EMBL

The EMBL Programme 2022–2026

Molecules to Ecosystems

Overview

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Executive Summary

EMBL – a unique track record of scientific excellence

Since its founding in 1974, the European Molecular Biology Laboratory (EMBL) has sought to serve its member states through fundamental discoveries in molecular biology that fuel a rich economy of knowledge, serving new technologies that meet societal needs in the areas of medicine, agriculture, and ecology.

EMBL is Europe's only intergovernmental laboratory for life science research. Established to advance the study and understanding of molecular biology across Europe, to nurture young talent, new ideas, and technologies, the Laboratory is constantly evolving and innovating. EMBL undertakes pioneering research and provides cutting-edge biological services and infrastructures. This foundational research has, during the past four decades, enabled a better understanding of the molecular basis of life. Since its creation during the era of classic molecular biology, EMBL has continued to play a leading role in the rapid evolution of modern biology, participating in major breakthroughs in the realms of cellular and developmental biology, the birth of genomics and molecular genetics, and, more recently, integrative approaches and systems biology. EMBL scientists have discovered many of the basic principles of how organisms are built – how these building blocks are generated, modified, and brought together over time and space.

EMBL occupies a unique position in European science, possessing incredibly strong foundations across all areas of molecular biology. It attracts talented individuals from many disciplines and trains the next generation of brilliant young scientists who then move on to become global leaders in Europe around the world. EMBL has played a major role in laying the ground of the current scientific revolution and spurred the development of many of the tools that scientists use today, including cryo-EM, genomics, and advanced imaging. The vital nature of these technologies is aptly illustrated by their global deployment in the current fight against COVID-19 and other diseases.

EMBL's vision is to advance our understanding of ecosystems at the molecular level, applying expertise in molecular biology to study life in its natural context. In so doing, EMBL aims to use fundamental science to tackle societal challenges.

Introducing Molecules to Ecosystems, the new EMBL Programme 2022–2026

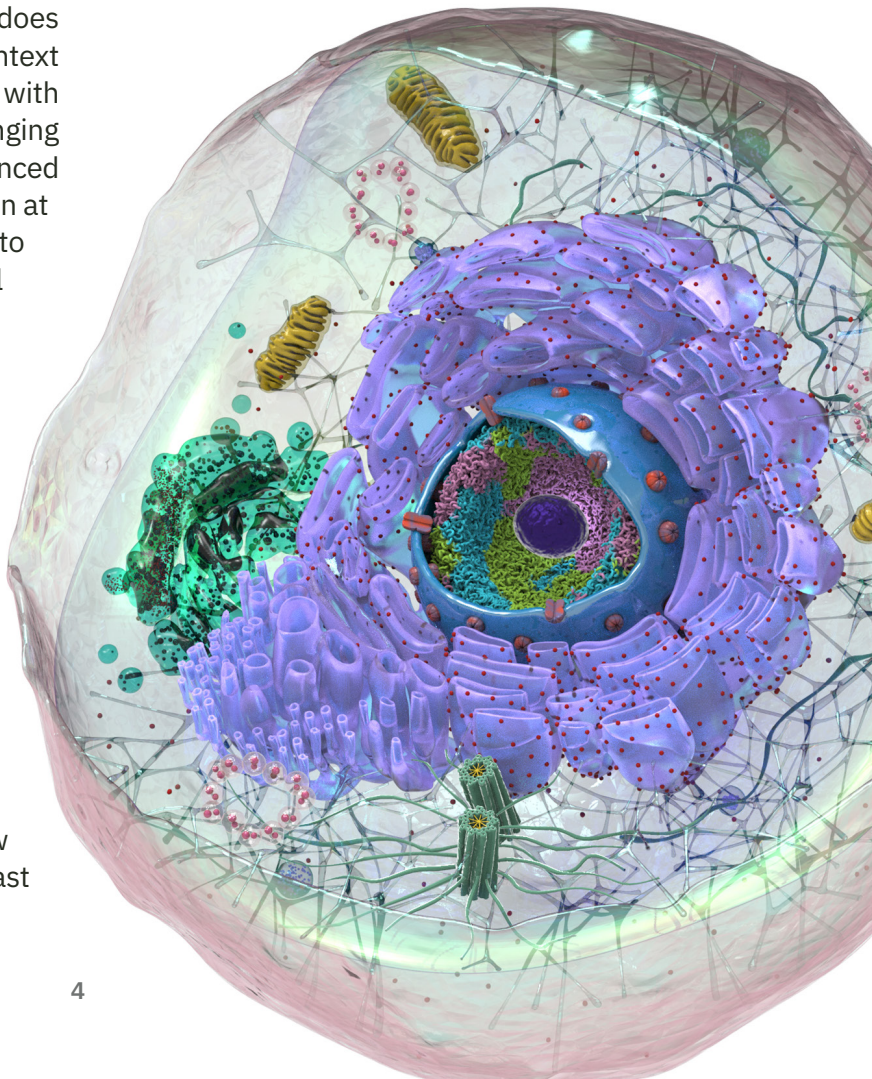
EMBL strives to be at the forefront of modern biology and to build the foundations of future successes. The curiosity-driven scientific discoveries by EMBL serve as the basis of the next generation of applications and discoveries.

Through its next five-year scientific Programme, EMBL intends to propel Europe into a new era of biological understanding, from the molecular building blocks of life through to the complexity of ecosystems - the very context within which all life forms exist. EMBL's ambition in the new Programme, titled Molecules to Ecosystems, is to establish the molecular basis of 'life in context', to gain new knowledge that is relevant to understanding life on earth, and to provide translational potential to support advances in both human and planetary health.

Most molecular research has entailed the study of organisms in the laboratory, performed under strictly controlled conditions. However, life does not happen in isolation, it occurs in the context of populations, where organisms interact with each other and respond to constantly changing physio-chemical parameters. Today's advanced technologies, which allow for data generation at multiple scales, coupled with the capacity to follow the dynamics of living matter in real time, mean that molecular biology can lead to a true understanding of the basis of life. Gaining new insight into how organisms coexist within changing environments will be of fundamental importance to understanding life – not just on a human scale but on a planetary scale.

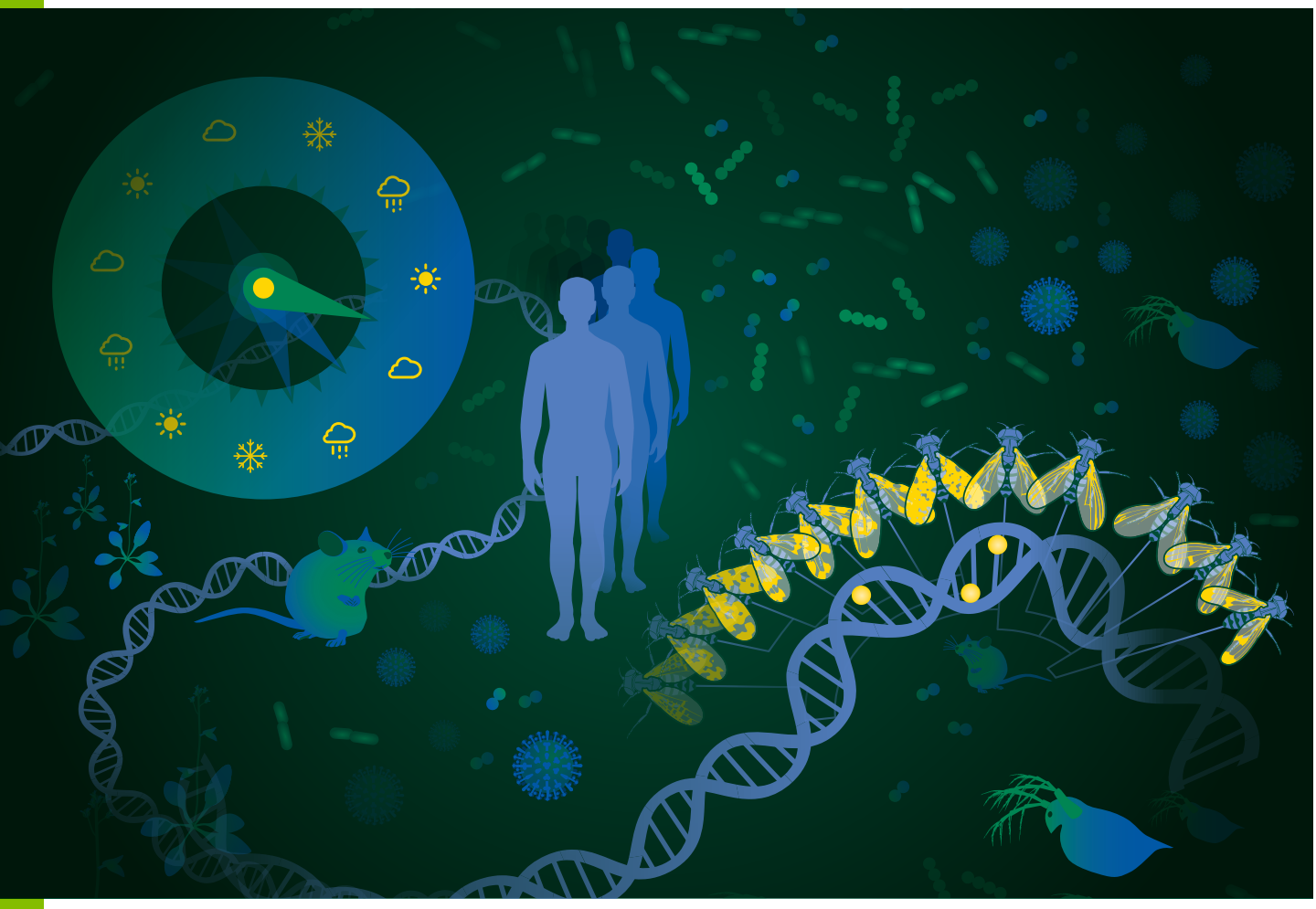
The challenges facing life on Earth today are huge, whether it be the spread of infectious diseases, the loss of biodiversity, environmental degradation, or climate change. As Tanya Steele, CEO at World Wide Fund for Nature (WWF) notes "We are the first generation to know we are destroying our planet and the last that can do anything about it". To take on these challenges, drastic improvements are needed in understanding the processes of life in natural environments. A better understanding of life means it can be better preserved.

Through the new Programme, EMBL will seek to build on its existing and globally recognised expertise in molecular biology to expand into new research areas including planetary biology, microbial ecosystems, human ecosystems, and infection biology. To understand the complexity of life in these different areas, central to the research strategy, will be the development of advanced data sciences and theoretical approaches. Through close collaborations with scientists from different domains, this Programme will reside at the intersection between biology, ecology, and epidemiology. EMBL will build new bridges between these disciplines, while keeping its firm foundations in molecular biology. Within this Programme EMBL will also look to train a new generation of interdisciplinary scientists who will address real-life scientific questions and prepare for future challenges.



EMBL seeks to seize this unique opportunity at a critical point in time for society, to undertake bold and potentially transformative discovery science that will also be a force for good for humankind and the planet. EMBL is well placed to fulfil its bold ambition to gain a molecular understanding of life in context and in doing so, will continue to uphold its special responsibility to lead, collaborate, and coordinate European life sciences in its role as Europe's flagship life sciences research organisation. The strong and dynamic collaborations and the networks of partnerships that EMBL has built over many years will be harnessed to bring its plans to fruition.

EMBL is an international organisation, made stronger by the breadth of its member states and by its physical presence at six sites across five host countries. EMBL's success is due to its dynamic turnover, interdisciplinarity, and a distinctive scientific culture that blends ambition, excellence, cooperation, and openness across borders and societies. EMBL's Programme sets out plans to enhance research coordination, to promote joint standards and open science, and to inform and impact international research and policymaking. The knowledge and technological advances unlocked as a result of this new Programme will directly assist EMBL's member states to better understand and address the planetary challenges of climate change, pollution, food security, and emerging pathogens.



Introduction to EMBL

EMBL is positioned at the heart of the current revolution in the life sciences. With its dynamic turnover model and its vibrant community of young scientists, EMBL is Europe's flagship laboratory for fundamental research in molecular biology. EMBL enables its 27 member states and two associate member states to be at the forefront of life sciences on the global stage. Professor Edith Heard was appointed as Director General of EMBL in 2019 by the governing body, the EMBL Council, composed of representatives of all member and associate member states. Her appointment corresponded to a wish by Council to usher in a new era at EMBL.

EMBL is the only intergovernmental organisation for life science research in Europe. Since its creation in 1974, EMBL's goal has always been to foster the development of excellent scientists and enable discoveries in molecular biology that fuel a rich economy in knowledge and technologies that meet societal needs in the areas of medicine, agriculture, and ecology. Today, almost 1800 personnel from 80 countries advance EMBL's activities across its six sites, each of which offers a unique and highly complementary mix of research and services.

The principle of regular staff turnover (nine-year rule) and the five-year programmatic funding, enable EMBL to be agile and to evolve rapidly through the recruitment of new scientific talent with exciting questions in biology and cutting-edge approaches. The regular turnover at EMBL also provides Europe with a regular supply of highly trained scientific personnel. EMBL's operational model has been employed across Europe and has served as a framework for many national centres of excellence.

