The Rosalind Franklin Institute

Pushing the boundaries

Technology innovation, transforming life sciences, improving health

Contents

Vivienne Cox, Chair

Foreword

As the founding Chair of the Franklin, I am proud to have seen the development of this national institute from plans on paper to a vibrant and productive centre at the heart of the Harwell campus.

As a national institute and charity, it is critical that we carry our mission at the core of everything we do. We were established with the clear and ambitious goal to **create and advance technology which will improve human health**. Guided by insight and support from our academic members and from industry, this is as critical and central to our work now as it was on our first day of establishment.

You will see in this prospectus the impact of the work the Franklin has undertaken in its first phase, driven by our research values of **Adventure**, undertaking projects with significant risk and reward, **Engagement**, across sectors and disciplines, **Novelty**, in the design and application of our projects, and **Utility**, holding closely the need to advance human health through our work.

The need for technology innovation to support our economy is clear. To create skilled jobs, new companies must form around new ideas, and these will be seeded through work at the very cutting edge of technology. We see already the innovations emerging from our first phase, and by working across the most fertile technology landscape in the UK around Harwell and the wider Oxford-Cambridge arc, and through work with national and global collaborators, we are determined to translate the economic and social benefits of our innovations.

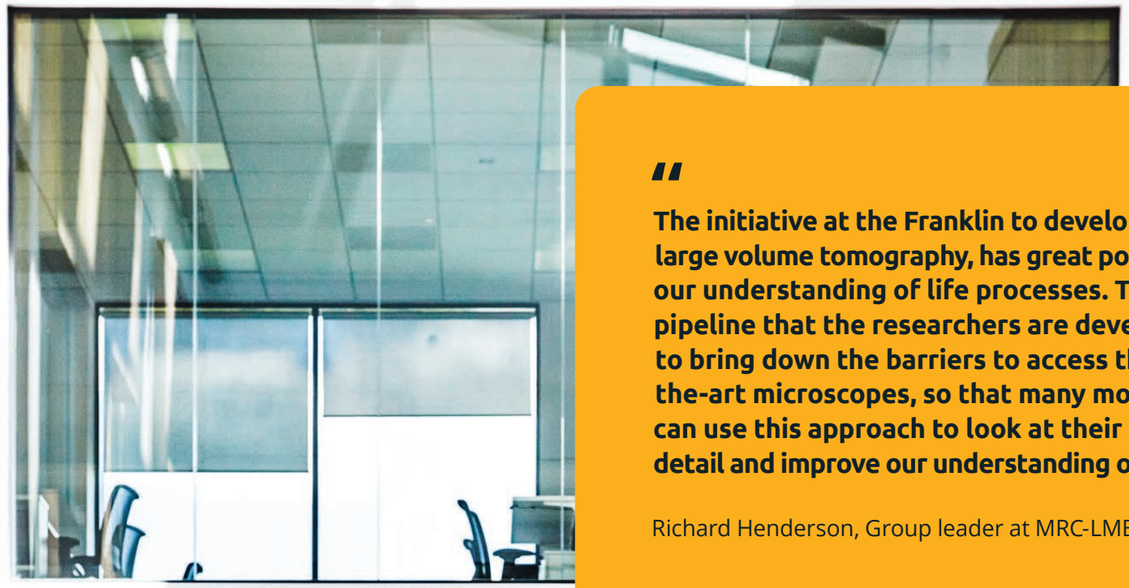
We enter our next phase with newly developed Challenges bringing together ambitious developments in technology with urgent and important work in life science, building on firm foundations of innovation and an exceptional home for our work.

Impact Examples

Since our inception in 2018, we have worked with global partners to pioneer new technologies in a unique environment that has allowed them to be applied immediately to advance life sciences and transform our views of disease and treatment.

