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FOREWORD BY THE INSTRUCT-ERIC **DIRECTOR & COORDINATION TEAM**

Instruct-ERIC in 2024

In 2024, we were energised by the interaction with the extended scientific community at the Instruct Biennial Structural Biology Conference. This edition took place in Cascais Portugal and showcased the power of integrated structural biology to tackle scientific challenges. We announced the 2024 Bertini Awardee, Dr. Martin Blackledge from IBS Grenoble. Martin embodies the principles which underpin our infrastructure: scientific excellence and frontier research that utilises an integrative structural biology approach. We look forward to the next Biennial hosted by Instruct-Belgium and a new Bertini awardee to join the prestigious list of scientists recognised by the award.

As Instruct community, we published a large consortium publication on the future of integrated structural biology (Structure. 2024 Oct 3;32(10):1563-1580. doi: 10.1016/j.str.2024.08.014).

2024 marked an inflection point in the evolution of our infrastructure; we conducted an ESFRI monitoring process and the Long-Term Assessment commissioned by the Instruct Council to analyse the operations of the organisation. Both processes provided a holistic review of Instruct by external experts, and in both exercises Instruct was very positively reviewed. We were delighted by the positive outcome in the ESFRI monitoring exercise which solidifies our position as a Landmark infrastructure operating in an efficient and transparent fashion.



FIG 1. Celebrating the membership of Germany in Instruct-ERIC at the Council Meeting in Ljubljana, May 2024.

We were delighted to welcome Germany as a new member of Instruct-ERIC, Germany was one of the founding members of Instruct when operations started formally in 2012 and now joins as a full Instruct-ERIC Member. Germany's structural biology community is a stalwart of European research in the field. We look forward to opening the doors of our facilities and, in the near future, to integrating the state-of-the-art technologies available at German facilities to the Instruct infrastructure.

Continuing the spirit of collaboration, a Memorandum of Understanding was signed with ELIXIR to enhance our strong mutual ties even further. Together with ELIXIR, we will work to make experimental data available and usable for researchers worldwide. Continued collaboration will also enrich the development of the federated European Open Science Cloud (EOSC).

2024 had a strong focus on engagement of national structural biology communities. Instruct Hub worked with national community champions to organise scientific networking events in Slovenia, Greece and Latvia. The events included scientific presentations from the local communities as well as demonstrating the technologies and expertise available at our centres. Next year we are looking forward to organising a showcase of events in the Netherlands and Finland.

All good things do sadly come to an end, and 2024 marked the end of iNEXT-Discovery which has a crucial impact with the provision of free and open access to facilities from the Instruct-ERIC infrastructure and other leading European facilities. Instruct was key in the development of a sustainability plan including the organisation of foresight meeting in Krakow. The future is challenging as the resources available to support access diminish. We will continue to add our voice and our effort to call for increased transnational access support.

Collaborating with colleagues from other ERICs is a highlight of our work, the ERIC Forum provides a great opportunity to share experiences and provide leadership in areas of expertise. In 2024 we were able to contribute to many areas including internationalisation, our contribution to EOSC and access provision.

Finally, we would like to highlight the great work carried out by everyone in the Hub and the centres and look forward to continuing this important work, and to the new and exciting opportunities that 2025 brings!

Dr Natalie Haley Head of Strategy

Prof Harald Schwalbe Instruct-ERIC Director Dr Claudia Alén Amaro Head of Operations

Notalia Haley

11. 411



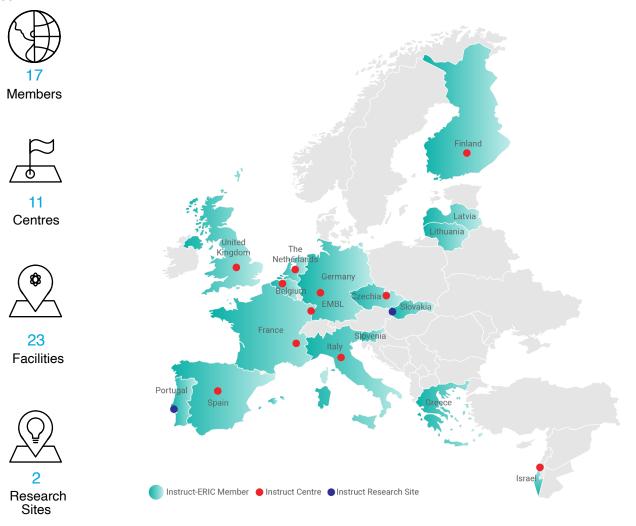


EXECUTIVE SUMMARY

INSTRUCT-ERIC MEMBERSHIP

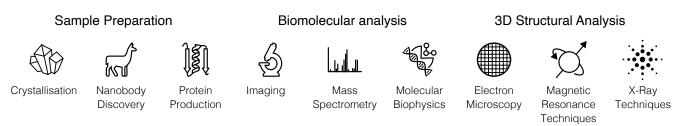
Instruct-ERIC had 17 Member Countries and Organisations with Germany joining in 2024.

The Members hosted 11 Instruct Centres with 23 facilities providing access to structural biology technology and expertise.



INSTRUCT-ERIC SERVICE CATALOGUE

Instruct-ERIC provides access to high-end structural biology services and techniques. In 2024, 80 services were offered across nine service types.



Access to those services is provided free at the point of use for researchers from Instruct Members and includes training, expert advice, and support before, during, and after the research visits.

Additionally, depending on the facility resources and user needs, services can be accessed in-person or remotely to result in optimal infrastructure use.

INSTRUCT-ERIC SERVICE PROVISION



Access proposals received



1535.5 Days of access provided



Scientific **Publications**

In 2024 Instruct-ERIC received 271 proposals for access from researchers in 26 countries.

Instruct-ERIC supported 180 research visits providing 1535.5 days of access to Instruct Facilities covering both national and transnational access.

Scientific output resulted in 338 publications in peerreviewed journals of which 88% are open access.

INSTRUCT-ERIC TRAINING AND CAREER DEVELOPMENT



Training Courses



Internships



R&D Awards

In 2024, Instruct-ERIC provided funding to support four training courses.

Additionally, Instruct-ERIC supported eight internships of three to six months for early career researchers.

Six Research & Development Pilot Awards were awarded, two in the TechDev call and four in the R&D Pilot Funding call.

INSTRUCT-ERIC HORIZON PROJECT PARTICIPATION



Projects

In 2024, Instruct-ERIC coordinated the Fragment-Screen project and participated in 13 other Horizon projects: Al4Life, BY-COVID, canSERV, EOSC Future, EOSC4Cancer, EOSC Beyond, ERIC Forum 2, eRImote, EU-LAC ResInfra Plus, FHERITALE, iNEXT-Discovery, IMAGINE, ISIDORe.

One new project was awarded to start in 2025: MALDIBANK

ARIA - ACCESS MANAGEMENT SYSTEM



ARIA is a cloud software platform, developed and maintained by Instruct-ERIC Hub, which provides an integrated suite of tools for research infrastructure management.

In 2024, ARIA supported 20755 registered users, an increase of 2717, the highest year on year increase on record. A record number of 770 proposals were submitted in ARIA resulting in 1458 peer reviews performed in 2024. Additionally, 2766 messages were sent in ARIA to connect the users, access managers, reviewers and facility teams.

COMMUNICATIONS







Science Highlights



Webinars

In 2024, Instruct published 27 news items on the website outlining the latest news from Instruct and partner projects, including new members, calls, and technologies.

Seven science highlights were published, putting a spotlight on research made possible by Instruct infrastructure.

Six webinars allowed Instruct scientists to outline their latest research to the structural biology community.

TIMELINE

selected events from 2024

Long-term assessment conducted

JAN Start of FHERITALE project



Germany joins as Member of Instruct-ERIC

Launch of Horizon Europe in UK

Start of EU-LAC
ResInfra Plus project



MAR

FEB

APR

Fourth International Call Launched

Start of EOSC Beyond Project

⊘eosc BEYOND≫

MAY

Instruct-ERIC Council Meeting in Slovenia

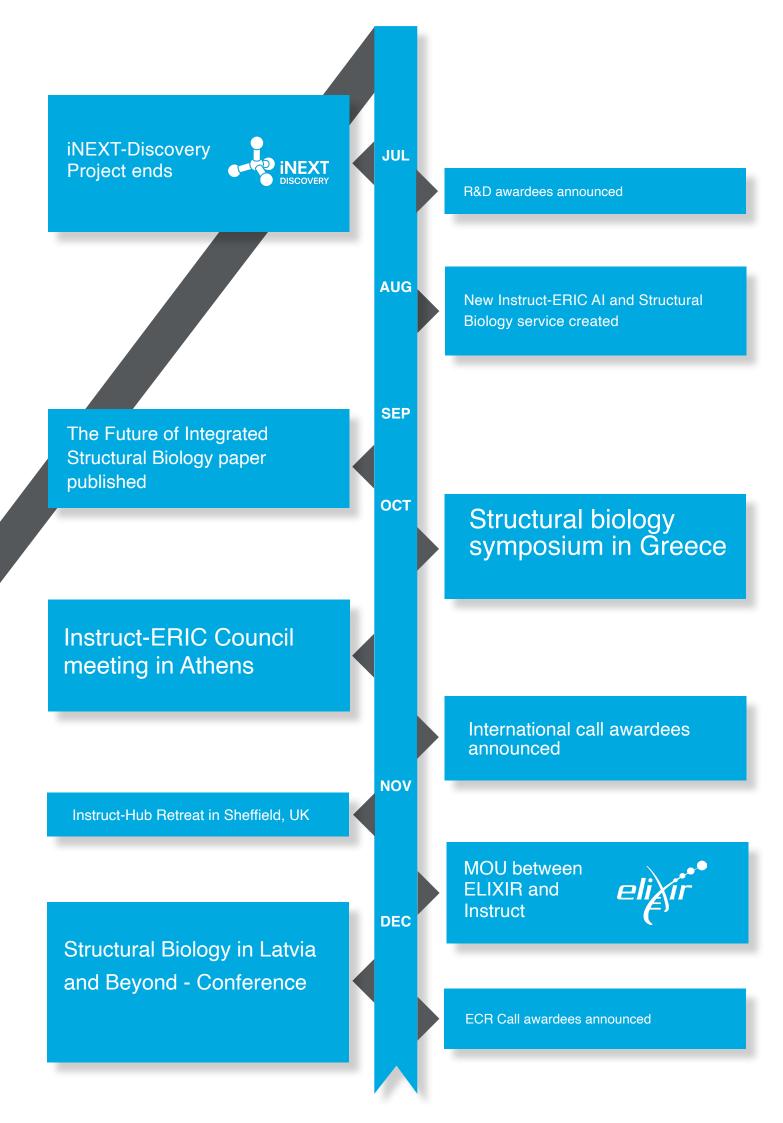
Bertini Award Winner announced as Martin Blackledge of IBS Grenoble

Launch of fandanGO ARIA metadata pipeline software as part of Fragment-Screen project

Structural Biology in Slovenia and Beyond - Minisymposium

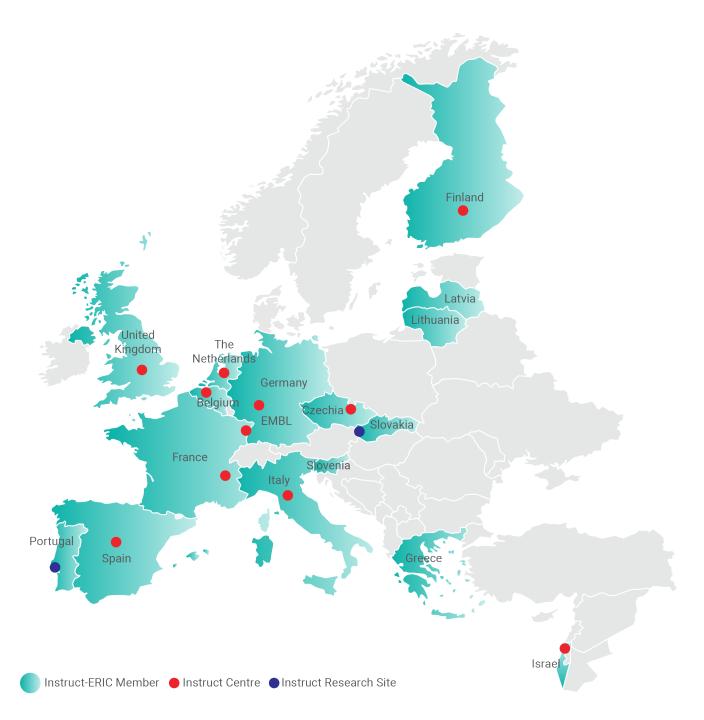
Instruct Biennial Structural Biology Conference 2024 - Cascais, Portugal

JUN



INSTRUCT-ERIC MEMBERSHIP

Germany became a Member of Instruct-ERIC in January 2024, growing the infrastructure further to 17 Members, following Slovenia and Greece who joined in 2023. As members, structural biologists in Germany could begin applying for access to services and technologies in the Instruct catalogue to advance their own research, whilst it also provided an opportunity for research teams in Europe to interact and collaborate with scientists in Germany. The news was accompanied by a plan to establish an Instruct Centre in Germany, providing access to users as well as utilising services offered by other facilities.



Instruct continued to collaborate with researchers in its Member Countries, organising three conferences in 2024 designed to bring together national structural biology communities, and promote the excellent research being conducted by its Members. This followed successful meetings of this kind in 2023, in Lithuania and Portugal. The first of these was in Slovenia, attached to the Council meeting in Ljubljana in May, with a "mini-symposium" highlighting the work done by early career researchers in the country, plus talks from experienced Instruct researchers detailing the opportunities available through Instruct. Attached to the October Council meeting in Athens was a similar event, highlighting the work done by researchers in Greece, and detailing the mechanisms by which researchers in the country can receive funded access and support for their structural biology research. Finally, in December, a dedicated one-day conference was organised in Riga, Latvia, showcasing the research conducting by the structural biology groups in the country, and offering a reminder of the services available to early-career researchers in Latvia, including training courses, internships, and R&D funding.

