to 200 participants, joining from 17 different countries, and the programme included a great collection of 15 internationally renowned experts, which were invited to present their latest results during three main sessions, and ten participants who had submitted an abstract were also invited to give a short talks. 53 posters were presented during a lively poster session in the evening of the 6th, and three "Best Poster" prizes were also awarded to Ondřej Bulvas (IOCB Prague, CZ), Jessica Harich (University of Hamburg, DE), and Shekhar Jadhav (EMBL Grenoble, FR). The organisation of the symposium was also the occasion to showcase the EPN campus and tours of some PSB platforms and instruments were organised for external participants on the first day.

The organisers wish to thank all the sponsors (Arinax, Bruker, Dectris, EMBO, Fédération Française de Diffusion Neutronique (2FDN), GRAL, Grenoble Alpes Metropole, Malvern Panalytical, MiTeGen, Thermofisher scientific, and the Université Grenoble Alpes) for their financial support, and all the participants for contributing to make this a great event. See you in 2025 for the fifth edition.

F. Bernaudat (PSB)

Instruct cryo-EM Workshop

© C. Argoud

On the 23rd to 25th May, the fifth edition of a 2.5-day practical workshop on the sample preparation for single particle cryo-EM took place. There were 12 participants in total, selected from a record number of applicants, who were hosted on the EPN campus to learn some theoretical aspects of cryo-EM sample preparation and also gain hands-on experience of the multiple steps needed for the production of good samples. The workshop was aimed at PhD students, post-docs, and scientists new to the field of cryo-EM and gave the participants the opportunity to bring some samples from projects currently being worked on.

The days were structured around practical sessions, including sample quality assessment by negative stain EM at the IBS, the preparation of grids using the Vitrobot, and screening of prepared grids using both the Glacios at the EMBL and the Glacios at the IBS, in addition to the CM01 Krios at the ESRF. Tutors from across campus led the sessions with additional help from Daouda Traore, now an Application Scientist at ThermoFisher, previously ILL.

The days finished with a session covering what techniques had been employed and opened the floor to questions and discussion, in order for the tutors to further share their experience with the attendees. Additionally, a poster session on the second day allowed the participants to showcase their current research and facilitated interesting discussions on the applications of cryo-EM in a variety of challenging projects.

Several of the samples brought by the participants showed promising results, so we hope to see these participants back on the EPN campus for data collections! The workshop was jointly organised by all four institutes, ESRF, EMBL Grenoble, ILL and IBS, and was funded by INSTRUCT-ERIC and ThermoFisher Scientific.

L. McGregor (ESRF)

Grenoble Host-Pathogen Interactions Club

From top left: Christine Clayton, Paul Tafforeau, and poster prize winners Christophe-Sebastien Arnold and Luis Vigetti

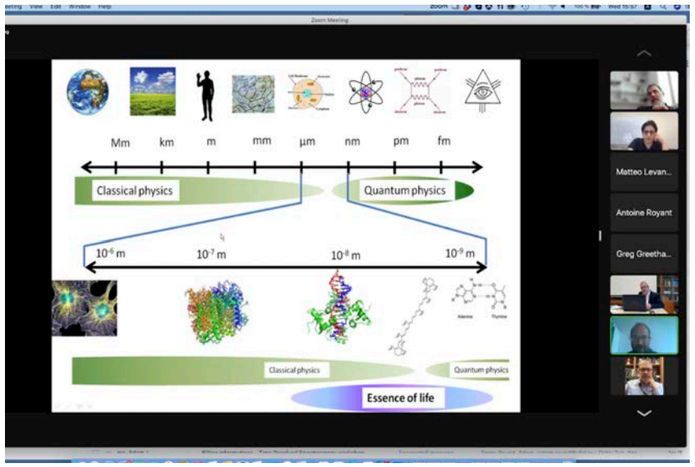
More than fifty registered participants gathered at the Institute for Advanced Biosciences (IAB) in La Tronche on 4 May 2023 for the 7th meeting of the Grenoble Host-Pathogen Interactions Club. The programme featured invited lectures from Christine Clayton (University of Heidelberg), who presented her research on mRNA turnover in trypanosomes, used as a model organism to better understand post-transcription regulation of gene expression in eukaryotes, and from Paul Tafforeau (ESRF Grenoble), who outlined his past palaeontological studies of fossils and described how the COVID-19 pandemic led him to his recent spectacular work on biomedical 3D imaging of human organs.

