The Rosalind Franklin Institute

Annual Report and Financial Statements 2019-2020

The Rosalind Franklin Institute Limited
(A Charitable Company Limited by Guarantee)
Annual and strategic report and financial statements Year Ended 31 March 2020

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Legal and administrative information

The Rosalind Franklin Institute is funded through UK Research and Innovation's Engineering and Physical sciences Research Council to be a national research centre for new technologies around molecular medicine. The Rosalind Franklin Institute is a collaborative, legally independent joint venture with 12 members and represents a £103 M investment from UK Government.

The Rosalind Franklin Institute registered address:

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Trustees and Strategic Report

Directors Foreword

Professor James Naismith FRS FRSE FMedSci

I am happy to present the annual accounts for The Rosalind Franklin Institute, 2019-2020. Our second year of operation has seen progress across all activities of the Institute.

We have transitioned from a team of interim leaders to permanent science directors. I would like to extend my thanks to the interim team, who have set the Institute firmly on a course to be an international leader in its field. The science directors, Professors Angus Kirkland, Ben Davis, Josephine Bunch, Zoltan Takats, and Dr Mark Basham are leading scientists. Paul McCubbin as Chief Operating Officer, a new team member this year brings a wealth of experience from industry and strong leadership skills. We are already attracting collaborations with academia and industry against global competition and producing exceptional science and have recently filed our first patents.

The technologies in our themes, details of which can be found later in this report, are now in development. All projects embody the 'Factor of Ten' which we strive to achieve – the major advances against the current state of the art which will see Franklin technologies revolutionise the capacity, capability and scope of life science research. Our external advisory boards are now in place and holding us to our high standards.

As a team, we are greater than the sum of our parts – the collaborations we create between our themes and with our communities will be the source of our most exciting research. We are all one team with a commitment to parity of esteem. Everything we do from research, through technology transfer, to operations, to public engagement will be marked by excellence.

During the course of the next year, we will move into our Hub building currently being constructed by Mace. The Hub will be the most efficient research space in the UK, world class in its facilities, and unique in its capabilities. From the a basic sketch in late 2017 to occupation in 2021 is a pace unmatched in lab construction. The building will be a stunning and inspiring space for research, and a beacon for collaboration, learning, and scientific excellence.

2020 marks the centenary of the birth of Dr Rosalind Franklin. An exceptional scientist best known to the public for her contribution to our understanding of the structure of DNA. Franklin, her family and scientific community recognised her work during her lifetime on the structure of viruses as ground breaking and of lasting impact. She pioneered structural analysis of Tobacco Mosaic Virus, and later Polio. Her collaboration with Aaron Klug set a course which would result in the awarding of his Nobel prize. She remains an inspiration for our work and sets a daunting standard to aspire to.

We are living through the greatest health crisis of our lifetimes and the economic damage threatens to exceed anything since the 1930's. Covid-19 has severely disrupted our plans and strained our staff. I want to acknowledge the personal efforts of all the team who have worked in the most difficult circumstances.

We recognise that we have an obligation to repay society's trust and investment in us. Therefore we have focused much of our work on the past few months helping defeat Covid-19. The Franklin team has made, I believe, important and significant contributions in the battle against the virus.

Chairs Foreword

Dr Vivienne Cox CBE

We are pleased to present these annual accounts, which represent the huge progress and transformation The Franklin has undergone in these last twelve months, and are also an indicator of the work which is still to come.

The projects described here will bring huge benefits to life science and to human health. We were pleased to be recognised this year by the Office for Life Science as a key institute for delivering scientific excellence in life science in the UK. This recognition that our research capabilities are leading and transformative is an important endorsement and places The Franklin alongside longer established peers at the Crick and at Laboratory of Molecular Biology.

The Franklin's unique position in the UK has attracted globally important researchers to the institute. Our ability to provide a home to truly transformative research – The Franklin 'Factor of Ten', requires our governance structures to hold the same values as our research team – of engagement, novelty, adventure and utility. All parts of The Franklin have worked together to deliver the outstanding science projects you see in this report against the backdrop of keeping our people safe during the Covid-19 pandemic: from the board, a team assembled largely thanks to the outstanding support of our members, to our theme advisory panels, our strategic advisory board, and our operations team. We also thank our funders at The Engineering and Physical Sciences Research Council for their commitment to the vision of the institute, and their huge support to all aspects of the Institute.

We were pleased this year to see engagement with our members deepen, with Franklin staff embedded at the Universities of Manchester, Oxford, Leeds, and Imperial College, and many research collaborations underway with our other member universities. We also welcomed Diamond Light source, our neighbours and close collaborators at Harwell, as a new member. This formalises an already close relationship, with several shared staff members and collaborations on key initiatives including electron tomography, protein production, next generation chemistry, and in correlated imaging. As hosts to both eBIC and ePSIC, the national electron imaging centres in life and physical sciences, and to the synchrotron, Diamond are welcome members and will enhance our governance and strategic development.

Looking to the future, 2021 will bring huge change to The Franklin and to the wider scientific community as we respond to the 'new normal'. The imperative to fund research which enables greater leaps in our understanding of biology has never been clearer, alongside the ability to respond quickly to urgent research problems. Our transition into the new building at Harwell places us in a uniquely privileged position to build research programmes with this responsiveness and ambition built in, having demonstrated already The Franklin's ability to react at pace to the coronavirus pandemic.

The transition to the Hub will see our activities expand hugely, and with that expansion will come further diversification of our income. We look forward to working with both our existing funders and with new partners from the charity and commercial sector.

It is clear in the community that there is a pressing need to bring diverse new talent into research, and to nurture early career researchers. We have been tasked with becoming a centre for skills development in UK research, and we take this role seriously. Our commitment for our first year in the new hub is to develop a studentship programme which will attract and supply the UK research community with researchers who share our vision and possess invaluable interdisciplinary skills. This unique programme will engage partners across our members and beyond and will provide the institute with the ideas and talent to support our future growth and development.

I would like to thank all the staff at The Franklin for their commitment and hard work during this most extraordinary year. The next years will also be challenging, but there is a lot to be proud and excited about.

Franklin research is driven by a need in the research community to speed up the design and delivery of novel drugs, create technologies which can advance our understanding of biological systems, and improve human health. Our technologies must deliver a Franklin Factor of Ten: significant and disruptive benefits to the bioscience community, which represent a factor of ten improvement on the current state-of-the-art.

Franklin strategic goals:

Our strategic goals encapsulate this drive - to deliver world class science, build a legacy to be proud of, and secure long term success for our world changing research programmes.

Delivering World Class Science

Adventure:
Franklin projects have significant risk, balanced by significant pay off if successful

Novelty:
Franklin technologies are globally original and ground breaking in their design and application

Engagement:
Franklin projects engage multiple partners from academic and industry and there is demonstrable support for their development

Utility:
Franklin technologies will be sought after by industrial and academic communities, generating research and economic benefits

Building a legacy to be proud of

Training the next generation in collaborative science: PhD, PDRA, Placements, Public engagement

Leverage:
Optimise the effectiveness of existing government investment in science infrastructure

Become a global Centre of Excellence:
for technology development and innovation, seed a new life science cluster, and enhance the UK skills base

Value our people:
Create an environment which develops staff to their full potential, supports career progression, and centres equality and diversity in STEM

Securing future success

Diversifying income:
- recurrent funding
- earned income
- partner contributions
- external funding
- charitable donations

Foster 'many-to-many' links:
across academia and industry, acting as a national focal point

Expand global network:
Establishing international partnerships. Position Franklin on global stage

Technology maturation:
Build bridges to clinical, robust IP and commercialisation planning for appropriate technoligies

Future Plans

- Delivery of the technologies detailed in our themes will be our primary driver in 2020-2021.
- We are taking delivery of state of the art instruments and designing beyond start of the art technologies.
- As delivery of wave one projects progresses, milestone project reviews will increase in frequency, linked to consultation on wave two technologies. Rigorous scrutiny for every technology will ensure that the 'Factor of Ten' test applies on delivery. The journey of a Franklin project from concept to maturation is summarised on the following page.
- We have committed to bringing AI and machine learning into the lab, automate the routine to focus on the extraordinary. Our plans for applying these technologies in imaging, mass spectrometry and chemistry are well advanced.
- Consultation on wave two technologies will begin with our Strategic Advisory Board, and with our science directors, Members, Theme Advisory Panels, and the wider community will be called on in due course to assess our future direction and test the ability to deliver factor of ten advances in each area, existing and potential new ones.
- As our current technologies mature, we will ensure that they are positioned for maximum success in their communities, through transition to national asset, commercialisation, or further development.
- As we develop technologies, we must also develop communities. At the heart of these new communities will be our PhD students, training alongside and contributing to the development of our technologies. In addition, we will build collaborations with partner universities, training industry partners, and hosting placements from around the world.
- As we grow and diversify our income, we will work with large funders alongside other collaborations and partnerships. Discussions on our core funding are in progress with UKRI, and commercialisation of our wave one technologies will diversify our income further.
- In an international partnership with Thermofisher, Diamond and the LMB we will revolutionise electron cryo tomography. This is hugely exciting and ambitious project that will allow us to see inside large volumes of a cell at close to atomic resolution.

Franklin Innovation Process

Origination for wave two technologies is underway, led by science directors and informed by the Strategic Advisory Board (SAB).

Origination

Life science and technology drivers

Project ideation: identification of factor of ten projects.

Led by science directors, guided by Strategic Advisory Board

Consultation

Test factor of ten and utility

Community engagement and development -establish communities of interest, project partners and assess utility. Test and review projects against Franklin research values.

Input from Theme Advisory Panels, Value for Money Panels, Franklin Board

Development

Create technologies and train communities

Established partnerships and development in process.

Governed by partners, science directors, theme leaders, and overseen and evaluated by Theme Advisory Panels, with internal project support. Training establishes community of practice and local experts in partner organisations and industry

Maturation

Continued development at The Franklin

Further technology development which can yield factor of ten advances

Transition to national asset

Large technologies to transition into national use at peer reviewed facilities

Technology transfer

Licensing, spin outs created at The Franklin or elsewhere, bridge to clinical and partner for appropriate onward development

Our response to COVID-19

In the unfolding COVID-19 pandemic, research teams across The Franklin have turned to applying their technologies and expertise towards treatments and diagnostics for SARS-CoV-2.

In February and March 2020, as lockdowns were implemented across the globe and research sites closed, Franklin teams worked extensively with partners to keep laboratories safely operational.

