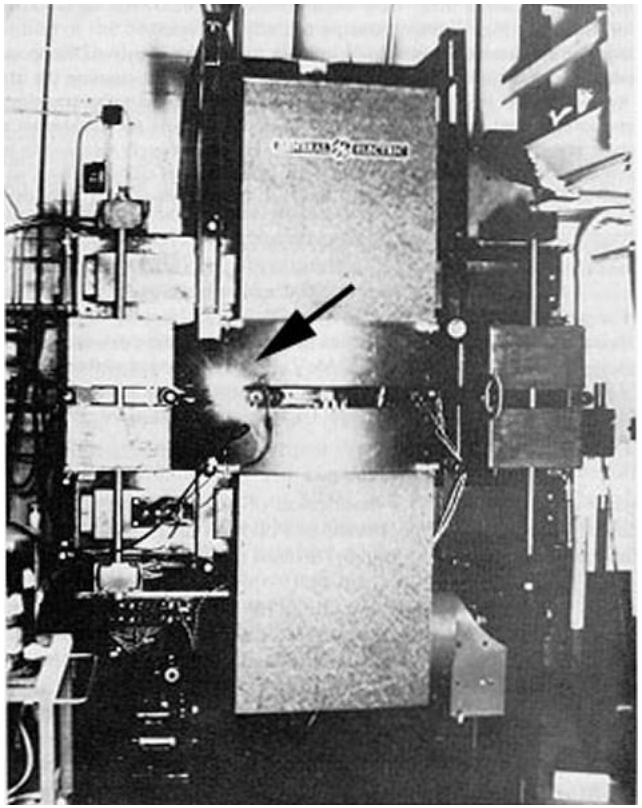

ESRF
The European Synchrotron

[New] Scientific Possibilities at the ESRF-EBS.

Gordon Leonard
ESRF Structural Biology Group

SYNCHROTRON RADIATION (SR) WAS FIRST OBSERVED 75 YEARS AGO

Leinard, A-M. (1898). Electric and Magnetic Field produced by an electric charge concentrated at a point and travelling on an arbitrary path. *L'Éclairage Électrique*, Vol 16.



Elder et al., (1947) "Radiation from Electrons in a Synchrotron" *Phys. Rev.*, **71**, 829-830. Published 1st June 1947

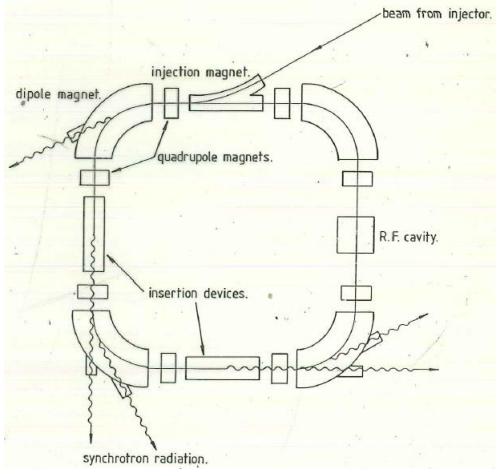
Radiation from Electrons in a Synchrotron

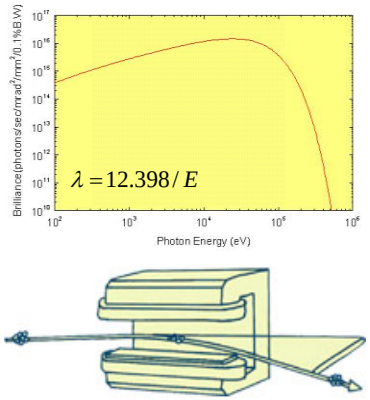
F. R. Elder, A. M. Gurewitsch, R. V. Langmuir, and H. C. Pollock
Research Laboratory, General Electric Company, Schenectady, New York
May 7, 1947

HIGH energy electrons which are subjected to large accelerations normal to their velocity should radiate electromagnetic energy.[1–4] The radiation from electrons in a betatron or synchrotron should be emitted in a narrow cone tangent to the electron orbit, and its spectrum should extend into the visible region. This radiation has now been observed visually in the General Electric 70-Mev synchrotron.[5] This machine has an electron orbit radius of 29.3 cm and a peak magnetic field of 8100 gausses. The radiation is seen as a small spot of brilliant white light by an observer looking into the vacuum tube tangent to the orbit and toward the approaching electrons. The light is quite bright when the x-ray output of the machine at 70 Mev is 50 roentgens per minute at one meter from the target and can still be observed in daylight at outputs as low as 0.1 roentgen.

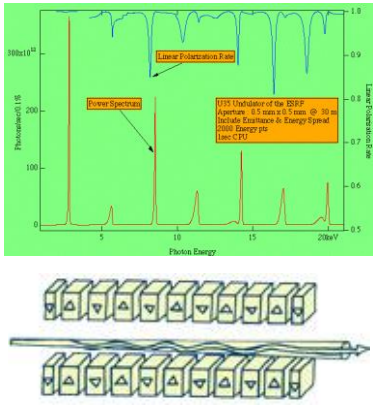
The synchrotron x-ray beam is obtained by turning off the r-f accelerating resonator and permitting subsequent changes in the field of the magnet to change the electron orbit radius so as to contract or expand the beam to suitable targets. If the electrons are contracted to a target at successively higher energies, the intensity of the light radiation is observed to increase rapidly with electron energy. If, however, the electrons are kept in the beam past the

SYNCHROTRON RADIATION SOURCES



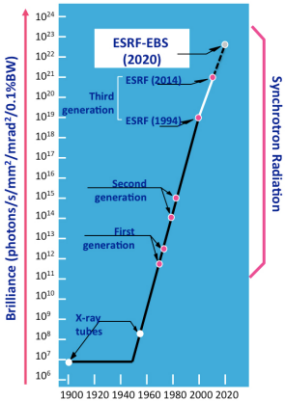


Bending magnet spectrum



Undulator spectrum

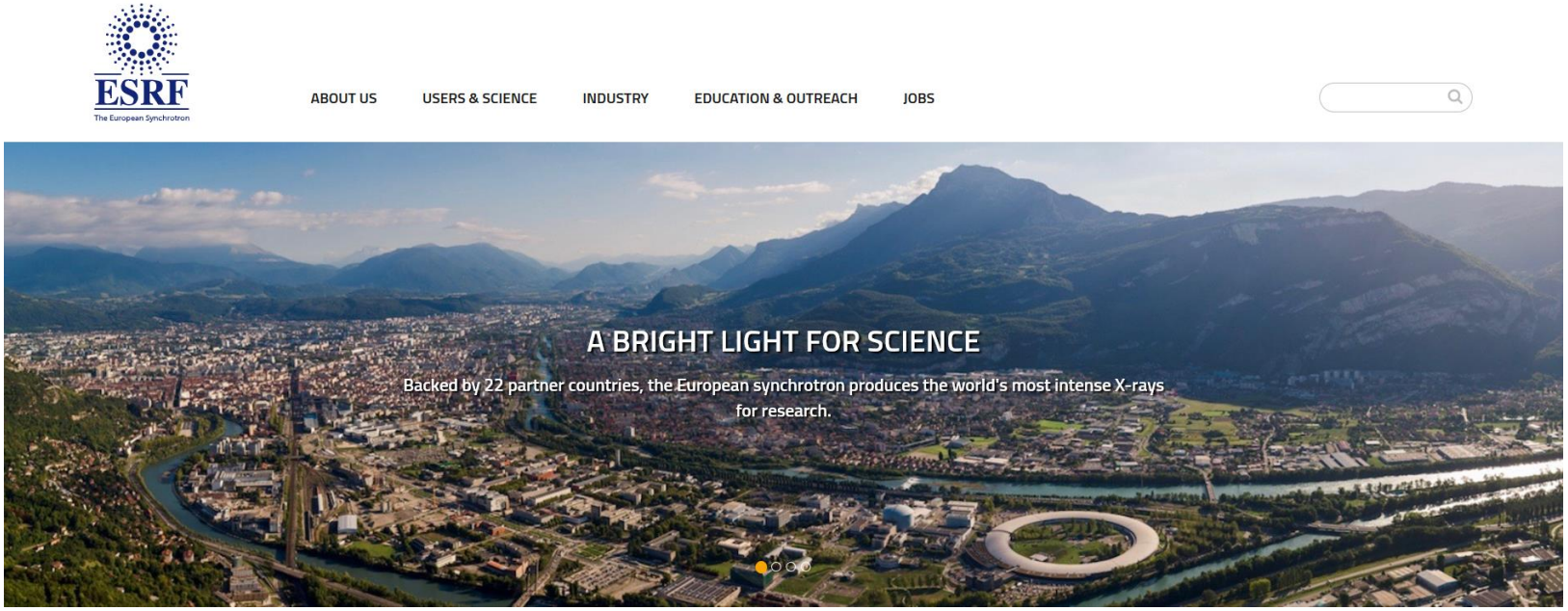
Intensity + collimation
= 'brilliance'



1st Generation - parasitic use
2nd Generation - dedicated
3rd Generation - dedicated, higher energy
4th Generation – dedicated, diffraction limited

THE ESRF

The world's most intense X-ray source and a centre of excellence for fundamental, innovation-driven research in condensed and living matter science.