INSTRUCT-BE

Instruct Centre BE

instruct-eric.org/centres/instruct-be/

Nanobodies4Instruct, Brussels Robotein for Instruct, Liège and Brussels



Services







Highlights in 2024

Meetings and Outreach

- Belgium announced as hosts of the upcoming Instruct Biennial Structural Biology Conference 2026
- Robotein® gave a talk in a postgraduate training course held at the University of Liège (Belgium, May 2024), focusing on quality control methodologies for protein samples.
- Platform manager, Dr Marylène Vandevenne, completed a two-week training program at the Biophysics Platform of the Pasteur Institute (Paris, November), aimed at deepening expertise in biophysical techniques routinely used at Robotein®.
- Prof. André Matagne gave three lectures (Siena, Leuven, Brasov) and a webinar (sponsored by Waters/Wyatt on protein quality control)
- Moderated Instruct Structure Meets Function Webinar 32, with speakers that accessed Robotein® through the ISIDORe project
- Els Pardon of Nanobodies4Instruct gave a talk "Nanobodies for structural biology and beyond" in the "Molecular perspective of cellular processes" session at FEBS 2024, in Milan

INSTRUCT-CZ

Instruct Centre CZ

instruct-eric.org/centres/instruct-cz/

BIOCEV - Biotechnology and Biomedicine Centre, Vestec, Prague

CEITEC - Central European Institute of Technology, Brno



















Highlights in 2024

New Instruments, Upgrades and Tools

- Installation of Falcon4i direct electron detector with Selectris energy filter and purchase of Cryo-FIB/SEM microscope for cryo-volume EM at CEITEC, CF Cryo-Electron Microscopy and Tomography
- New Refeyn mass photometer TwoMP, Fluorolog QM (modular spectrofluorometer) and Chirascan V100 (circular dichroism) at CEITEC, CF Biomolecular Interactions and Crystallography
- Updated Renishaw's InVia confocal Raman microscope, CEITEC, CF Nanobiotechnology
- Enhanced SAXS Instrumentation: MetalJet D2+, BIOCEV IBT, CF Diffraction Techniques
- New liquid chromatography system Agilent 1290 at BIOCEV IBT, CF Structural Mass Spectrometry
- New service of mammalian expression in HEK293T, Expi293, and Expi293F™ GnTI- cells, and baculoviral expression in Sf9 or High Five™ insect cells at BIOCEV IBT, CF Protein Production

- The XX Discussions in Structural Molecular Biology and 7th User meeting of CIISB was held in Nove Hrady, South Bohemia, March
- iNEXT-Discovery workshop cryo-FIB lamella preparation & cryo-ET, April 2024, at CEITEC
- 37th Central European NMR Meeting was held in Valtice, Czech Republic in May
- Final iNEXT-Discovery Consortium Meeting and 4th Symposium on Recent Advances in Cryo-EM CEITEC
- Practical Protein Crystallisation and Diffraction Course held at BIOCEV on October
- Vladimír Sklenář Memorial Conference on NMR & Structural Biology, CEITEC, November



INSTRUCT-DE

Highlights in 2024

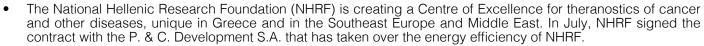
- Starting 2024, Germany became the 17th member of Instruct-ERIC.
- Prof. Harald Schwalbe, Instruct Director, said: "Scientific institutions and companies in Germany have contributed significantly in recent years to the development and establishment of structural biology methods and technologies. We will establish in Germany a network of Instruct centres with associated laboratories that meet European standards, which in turn will allow access to all facilities, across locations."



INSTRUCT-EL

Highlights in 2024

New Instruments, Upgrades and Tools



- The procurement of the state-of-the-art instruments for biophysical and structural characterisation including RF-MALDI-TOF, TIMS-TOF, cryoFIB/SEM, four (120 kV, 200 kV, 300 kV) cryo-TEMs (suitable for Electron Diffraction and Electron Tomography), vitrification robot, XRPD, SAXS, FTIR, NMR was completed.
- In September, NHRF signed an MoU with the Oncology Hospital Agios Savvas, one of the main anti-cancer hospitals in the center of Athens with a view towards the creation of a Comprehensive Cancer Center in Athensthe first one in Greece.
- The National Hellenic Research Foundation (NHRF), organised the Instruct-EL Structural Biology Symposium in October in Athens, Greece. The Symposium was addressed to Greeks interested in the field of Structural Biology, Decision Makers, Funders and End Users. The main objective of the Symposium was to celebrate the entry of Greece as a full member of ESFRI Landmark Instruct-ERIC and at the same time to inform all stakeholders about Structural Biology and its applications.







INSTRUCT-EMBL

Instruct Centre EMBL

instruct-eric.org/centres/instruct-embl/

EMBL Grenoble, EMBL Hamburg, EMBL Heidelberg



Services









Highlights in 2024

New Instruments, Upgrades and Tools

- EMBL Grenoble Staff at EMBL and ESRF developed a new method for using in situ serial crystallography (iSX) to study the structure of macromolecules. The method is now operational at the ID23-2 beamline, jointly operated by EMBL and the ESRF.
- EMBL Hamburg A key improvement at beamline P12 dedicated to SAXS has been the integration of a new stopped-flow mixing device (µSFM, Biologic), significantly reducing the volume of biological samples required, previously a limiting factor while maintaining experimental precision. The eSPC data analysis platform at EMBL Hamburg continues to expand, with the addition of the ChiraKit module for circular dichroism data.
- EMBL Heidelberg Steffen Klein, an ARISE fellow in Julia Mahamid's group was awarded an Instruct R&D grant 'Developing Technologies for accurately localizing macromolecules in cryo-electron tomography of intact cells'

Meetings and Outreach

- EMBL Heidelberg held an iNEXT-Discovery Workshop Cryo-FIB Lamella Preparation and Cryo Electron Tomography. A follow up course covering advanced sample preparation is planned and supported by Instruct-
- EMBL celebrated its 50-year anniversary in 2024. A year of events were organised culminating in a symposium in July 2024. 'From atoms to ecosystems – a new era in life sciences' showcased the foundational scientific research, service, technology and innovation that EMBL has fostered over the past 50 years.

INSTRUCT-ES

Instruct Centre ES

instruct-eric.org/centres/instruct-es/

CryoEM CNB-CSIC, Madrid 12PC - Instruct Image Processing Center, Madrid



Services



Highlights in 2024

New Instruments, Upgrades and Tools

- I2PC developed automatic workflows to support cryo-EM facilities, covering the entire processing pipeline, starting from the raw movies acquired at the microscope and leading to the generation of an initial 3D volume estimate
- As part of the Scipion Flexibility Hub, I2PC implemented a deep learning algorithm specifically designed for continuous heterogeneity analysis in single-particle cryo-EM. Developed new algorithms to detect and correct tiltseries misalignments in cryo-electron tomography datasets
- Cryo-EM Facility upgraded the Talos Arctica detector from a Falcon III to a Falcon 4i camera

- The new website of Instruct Spain is live at: instruct-eric.es
- Several courses I2PC Course on Single Particle Analysis by Cryo-EM (March), Instruct Course on flexibility analysis and integrative modelling using Scipion (June), I2PC - Instruct-RI Hubs hybrid course on Electron Tomography and Subtomogram Averaging (December)
- Courses included researchers from Latin America as part of the EU-CELAC Study Visit call, with attendees from Brazil, Argentina, and Paraguay



INSTRUCT-FI

Instruct Centre FI

instruct-eric.org/centres/instruct-fi/ University of Eastern Finland, Joensuu University of Helsinki, Helsinki University of Oulu, Oulu



Services















Highlights in 2024

New Instruments, Upgrades and Tools

- At the University of Helsinki, the direct electron detector on the Tecnai Arctica transmission electron microscope was upgraded to a Thermo Fisher Falcon 4i with fringe-free imaging. All single particle, electron tomography, microcrystal electron diffraction and processing software was updated at the Cryo-EM core facility. Ultracentrifugation rotors were updated at the Biocomplex Unit, plus Preomics BeatBox sample preparation at SCoPE-MS Unit.
- At the University of Oulu, Formulatrix NT8 crystallisation robot with a plate copy option that can setup hanging drop, sitting drop, micro-batch, LCP, and seeding experiments was installed.
- University of Eastern Finland Native MS facility acquired a high-precision capillary puller (P-1000; Sutter Instrument Company) for borosilicate nanospray emitter production. This boosts the quality native MS spectrum for difficult protein samples. An Äkta pure 25 M FPLC system (Cytiva) was purchased for protein purification and fractionation.

Meetings and Outreach

- Instruct-FI and FINStruct network was approved for the National Roadmap for Research Infrastructures 2025-2028.
- Structural Biology platform FINStruct and Instruct-ERIC Centre Finland 2024 Annual Meeting was held in Oulu in November 2024 and organised by the University of Oulu. The programme included scientific presentations, presentations by companies, infrastructure facilities or networks, and scientific and core facility posters.

INSTRUCT-FR

Instruct Centres FR1 & FR2

instruct-eric.org/centres/instruct-fr1/instruct-eric.org/centres/instruct-fr2/

IGBMC, Strasbourg IBS-ISBG, Grenoble



Services

















Highlights in 2024

New Instruments, Upgrades and Tools

- In crystallisation at FR1: a new Rock Imager System (Formulatrix) was installed in February 2024.
- New Agilent 6545XT LC-ESI-Q-TOF for intact mass determination at FR2, and new Malvern OMNISEC (SEC-MALLS) in FR2 the biophysical platform.
- Titan Krios delivered to FR2 and installed at the ESRF, and two CNRS positions created for EM and super resolution microscopy platforms

- iNEXT-Discovery workshop (April 2024): Cryo-FIB lamella preparation and cryo-ET at 4 Instruct centres eBIC/Diamond Light Source-EMBL-Heidelberg, CEITEC and FR1 (coordinator).
- Instruct Cryo-EM Workshop, Grenoble (FR2, May 2023).



INSTRUCT-IL

Instruct Centre IL

instruct-eric.org/centres/instruct-il/

ISPC - Weizmann Institute of Scince, Rehovot Centre for Bioinformatics, Tel Aviv University, Tel Aviv



Services







Highlights in 2024

New Instruments, Upgrades and Tools

- The Structural Proteomics Unit (SPU) has expanded its services to include in silico predictions of protein and protein complex structures using various software packages, including the advanced AlphaFold2. The predicted models are evaluated to determine their quality and accuracy.
- The EM Unit can provide data collection for protein structure determination using a Thermo Fisher Arctica microscope with a Falcon III direct electron detector.
- The Arctica microscope can also be used to collect tomographic data of thin samples (vesicles etc), or in scanningtransmission mode to collect cryo-STEM tomography data.
- The EM Unit's Talos microscope can give X-ray energy dispersive spectroscopy for vitrified samples.

INSTRUCT-IT

Instruct Centre IT

instruct-eric.org/centres/instruct-it/

CERM, Florence



Services







Highlights in 2024

New Instruments, Upgrades and Tools

- An NMR spectrometer has been installed at CERM/CIRMMP, within ITACA.SB NRRP, that allows 19F detection with high sensitivity, extending the possibilities of 19F NMR to characterise drugs and biomolecules in vitro and in cells.
- CERM/CIRMMP developed innovative strategies allowing to simultaneously map protein-protein binding sites on interacting partners in a ternary complex, by combining a complementary isotope-labelling approach with a multiple-receiver NMR detection scheme.
- A comprehensive protocol has been developed to systematically optimise 13C direct-detected NMR experiments on intrinsically disordered proteins ultra-high field
- A methodology based on the integration of NMR protein-based and ligand-based experiments, with several biophysical techniques and computational methods, enables the characterisation of protein-glycan complexes. This strategy can contribute to the design of new therapeutics against bacterial infections and cancer cells.

- The CERM/CIRMMP Infrastructure organised a special edition of the Chianti Workshop celebrating the 40th anniversary of the event, the 25th anniversary of the CERM and the 30th anniversary of the foundation of CIRMMP.
- The project FHERITALE, whose partnership include several ESFRI projects and Landscapes, provided several occasions for profitable exchange of ideas and setting the stage to broaden and increase the access provision.
- In the frame of the ITACA.SB NRRP, Instruct IT organised a series of webinars focusing on structural biology.

INSTRUCT-LT



Highlights in 2024

Meetings and Outreach

- On 19 November 2024, the Instruct-LT Webinar #36 from the "Structure meets function" series featured presentations on cryo-EM studies of Cas12 nucleases (Giedrius Sasnauskas), structure and mechanism of the anti-phage defence system retron Ec67 (Monika Jasnauskaitė) and structural studies of bacterial antiviral defence system Thoeris (Giedrė Tamulaitienė).
- On 29 November 2024, Instruct-LT representatives G. Sasnauskas and G. Tamulaitienė visited Kaunas, where they
 presented seminars titled "Structural Biology: Methods, Research in Lithuania, and Instruct-ERIC" at the Kaunas
 University of Technology and the Lithuanian University of Health Sciences, aiming to broaden the user base of
 Instruct-ERIC services in Lithuania.
- On 3rd December 2024 in University of Latvia, Riga, the Instruct-ERIC event "Structural Biology in Latvia and Beyond" was held. The meeting featured talks and discussions between leading experts in the field from the Instruct consortium and from the Latvian structural biology community. Researchers from Lithuania were invited to attend and speak at the symposium.



INSTRUCT-LV



Highlights in 2024

New Instruments, Upgrades and Tools

• In 2024, Latvian Institute of Organic Synthesis (LIOS) installed a 0.51 mm HCN solid-state MAS NMR probe. Using this probe structure, dynamics and interactions of biomolecules can be elucidated using only submiligram amounts of samples.

- From 2nd to 3rd May 2024 LIOS hosted the COST project "SPRINGBOARD" conference, dedicated to recent advances in drug discovery, featuring many structural biology related talks. The event took place in Riga Avalon Hotel and brought together 19 distinguished speakers and over 100 participants.
- On 3rd December 2024 in University of Latvia, Riga, the Instruct-ERIC event "Structural Biology in Latvia and Beyond" was held. The symposium was featuring talks and discussions between leading experts in the field from the Instruct consortium and from the Latvia structural biology community.





INSTRUCT-NL

Instruct Centre NL

instruct-eric.org/centres/instruct-nl/

Bijvoet Centre - Utrecht University, Utrecht NKI. Amsterdam NeCEN - Leiden University, Leiden

Services













Highlights in 2024

New Instruments, Upgrades and Tools

- NKI added new/updated AlphaFill and DSSP tools to the Instruct-ERIC Computational Services catalogue.
- Dutch national funding (Oncode Accelerator) allowed NKI to partially update their Protein Facility. Access to their new Malvern PEAQ-ITC can be requested, and a new OMNISEC SEC-MALS is being commissioned. A Single Molecule confocal microscope (LUMICKS) has been added and is currently being rolled out as an access service, with an aim to provide for Instruct-ERIC users.