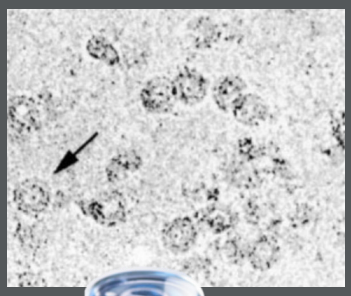
EMBL's Missions

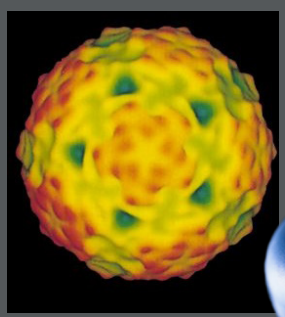
Mission 1: To perform excellent fundamental research in molecular biology

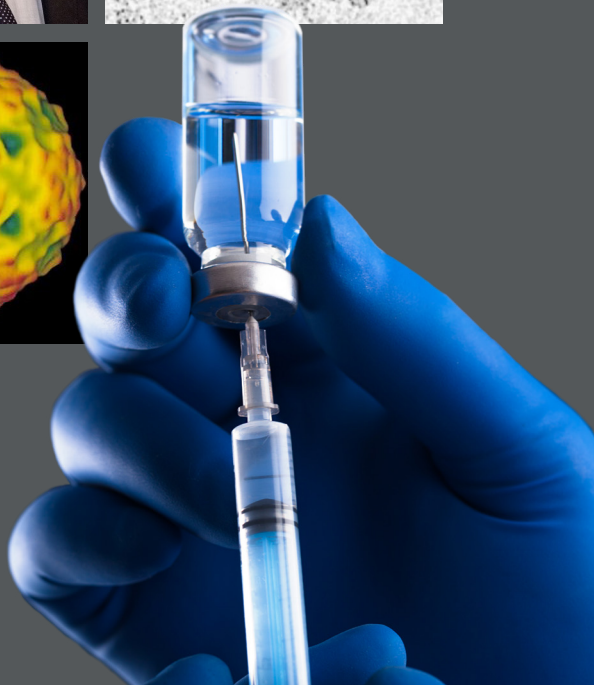
Research at EMBL emphasises experimental and computational analyses of biological organisation, from the molecule to the organism. Research areas cover a wide spectrum of biology, including structural biology, genome biology, cell biology, developmental biology, tissue and organ biology, neurobiology, microbiology, bioinformatics and computational biology, and molecular medicine. EMBL prides itself on the collaborative and interdisciplinary nature of its work, reflected in the percentage of papers published (~80% of papers written are published in high profile journals) and grants secured (a 65% success rate in grant applications in 2019) in collaboration with academic and industry research groups worldwide in 2019. Between 2014 and 2019, ~45% of research papers by EMBL scientists were published in the top 5% of journals.

EMBL has a long and distinguished history of ground-breaking scientific achievements; among the most notable contributions is the unravelling of genetic and molecular mechanisms by which multicellular organisms develop by Nobel laureates Christiane Nüsslein-Volhard and Eric Wieschaus. Such research has contributed to the subsequent understanding of the molecular pathways that are disrupted in the steps leading to cancer. EMBL has also made significant contributions to the study of the basic units of life, such as the cell and its molecular components. For example, EMBL research led to the characterisation of the cellular transport machinery, analysis of cytoskeleton organisation, and an understanding of the function and regulation of RNA metabolism.

In parallel, ground-breaking technologies are also developed at EMBL, driven by fundamental biological questions. For example, cryo-electron microscopy (cryo-EM) was developed by Nobel laureate Jacques Dubochet (pictured) during a quest to decipher protein structures. The further development of cryo-EM technology at EMBL has enabled scientists to study biological structures *in situ*, leading to new medicines and vaccines. Other notable inventions include the first functional light-sheet microscope by Ernst Stelzer used to track live cell movements in embryos, and mass spectrometry-based protein analyses by Matthias Mann. All of these technologies are widely used today in academia and industry.







Mission 2: To offer vital services to scientists in the member states and the world

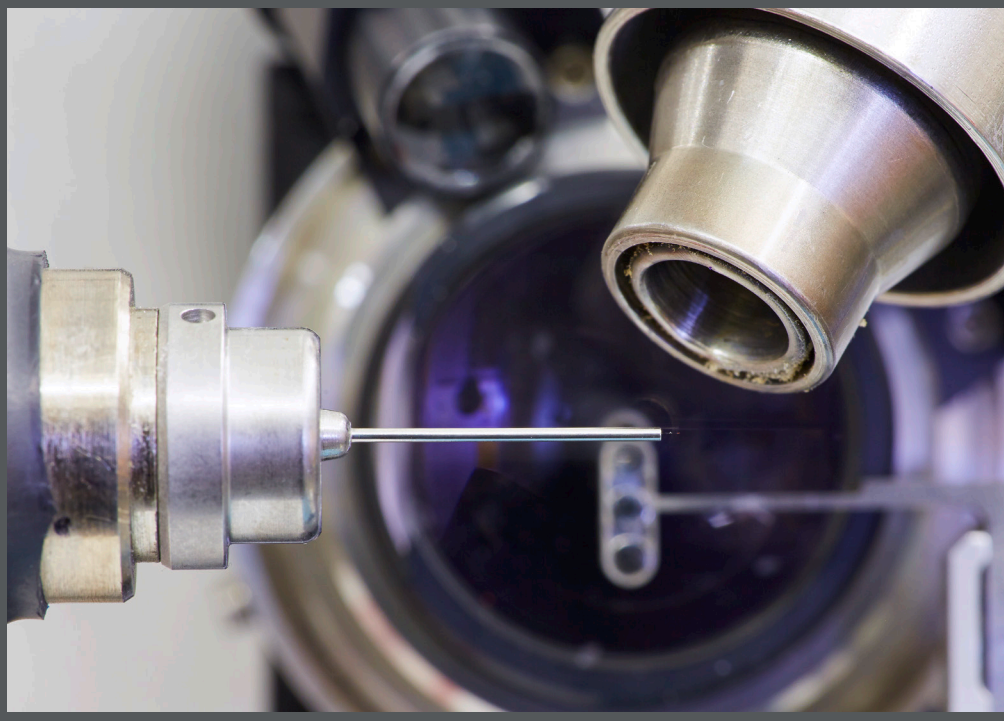
The scientific services provided by EMBL include data, structural biology, and imaging services as well as state-of-the art core facilities.

Core biomolecular databases and bioinformatics tools

EMBL pioneered open access data resources in the 1980s and currently hosts the most comprehensive, integrated set of open biomolecular data in the world. Over forty data resources are developed and made openly available to the worldwide scientific community by EMBL's European Bioinformatics Institute (EMBL-EBI). Databases include information on hundreds of millions of genome and RNA sequences, protein structures, protein folding domains, cell metabolites, phenotypes, and on the effects of drugs on cells and tissues, as well as biological image data. EMBL-EBI's open sharing of biological data in standardised formats with the life science community has been integral to generating countless research insights worldwide. These data resources have become a fundamental infrastructure for genomic medicine and the analysis of complex microbial ecosystems, and are becoming critical in other areas including agritech and biodiversity tracking.

Beamlines, instrumentation, and high-throughput technology for structural biology

EMBL provides structural biology infrastructure for biologists from all over Europe at the European Synchrotron Radiation Facility (ESRF) in Grenoble and Deutsches Elektronen-Synchrotron (DESY) in Hamburg. At both sites the synchrotron beamlines for macromolecular crystallography and small-angle X-ray scattering are complemented by advanced sample preparation facilities offering integrated access to services, expertise, and user training. These are widely used by the European and global scientific community in conjunction with EMBL scientists and have resulted in landmark discoveries, including the nature of protein–RNA complexes involved in viral replication, which is expected to inform research on diseases like COVID-19.



Imaging facilities with access to world-class microscopy and technologies

At EMBL Heidelberg, the new EMBL Imaging Centre is scheduled to begin operations in 2021. The centre will offer access to the latest light and electron microscopy technologies, along with data analysis facilities and expert support. In addition, EMBL Barcelona hosts a Mesoscopic Imaging Facility which, in conjunction with the Electron Microscopy Facility and Advanced Light Microscopy Facility in Heidelberg, provides scientists with access to microscopy and modelling technologies designed for studying tissues.

Core facilities which provide cost-effective and efficient access to methods and technologies

EMBL's core facilities offer scientists at EMBL and in its member states access to state-of-the-art equipment and expert support, enabling them to achieve their research goals. The facilities currently offer services in the following areas: advanced light microscopy, chemical biology, electron microscopy, flow cytometry, genomics, metabolomics, protein expression and purification, and proteomics. These services are provided by EMBL experts who also share their knowledge with the broader scientific community.

Mission 3: To train scientists, students, and visitors at all levels

EMBL's PhD and postdoctoral research programmes provide world-class training for scientists in a collaborative and interdisciplinary environment. The EMBL International PhD Programme, with over 200 PhD students at any one time, supports students in gaining early independence through a combination of dedicated mentoring and creative freedom. Co-funded by the EU's Marie Skłodowska-Curie Actions, the EMBL Interdisciplinary Postdoctoral (EIPOD) Programme provides training and career development opportunities for young researchers. A new fellowship programme, ARISE, was recently launched to train engineers and technology developers to become research infrastructure scientists and leaders. EMBL's courses and conferences cover a diverse range of topics and bring together experts to share new ideas and techniques, foster collaborations, and develop strategies to drive future research. In 2019, nearly 7,500 participants from 86 countries attended courses and conferences across EMBL's sites. EMBL also promotes scientific excellence through its Scientific Visitor Programme which provides opportunities for visiting scientists and students to benefit from new technologies and state-of-the-art equipment in EMBL laboratories and core facilities.

Mission 4: To actively engage in technology transfer and industry relations

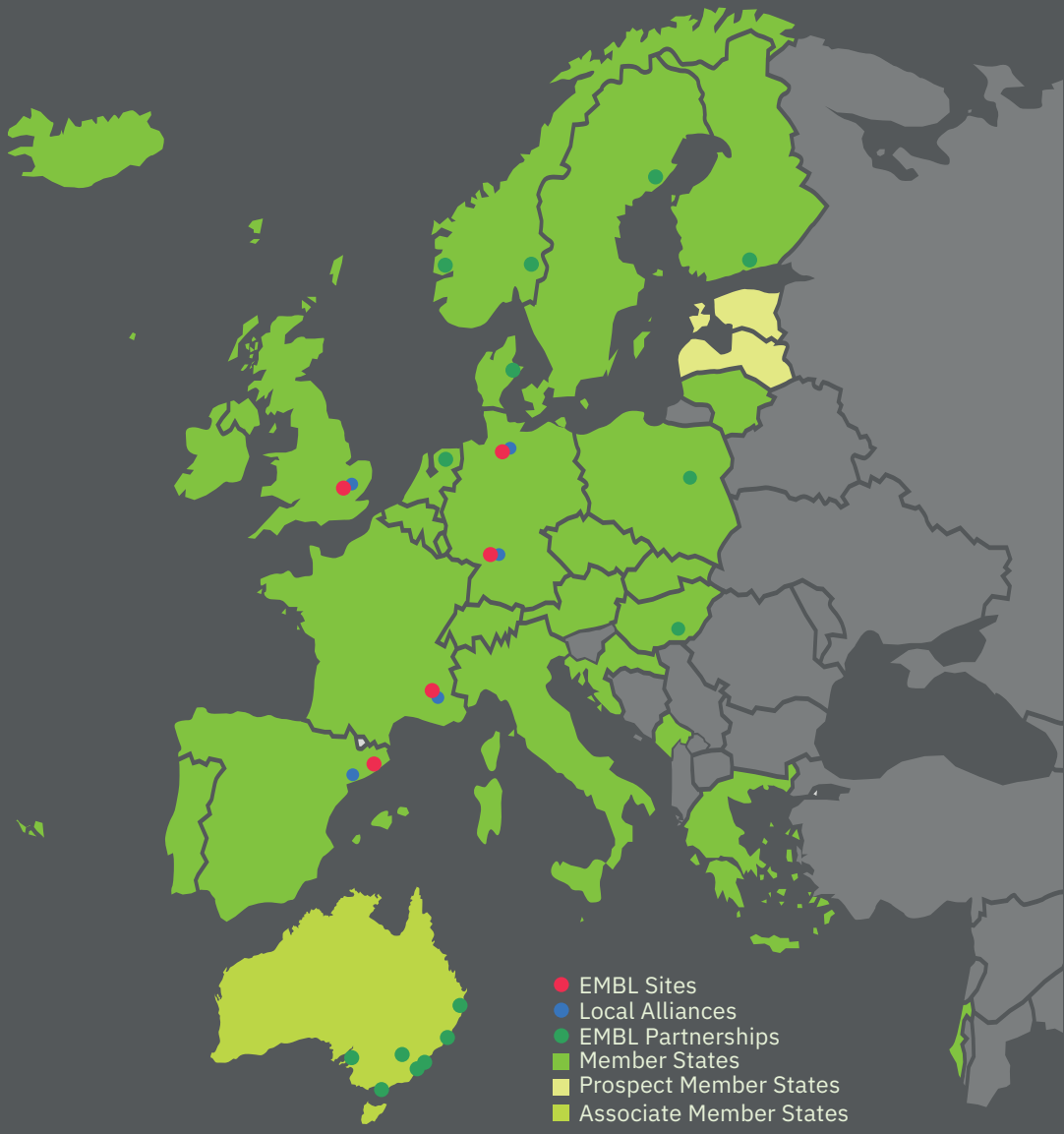
Scientists at EMBL often seek innovative ways to answer biological questions, frequently developing new technologies and methods in close collaboration with industrial partners as part of the process. EMBL's technology transfer arm, EMBLEM, facilitates the process of identifying and protecting intellectual property, enabling the establishment of EMBL spin-off companies, developing collaborative research agreements, and licensing technologies to third parties. EMBL also partners with industry in large-scale public-private research collaborations, such as Open Targets, which have led to publications and data platforms that further industry-driven questions.