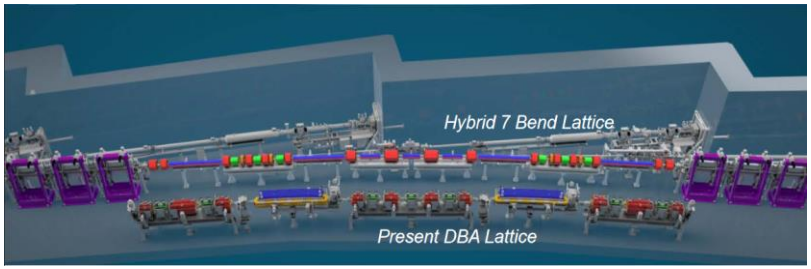
Member states

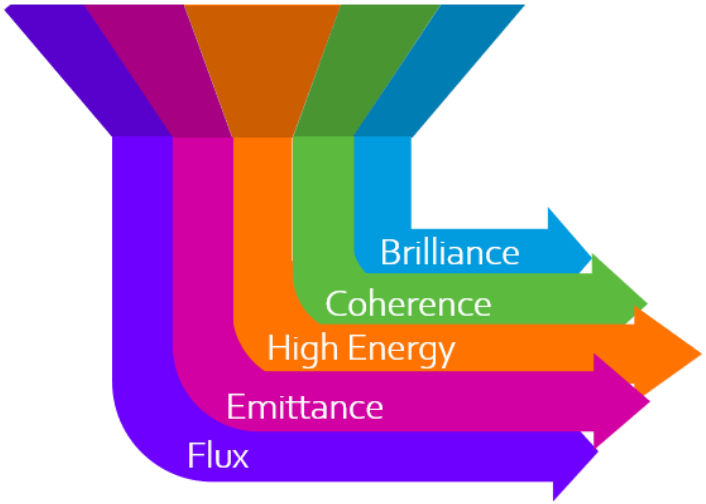
- 27.5% France
- 24% Germany
- 13.2% Italy
- 10.5% United Kingdom
- 6% Russia
- 5.8% Benesync (Belgium, The Netherlands)
- 5.0% Nordsync (Denmark, Finland, Norway, Sweden)
- 4% Spain
- 4% Switzerland

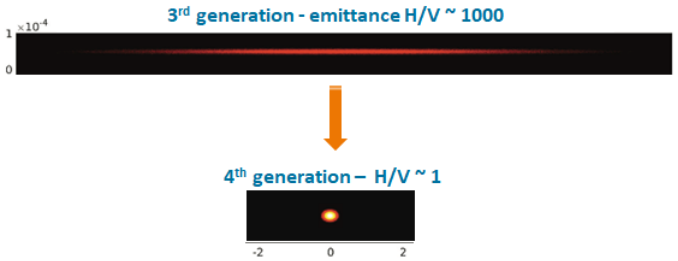
Scientific associates

- 1.75% Austria
- 1.75% Israel
- 1% Poland
- 1% Portugal
- 0.66% India
- 0.6% Czech Republic
- 0.3% South Africa
- 0.25% Hungary

ESRF-EBS (EXTREMELY BRILLIANT SOURCE): OPPORTUNITIES FOR USERS







Beam sizes from nm to half a meter

X-Ray Microscopies
Larger field of view

Greater coherence-based approaches

CDI, Phase Contrast, Holography, XPCS
High quality Optics

Photon hungry techniques

RIXS, RESX, NRS, XES, XDS, WDS, Lock in XBIC, XEOL

Higher flux at higher energies

Larger penetration
Low dose *in vivo* imaging
In situ, operando, Extreme (T,P,H), pump probe

Higher throughput with dose tolerance

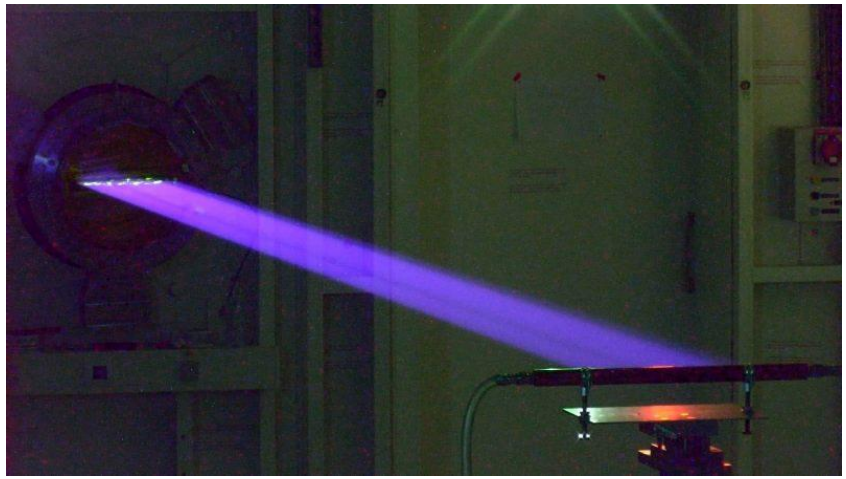
Faster dynamics
Time-resolved experiments, *cryo*...

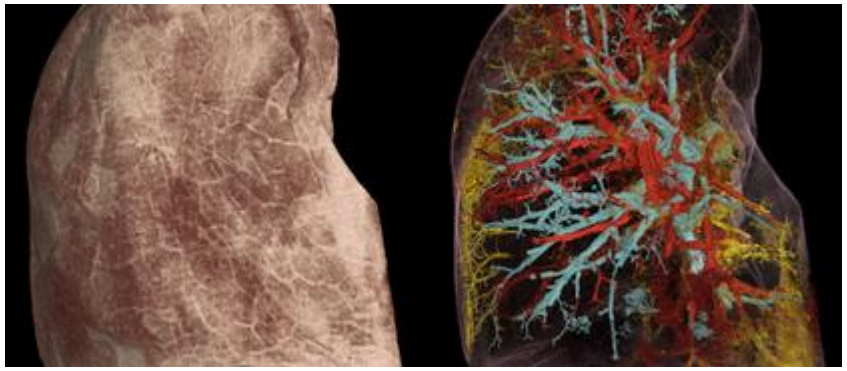
Better sensitivity Artifact mitigation

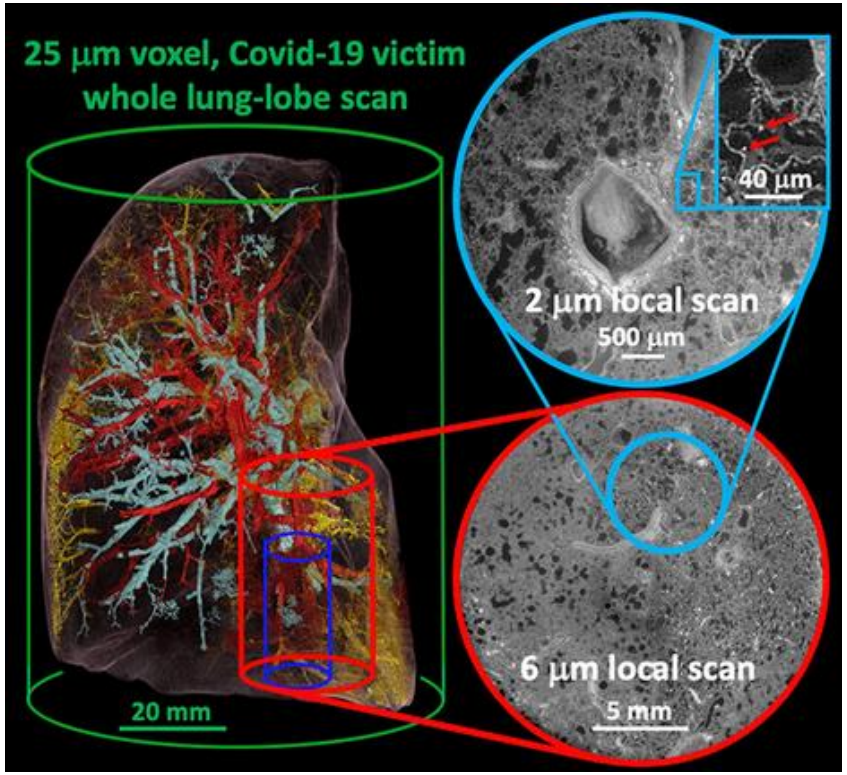
Single atom detection
Noise reduction

Courtesy Gema Martinez Criado

HIERARCHICAL PHASE-CONTRAST TOMOGRAPHY (HIP-CT)







HiP-CT was used to scan a lung of a COVID-19 victim. The whole lung lobe was first scanned at 25 micron voxel resolution (green cylinder, rendered to show the two vascular systems and occluded vessels). The researchers then zoomed in at 6 (red cylinder) then 2 micron voxels (blue cylinder), giving 100X more resolution than clinical CT and providing outstanding insight into the physiological effects of COVID-19. The cellular structure is resolved, including individual red blood cells (red arrows). (Credit: P.Tafforeau/ESRF).

https://youtu.be/zhPWCR7bBeI

Walsh, C.L., Tafforeau, P., Wagner, W.L. *et al.* Imaging intact human organs with local resolution of cellular structures using hierarchical phase-contrast tomography. *Nat Methods* **18**, 1532–1541 (2021). https://doi.org/10.1038/s41592-021-01317-x

THE HUMAN ORGAN ATLAS PROJECT (HTTPS://HUMAN-ORGAN-ATLAS.ESRF.EU/)

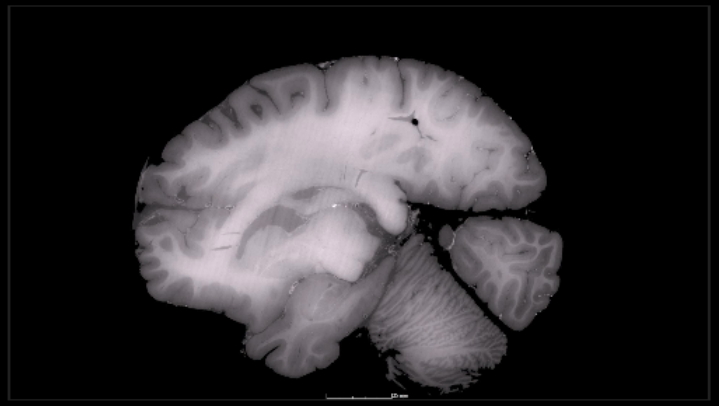
Human Organ Atlas EXPLORE SEARCH HELP

Welcome to the Human Organ Atlas

The Human Organ Atlas uses **Hierarchical Phase-Contrast Tomography** to span a previously poorly explored scale in our understanding of human anatomy, the micron to whole intact organ scale.

Histology using optical and electron microscopy images cells and other structures with sub-micron accuracy but only on small biopsies of tissue from an organ, while clinical CT and MRI scans can image whole organs, but with a resolution only down to just below a millimetre. HiP-CT bridges these scales in 3D, imaging intact organs with ca. 20 micron voxels, and locally down to microns.

We hope this open access Atlas, enabled by the ESRF-EBS, will act as a reference to provide new insights into our biological makeup in health and disease. To stay up to date, follow @HiP-CT



HiP-CT imaging and 3D reconstruction of a complete brain from the body donor LADAF-2020-31. More videos can be viewed on the HiP-CT YouTube channel.