The meeting then continued with flash presentations by 18 students and postdocs from the EMBL, IAB, IBS, and TIMC laboratories, and a lively poster session during which all participants were invited to vote for the best posters. Poster prizes were awarded to Christophe-Sebastien Arnold and Luis Vigetti, both students at the IAB.

To stay informed of future club events, please sign up to the mailing list by visiting: https://hostpathogen.fr

F. Bernaudat (PSB)

EMBO workshop "Time-resolved spectroscopy meets time-resolved crystallography: The future of dynamic photobiology"



The virtual EMBO workshop "Time-resolved spectroscopy meets time-resolved crystallography: The future of dynamic photobiology" has been recently organized (17-19 April 2023) by the University of Pécs (Sofia Kapetanaki and András Lukács) and the IBS (Giorgio Schirò). Understanding light signal transduction processes in biology is fundamental and has been so far mainly addressed by time-resolved spectroscopic methods that revolutionized the knowledge of protein function by probing excited states and revealing the kinetic profile of light-triggered intermediates. On the other hand, watching proteins at work at various time scales (from femtoseconds to the steady state) with atomic resolution has always been a dream in structural biology, which is now coming true thanks to the use of brilliant X-ray sources on protein microcrystals. None of these experimental techniques is however able to unravel dynamic processes in biomolecules by itself, whereas quantum mechanical and classical dynamics numerical calculations are needed to complement the experimental results.

The aim of the EMBO workshop has been to bring together scientists from the fields of time-resolved spectroscopy and time-resolved X-ray techniques as well as theoreticians in order to present their recent works and discuss the synergy of the experimental techniques to advance our understanding of light-induced biological dynamics processes and foster new collaborations between the different fields. The workshop also highlighted the cutting-edge instrumentation at X-ray and spectroscopy facilities promoting game-changing advances in the study of biological dynamical processes.

G. Schirò (IBS)

PROFILE


from EMBL Photo Lab

Professor Kristina Djinović-Carugo has been head of EMBL Grenoble since July 1st, 2022. Before joining EMBL she was head of the Department of Structural and Computational Biology as well as being a full professor in the Max Perutz Laboratories at the University of Vienna. As an established structural biologist the PSB newsletter met with her to discuss her career and vision for the PSB in Grenoble as head of EMBL Grenoble.

For those who don't know you so well, could you tell us in a few words who you are and what your scientific interests are?

In a few words I would say that I am a structural biologist. I studied chemistry at the University of Ljubljana, and then went for a masters, which was different compared with nowadays. You had to do some additional exams and lab research for 3 years, only then were you allowed to pursue a PhD. So I did my masters in crystallography in Ljubljana and then went to Italy to specialize in Structural Biology. I obtained a PhD fellowship to study at the Elettra synchrotron in Trieste. But at that time it was still under construction so I asked permission to go to the University of Pavia, the biggest structural biology laboratory in Italy at that time. For administrative reasons I actually defended in Ljubljana, but went back to Pavia as a postdoc for 3 years. From there I then went to EMBL Heidelberg, first as an EMBO fellow for a postdoc and then as a staff scientist in the group of Matti Sarastre. I was there for 5 years when the possibility to return to Eletta emerged. As head of the structural biology laboratory and subsequently head of the Structural biology and crystallography division I was managing beamlines for diffraction and SAXS, as well as the structural biology lab. I was there for 5 years and in 2004 I moved to University of Vienna to become a full professor in molecular structural biology, and from 2009 I was heading the Department for Structural and Computational biology, until 2022 when I started here.