Meetings and Outreach

- iNEXT-Discovery coordinator NKI co-organised a structural biology foresight meeting with Instruct-ERIC (Krakow; July 8-10, 2024), and successfully completed the entire iNEXT-Discovery H2020 structural biology project.
- Instruct-NL members attended the Biennial Structural Biology Conference and presented an Instruct-NL poster.
- NKI facility staff contributed to the Instruct-ERIC review paper "The future of integrated structural biology"

INSTRUCT-PT

Instruct Research Site PT

instruct-eric.org/content/instruct-research-sites-portugal

FC-ULisboa, Lisboa ITQB NOVA, Oeiras



Highlights in 2024

New Instruments, Upgrades and Tools

- Vitrobot Mark IV System (ThermoFisher Scientific) + clipping station
- PELCOeasyGlow Glow Discharge Cleaning System (TED Pella, inc)
- Humidity-controlled room
- Data processing infrastructure (cluster of 4GPUs, 5x 22TBRAID-5 storage, cryo-EM software packages Relion, CryoSparc and SCIPION

- Hosted Instruct-ERIC 6th Biennial Structural Biology Conference, Cascais, 23-24 May
- "How Time-Resolved X-Ray Crystallography is driving Structural Biology Forward", NOVA FCT, February workshop
- FEBS advanced course on Metals in biology: their importance and tools to study them, ITQB, May 26-June 2
- 10th National Meeting of Users of Synchroton Radiation, ENURS 2024, Caparica, 7 June
- 1st CryoEM X-Ray Crystalography Synergy Workshop, Caparica, 1-3 July
- Instruct Hands-on Workshop on Sample Preparation for Single Particle Analysis by CryoEM, INL, 7-10 October
- Pathprot-16 Workshop, an international forum on proteomics, systems biology, and structural mass spectrometry, FC-Ulisboa, 16-18 October
- European Researchers' Night 2024 initiatives: Seeing the invisible: Overcoming global biological challenges with Cryo-Electron Microscopy, and Hands-on activities (Structural Biology) for non-expert audiences, 27 September
- Exhibition "Investigarte" at "Pavilion of Knowledge" Centro Ciência Viva, 1 June 2024



INSTRUCT-SI

Highlights in 2024

New Instruments, Upgrades and Tools

- National Institute of Chemistry: Computer cluster in Ažman centre was upgraded. New 600 MHz Bruker Avance Neo NMR spectrometer designated primarily for solid-state measurements with 24 position sample case allowing for automated sample changing of solid and liquid state samples.
- Two instruments for mass photometry Refeyn TwoMP were installed, one at the National Institute of Chemistry and the other at the Faculty for Chemistry and Chemical Technology, University of Ljubljana.

- Website of the Instruct-SI consortium set up at instruct-eric.si
- The Instruct-SI consortium co-organised several workshops and conferences on structural biology. The 3rd MOSBRI conference took place in Ljubljana, aswell as the workshop Basics of Methodological Approaches in Structural Biology at the National Institute of Chemistry, which focused on cryo-EM, MX and NMR, and attracted more than 90 participants.
- On 15 May, the Instruct-ERIC Council meeting was held in Ljubljana, Slovenia, preceded by a mini-symposium Structural Biology in Slovenia and Beyond, at the National Institute of Chemistry (below)



INSTRUCT-SK

Instruct Research Site SK

instruct-eric.org/content/instruct-research-sites-slovakia IC SAS - Slovak Academy of Sciences, Bratislava



Highlights in 2024

New Instruments, Upgrades and Tools

New Sample Case Cooled on 600 MHz highresolution NMR spectrometer (right, top)

Meetings and Outreach

Discussion Group Meeting of the Slovak National NMR Centre (2nd Oct. 2024)





INSTRUCT-UK

Instruct Centre UK

instruct-eric.org/centres/instruct-uk/

Astbury Biostructure Laboratory, Leeds Harwell Campus. Didcot Oxford University, Oxford

Services















Highlights in 2024

- In July 2024, the Astbury Biostructure Laboratory installed a HydraBio FIBSEM for milling cryogenically prepared tissue and cellular samples to enable cryo-ET and volumetric studies.
- Instruct-ERIC talk at the Astbury Conversation, outlining the opportunities for cryo-EM researchers through Instruct
- The molecular Biophysics platform on the Harwell Campus is now available to Instruct-ERIC users. Techniques available include analytical ultracentrifugation (AUC), surface plasmon resonance (SPR), isothermal titration calorimetry (ITC), dynamic and multi angle light scattering, flow induced dispersion analysis (FIDA), nanodifferential scanning fluorimetry (nanoDSF) and stopped-flow spectroscopy.
- Harwell Campus courses included the iNEXT-Discovery Sample Preparation Course in January, iNEXT-Discovery workshop in cryo-FIB, lamella preparation & cryo-ET in April, Wellcome-iNEXT Cryogenic Electron Microscopy in Structural Biology 2024 in May, Wellcome Trust/MRC-Beginners Single Particle Cryo-EM course 2024 in September, Wellcome-MRC in situ Cryo-ET Workshop 2024 in October, Diamond-CCP4 Data Collection and Structure Solution Workshop 2024 in December, and the Early Career Scientists Symposium 2024 also in December.
- In July the Harwell campus was opened to the general public where we welcomed over 10,000 visitors to the site to learn about the groundbreaking research that happens at some of the UKs national research facilities, including Diamond Light Source, Research Compelx at Harwell, Central Laser Facility, ISIS Neutron and Muon Source, RAL Space and the Rosalind Franklin Institute. From supercomputing, accelerator science, and next generation telescopes to biological sciences and robotics, visitors were able to see first-hand how the different facilities deliver inspirational work and how it is improving life for current and future generations.



FIG 1. The Instruct-ERIC Centre Forum, part of the Instruct Biennial Structural Biology Conference held in May in Cascais, Portugal.





In-cell NMR suggests that DNA i-motif levels are less abundant that previously reported in human cells

Utilising access to technologies available at CEITEC, part of Instruct-CZ, the team devised an innovative incell NMR-based technique to study DNA gene regulators intercalated motifs (iMs) in different models. The in-cell NMR data showed that certain iMs can form inside living human cells at physiological temperatures.

Víšková, P. et al. (2024), In-cell NMR suggests that DNA i-motif levels are strongly depleted in living human cells. Nat Commun 15, 1992, doi.org/10.1038/s41467-024-46221-y

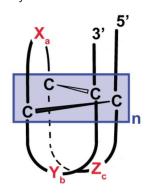


FIG 1. Schematic representations of the DNA i-motif structure with the minimal i-motif segment highlighted in the box. Xn, Yn, and Zn mark i-motif loop regions of variable length.



VDAC1-interacting molecules promote cell death in cancer organoids through mitochondrial-dependent metabolic interference

The voltage-dependent anion-selective channel isoform 1 (VDAC1) is a pivotal component in cellular metabolism and apoptosis. Biochemical characterisation showed that VDAC-antagonist (VA) molecules can directly interact with VDAC1 with micromolar affinity by competing with the endogenous ligand NADH for a partially shared binding site. Experiments performed on organoids derived from intrahepatic cholangiocarcinoma patients demonstrated a dose-dependent reduction in cell viability upon treatment with VA molecules with lower impact on healthy cells than conventional treatments like gemcitabine. The team hopes that this could pave the way for cancer treatments with fewer potentially harmful side effects.

Conti Nibali, Stefano et al. (2024), VDAC1-interacting molecules promote cell death in cancer organoids through mitochondrial-dependent metabolic interference, iScience, 27, 6, DOI:10.1016/j.isci.2024.109853

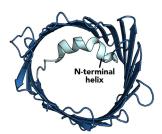


FIG 4. VDAC1 architecture and small molecule identification. β-strand topology of the channel



Using Nanobodies to Stabilise Previous "Undruggable" **Protein-Protein Interactions at Instruct-BE**

The research paper from Fischer et al (2024) describes the work conducted at VIB-VUB (Nanobodies4Instruct, part of Instruct-BE), utilising nanobodies to stabilise the binding of SOS1 and KRAS in their signalling complex, an interaction invlved in several cancers and previously thought to be undruggable.

Fischer et al. (2024), Allosteric nanobodies to study the interactions between SOS1 and RAS, 15 (6214): doi. org/10.1038/s41467-024-50349-2

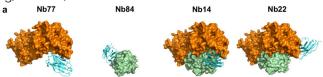


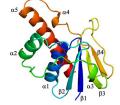
FIG 2. Crystal structures of the Nbs (cyan) in complex with SOS1 (orange) and/or RAS (green).



Unraveling multifaceted the resilience of arsenic resistant bacterium Deinococcus indicus

The ITQB NOVA team coordinated with the Weizmann Institute through Instruct-ERIC to study the effect of arsenic on *D. indicus*, an arsenic-resistant bacterium. The team characterised the structure of the proteins involved in arsenic reduction, which has potential applications in removing toxic arsenic from the environment.

Gouveia et al (2024), Unraveling the multifaceted resilience of arsenic resistant bacterium Deinococcus indicus, Frontiers in Microbiology, Volume 14, doi.org/10.3389/ fmicb.2023.1240798



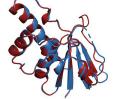




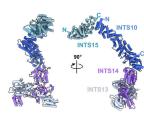
FIG 3. Figure 9. X-ray crystal structure of D. indicus arsenate reductase ArsC2.



Investigating the Structure of Integrator with Cryo-EM at Instruct-EMBL

The team utilised insect-cell expression, biomolecular characterisation including mass photometry, and cryo-EM at EMBL Grenoble, aiming to understand the structure of a sub-complex of Integrator, a key regulator of gene expression, to identify it's mechanism of binding with mRNA, telomerase RNA, and many other RNA forms.

Razew, M et al, (2024), Structural basis of the Integrator complex assembly and association with FIG 5. Atomic model of the transcription factors, Molecular Integrator arm module. Cell, 84,13, 2542 - 2552, DOI: 10.1016/j.molcel.2024.05.009





Structure and interactions the endogenous human Commander complex

The Commander complex, 16-protein assembly, plays multiple roles in cell homeostasis, cell cycle and immune response. Here, the team reports the structure and key interactions of the endogenous human Commander complex by cryogenicelectron microscopy and mass spectrometry-based proteomics, identifying the main interaction sites for its role in intracellular transport.



FIG 6. Composite cryo-EM map of the

Laulumaa et al. (2024), Structure complete Commander and interactions of the endogenous complex human Commander complex, Nature, (925-938).doi.org/10.1038/ s41594-024-01246-1

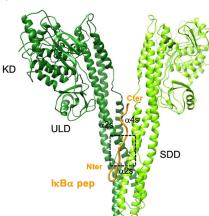


Revealing a molecular mechanism for IKK catalytic dimer docking with NFkB substrates at Instruct-FR1

Interactions between peptides IKK homodimers purified from insect cells (using Instruct funded access to the protein production platform at Instruct-FR1, IGBMC Strasbourg) were assessed by Isothermal Calorimetry (ITC) at the ITC Advanced platform at IBMC, Strasbourg. Li et al used Instruct-funded access to the crystallisation facility at Instruct-FR1 and X-ray crystallography to produce a 4.16-6.18A structure of IKKβ, and identify mechanisms to inhibit the protein and protect against pathologies emerging from IKK dysregulation.

Li, C., et al, (2024), Molecular mechanism of IKK catalytic dimer docking to NF-kB substrates. Nat Commun 15, 7692. doi.org/10.1038/s41467-024-52076-0

Figure Interaction between IKKB and IkBa peptide. Model of IKKβ bound to IκBa KD peptide based on the crystal structure obtained here for IKK β , with IkB α peptide modelled using distance constraints from cross linking mass spectrometry.



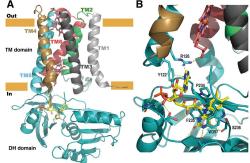


FIG 10. Full-length SpNOX. (A) Overall structure of SpNOX F397W at 3.6 Å with ribbons in the TM colored by helix, hemes (red sticks) and FAD cofactor (colored by atom). (B) The FAD binding site

Finding the Structure and Mechanism of **Bacterial Flotillin to Combat Antibiotic** Resistance

The team from the CNBmicrobiology facility (Ukleja et al, 2024) sought to understand how flotillin affects bacterial pathogenicity, and structure of its integration in the cell membrane by examining it in S. aureus, the bacteria behind MRSA. Ukleja, M., et al. (2024), Flotillin-mediated stabilization of unfolded proteins in bacterial membrane microdomains. Nat Commun 15, 5583, doi. ora/10.1038/s41467-024-49951-1



FIG 7. Cryo-EM map of the FloA-NfeD trimer (top). One FloA monomer is labeled in pink and the other FloA monomer in gray. The OBL of NfeD is shown in blue. Cryo-EM map with AF2 overlay (bottom).



Structural insights into Frizzled3 through nanobody modulators

Using Instruct-funded access to the VIB-VUB center for structural biology at Instruct-BE, Hillier & Zhao, et al were able to generate a series of specific nanobodies for Frizzled (FZD) receptors, transmembrane G-protein coupled receptors, enablling future studies into the effects of FZD in parkinsons disease and melanoma.

Hillier J, et al. (2024), Structural insights Frizzled3 into through modulators. nanobody Nat Commun. 2024 22;15(1):7228. doi: Aug 10.1038/s41467-024-51451-1.

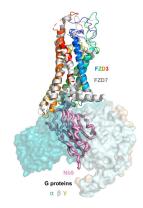


FIG 9. Schematic illustrating the Nb9 bound intracellular/TM portions of the FZD3 receptor overlayed with FZD7 bound to Gαβγ proteins



Unveiling the Key Insights into FR2 EMBL NADPH Oxidases through Study of Bacterial Model (Figure Left)

Researchers at the Institut de Biologie Structurale have made significant progress in understanding NADPH oxidases (NOX), enzymes critical for producing reactive oxygen species (ROS) used in immune defence and cellular signalling. This access was funded by the grants iNEXT-Discovery and Fragment-Screen, and through Instruct-ERIC. The published findings offer a deeper understanding of how electron transfer occurs within NOX

Petit-Hartlein, et al, (2024), X-ray structure and enzymatic study of a bacterial NADPH oxidase highlight the activation mechanism of eukaryotic NOX, eLife, DOI:10.7554/ eLife.93759



The Future of Integrated Structural Biology

The Instruct-ERIC review paper "The future of integrated structural biology" was published in Structure in 2024, detailing the current status of structural biology technologies, as well as discussing potential future developments in the field. With input from a host of leading experts, both within and external to the Instruct-ERIC consortium, the review examines

the existing challenges in structural biology, and how short and long-term developments may have profound benefits for science as a whole down the line.