Mission 5: To coordinate and integrate European life science research

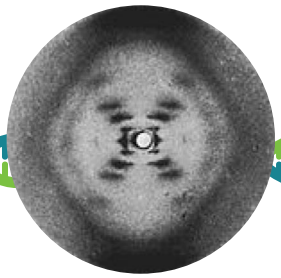
EMBL fosters international collaboration between scientific communities in Europe and around the world by playing a leading role in shaping scientific strategy and policy. EMBL has founded the European Strategy Forum on Research Infrastructures (ESFRI) projects ELIXIR and Euro-BioImaging, playing important leadership roles in both organisations and additionally is a member of the Instruct-ERIC. Via its Partnership Programme, EMBL has helped to establish institutes of excellence spanning life sciences in many of its member states, some with the aim of strengthening less research-intensive regions.

EMBL also maintains a strong relationship with the European Commission (EC) and regularly engages with the EC on European science policy issues, thereby contributing to the future direction of European framework programmes. EMBL also contributes to European science policy as a founding member of EIROforum, an alliance of eight intergovernmental research infrastructures in Europe.

EMBL's aim for its member states is to enable national research to grow and be transformative in furthering national strategies and priorities



The Foundations of Molecular Biology and the Birth of EMBL

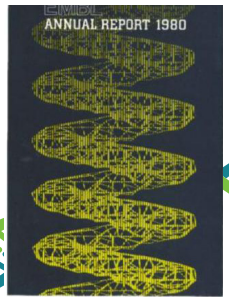


1953

DNA structure revealed

1962

EMBL founders, Kendrew and Watson, are each awarded a Nobel Prize for the discovery of the structures of myoglobin and DNA respectively



1980

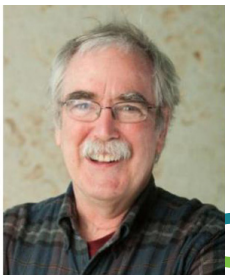
The first central depository of nucleotide sequence data in the world is founded at EMBL

1974

EMBL is founded by 10 member states

1990

Launch of the Human Genome Project



1995

Christiane Nüsslein-Volhard and Eric Wieschaus receive the Nobel Prize for research done at EMBL on genetic control of embryonic development

2015

Science *publish research made possible by EMBL's collaboration with* Tara Oceans

2003

Launch of the Encyclopedia of DNA Elements (ENCODE)

2017

Jacques Dubochet receives the Nobel Prize for technology development of cryo-electron microscopy done at EMBL

2021

EMBL Imaging Centre opens

2019

Professor Edith Heard becomes EMBL Director General

2022–2026

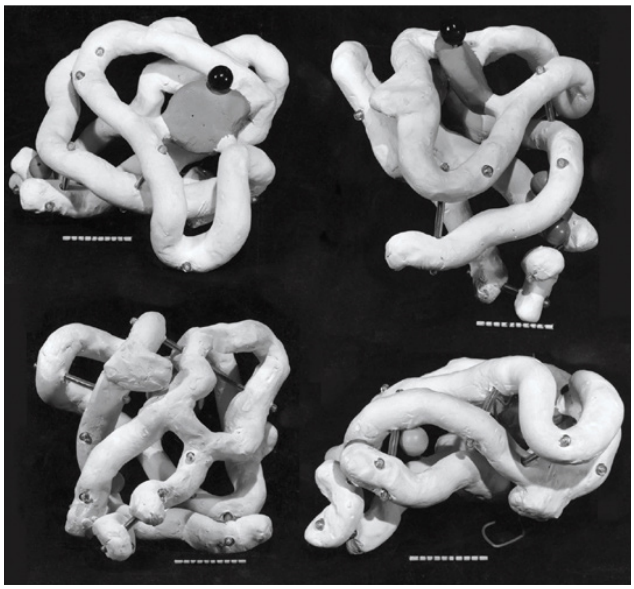
Molecules to Ecosystems: A new era of Molecular Biology at EMBL and beyond

The Future of Molecular Biology

The Foundations

Molecular biology can be considered to be the collective understanding of how the rich diversity of Earth works at the level of molecules, such as DNA, RNA, proteins, lipids, and others. This field of science was created more than half a century ago with the aim of deciphering how living things function, and has led to some of the greatest discoveries of the 21st century. Curiosity-driven research in molecular biology has given humanity a wealth of knowledge, including the capacity to read the blueprint of life, to observe and understand how organisms are formed, to identify the events that lead to disease, and to develop treatments.

Modern biology is in a period of spectacular progress and an unprecedented level of excitement. Transformative research technologies such as single-cell sequencing and cryo-EM, coupled with the ability to generate, perturb, and analyse biological systems at scale, have revolutionised our understanding of the core molecular processes that define life. Pioneering developments in molecular biology have applications in new areas of medicine, agriculture, and biotechnology, with genomics being used in patient diagnoses, cellular imaging for efficient food production, and structural biology being used to design drugs and create innovative consumer goods. The discoveries of basic molecular biology research include many of the genetic drivers of development and disease. However, despite the capacity to capture and read so much biological information, in reality only a modest fraction of the fundamental workings of living matter is actually known and what has been learnt in the past 50 years is just the beginning.



Discovery of the structure of myoglobin in 1962, by John Kendrew, Founder of EMBL.

Reconstructed by Alan Fersht, using the original figures in the archives of the Medical Research Council Laboratory of Molecular Biology, Cambridge, UK

The Next Frontier

Over recent decades, remarkable molecular insights have been made in model organisms ranging from bacteria to animals, using defined lab conditions. However, organisms do not live in isolation. From the plankton in oceans to the bacteria in the human gut, every organism in nature is part of a complex and dynamic ecosystem, living in community with other organisms, in physical and chemical environments. An ecosystem, or biome, is defined as a single environment comprising every living organism (biotic) and non-living factor (abiotic) contained within it. From unicellular to complex multicellular organisms, all living systems must respond and adapt to the environment in which they live in order to survive.

While the impact of the environment on phenotypes (the observable characteristics or traits of an organism) is well described at the organism and population levels, the underlying molecular processes and mechanisms remain relatively unstudied. The principles underlying phenotypic variation and the responsiveness of organisms to changing environments have hardly been tackled at the molecular level. Looking to the future, molecular biology can help to reveal these mechanisms in order to understand how organisms function in their natural contexts.

New technologies are now being developed to collect measurements of ecosystem components at unprecedented volumes, from molecules to cells, organisms, populations, and communities, alongside chemical and physical environmental parameters. Advances in computational power and artificial intelligence (AI) have also enabled the rigorous analysis and creative integration of these data. This tremendous technological progress in the life sciences can now be coupled with the capacity to gather and analyse data of greater scope, resolution, and quality than ever before. This means that measurements of environmental context can be collected in systematic ways, allowing for the integration of this new level of complexity into the study of biology. Building on its established expertise in molecular biology, EMBL can now take on the study of life in its natural context. **In this new scientific era, researchers at EMBL will strive to understand ecosystems at the molecular level.**

The Societal and Economic Value of Ecosystems

Healthy ecosystems, both in terms of biodiversity and balanced interrelationships among organisms, are fundamental to life on our planet and to human well-being. However, human action is destroying ecosystems on a massive scale. Accelerating pollution, deforestation, and climate change coupled with environmental policy failure, have created major environmental problems such as biodiversity loss, threats to public health including pandemics, and ecosystem collapse.

However, the value of healthy ecosystems to human welfare is severely underestimated. One estimate of the notional economic value of **ecosystem services** (such as for the provision of food, water, fuel, and other raw materials, the pollination of crops, or the prevention of floods or soil erosion) is $125 trillion per year; around two-thirds higher than global GDP (Living Planet Report 2018).

Leading the Future

The world is now facing an urgent need to find solutions to challenges such as climate change, the loss of biodiversity, environmental degradation, antibiotic resistance, environmentally-driven epidemics, and human diseases such as diabetes, cancer, and mental illness. It is crucial that the life sciences play a leading role in developing new knowledge and innovations for mitigating the impact of human action on ecosystems. A new era of molecular biology encompassing ecosystems is needed, to help us understand and revolutionise planetary and human health.

Knowledge of ecosystems at the molecular level will be pivotal for the next wave of scientific discoveries, such as an understanding of the emergence of infectious diseases, vaccine development for evolving pathogens, modelling the human brain, and providing ecological therapies for a burdened planet. These are some of the crises of modern society that can be transformed by molecular biology in the next decade.

Molecules to Ecosystems: EMBL's vision is to advance our understanding of ecosystems at the molecular level, applying expertise in molecular biology to study life in its natural context. In so doing, EMBL aims to use fundamental science to tackle societal challenges.

Molecules to Ecosystems: in the next Programme, EMBL will build on its core strengths in studying life at multiple scales (molecules, cells, tissues, and populations) to progress to studying life in context – including entire ecosystems – at the molecular level.

Molecules to Ecosystems

EMBL's ambitious Molecules to Ecosystems Programme will leverage EMBL's strengths in molecular biology, interdisciplinary research, and its collaborative spirit to work towards a fundamental understanding of life, including human life, in the context of populations and environments. This cutting-edge, interdisciplinary, and societally-relevant research will incorporate novel areas and technologies, and expand EMBL's horizons into a new era of life sciences.

The EMBL Programme will explore **biology in context** by studying **both classical and novel model organisms** in the context of their real world environment. Longitudinal studies will be performed collecting comprehensive data in specific areas of Europe, in close collaboration with institutes from EMBL's member states. **Fieldwork** bringing together molecular biologists and ecologists, epidemiologists, and environmental biologists will be a critical component to better understand environmental effects on molecular mechanisms and organism composition, symbiotic states, and host-pathogen interactions. Most importantly, to study life **across interconnected scales** (cells, tissue, organisms, populations) in different genetic and environmental contexts, **lab experiments** will be needed to induce **controlled perturbations of genetic or environmental factors** and to measure their impact to gain mechanistic understanding.

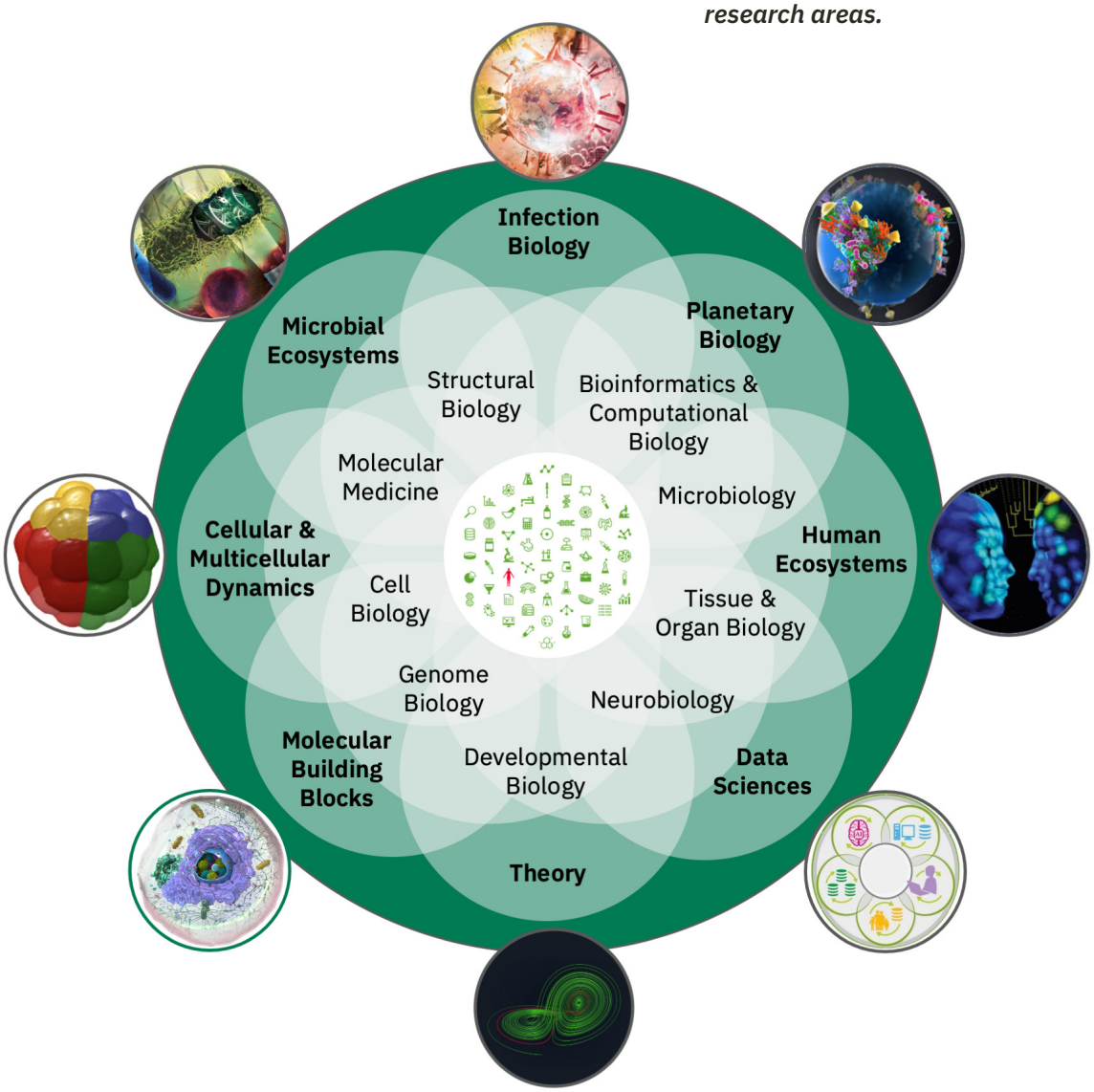
In collaboration with EMBL member states, EMBL will initiate specific projects within **mobile labs** containing equipment and staffed by dedicated personnel with technical and research expertise. EMBL will work in **partnership** with scientists from various fields, including ecologists, zoologists, epidemiologists, population geneticists, climatologists, and toxicologists, to realise these ambitions. EMBL aims to develop **advanced sampling approaches** for gathering data from observational studies. Appropriate computational tools, including AI and theoretical approaches, will be required to extract new knowledge and biological principles from these large and complex datasets.