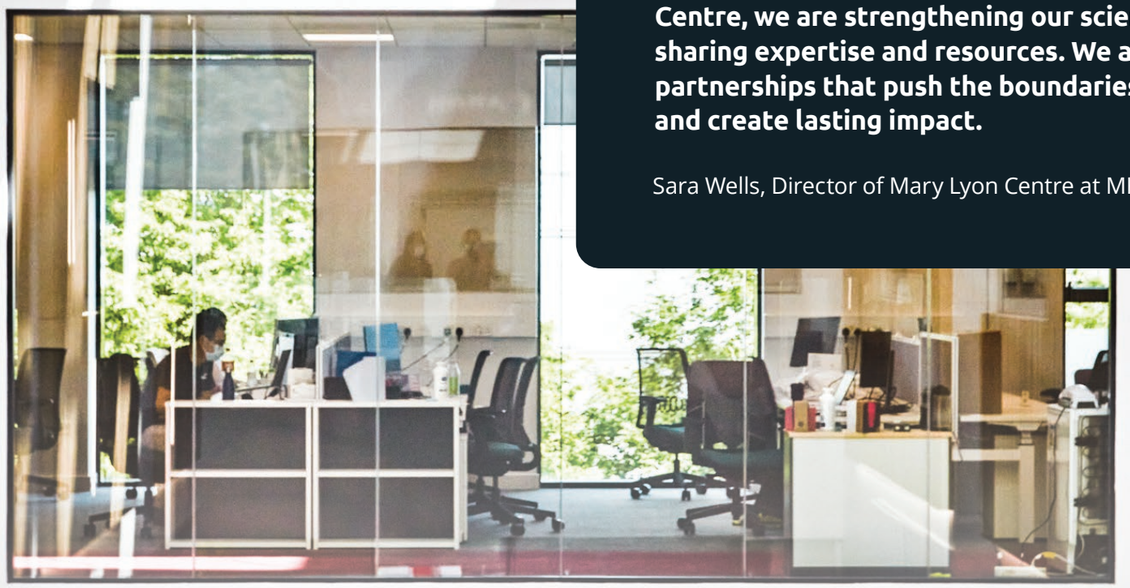
We have:

- Introduced novel chemistries for engineering biology through post-translational modification of proteins in the cell. This has generated a novel PET ligand for infection, which is now being used against Tuberculosis.
- Developed AI driven methods to rapidly generate highly targeted nanobodies and built new industrial partnerships for their exploitation based on a track record of pioneering applications of these as therapeutics for the Covid-19 virus.
- Worked with Bruker, Waters and Ionoptika to develop the next generation of mass spectrometry technologies, with improved TIMS resolving while retaining high mass resolution, and methods that are allowing new levels of sensitivity and accuracy for identification of molecules in intact cells.
- Partnered with Thermo Fisher Scientific to develop the next generation of electron microscopes for imaging the smallest structures of cells in intact tissues, bring these tools to market and establish new methods and standards for the community to enable their wide use. This work leveraged UKRI investment to attract major grant funding from Wellcome, and is now generating industrial and academic partnerships, including with MSD and AstraZeneca.
- Within the bespoke Franklin Hub, opened in 2021, we are creating an integrated analysis environment, capturing data from all major instrumentation. This digital lab of the future will be a key enabler for developing predictive biology models.



"The initiative at the Franklin to develop high-resolution large volume tomography, has great potential to deepen our understanding of life processes. The automated pipeline that the researchers are developing will help to bring down the barriers to access these state-of-the-art microscopes, so that many more researchers can use this approach to look at their samples in more detail and improve our understanding of human diseases.

Richard Henderson, Group leader at MRC-LMB and Nobel laureate



"Collaboration between scientific institutes drives innovation and accelerates discovery. By growing the partnership between the Franklin and the Mary Lyon Centre, we are strengthening our scientific ecosystem - sharing expertise and resources. We are committed to partnerships that push the boundaries of knowledge and create lasting impact.

Sara Wells, Director of Mary Lyon Centre at MRC Harwell

Franklin in Numbers

Since 2021, we have focused on assembling our world-leading science teams, kickstarting our scientific projects, and establishing our collaborations with academic and industry communities.