More specifically, the paper outlines the need for integrated structural biology: the combination of various techniques to ascertain both the structure and function of the fundamental elements of biology.

The synergy of NMR, cryo-EM, X-ray techniques, coupled with mass spectrometry and biomolecular analysis is crucial for truly in-depth studies of proteins, nucleic acids, and the other building blocks of biological life.

The advances in AI that have taken over the public consciousness in recent years, in particular prediction software such as AlphaFold, are already sending shockwaves through structural biology labs in Europe and beyond. How researchers can successfully integrate these tools into their projects is discussed in the review paper.

The five frontiers for future development in structural biology include:

Optimised sample preparation, deep automation, and broader availability of cryo-EM instrumentation

The explosion in data acquisition from optimisation of automated approaches will boost research efficiency

In situ cellular structural biology

Substantial parts of integrated structural biology will evolve living multicellular organisms – tomography techniques will become even more impactful

Correlating structural dynamics with biological function

Understanding that dynamic approaches to characterisation is vital to realising the full detail of the structure and function of biological molecules, not just increasingly high resolution static data

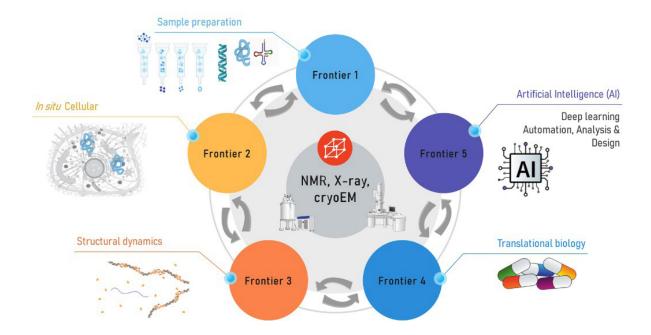
Bridging fundamental and applied research through translational biology

A growing relationship between academia and industry in translational research

Harnessing the data revolution, AI in structural biology

The aforementioned growth in data acquisition may come to rely on AI to identify key targets for drug discovery and future structural biology research projects

Future Direction: The Five Forces Analysis



All techniques at the current forefront of structural biology, and in its near and long-term future, are available through Instruct-ERIC. Researchers are invited to apply to access any of these techniques for their research; whilst early-career researchers can explore additional opportunities, including training courses, internships, dedicated access calls, and R&D funding.

ACCESS

What is Access?

As a research infrastructure, one of Instruct's core functions is to enable researchers to make use of scientific resources such as high-end technologies, equipment and expertise to facilitate innovation. This process by which researchers can use these scientific services is termed "access". Providing access to integrated structural biology infrastructure is a fundamental task of Instruct-ERIC. Any researcher worldwide can make use of Instruct-ERIC services. They must first submit a short research proposal detailing the research they would like to undertake, and the services from Instruct-ERIC's technology catalogue (instruct-eric.org/platform-catalogue) they wish to access. Proposals then undergo review by experts in structural biology to check that the proposal is of sufficient quality to warrant instruct-ERIC access. Selection is on the basis of scientific excellence. Following successful scientific review, a proposal is checked for technical feasibility by the Instruct-ERIC centres offering the requested services. If the proposal is deemed technically feasible access can proceed.

Funding for Access

A particular benefit for researchers working in Instruct-ERIC member countries and international organisations is that they are eligible for access funding. This means that access is provided free to the user in most instances, due to a service-dependent contribution to the cost of providing access paid to the Instruct-ERIC centres from the Instruct-ERIC budget and in many cases. Additionally, a contribution of € 400 is granted towards the travel and accommodation (or in the case of remote access, sample shipping costs) of the researcher. In 2024, a green bonus of € 50 was also made available for physical access for users travelling without taking a flight.

Access in 2024

Confirming the increase in access demand in the past years, 2024 saw record demand for Instruct's services with 277 proposals received for Instruct access. This figure includes proposals received for Instruct funded access, self-funded access and collaborations but also proposals received through the European projects ISIDORe and canSERV. To manage the increase in access requests, the Instruct evaluation process now includes a periodic selection panel, that makes final decisions on batches of applications which have been positively peer reviewed.

Some applications demonstrate scientific excellence but do not meet the threshold for Instruct funding due to competition induced by high demand. These are still offered funding from Instruct for travel and accommodation/ shipping along with the offer to self-fund their access with their own grants or resources.

In 2024, to tackle the specific needs of early career researchers (ECRs) (eg: post docs and early-stage PIs that need support to establish their independent research line), a specific ECR access call was launched, offering increased access support, travel and accommodation cost and a small grant for user consumables. Seven ECRs were supported through the Instruct ECR call in 2024 and a new ECR call will be launched in 2025.

Access through Horizon Europe projects

Complementing Instruct's core-funded access program, EU-funded TNA projects ISIDORe and canSERV continued in 2024. The 6 ISIDORe TNA calls closed in 2024. ISIDORe access to Instruct facilities was in high demand with a total of 48 applications received by Instruct, which led to 42 projects and 54 visits to Instruct Centres. Due to the high request for Instruct services in ISIDORe, Instruct was granted additional TNA budget within the project to meet some of this demand.

Infectious Disease

Cancer and Oncology

Translational Research

All Other Topics









canSERV opened 5 new access calls in 2024: 2 open calls and 3 targeted calls, with access management co-organised by Instruct through the ARIA access management platform. Similar to ISIDORe, the demand for Instruct services has been very high with 49 proposals requesting access to at least one Instruct service highlighting the importance of integrated structural biology services a broad range of research fields, including cancer research and infectious disease.

The final iNEXT-Discovery visits were completed in 2024, before the project came to an end in July. The outcomes of the iNEXT-Discovery project will continue to be realised over the coming years, as results from the research visits contribute to broadening the structural biology landscape.

ACCESS TO INFRASTRUCTURE 2024

Service demand

In the period from 1 January to 31 December 2024, demand for access reached a record high with 271 proposals. The increased demand in 2023 and 2024 results from a general increase in access requests to Instruct core access funding, and Instruct involvement in two access projects, canSERV and ISIDORe.

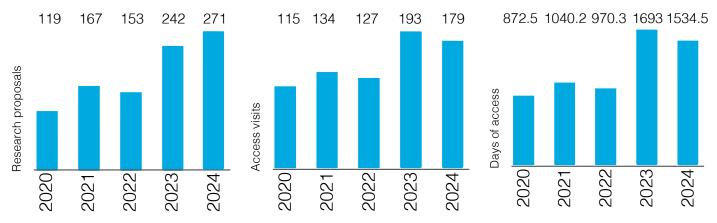


FIG 11. Instruct-ERIC access statistics [data retrieved 15.06.2025]

Service provision

In 2024, a 179 research visits were completed. 48 of those (27%) were national visits and the majority of 131 (73%) visits was transnational access to a research facility in a different county.

The visits combined to a total of 1534.5 days of access, of which 269 days were used nationally (17.5%) and 1265.5 transnationally (82.5%).

Services were provided to researchers from 20 different countries and organisations (AT, BE, BR, CH, CM, CY, CZ, DE, EL, ES, FI, FR, IL, IT, LT, NL, PT, SI, SK, UK). Those were primarily from Instruct-ERIC Members but special calls and research funded by the ISIDORe project allowed for access from non-Member countries.

3D structural analysis by electron microscopy was the most accessed service in 2024. This was followed by sample preparation services (protein production, crystallisation and nanobody discovery) which are essential for for subsequent 3D analysis (Fig. 12).

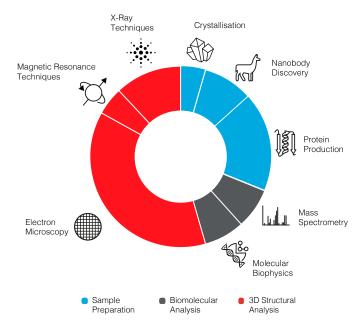


FIG 12. Instruct-ERIC access visits per service technology in 2024

[data retrieved 15.06.2025]

Peer-reviewed publications

A key performance indicator of success in this endeavour is the number of publications arising from use of Instruct-ERIC infrastructure, whether this is from the direct access to infrastructure through our access programme, or through the various training and career development opportunities that Instruct supports (for example, internships, R&D pilot awards and joint research activities).

The list of peer-reviewed papers published in 2024 that acknowledged Instruct-ERIC was 338 – the highest annual number achieved to date.

Structural biology has always been at the forefront in FAIR data sharing, and 88% of the 2024 Instruct publications are available as open access.

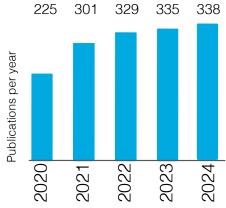


FIG 13. Instruct-ERIC publication statistics [data

TRAINING AND CAREER DEVELOPMENT

The Instruct-ERIC training programme helps researchers to develop new structural biology methods and skills. It includes structured courses, workshops, and online webinars, along with access to tools, resources and expertise.

TRAINING COURSES 2024

Since 2012, 77 training courses have been funded through the Instruct training programme. In 2024, the dedicated training programme included several courses focused on sample preparation for advanced structural biology techniques, ensuring that researchers have the tools and training for effective structural biology research projects.

Instruct-ERIC Practical School on Advanced Isotopic Labelling Methods for Integrated Structural Biology

21 - 27 May 2024 Instruct Centre FR2

This Instruct Practical School provided both practical and theoretical training in state-of-the-art isotopic-labelling approaches for NMR studies. The participants gained hands-on experience in a broad range of labelling methods, including innovative protocols for specific labelling, segmental labelling and in vitro expression of RNA and proteins. The Instruct school provided an environment in which attendees were able to exchange practical experience on protein labelling with instructors and other participants. Various links based on this discussion are already enabling future collaboration, mainly on cell-free facilities.

Instruct-ERIC spring workshop on sample preparation single particle crvo-electron microscopy

27 - 30 May 2024 Instruct Centre FR2

After five successful events, the sixth sample preparation workshop, co-organised by IBS, EMBL, and ESRF and funded by Instruct-ERIC, took place May 2024. Attendees were introduced to Partnership for Structural Biology (PSB) and ESRF facilities and the theory behind single particle cryo-EM sample preparation. The first day's practical session included negative-stain EM grid preparation and imaging along with vitrification trials using Vitrobot® equipment. Cryo-EM grids were examined using Titan Krioses. Participants quickly became comfortable with the Vitrobot, with many discovering their first cryo-conditions. Almost all the participants enthusiastically brought their own protein samples for the workshop.

Instruct-ERIC Hands-on Workshop on Sample Preparation for Single Particle Analysis by Cryo-Electron Microscopy

7 - 10 October 2024 Instruct Research Site PT

The workshop provided participants with a holistic understanding of the integrated use of biophysics, biochemistry, and cryo-EM for protein structure determination and analysis. The workshop was a unique opportunity for researchers to enhance their skills and stay at the forefront of structural biology. By the end of the course, attendees had a firm grasp of the individual aspects of sample preparation for SPA by cryo-EM, ready to apply these techniques to their research endeavours.

Instruct-RI Hubs hybrid course on Electron Tomography and Subtomogram Averaging

10 - 13 December 2024 Instruct Centre ES

The hybrid course provides a comprehensive overview of the entire image processing workflow in Electron Tomography (ET). This included tasks such as aligning the tilt series, reconstructing 3D tomograms, identifying particles, performing subtomogram averaging, and even carrying out tomogram segmentation, all within the Scipion integration framework. The course was aimed at researchers of all levels who wanted to adopt electron microscopy as one of the tools at their disposal for elucidating biological structures.



Instruct-ERIC Practical School on Advanced Isotopic Labelling Methods for Integrated Structural Biology



6th Instruct Hands-on workshop on sample preparation for Single Particle



Instruct-ERIC Hands-on Workshop on Sample Preparation for Single Particle Analysis by Cryo-Electron Microscopy

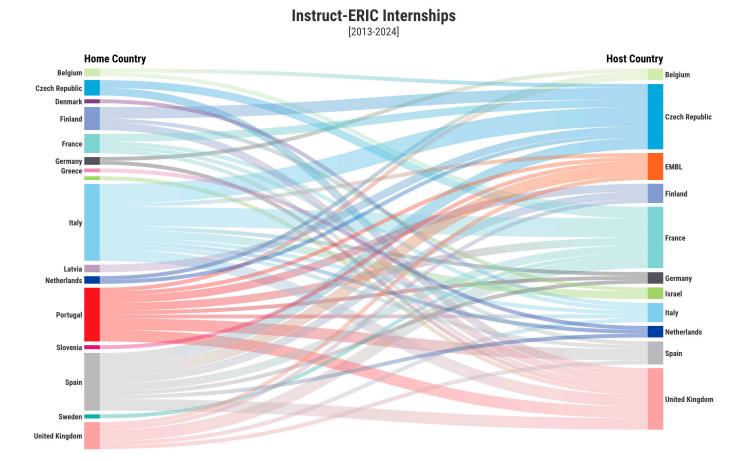


Instruct-RI Hubs hybrid course on ElectronTomography and Subtomogram Averaging

INTERNSHIPS

The Instruct-ERIC Internship programme aims to train structural and cell biologists in a wide range of technologies with three to six months visits to Instruct Facilities. The exchange programme provides in-depth skills training for predoctoral, and early-stage postdoctoral fellows, along with valuable experience of a different scientific environment, including the implementation of standards, processes and culture. Internships are hosted at an Instruct Facility that specialises in a method or technology from which the intern's own research can benefit. All internships require the intern to exchange with a facility in a different country or Member organisation to their own.

Since 2013, Instruct has awarded 84 internships that have facilitated research exchanges across Europe:



In 2024, eight internships applications were approved in three calls accross the year. The awards not only demonstrate a geographical distribution in the awardees, but also in the Centres hosting the internships.

