



2023

**INSTRUCT-ERIC
ANNUAL REPORT**

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FOREWORD BY THE INSTRUCT-ERIC DIRECTOR & COORDINATION TEAM



2023 has been another excellent year of providing funded access to structural biology technologies for researchers in Europe and beyond. Instruct-ERIC is the leading research infrastructure for integrated structural biology, bringing together researchers from member countries and organisations across Europe, and reaching structural biology experts worldwide. In our discussion within the global structural biology community, we often hear that Instruct serves as a role model on how to coordinate between different European countries and between different structural biology techniques.

2023 marked a notable year for Instruct, a key theme being growth. We were delighted that two new countries, Slovenia and Greece, joined as Members in July 2023 growing the participation of sovereign states in the infrastructure. The integration to Instruct was celebrated at the Council meeting in May. At the same time, Sarah Butcher of Finland, former Vice-Chair, and Jose Maria Carazo of Spain were elected as Council Chair and Vice-Chair, respectively. They follow Eric Guittet of France. We here wish to sincerely thank Eric for his work and service to Instruct.

Instruct started two major research infrastructure technology development projects, Fragment-Screen and IMAGINE, which will expand the technical capabilities in key technologies of interest for the field of structural biology and as a result, growing the services to be made available to our user community. Fragment-Screen marks the largest grant ever coordinated by Instruct-ERIC and will bring new breakthroughs and services in fragment-based drug discovery.

In the spirit of growing, Instruct, however, also experienced some growing pains. Whilst we were delighted that access demand grew significantly from 2022 to 2023, a new record, the demand was so substantial that for the first time ever the continually assessed call for funded access had to be closed as budget had been exhausted. To address this increased demand, future access awards will be made in regular batches throughout the year, so as not to compromise the rapid and thorough evaluation Instruct prides itself on.

We also welcomed some new faces to the Instruct family, both in the hub and in the Centres and wider infrastructure. Welcome to all.

Instruct has been central to hundreds of scientific publications in 2023, each displaying the importance of democratised access to structural biology technologies. Antibiotic resistance is a critical challenge of modern medicine, and researchers from the Bijvoet Centre in Utrecht have had the opportunity to collaborate with CERM/CIRMMP in Florence, developing several new antibiotics with low resistance. Instruct's collaboration with industry continued in 2023, as the team in Strasbourg coordinated with AstraZeneca to study the structure of glucocorticoids and their interaction with DNA and human development. Instruct also welcomed researchers from Sao Paulo to Diamond Light Source for their work on septins as part of the latest international call, highlighting our collaboration with global scientists.

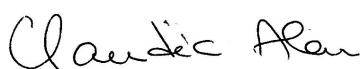
AI is an ever-increasing component of structural biology research, and in 2023, Diamond Light Source coordinated with IBM to conduct machine learning, identifying experimental drug targets from hundreds of thousands of potential antibodies. This is just a snapshot of what has been achieved in the lab in 2023, and the Instruct Scientific Strategic Plan aims to develop Instruct and the field of structural biology even further; presented to Council in 2023, and due to be published to the wider community in 2024.

Here at Instruct-ERIC we are continuously seeking ways to improve our service to the community, be that directly through the technology and expertise offering or indirectly through efficiency, quality and sustainability of the infrastructure operations. In 2023, we embarked upon two different exercises to analyse operations, results and impact of the infrastructure so far and to look into the future: the Long-Term Assessment (LTA) and the ESFRI Monitoring. Each of these activities will review Instruct's infrastructure and performance in detail, bringing in insights from external experts involved in the reviews. Insights gained will prove invaluable to us to pave the way for a bigger, better Instruct-ERIC in the future – to 2024 and beyond!

We wish to close by saying that we sincerely hope for peace in 2024. As scientists, we will continue to seek open scientific discussions and to share our knowledge to improve our lives.



Prof Harald Schwalbe
Instruct-ERIC Director



Dr Claudia Alén Amaro
Head of Operations



Dr Natalie Haley
Head of Strategy



EXECUTIVE SUMMARY

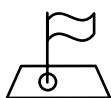
INSTRUCT-ERIC MEMBERSHIP

Instruct-ERIC had 16 Member Countries and Organisations with Greece and Slovenia joining in 2023. The Members hosted 11 Instruct Centres with 23 facilities providing access to structural biology technology and expertise.



16

Members



11

Centres



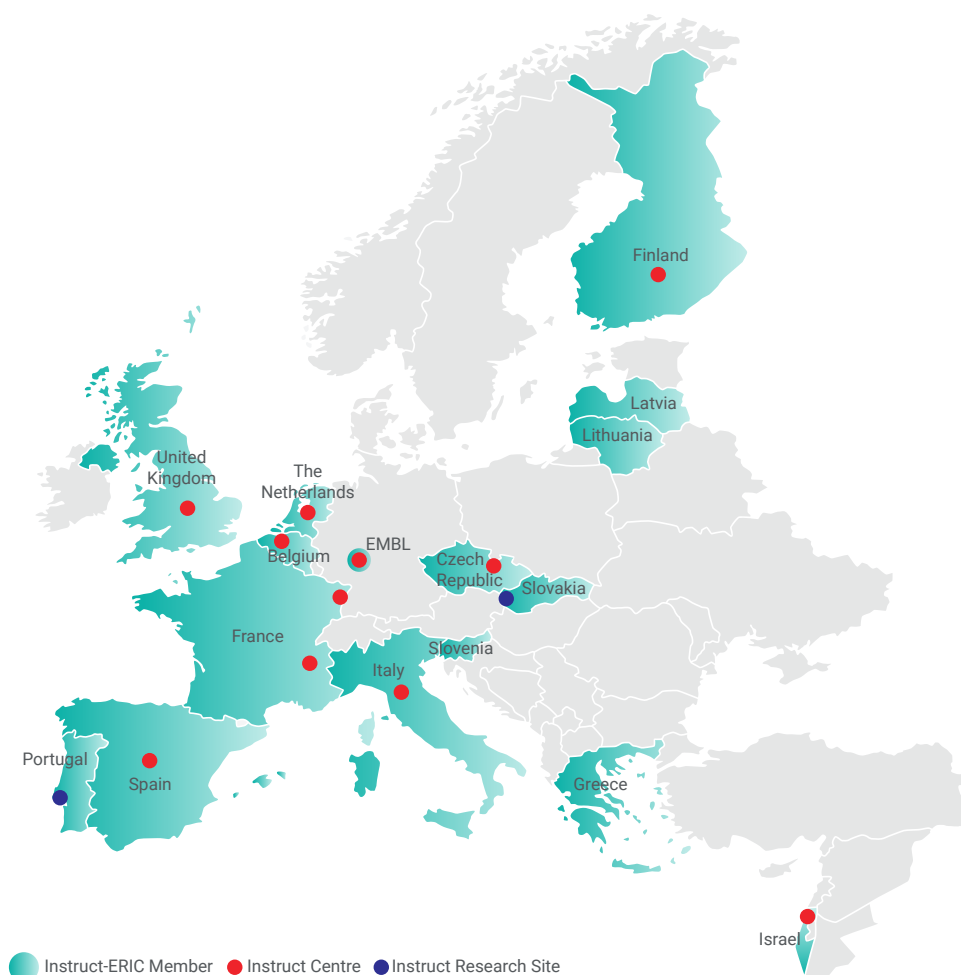
23

Facilities



2

Research Sites



INSTRUCT-ERIC SERVICE CATALOGUE

Instruct-ERIC provides access to high-end structural biology services and techniques. In 2023, 82 services were offered across nine service types.

Sample Preparation



Crystallisation



Nanobody
Discovery



Protein
Production



Imaging



Mass
Spectrometry



Molecular
Biophysics



Electron
Microscopy



Magnetic
Resonance
Techniques



X-Ray
Techniques

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.

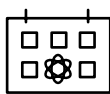
Additionally, depending on the facility resources and user needs, services can be accessed in-person or remotely to result in optimal infrastructure use.

INSTRUCT-ERIC SERVICE PROVISION



242

Access proposals received



1736

Days of access provided



335

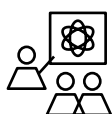
Scientific Publications

In 2023 Instruct-ERIC received 242 proposals for access from researchers in 23 countries of which 78% were approved.

Instruct-ERIC supported 193 research visits providing 1736 days of access to Instruct Facilities covering both national and transnational access.

Scientific output resulted in 335 publications in peer-reviewed journals.

INSTRUCT-ERIC TRAINING AND CAREER DEVELOPMENT



5

Training Courses



13

Internships



4

R&D Awards

In 2023, Instruct-ERIC provided funding to support five training courses.

Additionally, Instruct-ERIC supported 13 internships of three to six months for early career researchers.

Four Research & Development Pilot Awards were awarded for small scale pilot research projects in integrated structural biology.

INSTRUCT-ERIC HORIZON PROJECT PARTICIPATION



15

Projects

In 2023, Instruct-ERIC coordinated the new Fragment-Screen project and participated in 14 Horizon projects: AI4Life, BY-COVID, canSERV, EOSC Future, EOSC-Life, EOSC4Cancer, ERIC Forum 2, eRImote, EU-LAC ResInfra, iNEXT-Discovery, IMAGINE, ISIDORE, TRANSVAC-DS and TRANSVAC2.

Three new projects were awarded to start in 2024: EOSC Beyond, EU-LAC ResInfra Plus and FHERITALE.

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 2023, ARIA supported 18038 registered users. A record number of 693 proposals were submitted in ARIA resulting in 1307 peer reviews performed in 2023. Additionally, 2999 messages were sent in ARIA to connect the users, access managers, reviewers and facility teams.

COMMUNICATIONS



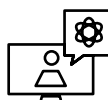
30

News Items Published



12

Science Highlights



5

Webinars

In 2023, Instruct published 30 news items on the website outlining the latest news from Instruct and partner projects, including new members, calls, and technologies.

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

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

TIMELINE

selected events
from 2023

JAN

Third International
Call Awarded

FEB

Start of the new
Horizon Europe project
Fragment-Screen

Fragment
Screen



Horizon 2020 projects EU-LAC ResInfra
and TRANSVAC-DS concluded

MAR

First canSERV TNA Call
opened

APR

Horizon 2020 project
TRANSVAC2 concluded

Start of RI-HUBS project



MAY

Instruct-ERIC Council
Meeting in Portugal

New Instruct-ERIC Council Chair

Sarah Butcher - Chair

Jose Maria Carazo - Vice Chair

Start of the
new Horizon
Europe
project
IMAGINE



IMAGINE

JUN

Instruct-ERIC Managers Meeting held in
Amsterdam, NL

JUL

2023 Instruct R&D Funding Projects Awarded

Instruct Hub retreat in Basingstoke, UK

New Horizon Europe Projects awarded: **FHERITALE, EOSC-Beyond, and EU-LAC ResInfra Plus**

Greece and Slovenia join as Instruct-ERIC Members

Horizon 2020 project EOSC-Life concluded

AUG

UK rejoins Horizon Europe Programme, and Diamond Light Source announces £500m funding plan

Registration opens for the Instruct Biennial Structural Biology Conference 2024

Instruct attends Spanish Presidency of the Council of the EU event, outlining how international collaboration benefits research infrastructures

