EMBL

The EMBL Programme 2022–2026

Molecules to Ecosystems

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 by making fundamental discoveries in molecular biology that fuel a rich economy of knowledge, training researchers and research leaders at the leading-edge for academic and industrial research, as well as by developing new technologies that meet societal needs in the areas of medicine, agriculture, and ecology.

EMBL is Europe's only intergovernmental organisation for life science research. Established to advance the study of molecular biology across Europe, to nurture young talent, new ideas, and technologies, EMBL is constantly evolving and innovating. EMBL undertakes pioneering research and provides cutting-edge biological services and infrastructures that are essential for European science. EMBL's 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 classical molecular biology, EMBL has played a leading role in the rapid evolution of modern biology, participating in major breakthroughs in the realms of structural, cellular and developmental biology, in the birth of genomics and molecular genetics, and – more recently – in integrative approaches and systems biology. EMBL scientists have discovered many of the fundamental principles by which organisms are built, including how their building blocks are generated, modified, and brought together in time and space. EMBL research has generated cutting-edge facilities to serve member states and beyond.

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 scientists who then move on to become global leaders in Europe and around the world. EMBL has played a major role in laying the groundwork of the current scientific revolution, and has spurred the development of many of the tools that scientists use today, including cryo-electron microscopy (cryo-EM), genomics, and advanced imaging. The vital nature of these technologies is aptly illustrated by their global deployment in the current fight a ainst COVID-19 and other diseases.

Molecules to Ecosystems, the New EMBL Programme 2022–2026

EMBL strives to be at the forefront of modern biology and to build the foundations for future success. The curiosity-driven scientific discoveries made at EMBL serve as the basis for the next generation of applications and discoveries, driving new technology developments and service provision.

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 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 human and planetary health.

Most molecular biology research has focused on studying organisms that are isolated in a laboratory setting, where environmental variation can be minimised. However, life does not happen in isolation, but in the context of communities where organisms interact with each other and respond to constantly changing physicochemical conditions. Due to incredible advances in technology and quantitative data generation, molecular biologists now have the capacity to follow the dynamics of living matter in real time and at multiple scales. Gaining molecular and mechanistic insights to understand how organisms respond to changing environments, and how they influence their environment, are at last feasible. This will be of fundamental importance in achieving a true understanding of the basis of life. It will also be relevant to the important issue of scientific reproducibility, as differences in biological samples due to subtle environmental parameters can influence the interpretation of experimental data.

The challenges facing life on Earth today are huge: the spread of infectious diseases, the loss of biodiversity, environmental degradation, and climate change. To take on these challenges, drastic improvements are needed in understanding the processes of life in their natural context. A better understanding of life means a greater ability to preserve it. EMBL will seize this unique opportunity at a critical time for society, and will undertake bold and potentially transformative discovery science that will also be a force for good for humankind and the planetary ecosystem services that sustain us.

Through the new Programme, EMBL will build on its existing and globally recognised expertise in molecular biology to expand into new areas including planetary biology, human ecosystems, infection biology, and microbial ecosystems. Central to the research strategy will be the development of advanced data sciences and theoretical approaches. Through close collaborations with scientists from different domains and within all of EMBL's member states, this Programme will enable EMBL to build new bridges with disciplines, including ecology and epidemiology, 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 is well placed to fulfil its bold ambition of gaining a molecular understanding of life in context. In doing so, EMBL will continue to uphold its special responsibility to lead and coordinate European life sciences in its role as Europe's flagship life sciences research organisation. The new Programme will be a truly pan-European initiative, providing scientific services and innovation, and sharing expertise with all of EMBL's member states, while harnessing the strong and dynamic collaborations and networks of partnerships that EMBL has built over many years.

As 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 is uniquely positioned to deliver this ambitious and timely programme. 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 help EMBL's member states to better understand and address the planetary challenges of climate change, pollution, food security, and emerging pathogens.

Introduction

The Foundations of Molecular Biology

Molecular biology can be considered as the collective understanding of how the rich diversity of life on 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 organisms function, and has led to some of the greatest discoveries of the 21st century. Curiosity-driven research in molecular biology has provided humanity with 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 new treatments.

Modern biology is in a period of spectacular progress, accompanied by 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 for the design of drugs and the creation of innovative consumer goods. The discoveries of fundamental 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.

The Future of Molecular Biology

The Next Frontier

Over recent decades, remarkable molecular insights have been made in model organisms ranging from bacteria to animals, under defined lab conditions. However, living things do not exist in isolation. From plankton in oceans to 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 processes and mechanisms in order to understand how organisms function in their natural contexts.**

The Societal and Economic Value of Ecosystems

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.