Name	Country of Home Organisation	Internship Host
Miriam Condeminas	Spain	Instruct Centre EMBL
Johan Pääkkönen	Finland	Instruct Centre CZ
Martina Rosati	Italy	Instruct Centre CZ
Stefano Morasso	Italy	Instruct Centre FR2
Roger Castano	Spain	Instruct Centre NL
Marta Palerma	Italy	Instruct Centre CZ
Chiara Baroni	Italy	Instruct Centre FR1
Anastasiia Herman	UK	Instruct Centre FI

R&D AWARDS

Instruct-ERIC has run several calls for R&D projects since 2013, with funding awarded to more than 60 projects. Resources are allocated to support a limited number of pilot studies within integrated structural biology proposed by researchers from Instruct Members, access technologies at one or multiple Instruct Centres. This intends to help researchers develop external funding for projects - the expectation is that a pilot study will lead to a grant submission to national or international funding bodies. In 2024, the eligibility criteria were adjusted to specifically target early career researchers to set the course for the next generation of excellent scientists. In addition, Instruct-ERIC expanded this successful programme by introducing a second R&D call focused on technology and method development for established researchers.

R&D CALLS

The R&D awards of the first call were specifically aimed at early career researchers as defined in the EU ERC programme. The ERC eligibility criteria state that researchers with two to seven years of experience since completion of their PhD as well as a scientific track record showing great promise and an excellent research proposal are eligible. Furthermore, Instruct-ERIC introduced the criterion that the proposal is required to contain aspects of technology and/or software development within integrated structural biology to be considered for the award. 15 applications were received of which four projects were awarded with a grant of € 15 000 per project. In addition to the R&D call for early career researchers, for the first time in 2024, Instruct-ERIC offered funding for projects in technology development (TechDev) on two specific topics up to a maximum of € 30 000 per project. The aim was to ensure that Instruct remains at the forefront of structural biology, offering the technology required by the community. This call was targeted at researchers with a proven track record in technology and methods development. Awarded projects must include the use of technologies available at Instruct Centres or develop technologies that will benefit the aims of Instruct and become available at Instruct Centres. 12 applications were received of which two applications were awarded.

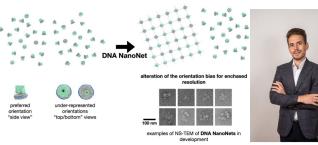
Piotr Stępień: R&D Award APPID 3671

DNA NanoNets for improving Cryo-EM imaging of bulky integral membrane proteins

Membrane proteins are among the essential constituents of living organisms, making up 20-30% of the proteins encoded by all genomes. As membrane proteins govern the transport of materials and information in and out of cells, they are privileged drug targets, with around 60% of small-molecule pharmacophores specifically targeting them. Recently, the study of membrane proteins and drug discovery connected to them was revolutionised by combining nanodiscs and cryo-EM. The nanodiscs are nanoscale lipid patches into which membrane proteins can be incorporated, effectively rendering them soluble, simplifying their handling and allowing for their facile single-particle analysis using cryo-EM.

Despite these advancements, obtaining the highest possible resolution with this combined approach is often challenging because bulky membrane proteins tend to adopt preferred orientations in vitreous ice. This restricts the available "views" of the proteins, resulting in reduced resolution.

In my Instruct-ERIC project, I am developing a tool to help overcome this obstacle. I am incorporating nanodiscs into DNA lattices to position the proteins into underrepresented orientations, creating "DNA NanoNets." These lattices are designed for easy integration into existing membrane protein preparation and analysis pipelines, enhancing the efficiency of analysis while reducing the number of micrographs which need to be collected.





Sarah O'Keefe: R&D Award APPID 3490

Towards a movie of nascent protein synthesis in the early secretory pathway

Our project leverages a photoswitchable translation inhibitor and a light-activated time-resolved cryo-EM approach to develop a new and accurate method to spatiotemporally map the early protein synthesis of any protein of interest, including those that cause human diseases. This method is applicable to capture moviesnapshots of how early protein synthesis is accurately co-ordinated in distinct cellular compartments and across cellular life.

First, we established a novel and universal pipeline for programming ribosomes of animal, plant or bacterial origin with stalled nascent chains, their rapid purification and small molecule light-activated ribosomal release. We are now applying these biochemically optimised methods in cryo-EM imaging to reveal new macromolecular insights in protein synthesis.

By enabling access to the technologies at the cryo-EM facility at the University of Helsinki, Instruct Centre-FI and the expertise of its staff and users (see photo), this R&D award has also provided invaluable training in instrument usage, sample preparation and image processing for the awardee. Our results integrated chemical and structural biology in this R&D project have already been used in grant submissions to external funding bodies.



Photo: left-right, Cristopher Mitchell (PhD researcher in Sarah Butcher Lab), Tuomas Niemi-Aro (cryo-EM facility Engineer), Sarah O'Keefe (Postdoctoral researcher in Sarah Butcher Lab, R&D pilot awardee), Kiran Ahmad (cryo-EM facility Engineer).

Sven Klumpe: R&D Award APPID 3485

Shaping focused ion beam in lamella preparation for cryo-electron tomography

In this project we explore the idea of using probe shaping (Figure 14a) in focused ion beam (FIB) milling in order to improve the resolution and speed of material removal in lamella preparation for cryo-electron tomography (cryo-ET) (Figure 14b-c). By using the available stigmator as a quasi-cylindrical lens similar to approaches in light sheet microscopy (Figure 14a), we stretch the beam profile into a highly elongated shape that we term 'ion knife'.

This improves the apparent resolution of spot burns one direction diameter) at the expense of the perpendicular direction (knife length) compared to a standard, Gaussian-like spot beam profile. In the future direction of the R&D award, we will investigate how specialised hardware could help improve our current approaches to increase the material retention in cryo-lift-out sectioning (Figure 14d). Additionally, we will develop open-source software to integrate shaped FIB probes into automated cryo-FIB lamella preparation routines.

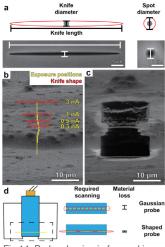


Fig 14. Probe shaping in focused ion beam milling process for cryo-electron tomography.

TechDev Award - Michal Sharon and Katharina Zittlau: **APPID 3331**

Uncovering Protein Complexity: A Novel Mass Spectrometry Approach for Examining Tissue-Specific Distribution and Functional Impact

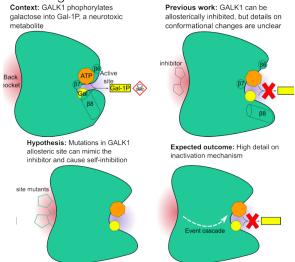
This project presents a novel strategy for examining protein diversity across tissues by integrating direct mass spectrometry (direct-MS) with machine learning. Building on our earlier success in applying direct-MS to crude cell lysates, we extended this approach to enable wholeorgan analysis with minimal sample preparation. Focusing on intrinsically disordered proteins (IDPs)—a dynamic and disease-relevant class of proteins—we developed a thermal enrichment protocol that selectively isolates IDPs from mouse tissues such as brain, heart, and liver. The project was driven by two primary goals: first, to establish a robust, tissue-compatible sample preparation method that preserves the native heterogeneity of proteoforms; and second, to create a data analysis pipeline using top-down proteomics in combination with deep learning techniques, including convolutional neural networks, to identify discriminative spectral features directly from raw data. By capturing proteoform complexity that is typically lost in bottom-up proteomic workflows, this methodology represents a significant advancement for structural biology and proteostasis research. With the analytical pipeline now in place, we are poised to uncover tissuespecific and age-dependent patterns of IDPs, offering new insights into their functional roles and pathological relevance.



Paola Lanzoni-Mangutchi: R&D Award APPID 3445

Giving GALK1 a stab in the back: the study of GALK1 inactivation through its allosteric site

Classic galactosaemia (CG) is a rare hereditary disorder of the galactose metabolism, causing a toxic buildup of galactose-1-phosphate (Gal-1P) inside the cells. Galactokinase 1 (GALK1) converts galactose into Gal-1P and is a validated therapeutic target against CG. Our group identified GALK1 inhibitors that act via an allosteric site, with a potential for selective drugs with fewer side effects. This project explores the mechanism of allosteric inhibition as a "stab on GALK1's back". We hypothesise that small amino acid modifications at the allosteric site are transmitted across the structure and disrupt the enzymatic activity, causing this mutant protein to selfinhibit in a similar manner as the wild-type would have been by a small molecule inhibitor. We mutated six candidate residues lining the allosteric site to tryptophan and histidine, due to their chemical similarity to our inhibitors, to test their impact on the enzyme's overall activity and structure. Initial single mutants show a slight decrease in kinase activity and thermostability. We anticipate that their crystal structures will provide us with an unprecedented understanding of allosteric inhibition.



TechDev Award - Maria Garcia Alai and Osvaldo **Burastero: APPID 3335**

KinGenie: An Online Tool for the Analysis of Solutionand Surface-Based Binding Data

As part of our Instruct-ERIC TechDev project, we are developing KinGenie, an intuitive and interactive online tool designed for the analysis of kinetic data. KinGenie will support users in planning their experiments by simulating both solution-based and surface-based binding interactions.

The tool incorporates a range of kinetic models, including one-to-one binding, conformational selection, induced fit, and one-to-one binding under mass transport limitation. In addition, KinGenie allows for data preprocessing (e.g., baseline subtraction) and supports global fitting of multiple datasets.

The software will be open source and integrated into the eSPC platform. A beta version is already available for exploration at Instruct Centre EMBL.



INSTRUCT BIENNIAL STRUCTURAL BIOLOGY CONFERENCE 2024

The sixth Instruct Biennial Structural Biology Conference took place in the seaside town of Cascais, Portugal, welcoming more than 230 attendees to the leading integrated structural biology conference.

The conference was built on a variety of sessions, covering AI, molecular dynamics, health and environment, imaging techniques, and the impact of structural biology on global sustainability. The sessions were organised and chaired by the Scientific Organising Committee:

Carlos Cordeiro
Harald Schwalbe
Margarida Archer
Maria Macias,
Roberta Pierattelli
Eaazhisai Kandiah
Friedrich Forster

- Friedrich Forster Kristina Djinovic-Carugo

The conference also included poster sessions and the gala dinner, providing space for interaction and networking among the global structural biology community.

The conference was formed around talks from several leading lights in the field of structural biology, each utilising a range of integrated techniques to conduct their research. This took attendees on a journey of sessions, kicking off with the timely topic of structural biology in combination with Artificial Intelligence (AI), but also with Molecular Dynamics (MD). From there, the impact of structural biology on health and the environment was discussed, opening the door for some cutting-edge talks on human disease and cell structures.

The second day began with a session on structural biology in combination with imaging studies – a wide range of structural characterisation techniques were displayed by invited and promoted speakers. The speaker programme closed with a selection of talks on structural biology's place in advancing global sustainability, from bacteria and viral structural determination to plant studies.

up to date with the latest research blossoming in integrated structural biology, and to forge new connections between facilities.

Martin Blackledge of IBS Grenoble was announced as the winner of the Ivano Bertini Award from Instruct-ERIC.

Martin was recognised for their pioneering work on intrinsically-disordered proteins using NMR. This ranges from identifying the conformational space of IDPs and their dynamic behaviour identified by varying techniques - to their interactions with highlyprocesses, such as viral replication.

a fantastic talk on their latest work on IDPs.











INVITED SPEAKERS

Jan Steyaert - VIB-VUB Brussels

Carmen San Martín - CNB-CSIC Madrid

Kresten Lindorff-Larsen - University of Copenhagen

Markus Weingarth - *Bijvoet Centre*

Olivier Duss - EMBL Heidelberg

Tanja Mittag - St Jude Children's Research Hospital

Jan Schuller - SYNMIKRO Research Centre

Tzviya Zeev-Ben-Mordehai - *Utrecht University*

Neil Kelleher - Northwestern University

Priya Ramakrishna - EPFL

Tassos Perrakis - Netherlands Cancer Institute

Stephan Rauschenbach - University of Oxford

Andrea Thorn - *Universiteit Hamburg*

ABSTRACT SPEAKERS

Courtney Tremlett - *University of Exeter*

Maria Del Rosario Fernandez Fernandez - CINN CSIC

Anna Stefanik Sobotkova - CEITEC

Jordan Chill - Bar Ilan University

Guilherme Vilela-Alves - UCIBIO, NOVA-FCT

Sarah Butcher - University of Helsinki

Sarah Lowen - *University College London*

Catarina Malta - iBET

Gints Kalnins - LBMC

Loïck Moisonnier - IBCP

Angela Sofia Tino - CERM/CIRMMP



ARIA is a cloud platform, developed and maintained by Instruct-ERIC Hub, which provides an integrated suite of tools for research infrastructure management.



The acronym "ARIA" is an abbreviation of "Access to Research Infrastructure Administration" and the functionality covers a range of access management functions: access catalogue, proposal submission, scientific peer review, technical evaluation, access delivery, feedback collection and access reporting. In addition, ARIA provides software tools for facility management such as instrument booking; website management, document management, events/ news/job postings, survey tool, CRM; and APIs for data integration. These tools are supported by context-dependent integrated internal messaging and automated notifications and reminders.

ARIA was initially developed to service Instruct's own needs due to a lack of suitable commercial software, however it has since grown to support projects and infrastructures throughout the life sciences, and beyond. As other research infrastructures reach maturity and begin offering access to their scientific communities the secure, scalable solution for access management offered by ARIA is required. ARIA currently manages the access provision of several European projects, facilities and research infrastructures.

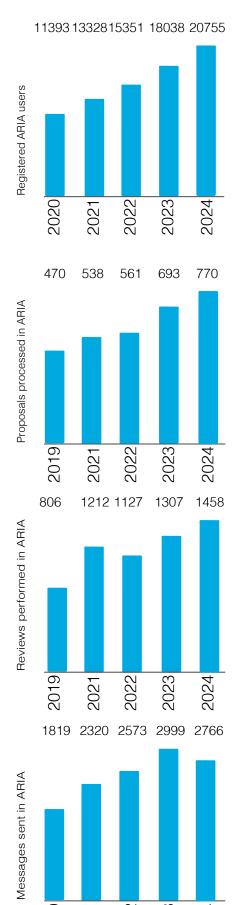
ARIA in numbers

Overall, ARIA welcomed 2717 new users in 2024, bringing the total number of registered users to 20755, a record increase year on year. 770 proposals were processed in ARIA in 2024, with more than 1450 reviews conducted throughout the year. Additionally, the access management was supported by the ARIA messaging system that processed 2766 messages in 2024 connecting the users, access managers, reviews and facility teams.