150

150 staff, 37 PhD students and 50 visiting researchers and students

85%

85% of our research grants are undertaken in collaboration with at least one external partner

£266m

Research collaborations valued at over £266 million

250

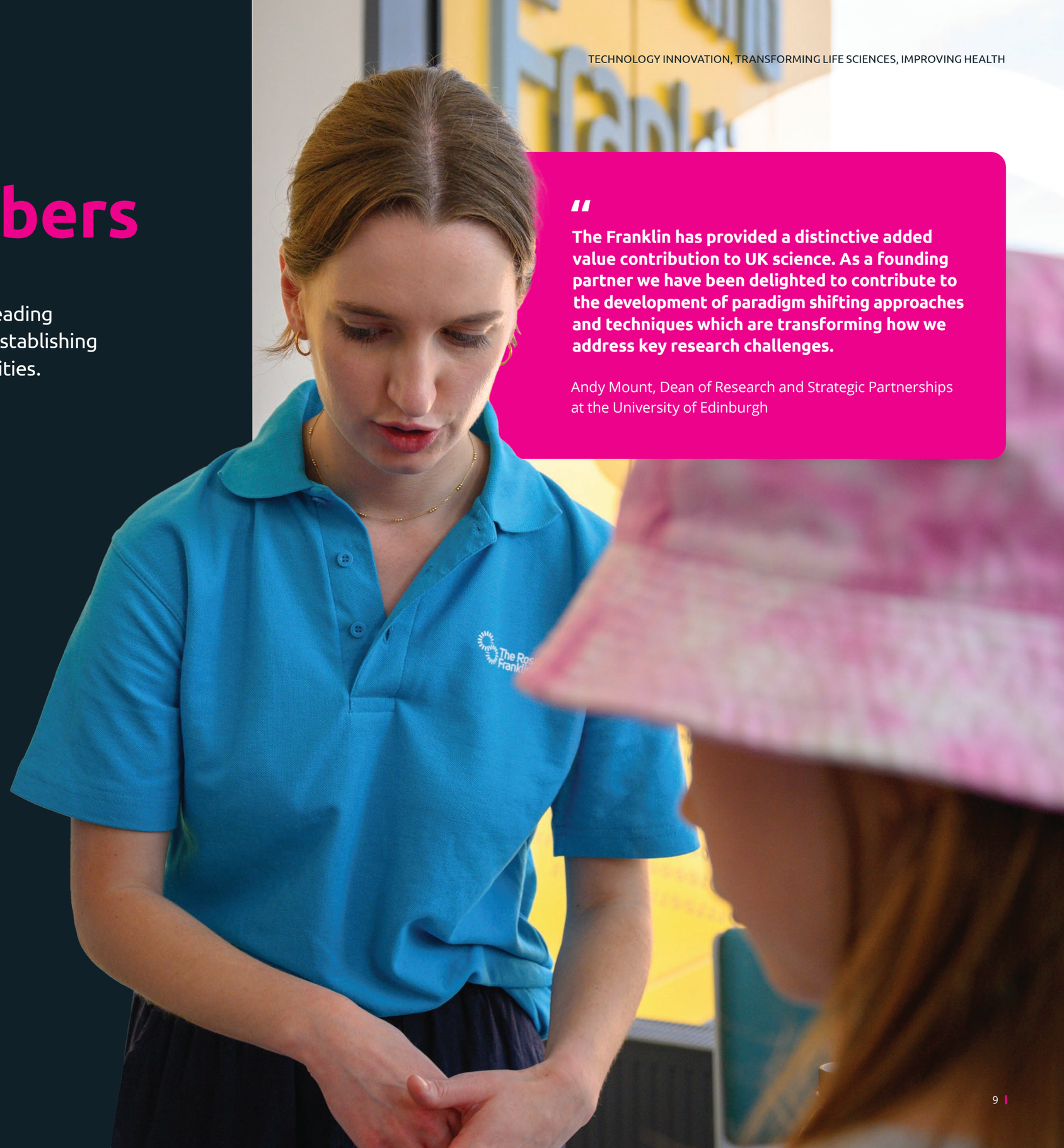
Our scientists have co-authored over 250 scientific publications