Although the ambition to gain a molecular understanding of ecosystems may be considered bold, EMBL is well placed to expand its horizons. Over the past decade, EMBL has built up the tools and knowledge base to begin to address the molecular basis of life in context and is ready to do this in partnership with its member states and collaborators. EMBL is recognised for excellence in structural biology, genomics, developmental biology, cell biology, bioinformatics, and instrumentation. The core strengths of EMBL, its expertise in studying life at multiple scales, its provision of biological data and key services, and its solid history in technology development, training, and innovation make EMBL an ideal organisation to lead and coordinate new scientific enterprises to investigate life in the context of its environment.

Programme Themes

Building on EMBL's existing strengths, the 2022–2026 Programme adds several exciting new scientific areas within which life can be explored in a variety of different contexts. Molecular processes and mechanisms underlying responses to environmental changes can be studied at multiple biological scales: from exploring the molecular components inside a cell, measurements of single cells and multicellular tissues to whole organisms, and studies of populations. In EMBL's new Programme these different dimensions will be explored, with specific ecosystems chosen as research areas of focus based on their potential for scientific opportunity when coupled with the current advances in experimental technologies and data sciences.

EMBL's current and new (shown in bold) research areas.



The first research theme of **Molecular Building Blocks in Context** delves into cellular function and subcellular components to determine systematically how responses to a changing environment are mediated at the molecular level. EMBL aims to understand mechanistically how these responses translate into adaptations of cells, tissues, and organisms in different contexts. Understanding how cellular components and processes change over time, how they are interconnected, and how they feedback to one another, lies at the core of EMBL's expertise.

EMBL's approaches for gaining a mechanistic understanding of how multiscale living systems function, respond to, and evolve in ever-changing environments are highlighted in the theme **Cellular and Multicellular Dynamics of Life.** EMBL will use cutting-edge technology developments and iterative computational and wet-lab experiments to measure and perturb living and dynamic systems and their interplay with the environment. Increasing knowledge about the robustness and plasticity of embryonic cell clusters, bioengineered systems, and complex tissues will be essential in revealing the mechanisms that drive normal development and living processes, and the way these processes respond to disruptive environmental changes.

Microbial communities colonise, proliferate on, and impact every surface and subsurface of the planet, even in its most inhospitable corners. To better understand microbial ecosystems, their functional capacities, and their molecular interplay with the environment, the diverse microbial communities residing within the human gut are taken as an exemplar community in the **Microbial Ecosystems** research theme. EMBL aims to use novel computational and experimental methods to understand the functional diversity of individual microbial species and strains, as well as the interactions and properties of gut microbial communities within the ecosystem of their human host. The ultimate goal is to be able to rationally modulate these microbial communities for the benefit of human and planetary health.

Infection Biology is an area that impacts humans and all life forms on Earth, with pathogens being able to cross species barriers, thereby adversely impacting biodiversity, planetary, and human health. The current COVID-19 pandemic highlights the urgent need to obtain insight into the emergence and spread of infectious disease. In the new Programme, EMBL will integrate multidisciplinary experimental and computational approaches to understand how pathogens and their hosts interact. These approaches will help to develop diagnostic and surveillance tools, to prevent the development and spread of antimicrobial resistance, and to work closely with frontline public health agencies to establish genome-based surveillance platforms. This has already begun with the provision of international data hubs for controlled data sharing, to empower scientists at EMBL and around the world to combat the COVID-19 pandemic.

Spanning multiple ecosystems, the **Planetary Biology** research theme aims to understand at the molecular, cellular, organismal, and population levels how microbes, algae, plants, and animals interact with each other and respond to environmental change. To achieve this, EMBL intends to systematically combine complementary global projects with local experimental analyses. TREC22, EMBL's flagship project to explore European coastlines in partnership with scientists in the member states, is a central part of this goal. By working together and learning from one another, EMBL and collaborators will help to address fundamental and pressing scientific questions about the influence of environmental parameters on biological processes, while also addressing societal questions about planetary health.

In **Human Ecosystems**, EMBL researchers aim to understand how the environment impacts humans, both as individuals and within populations. A central question is how environmental factors can cause disease and how genotype and the environment influence human phenotypes. In the context of this theme and in close collaboration with epidemiologists from member states, the environment will be studied through three distinct lenses focusing on the physical, biological, and social environments. Powerful computational, statistical, and experimental methods will address key questions that will bring a quantitative, mechanistic, and molecular understanding of environmental effects on humans.

Molecular biology experiments within all of these research themes will contribute to the growing volume and heterogeneity of biological and environmental data that are necessary to the study of life in context. To ensure these data are expertly generated, curated, annotated, managed, integrated, visualised, and shared, EMBL will launch a new **Data Sciences strategy**. As part of this strategy, data science centres connecting all EMBL sites will provide support and training, facilitate research advances in data sciences including novel AI methods, set technical standards, and offer critical public data resources to the molecular biology community, with the overall goal of maximising the value of the generated data. Through these efforts, EMBL aims to be a role model for life science institutions that face similar data-driven challenges.

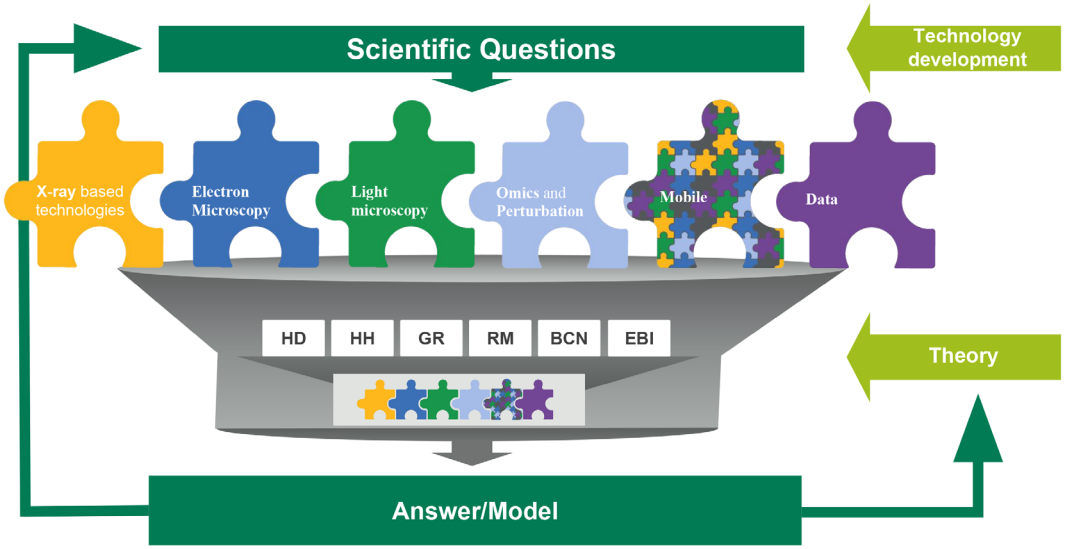
EMBL aims to create a new and highly integrated **Theory programme** to complement EMBL's research and data-driven approaches to studying life in context. The complexity of biology necessitates theoretical approaches. This design will build up approaches from first principles and will explain biological phenomena using mathematical formalism and models, turn data into understanding, and generate testable predictions. Theoretical approaches will be developed and applied to answer specific questions from all six research themes. The interplay between theoretical and experimental research, complemented by a theoretical training programme and visiting theoreticians, will be an integral requirement for achieving EMBL's scientific goals.

EMBL's **experimental and data Services** are set up to respond dynamically to the needs of research communities. EMBL's scientific services will be strengthened and integrated, to form a central pillar of EMBL's new Programme. Together, EMBL's scientific services help to advance research and technology development at EMBL, and across EMBL's member states:

- EMBL's cutting-edge technology development feeds into its **structural biology and imaging services**, which enable scientists to visualise molecules across scales. These services include robotically controlled beamlines that provide data on biological structures at the atomic level, and methods to integrate imaging by cryo-EM and light microscopes to show these molecules in their cellular context. By fully supporting the use of complex experimental apparatus, and by interfacing various scientific disciplines, EMBL services enable scientists from EMBL member states to access a range of structural biology and imaging techniques to answer complex biological questions.

- Advances in single-cell genomics and emerging developments in spatial omics will spur a range of new **multi-omics services**, based on new technologies. EMBL's ***in vivo* gene** editing service will enhance the study of human genetic variation in models such as the mouse, and will provide platforms for viral-mediated editing to offer insights into epigenetic mechanisms *in vivo*. New cross-site **chemical biology services** will help scientists explore novel drug targets and the effects of environmental factors. In conjunction with TREC22, EMBL's flagship project to explore European coastlines in partnership with scientists in the member states, the provision of **mobile services**, spanning imaging, genomics, environmental measures, and data services will enable EMBL to further support research in its member states.

- EMBL's biomolecular **data services** will also see significant enhancements in the provision of reference data, standards, and tools, including bioimage data, and human brain and behaviour data, as part of EMBL's data service repertoire. The **Genomic Medicine Platform** will engage with individual national initiatives, advising and proactively transferring technology to EMBL member states that have begun bringing precision medicine into their healthcare systems. EMBL will also provide **data portals** that can effectively coordinate new data types, which dynamically expand in size and relevance as research communities evolve.



EMBL **Training** activities will continue to provide state-of-the-art scientific training for EMBL fellows, including predoctoral and postdoctoral researchers, and will embrace the new research themes. The Course and Conference Programme will also reflect the new themes from the EMBL Programme and the EMBL Scientific Visitor Programme will increase the number of scientific visitors to its sites, by offering complementary sabbaticals and secondments. Training activities to strengthen capacity in EMBL member states will also be further developed. With remote working becoming a way of life for scientists all over the world, EMBL will build on its success in providing accessible e-learning materials. This will enhance the training impact and reach, while also contributing to environmental initiatives at EMBL through a reduction in travel.

Innovation and Translation at EMBL will be expanded to encompass the new scientific directions and spirit of this Programme. In addition to building a portfolio of innovation and commercialisation activities, EMBL will broaden and advance research collaborations and technology development via new public–private partnerships. A range of new activities will be implemented to develop an EMBL innovation culture, empower the next generation of EMBL fellows, and diversify the current instruments for training and knowledge exchange between EMBL and industry partners.

EMBL's mission to **Integrate European Life Sciences** reaffirms its commitment to its member states and associate member states. EMBL will continue to establish links and initiate collaborative relationships between scientific communities in Europe, especially in the new scientific areas of the Programme. EMBL will foster new and existing EMBL-modelled inter-institutional research partnerships across Europe, and will develop a series of initiatives to promote closer collaboration and knowledge exchange. EMBL will continue its key European coordination activities with EIROforum and with the European Commission (EC), including the EC-led project to establish the European Open Science Cloud (EOSC).