Funding

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- The European Synchrotron Radiation Facility (ESRF) — funding proposal MD-1252
- The Chan Zuckerberg Initiative, a donor-advised fund of the Silicon Valley Community Foundation
- The German Registry of COVID-19 Autopsies (DeRegCOVID), supported by the German Federal Ministry of Health
- The **Royal Academy of Engineering**, UK
- The **UK Medical Research Council**
- The **Wellcome Trust**

Collaborators

- UCL, London, England: **Peter D Lee, Claire Walsh, Simon Walker-Samuel, Rebecca Shipley, Sebastian Marussi, Joseph Jacob, David Long, Daniyal Jafree, Ryo Torii, Charlotte Hagen**
- ESRF, Grenoble, France: **Paul Tafforeau, Elodie Boller**
- Medizinische Hochschule Hannover, Germany: **Danny D Jonigk, Christopher Werlein, Mark Kuehnel**
- Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Germany:**M Ackermann**
- University Hospital of Heidelberg, Germany: **Willi Wagner**
- Grenoble Alpes University, Department of Anatomy, French National Center for Scientific Research: **A Bellier**
- Diamond Light Source, Harwell, UK: **Andy Bodey, Robert C Atwood**
- Imperial College London, UK: **JL Robertus**

Reference

Walsh, C.L., Tafforeau, P., Wagner, W.L. *et al.* Imaging intact human organs with local resolution of cellular structures using hierarchical phase-contrast tomography. *Nat Methods* (2021). https://doi.org/10.1038/s41592-021-01317-x

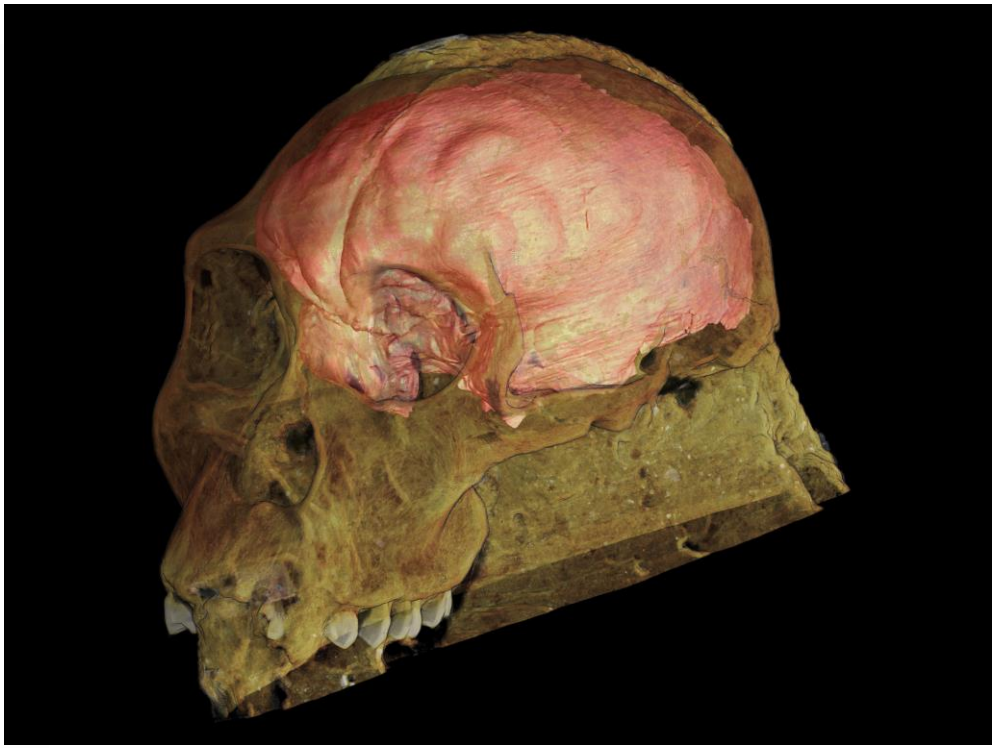
Aknowledgements

The development of this portal has been done as part of the PaNOSC project. PaNOSC has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 823852. The following people were involved in the development: Paul Tafforeau, Alejandro De Maria Antolinos, Axel Bocciarelli, Marjolaine Bodin and Andrew Götz from the ESRF, Jiří Majer from ELI, as well as the broader PaNOSC and ICAT communities.

NOT JUST ORGANS/HISTOLOGY

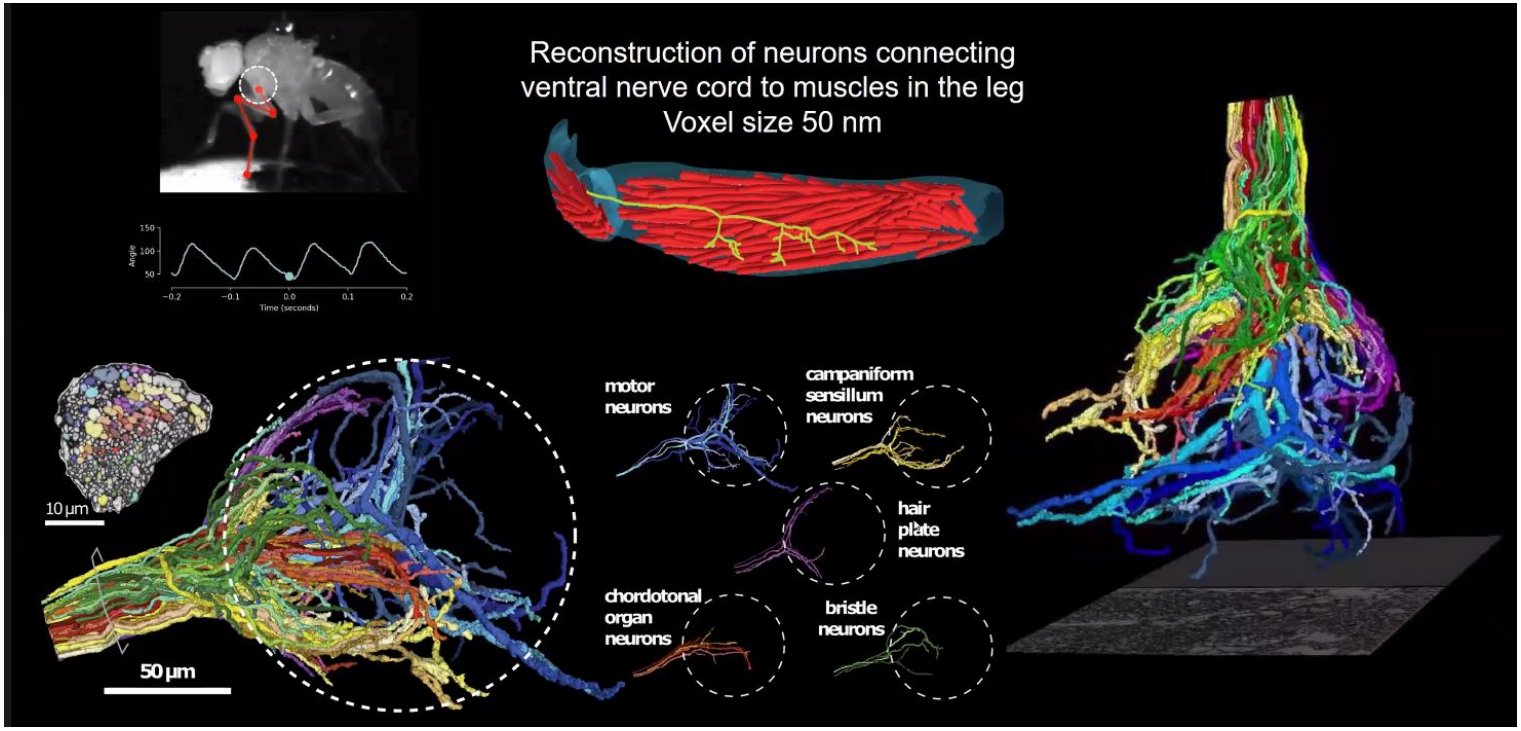
Materials Science

Paleontology



X-RAY HOLOGRAPHIC NANOTOMOGRAPHY (XNH)

Dense neuronal reconstruction through X-ray holographic nano-tomography

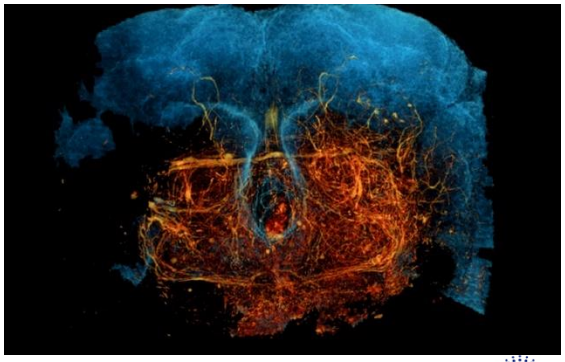


Deep learning algorithms applied to identify neurons

A.T. Kuan et al. Nature Neuroscience 23, 1637 (2020)