One major reason for this is that the value of ecosystems to human welfare is severely underestimated. A study carried out by environmental scientists and public policymakers (Living Planet Report 2018; Costanza, R. *et al.* Changes in the global value of ecosystem services. (2014) Global Environmental Change 26: 152-158) estimated the notional economic value of **ecosystem products and services** (such as the provision of food, water, fuel, and other raw materials, the pollination of crops, and the prevention of floods or soil erosion) to be US$125 trillion per year. This value, and conversely the cost to society of losing these products and services if they are not protected, is around two-thirds higher than global GDP. These services also include benefits for human health: the destruction of the planet's ecosystems means that, for the fir t time in modern history, humanity faces the prospect of losing many of the benefits that medicine has brought, possibly jeopardising advances made over the past two centuries.

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

Scientists now have many of the molecular tools needed to address fundamental questions about **life in context**. 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 (Figure IN1). 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**.

Figure IN1 | Molecules to Ecosystems.
EMBL's ambitious new 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 Programme will incorporate novel areas of research and new technologies. It will also expand EMBL's horizons, creating a new era for the life sciences, while maintaining EMBL's core values of scientific excellence and fundamental research.

The new EMBL Programme will explore **life 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 (theoretical and experimental), epidemiologists, and environmental biologists, will be a critical component in better understanding environmental effects on molecular mechanisms and organism composition, symbiotic states, and host–pathogen interactions. Most importantly, to study life **across interconnected scales** (cells, tissues, 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 specialised equipment and staffed by dedicated personnel with technical and research expertise. EMBL will work in **partnership** with scientists from various field , 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.

EMBL researchers working in areas relevant to many of the new themes have held or planned topic-specific workshops to bring together interdisciplinary experts, discuss strategic synergies, and solicit guidance for EMBL's future plans, providing a rapid horizon scan of the scope and challenges in these research areas. EMBL also plans to establish focused advisory boards for some of the new scientific themes, whose support and direction will be critical in pursuing research questions that are of the most scientific value. To explore the feasibility of expanding EMBL research in these new directions, EMBL initiated a set of **pilot projects**. Some of these were newly conceived proof-of-principle projects, while others were extensions of existing projects relevant to the Molecules to Ecosystems research themes. The projects are described in the chapters of the full Programme, preceded by the pilot project icon <>.

Why 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 join forces and be at the forefront of the life sciences on the global stage. Professor Edith Heard was appointed as Director General of EMBL in 2019 by EMBL's 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 Europe's only intergovernmental organisation for life science research. Since its creation in 1974, EMBL's goal has always been to foster the development of excellent scientists, to enable discoveries in molecular biology that fuel a rich economy in knowledge, and to develop technologies that meet societal needs in the areas of medicine, agriculture, and ecology. Today, almost 1,800 personnel from more than 90 countries advance EMBL's activities across its six sites: Heidelberg (headquarters) and Hamburg in Germany, EMBL's European Bioinformatics Institute (EMBL-EBI) in Cambridge in the United Kingdom, Grenoble in France, Rome in Italy, and Barcelona in Spain. Each site offers a unique and highly complementary mix of research and services (Chapter 14: People, Processes, and Places).

The principle of regular staff turnover (nine-year rule) and EMBL's five-year programmatic funding enable the organisation to be agile and to evolve rapidly via the recruitment of talented scientists studying exciting questions in biology using cutting-edge approaches (Figure IN2). 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.