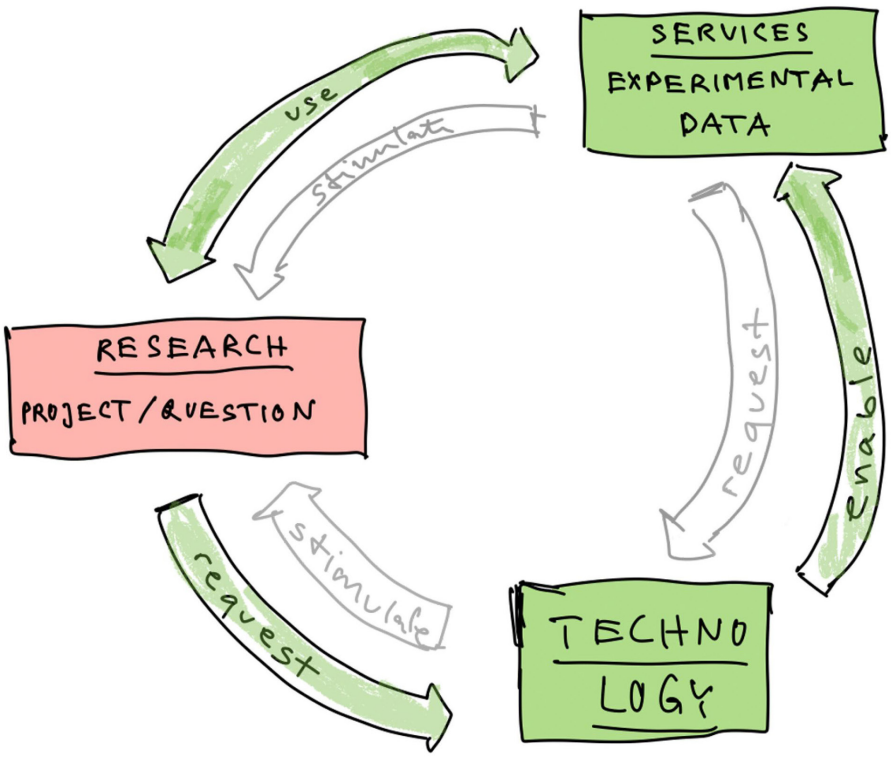
EMBL's **People, Processes, and Places** will be pivotal for the implementation of the new Programme, with the establishment of transversal themes across all EMBL sites, in order to launch some of the new research themes. The cross-disciplinary themes will require the recruitment of skilled professionals from diverse disciplines, including engineers, mathematicians, data scientists, theoreticians, physicists, and chemists. The development of an employer branding strategy will support these recruitment efforts. Across EMBL, schemes for career development and the promotion of equality and diversity will also be strengthened. EMBL's processes and systems will need to support modern ways of working alongside expanded IT infrastructures. EMBL's goal is to enable the creation of sustainable campuses across all sites and to firmly embed green working policies and practices. Through local collaborations, partnerships and engagements, each EMBL site will continue collaborations and exchanges with local institutes, regions, and national initiatives.

Given the societal and environmental relevance of EMBL's new Programme, strong **Public Engagement, Communications, and Outreach** will be key. EMBL aims to raise the visibility of its science and technology to inspire, inform, and educate a range of audiences. It will do this by increasing local public engagement at all EMBL sites, multiplying communications activity through collaborations and partnerships, embarking on the TREC22 outreach initiative in the member states, supporting European teachers and young learners, and engaging with policymakers to improve evidence-based decision making. EMBL also plans to strengthen public engagement and communication skills among staff and help increase communications capacity in its member states.

Critical Success Factors

EMBL's history of ground-breaking scientific achievements and other successes comes from a unique blend of flexibility, interactivity across disciplines, and a distinctive scientific culture which blends ambition, insistence on excellence, cooperation, and openness. The success of the new EMBL Molecules to Ecosystems Programme will rely on these same elements:

- A virtuous circle of novel research, technology development, and services
- Interconnection between experimental and computational science
- Open science
- Interdisciplinary research
- Intensive collaboration and coordination
- Sustainability practices as drivers of green research



The EMBL research–service–technology virtuous circle. Researchers can use EMBL experimental and data services to obtain answers otherwise not accessible to them. Research questions and service provision also drive novel technology developments. Conversely, novel technologies or services frequently trigger new research questions and projects.

Scientific and Societal Impact

Given the scale and pioneering nature of scientific research needed to tackle pressing environmental challenges, success is only feasible with an international effort involving collaboration between world-leading scientific institutions.

EMBL's new Programme aims to push the life sciences into a new era that will greatly strengthen the bridge between biology and disciplines such as epidemiology, ecology, toxicology, zoology, population geneticists, engineering, and mathematical theory. EMBL's unique international position enables it to coordinate and lead such efforts for the benefit of science and society, while also mediating joint community standards and promoting open science. Harmonised efforts will ensure informed and impactful national and international research and policymaking, especially concerning ecological issues.

As well as answering scientific questions, EMBL aims to rise up to answer societal questions, including questions about the impact of pollution, climate change, deforestation, and the loss of biodiversity; the spread of antibiotic resistance; the emergence of epidemics from zoonotic diseases; the destruction of our soils and oceans; the collapse of natural ecosystems; and human health challenges linked to environmental factors.

The powerful combination of EMBL's experience and expertise primes the organisation to lead this revolutionary direction in science. These strengths, paired with EMBL's collaborative, flexible, and inquiring scientific culture provide the ideal launch pad for the Molecules to Ecosystems Programme and create an ambitious new era of life science research in Europe.

Value Proposition

EMBL is a world leader in delivering and enabling high-quality and impactful research in molecular biology. The most immediate beneficiaries of EMBL's scientific activities are the scientists and public in EMBL's member states. In association with member state scientists, EMBL has created and designed this Programme with the aim of initiating a revolutionary new era of molecular biology to study ecosystems at the molecular level.

The diverse scientific directions and wide-reaching initiatives will be of differentiated value for each member state. EMBL's aim for its member states is to enable national research to grow and be transformative in furthering national strategies and priorities. Designed to address every aspect of the scientific process, EMBL's Programme is geared to enable member state participation, from collaborative research and training to the coordination, commercialisation, and communication of science.

International Coordination, Collaboration, and Representation

EMBL's future Programme, Molecules to Ecosystems, begins with boldly stepping outside of the laboratory to understand living systems in their natural context, at the molecular, mechanistic level. With climate change, epidemics, and rising pollution high on the agenda for Europe and the world, EMBL, as the only intergovernmental research institution specialising in molecular biology in Europe, can **efficiently coordinate** the efforts of multiple national initiatives to effectively pursue and further such societally-relevant research in an integrated manner. With its pan-European mandate, EMBL will play the role of a neutral broker to **facilitate a scientific approach** that will be essential to study cross-border ecosystems and enable projects which represent the interests of different parties. Establishing collaborations at all levels will be essential, whether they are strategic collaborations with institutes near EMBL host sites, or with different communities of researchers in the member states. The benefits of such relationships lie not just in research outputs but also in helping member states to indirectly gain access to landmark global projects and consortia-led collaborations, providing support to secure national funding, and allowing for representation in key European life sciences activities.

EMBL Services span sites and disciplines and enable scientists in EMBL's member states to access high quality, integrated infrastructure and expertise to answer and fuel further scientific questions

Open and Immediately Available Research Outputs

As EMBL pursues new avenues of research, new technologies and results will be generated. With EMBL's open science and open data mandate, research outputs from this EMBL Programme will be available for use and further development by member states and beyond. Some of the scientific discoveries from this Programme could lead to **solutions to address global societal challenges,** including the discovery of novel antibiotics and new therapeutics, or methods for detection and prevention of epidemics, carbon footprint reduction, plastic degradation, and bioremediation. Example outputs include concepts for molecular based sensors for environmental measurements or biomarkers that can enable evaluations of ecosystem collapse, or tools to more effectively classify biodiversity based on genetic diversity and molecular methods. Statistical methods developed by EMBL for human cohort analyses could also be used member state genomic medicine programs to enable patient stratification, diagnostics, and disease mitigation strategies, as well as help predict therapy outcomes. Other outputs include microbiome-based diagnostics and modulations for the treatment of major human diseases, or bioremediation strategies to reduce environmental toxicology based on naturally occurring or artificially introduced microorganisms. As well as these, molecular strategies for new viral epidemics and antibiotic resistance spread, and potential new therapies can be stimulated by an increased understanding of viral and bacterial communities and their interaction with their host.

Scientists across EMBL member states and beyond will have access to more data of different types than ever before, due to EMBL's commitment to promote open science principles and practices. The experimental directions proposed can also lead to the development of **databases and software tools** that allow for modelling of ecosystems or aid the discovery of associations between environmental exposures and human health. EMBL's at-scale and innovative experimental designs will also benefit scientists by providing **new experimental methods, protocols, and biological resources**.

Access to Deep, Multidisciplinary Expertise

EMBL's track record in combining research, service, and technology development is unparalleled for an international life sciences organisation. EMBL scientists have worldwide reputations as leaders in their respective fields, and this expertise is on call for member states to leverage in the delivery of national plans, from healthcare to environmental applications.

In embarking on new areas that will lead to a molecular understanding of ecosystems, EMBL's goal is to capitalise on its long-standing expertise in molecular biology to help **tackle the questions posed by ecologists and epidemiologists**. Through advisory committees and open calls for proposals, EMBL's experience in large international collaborations, both for experimental research and as a data coordination partner, will be critical to drive scientific discovery in these areas. EMBL's expertise will also become more locally accessible to member state scientists via EMBL's flagship project, TREC22, and the provision of novel, mobile laboratory services. Alongside **access to scientific services and cutting-edge technologie**s, EMBL's staff is able to help train national scientists to use specialist equipment and instrumentation at member state laboratories and via webinars, as well as provide after-care via mentoring schemes. Access to specialised EMBL personnel and the onward training of numerous member state scientists will enable discovery, collaboration and capacity building in projects relating to ecosystems at the molecular level. Through the TREC22 outreach arm, students, teachers, and members of the public in the member state communities surrounding the sampling sites visited by TREC22, will also have the opportunity to visit the mobile labs. Here, they will **learn about planetary health** topics such as biodiversity, antibiotic resistance, microplastics in the environment, and the importance of protecting ecosystems.

The complexity of emergent scientific areas at EMBL, such as planetary biology, human ecosystems, and theory needs an agile mechanism to boost the skills, knowledge, and career development for both academic and industry scientists. Through EMBL's expanded Visitor Programme, EMBL will host member state scientists for specialised and interdisciplinary **secondments**. With data sciences as a core area in all life sciences organisations, the EMBL Data Sciences Programme will provide training for member state scientists. This training, which will range from the basics of data analysis, statistics, and bioinformatics, to advanced and newly arising topics including AI and theoretical biology, can **empower scientists to work with big datasets**. AI communities within member states will benefit from a strengthening of AI research at EMBL through the establishment of a **critical mass of AI researchers within Europe** to help counteract the brain drain of this discipline to North America. EMBL's Data Sciences Programme will also stimulate natural collaboration with AI companies and information technology sectors for methods development, computing, and storage infrastructure.

EMBL has pioneered fundamental scientific services for the life sciences community and amassed expertise in various scientific technologies, such as molecular crystallography and open data services. With the opening of the EMBL Imaging Centre, new services in cutting-edge imaging will be provided, integrating the complementary techniques of electron microscopy and light microscopy. Bespoke user facilities will allow member state scientists to work together with EMBL scientists and industry specialists to develop technological solutions for specific experimental and data-driven questions. Clinical research and clinical practice are particular application areas for EMBL science which demands impactful knowledge and proactive technology transfer. EMBL has a rich interface to clinical research with joint research programmes, medical faculties, and hospitals. **Genomic medicine programmes** in member states can directly access EMBL's Genomic Medicine Platform and benefit from bespoke consultancy for their programmes, secondments to EMBL, access to reference data resources, and training schemes in genomic medicine.

National institutes which implement the EMBL model via the **EMBL Partnership Programme** benefit from the guiding principles of scientific openness, interdisciplinarity, and rejuvenation of research, through the staff turnover principle and a rigorous external evaluation of research activities and services. EMBL staff can help develop national institutes to create a critical mass of translational researchers, recruit excellent international talent, and enable the institutes to act as **multipliers of excellence locally and regionally**.

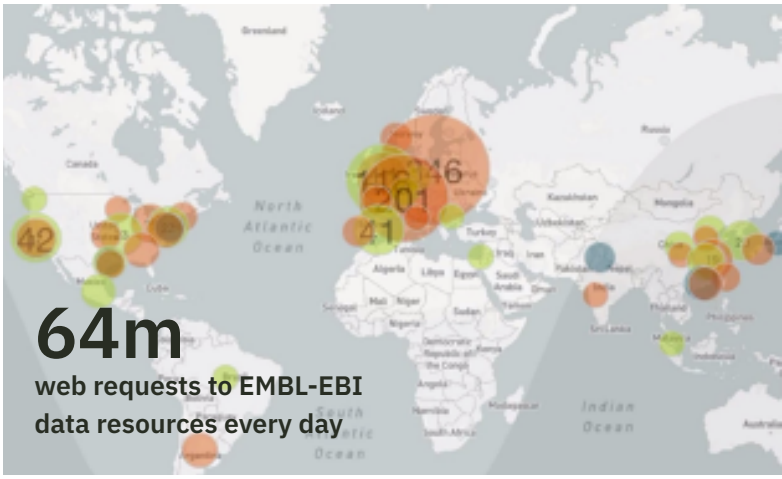
EMBL's new multi-component service, the Genomic Medicine Platform, will proactively transfer knowledge and technology into national precision medicine initiatives in EMBL member states through the five main components illustrated.

Access to Research Infrastructures

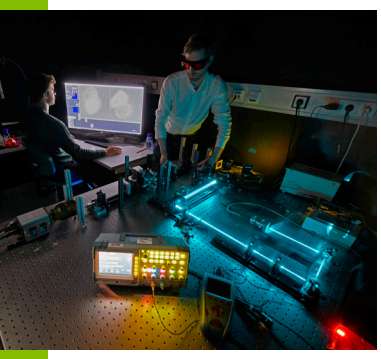
The Scientific Services mission of EMBL allows scientists and institutions in member states to access **research infrastructures** that will allow them to conduct investigations using a broad array of technologies. In the study of planetary biology, these infrastructures range from **mobile labs** that allow for **complex molecular surveillance projects**, to EMBL's micro- and mesocosms to perform (semi-) controlled experiments. Through collaborations with EMBL researchers, member state scientists can maximise the use of these artificial ecosystems and access state-of-the-art equipment.