The technique was able to trace neurites but not to visualize synapses

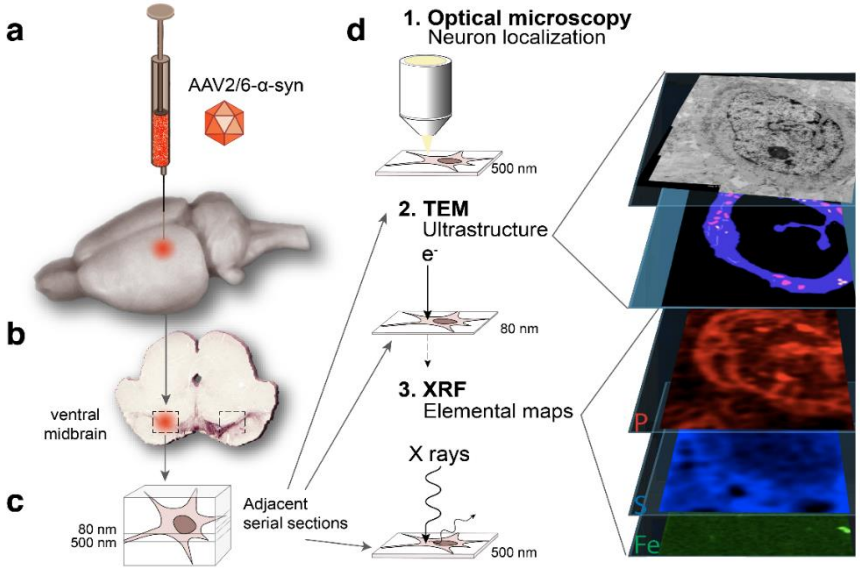
EBS → improved throughput & resolution



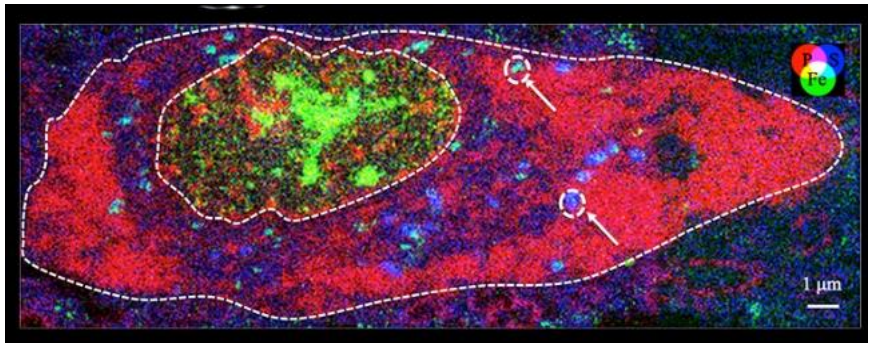
Fruit fly brain generated through XNH
Blue: tissue; orange: neurons

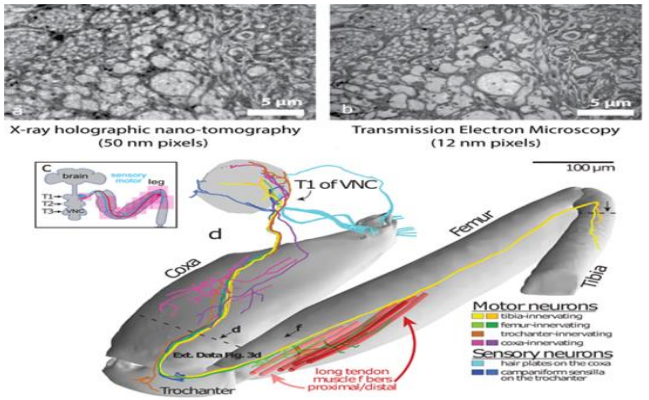
Courtesy Gema Martinez Criado

INFORMATION AT DIFFERENT [SPATIAL] RESOLUTION AND LENGTH SCALES



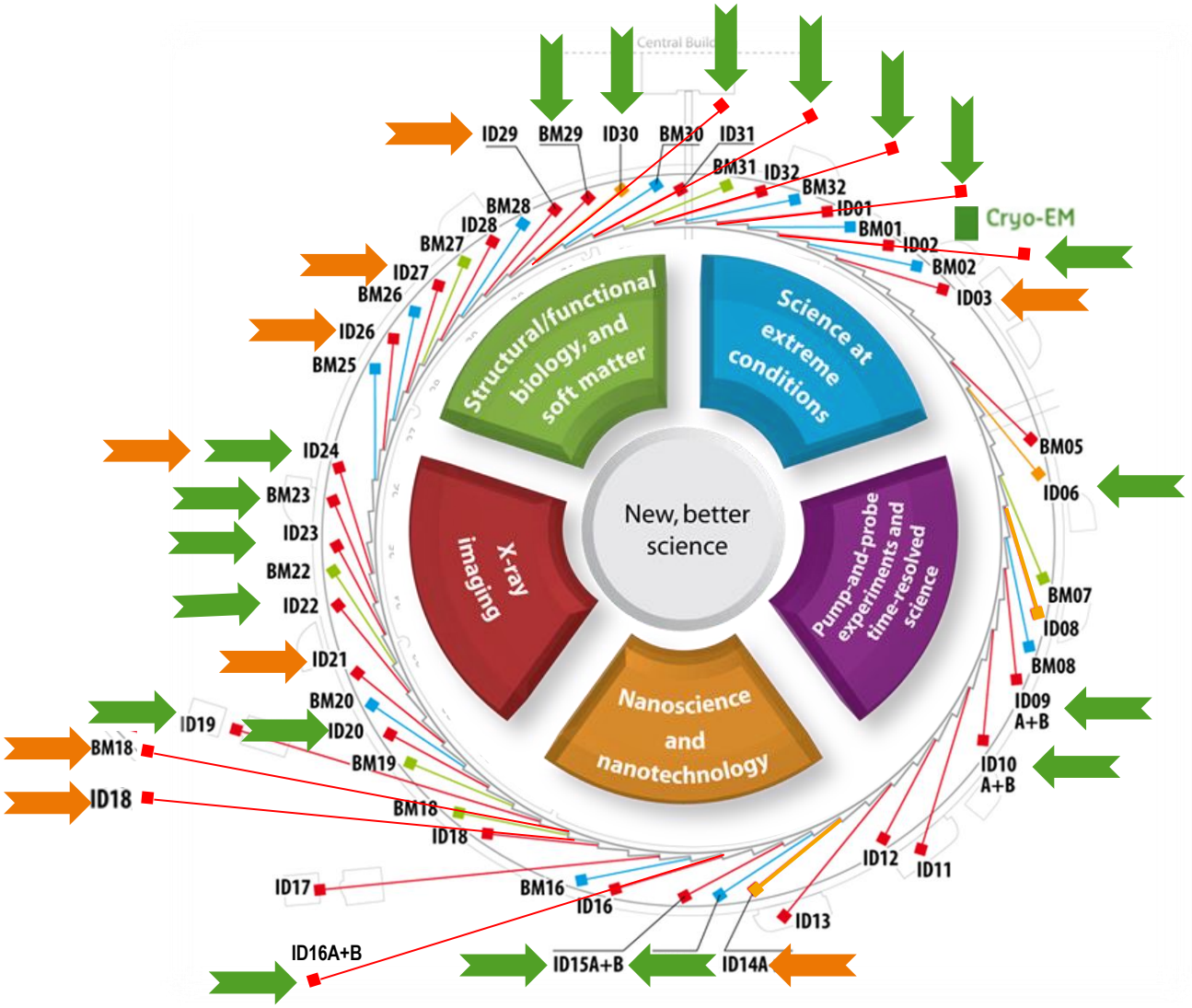
Correlative microscopy in the neurosciences: AAV2/6 vector encoding human α-syn is unilaterally injected in the rat substantia nigra. d (1) Optical imaging is used to localize neurons in the rat substantia nigra. (2) Ultrastructure mosaics are assembled from images recorded on a standard TEM (3) XRF images are recorded on the ID16-A nano-imaging beamline at ESRF and elemental maps compiled. Masks are defined from TEM images for each type of organelle and matched to the XRF maps of the neuron to calculate the elemental content per organelle type. This quasi-correlative imaging was applied to neuronal cell bodies in either the non-injected or α-syn-overexpressing hemisphere.





Correlative matching of regions Matched regions imaged with XNH and TEM. Strategy for covering the volume of interest and rendering of the reconstructed leg and the connection to the ventral nerve cord with several neurons traced from the VNC to the muscle insertion. Kuan AT et al., (2020). Dense neuronal reconstruction through X-ray holographic nano-tomography. Nat Neurosci. 2020 Dec;23(12):1637-1643. doi: 10.1038/s41593-020-0704-9. Epub 2020 Sep 14. PMID: 32929244; PMCID: PMC8354006.

ESRF-EBS: NOT JUST A NEW SOURCE



ESRF Upgrade Phase I

EBS & refurbishment programme

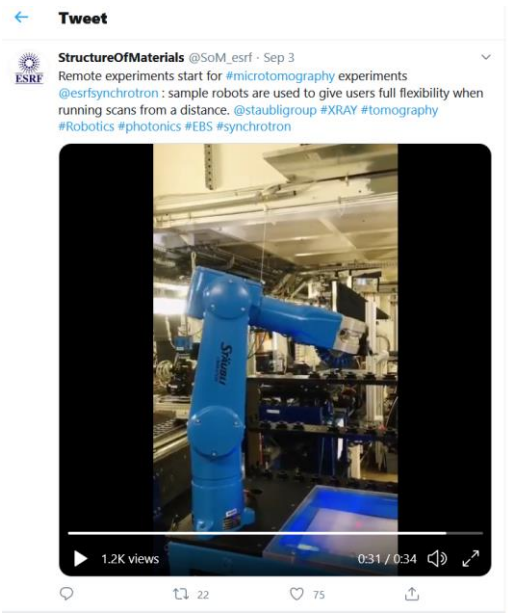
19 Upgraded or Refurbished BLs
2009 - 2015

4 New + 6 Refurbished Beamlines
2015 - 2023

Courtesy: Harald Reichert

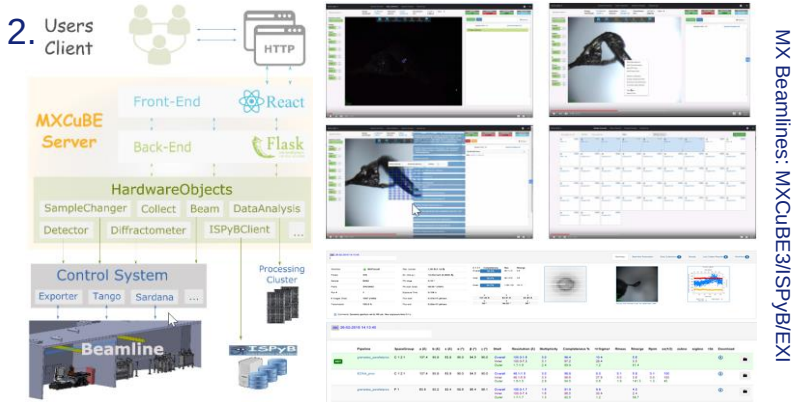
REMOTE ACCESS

1.