Start of new Horizon Europe project ERIC Forum 2



OCT

Instruct-ERIC Council meeting in Vilnius, LT

Structural Biology in Lithuania and Beyond Conference

NOV

ESFRI Monitoring process began

1000th completed Instruct access visit

DEC

iNEXT-Discovery 2nd Regional Structural Biology Meeting - Hungary

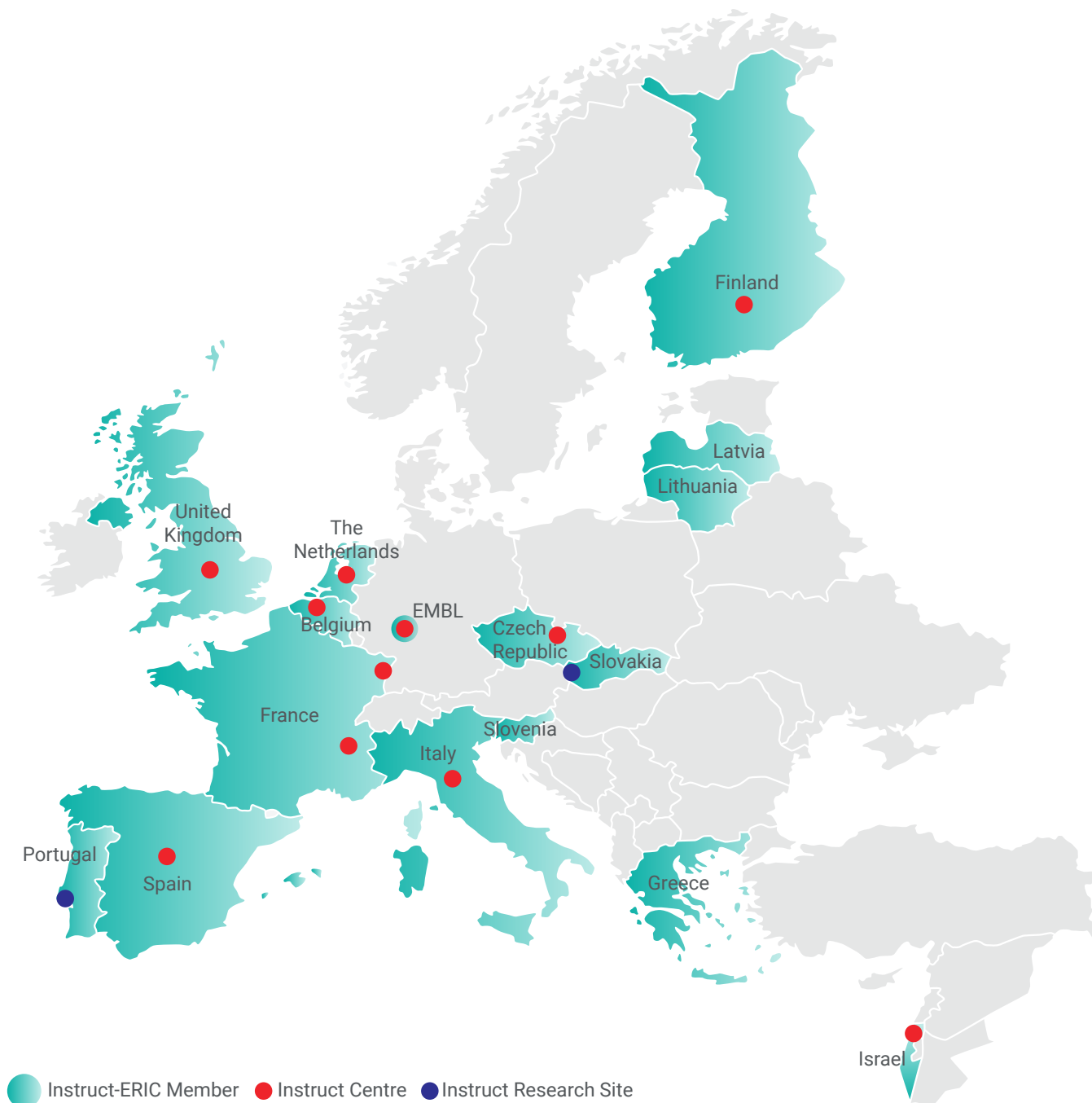
Instruct Image Competition winners announced

INSTRUCT MEMBERS



INSTRUCT-ERIC MEMBERSHIP

A clear highlight of 2023 was that Instruct was able to welcome two new Member countries to Instruct-ERIC, Slovenia and Greece, bringing the total number of members to 16. Membership of Instruct-ERIC ensures that researchers in Slovenia and Greece can now receive funded access to structural biology technologies at Instruct centres across Europe. Membership launch events in both countries will take place in 2024. Both Greece and Slovenia have a long history of structural biology expertise; the experience and the innovation that they can bring to the 11 Instruct centres as part of access visits, internships, and training courses will have profound effects on the structural biology community.



In October Instruct held an information event for the Lithuanian structural biology community at Vilnius University. At the event there were talks from local and Instruct speakers. This has resulted in a significant increase in applications from the structural biology researchers based in Lithuania.

Towards the end of 2023 discussions with Germany regarding membership concluded with an expectation that Germany will shortly submit their membership application. The application is eagerly anticipated in 2024.

INSTRUCT-BE

Instruct Centre BE

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



Nanobodies4Instruct, Brussels
Robotein for Instruct, Liège and Brussels

Services



Highlights in 2023

New Instruments, Upgrades and Tools

- Successful grant application to implement a High throughput Differential Scanning Fluorimetry (DSF) and a High Throughput Dynamic Light Scattering equipment (DLS). That we will be implemented in the Robotein lab in 2024.

Meetings and Outreach

- Robotein has been part of a post-graduate training course held in Breda (Netherlands, May 2023) dedicated to the methods used for the quality control of protein samples.
- Oral presentation of Robotein at the Workshop held in Brussels (Belgium), 27th April 23) "Challenges and Opportunities in Biotherapeutic Analytics".
- In January 2023 the 2nd Nb4Instruct training course was held. It was devoted to the hands-on discovery of nanobodies. Twelve participants could use their own protein samples to discover the most useful antibodies for applications in structural biology.

INSTRUCT-CZ

Instruct Centre CZ

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



BIOCEV - Biotechnology and Biomedicine Centre, Vestec, Prague-West
CEITEC - Central European Institute of Technology, Brno

Services



Highlights in 2023

New Instruments, Upgrades and Tools

- A 200kV (scanning-)transmission electron microscope for life-science applications Glacios 2 was installed to Cryo-EM facility at CEITEC
- From January 1, 2023, the laboratory of X-ray diffraction and BioSAXS was integrated into BIC facility at CEITEC. The protein diffractometer and Bio-SAXS including all services are now available under the Biomolecular Interaction and Crystallography Core Facility umbrella offering thus the full crystallography pipeline.

Meetings and Outreach

- The XIX Discussions in Structural Molecular Biology and the 6th User meeting of CIISB was held in Nove Hrad, South Bohemia, Czech Republic in March 2023
- 3rd CEITEC Symposium on Recent Advances in Cryo-EM took place in May 2023 at CEITEC
- 37th Central European NMR Meeting was held in Valtice, Czech Republic in April 2023
- CCP4 Practical Course 2023, a two-day hands-on course took place May 24th to 26th, 2023 in Biocev, Vestec

INSTRUCT-EL

Instruct Centre EL

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



Highlights in 2023

New Instruments, Upgrades and Tools

- The National Hellenic Research Foundation (NHRF) has been awarded 30.7 M€ in the frame of the project “Upgrade of Infrastructures of Research Centres supervised by the General Secretariat for Research & Innovation. New equipment 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 will be installed in the first quarter of 2025.

Meetings and Outreach

- The INSPIRED Structural Biology Conference was held in March 2023 at NHRF Athens, Greece organised by the National Research Infrastructure on Integrated Structural Biology, Drug Screening Efforts & Drug target functional characterization (MIS 5002550) with the aim to increase awareness of the services provided to interested key stakeholders.
- 2nd Regional Structural Biology Meeting was held in December 2023 at NHRF, Athens, Greece. The main aim of the meeting was to increase awareness of EU-wide iNEXT-Discovery and Instruct-ERIC structural biology services and to broaden the structural biology user community.

INSTRUCT-EMBL

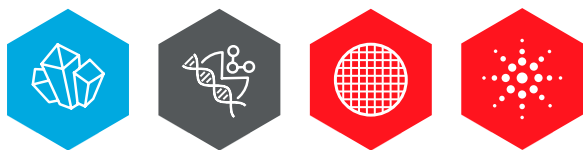
Instruct Centre EMBL

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



EMBL Grenoble, EMBL Hamburg, EMBL Heidelberg

Services



Highlights in 2023

New Instruments, Upgrades and Tools

- EMBL Grenoble - Continuation of the implementation of the CrystalDirect technology at the ESRF MASSIF 1 beamline, improving the beamline capacities and expanding the service portfolio of the HTX lab. EMBL and ESRF are jointly offering a completely automated ‘plate-to-beam’ service for both room temperature and cryogenic data collection.
- EMBL Hamburg - Contributed to the development of the Spitrobot, an experimental setup that will simplify time-resolved crystallography experiments. The SPC Facility introduced several new technologies to its portfolio, including Refeyn MP2 with MassFluidix HC, for measuring low affinity binding in micromolar concentrations.

Meetings and Outreach

- EMBL Heidelberg - Instruct was promoted at the Cryo-FIB lamella preparation and cryo-ET course, EMBO Practical Course In situ CLEM, EMBO/EMBL symposium Seeing is believing: imaging the molecular processes of life.
- EMBL Grenoble - ‘Science in the Mountains’ symposium celebrated Stephen Cusack’s career and the last 30 years of scientific and technological contributions from Grenoble teams. Kristina Djinic Carugo presented Instruct at the 15th Meeting of the Slovenian Biochemical Society

INSTRUCT-ES

Instruct Centre ES

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



CryoEM CNB-CSIC, Madrid

I2PC - Instruct Image Processing Center, Madrid

Services



Highlights in 2023

New Instruments, Upgrades and Tools

- I2PC Electron Microscopy FlexibilityHub - A platform for the study of the flexibility of a cryo-EM dataset
- Cryo-EM CNB-CSIC – Data acquisition for SPA and cryo-ET, using a 200 kV FEI TALOS Arctica, equipped with an autoloader and a Falcon 4i direct electron detector
- CryoCLEM sample characterisation – The facility provides support and expertise to researchers in the optimisation of cellular or tissue sample preparation for cryoCLEM workflow
- MicroED: Micro-Electron Diffraction data are acquired in a Talos Arctica 200 kV microscope

Meetings and Outreach

- Instruct-ERIC meets biological function (2023) - Presentation of the new services offered by the Instruct Centre ES.
- iNEXT Discovery - I2PC Course on Single Particle Analysis by CryoEM (March, 27-29, 2023)
- Instruct Course on flexibility analysis and integrative modelling using Scipion (June 19-23, 2023)
- I2PC Seminar series - 7 September - 19 October

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 2023

New Instruments, Upgrades and Tools

- DynaPro NanoStar II enables batch mode analysis of hydrodynamic size, aggregation and particle concentration at the Biomolecular Complex Purification (Biocomplex), University of Helsinki.
- Preomics BeatBox high-throughput sample preparation station at the Single-cell Proteomics (SCoPE-MS), University of Helsinki.
- A plate hotel and an automated protein crystallisation imager Formulatrix RockImager 182 replaces two RI54 imagers and offers visible, and UV light imaging options with increased plate storage capacity at the University of Oulu.

Meetings and Outreach

- Structural Biology platform FINStruct and Instruct-ERIC Centre Finland 2023 Annual Meeting was held in Turku in October 2023 and organised by the Universities of Turku and Åbo Akademi. 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 2023

New Instruments, Upgrades and Tools

- CHAMELEON system for EM sample vitrification: a new blot-free approach at FR1.
- In Molecular Biophysics at FR1: Bio-Layer Interferometry (Octet® R8 System, Sartorius) and Upgrade of the ITC equipment: Microcal PEAQ-ITC (Malvern).
- 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

Meetings and Outreach

- iNEXT-Discovery workshop (April 2023): Cryo-FIB lamella preparation and cryo-ET at 3 Instruct centres EMBL-Heidelberg, CEITEC and FR1 (coordinator).
- EMBO practical course on Preparation and biophysical/MS characterisation of multi-protein complexes for cryo-EM analysis (FR1: November 2023).
- Instruct Cryo-EM Workshop, Grenoble (FR2, May 2023).

INSTRUCT-IL

Instruct Centre IL

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

ISPC - Weizmann Institute of Science, Rehovot

Centre for Bioinformatics, Tel Aviv University, Tel Aviv



Services



Highlights in 2023

New Instruments, Upgrades and Tools

- In response to the growing demand over the past few years, 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.
- Although the 3D structure of a protein provides a wealth of valuable information, some researchers trained in the Life Sciences may lack the expertise to fully utilise this information and correlate it with their biological data. Therefore, upon request, once the SPU determines the protein structure, either experimentally (using X-ray or Cryo-EM) or through prediction, they perform extensive comparative analyses with a focus on correlating sequence, activity, and stability with the 3D structure.
- The centre provides a variety of services to the scientific community in the production of recombinant proteins such as: cloning, expression of different proteins in a variety of hosts and their purification and characterisation. Some of the proteins are crystallised and their structures determined by the in-house Liquid-metal-jet (LMJ) X-ray diffraction system. Protein structures are also determined by cryo-EM using in-house microscopes in collaboration with the WIS EM unit. The SPU also perform in silico predictions of the structures of proteins and protein complexes.

INSTRUCT-IT

Instruct Centre IT

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



CERM, Florence

Services



Highlights in 2023

New Instruments, Upgrades and Tools

- CERM/CIRMMP has optimised the workflow for ¹³C-detected NMR experiments at 1200 MHz, including some multiple receiver experiments, customized for the investigation of IDPs with varying molecular weights and structural complexity.
- A ligand-based real-time in-cell ¹⁹F approach to measure ligand binding affinities in human cells was demonstrated on a set of Hsp90α inhibitors.
- The combination of NMR tools (NOE and ROE) for probing protein–water interactions at a residue-specific level with molecular dynamics simulations and computational methods designed to provide a spatially resolved picture of solvent thermodynamics was employed to provide a complete panorama of solvent redistribution.