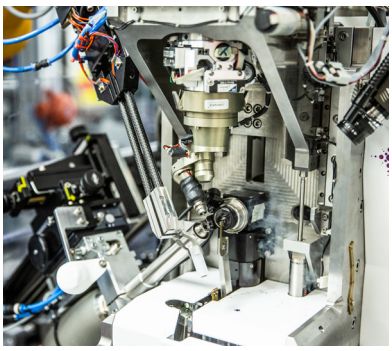
From sample preparation and instrumentation use, to data analysis and interpretation, member state scientists can access and learn to use the most cutting-edge imaging and cryo-EM technologies housed in the EMBL Imaging Centre. Member state scientists can also benefit from the technological developments ongoing at EMBL to integrate, and broaden the use of, key technologies such as light and electron microscopy. To facilitate access to non-experts and experts, EMBL will develop the Structural Biology and Imaging Centre Access Platform for biologists from member states who do not have expertise in classic structural biology techniques. The platform will enable them to easily and efficiently discover and choose complementary techniques that would be best for their experiments.

Member state scientists can access the EMBL multi omics experimental services; a set of integrative services which enable genomic sequencing, protein, and metabolomics analyses at the tissue or single-cell level. In addition, EMBL's high-throughput and systematic workflows as part of the Chemical Biology service can be accessed to screen for small molecules and optimise compounds to gain insights into protein function. The experimental workflows and quantitative assay systems to study the dark proteome or the effects of environmental pollutants, developed by the Chemical Biology core facility will offer further opportunities for collaborations with researchers in the drug discovery, environmental, and energy sectors.



Scientists around the world already benefit greatly from access to freely available, public data across a broad range of molecular data types within EMBL's open data resources. Many of these resources allow for member state scientists to rapidly compare their own unpublished data with open access datasets. Resources such as the BioImage Archive will also enable member state researchers to manage and better organise their own image data within the imaging community thanks to metadata and data formats developed by EMBL. EMBL's unique role in providing the most comprehensive and integrated suite of open data resources means that the standards and norms developed at EMBL set the global rules for data and knowledge sharing. An independent economic analysis conservatively estimated that in 2015, EMBL-EBI data resources directly underpinned £335 million of wider realisation of future research impacts, with the efficiencies delivered 20 times the operational cost of delivery.





In the future, scientists from other communities, such as ecologists, marine biologists, clinical neuroscientists, epidemiologists, and public health researchers may benefit from open access databases set up and/or maintained by EMBL, or develop data-sharing practices for their own data.

Best Practice and Principles

From open science to effective data management, EMBL's research practices can serve as a template for best practice and principles that can make research in the member states significantly more efficient. Member state scientists will be able to access tools, infrastructure, and training that embody open science in their research practice.

Member state scientists using EMBL's scientific services can capture increasing amounts of metadata and propagate EMBL's best practice for simpler and more coherent **data management**. Scientists would benefit from a more streamlined data flow, as well as being able to **reuse shared, standardised data processing workflows** to accelerate their research and improve the reproducibility of their analyses. Member state institutions facing issues with effective data management will benefit from EMBL's active participation in projects such as Euro-BioImaging and Instruct-ERIC. These projects aim to strengthen best practice; establish the FAIR principles of data sharing to make data findable, accessible, interoperable and reusable; and promote **Open Science**. Member state institutions can model EMBL's data management strategy or even directly use EMBL infrastructures to empower institutions which may lack the facilities and infrastructures to deal with storing and analysing large-scale datasets.

Sharing **best practice in technology transfer and open innovation collaboration** strategies is an important contribution by EMBL to the scientific community, especially for member states. EMBL and EMBLEM will continue to do this via the provision of on- and off-site training and advice for research institutes in the member states and EMBLEM internships, as well as through participation in the Horizon Europe Open Innovation pillar, to help the EU become a leader in breakthrough innovations in the health and environmental sectors.

Impact on National and European Policies and Guidelines

In the longer-term, EMBL aims to set up an Environmental Office to enable high-impact, global initiatives to be achieved. By combining resources and expertise and by working collaboratively across Europe, research in these new areas can stimulate the creation of new funding sources, help commercialise findings, lead to highly-cited publications, and generate outputs that have an impact on policy, clinical practice, or society. Depending on the scientific data gained, for example within the research themes described in this Programme, EMBL can play a role to effectively advocate for policy or practice changes. This could, for example, lead to reductions in pollution and thereby begin to slow detrimental changes to ecosystems or influence national health guidelines and patient stratification strategies. Policymakers in the member states and across Europe will be able to access information and advice from EMBL experts on key scientific, and sometimes contentious, topics more efficiently and effectively so that they can address ethical issues, technology developments, and societal impacts.

Training for the Next Generation

EMBL generates a constant stream of researchers at all career levels, enriching the skill set of European science. Formal training programmes such as the PhD and postdoctoral programmes, including the interdisciplinary EIPOD programmes, will also expand to allow more **member state students, researchers, and other professionals to receive advanced training by EMBL researchers**.

An array of EMBL courses, conferences, workshops, and EMBO | EMBL Symposia in 2015 to 2019. Of the 35,029 participants, 75% were from EMBL member states (MS).

Member states can also exchange best practice in training and career development with the EMBL International Centre for Advanced Training (EICAT) unit. This includes sharing **best practice in graduate and postgraduate education, career guidance, training formats, and workshops**. Programmes to benefit students from EMBL's member states include mentoring schemes for Master's students, summer research internships, and summer schools for undergraduates from STEM fields outside of biology. To benefit school pupils, EMBL organises guided campus visits for schools, teacher training sessions, educational resources for science teachers, and the new Junior Lab Programme for secondary school students. These programmes will enable students from member states to access expertise, science, and data which will complement national programmes.

EMBL enables scientists in and beyond its member states to maximally benefit from EMBL's state-of-the art **courses and conferences programme** with approximately 70% of the 6,000 to 8,000 participants each year coming from EMBL member states. EMBL's new models for delivering courses and conferences via videoconferencing and streaming capabilities aim to maximise participation. New initiatives, such as a structured programme for off-site training, will also be of immense benefit to the scientific community in each member state and could catalyse new collaborations between scientists in the member states and EMBL researchers.

Through EMBL's **Scientific Visitor Programme**, researchers, many of whom are pre- and postdoctoral fellows from EMBL member

states, have access to EMBL's state-of-the-art core facilities and technology platforms. These young researchers come to EMBL to carry out an important experiment or a part of their research project in collaboration with an EMBL research group.

Developing Excellent Personnel who Return to Member States

The new scientific areas outlined within the EMBL Programme will require EMBL to further attract talent in several new disciplines, including but not limited to, engineering, physics, mathematics, chemistry, theory, and ecology. Further integrating this mix of disciplines will continue to facilitate interdisciplinary science to answer questions outlined in many of the new themes in this EMBL Programme. The **experience gained** at EMBL by personnel in these unique and future-facing roles can be leveraged by member state research organisations as a result of EMBL's turnover model. In addition, the application of **professional development** competencies developed at EMBL is a significant benefit to future employers in the member states.

The direct exposure of EMBL scientists to industry science, via EMBL's various industry collaborations and entrepreneurship activities, has enabled greater career mobility between academia and industry, with national companies also benefiting from EMBL's turnover scheme. EMBL also plans to implement a number of new activities which seek to facilitate a mindset and culture change that will lead EMBL towards an innovation ecosystem and increase scientific impacts.

Multiplying Value

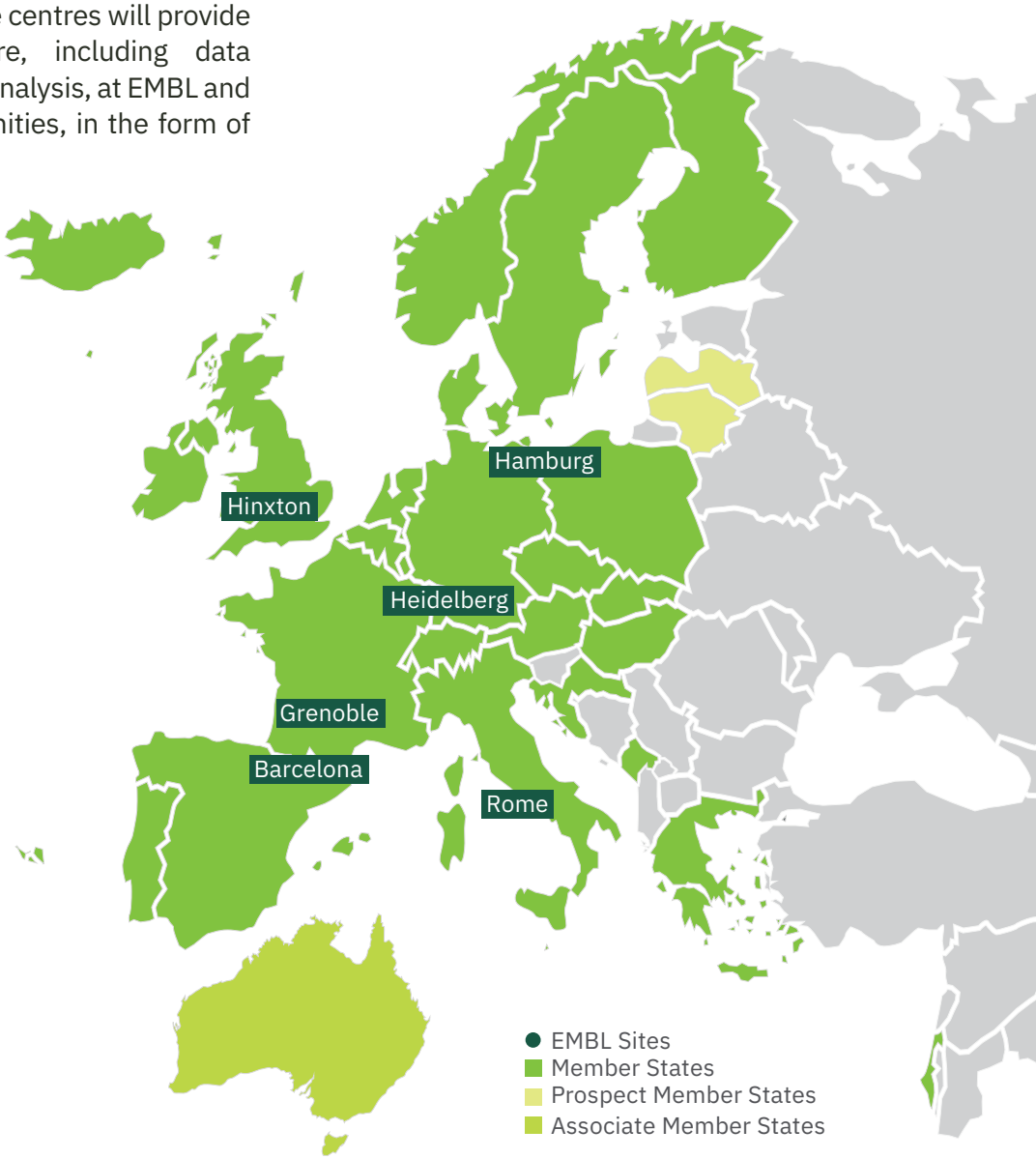
EMBL already leverages a significant amount of external grant funding from funders such as the EU, including the ERC, and various national funders in its host countries. In the next scientific Programme, EMBL will amplify its efforts to attract additional sources of funding. This will be of fundamental importance to absorb the additional costs related to the growth of the Programme and to realise the new initiatives. Most importantly, these additional sources of funding enable member states to realise an even greater return on investment in EMBL. Some initiatives, and/or sponsoring young talent, may also be an attractive cause for private philanthropists, foundations, and industry. EMBL's 50th anniversary in 2024 will also be an opportunity to celebrate, engage, and encourage fundraising.

In a world with increasing environmental, medical, and innovation demands, the fundamental rationale for EMBL is even more relevant today. EMBL is proud to embody the integrative, open, and progressive science values and be a beacon of excellence for the life sciences of Europe.

EMBL will continue to build collaborative relationships between scientific communities in Europe, especially in the new scientific areas.

EMBL Sites

Each EMBL site contributes individually and collectively to the delivery of all five EMBL missions and strategic priorities whilst specialising in particular research areas and scientific services. In the EMBL Programme, Molecules to Ecosystems, all EMBL sites will implement the scientific directions described under the previous headings, with the transversal themes cutting across sites, whilst building collaborations and networks that fully realise these ambitions. A key component of these will be the creation of the data science centres at each site to enable coordinated data science and bioinformatics research. The centres will provide services and infrastructure, including data research management and analysis, at EMBL and with member state communities, in the form of facilities, data resources, internal and external data science training.