8000+

We have reached more than 8,000 members of the public, 4,000 school students and 64 companies

34

Established 34 collaborations with countries globally, 105 universities, 31 industry partners and 7 other institutions or facilities



> **"The Franklin has provided a distinctive added value contribution to UK science. As a founding partner we have been delighted to contribute to the development of paradigm shifting approaches and techniques which are transforming how we address key research challenges.**
>
> Andy Mount, Dean of Research and Strategic Partnerships at the University of Edinburgh

Paul Matthews

Driving Innovation

As Director, I am proud to unveil a refreshed research strategy for the Rosalind Franklin Institute. This strategy will accelerate our science and boost its wider impact.

The overarching aim of the Franklin is to catalyse innovation at the interface between the physical and life sciences. Our work will enable transformative advances in biological understanding relevant to human health.

To achieve this, our strategy focuses on addressing an unashamedly ambitious set of technology innovation and life science challenges. These challenges unite our researchers in highly interdisciplinary, agile and dynamic matrix-style teams.

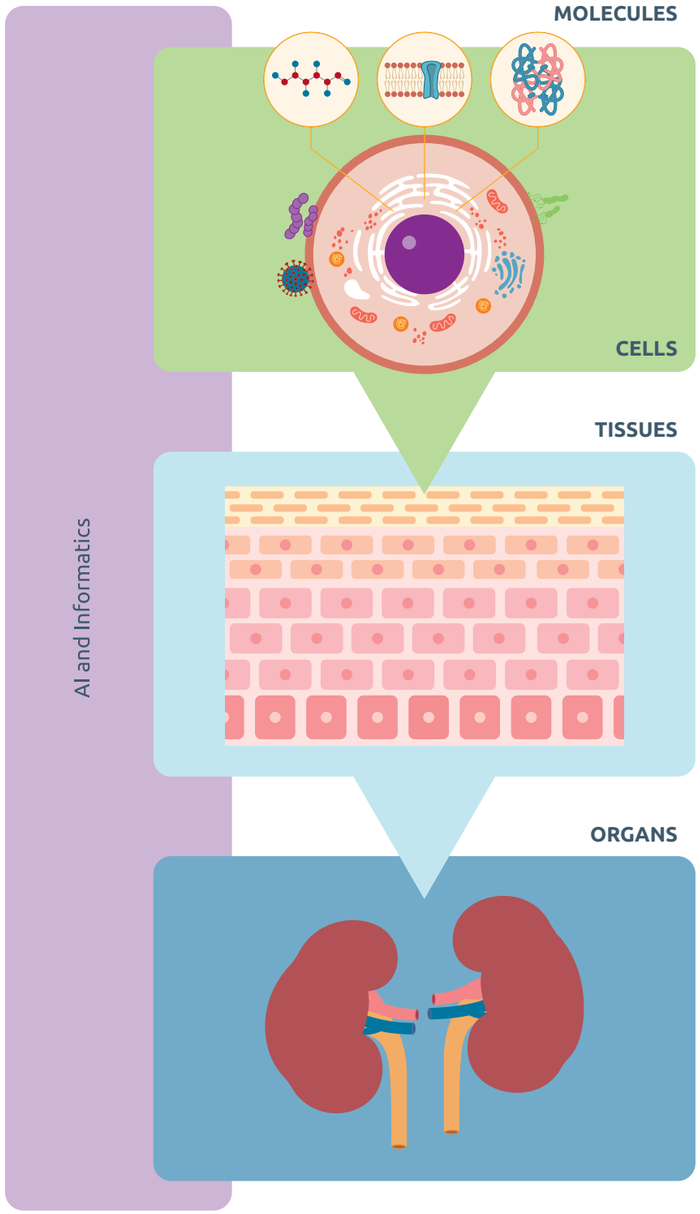
Collaborative work for these Challenges already is fostering increasingly close working relationships across UKRI, with our founder universities, with industry and with international partners. A particular strength arises from our location on the Harwell Science and Innovation Campus, where we can benefit from - and, in turn, provide benefits to - the UK's largest single cluster of national research facilities.