Meetings and Outreach

- ICGEB course “NMR for combatting diseases: from cancer to SARS-CoV-2”. Teaching both the basics and the more advanced potential of nuclear magnetic resonance.
- INEXT-Discovery / Instruct-ERIC training course on in-cell NMR. The course featured lectures and hands-on practicals on the following topics: mammalian protein expression, in-cell NMR of proteins/nucleic acids, NMR bioreactor, in-cell EPR.

INSTRUCT-LT



Highlights in 2023

New Instruments, Upgrades and Tools

- A new transmission electron microscope Talos L120C (ThermoFisher) was installed at Vilnius University Life Sciences Center.

Meetings and Outreach

- In June 2023, the iNEXT-Discovery 2nd regional structural biology meeting took place at the Vilnius University Life Sciences Center.
- Instruct-LT hosted a scientific seminar "Instruct-ERIC: Structural Biology in Lithuania and Beyond" (below), the purpose of which was to spread information about Instruct-ERIC, as well as to increase interest in activities and cooperation in the field of structural biology.



INSTRUCT-LV

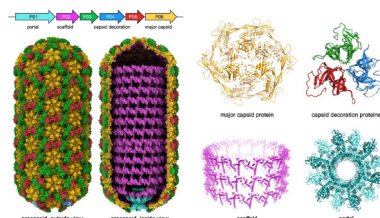


Highlights in 2023

- On March 29, 2023, the Latvian Institute of Organic Synthesis (LIOS) opened its new Biotechnology facility, located in a two-story building next to its main site.
- In 2023, a range of different instruments for molecular and structural biology research were installed, including a MALDI-TOF mass spectrometer Autoflex (Bruker) for protein sample characterisation, a microscale thermophoresis (MST) instrument Monolith NT.115 (Nanotemper) and an isothermal titration calorimeter (ITC) MicroCal PEAQ-ITC (Malvern Panalytical) for binding affinity measurements, a grating-coupled interferometry (GCI) system Creoptix WAVE (Creoptix) for high-throughput analysis of binding kinetics, as well as a circular dichroism (CD) spectrophotometer J-1500 (Jasco) for protein secondary structure evaluation.
- The new equipment will be used for structural and interaction studies in the contexts of rational drug design, biomaterials, biocatalytic processes and bio-pharmaceutical development.

Meetings and Outreach

- From 18th to 19th September 2023 LIOS hosted the ERA-Chair project “BioDrug” final conference, dedicated to recent advances in structural biology and drug discovery. The event took place in Riga and brought together 12 distinguished speakers and over 90 participants.
- From 27th to 29th June 2023 in University of Latvia, Riga, 6th Virus-like Particle & Nano-Particle Vaccines conference was held. While the main emphasis of conference was vaccine development, many talks included also structural biology aspects of virus-like particles and antigens.
- Recently researchers from Latvian Biomedical Research and Study Center solved cryo-EM structure of *Borrelia* bacteriophage ϕ BB1 procapsid.



Structure of the *Borrelia* bacteriophage ϕ BB1 procapsid

INSTRUCT-NL

Instruct Centre NL

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

Bijvoet Centre - Utrecht University, Utrecht
NKI Protein Facility, Amsterdam
NeCEN - Leiden University, Leiden



Services



Highlights in 2023

New Instruments, Upgrades and Tools

- 2.5 mm H/F/X/Y solid-state NMR probehead for 800 MHz NMR magnet. Probe allows for triple-resonance experiments such as H/P/C and can be tuned to low-gamma nuclei such as ^{43}Ca .

Meetings and Outreach

- 3-day workshop on NMR sensitivity enhancement on June 28-30 in Utrecht
- Symposium on “20 years of sailing the biomolecular interaction landscape with HADDOCK”, Huizen, the Netherlands, November 7-10, 2023
- NKI hosted on their premises in Amsterdam another recurring Instruct-ERIC Managers Meeting. The event, shared between Instruct-ERIC and iNEXT-Discovery, took place on June 26, 2023, once more allowing stimulated discussions among international life science facility managers and operators.

INSTRUCT-PT

Instruct Research Site PT

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



FC-ULisboa, Lisboa
ITQB NOVA, Oeiras

Highlights in 2023

New Instruments, Upgrades and Tools

- Opening of a cryo-EM facility based on a 200 kV Glacios 2 cryo-TEM at the Internacional Iberian Nanotechnology Laboratory in Braga (INL). Providing near atomic data for single-particle analysis, cryo-ET and Micro-ED applications in life and health sciences and strengthening the cooperation between Portugal and Spain in this area.
- Establishment of detailed methods and protocols for medium throughput of fragment screening by extreme resolution magnetic resonance mass spectrometry (MRMS), aiming to establish and consolidate mass spectrometry as the method of choice for fragment screen.
- Development of CAPIDOWN (Computational Annotation of Proteins In top-DOWN proteomics), a software package for sequence annotation of intact protein MSMS spectra.

Meetings and Outreach

- Final meeting of EU H2020 Twinning project “Imaging Life from Molecules to Cells”, IMpaCT (grant Nr 857203), INL, fostering Cryo-EM expertise within Instruct-PT researchers, supported by Instruct partners from UH, Finland, CNB-CSIC, Spain and WIS, Israel.
- Microscopy at the Frontiers of Science Conference (MFS2023), INL. September, focused on the latest breakthroughs and future developments in the field.
- Pathprot-15 Workshop, Gulbenkian Institute of Science, Oeiras, October, an international forum on proteomics, systems biology, and structural mass spectrometry.

INSTRUCT-SI



Highlights in 2023

New Instruments, Upgrades and Tools

- National Institute of Chemistry: LUMICKS C-Trap EDGE 350, a fluorescence TIRF microscope coupled to an optical tweezer and a microfluidics system. Prometheus Panta (Nanotemper) for quality control of biological samples. Eclipse Field-Flow Fractionation (FFF) instrument coupled to a multidetection system, Wyatt Technology. Computer cluster in Ažman centre was upgraded.
- Josef Stefan Institute: Mass spectrometer Orbitrap Exploris 480 (Thermo Scientific, USA).
- University of Ljubljana: high-resolution fluorescent microscopy: LSM 980 spectrometer (Zeiss), and Abberior STED. BioTek microplate reader Synergy H1 with fluorescence polarization; PEAQ ITC (Malvern) for isothermal microcalorimetry.
- University of Nova Gorica: a new phage display library of adhirons, an alternative to nanobodies.

Meetings and Outreach

- Slovenia joined Instruct-ERIC on 1st of July 2023.
- Prof. Marjetka Podobnik (National Institute of Chemistry) and Prof. Kristina Djinović-Carugo (EMBL Grenoble) presented Instruct-ERIC at the 15th Meeting of the Slovenian Biochemical Society, Portorož, Slovenia, September 20th to 23rd 2023.



Photo credit: consortium Instruct.SI

INSTRUCT-SK

Instruct Research Site SK

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



IC SAS - Slovak Academy of Sciences, Bratislava

Highlights in 2022

Meetings and Outreach

- A new partnership between the Institute of Molecular Biology SAS (Instruct-SK) and the Czech Infrastructure for Integrative Structural Biology (CIISB) in the Czech Republic (Instruct-CZ) has been signed to support the access to the full-service and self-service mode within the Call for research projects. The agreement supports collaboration in the field of Cryo-electron microscopy and tomography.



INSTRUCT-UK

Instruct Centre UK

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



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

Services



Highlights in 2023

Astbury Centre

- In April 2023, the Astbury Centre in Leeds installed a Talos L120C microscope.
- First in-person Wellcome training course at Astbury Centre in November 2023.

Harwell Campus

- Harwell Campus course included the Instruct-ERIC workshop on imaging cells using correlative soft X-ray tomography at cryogenic temperatures (Nov), SAS Analysis Course 2023 (Jun), Cryogenic Electron Microscopy in Structural Biology (Aug), iNEXT-Discovery Sample Preparation Course (Oct), Diamond-CCP4 Data Collection and Structure Solution Workshop 2023 (Dec), Early Career Scientists Symposium 2023 (Dec).

Oxford University

- The first commercial Arctis pFIB/SEM (plasma focussed ion beam Scanning Electron Microscope with fluorescent microscope for correlative experiments) in the UK has just been installed within the OPIC HG3 laboratory, as well as a Delmic CERES cleanstation, enabling sample loading in a dry environment at low energy and cost.
- Oxford Mass Spec Centre submitted EoI for new equipment to be installed in 2024.
- STRUBI Imaging Centre established in 2023, with first light microscopy facility accessible via Instruct-UK.



SCIENTIFIC HIGHLIGHTS



FR

Native Mass Spectrometry at Instruct-FR2 uncovers the cofactor and binding mechanism of adherent invasive *E. coli* protein IbeA

A team from University of Montpellier accessed structural biology technologies at IBS Grenoble, (Instruct Centre FR2), utilising a combination of size exclusion chromatography (SEC), mass spectrometry (MS), 3D modelling and various other techniques to investigate the structure, binding target(s), and binding mechanism of *E. coli* protein IbeA.

Paris et al. (2023), The IbeA protein from adherent invasive *Escherichia coli* is a flavoprotein sharing structural homology with FAD-dependent oxidoreductases 291 (1): 177-203. doi:10.1111/febs.16969

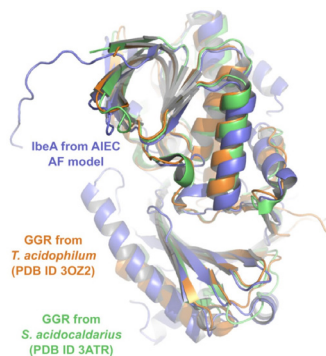


FIG 1. IbeA (purple) overlain with GGR structures (orange and green) using AlphaFold prediction software.

CZ

Conformational flexibility modulates distinct functions and coacervation properties of an intrinsically disordered region in RECQ4 helicase

The research teams of Konstantinos Tripsianes from CEITEC, Masaryk University, and Lumír Krejčí from Faculty of Science, Masaryk University, has uncovered a positively charged polyelectrolyte in the intrinsically disordered region of DNA helicase RECQ4, utilising solution NMR spectroscopy at Instruct-CZ, combined with biochemical, biophysical, and optical methods.

Papageorgiou et al. (2023), Recognition and coacervation of G-quadruplexes by a multifunctional disordered region in RECQ4 helicase, *Nature Communications*, 14 (6751). DOI: 10.1038/s41467-023-42503-z

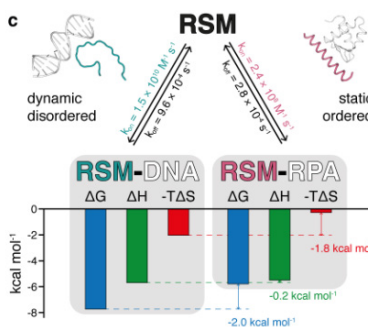


FIG 2. Distinct and competitive binding modes of RECQ4 IDR to DNA and RPA. Summary of kinetic, thermodynamic, and structural parameters of RECQ4-specific motif (RSM) interactions.

IL

Instruct-IL Project on the Impact of Multiple Factors in Studying the Crystal Structures of Ligand-Phosphotriesterase Complexes

The team at the Weizmann Structural Proteomics Unit, studied complexes of *B. diminuta* phosphotriesterase (PTE) with organophosphates (OPs), showing the factors that must be considered when obtaining crystals of ligand-protein complexes for X-ray data collection.

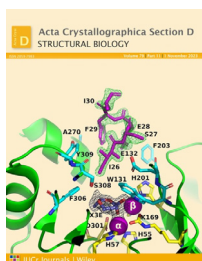


FIG 3. Ribbon representation of the A53_3 variant.

Dym et al (2023), The impact of molecular variants, crystallization conditions and the space group on ligand-protein complexes: a case study on bacterial phosphotriesterase, *Acta Cryst D*, Volume 79 (11), 992-1009. doi:10.1107/S2059798323007672

EMBL

ISIDORE Study at EMBL Grenoble Uncovers Potential SARS-CoV-2 Inhibitor

A collaboration between the Márquez group at EMBL Grenoble and Italian researchers from the European Biomedical Research Institute of Salerno (EBRIS) has led to the development and characterisation of a novel small molecule inhibitor, which shows promising activity against three SARS-CoV-2 variants.

Di Micco et al (2023), Rational design of the zonulin inhibitor AT1001 derivatives as potential anti SARS-CoV-2, *European Journal of Medicinal Chemistry*, Volume 244. doi.org/10.1016/j.ejmech.2022.114857

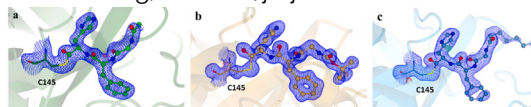


FIG 4. Co-crystal structures of the covalent inhibitors bound to SARS-CoV-2 Mpro C145.