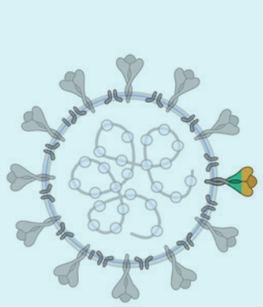
Nanobodies against SARS-COV-2

The Protein Production UK (PPUK) team, led by Professor James Naismith and Professor Ray Owens, have identified, produced, and refined nanobodies – potent antibody tools derived from camelids - against the SARS-CoV-2 spike protein. These nanobodies show powerful neutralising capabilities and have strong potential as a therapy.

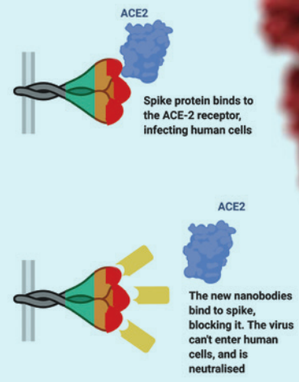
In less than two months, Franklin scientists:

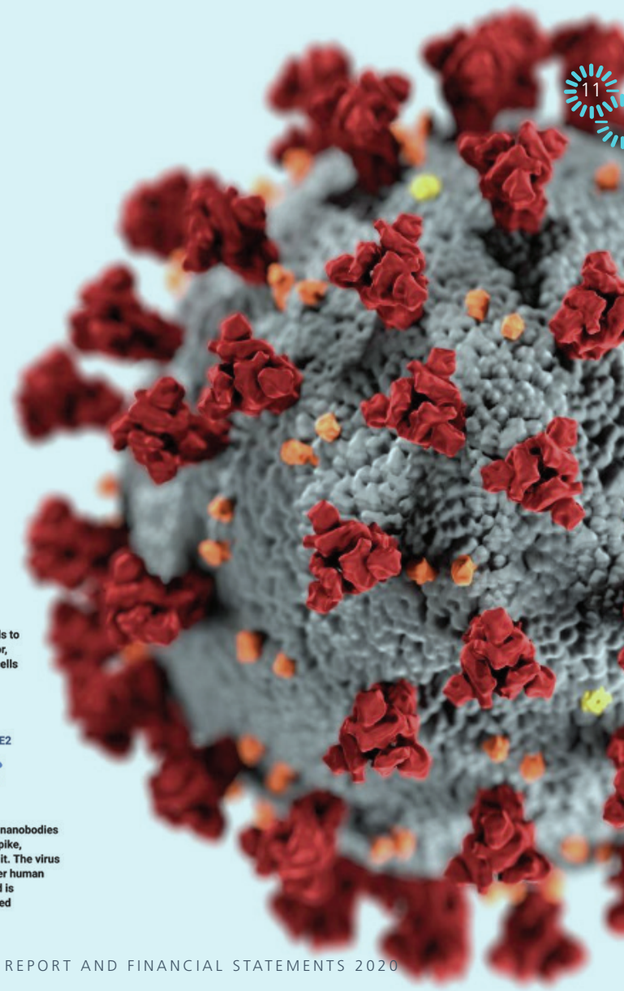
- Invented nanobodies that bind with nanomolar affinity to the receptor binding domain of the Covid-19 spike protein.
- Utilised single particle electron microscopy and X-ray crystallographic analysis to identify the interactions between amino acid side chains that drive the higher affinity achieved during in vitro affinity maturation of the nanobodies.
- These structural studies show The Franklin nanobody targets a new epitope and blocks the ability of the virus to bind its human target receptor.
- Developed an engineered antibody, combining human and nanobody components which shows potent neutralization activity against live SARS-CoV-2. A patent on these molecules has been filed.

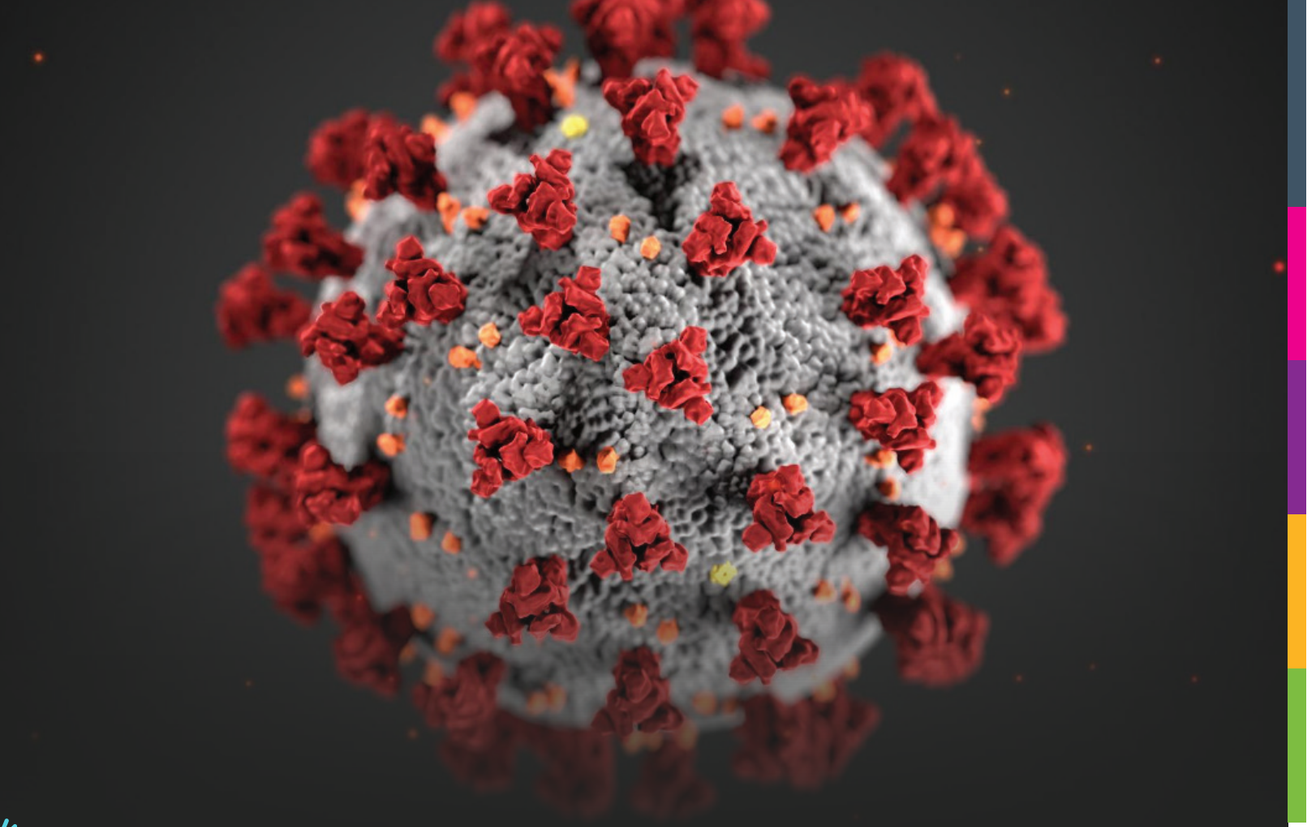
Combining expertise in advanced biological imaging with electrons and X-rays, and with a leading capability in in nanobody development, The Franklin has demonstrated the ability to make discoveries at the pace necessary to be relevant to an unfolding pandemic. This work is a powerful case study that validates The Franklin's choice to develop key technology platforms that will have applicability to other major problems in human health.



The SARS-CoV-2 virus. Spike proteins cover its surface.







Sugar decoys

Professor Ben Davis, Director of the Next Generation Chemistry Theme and Professor James Naismith, Institute Director, are investigating the role of sugars in guiding SARS-CoV-2 into place during the infective process. There is strong evidence that the virus uses sugars on the cell surface to 'stick' like Velcro before binding occurs between the viral spike protein to the host ACE-2 receptor. The team have already identified novel sugar molecules which bind to the Spike protein.

The aim is to synthesise sugar molecules that bind tightly to Spike and block binding to human cells, thereby reducing or preventing illness.

Rapid point of care testing

Rapid and accurate SARS-CoV-2 testing could be critical in clinical settings for patient triage, in addition to other settings where rapid and high throughput testing is required.

Current methods using PCR and immunochemical tests rely on primers, reagents, solvents and extraction methods. The fastest available tests currently take hours from sample to result. The development of tests which give near-instant results without the need for laboratory analysis would have huge benefits and could be transformative for testing regimens in a range of settings.

Ambient mass spectrometry could provide this tool. Using mass spectra of patient test samples and quickly analysing for the presence of virus enables tests to be completed in seconds, without the need for expensive primers or reagents. The technology could be developed for point of care, such as hospital admissions, for direct diagnosis.

The Franklin Biological Mass Spectrometry theme leaders, in collaboration with Imperial College, NPL, and Waters, are investigating testing based on nasopharyngeal sampling swab analysis by ambient MS.

Research activity and technology portfolio

Projects are underway in the five Franklin Themes, led by the Science Directors. Funding for capital projects is awarded through standard governance procedures, which test projects against The Franklin research values and seek external views on their transformational capacity. Collaborations and partnerships with industry and academic partners are in place in each theme, with additional funding sought through grants.

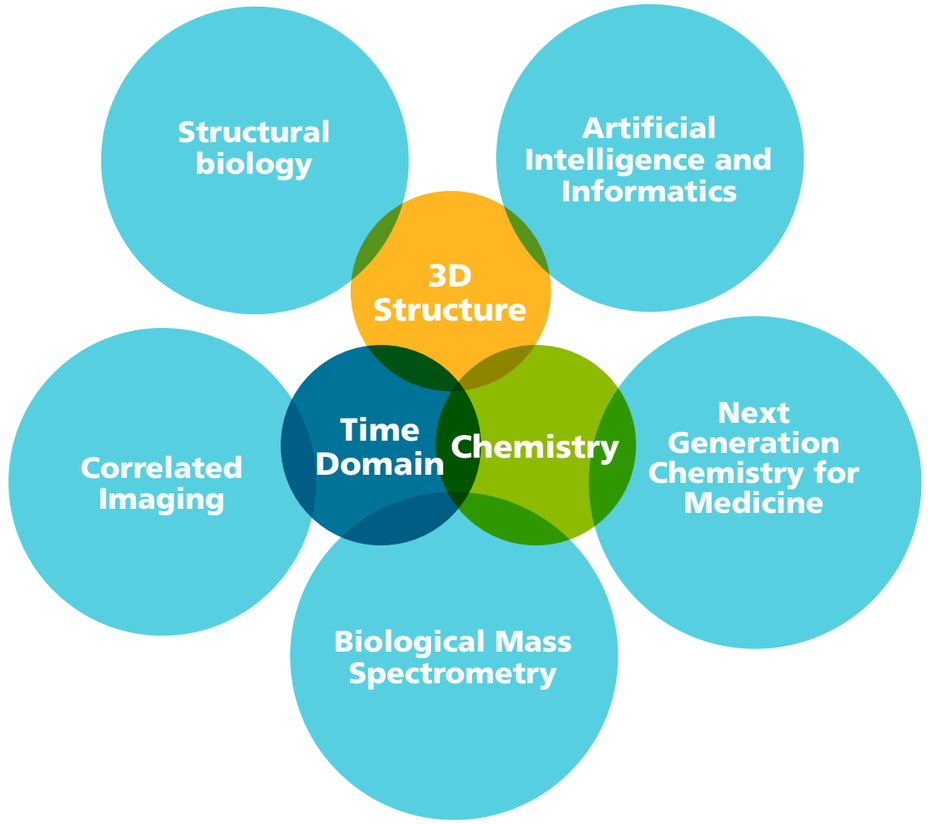
All funding for capital projects indicated is allocated from The Franklin core funding, which runs to 2021. Grants are either allocated directly, or via member universities.