What brought you to Grenoble and to EMBL?

I had seen the opening to become head of EMBL Grenoble, but initially I did not consider to apply for it. However, I was then contacted by the EMBL search committee, who asked me if I had seen the position, and I thus started to think about it and reconsider. Firstly, I had this excellent past experience of being a staff scientist at EMBL, and I also knew the European Photon and Neutron (EPN) science campus and the local ecosystem. I have been an ESRF user since the beginning, and a member of various evaluation committees, as well as some collaborations with IBS on X-ray induced radiation damage studies and IDPs. This is a special place, and I thought it was a real opportunity, where you feel that you can make a difference.

What is the focus of your research?

My group works on the cytoskeleton of striated muscles, where we're particularly looking at Z-discs, the boundaries between two adjacent sarcomeres that are the basic contractile units. Z-discs are quite complex assemblies composed of more than 60 different proteins and we study both the architecture and how these protein complexes assemble. We are studying those structures looking mostly at reconstituted complexes, but now we are also starting to go into cells, using stem cells derived into cardiomyocytes. I believe these are a nice tool because you can control and manipulate them to look at different stages of maturation during biogenesis. We use a compilation of techniques such as crystallography, cryo-EM, SAXS, NMR (as many are intrinsically disordered), binding studies, chemical crossing linking, and we recently started to do expansion microscopy in collaboration with Niccolo Banterle at EMBL Heidelberg. With our research, we want to understand how the sarcomeric Z-disc form highly ordered structures form initially disordered assemblies, as well as the molecular basis of diseases, linked to mutations in the Z-disc, that are affecting muscles (myopathies), and in particular the heart (cardiomyopathies), as they are among the most deadly diseases worldwide.

What is your vision for EMBL Grenoble research and activities (in relation to the PSB?)

I believe that structural biology is in its golden age because we now have advanced infrastructure, like the extremely brilliant X-ray source at the European Synchrotron Facility (ESRF), and a whole range of very mature structural biology techniques, like crystallography, cryo-EM, and others, which can be combined with developments in stem cell biology and genome engineering technologies. EMBL Grenoble, being located on the EPN campus and a partner of the PSB, is thus the right place to exploit all this potential. On top of that, being at EMBL also provides an additional dimension, because it gives this opportunity to really do fundamental biology related research and to establish different collaborations with other researchers across the institution, and also offers access to a number of EMBL core facilities in addition to what we already have here.

What do you consider to be the major strengths of the PSB?

The EPN campus is a really special campus, where you have the best synchrotron and neutron sources on the planet. There is only one such place! In addition, with the presence of the IBS and EMBL, all together there are around 350 structural biologists in the PSB. This represents a huge community, which comes with a number of expertises and everything that is possible to do through the top-notch platforms and facilities we have at our disposal. This puts us in a very special position. Moreover, all the ongoing events, such as the PSB Symposium that took place in early July, are also very nice, and for the future, I would like to put in place a common PSB seminar series of invited speakers.

As a female research director in Vienna previously what is your vision for science and diversity in Grenoble?

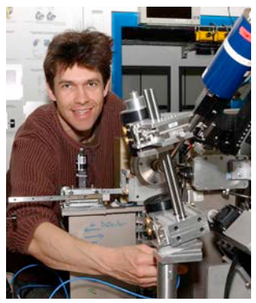
When I arrived at the University of Vienna I landed in the Faculty of Natural Sciences and Mathematics. At that time there were 102 full professors but I was only the third female professor, which all came with some experiences! Of course, one should promote diversity and I am the first to say so, but I am also the first to say that the main criteria for selection need to be excellence, and I do trust that I was actually appointed because of this. However, if all is equal, then of course people who are diverse should not be suppressed but instead promoted.

What will you miss in Vienna and how do you plan to relax in Grenoble?