NL

Instruct-NL Develop Clovibactin: The Potential New Antibiotic with Low Bacterial Resistance

The group led by Markus Weingarth initially uncovered teixobactin (following access to Instruct Centre IT) which blocks cell wall development in bacteria, making it a prime antibiotic candidate. Now, the group have uncovered another potential antibiotic candidate: clovibactin. A lack of specific interaction between clovibactin and cell wall lipid II sugars is what allows clovibactin to bind effectively with many cell wall precursors, with a lipid-anchored PPI group.

Shukla et al (2023), An antibiotic from an uncultured bacterium binds to an immutable target, *Cell*, 186(19):4059-4073. DOI: 10.1016/j.cell.2023.07.038.

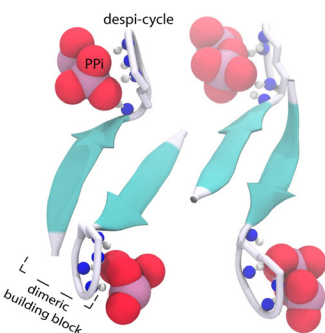


FIG 4. The structure of the clovibactin (blue) despi-cycle (grey) in complex with the lipid II PPI group (red).

FI

University of Helsinki Identifies an Intranasal Prophylactic Treatment of SARS-CoV-2 and Variants

Insight into the molecular mechanisms underlying strong neutralisation of SARS-Cov-2 by prophylactic treatment by sherpabody Sb92 was determined through cryo-EM structure determination, where the cryo-EM facilities at University of Helsinki, part of Instruct Centre FI, were instrumental.

Mäkelä et al. (2023), Intranasal trimeric sherpabody inhibits SARS-CoV-2 including recent immunoevasive Omicron subvariants, Nature Communications, 14 (1637). DOI:10.1038/s41467-023-37290-6

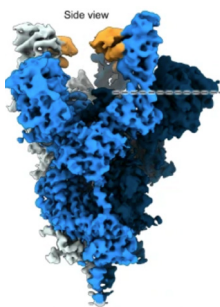


FIG 5. SARS-CoV-2 Spike trimer in complex with TriSb92.

IT

Instruct-IT develops new in-cell NMR approach to observe fluorinated proteins in mammalian cells

CERM/CIRMMP has developed a novel approach that allows the observation of fluorinated proteins in intact human cells by in-cell ¹⁹F NMR. The approach allows the observation of proteins otherwise 'invisible' due to interactions with cellular components. J. Am. Chem. Soc. 145, 2, 1389–1399, 2023 - DOI: 10.1021/jacs.2c12086

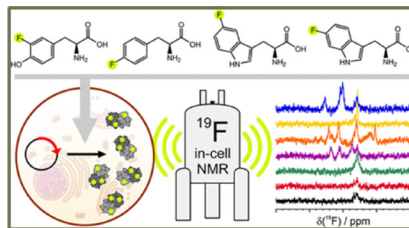


FIG 6. Fluorine incorporation in mammalian cells allows to study protein structure and function in the native cellular environment.

ES

UK

Understanding the Mechanism of Transposase Complex Formation by Cryo-EM

Cryo-EM was used to identify the self-assembled three-dimensional tetramer formed by IstA in formation with transposon IS21. This cryo-EM experiment took place at Diamond Light Source (part of Instruct Centre UK) and initial data processing was performed at I2PC (Instruct Centre ES) following a successful application to get access to structural biology services through Instruct-ERIC.

Spínola-Amilibia et al. (2023), IS21 family transposase cleaved donor complex traps two right-handed superhelical crossings, Nature Communications, 14 (2335). DOI:10.1038/s41467-023-38071-x

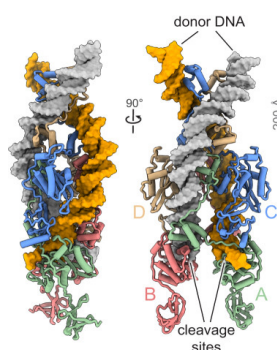


FIG 7. Cryo-EM structure of IstA tetramer bound to donor DNA.

FR

Instruct-FR1 and AstraZeneca combine to determine DNA and ligand-bound structure of glucocorticoid receptor

This study aimed to determine the structure of glucocorticoid receptor, and explore how the various domains differ and communicate with one another. This was done with the experience of the team at IGBMC and with AstraZeneca, showcasing a strong collaborative effort between academia and industry.

Postel et al. (2023), Quaternary glucocorticoid receptor structure highlights allosteric interdomain communication, Nat Struct Mol Biol, 30, 286–295. DOI:10.1038/s41594-022-00914-4

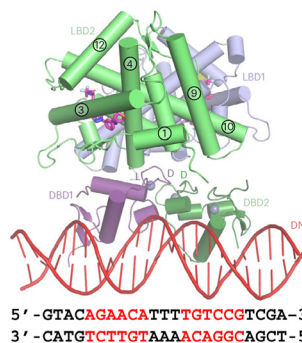


FIG 8. The LBD dimer bound in the centre of the DBD dimer, which is then bound to the DNA strand.

BE

New insights into antibody response to COVID-19 from Instruct-BE

Analysis over the course of 2022 and 2023 of effects and efficacy of the SARS-CoV-2 vaccine on specific demographics: nursing home residents, younger children, and kidney transplant recipients - utilising biomolecular analysis and protein production services of the Robotein facility.

Pannus et al. (2023), Third dose of COVID-19 mRNA vaccine closes the gap in immune response between naïve nursing home residents and healthy adults, Vaccine, 2023;41(17):2829-2836. doi:10.1016/j.vaccine.2023.03.047

Kemlin et al. (2023), Humoral and cellular immune correlates of protection against COVID-19 in kidney transplant recipients, 23(5), 649-658. DOI:10.1016/j.ajt.2023.02.015

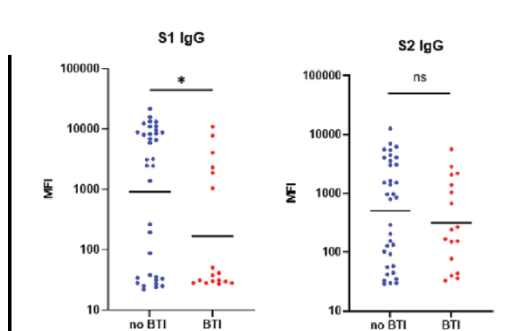


FIG 9. Difference in S1 and S2-binding antibodies between no BTI and BTI affected SOT patients. S1 binding is lower in BTI patients, however there is minimal difference between BTI and no-BTI patients for S2-binding antibodies.

CORE ACTIVITIES



8CK0

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. 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.

Access in 2023

2023 saw record demand for Instruct's services with 188 approved visits. The previous highest demand was in 2021 with 144. The increase in demand for Instruct services saw the access budget consumed in record time, and as a result, for the first time ever, Instruct temporarily closed its call for access between October and December. Demand is expected to remain strong in the coming years, therefore Instruct has now taken measures to ensure access can remain open throughout the call. This was achieved by moving 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. Applications demonstrating scientific excellence which do not meet the threshold for Instruct funding due to competition induced by high demand, will still be offered funding from Instruct for travel and accommodation/shipping along with the offer to self-fund their access with their own grants or resources.

New technologies available in 2023

In 2023, Instruct-ERIC expanded its catalogue with several new technologies: A new focused ion beam scanning electron microscope, the Helios Hydra V, and a new Glacios Plasma-FIB/SEM microscope, available for service at cryo-electron microscopy and tomography core facility (CEMCOF) at CEITEC in Instruct Centre CZ. IGBMC (Instruct Centre FR1) added the Chameleon automated freezing device for ultra-consistent sample vitrification for Cryo-EM. Additionally, IGBMC introduced the BLI and FIDA technologies to its molecular biophysics catalogue. Instruct Centre ES opened the FlexibilityHub, an innovative approach for image processing of challenging samples presenting a large degree of flexibility, as well as the cryo correlative light and electron microscopy (CryoCLEM).

Access through Horizon Europe projects

Complementing Instruct's core-funded access programme, EU-funded TNA projects ISIDORE and CanSERV continued in 2023. canSERV opened its first calls in 2023: A "challenge-driven" call for service provision "Advancing personalised oncology" which launched in February and the broader-scope "Open Call" which opened in September. Service provision is expected to commence in 2024.

Infectious Disease



Cancer and Oncology



Translational Research



All Other Topics



The ISIDORE project ran six open calls in 2023, offering researchers access to structural biology services in different thematic areas: Two in emergency areas for ongoing pandemics (SARS-Cov-2, and Monkeypox virus), and four in pandemic preparedness (Risk Group 4 Pathogens, Respiratory Pathogens, Vector-Borne Pathogens and Their Vectors, and Other Pathogens with Epidemic Potential). 54 visits took place in 2023 to access Instruct facilities through ISIDORE, whilst three Joint Research Activity projects started in 2023 with involvement of Instruct partners.

ACCESS TO INFRASTRUCTURE 2023

Service demand

In the period from 1 January to 31 December 2023, demand for access reached a record high with 242 proposals received of which 188 were approved, equating to a 78% approval rate. This high approval rate shows the excellent quality of the research project proposed.

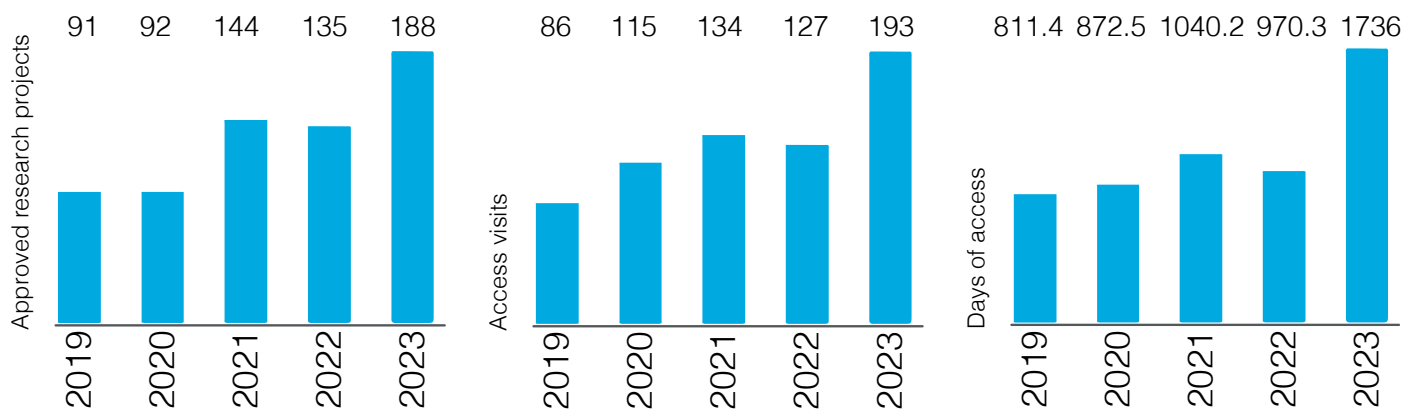


FIG 1. Instruct-ERIC access statistics [status 02.07.2024]

Service provision

In 2023, a new high of 193 research visits were completed. 55 of those (29%) were national visits and the majority of 138 (71%) visits was transnational access to a research facility in a different country.

The visits combined to a total of 1736 days of access of which 324 days were used nationally (19%) and 1412 transnational (81%).

Services were provided to researchers from 20 different countries and organisations (AR, AT, BE, BR, CZ, DE, DK, EL, EMBL, ES, FI, FR, IL, IT, LT, LV, NL, PT, SK, UK, ZA). 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 technologies (EM, NMR and X-Ray) were the most accessed services in 2023. This was followed by sample preparation services (protein production, crystallisation and nanobody discovery) which are essential for subsequent 3D analysis (Fig.2).

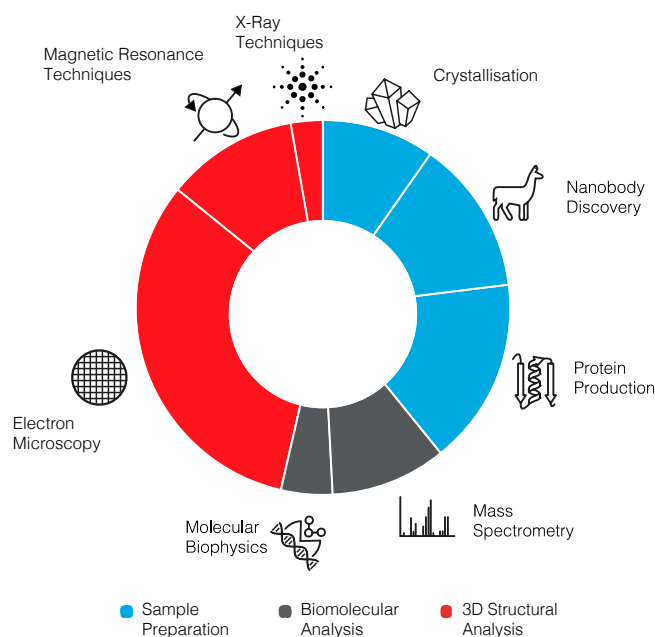


FIG 2. Instruct-ERIC access visits per service technology in 2023 [status 02.07.2024]

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 2023 acknowledged Instruct-ERIC was 335 – the highest annual number achieved to date.