Team members are correct as of July 2020.

Wave One Technologies

Wave one technologies are linked by a unifying goal to understand life in five dimensions - the shape, chemistry, and movement of biological systems.

This understanding will enable the observation of drug entry and action in cells, bring insights into the chemistry of disease, and the ability to edit and alter the molecules of life in the cell.



Biological Mass Spectrometry

The Biological Mass Spectrometry theme at The Franklin will deliver unique mass spectrometry instruments for characterising and imaging molecules ranging from metabolites to proteins. Bringing together researchers at the Universities of Manchester, Oxford, Birmingham, Imperial College London and Edinburgh, collaborators at The National Physical Laboratory, Bruker and Ionoptika as industrial partners, staff are creating a suite of novel instruments which will come together in The Franklin hub in 2021.

Science directors: Professor Josephine Bunch and Professor Zoltan Takats

Projects underway:

A new hybrid instrument for high resolution imaging

Enabling detailed mapping of biological molecules

Modern mass spectrometry (MS) methods allow detailed analysis of biological molecules ranging from metabolites to proteins. These experiments involve ionisation of molecules and manipulation the resulting ions in electro-magnetic fields in vacuo to determine their "masses". MS can now be efficiently coupled with imaging technologies (MSI) allowing generation of molecular maps of biological samples. However, the sensitivity of MSI and the molecular coverage of MSI imaging technologies, particularly for larger molecules, is not competitive with high performance instruments used for traditional experiments with, for example chromatography. The BMS theme at The Franklin is developing new concepts and related instruments to close this gap in collaboration with Bruker Ltd. a leading vendor in MS and MSI. Our flagship instrument under design and development will feature a number of MS ion sources with a fast mass analyser, as well as mass analysers for enhanced sensitivity, high resolution MS and methods for measuring the "shape" of molecules using trapped ion mobility spectrometry (IMS). The combination of ion sources and novel analyser configuration will allow broader analyte coverage than is currently achieved.

Importantly, structural characterisation experiments, including protein conformation studies, can be performed.

High resolution MSI

Pushing the limits of secondary ion mass spectrometry

MSI in super high resolution mode is currently achieved by bombarding samples with focused ion beams and analysing the ejected secondary ions by secondary ionisation MS (SIMS). We have selected an Ionoptika J105 instrument, with a water cluster ion beam, which will be used to map surfaces in a very gentle way. We will use this to push the current limits in sensitivity and size of molecules which can be detected, extending the range from small metabolites and lipids to small peptides and proteins. The project explores coupling the instrument with lasers to boost secondary ion yields. The aim is to establish optimum regimes for surface sampling and post-ionisation. In the future this may inform ion source design in other theme instruments.

Microscope mode MSI

Ultrafast, high throughput mass spectrometry imaging

Current MSI instruments operate in "one pixel – one analysis" mode meaning that the mass analyser only measures molecules from a single pixel area at a time and pixels need to be analyzed one after the other. This common approach severely limits throughput as the higher the resolution map desired, the longer the experiment takes. In collaboration with researchers at Oxford and industrial partner Ionoptika, the BMS theme at The Franklin is developing a new microscope mode (or stigmatic mode) secondary ion mass spectrometry imaging platform, with a view to simultaneously determining molecules from multiple pixel locations at once.

Correlated Imaging

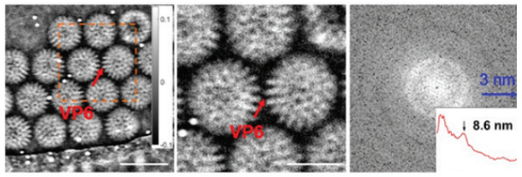
The primary focus is to develop novel electron optical instruments with high temporal and spatial resolution, and associated imaging methods. These instruments will allow the visualisation of dynamic biological events at the atomic level by shifting the time scale from milliseconds to microseconds or even 100s of nanoseconds.

Science directors: Professor Angus Kirkland and Dr Judy Kim

Time-Resolved Electron Microscopy

This instrument will enable structural studies of smaller molecules in native environments

The Franklin is developing a new double aberration corrected column, which will open up new imaging modes not available in conventional cryo-EM instruments. The increased phase sensitivity of ptychography will enable structural studies of smaller molecules at lower doses and will require fewer particles for single-particle 3D reconstruction. This instrument will also include high speed electrostatic shutters which will enable a pulsed mode operation.



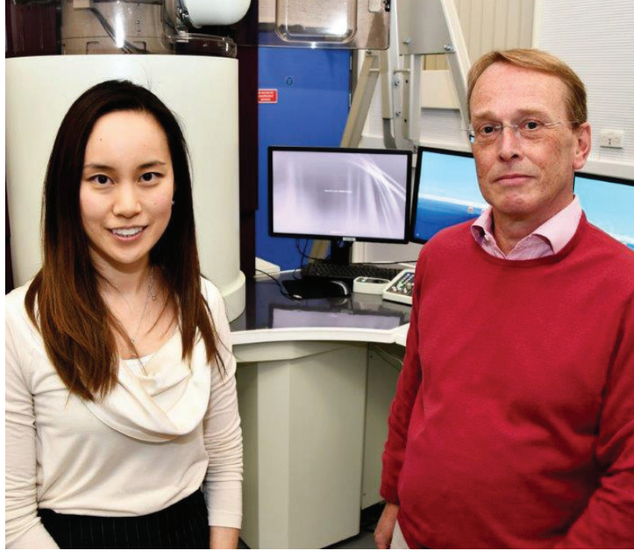
Pytchographic imaging of single virus particles. From Zhou et al. See Theme Publications.

Chromatic correction

Enabling structural studies of thicker biological samples.

Currently TEM imaging of thicker samples is resolution limited by the effects of chromatic defocus, an effect which becomes more severe at lower voltage. The Franklin is developing a chromatically corrected column fitted with a new corrector design.

This instrument will also be fitted with high speed electrostatic shutters and a robotic autoloader.



Liquid cells

Novel liquid cells to study biological processes in situ.

To fully understand biological structure and function it is necessary to study molecules in their native state. This requires imaging in liquid environments that mimic those found in-vivo.

The Franklin together with Manchester University and Kings College London are developing new liquid cell technologies for EM.

Theme publications:

Zhou et al. (2020) Low-Dose Phase Retrieval of Biological Specimens using Cryo-Electron Ptychography, Nature Communications, doi: 10.1038/s41467-020-16391-6

Next Generation Chemistry for Medicine

In November 2019 Professor Ben Davis FRS FMedSci took up the role of permanent scientific director for Chemistry bringing a new programme of chemistry and chemical biology projects to The Franklin. This follows the excellent intermediate leadership of Professor Adam Nelson (Leeds).

The ability to edit the molecules of life within the cell without altering the genome is a challenging target, but one which could revolutionise how we understand and treat disease. This 'in-cell chemistry' creates a route to understand and manipulate the molecules of life with precision.

Amongst various sub-theme projects [others include novel methods in BioPhysics for Function, Synthetic Biologic, Theranostics and Chemical Microbiology] highlighted focuses include:

Post-translational mutagenesis and synthetic biologics

Chemical editing of biological systems

Cellular processes, such as movement or cell-cell communication dominate many functions in higher organisms but are only understood in gross terms. Control of cells through the "editing" of functional biomolecules could allow reprogramming of events as diverse as inflammatory response to tissue formation. We are developing methods to break and form bonds in vitro and in vivo that can be applied to, for example, selective change of proteins and glycans. These include attractive targets such as proteoglycans for such chemical editing as their complexity prevents precise control by biological methods. Intracellular applications can also be explored for epigenetic programming allowing de novo cellular epigenetic control of chromosomal gene expression and transmission in living cells and organisms. Other live applications include the design of conditional responsive functional groups and their chemical editing to invent a new generation of "biologics" programmed to respond to multiple stimuli and signals.

Mechanistic Proteomics

Mechanistic biology at the molecular level

Multi-scale models suitable for precise biomolecule editing and programming and interrogation by widescale gene-product-omics will be established with a focus on the exploitation, control and understanding of chemical structure. A goal is to fully exploit the >4000 serum proteins that are predicted to exist as potential quantifiable biomarkers. Development of high-throughput high-sensitivity mass spectrometry-liquid chromatography workflows will lead to improved pathway detection and insights into cellular function. Unnatural amino acids and glycans will be utilised not only to allow quantitation in proteomics and longitudinal studies in living model systems but also the identification of modification and functional group states that truly determine mechanism in those same models.

High-throughput discovery

Integrating diversity of synthesis with contextual functional effects

Chemistry is a cornerstons of molecular discovery in Biology and the innovative High-throughput Discovery facility, started by Adam Nelson will be integrated with other sub-theme projects to enable the rapid synthesis and, critically, assessment of novel compounds (large and small), so that we can reach and act on disease targets. The project aims to expand the reaction toolkit used in molecular discovery, enabling new regions of biologically relevant chemical space to be explored. The current reaction toolkit, that underpins discovery workflows, has to date been dominated by a small number (<10) of reaction classes that have remained unchanged for 30 years. This has led to high attrition and stagnation in drug discovery. The High-Throughput Discovery facility hopes to disrupt this using new methods and direct functional assessment in context to lead the way in the production of new starting points for drug discovery.

The facility has been designed to deliver a step-change in molecular discovery: both in increased efficiency, through faster and parallel design-make-test cycles, and effectiveness, by harnessing chemistry that is currently outside the discovery toolkit. This will require the integration of artificial intelligence, synthetic chemistry, engineering, structural biology and biophysics capabilities. By embedding high-throughput closed-loop methods in direct functional biological contexts *in vitro, in crystallo,* and *in cellulo*, we aim to guide and select data that will refine chemical structures towards precise biological modulation.