What I am missing from Vienna is the cultural offer. There, as a capital city, the number of ongoing exhibitions, music concerts, and theatre performances is huge. Vienna is also consistently ranked among the top for quality of life cities in the world, and I can confirm that it is a nice and enjoyable place to live. But what I like about Grenoble is the great surroundings and the possibility of going to mountains and lakes whenever you want. We are close to Lyon and Geneva, and Provence is not so far either, and by hopping on a train you can easily get to Paris.

F. Bernaudat (PSB Coordinator), L. Gajdoš (ILL) and A. McCarthy (EMBL)

ANNOUNCEMENTS



In memoriam of Raimond Ravelli.

Raimond Ravelli, Professor of Structural Biology at Maastricht university, and former team leader at EMBL Grenoble between 1998 and 2007, passed away on 30 June 2023 at the age of 55 after a 10 week battle with a sudden unexpected illness. He was a brilliant scientist, thoughtful and inspiring mentor and a much appreciated colleague within EMBL, ESRF, and the wider structural biology community. Raimond was instrumental to the success of the EMBL-ESRF Joint Structural Group Beamlines and well known for spending long hours optimizing ID14-4 at ESRF for user experiments as the beamline responsible. Below is a link to an EMBL obituary page for those who wish to leave a condolenc message.
https://www.embl.org/about/info/alumni/community/obituaries/raimond-ravelli/
Raimond will be dearly missed by his family, his partner Maaike de Backer, a talented scientist herself who did her PhD studies at the ESRF, their son Seppe and daughter Noé.

José Antonio Márquez, Team leader and head of the high throughput crystallisation facility at EMBL Grenoble has been appointed as an EMBL Senior Scientist. With this appointment, which was confirmed by the EMBL Council in June, he will gain additional responsibilities including advising EMBL director general, along with the Unit Head as well as representing EMBL externally.

Dr. Ken Andersen has been appointed as the new Institut Laue-Langevin (ILL) director, and will assume his responsibilities on October 16, 2023. Dr. Andersen currently holds the position of Associate Laboratory Director for Neutron Sciences at Oak Ridge National Laboratory. In this role, he is responsible for managing and overseeing two neutron facilities, namely the Spallation Neutron Source (SNS) and the High Flux Isotope Reactor. Previously, Dr. Andersen served as the director of the Neutron Technologies Division within the Neutron Sciences Directorate. From 2010 to 2019, he held the position of head of the Neutron Instruments Division at the European Spallation Source in Lund, Sweden. Before that, he was in charge of the Neutron Optics lab at the ILL and worked as an instrument scientist at both ILL and ISIS in the UK. Additionally, he spent a brief period as a post-doctoral researcher at the KENS neutron facility in Japan. Dr. Andersen's research interests revolve around the design and optimization of neutron instruments for both steady-state and pulsed neutron sources. He obtained his PhD in physics from the University of Keele in the UK and ILL in 1991.

DATES FOR YOUR DIARY

14th September to 7th December 2023 - Recent Advances and Applications in Structural Biology seminar series
This lecture series is organised within the Master 2 programme "Structural Biology of Pathogens" at the UGA, but is open to all scientists on the EPN campus. The lectures will take place at 14:00 every Thursdays, from 14th September to 7th December, in the CIBB seminar room, and will include speakers from the IBS, EMBL Grenoble, IAB, and the I2BC Paris Saclay.
For more information on the lectures and programme: https://www.psb-grenoble.eu/

15th September 2023 – Science in the Mountains
This symposium is organised to celebrate Stephen Cusack's scientific career at EMBL Grenoble, and will be held in the ESRF auditorium on the EPN campus in Grenoble. More information: https://www.embl.org/events/cusack-symposium/

2nd to 4th October 2023 – Symposium "Signaling through Chromatin"
This 3 days symposium focused on "Signaling through Chromatin: from molecules to ecosystems" will cover innovative aspects of chromatin and epigenetics, from the atomic to cellular, organismal, and population scales. The symposium will be comprised of eight sessions, exploring chromatin dynamics and its link to several DNA and RNA-based processes such as transcription, DNA replication, repair and recombination. Dedicated sessions will feature the translational implications of epigenetic studies and the development of epidrugs. Internationally renowned speakers will present their latest research results using multiple approaches, such as quantitative proteomics, metabolomics, structural biology, single-cell epigenomics and population studies in different model organisms, from yeast to plants and mammals, including 3D culture models.