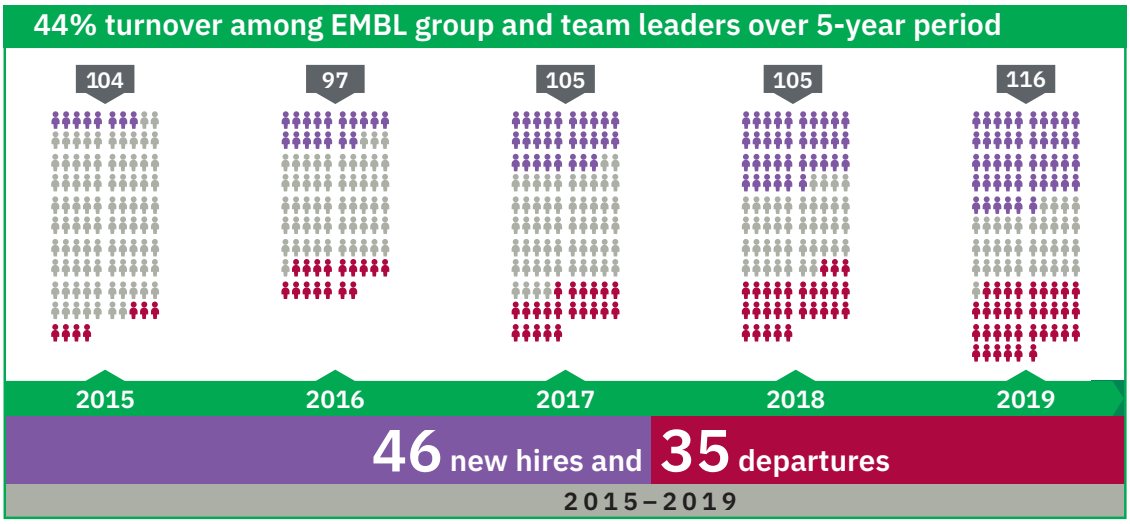


Figure IN2 | EMBL's dynamic turnover among group and team leaders.
In the five-year period up to and including 2019, nearly half of EMBL's group and team leaders joined EMBL (purple) or departed (red). This model, based on a nine-year rule, ensures that EMBL can quickly and seamlessly adapt and develop its scientific directions via the continuous intake of new group and team leaders.

EMBL's Missions and Achievements

Mission 1: To perform excellent fundamental research in molecular biology

EMBL's **overarching goal** is to understand the molecular basis of life. 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 high percentage of papers published and grants secured in collaboration with academic and industry research groups in EMBL member states and worldwide (Figure IN3).

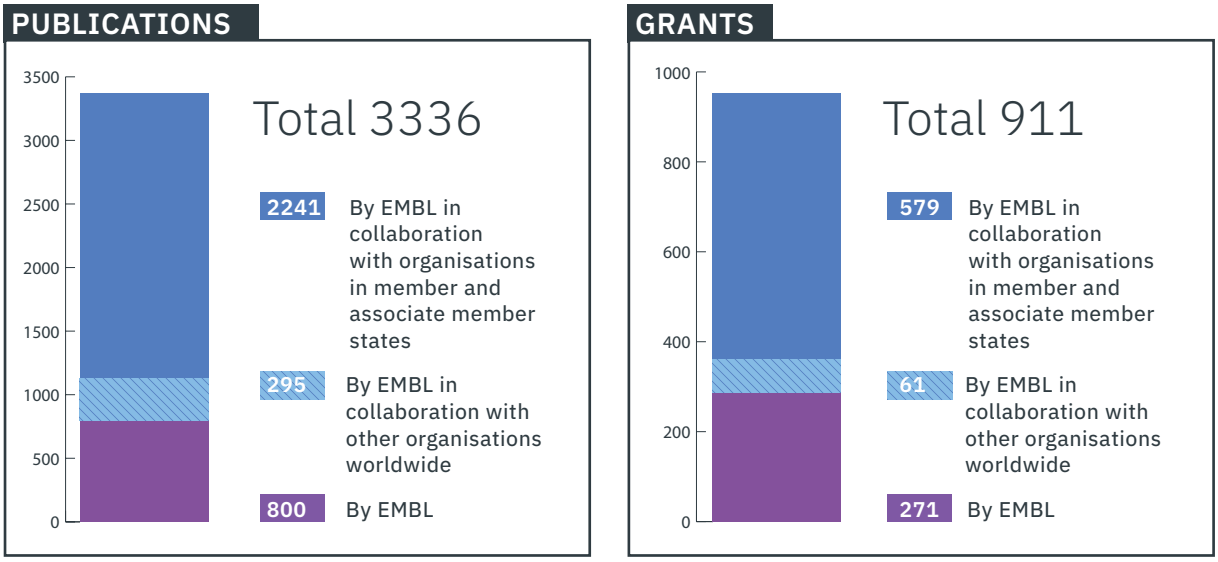
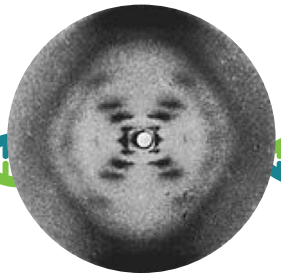


Figure IN3 | EMBL collaborations: publications and grants (2015–2019).
Of the 3,336 scientific publications by EMBL from 2015–2019, more than three-quarters (76%) were published as part of collaborations with other organisations worldwide, many of which are in member states. Among the 911 grants secured by EMBL during the same period, including 45 ERC grants, a similar proportion (70%) involved collaborations with organisations worldwide, with the majority of those organisations also in EMBL member states.

EMBL has a long and distinguished history of groundbreaking scientific achievements (Figure IN4). Among the most notable contributions is that made by Nobel laureates Christiane Nüsslein-Volhard and Eric Wieschaus, who unravelled the genetic and molecular mechanisms by which multicellular organisms develop. Such research has contributed to the subsequent understanding of the molecular pathways that are disrupted in the development of cancer. EMBL has also made significant contributions to the study of the fundamental units of life, such as the cell and its molecular components. For example, EMBL research has 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, groundbreaking technologies are also developed at EMBL, driven by fundamental biological questions. For example, cryo-EM was developed by Nobel laureate Jacques Dubochet 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.