Theme publications:

Calabrese et al. (2020) Observation of the unbiased conformers of putative DNA-scaffold ribosugars, ACS Central Science, doi: 10.1021/acscentsci.9b01277

Josephson *et al. (in press)* Light-driven posttranslational installation of reactive protein side chains, Nature.

Karageorgis et al. (2020) Activity-directed synthesis: A flexible approach for lead generation, ChemMedChem, doi: 10.1002/cmdc.202000524

Structural Biology

Determining biological structures with atomic detail has revolutionised our understanding of biology and transformed the search for new medicines. A new era of discovery, however, requires a paradigm shift in structural biology; structural biology must be able to study proteins in the context of the cell, be ubiquitous and deliver with a higher rate of success.

Science director: Professor James Naismith

Protein Production UK

Right sample, right time, right experiment

Rapidly growing knowledge of the human genome and proteome has resulted in a bottleneck for researchers interpreting protein structure and function as proteins of interest are being identified far faster than they can be produced for analysis. Protein Production UK is a national hub hosted at The Franklin to revolutionise how proteins are produced, stabilised, delivered and transferred. In partnership with Diamond Light Source, the UK's national synchrotron facility, PPUK is tasked with devising new ways to deliver "the right sample, at the right time, for the right experiment". This involves improving existing technology and developing new methods that will enable the structural biology community to keep pace with the rapidly expanding range of tools available for analysis using X-rays and electrons.

Key to delivering PPUK's aims are two projects, Nanobodies and Chameleon, described in detail below:

Nanobodies

Enabling analysis of complex macromolecules and small proteins.

The small molecular size, facile expression, high affinity and stability of nanobodies (recombinant antigen-specific single domain antibodies derived from the heavy chain of camelid immunoglobulins) make them unique targeting reagents with multiple applications in the biomedical sciences. In structural biology, the use of nanobodies has been transformative enabling the analysis of complex macromolecules including integral membrane proteins by both X-ray crystallography and cryo-EM. Using nanobody-based scaffolds to build up the size of proteins that are otherwise too small to image by cryo-EM is a new and exciting application of nanobody technology. The Franklin's goal is to develop high throughput nanobody technologies (50 campaigns a year) to address the barriers to use of poor access and high cost for the UK community.

Chameleon

Automating cryo-EM sample preparation for better, more reliable results

Recent advancements in cryo-EM have opened the possibility of determining atomic resolution structures for both traditional targets and more challenging sample (e.g. integral membrane proteins), which could have profound effects on drug discovery processes. However, sample preparation for cryo-EM is low-throughput due to it still being largely a manual process. The process gives inconsistent, non-repeatable results, and is prone to manual handling errors.

To deal with these issues, The Franklin has partnered with STP Labtech to produce Chameleon, which will provide automatic sample preparation. This system will offer the users reduced variability, improved sample yields and reduced sample consumption through the real-time user feedback, which will guide sample preparation and quality control. Alongside, a simplified workflow and user interface to ensure the machine is easy to use.

Amplus

High resolution molecular mapping of whole cells

The ability to visualise the atomic structure of proteins in the context of the cell (or tissue) has always been an aspiration for structural biology. Realising this goal has never been more urgent as we discover complex molecular machines and assemblies that regulate life. High-resolution large-volume electron cryo tomography is the most promising technology to deliver this ambition. However, electron cryo tomography is currently labour intensive, with poor resolution and even experienced labs report >80% failure rate. The Franklin's Amplus project is set to transform this workflow and push the capability of the technique to yield molecular resolution of "just-in-time" biological samples.

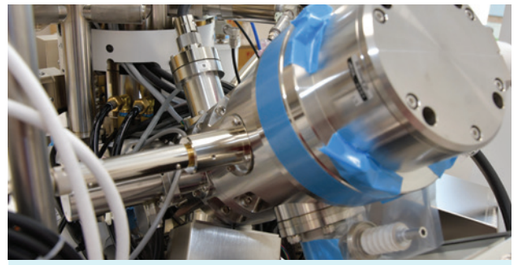
Proof-of-concept projects in microbial pathogenesis are being explored to support development of the novel instruments.

C100

This new detector, named C100, is the critical first step in this democratisation of the cryo electron microscopy method.

The goal of the project is to develop a detector which can work at a much lower energy, 100 keV, versus the current industry standard 300 keV, to obtain atomic scale images of biological samples. Cryo-EM currently requires large and expensive technology, which is housed in highly specialist environments. Lowering the energy of the electrons enables the use of a simpler, and cheaper, electron gun. Crucially, the new detector will produce better data from the lower energy microscope than existing detectors working with higher energy microscopes.

The ultimate aim is to encourage faster scientific progress by bringing a quick, simple and reliable cryo-EM to medical research laboratories and drug companies around the world, allowing a massive shift in the accessibility of this revolutionary technique.



Theme publications:

Gao et al. (2020) Uncovering the chemistry of C–C bond formation in C-nucleoside biosynthesis: crystal structure of a C-glycoside synthase/PRPP complex, Chemical Communications, doi: 10.1039/D0CC02834G

Huo et al. (2020) Neutralizing nanobodies bind SARS-CoV-2 spike RBD and block interaction with ACE2, Nature Structural & Molecular Biology, doi: 10.1038/s41594-020-0469-6

Song & Naismith (2020) Enzymatic methylation of the amide bond, Current Opinion in Structural Biology, doi: 10.1016/j.sbi.2020.06.004

Zhou et al. (2020) Structural basis for the neutralization of SARS-CoV-2 by an antibody from a convalescent patient, Nature Structural & Molecular Biology, doi: 10.1038/s41594-020-0480-y

Bell (2020) Uncovering a novel molecular mechanism for scavenging sialic acids in bacteria, Journal of Biological Chemistry, doi: 10.1074/jbc.RA120.014454

Song et al. (2020) Substrate plasticity of a fungal peptide αN-Methyltransferase, ACS Chemical Biology, doi: 10.1021/acschembio.0c00237

Song et al. (2020) The Biosynthesis of the Benzoxazole in Nataxazole Proceeds via an Unstable Ester and has Synthetic Utility, Angewandte Chemie International Edition, doi: 10.1002/anie.201915685

Moynié et al. (2019) The complex of ferric-enterobactin with its transporter from Pseudomonas aeruginosa suggests a two-site model, Nature communications, doi: 10.1038/s41467-019-11508-y

Artificial Intelligence and Informatics

Our aim is to automate the mundane scientific activities at The Franklin, allowing our scientists to highlight the extraordinary.

Science director: Dr Mark Basham

A Cross-cutting Theme

Artificial Intelligence and Informatics plays a key role in augmenting the other scientific themes at the Rosalind Franklin Institute, applying the latest methods in AI and machine learning to enhance performance in areas such as data processing and analysis. Data is critical to many areas of AI, including machine learning, and so the team is also responsible for data storage and management at the Franklin.

AI and Machine Learning

One of the big challenges in modern science is handling the vast quantities of data collected by state-of-the-art equipment of the type housed at The Franklin. This is where AI and machine learning techniques come in: tasks that would take researchers months or even years to carry out manually can be automated, generating order-of-magnitude efficiencies in the processing and analysis of data. By training a machine learning algorithm to spot patterns or anomalies in these huge volumes of data, time-consuming tasks can be sped up considerably – freeing researchers to focus on what's important.

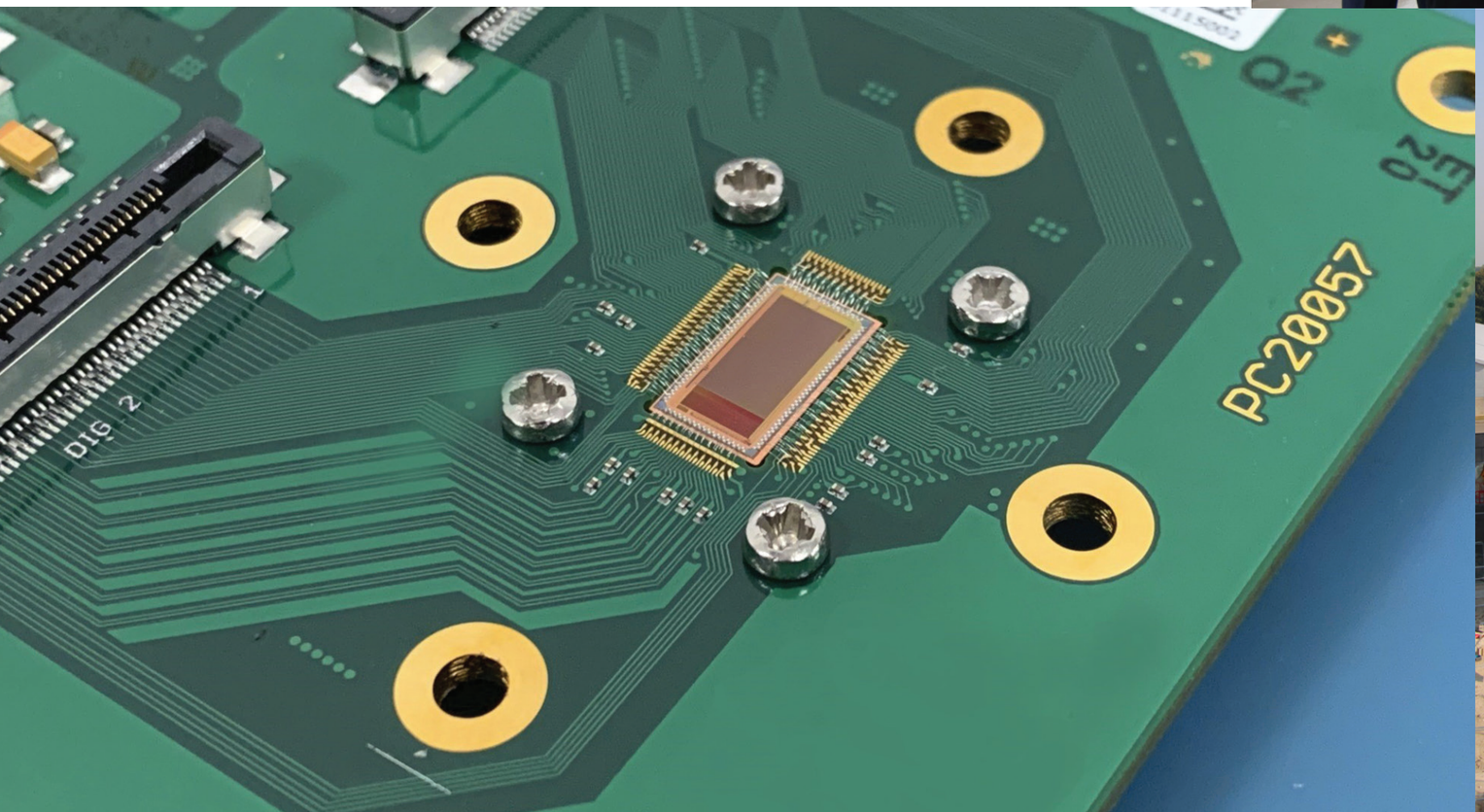
Data Management and Storage

The AI and Informatics theme is also responsible for the general management of data at the Franklin, making sure any data collected on its instruments is stored safely and effectively, and made accessible to researchers for mining and processing. The theme's methods can also be applied to areas such as manufacturing – for example, to create efficiencies in the quality assurance process.