More information at: https://epigenetics.fr/sympo-iv-signaling-through-chromatin-oct-2-4-2023-grenoble-fr/

9th November 2023 – Grenoble Drug Discovery Club 5th meeting

This one-day event will take place at the Institute for Advanced Biosciences (IAB) in La Tronche, and the programme will include talks by invited speakers: Roman Chabanon (Institute Gustave Roussy, Villejuif, FR), Giovanna Lollo (Faculty of Pharmacy-ISPB, Lyon, FR), and Christopher Swale (IAB, La Tronche, FR).

For more information about the club and the updates of the programme: https://grenobledrugdiscovery.fr/

21st to 23rd November 2023 - Advanced Methods for Ambient Crystallography at ESRF-EBS Workshop
The ESRF and EMBL Joint Structural Biology Group, with the support of EU project Streamline, is organizing a workshop on sample preparation, data collection and data processing for Ambient Temperature Crystallography.
The ESRF and EMBL have been laying the groundwork for the future development of this field with two main projects: the refurbishment of MASSIF1 (https://www.esrf.fr/MASSIF1), including a CrystalDirect Harvester, allowing full automation of single crystal RT data collection and the new ID29 (https://www.esrf.fr/id29) for Time Resolved Serial Crystallography experiments with microseconds X-ray pulses.
This 2.5 days workshop will cover the different practical and theoretical aspects of room temperature data collection and structure determination on the first day, followed by practicals at the beamlines and data processing on the following days.

More information at: https://www.esrf.fr/home/events/conferences/2023/amax2023.html

30th November 2023 – CRISPR/Cas and genome engineering meeting
This meeting will take in the afternoon of 30th November in the IBS seminar room on the EPN campus. The programme will include talks by invited speakers: Michael Schmitz (University of Zurich, CH), Alexandre Paix (EMBL Heidelberg, DE), Neil Humphreys (EMBL Rome, IT), and Michel Wassef (Curie Institute, Paris, FR)
More information at: https://www.psb-grenoble.eu/

5th to 7th February 2023 – ESRF User Meeting
The 33rd ESRF User Meeting took place onsite in February 2023, marking the return to in-person gatherings after two years of remote meetings. It was a delightful experience to witness the auditorium filled with scientists from all across Europe, engaging in discussions and sharing ideas over a communal buffet. Last year, the User Meeting set a new record for attendance, and we look forward to the same level of enthusiasm and participation in the 2024 ESRF User Meeting.
The User Meeting holds great significance in the scientific life of ESRF, providing users with valuable opportunities for training in data analysis through Tutorials. Attendees can also benefit from attending cutting-edge scientific presentations showcasing the forefront capabilities of the ESRF beamlines. Additionally, micro-symposia offer a platform for gathering with their scientific communities. With the meeting being held onsite, fruitful discussions can take place with local ESRF staff, fostering collaborations, reflecting on previous experiments, and preparing proposals that leverage the unique performance of the ESRF-EBS.....

More information at: https://www.esrf.fr/home/events/conferences/2024/user-meeting-2024.html

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The Partnership for Structural Biology (PSB) is a collaboration between a number of prestigious European and French scientific laboratories in Grenoble. The PSB is unique in combining world leading user facilities for synchrotron X-ray and neutron scattering with NMR, electron microscopy, molecular biology and high throughput techniques on a single site together with strong projects in a broad range of structural biology.