Our research and our partnerships have created an exciting, highly multidisciplinary training environment. We are passionate about building the skills base and capabilities needed to keep the UK at the forefront of physical methods for the life sciences.

In the first five years since construction of our facilities, the Franklin is already realising impacts on international research practice and standards, inward investment and growth in technology and pharma and the national science skills base.

Our Technology Innovation and Life Science Challenges

Technological innovation for transformative science and healthcare impact



Multidimensional Imaging of Molecular Structures
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Molecular Perturbations: Chemistry Engineering Biology
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AI and Informatics for Predictive Biology
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Technology Innovation Challenge

Molecular Perturbations: Chemistry Engineering Biology

Our aim:

To use innovative chemistries and chemical thinking to better understand and modulate the molecules of life.

What are we doing?

We are developing techniques to selectively manipulate the structure of molecules that 'do the work' in living systems, such as proteins, sugars and lipids *in vitro* and *in vivo*.

Why?

Making specific structural changes to these molecules in the place that they are working gives us unique insights into their cellular functions. These provide greater understanding of biology at a molecular level. We are using these approaches to gain insight into important cellular processes including, for example, how pathologies arise and the consequences.

The techniques developed may create new classes of therapies and biotechnologies, and enable new ways of visualising and diagnosing pathology. Applying in vivo covalent chemistries as treatments is a bold goal – they represent new modes of treatment, creating fresh possibilities for tackling hard-to-treat diseases.

> **"These technologies could provide a new era of biological chemistry – helping us to more fully understand the functions of cellular workhorse molecules such as sugars, proteins and lipids.**
>
> **This is highly ambitious research which could also have unlimited real-world applications in biology and medicine.**
>
> Ben Davis, Challenge Lead

Technology Innovation Challenge

AI and Informatics for Predictive Biology

> **We are putting AI at the centre of our biological research, meaning that we are generating the type of data that is needed to drive AI and machine learning. This will supercharge our science so we can find out more about human biology and health.**
>
> Mark Basham, Challenge Lead

Our aim:

To embed data management and science into all of our research groups to best use AI and machine learning to drive life sciences research and create new research tools.

What are we doing?

Data scientists are an integral part of our matrix research teams tackling complex life sciences challenges. By being involved from the earliest stages of the project, and throughout the whole project lifespan, the highest quality data will be generated, and the most appropriate AI and machine learning tools will be used.

Our tools and data generated will be open source to allow researchers internally and externally to create new- and modify existing- machine learning tools and AI algorithms. We hope these tools will be used to accelerate research and to help prioritise life sciences research efforts.

Why?

Adapting AI and machine learning for use in biology presents a number of challenges. Biology is complex, every person, patient and sample in biology has unique variations, which creates huge challenges. Harnessing the power of AI and machine learning to understand biology is in its infancy, and as a result is often used inefficiently or in ways that doesn't yield helpful results. Our work in this area will address these difficulties and our learning show how AI can be used more efficiently and effectively.

Technology Innovation Challenge

Integrated Chemical Imaging in Cells and Tissues

Our aim:

To drive innovations in mass spectrometry, alongside other structural biology techniques, to find out more about the role of molecules in biology so that we can better understand health and disease.

What are we doing?

We are developing ways to unlock the most information possible from our biological samples. We plan to achieve this by bringing together mass spectrometry with other structural biology techniques, including high resolution microscopy, to map molecules across scales - from inside cells, to groups of cells, through to tissues and organs.

Mass spectrometry will give us valuable insights into the identity, characteristics, chemistry and environment of biological molecules, from large protein assemblies to small metabolites. We will also use computing and machine learning to speed up data acquisition and analysis to build three-dimensional maps of the molecules of life at different scales.