Hub at Harwell Update:

The hub building is situated on the Harwell Campus, and will be the home of The Franklin. Once complete the hub will be home to 235 researchers. It will also house many of our world leading technologies.

In May 2019, groundbreaking at Harwell took place, with the Hub's sophisticated piled foundations laid shortly after. By November 2019 we celebrated topping out, with the building watertight in March 2020. Progress has continued throughout lockdown and we would like to thank our partners at MACE , AECOM and STFC for their support and ingenuity during this difficult period. We look forward to moving equipment and staff into the Hub for opening in 2021.



Engagement

Academic and Industry Engagement

Throughout this year we have held events with several of our partner organisations, including Universities of Edinburgh, Southampton, Manchester and Leeds. These events are critical to deepening our connections with members of these universities, to keep them updated with what is happening at The Franklin, and to find projects upon which we can collaborate.

We delivered the first Interfaces in Cryo-EM conference, which aims to bring together researchers from industry and academia around cutting edge techniques in cryo-EM. The first event, held in July 2019, attracted 80 delegates form industry and academia. Following on from the success of the 2019 conference, in 2020 we will hold a virtual training event. This event will tackle various forms of image data analysis, we believe that it will provide both academics and industry specialists with important skills, and give them important contacts for support with data analysis in the future.

We were pleased to celebrate two major building milestones with our members and community in 2019 – the groundbreaking and topping out of the building. The Groundbreaking in May 2019 coincided with our annual members symposium, which brought member from academia and project partners together to discuss progress at The Franklin. This annual meeting is a key opportunity for members and our communities to meet, discuss collaborations, and hear about future plans at The Franklin.

Engaging with industry on projects will be a key focus in the coming year, with strong engagement already in place with the technology sector, and strong collaboration with our colleagues at the Harwell HealthTec cluster.

Public Engagement

Here at The Franklin we aspire not only to do great science but also to inspire the next generation of scientists. Since we were established, we have carried out activities which inform and engage the public with our science. We have done this through all available channels, including traditional and social media. In 2019, we again had a presence at Bluedot festival, where we ran activities about cells and the human body, which thousands of attendees enjoyed, and hosted a public talk on The Franklin.

In addition to sharing our own science, we also like to talk about our namesake, Rosalind Franklin, and her legacy whenever possible. This has been especially important to us in 2020 as it is the centenary of Franklin's birth. Throughout 2020, representatives from The Franklin have given talks about Franklin's legacy at range of events, from Cheltenham Science Festival at Home to the STFC lecture series 'Talking Science', to the Willesden Cemetery's (where Franklin is buried) Rosalind Franklin Centenary Celebration.

In this year, we have built important relationships with a number of local schools. For this work, we have partnered with Education Business Partnerships based in West Berkshire and are taking part in their Hi-Tech Horizons programme, which introduces school students to businesses in the tech industry. Designed to reach 10,000 students per year, the scheme targets state school students in the Berkshire, Hampshire and Wiltshire region. These students are often based in rural communities with poor access to traditional science outreach programmes.

When visiting schools, we discuss a range of topics, including Rosalind Franklin's work and career, the impact The Franklin hopes to have on the life sciences field. We also discuss future career options at the Franklin and in generally in science.

These school visits are vitally important in raising the aspirations of local students. Research by King's College London into the aspirations of 10-14 year olds has shown that one of the primary barriers to students aspiring to be scientists is a lack of family science capital. Family science capital is the amount of science-related qualifications, understanding, knowledge (about science and science careers), interest and social contacts (knowing someone in a science-related job). Those coming from families with little or no science capital can often find it difficult to understand the range of career opportunities available within the science and technology field. Also, even if they are aware of the opportunities, they may find it difficult to imagine themselves in such roles. Therefore, the opportunity to meet and interact with scientists is extremely important in removing these barriers.

We look forward to continuing and building upon these events in the coming years.

Equality, Diversity and Inclusivity (EDI)

Our approach to working is collaborative, welcoming and encourages diversity in all its forms. We believe that these working approaches, together with our research values, make The Franklin a unique environment for research and researchers.

We endeavour to put policies and systems in place to ensure that we are welcoming and accommodating to staff with protected characteristics, from underrepresented groups and backgrounds, and to support staff with caring responsibilities. For example, by actively discussing flexible working at our interviews, we hope to normalise and encourage flexible working practices. In addition, we have now made unconscious bias training available to all Franklin staff.

We have also been gathering data about our recruiting and hiring processes, so that this year's data will provide a benchmark for subsequent years and will allow us to set reasonable goals moving forward. We will also benchmark ourselves against other similar institutes as we believe to grasp these issues and understand how best to tackle them, we must place what we are doing in the larger context.

Sustainability and Environmental Impact

We are committed to reducing our environmental impact. Where possible we hope to eliminate, or where not possible, to mitigate and measure our impact on the environment. A few key examples of these areas and the steps we intend to take are given below.

Construction

We are proud that the Hub is on target to receive a BREEAM 'very good' status. The 'very good' rating reflects the work carried out in designing the Hub, in selecting sustainable materials, designing spaces to be heat and power efficient, and integrating efficient management into the building. The building contractors, Mace, also measure sustainability in their construction processes, and report monthly on their progress. Our site has a current sustainability rating of gold from Mace.

Utilities

In the new building we will work with STFC to measure the electricity, gas and water usage of our new building, we will create a reporting matrix which we will annually send to the board and any external companies if required. We will aim to reduce our consumption as much as possible.

Lab practices

Once in the new building, we will aim to have good lab practices which limit the environmental impact, through receiving training and accreditation through schemes like the Laboratory Efficiency Accreditation Scheme (LEAF).

Events management

When hosting events, we will where possible to reduce the impact of these events. We provide only vegetarian catering options and are working to reduce the number of single-use items given out during events.

Travel

Travel is important in research – bringing together colleagues to share and learn. Science is by its nature global, so travel is sometimes unavoidable in international collaborations. However, the impact of global and domestic travel in climate change is unarguable.

We intend to minimise our travel whenever possible and necessary travel should be taken by the lowest impact means. It is essential that we measure our carbon emissions from travel, to understand the impact our travel has on the environment, and report appropriately. We will benchmark against our colleagues and be aspirational in our targets. We plan to invest in carbon offsetting projects to mitigate the effects of our travel.

At Harwell, we support green travel initiatives, and encourage staff to cycle to work, or use public transport.

Directors/Trustees

The Directors of the charitable company are its Trustees for the purposes of charitable law and throughout this report are referred to as the Directors.

- Dr Gillian Burgess
- Professor Stephen Caddick
- Dr Vivienne Cox CBE
- Mr Stephen Dauncey
- Dr Joanne Dekkers (Resigned 9 May 2019)
- Dr B M G Ghinelli
- Dr Jennifer Jennings (Appointed 9 May 2019)
- Professor Andrew Livingston
- Professor Ewan McKendrick
- Professor J H Naismith (Appointed 22 July 2019)
- Professor Peter Smith
- Professor Nigel Titchener-Hooker (Appointed 7 May 2019)
- Dr Anthony Wood

Members of the Rosalind Franklin Institute

University of Birmingham

University of Cambridge

Diamond Light Source

University of Edinburgh

Imperial College London

University of Leeds

Kings College London

University of Manchester

University of Oxford

University of Southampton

University College London

UKRI-STFC

Bankers

Barclays

Solicitors

Royds Withy King
North Bailey House,
New Inn Hatt Street
Oxford
OX1 2EA

Keystone Law
48 Chancery Ln,
Holborn,
London
WC2A 1JF

Executive Group

Institute Director	James Naismith	Seconded from Oxford
Director of Structural Biology	James Naismith	Seconded from Oxford
Director of Next Gen Chemistry	Ben Davis	Employed Rosalind Franklin Institute
Interim Theme Leader	Adam Nelson	Seconded from Leeds University
Director of Correlated Imaging	Angus Kirkland	Seconded from Oxford
Director of Artificial Intelligence and Informatics	Mark Basham	Employed Rosalind Franklin Institute
Directors of Mass Spectrometry	Josephine Bunch	Seconded from National Physical Laboratory and Imperial College London
	Zoltan Takats	Seconded from Imperial College London
Chief Operating Officer	Tim Venables (to April 2019)	Seconded from Imperial
	Ellanore Johnson Searle (interim April-November 2019)	Employed Rosalind Franklin Institute
	Paul McCubbin (Nov 2019-)	Employed Rosalind Franklin Institute
Director of Communications and Culture	Laura Holland	Employed Rosalind Franklin Institute
Head of Partnerships and Business development	Roisin NicAmhlaoibh	Employed Rosalind Franklin Institute
Financial Controller	Catherine Tysoe (April 2020 -)	Employed Rosalind Franklin Institute

Objectives and activities

The Rosalind Franklin Institute is devoted to addressing important challenges through the development and use of innovative technology. Many of our challenges relate to our ability to see the structures of life more clearly; from novel imaging techniques which will allow us to see better into living systems, to the atomic detail of a drug binding with a target protein.

This ability to visualise the inner workings of life, and to draw new understanding from this, is one of the reasons we are named in honour of Rosalind Franklin who celebrates her centenary year in 2020. A great experimental scientist, Franklin worked on a number of diverse scientific problems, most famously DNA, bringing incredible experimental skill, technological expertise and knowledge from across the sciences.

The charitable objectives of the Rosalind Franklin Institute are for the public benefit

- the promotion and preservation of human health, including without limitation by furthering the progress of scientific discoveries and new technologies arising from research into therapeutic treatments, drugs, diagnostics, other technologies and/or information resources by conducting its own research and development activities and by means of collaboration with universities, industry, charities, the state and other relevant bodies.
- the furtherance of education, in the fields of the physical sciences, engineering, health and life sciences, engineering, health and life sciences by means including
- conducting research and publishing the useful results of such research
- collaborating and exchanging knowledge with universities, industry, charities and other not-for-profit organisations, the state and other relevant bodies
- public engagement through educational outreach activities, in each case with a view to advancing the state of our collective knowledge and understanding of such fields of study

The income of the Rosalind Franklin is derived from grants from UKRI, administered by the Engineering and Physical Sciences Research Council (UKRI/EPSRC) and grants awarded for specific research projects and collaborations, and a one-off Membership fee paid by our new Academic Member Diamond Light Source.