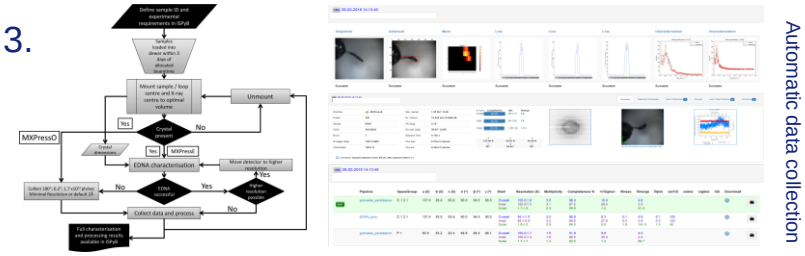
ID19: Guacamole/remote desktop to BL control computer/Zoom

2.



MX Beamlines: MXCuBE3/ISPyB/EXI

3.

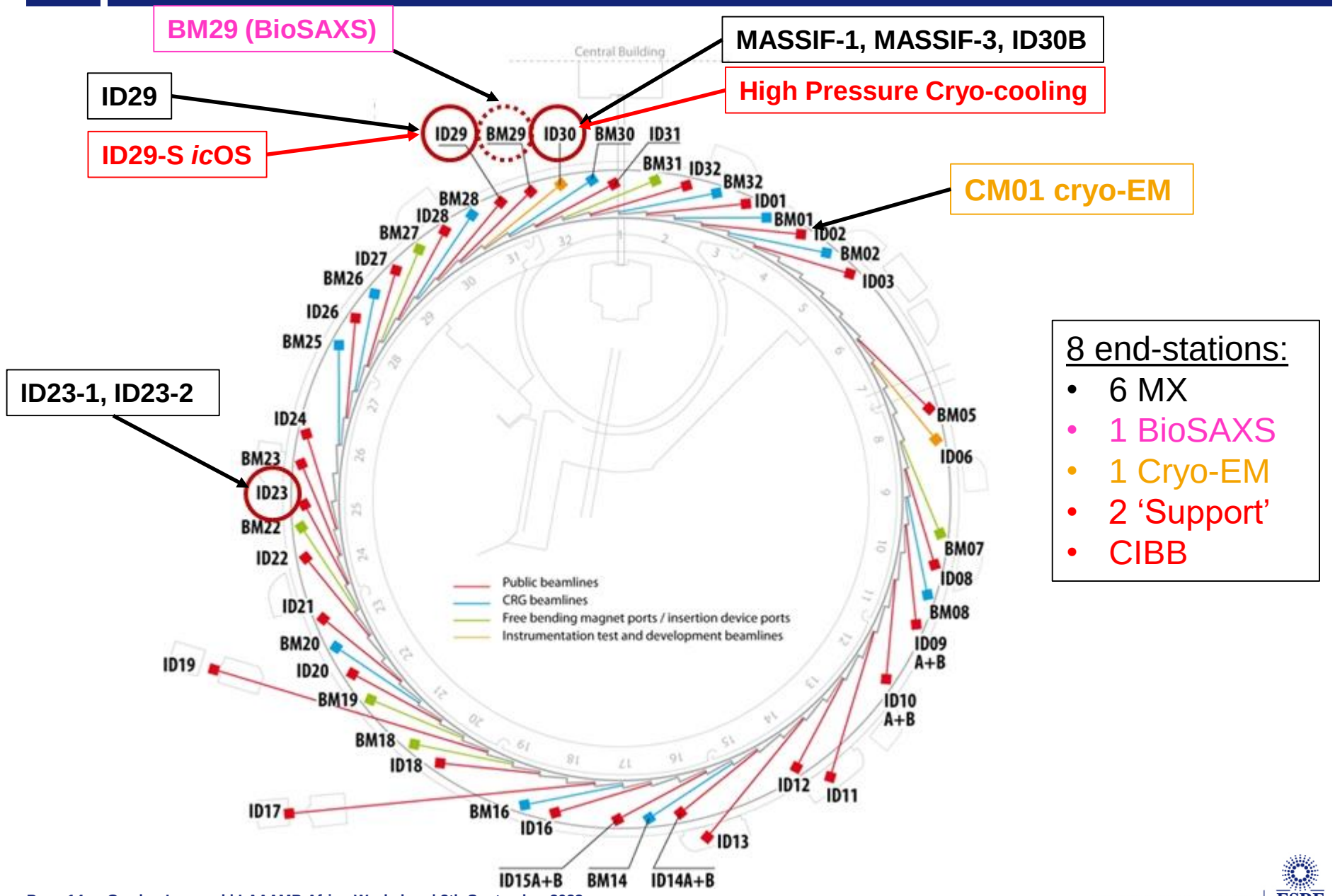


Automatic data collection

Refurbished MASSIF-1 (ID30A-1; ESRF-EMBL collaboration)

4. Users send samples. Beamline staff do everything
- Often 24h/24h

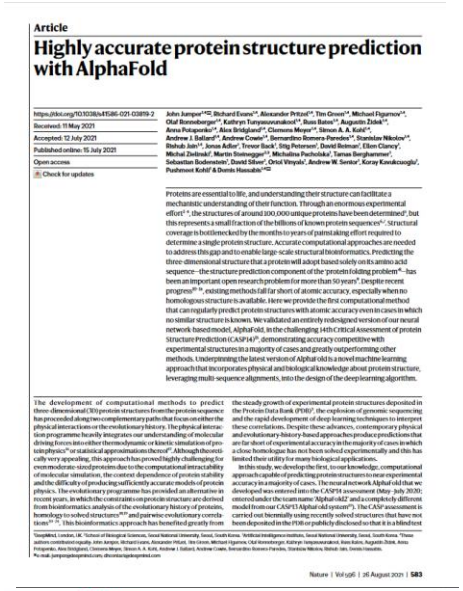
ESRF FACILITIES FOR INTEGRATED STRUCTURAL BIOLOGY



8 end-stations:

- 6 MX
- 1 BioSAXS
- 1 Cryo-EM
- 2 'Support'
- CIBB

PROTEIN STRUCTURE PREDICTION: IS IT A 'MAGIC BULLET'?



Article

Highly accurate protein structure prediction with AlphaFold

https://doi.org/10.1038/s41586-021-03819-2
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Open access
Check for updates

John Jumper[1,2]✉, Richard Evans[1]✉, Alexander Pritzel[1]✉, Tim Green[1]✉, Michael Figurnov[1]✉, Olaf Ronneberger[1]✉, Kathryn Tunyasuvunakool[1]✉, Russ Bates[1]✉, Augustin Žídek[1]✉, Anna Potapenko[1]✉, Alex Bridgland[1]✉, Clemens Meyer[1]✉, Simon A. A. Kohl[1]✉, Andrew J. Ballard[1]✉, Andrew Cowie[1]✉, Bernardino Romera-Paredes[1]✉, Stanislav Nikolov[1]✉, Rishub Jain[1]✉, Jonas Adler[1]✉, Trevor Back[1]✉, Stig Petersen[1]✉, David Reiman[1]✉, Ellen Clancy[1]✉, Michal Zielinski[1]✉, Martin Steinegger[2,3]✉, Michalina Pacholska[1]✉, Tamas Berghammer[1]✉, Sebastian Bodenstein[1]✉, David Silver[1]✉, Oriol Vinyals[1]✉, Andrew W. Senior[1]✉, Koray Kavukcuoglu[1]✉, Pushmeet Kohli[1]✉ & Demis Hassabis[1]✉

Proteins are essential to life, and understanding their structure can facilitate a mechanistic understanding of their function. Through an enormous experimental effort[1–4], the structures of around 100,000 unique proteins have been determined[5], but this represents a small fraction of the billions of known protein sequences[6,7]. Structural coverage is bottlenecked by the months to years of painstaking effort required to determine a single protein structure. Accurate computational approaches are needed to address this gap and to enable large-scale structural bioinformatics. Predicting the three-dimensional structure that a protein will adopt based solely on its amino acid sequence—the structure prediction component of the 'protein folding problem'[8]—has been an important open research problem for more than 50 years[9]. Despite recent progress[10–15], existing methods fall far short of atomic accuracy, especially when no homologous structure is available. Here we provide the first computational method that can regularly predict protein structures with atomic accuracy even in cases in which no similar structure is known. We validated an entirely redesigned version of our neural network-based model, AlphaFold, in the challenging 14th Critical Assessment of protein structure Prediction (CASP14)[16], demonstrating accuracy competitive with experimental structures in a majority of cases and greatly outperforming other methods. Underpinning the latest version of AlphaFold is a novel machine learning approach that incorporates physical and biological knowledge about protein structure, leveraging multi-sequence alignments, into the design of the deep learning algorithm.

The development of computational methods to predict three-dimensional (3D) protein structures from the protein sequence has proceeded along two complementary paths that focus on either the physical interactions or the evolutionary history. The physical interaction programme heavily integrates our understanding of molecular driving forces into either thermodynamic or kinetic simulation of protein physics[17] or statistical approximations thereof[18]. Although theoretically very appealing, this approach has proved highly challenging for even moderate-sized proteins due to the computational intractability of molecular simulation, the context dependence of protein stability and the difficulty of producing sufficiently accurate models of protein physics. The evolutionary programme has provided an alternative in recent years, in which the constraints on protein structure are derived from bioinformatics analysis of the evolutionary history of proteins, homology to solved structures[19–21] and pairwise co-evolutionary correlations[22–24]. This bioinformatics approach has benefited greatly from the steady growth of experimental protein structures deposited in the Protein Data Bank (PDB)[5], the explosion of genomic sequencing and the rapid development of deep learning techniques to interpret these correlations. Despite these advances, contemporary physical and evolutionary history-based approaches produce predictions that are far short of experimental accuracy in the majority of cases in which a close homologue has not been solved experimentally and this has limited their utility for many biological applications.