These publications featured work of researchers from more than 59 different countries. This is indicative of Instruct-ERIC's presence within the global structural biology community – and is further emphasised by Instruct's growing international reputation.

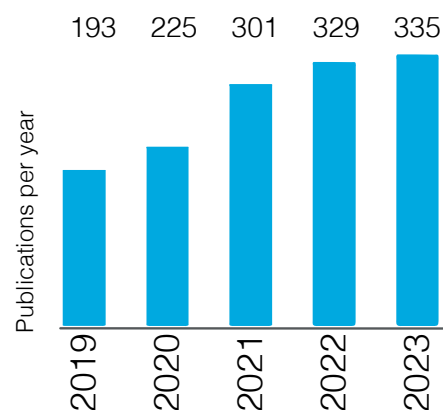


FIG 3. Instruct-ERIC publications statistics [status 02.07.2024]

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 2023

Since 2012, 77 training courses have been approved for Instruct funding or co-funding. In 2023, the dedicated training programme included courses focused primarily on cryo-EM and X-ray crystallography and tomography, as well as workshops on analysing this data further for more accurate and impactful results.

[Instruct course on flexibility analysis and integrative modelling using Scipion](#)

19 - 23 June 2023

Instruct Centre ES

The course mapped out how to construct an atomic model for a cryo-EM map and how to analyse macromolecular flexibility from cryo-EM images. It outlined the tools within Scipion for both steps (modelling and flexibility analysis). In addition to the hands-on training with the software and tools, long-term collaborations have been generated via the workshop.



Fig1. Instruct course on flexibility analysis and integrative modelling using Scipion

[5th Instruct Hands-on workshop on sample preparation for Single Particle cryo-EM](#)

23 - 25 May 2023

Instruct Centre FR2

The practical workshop is jointly organised by ESRF, EMBL and IBS, including sample preparation theory talks from Thermofisher speakers, followed by hands-on sessions in sample preparation of cryo-EM grids. Several positively prepared samples were produced, as students learned use of Vitrobot, Titan Krios, and Glacios machinery.



Fig2. 5th Instruct Hands-on workshop on sample preparation for Single Particle cryo-EM

[Instruct-ERIC workshop on Nanobodies for Structural Biology and beyond](#)

8 - 17 Jan 2023

Instruct Centre BE

The second Nanobody4Instruct Training Course in Brussels was devoted to the hands-on discovery of nanobodies (Nbs) for applications in structural biology. Trainees were introduced to applying Nbs in X-ray crystallography and cryo-EM. New developments in the field (Megabodies, Fluobodies) were also introduced. During the course, participants used their own protein samples to discover the most useful antibodies for solving the structure of their target.



Fig3. Instruct-ERIC workshop on Nanobodies for Structural Biology and beyond



Fig4. Instruct workshop on imaging cells using soft X-ray tomography at cryogenic temperatures

[Instruct workshop on imaging cells using soft X-ray tomography at cryogenic temperatures](#)

11 - 14 September 2023

Instruct Centre UK

The course aimed to introduce soft X-ray tomography facilities to users and train students from different labs to the use of the method. On each day of the workshop, theory sessions were streamed to a hybrid audience, followed by hands-on training on sample preparation and data collection, delivered to 12 on-site students.

[Instruct-ERIC course on X-ray, electron and neutron crystallography](#)

29 June - 6 July 2023

Instruct Centre FI

The hybrid course contained a range of hands-on practical sessions on data processing of X-ray, neutron and electron diffraction methods, while the lectures were also open for online participation after a light registration procedure. Also, time-resolved serial-crystallography methods to study dynamic biomolecular processes and data curation and archiving were discussed towards the end of the course.



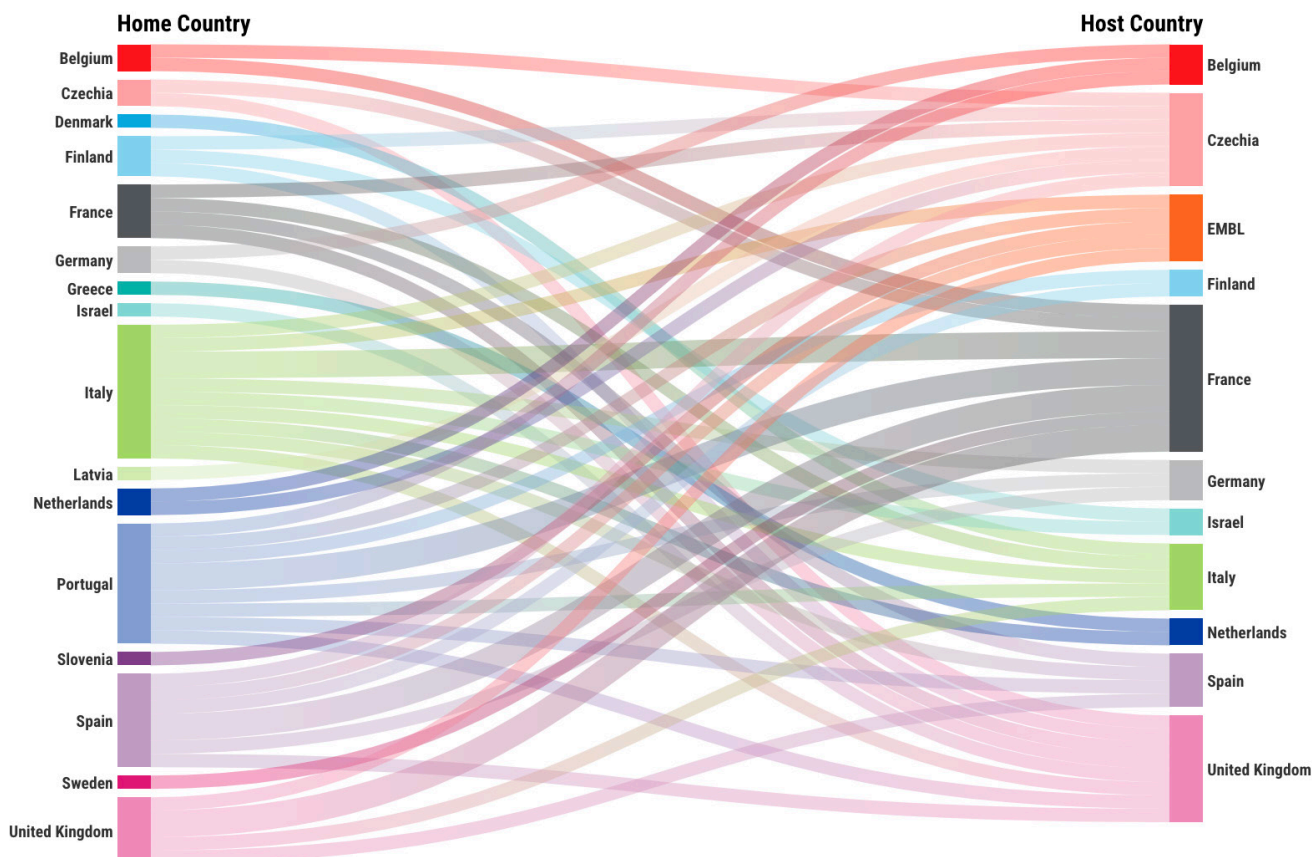
Fig5. Instruct-ERIC course on X-Ray, electron and neutron crystallography

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 pre-doctoral, 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 76 internships that have facilitated research exchanges across Europe:

Instruct-ERIC Internships [2013-2023]



In **2023**, 13 internships applications were approved in three calls across 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
Nika Žibrat	Slovenia	Instruct Centre EMBL
Tsouri Angeliki	Greece	Instruct Centre NL
Hannula Liina	Finland	Instruct Centre UK
Liedtke Janine	Netherlands	Instruct Centre CZ
Costanzo Antonella	Italy	Instruct Centre ES
Borja Sáez	Spain	Instruct Centre FR2
Sharda Bharti	Italy	Instruct Centre EMBL
Marialaura Giannaccari	Italy	Instruct Centre FR1
Lucía-Sánchez Alba	Spain	Instruct Centre FR1
Daniel Muñoz-Reyes	Spain	Instruct Centre UK
Stephanie Spada	UK	Instruct Centre EMBL
Matteo Amadei	Italy	Instruct Centre UK
Marta Cozzaglio	Italy	Instruct Centre CZ

R&D AWARDS

Instruct-ERIC publishes calls for pilot research projects in integrated structural biology. Resources are allocated to support a limited number of pilot studies proposed by researchers from Instruct Member countries, utilising integrated structural biology techniques, and working alongside multiple centres within the Instruct consortium. Pilot projects may be funded up to a maximum of €15,000. The funds are expected to cover research expenses but not normally salaries or overheads. The intent of this support is to help researchers develop external funding for projects, i.e. the expectation is that a pilot study will lead to a grant submission to national or international funding bodies.

Instruct has run several calls for R&D projects since 2013, with funding awarded to more than 50 projects in that time. The seventh call was opened in February 2023 and received 58 applications of which four applications were awarded:

Name and Home Organisation Country

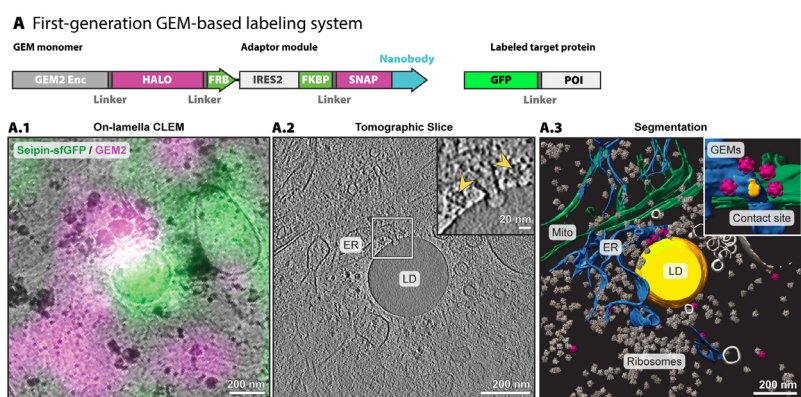
Francesca Paoletti	Italy
Alexandre Ourjountsev	France
Steffen Klein	EMBL
Heikki Saari	Finland

R&D Award Highlights

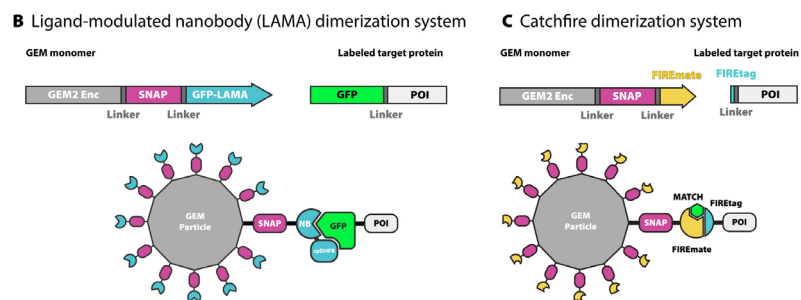
Steffen Klein: R&D Award APPID 2735

Optimising labels for accurately localizing macromolecules in cryo-electron tomography of intact cells

In this project, we develop a correlative method using fluorescent and structurally defined tags that can be directly localized in cryo-ET data to allow identification and pinpointing the location of new targets in human cells for structure determination by subtomogram averaging. Based on our previously developed tags, we aim to optimise the method by generating a simplified one-component labeling system and improving its efficiency. By coupling different inducible dimerisation modules directly to genetically encoded multimeric particles (GEMs), we reduce the complexity and size of the tags while allowing tight temporal control of target labeling. The reduced distance between the GEM tag and the target protein will increase the localisation accuracy of the target position, potentially improving automated particle picking during data analysis, which is essential for structure determination.