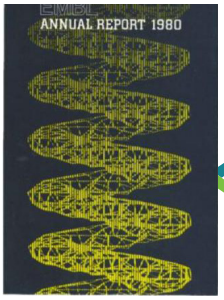


1953

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

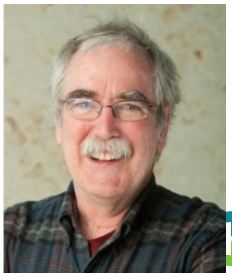
The first central depository of nucleotide sequence data in the world is founded at EMBL

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

Figure IN4 | The foundations of molecular biology and the birth of EMBL.
EMBL's foundations and successes have been built upon the discoveries and visions of its scientific predecessors. EMBL's future will rely on its expertise, experience, and collaboration with the scientific community to drive forward a new era of life science research.

Mission 2: To offer vital services to scientists in the member states and around 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-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 each site, 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. One recent illustrative example is the discovery of 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 that provide cost-effective and efficient a cess 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, genetic and viral engineering, histology, gene editing and embryology. These services are provided by EMBL experts who also share their knowledge with the broader scientific ommunity.

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. Cofunded by the EU's Marie Skłodowska-Curie Actions, the EMBL Interdisciplinary Postdocs (EIPOD) Programme provides training and career development opportunities for young researchers. A pioneering 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 advance 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 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 Instruct-ERIC. Via its Partnership Programme (Figure IN5), EMBL has helped to establish institutes of excellence spanning the 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.

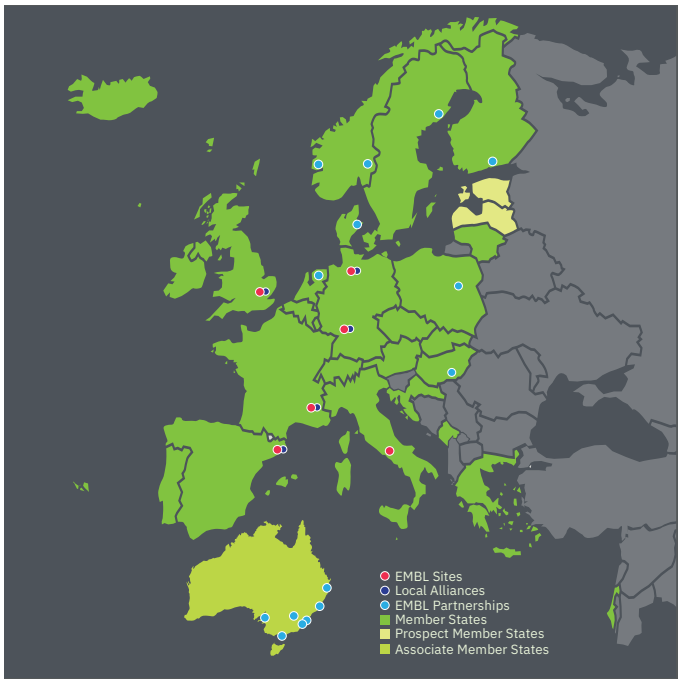


Figure IN5 | EMBL member states, partnerships, and local alliances.

EMBL works to establish links and promote collaborative relationships between EMBL and institutions in the EMBL member states, including EMBL's successful network of partnerships (green dots). The aim of these partnerships is to increase integration and participation of national scientific communities in EMBL's research and activities and also support member states to recruit excellent international talent. EMBL's local alliances (blue do1ts) represent close collaborations with EMBL's sites (red dots) and are instrumental in the creation of a critical mass of life sciences research within the local area.

Moving Towards the Next Frontier

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 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 (Figure IN6). 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 en erprises to investigate life in the context of its environment.

EMBL researchers will build upon experience and models from previous research projects. EMBL has initiated and participated in collaborative expeditions with the Tara Oceans Consortium to monitor oceans around the world, revealing an extraordinary and previously unexplored biodiversity. Studying the impact of climate change on biodiversity is vitally important, given the role many ecosystems play in regulating climate. Researchers at EMBL have shown that the relative abundance of bacteria and fungi in terrestrial topsoil is critical for nutrient cycling and may also have a profound impact on the appearance of antibiotic resistance genes. Understanding the molecular basis of antibiotic resistance transmission in natural contexts is a key endeavour for EMBL scientists. Computational tools, including lightweight apps, have also been developed by EMBL scientists to enable genome-based surveillance of infectious diseases. Scientists across EMBL and its member states are carrying out a range of other research to study the emergence and spread of pathogens. This is highly relevant, given that biodiversity loss facilitates the emergence of new pathogens and frequently increases rates of transmission. Finally, in the context of human health, there is now a plethora of studies demonstrating correlations between gut microbiome composition, nutrition, and common disorders such as metabolic disease or cancer. The hope is that these correlations can be translated into therapies using mechanism-based approaches. Ultimately, **EMBL's future discoveries, made through a combination of research in the field and in the laboratory, will provide key mechanistic insights with potential applications**.