In this study, we develop the first, to our knowledge, computational approach capable of predicting protein structures to near-experimental accuracy in a majority of cases. The neural network AlphaFold that we developed was entered into the CASP14 assessment (May–July 2020; entered under the team name 'AlphaFold2' and a completely different model from our CASP13 AlphaFold system[25]). The CASP assessment is carried out biennially using recently solved structures that have not been deposited in the PDB or publicly disclosed so that it is a blind test

Science

Accurate prediction of protein structures and interactions using a three-track neural network

Deep learning takes on protein folding

In 1972, Anfinsen won a Nobel prize for demonstrating a connection between a protein's amino acid sequence and its three-dimensional structure. Since 1994, scientists have competed in the biannual Critical Assessment of Structure Prediction (CASP) protein-folding challenge. Deep learning methods took center stage at CASP14, with DeepMind's AlphaFold2 achieving remarkable accuracy. Baek *et al.* explored network architectures based on the DeepMind framework. They used a three-track network to process sequence, distance, and coordinate information simultaneously and achieved accuracies approaching those of DeepMind. The method, RoseTTA fold, can solve challenging x-ray crystallography and cryo–electron microscopy modeling problems and generate accurate models of protein-protein complexes. —VV

Abstract

DeepMind presented notably accurate predictions at the recent 14th Critical Assessment of Structure Prediction (CASP14) conference. We explored network architectures that incorporate related ideas and obtained the best performance with a three-track network in which information at the one-dimensional (1D) sequence level, the 2D distance map level, and the 3D coordinate level is successively transformed and integrated. The three-track network produces structure predictions with accuracies approaching those of DeepMind in CASP14, enables the rapid solution of challenging x-ray crystallography and cryo–electron microscopy structure modeling problems, and provides insights into the functions of proteins of currently unknown structure. The network also enables rapid generation of accurate protein-protein complex models from sequence information alone, short-circuiting traditional approaches that require modeling of individual subunits followed by docking. We make the method available to the scientific community to speed biological research.

5. A. Pozzer, A. P. Tsimpidi, V. A. Karydis, A. de Meij, J. Lelieveld, *Atmos. Chem. Phys.* **17**, 12813 (2017).
6. R. M. Hoesly *et al.*, *Geosci. Model Dev.* **11**, 369 (2018).
7. G. D. Thurston *et al.*, *Environ. Health Persp.* **79**, 73 (1989).
8. A. R. McLeod *et al.*, *Nature* **347**, 277 (1990).
9. X. Zhang *et al.*, *Nat. Commun.* **11**, 4357 (2020).

10.1126/science.abn7647

The protein-folding problem: Not yet solved

We agree with H. H. Thorp ("Proteins, proteins everywhere," Editorial, 17 December 2021, p. 1415) and numerous others (*1*) that the advance in protein structure prediction achieved by the computer programs AlphaFold (*2*) and RoseTTAfold (*3*) is worthy of special notice. The accuracies of the predictions afforded by these new approaches, which use machine-learning methods that exploit the information about the relationship between sequence and structure contained in the databases of experimental protein structures and sequences, are much superior to previous approaches. However, we do not agree with Thorp that the protein-folding problem has been solved.

AlphaFold achieves a mean C-alpha root mean square deviation (RMSD) accuracy of ~1 Å for the Critical Assessment of Structure Prediction 14 (CASP14) dataset (*2*). This accuracy corresponds to that of structures determined by x-ray crystallography or single-particle cryo–electron microscopy at very low resolution. The accuracy of these methods is several times better than machine learning methods; for example, at 3 Å resolution, the coordinate C-alpha RMSD accuracy for empirically determined structures is far better than 1 Å. At present, for the best cases, the C-alpha coordinate RMSD accuracy of AlphaFold-predicted structures roughly corresponds to the accuracy expected for structures determined at resolutions no better than ~4 Å. Thus, although structural predictions by AlphaFold and RoseTTAfold may be accurate enough to assist with experimental structure determination (*3*), they alone cannot provide the kind of detailed understanding of molecular and chemical interactions that is required for studies of molecular mechanisms and for structure-based drug design.

A further complication for structure prediction is the dynamic structural variation in a given sequence. Allosteric states, which can differ dramatically, may be in an intrinsic equilibrium or depend on a binding partner, which may be a ligand or cofactor (e.g., ATP or cobalamin), another macromolecule (e.g., DNA or a protein partner), or aberrant self-association (e.g., pathogenic amyloids). Work is in progress to address protein complexes (*4*, *5*), but structure prediction remains to be achieved for those in complicated molecular machines and for those with ligands that affect conformation, which may be as yet unidentified.

Recent advances should be taken as a call for further development. Moreover, lessons should be learned from history. In 1990, Alwyn Jones and Carl-Ivar Brändén published a commentary on errors in x-ray crystal structures (*6*) that stimulated the development of cross-validation and validation tools for structural biology (*7*–*9*) and that ultimately made the databases of experimental structures much more reliable. Thus, tools should be developed to assess coordinate accuracy of predictions and alleviate bias toward structural patterns observed in repositories.

Finally, it is necessary to reflect on what the word "solved" might mean in the context of the protein-folding problem. Some may feel that this problem will have been solved once any method has been found that enables one to obtain accurate predictions of the structures of proteins from their sequences. AlphaFold and RoseTTAfold represent a major step forward in that direction, but they are not the final answer. Others, including us, feel that solving the protein-folding problem means making accurate predictions of structures from amino acid sequences starting from first principles based on the underlying physics and chemistry. Despite these major advances in protein structure prediction, experimental structure determination remains essential.

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2. J. Jumper *et al.*, *Nature* **596**, 583 (2021).
3. M. Baek *et al.*, *Science* **373**, 871 (2021).
4. I. R. Humphreys *et al.*, *Science* **374**, eabm4805 (2021).
5. R. Evans *et al.*, bioRxiv, 10.1101/2021.10.04.463034 (2021).
6. C. Branden, T. Jones, *Nature* **343**, 687 (1990).
7. A. T. Brunger, *Nature* **355**, 472 (1992).
8. R. J. Read *et al.*, *Structure* **19**, 1395 (2011).
9. R. Henderson *et al.*, *Structure* **20**, 205 (2012).

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https://www.embl.org/news/science/alphafold-potential-impacts/

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Guest author(s)

22 July 2021
Science

Great expectations – the potential impacts of AlphaFold DB

A discussion of the applications that AlphaFold DB may enable and the possible impact of the resource on science and society

Protein structural biology. Image credit: Karen Arnott/EMBL-EBI

Authors
Stephen Cusack, Sebastian Eustermann, Gerard Kleywegt, Jan Kosinski, Julia Mahamid, José Antonio Marquez, Christoph Müller, Thomas Schneider, Janet Thornton, Jessica Vamathevan, Sameer Velankar, Matthias Wilmanns

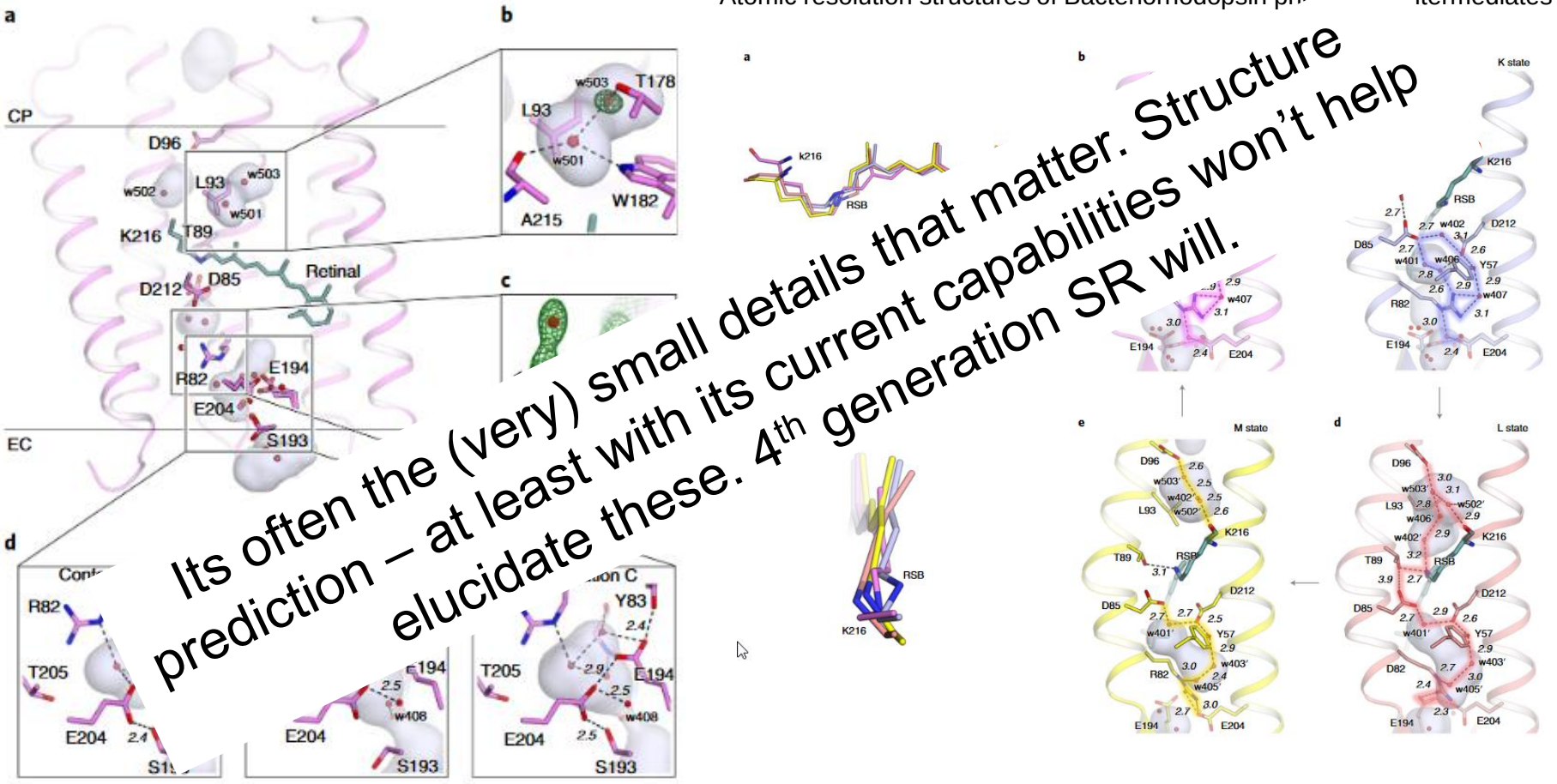
Modelling of large macromolecular complexes using integrative and hybrid methods for structure determination (I/HM) will similarly benefit from the availability of predicted models for the building blocks of such complexes as well as from the anticipated increase in the number of macromolecular complex structures. Rapid advances in cryo-EM have made it possible to study macromolecular complexes in their biological context (the cell) using *in-situ* experiments. The predicted models may help to elucidate the identity of proteins that interact with large complexes in various contexts in a cell.