Fung et al., Nature Methods, 2023



Alexandre Ourjountsev: R&D Award APPID 2683

New tools and concepts for efficient real-space refinement and validation of macromolecular atomic models versus inhomogeneous cryo electron microscopy or crystallographic maps (Full Map Images - Bottom, overleaf)

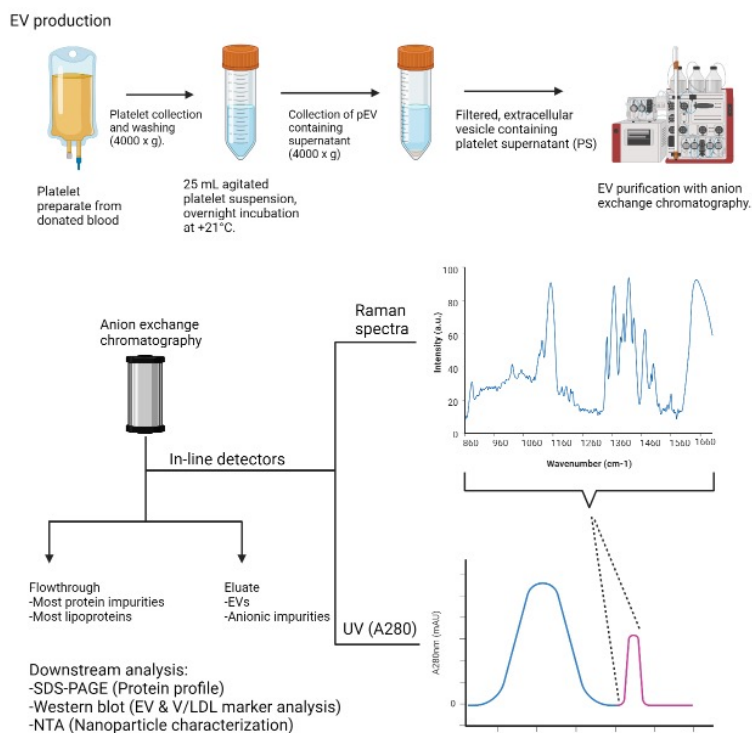
Proposed new type of modelling based on a specially designed function allows a new representation of information about cryo-EM and crystallographic maps and about atomic models refined versus these maps, leading, respectively, to new refinement procedures. To numerically compare model maps with the experimentally obtained ones, the former, mimicking major imperfections of the latter, are calculated as a sum of atomic images expressed by analytic functions of atomic position, values of the displacement parameter (B), occupancy and a local resolution (D). This resolution is associated now with atoms contributing to the given map point. The proposed method requires no Fourier transform and allows the generation of variable-resolution maps in a single run. Inversely, developed analytic expressions for finite-resolution atomic images, together with analytic expressions for the target functions comparing two maps, allow the estimation and simultaneous refinement of the values of all atomic parameters. The algorithms already implemented recover B and D values assuming that atomic positions are known. In particular, several cases of such values, previously incorrectly assigned by conventional software, have been identified and fixed. The values found with the new method made the calculated maps much more similar to the respective experimental ones. Development of full-parameters refinement software is under development.

Heikki Saari: R&D Award APPID 2729

In-line Raman detector for flow analytics of macromolecular biocomplexes

Our Instruct-ERIC R&D pilot project is focused on establishing a novel inline Raman detector to be used for preparative or analytic methods using liquid flow. Usually, Raman spectroscopy is applied for dried samples, as the Raman scattering of photons is rare, and the intensity of an acquired spectra is dependent on sample concentration. A special focus is using it during extracellular vesicle (EV) isolation to monitor the purification process. As Raman spectroscopy is a non-destructive analysis method that provides information regarding chemical functional groups in a given sample, it can be used to identify and assess several types of biomolecules, including proteins and lipids.

For our first sub-project, we have been applying the inline Raman detector in conjunction with an anion exchange chromatography purification scheme for platelet derived EVs. Since anion exchange is simultaneously able to concentrate and purify EVs, we found that the EVs are quite specifically enriched into the eluate and most of the impurities are discarded in the flowthrough. These phases can be identified with the inline Raman detector, and changes such as additional impurities or increased sample load can also be distinguished from a standard sample based on the Raman spectra.



Francesca Paoletti: R&D Award APPID 2784

Illuminating the role of the intrinsically disordered regions of pro-neurotrophins and their interacting cartography with ligands and receptors by integrative structural biology with hybrid methods.

Nerve growth factor (NGF), the prototypical neurotrophin (NT), is involved in the maintenance and growth of neuronal populations, whereas its precursor, proNGF, is involved in neuronal apoptosis. Binding of NGF or proNGF to TrkA, p75NTR, and VP10p receptors triggers complex intracellular signalling pathways that can be modulated by Small Endogenous Ligands (SELs). Due to the wide spectrum of diseases involving NTs (e.g. Alzheimer's Disease, corneal pathologies, chronic pain, etc.), there is a wide pharmacological interest in targeting NTs with SELs. The role of SELs in these processes remains poorly understood because of the lack of architectural details on the pro-NTs pro-peptide, predicted to be intrinsically unstructured.

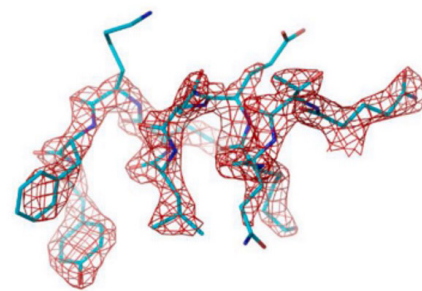
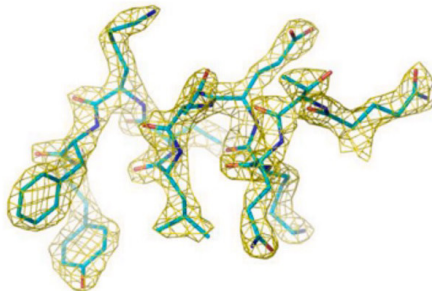
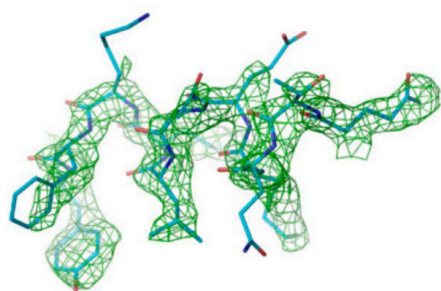
This proposal aims at widening the molecular understanding of proNGF biological responses, through integrative structural biology. The NMR spectral assignment of proNGF represents a fundamental milestone for interaction biophysical studies (HDX-MS, AUC, ITC, GCI...) aimed to unravel the molecular determinants of SELs in the modulation of receptors' binding. The optimisation of a workflow for proNGF would allow to extend it to different SELs, as well as to other pro-NTs. The project foresees to overcome resilience in unravelling how proNTs structure affect their function and to foster advances in their diagnostic and pharmacological applications.



cryoEM map

maps calculated: with the deposited parameters

using the new model



Alexandre Ourjountsev: R&D Award APPID 2683



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.

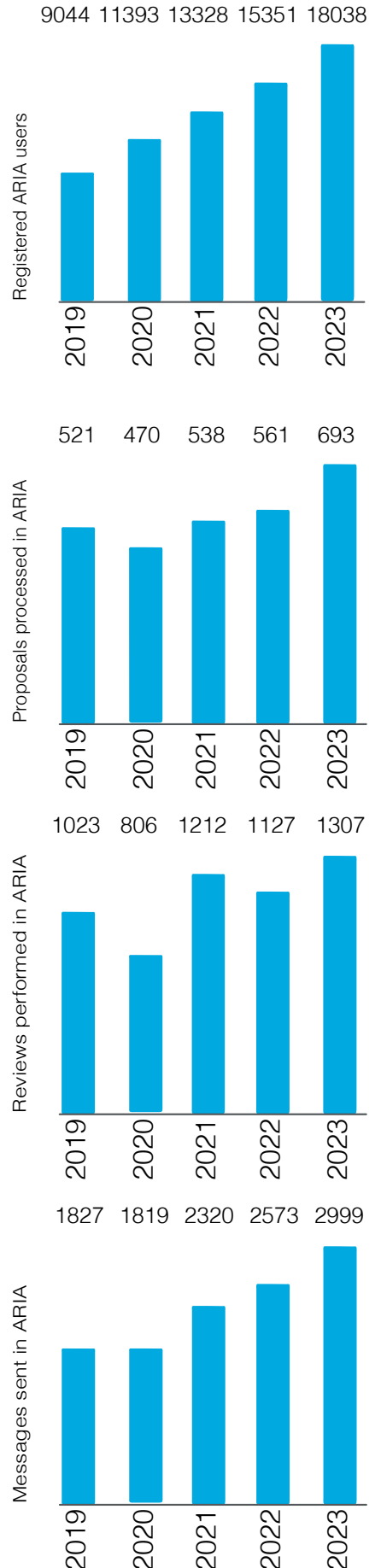
2023 saw the introduction of some powerful new functionality, further expanding the capability of the ARIA platform.

ARIA in numbers

Overall, ARIA welcomed 2687 new users in 2023, bringing the total number of registered users to 18308. 693 proposals were processed in ARIA in 2023, with more than 1300 reviews conducted throughout the year. Additionally, the access management was supported by the ARIA messaging system that processed 2999 messages in 2023 connecting the users, access managers, reviews and facility teams.

ARIA: New Updates

Access on such a large scale requires intensive process support, enabled by a dedicated team in the Instruct-ERIC Hub and our pioneering access management software ARIA. ARIA is constantly evolving to encompass new features for access management, reporting and application handling. In 2023 developments included the enhanced compatibility with external systems (crucial for integration with projects such as ISIDORe and canSERV), enhanced control of visits and reporting, and increasing useful notifications and communication to users. User experience improvements to the interface of ARIA both in the back-end dashboard and for front-end navigation were also made, plus an update to the Instruct-ERIC homepage in terms of design.



COLLABORATIVE WORK



EUROPEAN PROJECTS



Fragment-Screen: Fragment-based drug discovery through structural biology, medicinal chemistry, and AI
February 2023 to February 2026



canSERV

canSERV: Providing cutting edge cancer research services across Europe
September 2022 to August 2025



EOSC4Cancer: A European-wide foundation to accelerate Data-driven Cancer Research
September 2022 to February 2025



EU-LAC ResInfra: Towards a new EU-LAC partnership in Research Infrastructures
December 2019 to February 2023



TRANSVAC-DS: Towards a sustainable European vaccine infrastructure
May 2017 to April 2023



AI4Life: Artificial Intelligence for Image Data Analysis in the Life Sciences
September 2022 to August 2025



EOSC-Future: Advancing European research through Open Science
April 2021 to September 2023



eRImote: Pathway to Improved Resilience and Digital and Remote Access
June 2022 to November 2024



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



TRANSVAC2: European vaccine research and development infrastructure
May 2017 to April 2023



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



EOSC-Life: Providing an open collaborative space for digital biology in Europe
March 2019 to August 2023



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



ISIDORe: Integrated Services for Infectious Disease Outbreak Research
February 2022 to January 2025



IMAGINE: Next generation imaging for biology across scales
May 2023 to April 2028

EUROPEAN PROJECTS

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 persisted in 2023, as impactful projects continued to provide new technologies and software for structural biologists to use for their research.

Fragment-Screen (began February 2023)

The Fragment-Screen project is coordinated by Instruct-ERIC. It commenced with a Kick-Off Meeting held in Frankfurt, a two-day gathering of scientific talks and project discussions bringing together participants from across the consortium, both in person and remotely.

The Fragment-Screen project aims to develop innovative instrumentation, workflows and experimental and computational methodologies for fragment-based drug discovery (FBDD) enabling access to early phase structure-based drug discovery for all biological targets and for scientists both in industry and academia. The established workflows will use structural biology insights and associated data to feed artificial intelligence (AI) methodology to guide medicinal chemistry in drug development. Fragment-Screen brings together scientists from four ESFRI Landmark research infrastructures (RIs): ESRF (the European synchrotron) and the distributed RIs EU-OPENSCREEN ERIC (medicinal chemistry), ELIXIR (data resources for life science) under the coordination of Instruct-ERIC and seven industry partners in scientific instrumentation and computational and AI sectors including SMEs to remove crucial bottlenecks in early phase drug discovery.

Fragment Screen



FIG 1. Full Fragment-Screen consortium during the Kick-Off Meeting in March 2023, held in Frankfurt, Germany.

EOSC-Life (ended August 2023)

The EOSC-Life project brought together 13 Life Science RIs to create an open, digital and collaborative space for data resources and data processing workflows in the European Open Science Cloud (EOSC).