Structure, Governance and Management

The Rosalind Franklin is governed by its Board of Trustees whose members are also its Directors.

Recruitment and appointment of Trustees

The members of the Board who served during the year and up to the date of the Report are listed on page 26. The Members of the Board are Directors for the purpose of company law, and Trustees for the purpose of charity law. Under the Joint Venture Agreement and Company's Articles, Independent Board Members are elected to serve on the Board for a period of three years. In order to ensure continuity during the Covid19 lockdown period, both directors who were due to step down on 31 March had their terms extended to 30 September 2020, as approved by members. Terms may be extended by re-election to a maximum of two terms.

The Board seeks to recruit a diverse membership. Periodically, they consider the skills mix of the Board as a means of succession planning. Other than our Independent Non-Executive Chair, Board Members do not receive fees or other remuneration as Directors and Trustees but are entitled to recover expenses as outlined in the notes to the Accounts.

The induction programme seeks to inform Directors of the strategic priorities through a schedule of meetings and briefing documents as appropriate. As per our governance there is an annual rotation of Member Directors and as we receive feedback from 'retirees' we will review and refine this process.

Organisational structure

The Rosalind Franklin has a clear organisation structure with documented lines of responsibility and authority and that sets out the composition of each group and committee within the structure.

Member Representatives - represent the interests of the member organisations, and their role is to ensure that the institute is delivering strong partnerships with its members

and delivering its aims. Collectively, they drive the direction of The Franklin. The Joint Venture Agreement sets out a number of decisions that are reserved for the Members and those matters that are delegated to the Board, Institute Director and Executive Group. The Members appoint the external auditors.

The Board - have primary responsibility for The Franklin (Joint Venture Agreement and Memorandum and Articles). The Board is responsible for setting the aims and strategic direction of The Franklin. They monitor risks, approval the annual business plan, budget and expenditure targets, and monitor the financial results (actual and forecast). The Board has final approval of funding bids and the resourcing of projects.

UKRI/EPSRC may nominate a representative to attend Board meetings as an observer, but such representative will not be a Director.

The Board meets four times a year to monitor the operations of The Franklin and there is regular contact with Board Members in between meetings.

During the financial year 2019/2020 the Board oversaw all of the organisations finances and activities. Three sub-committees have been established by the board prior to this reporting year; The Value for Money Panel, Remuneration committee, and the Audit and Risk Committee. The Strategic Advisory Board also advises on the direction and development if scientific themes via the board.

The Value for Money Panel – considers all major funding proposals prior to them being considered by the Board. They assess their viability and value for money. Only proposals with the support of the Executive Group and relevant Theme Advisory Panels are submitted to the Value for Money panel which is chaired by the Institute Director. Recommendations from the Value for Money Panel are presented to the Board of Trustees for final approval.

Strategic Advisory Board – has been established to advise the Franklin, via its Board on the development and implementation of the research and development strategy of the institute. Members are independent experts from academia and industry, both national and international. The Board met for the first time in February 2020 and reviewed the current direction and future plans for each theme.

Remuneration committee (RemCom) - has oversight of the preparation of policies and procedures in respect of salaries, emoluments and conditions of service of employees of The Franklin and in particular as they relate to Equality and Diversity, performance reviews and personal development.

Audit committee – is responsible for audit, finance and risk management. They review The Franklin's internal controls, risk management processes and compliance with funding and reporting requirements. They monitor the work of the external auditors and the resulting financial statements and receive and review the annual audit report.

Theme Advisory Panels – each theme has a panel of international experts from across academia and industry who contribute to the development and review of the road-maps, technology and funding proposals for each theme.

The day to day management of The Franklin has been delegated to the Institute Director who works with the Executive Group to deliver The Franklin's operations, activities and projects.

The Executive Group – the Group is made up of the senior operations team and the science directors. They consider developments across the themes and form part of the decision-making in advancing proposals to the Value for Money Panel. They are responsible for implementing the agreed strategy and policies and report on performance to the Board.

Remuneration policy

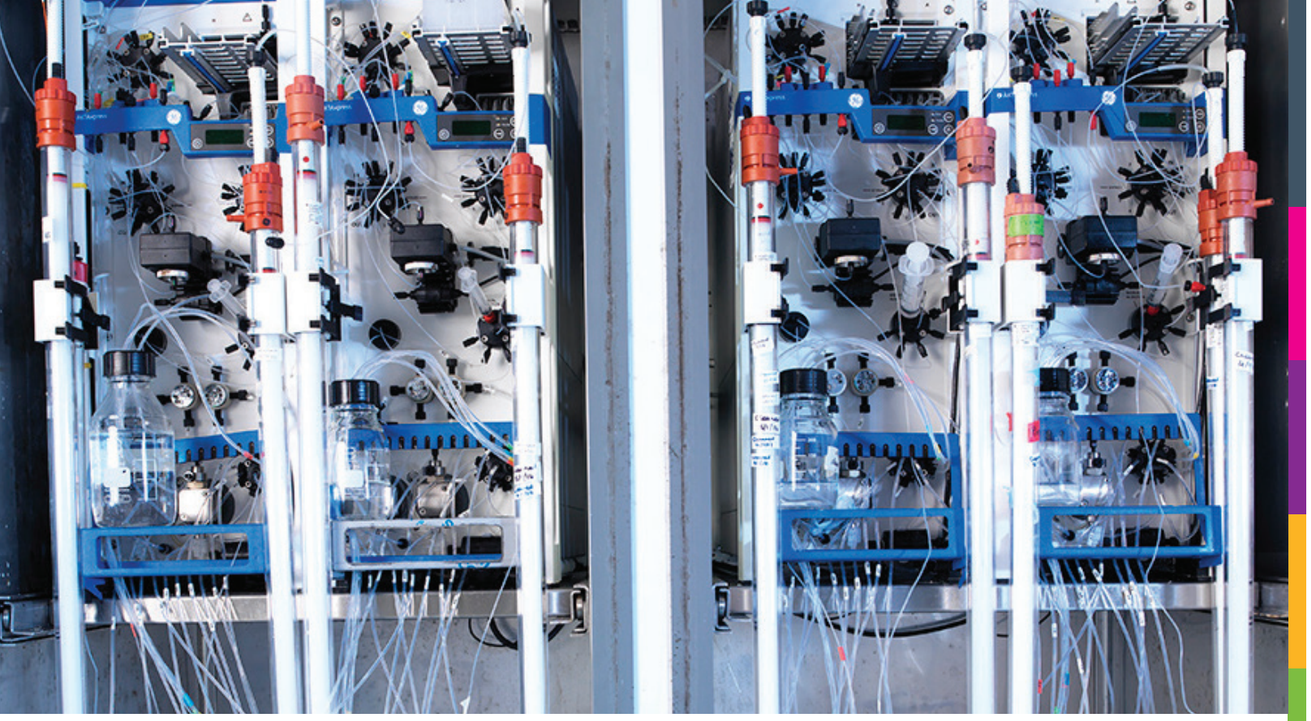
In determining the remuneration we offer to employees, the Rosalind Franklin Institute has established a set of principles. We appreciate that we employ a wide variety of people with varying skills, experience and lifestyles. We are mindful that individuals' needs will be different and, as far as possible take this into account in shaping our remuneration package; in developing and implementing our people policies; and in how we work together. The same benefits, including pensions, and terms and conditions apply to all employees irrespective of role or pay grade.

It is important to The Franklin to pay competitive salaries in the sector and location where we employ people. Base pay rates are benchmarked against sector pay and taking into account our location - we do this on a continuous basis. In addition, each year we take into account inflationary indices and organisational affordability. All pay levels are reviewed annually.

Risk management

Effective risk management is central to the role of The Franklin Board in providing strategic oversight and stewardship.

Led by the Institute Director and the Chief Operating Officer, the Executive Group is responsible for reporting and managing risks, ensuring they are assessed and mitigated in accordance with our risk policy. Risks are detailed using an organisation-wide risk register which offers a rating score, pre and post mitigation. Significant risks are reported formally to the Audit Committee and Board as they have the ultimate responsibility for risks.



Examples of risks that the Rosalind Franklin currently faces include

- ***Future funding structure:*** Securing ongoing funding beyond March 2021. Failure to attract adequate future funding risks the success of current technologies and diminishes the value to UK research of the new Hub.
- ***Successful transition into Hub:*** commissioning and installing technologies, seamless transition into new space for operational teams. Failure to transition successfully risks delays in key technologies and operational disruption.
- ***Strategic development:*** Identifying the next wave of science themes and technologies. The Franklin's themes must represent a clear factor of ten area for development, with appropriate support from the community. Robust governance must apply appropriate tests.
- ***Resilience:*** Creating operational resilience, while maintaining a lean and high value organisation. Operational disruption may be caused by a failure to recruit suitably qualified and experienced individuals to support the scientific aspirations and operational expansion of the Institute.
- ***Managing scientific risk*** – closely monitoring technologies in progress to identify risks. Not all Franklin projects will succeed by their nature, but resources should be transferred as early as possible where this is the case.

The Board seek to ensure that risks are mitigated, so far as is reasonably possible by the actions to be implemented and noted in the register. The mitigation for risks noted above includes

- Engage with Members and funders; communicate the clear vision for The Franklin's future; ensure adequate consultation with Members, academic community and industry. Science directors to contribute to funding strategy.
- Liaise with STFC to plan appropriate 'soft landing' and transition into building.
- Deliver clear consultation on wave two, based on recommendations of the Strategic Advisory Board. Maintain awareness and understanding of the current portfolio of scientific projects with the Board and Members.
- Review the composition and organization of the operations team, ensuring that the skills and structure will support future growth of the Institute.
- Ensure an appropriately developed project governance framework, with cost controls and clear accountability across the organisation. Commitment from research teams to regular peer review and engagement with Theme Advisory Panels.

Financial Review

For the 12 month period ended 31 March 2020, the Institute recorded a surplus on general unrestricted funds of £1,741,687.

Total income in 2019/20 was £18,722,993, £4,726,548 of which was unrestricted. Income is made up of funding from an unrestricted grant of £4,726,548 from UKRI/EPSRC, funding from a restricted grant of £13,922,123 from UKRI/EPSRC, membership fees of £20,000 and collaboration income from a Member of the Institute, a commercial partner and also an academic partner based overseas.