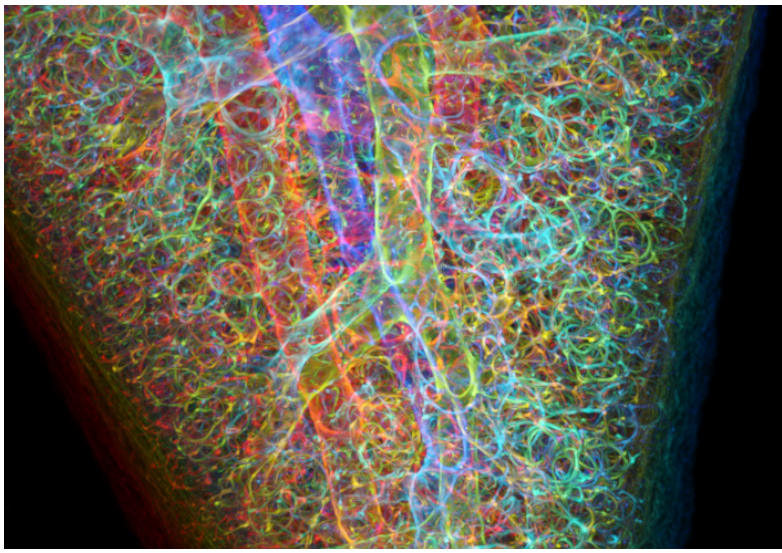


EMBL Barcelona

EMBL Barcelona, the youngest of the EMBL sites, focuses on tissue biology and disease modelling, from questions about the molecular control of embryonic tissues to applied projects which model a wide range of disease types using 3D *in vitro* human tissues. Since its opening in 2017, the unit has created a strong brand for itself in the field of **multicellular engineering**. This perspective of 'reconstructing biology' runs through its research: cells are coaxed into re-building 3D tissues showing, for example, dynamical oscillations of gene expression, spatial patterns of cartilage formation, or functional vasculature, through which blood cells can be perfused. Putting cells back into their true environmental context - as multicellular tissue collectives with emergent behaviours - allows the study of tissues in health and in disease, such as human congenital defects, cardiovascular disease and malaria infection of the blood brain barrier. An interdisciplinary mix of technical expertise supports this vision: microfluidics engineering, state-of-the-art mesoscopic imaging technologies, and increasingly the use of mathematical and computational models, in line with EMBL's goal to strengthen the area of theory.

EMBL Barcelona is hosted in the Barcelona Biomedical Research Park (PRBB), one of the largest infrastructures in Southern Europe dedicated to translational research. In this highly collaborative, interdisciplinary, and international environment, EMBL researchers benefit from its partnership with the Centre for Genomic Regulation (CRG) which offers opportunities for collaboration with this pioneering research institute. From its focus on tissue engineering approaches, EMBL Barcelona also has a strategic alliance with the Institute for Bioengineering of Catalonia (IBEC), a cutting-edge, multidisciplinary research centre that connects engineering, mechanobiology, and life sciences to generate new knowledge and applications in biomedicine.

EMBL Barcelona will embark on several new initiatives in the context of ecosystems at the molecular level, for example, partnering with the



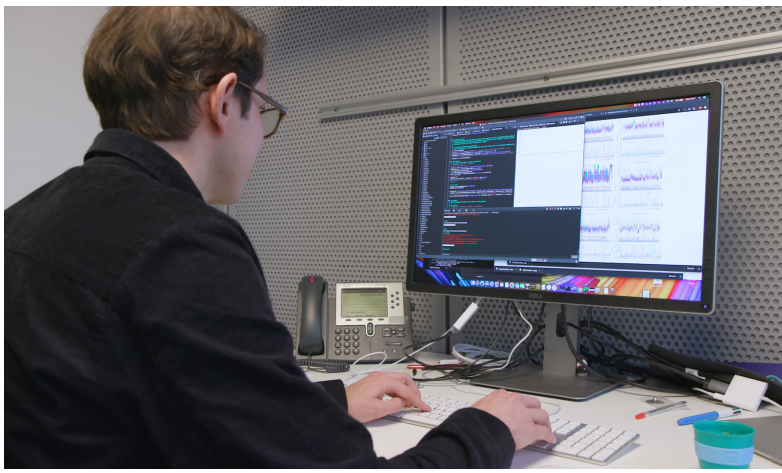
Pompeu Fabra University and Alicante University in a project called SYNTERRA, whose goal is to take the first steps in exploring ecological engineering, or terraformation of arid soil ecosystems. Within the context of planetary biology, EMBL Barcelona is also partnering with the Institute of Evolutionary Biology (IBE), the Barcelona Zoo, and the CRG, to create a global reference European Cryo-Zoo for a cell line biobank which supports the study of biodiversity at the omics level. EMBL Barcelona will create iPS cell lines for selected species, creating a unique cellular resource. These stem cells will be used in various in vitro tissue engineering projects, thus allowing comparative studies of tissue structure and function across multiple species.

To capitalise fully on the collaborative potential that is enabled through the local alliance, EMBL is in discussions with the CRG to establish a new joint activity that is expected to benefit not only EMBL and the CRG, but also the broader local and national research ecosystem: the EMBL-CRG Collaborative Environment for Data-Driven Predictive Modelling. Combining EMBL and CRG researchers with visiting fellows and sabbaticals, this exciting new initiative would be purely theoretical, or dry-lab, focused on computational modelling and related topics and thus be a key part of EMBL's distributed initiative to strengthen theory within this EMBL Programme.

EMBL-EBI

EMBL's European Bioinformatics Institute makes the world's public biological data freely available to the scientific community via a range of data services and tools, whilst performing basic research and providing professional training in bioinformatics. **EMBL-EBI Services** maintain and openly host more than 40 core biological **data resources** such as the European Nucleotide Archive (ENA), UniProt, Ensembl and InterPro, as well as emerging resources like the BioImage Archive, which continues to be developed to serve as the central bioimage data repository for the scientific community. These databases and tools help scientists share data efficiently, perform complex queries and analyse the results in different ways. Included within these data resources are data on the genome, proteome, cell types, literature and many more. The use of EMBL-EBI's websites continues to grow exponentially, with data resource websites accessed by the global research community on average **64 million** times per day in 2019. At the close of the year, EMBL-EBI had more than 300 petabytes of data storage capacity. EMBL-EBI data services are used either directly or indirectly by nearly every life scientist in the world. **EMBL-EBI Research** performs active data science research in biology and broadly mirrors the areas of EMBL-EBI's data services. Independent group leaders use the large-scale data and associated compute to make novel inferences of the world.

EMBL-EBI is situated on the Wellcome Genome Campus in Hinxton, Cambridge, UK, alongside the Wellcome Sanger Institute, a charitably funded, genomic research centre focused on understanding the role of genetics in health and disease. This campus is one of the world's largest concentrations of scientific and technical expertise in genomics. EMBL-EBI has had a long-term partnership with the Wellcome Sanger Institute, with the proximity between both institutes permitting the fostering of close collaborations such as the Darwin Tree of Life Project, an effort to sequence 66,000 UK species and where EMBL-EBI will play a key role in the annotation and distribution of this collected data.



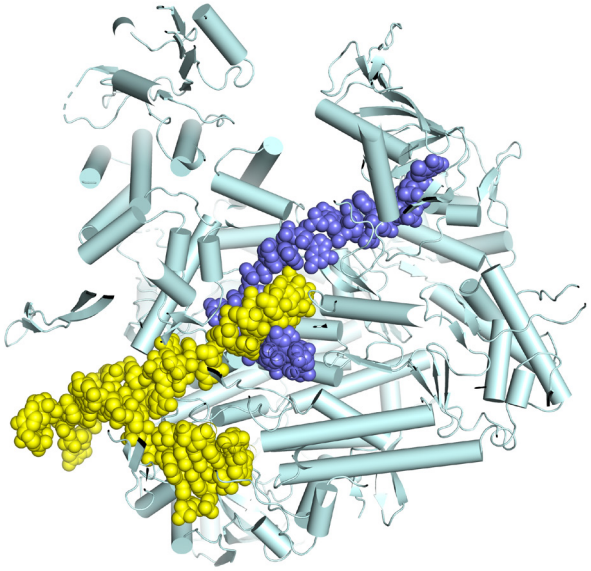
The early adaptation of the EMBL-EBI SARS-CoV-2 Data Hubs to organise the flow of SARS-CoV-2 outbreak sequence data from Europe and beyond and provide comprehensive open data sharing for the European and global research communities is a further example of the benefits that accrue from these collaborations.

To provide for the growing volumes of biomolecular data, the diversity of biological applications, and the diverse needs of a growing and global scientific community, EMBL-EBI will focus on five strategic priorities which aim to (i) increase the usage, utility, and application of bioinformatics; (ii) extend collaboration and coordination activities; (iii) grow the culture of continuous improvement to maximise efficiency; (iv) build bioinformatics capacity and capability; and (v) support the global sustainability of biomolecular resources. This structured approach to change also helps to focus and distribute resources sensibly, while building on EMBL-EBI's strong foundations as a technology innovator, cross-sector collaborator, and neutral intermediary across various communities. One new initiative EMBL-EBI will implement in the next EMBL Programme is a bespoke, multi-component service, the Genomic Medicine Platform, that will engage with individual national healthcare initiatives, to advise and proactively transfer knowledge and technology into those EMBL member states that have embarked on bringing precision medicine into their healthcare systems.

EMBL Grenoble

EMBL Grenoble is situated on the European Photon and Neutron (EPN) Campus, along with three other research institutes, the European Synchrotron Radiation Facility (ESRF), the Institut Laue-Langevin (neutron scattering), and the Institut de Biologie Structurale (IBS). Operating as the Partnership for Structural Biology (PSB), these institutes create a dynamic and multidisciplinary environment that provides a uniquely comprehensive range of structural biology platforms for both in-house research and external users. EMBL Grenoble and the ESRF jointly develop and operate the beamlines for macromolecular crystallography (MX) and small-angle X-ray scattering (SAXS). After a long shutdown for refurbishment, the ESRF restarted in early 2020 as the world's first high-energy, fourth-generation synchrotron. The increase in brilliance and coherence of the X-ray beams by up to 100 times, opens up new exciting opportunities including microsecond-scale serial crystallography and high-resolution X-ray imaging. In addition, EMBL Grenoble participates in a joint cryo-electron microscopy facility on the EPN campus, currently with one Krios machine, that, given the power and importance of this technique, is likely to develop further in the future.

A particular strength of EMBL Grenoble is its leading expertise in designing and building automated sample-handling instrumentation for synchrotron MX and SAXS, providing innovative technologies that benefit the structural biology community worldwide. The same expertise is now being applied to cryo-EM sample preparation. High-throughput methods have also been introduced upstream of data collection, including the unique CrystalDirect system which performs automated crystal mounting and cryo-cooling. This has prompted development of highly efficient, fully automated crystallisation to structure-determination pipelines that are being exploited for large-scale ligand screening campaigns by academia and the pharmaceutical industry, as an aid to drug development.



Research at EMBL Grenoble focuses on structural biology of complexes involved in RNA biology, gene-expression, signalling, and host-pathogen interactions, mainly in eukaryotic systems. EMBL Grenoble uses the full spectrum of structural biology technologies available on the site, as well as proteomics and cell biology approaches. Many projects have developed a translational aspect in collaboration with EMBLEM.

With the opportunities offered by the new synchrotron source, as well as by the rapid developments in cryo-EM, EMBL Grenoble is in the exciting position of being able to drive forward a future in integrated structural biology with broad applications in fundamental and translational research. Additional services that should be developed include *in situ* cryo-EM tomography, serial crystallography, molecular and ligand modelling, and X-ray imaging. Reinforced or newly formed links with the Université Grenoble Alpes (UGA), the French Alternative Energies and Atomic Energy Commission (CEA), and the Institute for Advanced Biosciences (IAB) in Grenoble can help drive forward the scientific directions, particularly in infection biology, planetary biology, human ecosystems, and microbial ecosystems.

EMBL Hamburg

EMBL's unit in Hamburg has existed since the founding of the **laboratory** to pursue a long-standing aim to harness the enormous potential of synchrotron radiation for applications in the life sciences, in a strategic alliance with the Deutsches Elektronen-Synchrotron (DESY). EMBL Hamburg operates its own synchrotron radiation beamlines for applications in macromolecular X-ray crystallography (including a new instrument dedicated for time-resolved studies) and small angle X-ray scattering for applications in the life sciences, for use by external research groups, mostly from EMBL member states. EMBL Hamburg also operates an associated Sample Protein Characterisation facility, suitable for a broad range of mostly biophysical characterisation approaches and automated crystallisation and also participates in the operation of a laboratory for sample preparation for experiments on the European X-Ray Free Electron Laser (X-FEL). The current beamlines at the PETRA III storage ring, representing one of the most powerful synchrotron infrastructures globally, provide robust, high-end services to a large and growing user community. EMBL Hamburg also supports the wider scientific user community through additional service activities such as software suites for structural analysis, as well as various technical developments on beamline and instrument operation.

The main research focus of the Hamburg Unit, in cooperation with research groups from the neighbouring Center for Structural Systems Biology (CSSB), is in the field of studying infection processes from pathogenic bacteria by structural/functional approaches. Research programmes at EMBL Hamburg address questions such as the structures of membrane transport proteins, complex networks and pathways such as the influenza virus infection cycle, and advanced modelling based on core principles of protein structure and dynamics. EMBL Hamburg also has strong research links with groups at the Universität Hamburg, the Center for Free Electron Laser Science (CFEL), and the Hamburg Advanced Research Centre for Bioorganic Chemistry (HARBOR).