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

The powerful combination of EMBL's experience, expertise, and position prime the organisation to lead this revolutionary endeavour in science. EMBL will remain a stronghold of molecular biology research and will utilise its strengths in this field to drive scientific discovery in new areas. Research in molecular biology will always be EMBL's focus and area of excellence. 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.

Why Now? An Optimal Time for Investment

Measuring and understanding community dynamics, interactions including infections, the principles underlying phenotypic variation, and the responses of organisms to changing environments are challenges that have hardly been tackled at the molecular level.

Early attempts to measure and understand the reciprocal interactions between environment (nurture) and genotype (nature) to explain phenotypes were made by developmental biologist Conrad Waddington, following Darwin's explanation of evolution through heritable variation and natural selection, and Mendel's laws of genetics. For much of the 20th century, genetic determinism prevailed, and the impact of environmentally induced phenotypic variation of any kind was recognised, but largely ignored experimentally. This was due to the limited quality and quantity of biological data available, and to limited experimental possibilities at the time for perturbing living systems. The additional levels of complexity brought about by the integration of environmental factors at the molecular level have meant that much of molecular biology has focused on reducing environmental fluctuation to a strict minimum, in order to study the impact of genetic and stochastic variation on phenotypic variation.

Over recent decades, remarkable molecular insights have been made in model organisms at EMBL, from bacteria to animals, using defined lab conditions. These have paved the way for EMBL to tackle the urgent need to understand life in context. Emergent technologies are now being developed to collect measurements of ecosystem components at unprecedented volumes, from molecules to cells, organisms, populations, communities, and their chemical and physical environments. Exceptional advances in computational power, AI, and causal reasoning have also enabled the rigorous analysis and creative integration of these data. This tremendous technological progress in the life sciences, coupled with the capacity to gather and analyse data of greater scope, resolution, and quality than ever before, means that measurements of environmental context can be collected in systematic ways, allowing the integration of this new level of complexity into the study of biology. **With these technological and computational advances, Europe – via EMBL – will lead the development of a new way of performing molecular biology: the study of biological components in their natural context**.

Programme Roadmap

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 contexts (Figure IN6). Molecular processes and mechanisms underlying responses to environmental changes can be studied at multiple biological scales: from exploring the molecular components inside a cell, to 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 the selection of specific areas of focus based on their potential for scientific opportunity when coupled with current advances in experimental technologies and data sciences.