The UKRI/EPSRC grants and the collaboration income are awarded in respect of the delivery of specific projects including the purchase of instrumentation.

For the 12 month period ended 31 March 2020, total expenditure was £2,061,565.

This review does not include funds paid directly to certain Member Institutions UKRI/EPSRC for science projects being delivered as part of our grant portfolio.

Reserves

At the end of the financial year, the retained reserves of the charity were £20,524,339 of which £16,889,569 were restricted and not available for the general purposes of the charity. Of these funds, £13,733,114 has been designated, or otherwise committed, at the end of the reporting period.

The timing of spend of these financial commitments remains under review with our grant funding bodies and relevant suppliers. Whilst purchase orders and collaboration agreements have been entered into, the construction of instrumentation and therefore timing of payments has been impacted by delays due to Covid-19 which were not foreseen at the time of the grant drawdown.

After making an allowance for these restricted, designated funds – the charity holds reserves of £6,791,225.

Reserves Policy

In accordance with Charity Commission guidance and best practice the Reserves Policy for the Institute is to ensure the stability of the on-going operations of the organisation. The reserves are intended to provide a cushion against unexpected situations, large unbudgeted expenses, and unanticipated losses in funding and is in keeping with the careful management of our charity funds.

It is the policy of the Institute to retain sufficient unrestricted reserves to cover liabilities relating to liquidation and that the Audit and Risk Committee will monitor the level of reserve required in this respect as the organisation grows and becomes established.

Surplus reserves were held at the end of the financial year due, in part, to the deceleration of spend as the Covid-19 pandemic unfolded. Grant funds are awarded by UKRI/EPSRC in respect of recurrent spend based on pre-approved and authorised cash flow forecasts.

Investment Policy

At this stage, the investment policy continues to be limited to the management of instant access, liquid funds. Moving forwards, it is anticipated that the investment policy will be developed to facilitate the secure investment of excess cash resources through diversification of the portfolio. Investments will remain risk averse and non-speculative in line with charitable objectives.

Funding Sources and Sustainability

The principal funding source of the Institute in the year was the award of grant applications. The Institute does not engage in fundraising.

The Institute works in close partnership with funders to ensure that the grant profiles and project funding remain appropriate and support financial sustainability.

Looking ahead, the Institute remains in discussion with UKRI/EPSRC in respect of core funding post March 2021, in accordance with the planned quinquennial review. In addition, the Institute continues to work with both existing and new partners, seeking to diversify income in order to support new projects in line with charitable objectives.

Going Concern

Whilst future funding of the Institute beyond March 2021 remains under review with UKRI/EPSRC; having made due enquiries the Board believe that it is appropriate to prepare the accounts on a going concern basis.

The Board consider that the Institute has adequate resources available to cover the working capital requirements of the charity for at least 12 months from the date of signing this report and financial statements. Cash flow forecasts and budget reviews are carried out monthly by the Executive Team and reforecasts allow activity to be adjusted to respond to any unexpected variations.

Statement of Trustees Responsibilities

The trustees, who are also the directors of The Rosalind Franklin Institute for the purpose of company law, are responsible for preparing the Trustees' Report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards (United Kingdom Generally Accepted Accounting Practice).

Company Law requires the trustees to prepare financial statements for each financial year which give a true and fair view of the state of affairs of the charity and of the incoming resources and application of resources, including the income and expenditure, of the charitable company for that year.

In preparing these financial statements, the trustees are required to:

- select suitable accounting policies and then apply them consistently;
- observe the methods and principles in the Charities SORP;
- make judgements and estimates that are reasonable and prudent;
- state whether applicable UK Accounting Standards have been followed, subject to any material departures disclosed and explained in the financial statements; and
- prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charity will continue in operation.

The trustees are responsible for keeping adequate accounting records that disclose with reasonable accuracy at any time the financial position of the charity and enable them to ensure that the financial statements comply with the Companies Act 2006. They are also responsible for safeguarding the assets of the charity and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

Disclosure of information to auditor

Each of the trustees has confirmed that there is no information of which they are aware which is relevant to the audit, but of which the auditor is unaware. They have further confirmed that they have taken appropriate steps to identify such relevant information and to establish that the auditor is aware of such information.

The trustees' report was approved by the Board of Trustees.

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Dr Vivienne Cox CBE
Chair of Trustees

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Dated: ?????????

Independent Auditor's Report to the members of The Rosalind Franklin Institute

Opinion

We have audited the financial statements of The Rosalind Franklin Institute (the 'charity') for the year ended 31 March 2020 which comprise the statement of financial activities, the balance sheet, the statement of cash flows and the notes to the financial statements, including a summary of significant accounting policies. The financial reporting framework that has been applied in their preparation is applicable law and United Kingdom Accounting Standards, including Financial Reporting Standard 102 *The Financial Reporting Standard applicable in the UK and Republic of Ireland* (United Kingdom Generally Accepted Accounting Practice).

In our opinion, the financial statements:

- give a true and fair view of the state of the charitable company's affairs as at 31 March 2020 and of its incoming resources and application of resources, for the year then ended;
- have been properly prepared in accordance with United Kingdom Generally Accepted Accounting Practice; and
- have been prepared in accordance with the requirements of the Companies Act 2006.

Basis for opinion

We conducted our audit in accordance with International Standards on Auditing (UK) (ISAs (UK)) and applicable law. Our responsibilities under those standards are further described in the Auditor's responsibilities for the audit of the financial statements section of our report. We are independent of the charity in accordance with the ethical requirements that are relevant to our audit of the financial statements in the UK, including the FRC's Ethical Standard, and we have fulfilled our other ethical responsibilities in accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Conclusions relating to going concern

We have nothing to report in respect of the following matters in relation to which the ISAs (UK) require us to report to you where:

- the trustees' use of the going concern basis of accounting in the preparation of the financial statements is not appropriate; or
- the trustees have not disclosed in the financial statements any identified material uncertainties that may cast significant doubt about the charity's ability to continue to adopt the going concern basis of accounting for a period of at least twelve months from the date when the financial statements are authorised for issue.

Other information

The trustees are responsible for the other information. The other information comprises the information included in the annual report, other than the financial statements and our auditor's report thereon. Our opinion on the financial statements does not cover the other information and, except to the extent otherwise explicitly stated in our report, we do not express any form of assurance conclusion thereon.

In connection with our audit of the financial statements, our responsibility is to read the other information and, in doing so, consider whether the other information is materially inconsistent with the financial statements or our knowledge obtained in the audit or otherwise appears to be materially misstated. If we identify such material inconsistencies or apparent material misstatements, we are required to determine whether there is a material misstatement in the financial statements or a material misstatement of the other information. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact.

We have nothing to report in this regard.

Opinions on other matters prescribed by the Companies Act 2006

In our opinion, based on the work undertaken in the course of our audit:

- the information given in the trustees' report, which includes the directors' report prepared for the purposes of company law, for the financial year for which the financial statements are prepared is consistent with the financial statements; and
- the directors' report included within the trustees' report has been prepared in accordance with applicable legal requirements.

Independent Auditor's Report (cont) to the members of The Rosalind Franklin Institute

Matters on which we are required to report by exception

In the light of the knowledge and understanding of the charity and its environment obtained in the course of the audit, we have not identified material misstatements in the directors' report included within the trustees' report.

We have nothing to report in respect of the following matters in relation to which the Companies Act 2006 requires us to report to you if, in our opinion:

- adequate accounting records have not been kept, or returns adequate for our audit have not been received from branches not visited by us; or
- the financial statements are not in agreement with the accounting records and returns; or
- certain disclosures of trustees' remuneration specified by law are not made; or
- we have not received all the information and explanations we require for our audit; or
- the trustees were not entitled to prepare the financial statements in accordance with the small companies regime and take advantage of the small companies' exemptions in preparing the trustees' report and from the requirement to prepare a strategic report.

Responsibilities of trustees

As explained more fully in the statement of trustees' responsibilities, the trustees, who are also the directors of the charity for the purpose of company law, are responsible for the preparation of the financial statements and for being satisfied that they give a true and fair view, and for such internal control as the trustees determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, the trustees are responsible for assessing the charity's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the trustees either intend to liquidate the charitable company or to cease operations, or have no realistic alternative but to do so.

Auditor's responsibilities for the audit of the financial statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with ISAs (UK) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

A further description of our responsibilities for the audit of the financial statements is located on the Financial Reporting Council's website at: http://www.frc.org.uk/auditorsresponsibilities. This description forms part of our auditor's report.

Use of our report

This report is made solely to the charitable company's members, as a body, in accordance with Chapter 3 of Part 16 of the Companies Act 2006. Our audit work has been undertaken so that we might state to the charitable company's members those matters we are required to state to them in an auditors' report and for no other purpose. To the fullest extent permitted by law, we do not accept or assume responsibility to anyone other than the charitable company and the charitable company's members as a body, for our audit work, for this report, or for the opinions we have formed.

Jemima King (Senior Statutory Auditor)

for and on behalf of Richardsons

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Chartered Accountants Statutory Auditor

Statement of financial activities including income and expenditure account For the year ended 31 March 2020

	Notes	Unrestricted funds 2020 £	Restricted funds 2020 £	Total 2020 £	Unrestricted funds £	Restricted funds 2019 £	Total 2019 £
Income and endowments from:							
Donations and legacies	3	-	-	-	921,606	2,993,002	3,914,608
Charitable activities	4	4,726,548	13,922,123	18,648,671	-	-	-
Other income	5	-	74,322	74,322	-	220,000	220,000
Total income		4,726,548	13,996,445	18,722,993	921,606	3,213,002	4,134,608
Expenditure on:							
Raising funds	6	46,354	-	46,354	63,044	-	63,044
Charitable activities	7	1,694,250	319,878	2,014,128	208,638	-	208,638
Other	11	1,083	-	1,083	15	-	15
Total resources expended		1,741,687	319,878	2,061,565	271,697	-	271,697
Net income for the year/ Net movement in funds		2,984,861	13,676,567	16,661,428	649,909	3,213,002	3,862,911
Fund balances at 1 April 2019		649,909	3,213,002	3,862,911	-	-	-
Fund balances at 31 March 2020		3,634,770	16,889,569	20,524,339	649,909	3,213,002	3,862,911

The statement of financial activities includes all gains and losses recognised in the year. All income and expenditure derive from continuing activities.

The statement of financial activities also complies with the requirements for an income and expenditure account under the Companies Act 2006.