In EOSC-Life, a series of training workshops and open calls were organised to select and support pilot projects that would develop solutions for the FAIR handling of data resources in the life sciences. Projects involving 7 Instruct Centres were selected and benefited from EOSC-life financial and technical support:

- Development of the Fragalysis platform for fragment-based drug discovery – Diamond Light Source
- Increasing the FAIRness of data and image processing workflows in Cryo-EM (2 projects) – CNB-CSIC, CEITEC
- Development of ICEBEAR: Macromolecular crystallography data management in the cloud – University of Oulu, Weizmann Institute of Science, Diamond Light Source
- Development and refinement of PDB-REDO Cloud for FAIR protein structures (2 projects) – NKI
- Towards FAIR data for X ray-based structure-guided drug design – EMBL Grenoble

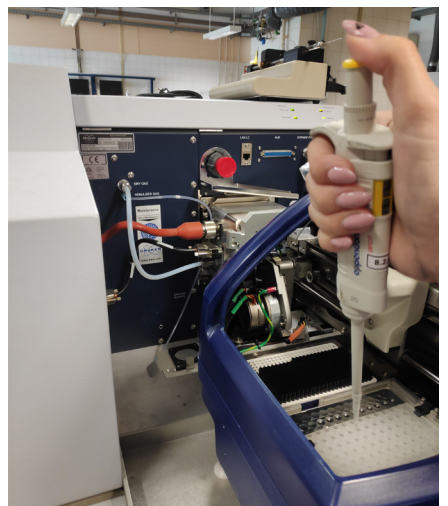
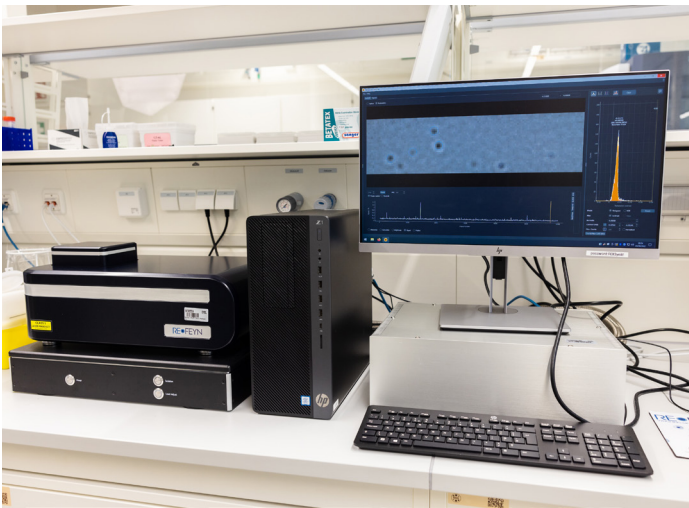
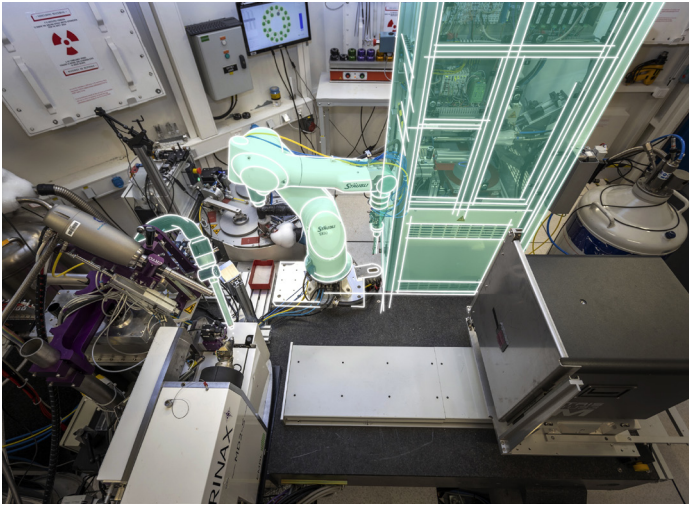
Instruct partners delivered training programs focusing on: 1) data validation and fairness in cryo-EM delivered by CNB-CSIC in Instruct-ES; 2) remote access and remote training organised by Instruct and Euro-Biolmaging with the participation of several Instruct Centres. Instruct-IT was involved in the development of solutions for the handling of tools and workflows such as the WorkflowHub, a powerful registry for sharing scientific workflows. Cloud deployment and further development of key software such as ARIA in the Instruct Hub with the integration of the LS Login system in ARIA and Proteopedia in Instruct-IL were also supported by EOSC-life.



EOSC-Life



FIG 2. EOSC-Life consortium at the Final Annual General Meeting, which took place in June 2023, in Brussels, Belgium.



SUPPORTING ACTIVITIES AND OUTPUTS





Newsletter

The Instruct-ERIC Newsletter continued its distribution in 2023, to almost 4,000 accounts in the ARIA network. The themes for the Summer (New Members) and Winter (Access Demand) were apt, as the major stories concerning Instruct throughout the year. In addition, the newsletters kept readers informed of project information, science highlights and testimonials, as well as new technologies and equipment available at Instruct centres..



Social media

Instruct-ERIC social media presence continued to develop further in 2023, reaching more than 5,600 followers on X/ Twitter, and more than 700 on LinkedIn. Social media is a powerful tool for engagement and promotion, as well as a mechanism to reach new users to further develop structural biology on a global scale. The use of X/Twitter has been impacted by new developments, such as paid-only access to scheduling and analytical services.



Scientific Highlights

Instruct-ERIC published twelve science highlights in 2023, covering a wide variety of techniques available in the Instruct catalogue: NMR, cryo-EM, X-Ray studies, and mass spectroscopy. In addition, burgeoning studies involving AI, and machine learning, started to be developed acknowledging Instruct. Instruct's role in facilitating such research, through partner projects like Fragment-Screen, opened new avenues for publications.



Webinars

The "Structure Meets Function" webinar series continued to provide information and background to Instruct services and centres. This year, the focus shifted towards novel approaches in Instruct: new technologies added to the catalogue, publications and science borne out of Instruct partner projects such as ISIDORe, as well as continued celebration of Instruct centres and facilities.



ARIA Communication

In addition to core Instruct-ERIC communication, great attention was paid towards disseminating the power and importance of ARIA to the Instruct and research infrastructure community. All ARIA releases are communicated to the community, outlining the latest features available through the system, as well as updates and any optimisations to enhance the user experience - crucial to maximise its use and effectiveness for structural biology researchers, and boost its use in partner projects such as canSERV.



23-24 May, 2024

Join us in Cascais, Portugal for [#IBSBC2024](#) - the leading integrated structural biology conference, with more than 20 expert speakers, abstract talks, poster sessions and the announcement of the Bertini Award Winner!

instruct-eric.org/ibsbc2024



Access the full structural biology workflow through Instruct-ERIC. From sample prep to CryoEM, from protein production to NMR. Structural biology services are available here - instruct-eric.org/submit-proposals



It was fantastic to be part of the Kick-Off Meeting for the new IMAGINE project, which focuses on boosting imaging technology in the life sciences and beyond, featuring partners from Instruct facilities including [@embl](#) and [@NeCEN_2p0](#)!

instruct-eric.org/news/ imagine-p...



EMBL Heidelberg and 2 others

INSTRUCT-ERIC HUB

In 2023 the Instruct Hub team saw more comings and goings of staff members. We welcomed Project Manager Eirini Xemantilotou to the team who will be overseeing the progression of our ground-breaking new project Fragment-Screen as lead project manager for the coordinator. Eirini brings both academic and industrial experience to the role from previous positions. Eirini is joined by Yvonne de Jong-Leung and Lucien Holliday in the ARIA team who will be working on implementation of Instruct's ambitious data management strategy – enabling automatic facility-led collection, deposition and preservation of experimental data.

On the administrative side, Instruct welcomed Sarah King as new Senior Finance Officer who has previous experience working in both university and SME settings. Sarah will be taking over leadership of the finance function within Instruct, supported by Lorraine Donaldson who has been Finance Manager throughout the setup of Instruct and continues to work with us part-time.

Sadly, we said goodbye to Joshua Ruff from the ARIA team at the start of the year. Marcus Lowndes progressed to developer in recognition of their growth since taking on the role of junior developer in 2020 and took on additional responsibilities within the team.

Following the success of the first hub team retreat in 2022, in 2023 we descended upon Basingstoke for two days of team building and planning, supported by Helen Duyvesteyn from Instruct Centre UK who performed the role of moderator during discussions.

SPOTLIGHT ON STAFF - FINANCE

Instruct expanded the Finance department in 2023, aiming to enhance the experience level in the team, as well as reorganise workload among the team. With many new members and Horizon Europe projects, the need to increase personnel within the team was heightened.



Lorraine Donaldson
Finance Officer

Lorraine Donaldson has been Financial Manager at Instruct-ERIC since its inception, covering all financial aspects of the research infrastructure. Lorraine is based at Instruct one day per week.

Sarah King is the Senior Finance Officer at Instruct-ERIC. They spent ten years in various finance roles at the University of Oxford, including five years as Finance Manager at the Department of Pharmacology, where their responsibilities included post-award grant management, as well as the day-to-day management of the finance function.

Sarah completed their ACCA studies in December 2022, becoming a fully qualified member in January 2023. They joined Instruct-ERIC in November 2023. Sarah's responsibilities include:

- Day to day management of financial matters
- Line management of Finance Assistant
- Bank reconciliations
- Preparation of monthly Working Budget report (Actuals v Budget) and budget forecasts to year end
- Oversee EU project overhead allocation to Instruct
- Oversee staff allocation to EU projects
- Liaise with external auditors
- Assist with Audit and year-end tasks
- Process purchase invoices



Sarah King
Senior Finance Officer

Francisco Guimaraes has been at Instruct-ERIC since June 2020 operating as the Finance Officer. Francisco is a full member of AAT: Association of Accounting Technicians. Until 2023, Francisco was the only full-time member of the finance team, hence the need for expansion. Francisco fulfils many roles within the finance department, covering both internal and external expenses and income. A full summary of their role includes:

- Raising invoices for Membership, ARIA Support, Biennial Structural Biology Conference, and other core activities
- Processing external payments
- Allocation of costs to projects
- Expenses
- Timesheets
- Contact with facilities and users to chase claims



Francisco Guimaraes
Finance and Admin Officer

HUB TEAM MEMBERS



Harald Schwalbe
Director



Claudia Alén Amaro
Head of Operations



Natalie Haley
Head of Strategy



Pauline Audergon
Project Manager



Regina Guenster
Project Manager



Corinna Brockhaus
Trainee Project
Manager



Eirini Xemantilotou
Project Manager



Madalena Gallagher
Administrative Officer



Carla Marques-Wood
Administrative
Support



Lorraine Donaldson
Financial Manager



Sarah King
Senior Finance
Officer



Francisco Guimaraes
Finance Officer



John Dolan
Communications
Officer



Marcus Povey
Senior Software
Developer



Marcus Lowndes
Software Developer



Joshua Ruff
Software Developer



Omran Alhaddad
IT Developer



Alec Matthews
IT Developer



Yvonne de Jong-
Leung
IT Developer



Lui Holliday
Software Developer

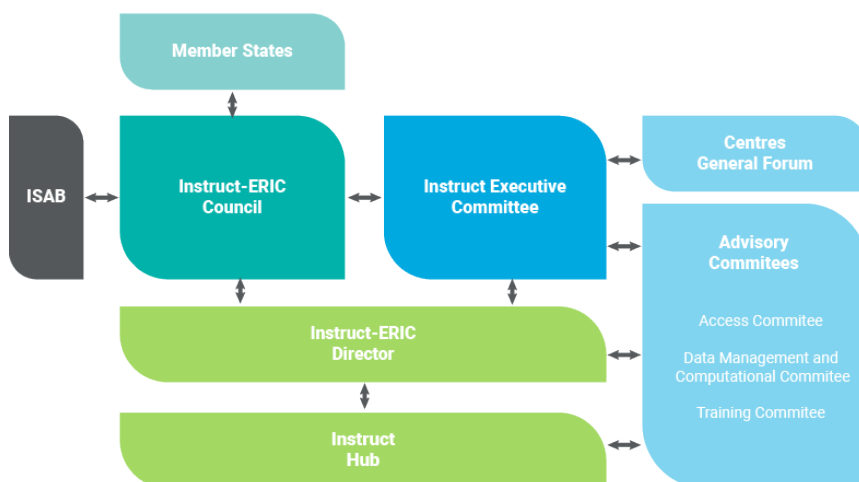


FIG 1. Instruct Hub members at the summer picnic, retreat and christmas party (left to right).

GOVERNANCE

The Instruct-ERIC Council continued to be chaired by Eric Guittet (FR) and Sarah Butcher (FI) 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 decision-making body responsible for the overall direction and supervision of the ERIC. It consists of representatives from each Instruct Member. In 2023 Instruct welcomed Prof Sarah Butcher (FI) and Prof Jose-Maria Carazo (ES) as the new Chair and Vice-Chair of Council respectively. Council approved the membership applications of Greece and Slovenia in May 2023, welcoming them as new Members 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 launched in September 2023 and expected to be 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 an important document for Instruct it is also of high-importance and relevance to the structural biology community as a whole and was developed into a review document with the aim of publishing it as a position paper.

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 2023 the Executive Committee supervised the changes to the access process recommended by the Access Committee. 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 (see p22 for more details). 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. The Executive Committee also oversaw the organising committee of the Instruct Biennial Structural Biology Conference 2024 for which the scientific programme was completed and registrations opened in 2023. During 2023 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. In 2023, Rommie Amaro was added to the existing members of the ISAB, bringing expertise on state-of-the-art computational methods in drug discovery and molecular-level biophysics.