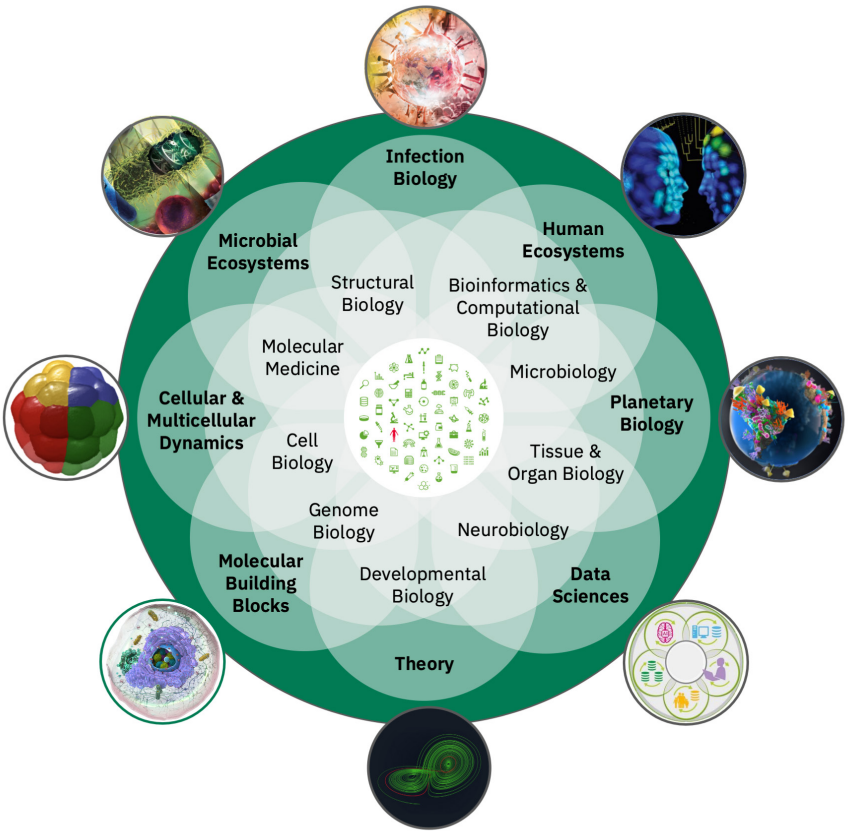


Figure IN6 | The research themes of the Molecules to Ecosystems Programme.
EMBL's current and new research themes are represented by the inner and outer rings, respectively. EMBL will build upon its existing strengths and expertise to conduct and enable collaborative, interdisciplinary research in these areas with scientists in EMBL's member states and beyond.

Section II of the full Programme begins with the first research theme of **Molecular Building Blocks in Context**, which 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 molecular 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 feed back to one another, lies at the core of EMBL's expertise.

EMBL's approaches for gaining a mechanistic understanding of the genetic and environmental sources of variability in living systems, and understanding responsiveness at the cellular level and in a multicellular context, are highlighted in the theme **Cellular and Multicellular Dynamics of Life.** EMBL will use novel experimental strategies, cutting-edge technology developments, and predictive computer modelling to measure and perturb dynamic living systems and their interplay with the environment. Increasing knowledge about the robustness and plasticity of embryonic cell clusters, bioengineered tissues, and model systems 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 f 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 and human health. The current COVID-19 pandemic highlights the urgent need to obtain insight into the emergence and spread of infectious diseases. In the new Programme, EMBL will integrate multidisciplinary experimental and computational approaches to understand how pathogens and their hosts interact. These approaches will aid the development of 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.

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.

Spanning multiple ecosystems, the **Planetary Biology** research theme will enable scientists to understand at the molecular, cellular, organismal, and population levels how microbes, algae, plants, and animals interact with each other and respond to natural and anthropogenic environmental changes. The main objectives will be to recognise and understand phenotypic changes that are environmentally induced in nature, using the plethora of tools available for molecular, structural, genomic, cellular, and developmental biology, and the powerful technologies that enable visualisation and perturbation of processes. TREC22, EMBL's flagship project to explore European land–water interfaces including coastlines, rivers, and lakes, in partnership with scientists in the member states, is a central part of this theme. 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 the state of ecosystems.

All these research themes will contribute to the growing volume and heterogeneity of the biological and environmental data that are necessary for 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** programme, which will lie at the heart of EMBL's research 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 methods for studying life in context. The complexity of biology necessitates theoretical approaches. This programme 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. Conceptual theories 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 **Scientific Services** are set up to respond dynamically to the needs of research communities. EMBL's experimental and data services will be developed and integrated to form a central pillar of the new Programme:

- 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.
- A wide array of **perturbation** approaches will be critical for mechanistic tests. EMBL's ***in vivo* gene editing service** will enhance the study of genetic variation in animal models, and will provide platforms for viral-mediated editing to offer insights into mechanisms *in vivo.*
- New cross-site **chemical biology services** will help scientists explore the effects of environmental factors and novel drug targets.
- 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 embrace the new research themes in providing state-of-the-art scientific training for EMBL fellows, including predoctoral and postdoctoral researchers. The Course and Conference Programme will also reflect the new themes from the EMBL Programme, and the 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 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 impact and reach of EMBL's training activities, while also contributing to environmental initiatives at EMBL.

Innovation and Translation at EMBL will be expanded to encompass the translational potential of the new scientific directions in 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 establish new links and initiate collaborative relationships between scientific communities in Europe, especially in the new scientific areas of the Programme. EMBL will foster additional 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 EC, including the EC-led project to establish the European Open Science Cloud (EOSC).

Section III of the full Programm outlines plans for EMBL's **People, Processes, and Places**, which 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 firm y embed green working policies and practices. Through local collaborations, partnerships, and engagements, each EMBL site will continue research activities 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 to help increase communications capacity in its member states.

Critical Success Factors

EMBL's history of groundbreaking scientific achievements and other successes comes from a unique blend of ambition, insistence on excellence, cooperation, and openness across disciplines, all of which contribute to a distinctive scientific culture. These factors will embody every part of the new EMBL Molecules to Ecosystems Programme and will be key to its success.