EMBL's strategic partner in Hamburg, DESY, has recently started to plan a major upgrade of the present synchrotron PETRA III to PETRA IV, which is expected to have world-leading capability in terms of spectral brilliance and coherence, with an expected completion around 2026/27. EMBL Hamburg, which is centrally involved in the planning especially for applications in the life sciences, views this as a major future opportunity for both upgrading research activities where there is already a strong, long-term record (X-ray crystallography, SAXS) and also for further diversifications, where the application of different structural and imaging technologies to related questions and systems has the potential to allow researchers to achieve a holistic and integrated view of organisms. Key to these endeavours is the availability of correlated multiscale and dynamic structural information from molecules and cells to tissues and organisms, where EMBL Hamburg is planning to contribute by establishing a new activity in X-ray imaging, with superior perspectives for thick specimen penetration and throughput.

As EMBL Hamburg is presently located in different areas of the DESY campus, the unit plans to bring together all activities for the operation and use of research infrastructures under one roof: a new Hamburg Hub for Integrative Structural Biology (HISB), during the timeframe of the next EMBL Programme. This applies in particular to the operation and constant further development of synchrotron measuring stations, including the operation of online data evaluation and data interpretation, relevant research projects and the operation of a future user facility for electron microscopy and tomography of biological samples. The HISB project is embedded into one of the largest city development projects in Europe, the new "Science City Bahrenfeld".

EMBL Heidelberg

EMBL Heidelberg is the first and largest of EMBL's six sites and brings together the most diverse range of life sciences disciplines including molecular, cellular, and structural biology. The current units are Cell Biology and Biophysics, Developmental Biology, Genome Biology, and Structural and Computational Biology.

Many of the directions in the new EMBL Programme will need to bring together various technologies and fields of research in specialised laboratories of the planned Molecular Biology Centre for Human and Planetary Health, in order to examine organisms, microbial communities, and ecosystems at the molecular level. EMBL Heidelberg plans to expand its research into specialised laboratory systems that can be environmentally controlled (micro- and mesocosms) in order to test the findings of global field research in nature, with specific experiments that allow for long-term investigation of organisms and their ecosystems under near-natural, but controlled, conditions.

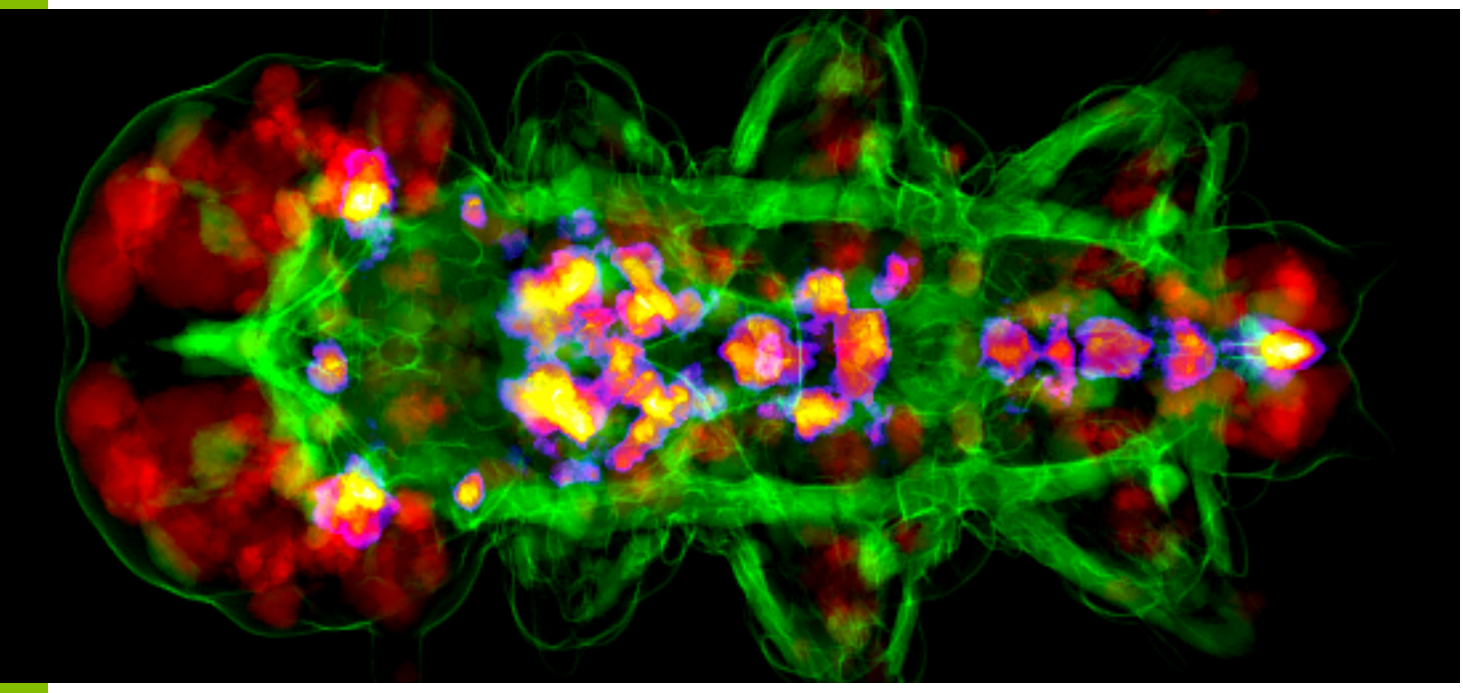
To achieve a molecular understanding of complex ecosystems, it is necessary to integrate innovative molecular biological methods of genomics, transcriptomics, proteomics and metabolomics, and state-of-the-art imaging technology across several spatial scales, and to analyse the resulting large data volumes with bioinformatics. Here, EMBL Heidelberg plans to develop new 'integrative spatial omics' methods for the quantitative analysis of DNA, RNA, proteins, and metabolites in cells, tissues, organisms, and biocoenosis and of their spatio-temporal changes due to critical environmental parameters.

Experimental scientific services at EMBL Heidelberg are currently driven by the Core Facilities which enable scientists to access cutting-edge technologies and the expertise required to effectively gain high-quality data. Services which span imaging and structural biology techniques will be further enhanced by the opening of the EMBL Imaging Centre in 2021. The ability to develop new technologies within the EMBL Imaging Centre will be further accelerated through technology development partnerships between on-site research groups and industry partners, with the aim to be the European hub for introducing the latest pre-commercial imaging technologies to ground-breaking life science applications. Spin-outs, public-private partnerships, and proof of concept projects generated by the scientific activities within molecular-level ecosystems for the development of new technological advances (such as molecular sensors for environmental measurements, biomarkers that can enable evaluations of ecosystem collapse, new drug targets as well as software and databases that allow for modelling of human and planetary ecosystems) are also envisaged.

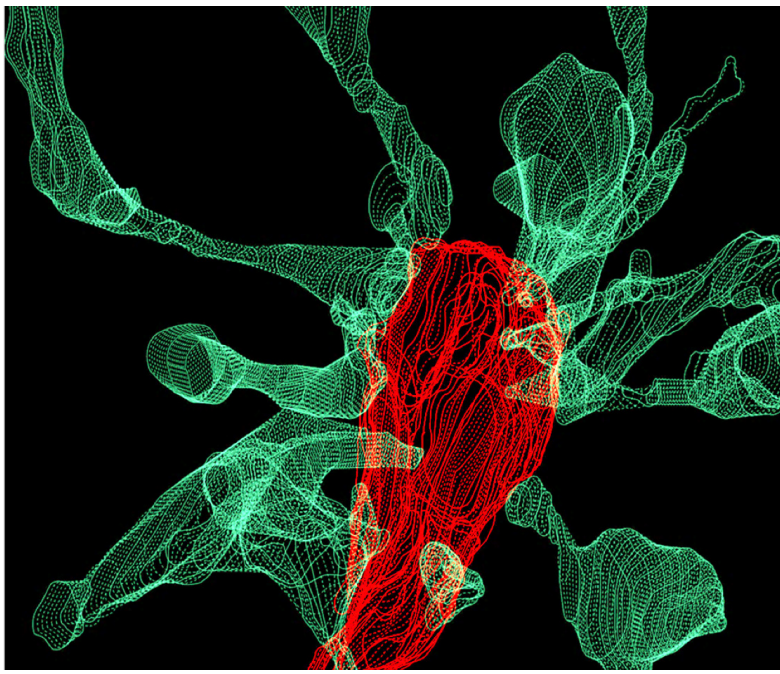
With the planned growth in data sciences across the organisation, EMBL Heidelberg will enlarge its IT infrastructure to support centres in Heidelberg and the other sites, which will enable the management, integration and interpretation of data for molecular-level ecosystems, with emphasis on machine learning and artificial intelligence approaches. Taking advantage of the large data volumes and novel experimental labs, will be the Theory at EMBL strand, aimed

at uncovering the general principles in living systems on Earth. These capabilities will be key to EMBL's role in German initiatives such as Cyber Valley Health in Tübingen and EMBL's leadership in the establishment of the German Human Genome Phenome Archive. EMBL Heidelberg also houses much of EMBL's external training, with the vast majority of EMBL's on-site courses and conferences held within the Advanced Training Centre. Many new courses and conferences are planned in the topics that emerge from the study of ecosystems at the molecular level, to train researchers in the latest methods in the life sciences.

Many bilateral links between scientists at EMBL and other Heidelberg research institutions have been established. Alongside these, EMBL participates in several larger projects with the German Cancer Research Centre (DKFZ) and the Max Planck Institute for Medical Research. A joint venture with the Medical Faculty of the University of Heidelberg which drives innovation and its translation into medicine is also facilitated by the Molecular Medicine Partnership Unit (MMPU), which will be furthered under the human ecosystems direction.



EMBL Rome



Research at EMBL Rome focuses on the interface between epigenetics and neurobiology. In particular, the unit provides an anchor for neurobiology research across all EMBL sites and has extensive links to chromatin biologists, *in vivo* imaging technologists, and bioinformatics experts across the organisation. Key areas of inquiry at present include understanding how internal brain states (e.g. hunger, activity, anxiety, territoriality, social experience) adapt to drive context-specific, instinctive behavioural programmes and how these internal states impact sensory processing. The unit is also working to resolve long-standing questions about the causal relationship between chromatin marks (e.g. DNA methylation, histone modifications) and gene transcription and trying to understand how these mechanisms can store and transmit information about the environment across generations. Several joint projects between epigeneticists and neurobiologists at the unit are exploring the peculiar role of chromatin modifications in neural tissues and plasticity and these links will be deepened with additional faculty hires at the interface between these fields during the next EMBL Programme. *In vivo* research in the laboratory mouse is a core strength of the unit, supported by a series of core facilities, including advanced gene editing, viral gene delivery, and imaging approaches. Recent advances in in vivo gene editing technologies have dramatically increased the precision and speed with which genetic and epigenetic perturbations can be introduced into the mouse genome, including viral-mediated cell-type specific knockout and tagging, and humanised and point mutant mice and these are routinely produced at the unit for internal and external researchers.

As part of a major programme to enhance links to Italian research centres, EMBL Rome has established a three-way joint interdisciplinary postdoctoral programme with EMBL-EBI and the Italian Institute of Technology (IIT) in the areas of nanotechnology, genomics, and systems neuroscience. In addition, EMBL Rome has close local links and collaborations with Sapienza University with whom it runs a highly successful seminar series in epigenetics and neurobiology. As part of a strategy to build on these collaborations and leverage its unique expertise linking genomics, environment, and neuroscience, EMBL Rome plans to establish a Centre for Human Brain Phenomics. This bioinformatics initiative will carry out research to develop novel methods to link human genetic and environmental variation to brain and behaviour-relevant phenotypes and make these available to the research community. Discussions are in progress that would enable the Centre for Human Brain Phenomics to be established as a partnership between EMBL Rome and the IIT-Sapienza Centre for Life-Nano Science with whom it would share infrastructure, scientific interests and public engagement capacities. The close integration of EMBL Rome's Centre for Human Brain Phenomics with IIT and Sapienza will provide critical mass and complementary expertise and will sow the seed for further life sciences research initiatives in Rome.

Although discrete entities in their own right, EMBL's six sites are highly connected through scientific collaboration, overlapping operational processes as well as professional and personal networks forged through EMBL-wide initiatives. Each site contributes to EMBL's success by adding its distinct specialism and expertise. These specialisms allow the sites to easily integrate into their own local scientific landscapes. Thereby, through local collaborations, partnerships and engagements, the sites continue their positive exchanges with local institutes, regions, and national initiatives.

Going forward, EMBL will both deepen its interactions on these six sites and also broaden the interface to the wider life sciences expertise across Europe. The deepening will be due to joint programmes in regional, national, European, and global contexts, aiming to deliver on EMBL's scientific missions from a transnational European base. The broadening will be due to a series of innovations: firstly, increased research collaborations with both partner institutes across Europe and to diverse European collaborators; secondly, via revitalised or new instruments explicitly with collaborative components, such as EIPOD and ARISE programmes; and thirdly, via the new aspects of sabbaticals and secondments with member states. By working together across Europe, with these six physical sites united in a single legal structure, and with deep connections across all its member states, EMBL will deliver a new era of critical scientific missions for the benefit of society.

With the ambitious scientific directions set out in the new Programme, EMBL will strengthen European science, tightly connecting its member states and providing new services, technologies and expertise, from molecules to ecosystems. Ultimately, this knowledge economy should enable a comprehensive understanding of the molecular basis of human and planetary health, and the emergence and spread of disease in populations and individuals. These discoveries, including improved understanding of biodiversity and ecosystems, are vital to foster change at the public and political levels. In doing so, EMBL's aim is to help Europe become the scientific leader in this new interdisciplinary area, to help both human and planetary health.

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