Why?

Traditionally our understanding of the spatial biochemistry of cells, tissues and organs has been limited to specific molecular classes. The techniques we are developing will give us highly detailed information about proteins, their structure and their broader molecular environment.

"The techniques we develop will have wide applications in the life sciences. For example, we want to create a three-dimensional protein atlas of the mouse brain. Such a resource will enable new insights into neurodegeneration conditions such as Motor Neurone Disease.

Helen Cooper, Challenge Lead

Technology Innovation Challenge

Multidimensional Imaging of Molecular Structures

Our aim:

To develop new technologies to see the molecules of life and their dynamics with unprecedented detail.

What are we doing?

We are developing new technologies that can detect low levels of multiple signals combined with innovative sample preparation.

This will allow us to see biological structures at a molecular level and gain insights into the dynamics of their interactions. We are working to be able to routinely see structures in cellular context with near atomic resolution and to follow how single molecules change over time in performing their functions. The tools to give this information do not yet exist – we are working with manufacturers and developing our own technologies in house to achieve this ambitious goal.

Why?

Our work promises new tools that will provide near atomic resolution of molecules in the context of the native cell. Giving valuable new insights into amino acids, proteins, sugars and lipids, including how they function in a healthy system and how their malfunction may contribute to disease. The ability to see interactions between biomolecules is vital as many imaging techniques approaching this resolution are static, whereas in life, biomolecules move and interact constantly.

> **"The Franklin is giving us the time and expertise to dream big and create technologies to look more closely at life at a molecular level. We are developing the instruments and techniques which will allow biologists to do experiments they never thought possible.**
>
> Angus Kirkland, Challenge Lead

Life Science Challenge

Quantitative Biology Across Scales

Our aim:

To combine innovative imaging techniques and AI in ways that will allow researchers to flexibly image across large and small scales - from seeing whole organs to views of cells and the intricate structures within them, to transform how doctors treat patients.

What are we doing?

We are mapping cells, tissues and organs in the same sample, then using this information to create simulated systems to better understand disease. To do this, we are bringing together imaging techniques, including MRI, synchrotron CT, X-ray, electron microscopy and mass spectrometry, with advanced data science and machine learning.

Why?

A lot of what we know about tissue and organ structure and function is taken from imaging two-dimensional, small samples using one technique. Developing ways to bring together many, three-dimensional techniques will allow us to see cells and tissues in greater detail combining information across scales in simulated systems, including where they sit in the wider context of the tissue or organ. This could give us vital information about mechanisms of disease and help the development of new treatments, or improve the use of existing treatments.

"We will develop game changing techniques to map out the biology of our organs. We will begin by studying the placenta to understand what causes it not to function effectively in some circumstances. Our hope is to use computational modelling to understand better how to reduce stillbirth by identifying women most at risk, and improving treatments to reduce babies' exposure to hypoxia.

Michele Darrow, Challenge Lead

Life Science Challenge

How Pathogens Interact with Human Cells

Our aim:

To discover new ways of detecting, preventing and combatting human infectious diseases by discovering the mechanisms by which viruses and bacteria interact with human cells and tissues.

What are we doing?

We will use innovative nanometre scale imaging techniques combined with data science, to visualise the dynamic interactions between a virus or bacterium and human cells, at the level of macromolecules, cells, and ultimately tissues.

Our platform technology for producing llama nanobodies, which are single domain antibodies, will help us identify, and track the specific proteins essential in host cell pathogen interactions. Nanobodies are ten times smaller than antibodies so that, in combination with advanced imaging techniques, they can be used to pinpoint the location of targeted proteins very precisely. The application of novel chemistry within cells to modify protein function will give us even greater insights into the factors important in host pathogen interactions.

Why?

As human disease-causing viruses and bacteria continue to evolve and evade current anti-microbial drugs and vaccines, there is a growing need for new treatments. A better understanding of how pathogenic viruses and bacteria interact with human cells and tissues could find vulnerabilities that provide targets for the development of new medicines.