A Virtuous Circle of Novel Research, Technology Development, and Services

EMBL has longstanding expertise in technology development in molecular crystallography, microscopy, genomics, and microfluidics methods, with several important contributions and successful examples of commercialisation. This is fuelled by EMBL's unique capacity to host research groups in proximity to facilities for the creation of instrumentation and software. The collaborative spirit and shared desire to creatively solve problems promotes a virtuous circle (Figure IN7). Research questions drive technological developments that, in turn, drive further research. These technological developments can then be made available to the scientific community via EMBL scientific services. The broad range of research areas and the juxtaposition of curiosity-driven researchers and experienced engineers who are able to build new equipment, often from raw materials or individual components, makes EMBL unique among life science research organisations in Europe. The technology powerhouse that sustains this virtuous circle is essential to EMBL's continued success. EMBL has developed and uses an impressive range of technologies, and the full Programme document includes chapters referring to the application of several technology developments, which are showcased in **Technology Development Boxes**. In the new Molecules to Ecosystems Programme, many new and ambitious technologies and services are being proposed and will be shared with EMBL member states.

A Guide to Technologies at EMBL (Appendix I in the full Programme) provides brief descriptions of the technologies referred to in this Programme, covering the areas of structural biology and imaging, computational methods, and omics technologies, as well as the convergence of these fields with one another.

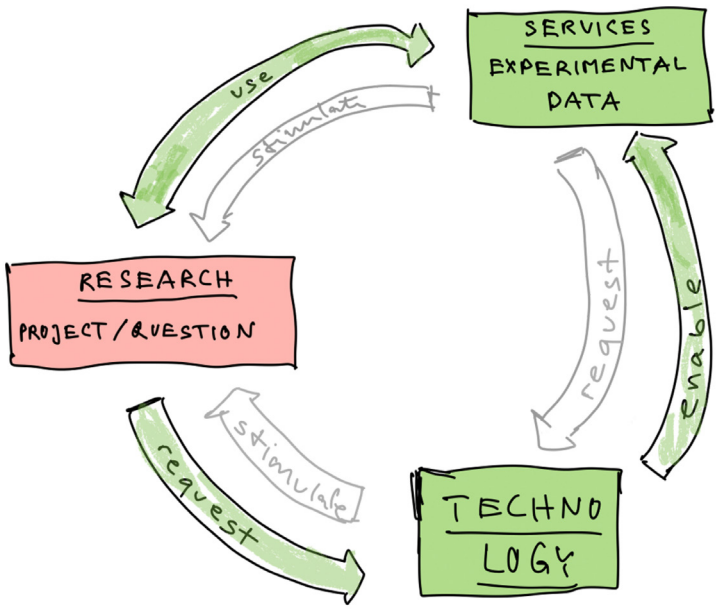


Figure IN7 | The EMBL research–service–technology virtuous circle.

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.

Interconnection Between Experimental and Computational Science

EMBL's computational research spans multiple areas and all EMBL units and sites. Over 50% of researcher time is spent on computational research, and there are dedicated computational group leaders present in nearly all units. This deep commitment to computational research is important, as much of the integration between research themes is achieved computationally, by analysing the results of well-designed experiments. EMBL's research expertise is enabled by a clear view of the most important prevailing research questions, a view that benefits from EMBL's programme of international courses and conferences. Key to EMBL's future success will be maintaining this close alliance between experimental research, the development of new tailored mathematical algorithms, and AI-based approaches, and nurturing the next generation of scientists who combine experimental and computational expertise in their research.

Open Science

Open science is the movement to make scientific research accessible and transparent, and to remove barriers that may restrict the availability of research to privileged groups or to those prioritising financial gain. Motivated by a desire for science that is high quality, more efficient, and more useful for society at large, open science is promoted by a range of actors, including the EC, EMBL member states, funding bodies, and many scientists themselves.

This motivation and commitment to open science is shared by EMBL. The organisation has a special responsibility to be a leader and innovator in open science, not only in terms of the scientific results it produces, but also in the way research in molecular biology is performed. EMBL also provides scientific facilities and data services that are crucial for all European life science research, thus connecting Europe with global open

science infrastructures. Open science practices at EMBL comprise policies that cover all scientific outputs. This includes the deposition of data in open data resources, publishing preprints and accepted manuscripts to Europe PMC (EMBL's database of open access literature), and making open source software available. The way EMBL delivers open science will be a template for open science practices for life science organisations across Europe.

Interdisciplinary Research

As our understanding of the living world grows and new technologies for the life sciences emerge, there is an increasing need for interdisciplinarity. EMBL has long embraced the integration of researchers from a variety of biological disciplines, as well as physics, chemistry, computer science, and engineering science, into multidisciplinary teams in which traditional silos are broken down. EMBL has always combined groundbreaking curiosity-driven research with innovative technology development: an approach that has been made possible by the collaboration of experimental life scientists, technology developers, and data scientists at EMBL. The new Programme will require an even greater commitment to interdisciplinary collaborative research, with diverse areas such as **ecology, epidemiology, public health, zoology, toxicology, and theory**. Ultimately, a critical mass in many new disciplines will be needed at EMBL for the provision of new expertise and facilities. This will also foster connections with experts in other fields, whose work may benefit from interactions with molecular biology research and its methods.