ARIA: New Updates

Considerable updates, improvements and new features were released, including the access calls and panel reviews. Instruct, in collaboration with CNB-CSIC in Spain, introduced a new data management toolset, fandanGO. This will revolutionise the FAIRness of data arising from the Instruct infrastructure. fandanGO is deployable directly at facilities to allow them to capture research metadata and store on the Instruct Federated Cloud. Several Instruct facilities have been onboarded with fandanGO, with more to be onboarded in 2025.

A brand new feature to enable interactive review of batches of by panels of experts in ARIA was released in 2024, and served in many of Instruct's review panels throughout the year. Several improvements were also made to enhance ARIA's end-user experience. A new feature was also added to introduce newly registered users to the RI or project portal. This includes welcoming them to the site and reminding them to complete their user profile for submission and review and, check their ARIA email settings to ensure they stay up to date with ARIA notifications and project updates. User experience was also enhanced for managing visits from the facility manager's perspective, including enabling more customisation in how access can be reported, and various interface improvements.





EUROPEAN PROJECTS



Fragment-Screen: Fragmentbased drug discovery through structural biology, medicinal chemistry, and Al

February 2023 to January 2026



Al4Life: Artificial Intelligence for Image Data Analysis in the Life Sciences

September 2022 to August 2025



BeYond-COVID. BY-COVID: tackling the challenges that can hinder pandemic response October 2021 to September 2024



canSERV: Providing cutting edge cancer research services across Europe

September 2022 to August 2026



Beyond: Advancing innovation and collaboration for research

April 2024 to March 2027



EOSC4Cancer: A Europeanwide foundation to accelerate Data-driven Cancer Research September 2022 to May 2025



EOSC Future: Advancing innovation and collaboration for research

April 2024 to March 2027



ERIC Forum 2: The ERIC Forum implementation project September 2023 to August 2027



eRImote: Pathway to Improved Resilience and Digital and Remote Access

June 2022 to November 2024



EULAC ResInfra Plus:

Towards a Sustainable EU-LAC Partnership In Research Infrastructures

January 2024 to December 2025



FHERITALE: Food, Health and Environment Research Infrastructures to Tackle **Emerging Priorities** January 2024 to December 2026



IMAGINE: Next generation imaging for biology across scales

May 2023 to April 2028



iNEXT Discovery: Structural biology for translational research and discovery February 2020 to July 2024



ISIDORe: Integrated Services for Infectious Disease Outbreak Research

February 2022 to July 2025

EUROPEAN PROJECTS SPOTLIGHT

Instruct-ERIC is involved in several European projects each year, each with specific aims and activities which are of specific benefit to the European structural biology community. This continued in 2024, as impactful projects continued to provide new technologies and software for structural biologists to use for their research.

iNEXT-Discovery (February 2020 - July 2024)

iNEXT-Discovery, a structural biology project funded from the European Commission Horizon 2020 scheme, ended on July 31 2024. iNEXT-Discovery made X-ray, NMR, cryo-EM and macromolecular biophysics services available to external user communities, often researchers without prior experience in the field. In addition to providing access to existing infrastructure, partners developed methods through joint research, and organised meetings, theoretical courses, and practical workshops.

In addition to providing access in the project to its centres, Instruct had a key role in the role in the access management for the project, adapting ARIA to the needs of the project from submission to reporting of each proposal. The use of ARIA in projects is an effective management of resources, using already available tools, saving funds and time in the setting up of the complex procedure of managing transnational access.

With the end of iNEXT-Discovery, resources available to researchers to access the structural biology infrastructure they need for their research has greatly diminished. Instruct worked together with coordination and all partners to develop a sustainability plan including the organisation of foresight meeting in Krakow. All services offered by Instruct and iNEXT-Discovery were mapped to analyse the future provision for users, making recommendation to service providers and other stakeholders.

eRImote (June 2022 - November 2024)

The eRImote project started on 1 June 2022, before coming to an end in November 2025. The project, developed during the Covid-19 pandemic, succeeded in its aims to make sure European RI are suitably equipped to provide and manage remote access. It aimed to gather a knowledge base on remote and virtual access to research infrastructures (RI) in Europe, and develop recommendations based on use cases, expert groups, surveys and the analysis of best practices. The ambition was to enhance and improve the resilience and accessibility of research infrastructures overall.

Instruct's role in the project was to use its experience and resources with ARIA, data management, and remote access contacts worldwide, to generate an Information Platform. The platform was made up of databases, documents, and webinars, allowing researchers, facility managers, and any other role within access providing communities, to find and utilise the resources most useful to them. The platform also showcased external tools, those which had been developed by eRImote partners, sister projects, and industrial users and providers.

The platform is located on the project website (erimote.eu/ resources). The website was built by the ARIA SiteBuilder tool, which allowed the website and Information Platform to be built with flexibility and speed, and ensures that the resources collected will be available on the platform indefinitely. This also provides long-term visibility for Instruct through eRImote and other SiteBuilder sites.





iNEXT-Discovery Foresight Meeting at the end of the project, looking at sustainability of structural biology access provision.





Final Meeting of the eRImote project in Brussels, in October 2024.

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Newsletter

The Instruct newsletter continued its distribution in 2024, to more than 3,500 accounts in the ARIA network. The themes for the summer (Biennial Conference) and winter (Artificial Intelligence) were appropriate, as the significant news and advances made in Instruct in 2024. In addition to these central news stories, the newsletters provided a snapshot of the latest projects, science highlights, and news from Instruct Centres.



Social media

Instruct's social media profile changed throughout 2024. The Instruct LinkedIn account grew significantly, with more than 3,600 connections and followers. The X (Twitter) account has begun to stagnate in terms of follower growth and engagement, as it became increasingly clear that the scientific community was moving to Bluesky. An account was set up on the new platform, and by the end of 2024 had more than 1,000 followers.



Scientific Highlights

Instruct published seven science highlights in 2024, covering a wide variety of topics and technologies, providing users with an idea of the sort of research that they can perform at Instruct facilities. Techniques including cryo-EM, NMR, and X-ray studies were highlighted in 2024, as well as nanobody discovery and protein production studies.



Webinars

The Structure Meets Function webinar series continued to provide information and background to Instruct services and centres. Eight webinars in 2024 provided a platform for users of Instruct-ERIC services, R&D Calls, and partner TNA projects such as ISIDORe. The webinar series has also been used as a platform for the Fragment-Screen project, allowing users to hear the latest in fragmentbased drug discovery and AI and machine learning tools.



Instruct Website

The website has continued to be updated with informative and novel features and pages for structural biology users. For example, the website now includes a dedicated page on "Al and Structural Biology", providing users and researchers with the resources they need for utilising Al in their research, as well as contact with experts on how to validate AI predictions using experimental structural biology. This fits neatly with news items, science highlights, and European projects with an Al focus.





A fantastic Instruct Biennial Structural Biology Conference! Stunning talks, so many fantastic posters, and a great forum for discussion on structural biology. Thanks to all of you who made it happen - see you in Brussels in 2026!





INSTRUCT-ERIC HUB

In 2024 the Instruct Hub saw the addition of more team members. We welcomed Sarah Townend and David Marshall to the project management team. Both Sarah and David bring direct expertise in structural biology, having both completed PhDs in cryo-ET and cryo-EM respectively. Whilst both new team members are involved in several Instruct projects, Sarah is the lead project manager for the IMAGINE project, and David organises Instruct's role in FHERITALE, as well as iNEXT-Discovery.

In addition to the project management team, Instruct appointed an Administration and Communication Assistant, Wahida Alam. Wahida's role covers both the administration team, assisting with the day to day running of the Instruct-Hub and coordinating with centres, as well as the communication team, generating content for social media, the website, and external projects to help disseminate and promote Instruct activities.

Following the success of previous Hub team retreats, in 2024 we visited Shefield for two days of team building and planning, supported by Josh White from Instruct Centre UK who performed the role of moderator during discussions. The team then had the opportunity to visit the Astbury Centre in Leeds, the UK centre, for a guided tour of the technologies available to researchers through Instruct.

SPOTLIGHT ON STAFF

Pauline Audergon - Senior Project Manager

Pauline Audergon was promoted to Senior Project Manager in 2024, recognising their advancement since joining Instruct-ERIC in 2020. Pauline is involved in a wide range of Horizon projects, and plays an integral role in Instruct access management.

Pauline leads the Instruct access management team at Instruct. This involves making sure that users are able to apply for access through Instruct, managing proposals for efficient review and panel evaluation, and timely interaction with research teams and Instruct facilities to ensure visits go smoothly and successfully.

Pauline has been the lead Instruct Project Manager for the ISIDORe project, which provides funding for access to research infrastructure services for infectious disease studies. As part of the project, Pauline acts as the main contact for both structural biology users in ISIDORe accessing technologies through Instruct, as well as the project coordination team to ensure the best service is provided for the users themselves.

In addition, in 2024, Pauline worked on the BY-COVID project, which aimed to identify data management solutions for infectious disease-related data, as a sister project to ISIDORe.

In 2024, Pauline also helped to manage the access-providing project canSERV, another Horizon Europe grant providing funded access to technologies through Instruct, with a focus on cancer-related research.



Senior Project Manager

John Dolan - Communication and Project Manager

A new member of the Project Management team is John Dolan. John started at Instruct in 2021 as a Communication Officer, and following their work in various Horizon Europe projects, as well as Instruct's international collaboration work, is now Communication and Project Manager, as of 2024.

John oversees the communication, dissemination, and visibility activities at Instruct, ensuring a wider reach of the technologies and services offered to new users and members.

John helped to organise the Instruct Biennial Structural Biology Conference 2024, alongside Administrative Officer Madalena Gallagher. John and Madalena ensured that registration, communication, and running of the conference went smoothly, to ensure delegates and speakers got full value in terms of talks, networking opportunities, and the poster presentation sessions.

John is involved in several Horizon Europe projects at Instruct, including the internationalisation component of ERIC Forum 2, helping to manage the information platform in eRImote, and is the lead Instruct Project Manager in the AI4Life project. As part of their role, John manages the communication from Instruct in all other Horizon Europe projects, including Fragment-Screen, EU-LAC ResInfra Plus, and FHERITALE.



John Dolan Communication and Project

HUB TEAM MEMBERS



Harald Schwalbe Director



Claudia Alén Amaro **Head of Operations**



Natalie Haley Head of Strategy



Pauline Audergon Senior Project Manager



Regina Guenster Project Manager



Corinna Brockhaus **Project Manager**



Eirini Xemantilotou **Project Manager**



Sarah Townend **Project Manager**



David Marshall Project Manager



John Dolan Communication and **Project Manager**



Madalena Gallagher **Administrative Officer**



Lorraine Donaldson Financial Manager



Sarah King Senior Finance Officer



Francisco Guimaraes Finance Officer



Wahida Alam Admin and Communication **Assistant**



Marcus Povey Senior Software Developer



Marcus Lowndes Software Developer



Omran Alhaddad **IT Developer**



Alec Matthews **IT** Developer



Yvonne De Jong Junior IT Developer



Lui Holliday Software Developer



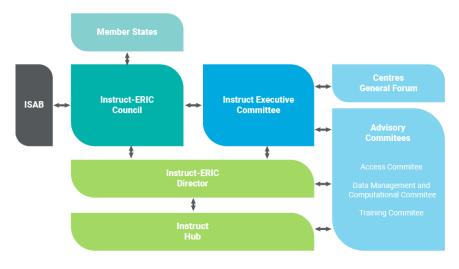


Instruct Hub members at the Christmas dinner and the retreat (left to right).

GOVERNANCE

The Instruct-ERIC Council continued to be chaired by Sarah Butcher (FI) with Jose-Maria Carazo (ES) as Vice-Chair. The Independent Scientific Advisory Board (ISAB), chaired by Stephen Burley remained in place to advise the Council.

The Instruct Council is the ultimate decisionmaking body responsible for the overall direction and supervision of the ERIC. It consists of representatives from each Instruct Member. In 2024, Instruct Council was led by Prof Sarah Butcher (FI) and Prof Jose-María Carazo (ES) as the Chair and Vice-Chair of Council respectively. Council approved the membership application of Germany in January 2024, welcoming them as the 17th Member of Instruct-ERIC. To identify areas of improvement in Instruct's governance and operations, Council launched a long-term assessment exercise. Furthermore, Council supported the Hub in the document preparation for the ESFRI Landmark monitoring exercise the was successfully completed in July 2024. In addition, a comprehensive



scientific plan was presented to Council detailing the Director's scientific vision for Instruct-ERIC for the coming five years. The document focuses on The Future of Integrated Structural Biology and addresses the current state-of-the-art as well as future challenges and opportunities for the field. In addition to being important for Instruct it is also of highimportance and relevance to the structural biology community as a whole and was published as a review paper in the journal Structure in October (DOI:10.1016/j.str.2024.08.014).

The Instruct Centres are distributed in the Instruct Member countries and organisations. Each Centre has a nominated lead, the Centre Coordinator, sitting on the Executive Committee which is the supervisory body for the execution of the strategy developed by the Director and approved by Council. The Executive Committee is responsible for overseeing workplans, progress and infrastructure service provision of Instruct. Subcommittees of the Executive Committee oversee access, training and data management for Instruct. The leadership of the Executive Committee (chair Harald Schwalbe), the Training Committee (Chair Lucia Banci) and the Access Committee (Chair Darren Hart) remained unchanged while the Data Management and Computational Committee (DMCC) welcomed Josan Marquez as the new committee chair. During 2024 the Executive Committee supervised the recommendations from Instruct's various subcommittees. Instruct moved from a continuous assessment and decision to a gathered field decision by introducing periodic panel decisions on batches of applications which have been positively peer reviewed. Additionally, the collaboration with the European Open Science Cloud (EOSC) was strengthened with the support of the DMCC. As a member of the EOSC Association, activities were monitored providing input for further activities. During 2024 the Executive Committee also provided guidance on which Horizon Europe calls to apply to as well as contributed to the applications through the involvement of appropriate Centres.

The Independent Scientific Advisory Board (ISAB) provides independent advice to the Director and Council on the scientific direction and service provision to the scientific community. For this role, members are selected considering diversity in their scientific expertise, industrial background, and knowledge of research infrastructure. There was a change of personnel of the ISAB in 2024, as Tanja Mittag joined in August, and Angela Gronenborn and Juergen Plitzko concluded their terms at the end of the year. We thank them for their guidance and support.