> **We want to apply cutting edge imaging technologies to investigate the interactions of viruses and bacteria with human cells over time and with higher resolution than ever before. We hope that the knowledge we generate will lead to the development of new approaches for the treatment of infectious diseases.**
>
> Ray Owens, Challenge Lead

We Work Differently

High ambition

The Franklin provides a different environment for research, where highly ambitious projects are encouraged. Technology innovation is a priority. Our approaches are driven by creative joint leverage of the “push” of new technology and the “pull” of the need to address major life sciences challenges.

> **“At the Franklin we are surrounded by researchers with different expertise to our own who don’t share the same assumptions as us. The whole environment is designed to encourage exchange of ideas and generation of new projects and approaches.**
>
> Felicia Green, Associate Investigator

> **“I wanted to work at the Franklin because its technology development focus allows me to use my engineering background in the life sciences to build tools which improve research. The criteria of success we are judged against is different. We are as highly recognised for our work in technology development as we are for our own research papers, resulting in greater long-term impact of our work here beyond single studies.**
>
> Elaine Ho, Research Software Engineer

Truly multidisciplinary working

The Franklin brings together researchers with diverse backgrounds and skills, coming from chemistry, physics, mathematics, material science, engineering, computing and life sciences. The Franklin encourages and rewards matrix working. Agile, multidisciplinary teams flexibly assemble around our strategic priorities to accelerate our progress.

Cross-sector science

We have a broad range of stakeholders in academia, the NHS, industry and government. We work through partnerships with UKRI, government and academic researchers, clinicians and industry to develop our technologies and to demonstrate their potential to transform science and have an impact for healthcare.

"Our work is very collaborative. My research uses laser-based techniques to study protein modifications, and then trains machine learning algorithms to predict outcomes of future reactions. We are working with the University of Bath Chemical Engineering Department, the STFC Central Laser Facility and with the X-ray Spectroscopy team at Diamond Light Source. Bringing this expertise together gives us the best opportunity to make progress.

Ajay Jha, Associate Investigator

Training researchers for the future

We offer our PhD students and early career researchers a unique training experience. They gain an exposure to multiple domains including imaging physics, novel chemistries, cell biology, advanced computing and AI. Our goal is to help younger researchers develop a depth of understanding of cutting edge methods or areas of biology while also learning how to integrate complementary expertise provided by others.

"Being at the Franklin is an incredible learning experience. The nature of our research teams means everyone has some understanding of biology, chemistry, physics, and computing, and we have become brilliant communicators through collaboration and communication between different research teams. We also learn many specialist skills because of the access we have to remarkable pieces of scientific equipment.

Angharad Smith, Franklin PhD Student

Creating a Home for Technology Innovation for the Life Sciences

The Rosalind Franklin Institute has the infrastructure, expertise and local partnerships needed to catalyse technology innovation for life sciences discovery and healthcare impact.

Our building and resources

Our 5300m^2 building has a bespoke design to house our advanced scientific instrumentation and provide adaptable laboratory, office and collaboration spaces. Our open design encourages interactions between interdisciplinary teams. The central hub at the core of the building is used by the entire staff flexibly for seminars, lunch or just meeting over coffee through the day.

The Harwell Campus

Our co-location with national laboratories on the Harwell Science and Innovation campus provides us with access to world-leading facilities and the complementary technical skills and expertise needed to develop cutting edge equipment and maintain it going forward. We benefit from the experience in these laboratories and their well-established mechanisms for making advanced instrumentation open and accessible to the wider research community.