Intensive Collaboration and Coordination

Collaborative research has become more prevalent globally, across all scientific disciplines, over the past 50 years. Tackling grand societal challenges such as climate change, food security, and threats to human health, as well as dealing with increasingly data-rich and computationally heavy projects, requires intensively collaborative work, which cannot be done by a single individual, laboratory, or company. The new themes of the Programme will build on EMBL's existing strengths and expertise, but will need to bridge disciplines more than ever before. EMBL can succeed in this endeavour thanks to in-depth **collaborations with scientists in EMBL member states** and around the world. Together, these collaborations will enable the development of unexplored concepts, novel tools, and innovative technologies. **EMBL aims to reach out across scientific domains and forge strong links with academics, governments, policymakers, and citizens to co-produce and co-create a new era of biology that will provide a molecular understanding of ecosystems**.

Sustainability Practices as Drivers of Green Research

Given EMBL's scientific commitment to the environment in its new Programme, sustainable practices are being strengthened across all of EMBL's sites, driven by a recent **Green EMBL** initiative. An Environmental Officer was recently appointed to ensure the implementation of these practices. The novel discoveries and tools expected from the new Molecules to Ecosystems Programme should make EMBL a model for research and services in ecologically relevant areas, as well as creating an environmentally friendly workplace. EMBL aims to be a leader in developing new ways to carry out environmentally conscious, responsible research practices.

In the longer term, EMBL aims to set up an Environmental Office to enable the realisation of high-impact global initiatives. By combining resources and expertise and working collaboratively across Europe, research in the new areas to study life in its natural context can stimulate the creation of new funding sources, help to commercialise finding, lead to highly cited publications, and generate outputs that have an impact on

environmental policy, clinical practice, or public health. Supported by trusted research data and critical analysis of validated results, EMBL may be able to target specific sectors of society and provide evidence that supports decisions to strengthen ecosystems through careful, positive change. Depending on the scientific data gained, EMBL could play a role in lobbying for changes in policy or practices. This might involve reducing pollution and thereby slowing detrimental changes to ecosystems. Alternatively, through collaborations with industry, research data may spark innovative and creative solutions to actively strengthen at-risk ecosystems.

Value and Impact

The knowledge and understanding gained from experimental molecular biology has always enabled further discoveries and applications. This knowledge benefits scientists and other members of society in multiple ways; to understand how the rich diversity of life on Earth works at the level of molecules, and to tackle societal challenges and develop solutions.

With this new Programme, EMBL will address fundamental questions about the impact of the environment on biological processes, while addressing societal questions about human and planetary health. Ultimately, this knowledge economy should enable a comprehensive understanding of the molecular and mechanistic basis of life in context, including an understanding of biodiversity and ecosystems. As well as answering scientific questions, EMBL aims to answer societal questions, including questions about the impact of humans on the environment, such as the effects of pollution, climate change, deforestation, and biodiversity collapse; 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.

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 genetics, 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. EMBL will implement and deliver **large-scale collaborative projects** involving molecular profiling in various contexts. With EMBL's philosophy of open science, the framework for such research can be a model for other ecosystem molecular biology research initiatives in the future. 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 (Chapter 16 in the full Programme: Value Proposition).

With the ambitious scientific directions set out in the new Programme, EMBL will strengthen European science, closely connecting our member states and providing **new services, technologies, and multidisciplinary expertise**, from molecules to ecosystems. EMBL will continue to lead the world in the provision of **open research data and standards**, in collaboration with the worldwide scientific community, and to develop the knowledge databases and tools that will enable the study of the complexity of life in the context of ecosystems.

Alongside these, EMBL aims to **train the next generation** of scientists, providing them with an awareness of planetary biology and the need to integrate environmental concepts. EMBL's various external training initiatives will make these opportunities accessible to scientists beyond EMBL, and will increase public awareness of scientific and societal challenges. As a result of EMBL's turnover model, when **EMBL personnel return to member states** their expertise can be leveraged by member state research organisations, which will benefit from having experienced personnel in unique and future-facing roles related to the Programme themes.

EMBL's scientific endeavours will integrate many scientific disciplines in an international, innovative, and interdisciplinary way. These, in turn, will facilitate new ways of bringing technologies to member states with the practical goal of **developing solutions** to mitigate the effects of environmental damage. Harmonised efforts will ensure informed and **impactful national and European policy and guidelines**, especially concerning ecological issues. EMBL's aim is to help Europe become the scientific leader in this new interdisciplinary area, to help both human and planetary health.

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

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