INDEPENDENT SCIENTIFIC ADVISORY BOARD

Chair: Stephen Burley, Rutgers University, USA

Members

Angela Gronenborn, Pittsburgh University, USA Juergen Plitzko, Max Plank Institute for Biochemistry, Germany Ilaria Ferlenghi, GSK, Italy Marjolein Thunnissen, Max IV, Sweden Rommie Amaro, University of California, USA Tanja Mittag, St Jude Children's Research Hospital, USA

COUNCIL

The Instruct-ERIC Council is the ultimate decision-making body of the consortium. It consists of scientific and administrative representatives from each Instruct-ERIC Member.

Chair: Sarah Butcher, FI

Vice-Chair: Jose Maria Carazo, ES

Country	Delegates
Belgium	Michele Oleo & Virginie Storms
Czech Republic	Pavel Plevka / Jiri Nováček & Jan Burianek
EMBL	Christoph Mueller & Plamena Markova
Finland	Sarah Butcher & Anni Kleino
France	Winfried Weissenhorn & Catherine Le Chalony
Germany	Julia Engert & Martin Voss
Greece	Evangelia Chrysina & Denis Sarigiannis
Israel	Joel Sussman & Iris Eisenberg
Italy	Lucia Banci & Fabio Mazzolini
Latvia	Kaspars Tars & Uldis Berkis
Lithuania	Giedrius Sasnaukas & Gintaras Valincius
Netherlands	Reinout Raijmakers & Naomi Chrispijn-Steenbeek / Ana de Castro
Portugal	Maria Armenia Carrondo & Marta Abrantes
Spain	Jose Maria Carazo & Ignacio Baanante Balastegui
Slovakia	Milos Hricovini & Simona Tanhäuserová / Jan Kočišek
Slovenia	Marjetka Podobnik & Albin Kralj
United Kingdom	Robert Deller & Charlotte Durkin

EXECUTIVE COMMITTEE

The Executive Committee is the principal executive management committee for Instruct-ERIC, comprising representatives drawn from Instruct Centres. It is the supervisory body for the execution of Instruct which reports to and is accountable to the Instruct-ERIC Council.

Chair: Harald Schwalbe (Instruct Director)

Instruct Centre	Head of Centre	Deputy
Instruct BE	Jan Steyaert	Han Remaut
Instruct CZ	Pavel Plevka / Jiri Nováček	Ondrej Hradil
Instruct EMBL	Kristina Djinovic Carugo	Matthias Willmans
Instruct ES	Jose Maria Carazo	Carlos Oscar Sanchez Sorzano
Instruct FI	Sarah Butcher / Hanna Oksanen	Markku Varjosalo
Instruct FR1	Patrick Schultz	Arnaud Poterszmann
Instruct FR2	Darren Hart	Martin Blackledge
Instruct IL	Shira Albeck	Joel Sussman
Instruct IT	Lucia Banci	Roberta Pierattelli
Instruct NL	Ariane Briegel / Reinout Raijmakers	Rolf Boelens / Bert Janssen
Instruct UK	David Stuart	Andrew Quigley
Research Site	Head of Research Site	
Instruct PT Instruct SK	Margarida Archer / Carlos Cordeiro Milos Hricovini	



TNANCIAL DAIA

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FINANCIAL DATA

This report presents the financial statements for the period 1 January 2024 to 31 December 2024.

Statement of Council Members' responsibilities in respect of the Council's Report and the Financial Statements

The Council Members are responsible for preparing the Council's Report and the financial statements in accordance with applicable law and regulations.

The financial statements are prepared in accordance with applicable law and the statutes of Instruct.

In preparing these financial statements, the Council Members accept the recommendations of the auditor and approve the application of the appropriate policies in the following decisions:

- Making judgements and estimates that are reasonable and prudent:
- Stating whether UK Accounting Standards have been followed, subject to any material departures and explained in the financial statements;
- Assessing Instruct-ERIC's ability to continue its activities, disclosing as applicable matters related to financial
- Using the 'going concern' basis of accounting unless they intend to cease operations or have no realistic alternative but to do so.

The Council is responsible for ensuring the Financial Statements are accurate and that the accounting records are sufficient to show and explain Instruct-ERIC's transactions and disclose with reasonable accuracy at any time the financial position of Instruct-ERIC and enable Council Members to ensure that the financial statements comply with the appropriate regulations and applicable law. Council Members aver that they are free from material misstatement, whether due to fraud or error, and have general responsibility for taking such steps as are reasonably open to them to safeguard the assets of Instruct-ERIC and to prevent and detect fraud and other irregularities.

This report covers the period 1 January 2024 – 31 December 2024.

BALANCE SHEET FOR INSTRUCT-ERIC

For Year Ended 31 December 2024

Assets	GBP	EUR	Notes	
Euro bank	2,996,878	3,621,999	••••••	
Sterling bank	210,657	254,598		
Total Bank	3,207,535	3,876,597		
Current Assets				
Accounts Receivable	2,515	3,040	1	1. ARIA support income
Prepayments	12,476	15,078		receivable
Accrued income	218,751	264,381	2	2. Grant income recoverable
Rental deposits	3,713	4,488		at report period end
Total Current Assets	237,455	286,987		
Fixed Assets				
Computer Equipment	9,408	11,370		
Depreciation on Computer Equipment	-8,891	-10,746		
Office Equipment	2,528	3,055		
Depreciation on Office Equipment	-1,428	-1,726		
Total Fixed Assets	1,617	1,953		
Total Assets	3,446,607	4,165,537	•	
Liabilities	GBP	EUR	Notes	
Current Liabilities		•••••	••••••	
Accruals	12,500	15,107		
Amounts to be paid and Unclaimed Access Awards	1,394,250	1,685,078	3	3. Access and other service accruals
Income in Advance - Other inc deferred grants	1,426,505	1,724,061	4	4. Deferred project income
Income in Advance - ARIA Support	10,684	12,912		
Other creditors	2,211	2,672		
Payroll taxes due	20,138	24,339		
Pensions due	-	-		
Total Current Liabilities	2,866,288	3,464,169		
Total Liabilities	2,866,288	3,464,169		
Net Assets	580,319	701,368		
Surplus Brought Forward	264,356	304,983		
Exchange rate movement - revalue opening reserves	-12,009	-	5	5. Revalue opening reserves from prior year exchange rate to the exchange rate
Surplus for the Year	327,972	396,385		used for current reporting
Surplus Carried Forward	580,319	701,368		period.
	000,010	, , , , , , , ,		
Exchange rate for reporting period: 0.82741 (2023: 0.	.86680)			

PROFIT AND LOSS FOR INSTRUCT-ERIC

For Year Ended 31 December 2024

Income	GBP	EUR	Notes
Member state contributions	1,171,306	1,415,630	6
External grant income	1,112,045	1,344,007	7
External grant overhead contribution income	185,485	224,176	
Other miscellaneous income	129,373	156,359	8
Total Income	2,598,209	3,140,172	
Less Cost of Service Provision			
Access Cost	413,092	499,259	
Internships	26,735	32,312	
R&D Pilot awards	99,289	120,000	
Training Courses	30,329	36,655	
Conference costs	90,652	109,561	
Instruct core staff salaries	312,121	377,227	
External grant TNA costs	396,693	479,440	9
Project activities (staff, ODC, subcontracting)	728,808	880,830	10
Total Cost of Service Provision	2,097,719	2,535,284	
Gross Surplus	500,490	604,888	
Less Operating Expenses			
Premises and support	64,210	77,604	
Equipment, Licenses & Software	7,331	8,860	
Commissioned services (insurance, financial, HR,	34,557	41,765	
legal)			12
Meetings	39,584	47,841	
Overhead expenses	16,310	19,712	
Publicity	4,456	5,385	
General admin (postage, copying, bank charges)	2,013	2,433	
Profit on disposal of fixed assets	-	-	
Depreciation charge	2,873	3,472	
Foreign Currency (Gains)/Losses	1,184	1,431	
Total Operating Expenses	172,518	208,503	
Net Surplus	327,972	396,385	••••••

- **6.** Membership income receivable
- 7. Project income excluding 25% contribution to Instruct-ERIC overheads, against expenditure
- ARIA support and conference sponsorship
- 9. TNA access awards relating to externally funded projects (ISIDORe, CanSERV)
- **10.** WIP on research grants. Project activities delivered.
- **12.** Staff costs recharged from the University of Oxford and external consultancy

SUPPORTING INFORMATION FOR THE FINANCIAL STATEMENTS

Accounting Policies

The financial statements are prepared under the historical cost convention, and in accordance with the Statutes of Instruct.

The principal accounting policies set out below have, unless otherwise stated, been applied consistently to all periods presented in these financial statements.

Reporting and Disclosure Exemptions

The financial statements have been prepared on the assumption that Instruct-ERIC will continue as a going concern. Instruct-ERIC is expected to generate positive cash flows on its own account for the foreseeable future. The Council Members have a reasonable expectation that Instruct-ERIC has adequate resources to continue in operational existence for the foreseeable future. Thus the Council Members continue to adopt the going concern basis in preparing the financial statements.

Expenditure

Awards are recognised as expenditure when the relevant committee formally approves the award. Awards are given a 12 – 18 month window after which the beneficiary must reapply if unclaimed. The exception to the above is where training courses have been awarded on the condition that they will take place in a future financial year. In such cases liability and cost is recognised by Instruct-ERIC at the start of the financial year the course is due to take place.

Foreign Exchange

Currency transactions are recorded at the rate of exchange on the transaction date. Monetary assets and liabilities denominated in non-UK currencies are reported at the rates of exchange prevailing on the balance sheet. Non-monetary assets and liabilities measured at historical cost in a non-UK currency are translated using the exchange rate at the date of the transaction. Currency exchange differences are recognised in the Profit and Loss statement.

Corporation Tax

In our opinion and under the terms of the Council Directive 2006/112/EC of 28 November 2006 on the common system of value added tax and Council Directive 92/12/EEC of 25 February 1992 on the general arrangements for products subject to excise duty and on the holding, movement and monitoring of such products, Instruct-ERIC has no liability to Corporation Tax.

Basis of preparation

The financial statements have been prepared in accordance with applicable United Kingdom accounting standards, and under the historical cost accounting rules used and approved for Instruct-ERIC in accordance with the requirements of the ERIC Regulation.

Income

- the amounts derived from membership subscriptions. This income is recognised evenly over the subscription period.
- EC Grants and projects income is recognized when the costs are incurred, attributing the contribution to overheads as per the Grant Agreement.

Depreciation

Tangible assets are calculated using an initial measurement at cost (including delivery and handling costs, installation costs) and the straight line method of depreciation to a zero salvage value at the end of the depreciation term. For computer equipment the depreciation term is 3 years. For furniture, fixtures and fittings, the depreciation term is 5 years. The following costs are not capitalised in this measurement: communication or training costs, repairs and maintenance. Software licenses are classified as intangible assets.

Taxation

The United Kingdom, as host Member State of Instruct-ERIC, has made a declaration to recognize the ERIC as an international body or organization for the purpose of the application of Council Directive 2006/112/EC of 28 November 2006 on the common system of value added tax and Council Directive 92/12/EEC of 25 February 1992 on the general arrangements for products subject to excise duty and on the holding, movement and monitoring of such products as of its setting up. Instruct-ERIC therefore benefits from certain exemptions as an international organisation for the purpose of applying Directive 2004/18/EC of the European Parliament and of the Council of 31 March 2004 on the coordination of procedures for the award of public works contracts, public supply contracts and public service contracts, in conformity with State aid rules.

Instruct-ERIC operates and reports on this basis of tax exemption except where irrecoverable tax is shown.

Cash and cash equivalents

Cash and cash equivalents comprise cash balances and cheque deposits.

ACCOUNTING JUDGEMENTS AND ESTIMATES

In its preparation of these financial statements, Instruct-ERIC has made material judgements, estimates and assumptions. Discussion of these judgements, estimates and assumptions and their impact is included in the relevant note disclosures; the main areas being:

Judgements: Grant Income recognition

Estimations, uncertainties and assumptions: Going concern

B. Income

List of Members and their cash contribution (EUR)

Member Country	Membership contribution 2024
UK	123,650
FR	123,650
DE	123,650
ES	92,740
IT	92,740
BE	92,740
NL	92,740
IL	92,740
CZ	61,830
PT	61,830
SK	61,830
LV	61,830
EMBL	61,830
FI	61,830
LT	61,830
SI	61,830
EL	61,830
Host contribution	24,510
Total	1,415,630

Grant Recipts (EUR)

EU Grants	Staff and other direct cost income	TNA cost income	Overhead income
Al4Life	9,649		2,412
BY-COVID	20,752		5,451
canSERV	225,719	279,472	56,430
EOSC Future	16,304		4,581
EOSC4Cancer	35,399		8,850
EOSC BEYOND	16,686		4,171
ERIC Forum 2	22,932		5,733
eRImote	102,714		27,527
EU-LAC ResInfra Plus	40,555		10,139
FHERITALE	22,759		5,690
Fragment-Screen	226,931		56,733
iNEXT-Discovery	31,395		7,440
IMAGINE	37,050		9,262
ISIDORe	73,152	199,968	18,288
EOSC-LIFE (CLOSED)	(16,141)		182
EU-CELAC (CLOSED)	(1,287)		1,287
Total	864,569	479,440	224,176

Overhead contribution recognised: 25%

C. Deficit/surplus on activities: € 396,385

D. Employees

EMBL in-kind contribution in lieu of membership fees supported 1 FTE Project Manager.

E. Debtors

Invoices outstanding from Members (present total figure outstanding against 2024 invoices): € 0

Prepayments: € 15,078 Accrued income: € 264,381

F. Creditors

Accruals for services and awards (Access, Internships, R&D, Training, unclaimed access): € 1,685,078 Income in Advance - Other inc deferred grants: € 1,724,061

Accruals: € 15,107

G. Related Parties

Third parties are specified within each project Grant Agreement, particularly Articles 11-15 and in the Consortium Agreements (based on the DESCA Model Consortium Agreement) between consortium partners.

The Consortium Agreement defines the responsibilities of beneficiary partners towards third parties that undertake project work, as follows:

"A Party (beneficiary or associated partner) that enters into a subcontract or otherwise involves third parties (including but not limited to Affiliated Entities or Third parties linked to a Beneficiary identified under the Grant Agreement) in the Project remains responsible for carrying out its relevant part of the Project and for such third party's compliance with the provisions of the Consortium Agreement and of the Grant Agreement. The Party has to ensure that the involvement of third parties does not affect the rights and obligation of the other parties under the Consortium Agreement and the Grant Agreement. Each Party shall be solely liable for any loss, damage or injury to third parties resulting from the performance of the said Party's obligations by it or on its behalf under the Consortium Agreement or from its use of Results or Background whether owned by that Party or obtained by it from another Party according the Grant Agreement or the Consortium Agreement."