> **"The Franklin is located on one of the largest Science and Innovation Campuses in Europe. The growth and impact of the HealthTech cluster continues to attract investors from around the world and cements Harwell's position as a key location for life sciences organisations in the UK. The cross-disciplinary knowledge, skills and technical facilities that exist across our collaborative community are unparalleled. These capabilities support organisations from start-ups and scale-ups to large corporates to accelerate their research, validate their technology and products, positioning them at the forefront of health and medical innovation.**
>
> Barbara Ghinelli, Innovation Clusters and Harwell Campus Director at Science and Technology Facilities Council (STFC)

Our partnerships

The Franklin was founded by a group of ten university partners from across the UK, Diamond Light Source, and the UKRI Science and Technology Facilities Council. These partnerships are central to our science strategy and to how our science and training missions are implemented. We also work closely with industry partners to develop new technologies and apply them for impact.

Supporting UK life sciences

As a national institute, we support the wider UK research community through collaborative research, by prioritising open science, by training other researchers on our instruments and by sharing data, tools and workflows.

"The combination of the Franklin's focus on transformative imaging techniques in the Life Sciences and the proximity of the Diamond synchrotron and the Central Laser Facility, with its expertise in both microscopy and high-intensity lasers means that the Harwell Campus is the ideal place to develop a new microscope based on laser generation of soft X-rays. If you want to do correlative imaging on length scales from microns to Angstroms, within a few hundred metres there are world experts in every aspect.

Bill Brocklesby, Associate Professor in Photonics, University of Southampton

"From its inception the Franklin has aimed to do things differently. Following some impressive early impacts, the new strategy will help further focus research efforts to make the technology innovations to boost our understanding of biology and health.

Andrew Bourne, Executive Director for Innovation and Partnerships at EPSRC

Collaborate With Us

We believe that big challenges must be tackled in collaboration. We work with academia, government and industry, both in the UK and internationally, to set our objectives and then to develop new technologies and apply them to address major Life Science Challenges.

Our collaborations are flexible. We actively seek partners whose interests are aligned with our Technology Innovation and Life Sciences Challenges. We look towards building long-term partnerships through collaboration. Well-precedented routes to collaboration include studentships, training on advanced techniques, collaborative grants, sponsored research and the creation of consortia. We are also happy to use our links across our wide research network and convening power just to explore questions in their early stages.

If you interested in collaborating with the Franklin, please get in touch with us and we can connect you with the right people

collaboration@rfi.ac.uk

> **Thermo Fisher Scientific is a company driven by the needs of scientists. It has been thrilling to work with the Franklin because they want to make breakthrough innovations, not just incremental changes, so working to meet their scientific needs has been a really exciting challenge.**
>
> Steve Reyntjens, Senior Director of Product Marketing for Life Sciences at Thermo Fisher Scientific

> **As a national user facility, it is essential that our technologies reflect rapidly changing needs of our user communities. The Rosalind Franklin Institute here on the Harwell Campus is a valuable partner to us, and together we look forward to creating next generation technologies with real impact.**
>
> Gianliugi Botton, CEO of Diamond Light Source

Our work would not be possible without the funding and support of UKRI-EPSRC, through which the Franklin is funded.

Our project work is supported and developed through additional grant funding from a range of sources, including Wellcome, UKRI-MRC, UKRI-BBSRC, the Chan Zuckerberg Initiative, Wellcome LEAP, and others. We are proud to participate in international consortia supported through European funding.

We also thank our founding members for their ongoing support:

diamond
IMPERIAL
KING'S College LONDON
UKRI Science and Technology Facilities Council
UNIVERSITY OF BIRMINGHAM
UNIVERSITY OF CAMBRIDGE
UCL
THE UNIVERSITY of EDINBURGH
UNIVERSITY OF LEEDS
MANCHESTER 1824 The University of Manchester
UNIVERSITY OF OXFORD
University of Southampton

We are proud to work in collaboration with partners across sectors, including:

ThermoFisher SCIENTIFIC
JEOL
BRUKER
Waters
IONOPTIKA ion beam technology
UKRI Mary Lyon Centre at MRC Harwell
novo nordisk®
evotec
MSD
AstraZeneca

More information about our strategy and impact can be found on our website: **www.rfi.ac.uk**

The Rosalind Franklin Institute

Engineering and Physical Sciences Research Council

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