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

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: Eric Guittet, FR (Q1/Q2) & Sarah Butcher, FI (Q3/4)

Vice-Chair: Sarah Butcher, FI (Q1/2) & Jose Maria Carazo, ES (Q3/4)

Country	Delegates
Belgium	Michele Oleo & Virginie Storms
Czech Republic	Vladimir Sklenar/ Pavel Plevka & Jan Burianek
EMBL	Christoph Mueller & Plamena Markova
Finland	Sarah Butcher & Anni Kleino
France	Winfried Weissenhorn & Eric Guittet/ Catherine Le Chalony
Greece	Evangelia Chrysina & Denis Sarigiannis
Israel	Joel Sussman & Iris Eisenberg
Italy	Lucia Banci & Grazia Pavoncello/ Fabio Mazzolini
Latvia	Kaspars Tars & Uldis Berkis
Lithuania	Giedrius Sasnauskas & Gintaras Valincius
Netherlands	Reinout Raijmakers & Nienke Klomp/ Naomi Chrispijn-Steenbeek
Portugal	Maria Armenia Carrondo & Marta Abrantes
Spain	Jose Maria Carazo & Ignacio Baanante Balastegui
Slovakia	Milos Hricovini & Barbora Liptakova/ Simona Tanhäuserová
Slovenia	Marjetak Podobnik & Albin Kralj
United Kingdom	Robert Deller & Megan Dowie/ 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 the project 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	Vladimir Sklenar/ Pavel Plevka	Ondrej Hradil
Instruct EMBL	Stephen Cusack/ Kristina Djinovic Carugo	Matthias Willmans
Instruct ES	Jose Maria Carazo	Carlos Oscar Sanchez Sorzano
Instruct FI	Sarah Butcher	Markku Varjosalo
Instruct FR1	Patrick Schultz	JeanCavarelli/Arnaud Poterszmann
Instruct FR2	Darren Hart	Martin Blackledge
Instruct IL	Shira Albeck	Joel Sussman
Instruct IT	Lucia Banci	Roberta Pierattelli
Instruct NL	Ariane Briegel	Rolf Boelens
Instruct UK	David Stuart	Andrew Quigley



FINANCIAL DATA

8CDP



FINANCIAL DATA

This report presents the financial statements for the period 1 January 2023 to 31 December 2023.

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 resilience;
- 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 2023 – 31 December 2023.

BALANCE SHEET FOR INSTRUCT-ERIC

As at 31 December 2023

Assets	GBP	EUR	Notes
Euro bank	1,843,386	2,126,657	
Sterling bank	117,671	135,753	
Total Bank	1,961,057	2,262,410	
Current Assets			
Accounts Receivable	2,635	3,040	1
Prepayments	13,488	15,561	
Accrued income	313,695	361,902	2
Rental deposits	3,890	4,488	
Total Current Assets	333,708	384,991	
Fixed Assets			
Computer Equipment	16,747	19,321	
Depreciation on Computer Equipment	(13,996)	(16,147)	
Office Equipment	1,802	2,079	
Depreciation on Office Equipment	(1,466)	(1,691)	
Total Fixed Assets	3,087	3,562	
Total Assets	2,297,852	2,650,963	
Liabilities			
Current Liabilities			
Accruals	13,776	15,893	
Amounts to be paid and Unclaimed Access Awards	1,006,044	1,160,641	3
Income in Advance - Other inc deferred grants	968,707	1,117,567	4
Income in Advance - ARIA Support	12,650	14,594	
Other creditors	4,939	5,698	
Payroll taxes due	16,519	19,057	
Pensions due	10,861	12,530	
Total Current Liabilities	2,033,496	2,345,980	
Total Liabilities	2,033,496	2,345,980	
Net Assets			
Surplus Brought Forward	111,897	126,411	
Exchange rate movement - revalue opening reserves	(2,329)	-	5
Surplus for the Year	154,788	178,572	
Surplus Carried Forward	264,356	304,983	

Exchange rate for reporting period: 0.86680 (2022: 0.88519)

1. ARIA support income receivable

2. Grant income recoverable at report period end

3. Access and other service accruals

4. Deferred project income

5. Revalue opening reserves from prior year exchange rate to the exchange rate used for current reporting period.

PROFIT AND LOSS FOR INSTRUCT-ERIC

For Year Ended 31 December 2023

Income	GBP	EUR	Notes
External grant income	1,104,540	1,274,271	7
External grant overhead contribution income	134,910	155,642	
Member state contributions	1,024,545	1,181,986	8
Other miscellaneous income	11,301	13,038	9
Total Income	2,275,296	2,624,937	
Less Cost of Service Provision			
Instruct core staff salaries	210,262	242,573	
R&D Pilot awards	52,008	60,000	
Training Courses	27,494	31,719	
Internships	21,669	24,999	
External grant TNA costs	562,131	648,513	10
Access Cost	498,667	575,297	
Meetings	22,109	25,507	
Project activities	550,663	635,283	11
Total Cost of Service Provision	1,945,003	2,243,891	
Gross Surplus	330,293	381,046	
Less Operating Expenses			
Commissioned services (Insurance, financial, HR, legal)	36,683	42,320	
Conference costs	-	-	
Consultants	13,840	15,967	12
Depreciation charge	4,848	5,593	
Foreign Currency (Gains)/Losses	6,965	8,035	
General admin (postage, copying, bank charges)	1,974	2,277	
Licenses & software	16,093	18,566	
Miscellaneous	634	731	
Premises and support	59,958	69,172	
Project overhead expenses	35,875	41,388	
Publicity	406	468	
Telephone	1,271	1,466	
Total Operating Expenses	178,547	205,983	
Other Operating Gains/(Losses)			
Profit on disposal of fixed assets	3,042	3,509	
Total Other Operating Gains/(Losses)	3,042	3,509	
Net Surplus	154,788	178,572	

7. Project income excluding 25% contribution to Instruct-ERIC overheads, against expenditure
 8. Membership income receivable
 9. ARIA support and conference sponsorship income

10. TNA access awards relating to an externally funded project, ISIDORe

11. WIP on research grants. Project activities delivered.

12. Staff costs recharged from the University of Oxford and external consultants

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

Going concern

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

1. the amounts derived from membership subscriptions. This income is recognised evenly over the subscription period.
2. 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 call 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 01/01/23 - 31/12/23
UK	121,232
FR	121,232
ES	90,922
IT	90,922
BE	90,922
NL	90,922
IL	90,922
CZ	60,614
PT	60,614
SK	60,614
LV	60,614
EMBL	60,614
FI	60,614
LT	60,614
SI	30,307
EL	30,307
Total	1,181,986

Grant Receipts (EUR)

EU Grants	Staff and other direct cost income	TNA cost income	Overhead income
AI4Life	8,032		2,008
BY-COVID	10,800		2,700
canSERV	207,851		51,963
EOSC Future	67,926		16,982
EOSC-Life	32,957		8,239
EOSC4Cancer	9,053		2,263
ERIC Forum	-2,732		0
ERIC Forum 2	5,498		1,374
eRImote	80,419		20,105
EU-LAC ResInfra	10,712		1,918
Fragment-Screen	113,500		28,375
iNEXT-Discovery	17,746		4,437
IMAGINE	4,692		1,173
ISIDORe	53,227	648,513	13,307
TRANSVAC-DS	67		23
TRANSVAC2	6,011		776
Total	625,759	648,513	155,643

Overhead contribution recognised: 25%

C. Deficit/surplus on activities: 178,572

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 2023 invoices): €0

Other accrued income: €15,561

Grant accrued income: €151,906

F. Creditors

Accruals for services and awards (Access, Internships, R&D, Training, unclaimed access) €1,169,258

Advances on Research Grants: €600,376

Other creditors: €15,893

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.

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:

AI4Life €34,500

BY-COVID €166,316

canSERV €1,376,753* **

EOSC Future €126,421

EOSC-Life €978,986

EOSC4Cancer €82,500

ERIC Forum 2 €114,126

eRImote €272,375

EU-LAC ResInfra €138,153

Fragment-Screen €1,647,815*

iNEXT-Discovery €147,500

IMAGINE €1,012,895

ISIDORe €736,245 * **

TRANSVAC-DS €5,193

TRANSVAC2 €27,886

* 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.
AI	Artificial intelligence
AI4Life	AI4Life 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 Management and 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

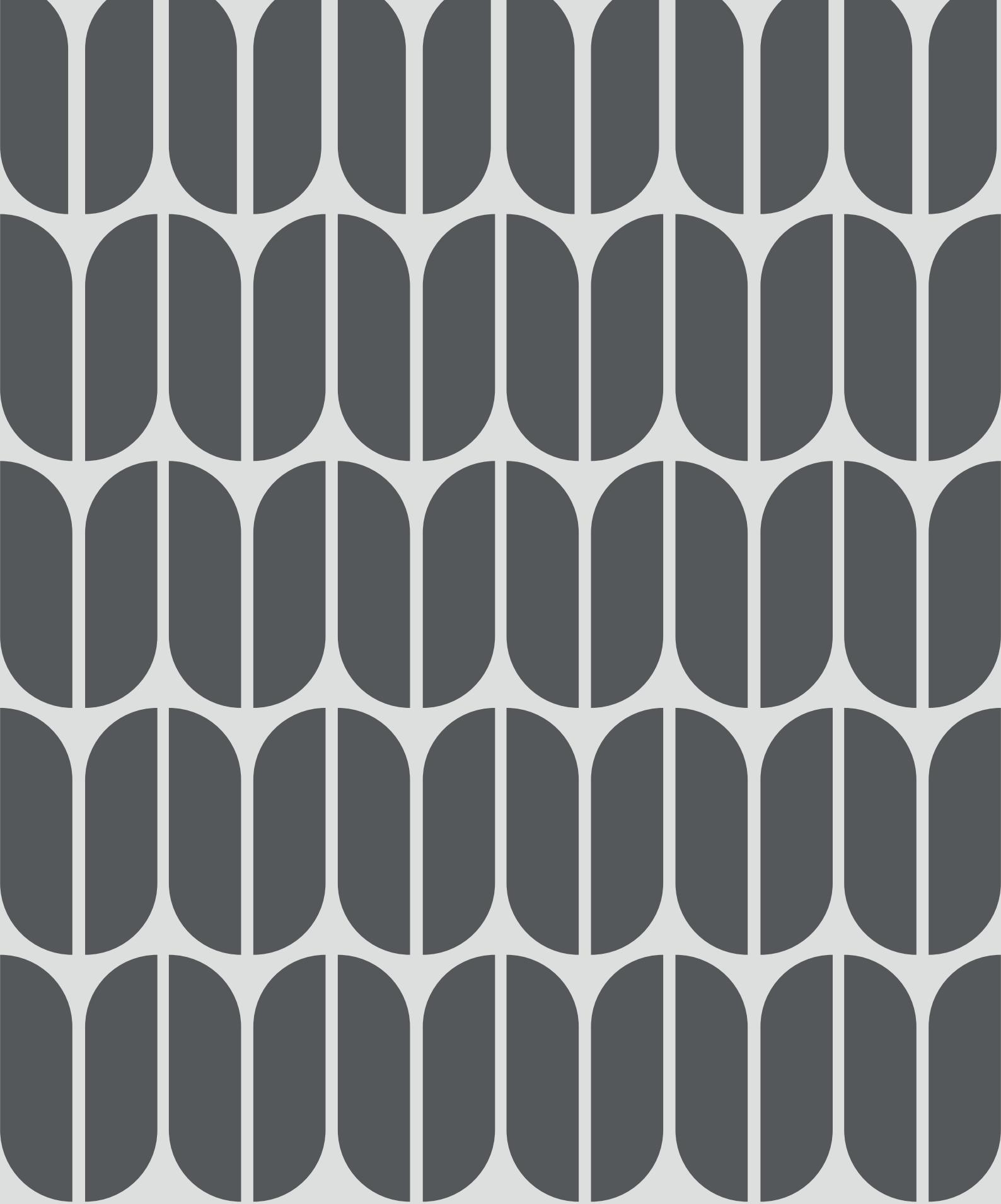
Term	Definition
ERIC Forum	A Horizon 2020 project bringing together European Research Infrastructure Consortia to strengthen their coordination and enhance their collaborations.
eRImote	eRImote finds solutions for digital and remote service provision across RI domains.
ESFRI	European Strategy Forum on Research Infrastructures: an organisation with members nominated by European member states ministries to support a coherent and strategy-led 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-Biolmaging	A European Research Infrastructure providing open access to a broad range of technologies in biological and biomedical imaging for life scientists.
EU-OPENSREEN	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 Site	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 Chromatography - 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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