H. Commitments

Instruct-ERIC has a lease agreement with PURE Offices Ltd. The Blade, Abbey Square, Reading, Berkshire RG1 3BE, UK to provide office space comprising Suites 8-11 including telephone, wireless and infrastructure services. The lease has a 3 month notice period for termination.

I. Pensions

A Defined Contribution Pension Plan has been established through Aviva (www.aviva.co.uk/business/workplace-pensions/) with 8% employee contribution and 18% employer contribution. The Plan operates with an annual management charge of 0.3% which is levied annually on each Member portfolio investment. The Plan has been running successfully and has been implemented to comply with the UK terms of mandatory pension enrolment of all eligible employees within 1 month of employment. In 2024 the scheme was extended to enable salary exchange with any NI savings passed on to the employee.

J. Grant Agreements

Instruct-ERIC acts as host (Coordinator) in respect of the following grants:

Fragment Screen: €8,265,080 (total value) – start date 01 February 2023, end date 31 January 2026.

Instruct-ERIC is a beneficiary partner in the following grants with a project lifetime award to Instruct-ERIC shown below:

Al4Life €34,500

BY-COVID €166,316

canSERV €1,376,753* **

EOSC Beyond €153,405

EOSC Future €126,421

EOSC4Cancer €82,500

ERIC Forum 2 €114,126

eRImote €272,375

EU-LAC ResInfra €138,153

FHERITALE €277,763

Fragment-Screen €1,647,815*

iNEXT-Discovery €147,500

IMAGINE €1,012,895

ISIDORe €736,245 * **

^{*} Grant amount includes budget held on behalf of other partners.

^{**} Grant amount includes flexible TNA budget which is adjusted based on user demand.

ABBREVIATIONS AND GLOSSARY

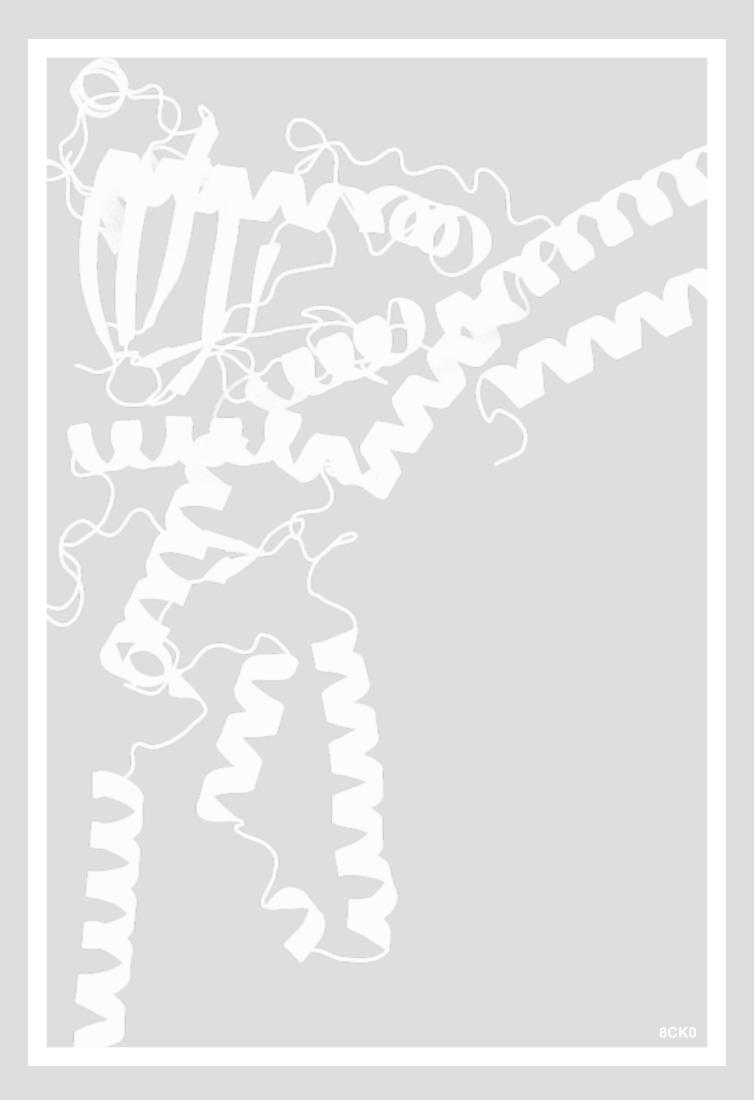
Term	Definition
Access	The unit of use of Instruct Research Infrastructure in person or remotely (sending samples)
Access Committee	A body established to manage the review of prospective users' proposals and applications for access to the tools and services provided by the Instruct-ERIC.
Al	Artificial intelligence
Al4Life	Al4Life aims to build bridges between the life science community and the machine learning/artificial intelligence community
AlphaFold	AlphaFold is an artificial intelligence program developed by DeepMind which performs predictions of protein structure.
API	Application Programming Interface
ARIA	Access to Research Infrastructure Administration: Instruct-ERIC's access management system
BIOCEV	Biotechnology and Biomedicine Centre (Czech Republic)
BLI	Biolayer Interferometry
BY-COVID	The BeYond-COVID project aims to make COVID-19 data accessible to scientists in laboratories but also to anyone, such as medical staff in hospitals or government officials.
canSERV	canSERV's mission is to make cutting-edge and customised research services available to the cancer research community EU wide, enable innovative R&D projects and foster precision medicine for patients benefit across Europe.
CEITEC	Central European Institute of Technology (Czech Republic)
CERM	Magnetic Resonance Center of the University of Florence (Italy)
CIISB	The Czech Infrastructure for Integrative Structural Biology
CIRMMP	The Interuniversity Consortium for Magnetic Resonance of Metallo Proteins (Italy)
CLEM	Correlative light and electron microscopy
CNB	Spanish National Centre for Biotechnology
COVID-19	Coronavirus disease caused by the SARS-CoV-2 virus
CSIC	Spanish National Research Council
DLS	Dimond Light Source (UK)
DMCC	Data Managementand Computational Committee
eBIC	Electron Bio-Imaging Centre (UK)
EC	The European Commission
EM	Electron Microscopy
EMBL	The European Molecular Biology Laboratory: an intergovernmental organisation specialising in research in the life sciences, funded by its 28 member states.
EOSC Future	EU-funded EOSC Future project to integrate and connect e-infrastructures, research communities and initiatives in Open Science to advance the EOSC platform of services.
EOSC-Life	The European Open Science Cloud: bringing together biological and medical Research Infrastructures to create an open, collaborative space for digital biology.
EOSC4Cancer	EOSC4Cancer will make cancer data accessible, using and enhancing existing federated and interoperable systems for securely identifying, sharing, and processing FAIR cancer data
ERIC	European Research Infrastructure Consortium: a specific legal form that facilitates the establishment and operation of Research Infrastructures with European interest.

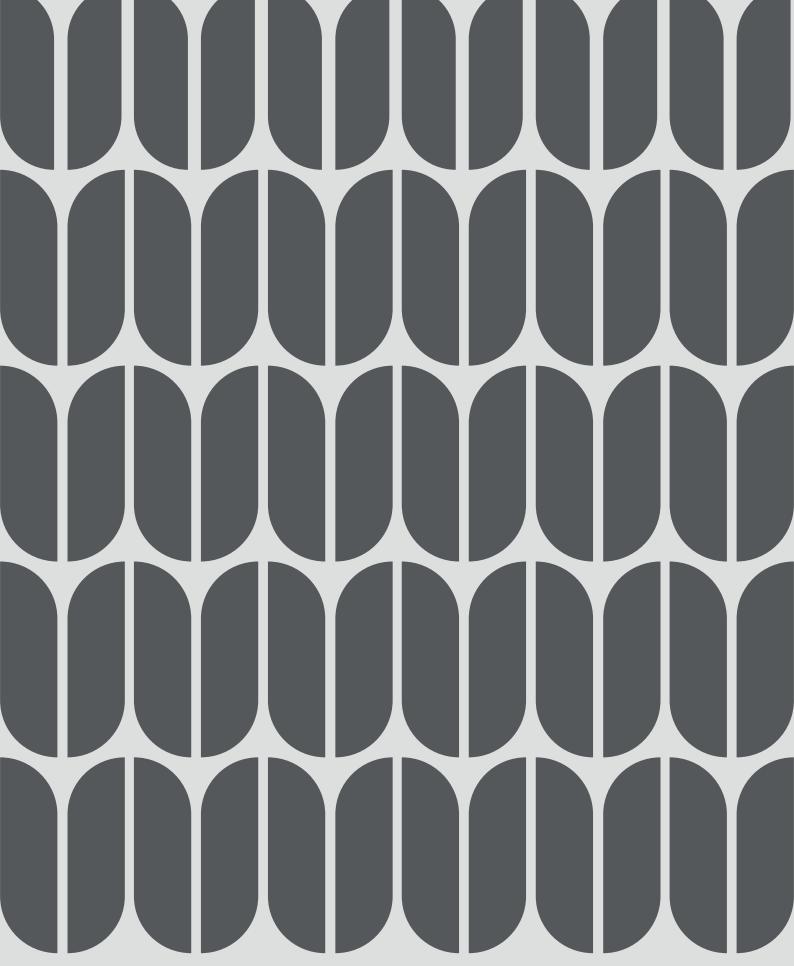
ABBREVIATIONS AND GLOSSARY CONTINUED

Term	Definition
ERIC Forum	A Horizon 2020 project bringing together European Research Infrastructure Consortia to strengthen their coordination and enhance their collaborations.
eRImote	eRImote finds solutions for digital and remote service provision across RI domains.
ESFRI	European Strategy Forum on Research Infrastructures: an organisation with members nominated by European member states ministries to support a coherent and strategyled approach to policy-making on Research Infrastructures in Europe.
ESRF	The European Synchrotron Radiation Facility (France)
ET	Electron Tomography
EU-LAC ResInfra	The European Union – Latin America and Caribbean partnership in Research Infrastructures pursues the construction of a bi-regional collaboration between European Union and the LAC countries.
Euro-BioImaging	A European Research Infrastructure providing open access to a broad range of technologies in biological and biomedical imaging for life scientists.
EU-OPENSCREEN	A European Research Infrastructure providing access to all stages of a chemical tool development projects.
FIB-SEM	Focused Ion Beam Scanning Electron Microscopy
Fragment-Screen	Horizon Europe project: From fragments to high affinity binders interfacing integrated structural biology, medicinal chemistry and artificial intelligence.
FRISBI	The French Infrastructure for Integrated Structural Biology: an infrastructure for integrative structural biology approaches.
H2020	Horizon 2020 is the biggest EU Research and Innovation programme, making €80 billion of funding available over 7 years.
I2PC	Instruct Image Processing Center (Spain)
IBS	Institute of Structural Biology (France)
IGBMC	The Institute of Genetics and Molecular and Cellular Biology (France)
IMAGINE	Horizon Europe project: Next generation imaging technologies to probe structure and function of biological specimen across scales in their natural context
iNEXT-Discovery	A consortium funded by the Horizon2020 program, offering European researchers access to a range of structural biology technologies.
Instruct Centre	An organisation that delivers access through the Instruct funding route.
Instruct Council	The governing body of Instruct-ERIC, deciding all issues of major importance including strategic objectives and targets and the deployment of finances and resources.
Instruct Executive Committee	The supervisory body for the execution of the project that reports to, and is accountable to the Instruct Council. Responsible for maintaining the progress and direction of the project.
Instruct Hub	The team responsible for coordinating Instruct-ERIC's operational activities.
Instruct Member	A country paying a membership fee to allow its scientists to apply for funding to access Instruct-ERIC services.
Instruct Observer	Countries or international organisations that are considering Instruct membership can become an Observer for a period of 1 year.
Instruct Research Sit	An Instruct facility or organisation, or a consortium of organisations within a country that can offer a centralised national hub to provide training, outreach or networking activities of interest to Instruct users and members.
Instruct User	A person that has applied, or is in the process of applying to access Instruct services.

ABBREVIATIONS AND GLOSSARY CONTINUED

Term	Definition
ISAB	Independent Scientific Advisory Board
ISBG	Integrated Structural Biology Grenoble (France)
ISIDORe	The ISIDORe project provides research services from structural biology through to clinical trials to support infectious disease epidemic research including SARS-CoV-2.
ISPC	The Israel Structural Proteomics Center
ITQB	Institute of Chemical and Biological Technology (Portugal)
LIOS	Latvian Institute of Organic Synthesis
LMJ	Liquid-metal-jet
MALDI-TOF-MS	Matrix Assisted Laser Desorption/Ionisation tuned to time-of-flight mass spectrometry
Moderator	A person assigned to an Instruct proposal by the Secretary of Moderators in order to select reviewers and decide the outcome of user proposals.
MoU	Memorandum of Understanding
MS	Mass Spectrometry
MX	Macromolecular Crystallography
NeCEN	Netherlands Centre for Electron Nanoscopy
NKI	Netherlands Cancer Institute
NMR	Nuclear Magnetic Resonance
OPIC	Oxford Particle Imaging Centre (UK)
PID	Proposal Identification number
Proposal	A user's request for access to technology or other services.
R&D	Research and development
Reviewer	A reviewer assesses the science of an Instruct proposal. Three reviewers are assigned to each proposal: all are external to the Instruct Centre that has been requested for access, and at least one is external to Instruct-ERIC.
RI	Research Infrastructure
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2 causing the COVID-19 pandemic
Scipion	Integrative image processing workflow engine
SEC-MALLS	Size Exclusion Chomatography - Multi-Angle Laser Light Scattering
SPC	Sample Preparation and Characterisation Facility, EMBL Hamburg
SPU	Structural Proteomics Unit
ssNMR	solid-state NMR
TRANSVAC-DS	The TRANSVAC-DS project aims to consolidate the conceptual and technical design and ultimate implementation of a European vaccine R&D infrastructure.
TRANSVAC2	The TRANSVAC2 consortium comprises a comprehensive collection of leading European institutions that propose to further advance with the previous initiative towards the establishment of a fully operational and sustainable European vaccine R&D infrastructure.
WIS	Weizmann Institute of Science (Israel)







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