While AlphaFold DB will, in general, accelerate structural biology research, it will likely also induce a shift in emphasis from initial structural determination to the study of the more mechanistic and functional aspects of protein structures. Although this in turn may lead to an objective re-evaluation of the large-scale structural biology infrastructures devoted to structure determination (e.g. synchrotron X-ray crystallography beamlines), it is likely that for the foreseeable future they will be essential to validate and thus fully harness the potential of structure prediction, and to enable structural investigations for which no reliable predictions can be made at this time (structure of nucleic acids and large complexes, ligand and fragment screens, investigations of dynamics, etc.).

The European Synchrotron | ESRF

TRUE ATOMIC RESOLUTION WILL STILL BE NEEDED TO DECIPHER [BIOLOGICAL] MECHANISM.

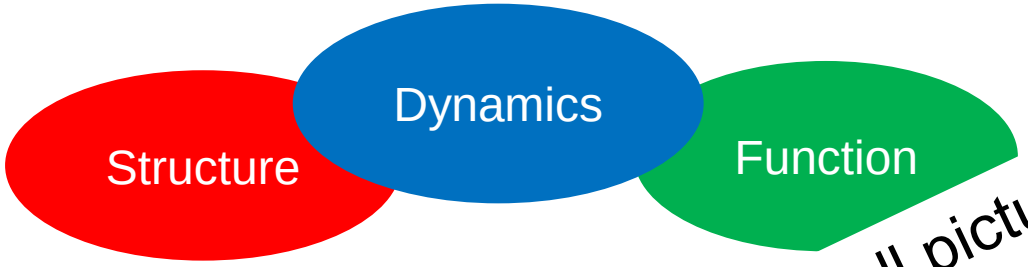
Atomic resolution structures of Bacteriorhodopsin pho[illegible]ntermediates



Its often the (very) small details that matter. Structure prediction – at least with its current capabilities won't help elucidate these. 4th generation SR will.

Borshchevskiy, V. *et al.*, (2022). True atomic-resolution insights into the structure and functional role of linear chains and low-barrier hydrogen bonds in proteins. Nat Struct Mol Biol 29, 440 –450. https://www.nature.com/articles/s41594-022-00762-2.

ENSEMBLES OF STRUCTURES WILL HELP PROVIDE AN UNDERSTANDING OF CONFORMATIONAL VARIABILITY/DYNAMICS



Ensemble of structures of a given protein obtained by X-ray crystallography under various conditions.

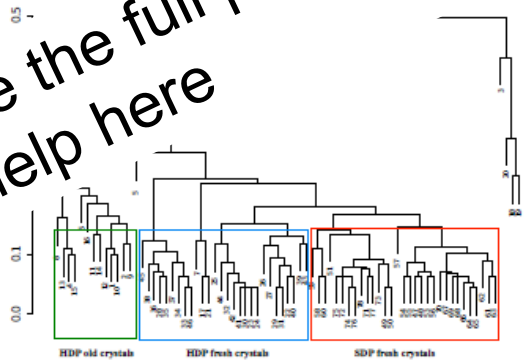
Cryo T Ambient P | Room T Ambient P | Cryo T Increasing P | Room T Increasing P

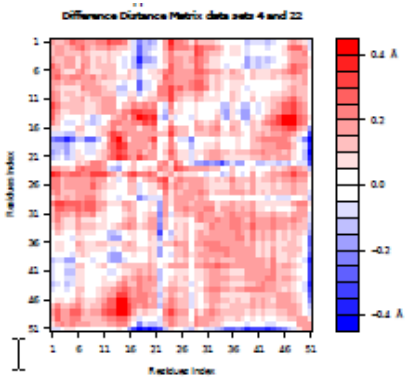
Additional restraints to gi… details of change…

…c Crystallography – Small-scale movements (a few atoms)

…lecular Dynamics Simulations – to validate a scenario involving all available structures, including restraints, and fill up the missing bits

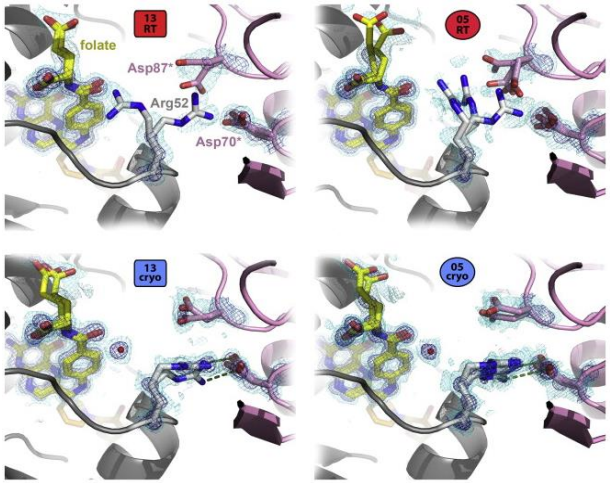
A single structure/data point will not give the full picture. Again 4th generation SR will help here

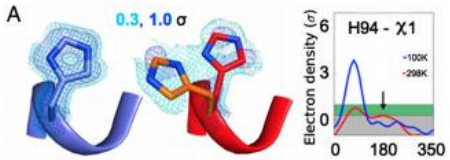




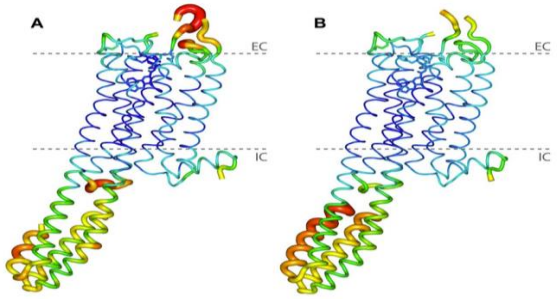
Ensembles of structures not a single structure

ROOM TEMPERATURE DATA COLLECTION





Fraser et al., PNAS 2011

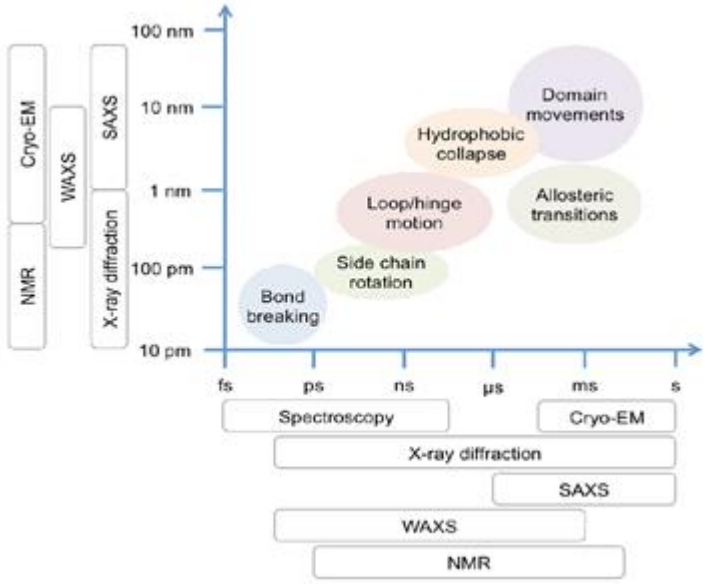


XFEL (RT) Synchrotron (100 K)

Liu et al. 2013

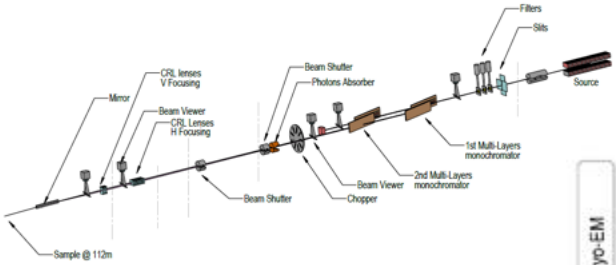
- CryoMX was one of the keys for success
- Cryo-structures do not display the same range of conformations as the RT structures.
- They might hide functional conformations and prevent binding of substrates or inhibitors
- RT temperature crystal structures reveal physiologically relevant conformations “hidden” at 100 K
- Present thermal motion closer to “native” conditions
- Better interpretation of crystal structures, including for the design of new therapeutic agents
- Because of radiation damage, serial crystallography is the most valuable route to obtaining RT structures.

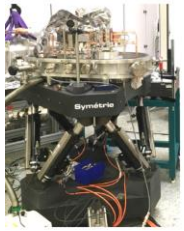
- **Hydrated microcrystals at room temperature can:**
  - **be activated**
  - **be soaked**
  - **We can carry out (and follow) reactions in them**



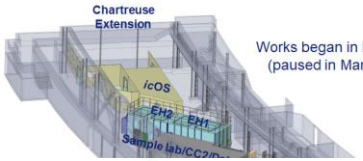
ID29/EBSL8: A BEAMLINE FOR (TIME-RESOLVED) SERIAL CRYSTALLOGRAPHY

- High flux (10^{16} ph/s), large bandwidth (0.3%, 1.0%)
- Beamsize: 0.5 µm – 10 µm
- Tuneable: 10-15 keV; 35 keV

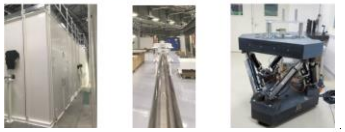




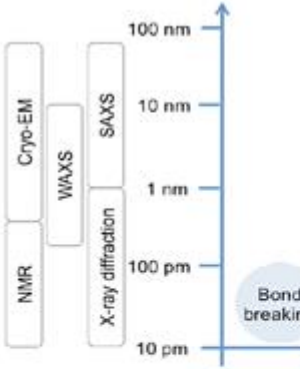
Double multilayer monochromator
Installation in Week 23



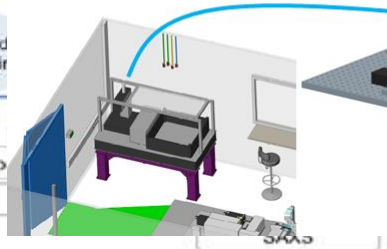
Works began in November 2019
(paused in March-July 2020)

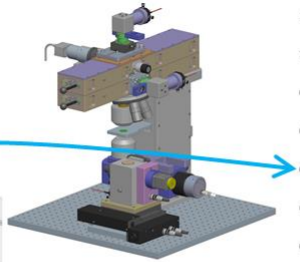


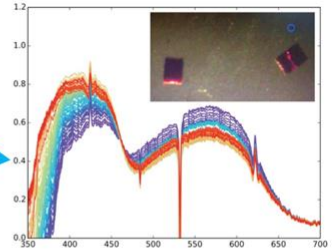
Works began in July 2020
ined in March 2020)
ses due to Covid-19



Domain

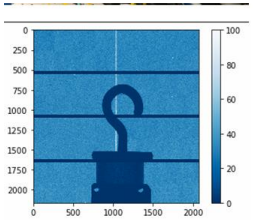






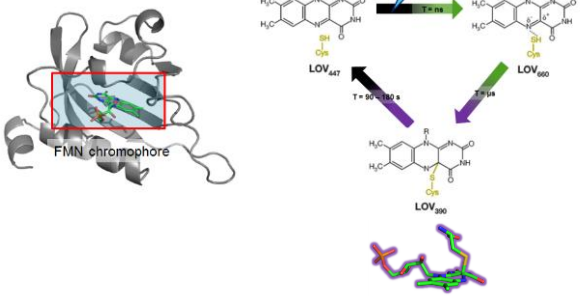
Time series of UV-vis abs spectra from a bacteriorhodopsin crystal following an actinic flash (10 microsecond time scale)

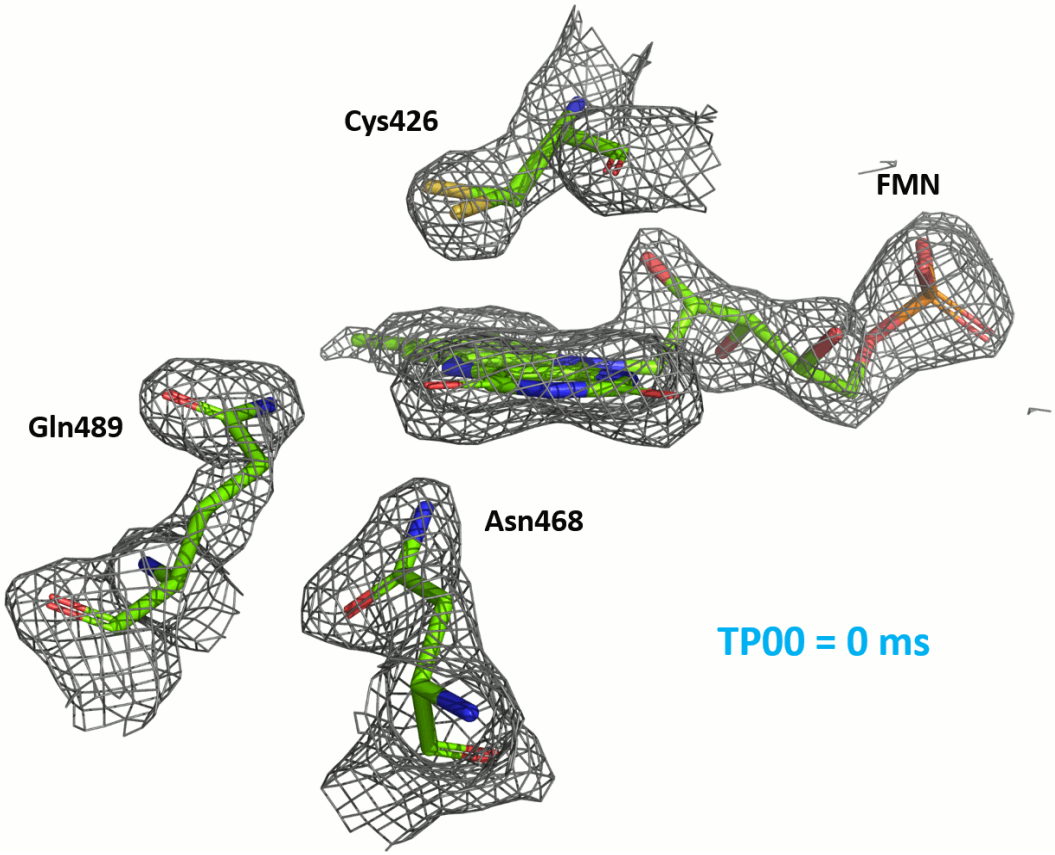
synchronous data collections. Target moves synchronously with a 1kHz clock with ~ 1 µm positioning accuracy (Collaboration with EMBL Grenoble). Test with ESRF timing system (RF clock) and heat load chopper in coming weeks.



Jungfrau 4M (Collaboration with PSI) delivered at the end of April. SAT on going with ESRF Lima library. Development of Lima2 and compression algorithm on going.

MOLECULAR MOVIE OF LOV-2 PHOTORECPTOR ADDUCT FORMATION

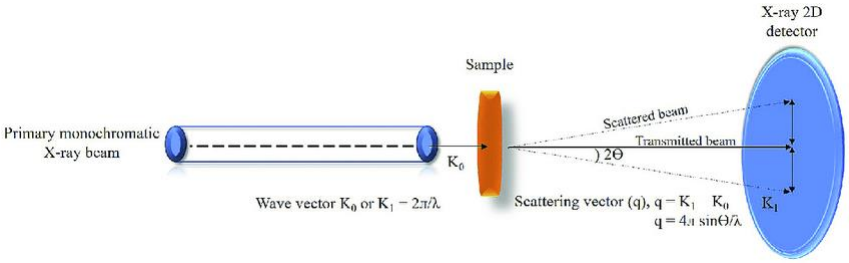


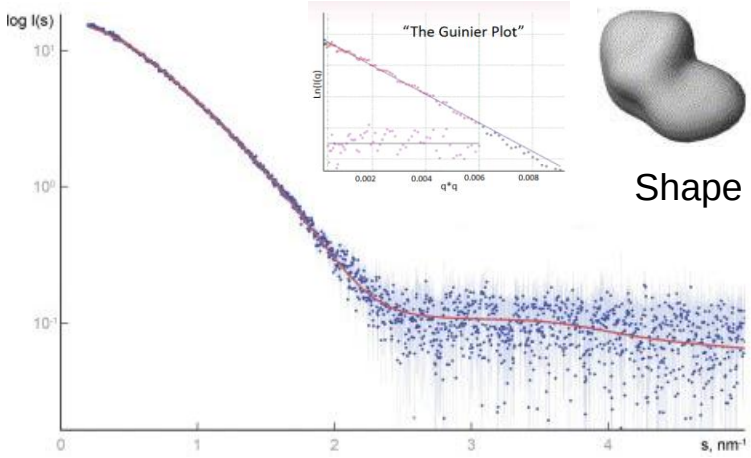


Aumonier, S., et al. (2020). Millisecond time-resolved serial oscillation crystallography of a blue-light photoreceptor at a synchrotron. *IUCrJ* **7**, 728-736.

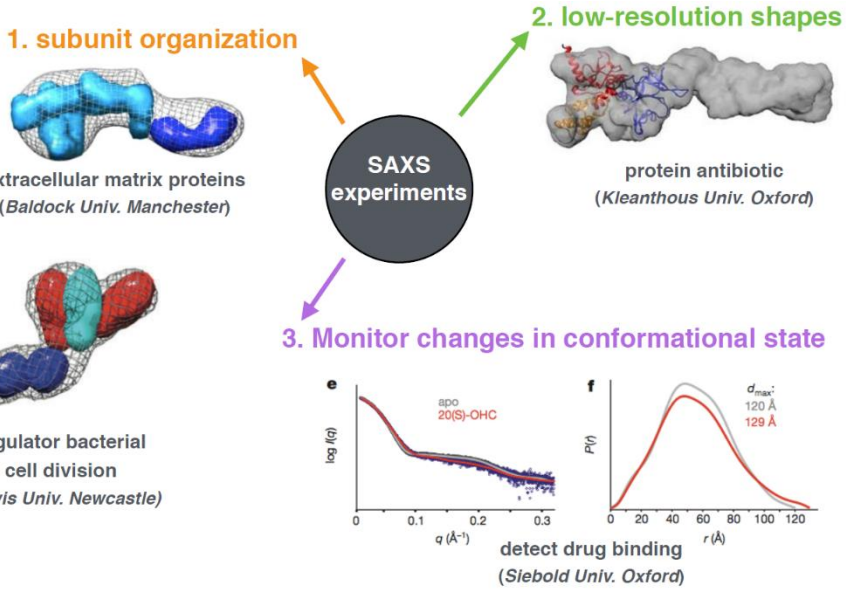
SMALL-ANGLE X-RAY SCATTERING (SAXS, BM29)

SAXS measures the solution state of protein or biopolymer





Shape



ELECTRON MICROSCOPY AT ESRF-EBS: CM01

Rolling proposal

↓

BTAP evaluation

↓

Approved proposal

Pre-evaluated project
(sample preparation established)

Grids available → KRIOS

Grids NOT available → GRID preparation @ ESRF cryoEM lab → KRIOS

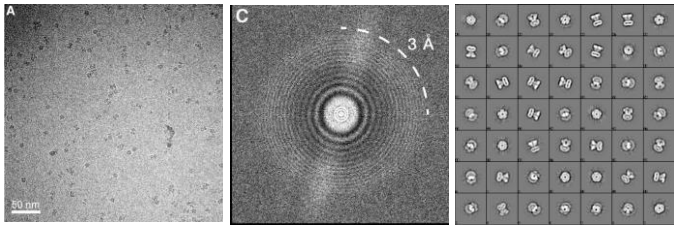
New project
(sample preparation to be established)

↓

First quality test @ PSB cryoEM Platform (IBS/EMBL(?))

High sample quality → KRIOS

Average sample quality → cryoEM @ PSB → end



Thank you for your attention

ESRF LAAMP Contact: Prof. Ed Mitchell, Head of Business Development
Email address: mitchell@esrf.fr

https://www.youtube.com/watch?v=joY1vMQkzUk