Balance Sheet as at 31 March 2020

	Notes	2020 £	2020 £	2019 £	2019 £
Fixed assets					
Tangible assets	**12**		11,964,438		3,614,680
Current assets					
Debtors	**13**	250,254		3,020,162	
Cash at bank and in hand		8,715,328		904,462	
		8,965,582		3,924,624	
Creditors: amounts falling due within one year	**14**	(405,681)		(3,676,393)	
Net current assets			8,559,901		248,231
Total assets less current liabilities			20,524,339		3,862,911
Income funds					
Restricted funds			16,889,569		3,213,002
Unrestricted funds			3,634,770		649,909
			20,524,339		3,862,911

The financial statements were approved by the Trustees on .....

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Dr Vivienne Cox CBE
Chair of Trustees

Company Registration No. 11266143

Statement of Cash Flows for the year ended 31 March 2020

	Notes	2020 £	2020 £	2019 £	2019 £
Cash flows from operating activities					
Cash generated from operations	**18**		16,459,290		4,520,281
Investing activities					
Purchase of tangible fixed assets		(8,648,424)		(3,615,819)	
Net cash used in investing activities			(8,648,424)		(3,615,819)
Net cash used in financing activities		-			-
Net increase in cash and cash equivalents			7,810,866		904,462
Cash and cash equivalents at beginning of year			904,462		-
Cash and cash equivalents at end of year			8,715,328		904,462

Notes to the Financial Statements for the year ended 31 March 2020

1. Accounting policies

Charity information

The Rosalind Franklin Institute is a private company limited by guarantee incorporated in England and Wales. The registered office is The Research Complex at Harwell, Rutherford Appleton Laboratory, Harwell, Oxfordshire, OX11 0FA.

1.1 Accounting convention

The financial statements have been prepared in accordance with the charity's Memorandum and Articles of Association, the Companies Act 2006 and "Accounting and Reporting by Charities: Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102)" (as amended for accounting periods commencing from 1 January 2016). The charity is a Public Benefit Entity as defined by FRS 102.

The financial statements are prepared in sterling, which is the functional currency of the charity. Monetary amounts in these financial statements are rounded to the nearest £.

The financial statements have been prepared under the historical cost convention. The principal accounting policies adopted are set out below.

1.2 Going concern

At the time of approving the financial statements, the trustees have a reasonable expectation that the charity has adequate resources to continue in operational existence for the foreseeable future. Thus the trustees continue to adopt the going concern basis of accounting in preparing the financial statements. Further details on this assessment can be found within the Trustees' Report.

1.3 Charitable funds

Unrestricted funds are available for use at the discretion of the trustees in furtherance of their charitable objectives.

Restricted funds are subject to specific conditions by grant providers as to how they may be used. The purposes and uses of the restricted funds are set out in the notes to the financial statements.

1.4 Incoming resources

Income is recognised when the charity is legally entitled to it after any performance conditions have been met, the amounts can be measured reliably, and it is probable that income will be received.

1.5 Resources expended

Liabilities are recognised as expenditure as soon as there is a legal or constructive obligation committing the charity to that expenditure, it is probable that a transfer of economic benefits will be required in settlement and the amount of the obligation can be measured reliably. Expenditure is accounted for on an accruals basis and has been classified under headings that aggregate all cost related to the category. Where costs can not be directly attributed to particular headings that have been allocated to activities on a basis consistent with the use of resources.

1.6 Tangible fixed assets

Tangible fixed assets are initially measured at cost and subsequently measured at cost or valuation, net of depreciation and any impairment losses.

Depreciation is recognised so as to write off the cost or valuation of assets less their residual values over their useful lives on the following bases:

Scientific Equipment	20% Straight Line
Office equipment	25% Straight Line
Computer equipment	33% Straight Line

No depreciation is charged on assets under construction.

The gain or loss arising on the disposal of an asset is determined as the difference between the sale proceeds and the carrying value of the asset, and is recognised in net income/(expenditure) for the year.

1.7 Impairment of fixed assets

At each reporting end date, the charity reviews the carrying amounts of its tangible assets to determine whether there is any indication that those assets have suffered an impairment loss. If any such indication exists, the recoverable amount of the asset is estimated in order to determine the extent of the impairment loss (if any).

1.8 Cash and cash equivalents

Cash and cash equivalents include cash in hand, deposits held at call with banks, other short-term liquid investments with original maturities of three months or less, and bank overdrafts. Bank overdrafts are shown within borrowings in current liabilities.

1.9 Financial instruments

The charity has elected to apply the provisions of Section 11 'Basic Financial Instruments' and Section 12 'Other Financial Instruments Issues' of FRS 102 to all of its financial instruments.

Financial instruments are recognised in the charity's balance sheet when the charity becomes party to the contractual provisions of the instrument.

Financial assets and liabilities are offset, with the net amounts presented in the financial statements, when there is a legally enforceable right to set off the recognised amounts and there is an intention to settle on a net basis or to realise the asset and settle the liability simultaneously.

Basic financial assets

Basic financial assets, which include debtors and cash and bank balances, are initially measured at transaction price including transaction costs and are subsequently carried at amortised cost using the effective interest method unless the arrangement constitutes a financing transaction, where the transaction is measured at the present value of the future receipts discounted at a market rate of interest. Financial assets classified as receivable within one year are not amortised.

Basic financial liabilities

Basic financial liabilities, including creditors and bank loans are initially recognised at transaction price unless the arrangement constitutes a financing transaction, where the debt instrument is measured at the present value of the future payments discounted at a market rate of interest. Financial liabilities classified as payable within one year are not amortised.

Debt instruments are subsequently carried at amortised cost, using the effective interest rate method.

Trade creditors are obligations to pay for goods or services that have been acquired in the ordinary course of operations from suppliers. Amounts payable are classified as current liabilities if payment is due within one year or less. If not, they are presented as non-current liabilities. Trade creditors are recognised initially at transaction price and subsequently measured at amortised cost using the effective interest method.

Derecognition of financial liabilities

Financial liabilities are derecognised when the charity's contractual obligations expire or are discharged or cancelled.

1.10 Retirement benefits

Payments to defined contribution retirement benefit schemes are charged as an expense as they fall due.

2 Critical accounting estimates and judgements

In the application of the charity's accounting policies, the trustees are required to make judgements, estimates and assumptions about the carrying amount of assets and liabilities that are not readily apparent from other sources. The estimates and associated assumptions are based on historical experience and other factors that are considered to be relevant. Actual results may differ from these estimates.

The estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognised in the period in which the estimate is revised where the revision affects only that period, or in the period of the revision and future periods where the revision affects both current and future periods.

3 Donations and legacies

	Total	Unrestricted funds	Restricted-funds	Total
	2020 £	2019 £	2019 £	2019 £
Grants	-	921,606	2,993,002	3,914,608

Notes to the Financial Statements for the year ended 31 March 2020 (cont)

4 Charitable activities

	2020	2019
	£	£
Grant income	18,648,671	-
Analysis by fund		
Unrestricted funds	4,726,548	-
Restricted funds	13,922,123	-
	18,648,671	-

5 Other income

	Restricted funds 2020	Restricted funds 2019
	£	£
Other income	54,322	-
Members' contributions	20,000	220,000
	74,322	220,000

6 Raising funds

	Unrestricted funds 2020	Total 2019
	£	£
Engagements & Publicity	46,354	63,044
	46,354	63,044

7 Charitable activities

	Operational Expenditure 2020	Operational Expenditure 2019
	£	£
Staff costs	730,333	60,264
Depreciation and impairment	298,666	1,139
Entertainment	222	77
Catering and events	44,960	1,286
Printing, postage and stationary	7,786	2,046
Recruitment	84,757	34,854
Insurance	17,790	1,637
Rent	111,632	12,044
Secondments and temp staff	444,145	45,000
Travel and accommodation	33,404	2,457
IT costs	47,432	10,258
Project costs	123,504	-
Partnerships & Business Development costs	35,150	-
Equipment hire	568	-
Sponsorship	800	-
	1,981,149	171,062
Share of support costs (see note 8)	9,039	21,686
Share of governance costs (see note 8)	23,940	15,890
	2,014,128	208,638
Analysis by fund		
Unrestricted funds	1,694,250	208,638
Restricted funds	319,878	-
	2,014,128	208,638
For the year ended 31 March 2019		
Unrestricted funds	208,638	

Notes to the Financial Statements for the year ended 31 March 2020 (cont)

8 Support costs

	Support costs	Governance costs	2020	Support costs	Governance costs	2019
	£	£	£	£	£	£
Accountancy	5,130	-	5,130	21,686	-	21,686
Legal and professional	3,909	-	3,909	-	-	-
Audit fees	-	3,600	3,600	-	3,450	3,450
Legal and professional	-	20,340	20,340	-	12,440	12,440
	9,039	23,940	32,979	21,686	15,890	37,576
Analysed between						
Charitable activities	9,039	23,940	32,979	21,686	15,890	37,576

Governance costs includes payments to the auditors of £3,600 (2019: £3,450) for audit fees.

9 Trustees

One (2019: One) of the trustees received remuneration of £20,000 (2019: £15,000) during the year ended 31 March 2020 for trustee duties. None of the trustees (or any persons connected with them) received any benefits from the charity during the year.

10 Employees

The average monthly number of full time equivalent employees during the year was 12 (2019: 1.3).

Employment costs	2020	2019
	£	£
Wages and salaries	571,226	52,642
Social security costs	63,233	2,208
Other pension costs	95,874	5,414
	730,333	60,264

The number of employees whose annual remuneration was £60,000 or more were:

	2020	2019
	Number	Number
£60,000 - £69,999	1	-
£70,000 - £79,999	1	-
£80,000 - £89,999	1	-
£90,000 - £99,999	1	-

11 Other

	Unrestricted funds	Unrestricted funds
	2020	2019
Financing costs	1,083	15
	1,083	15

12 Tangible fixed assets

	Assets under construction	Scientific Equipment	Office equipment	Computer equipment	Total
	£	£	£	£	£
Cost					
At 1 April 2019	3,600,862	-	7,698	7,259	3,615,819
Additions	8,592,927	5,447,560	4,407	51,091	14,095,985
Other changes	(5,447,560)	-	-	-	(5,447,560)
At 31 March 2020	6,746,229	5,447,560	12,105	58,350	12,264,244
Depreciation and impairment					
At 1 April 2019	-	-	481	658	1,139
Depreciation charged in the year	-	288,543	2,613	7,511	298,667
At 31 March 2020	-	288,543	3,094	8,169	299,806
Carrying amount					
At 31 March 2020	6,746,229	5,159,017	9,011	50,181	11,964,438
At 31 March 2019	3,600,862	-	7,217	6,601	3,614,680

13 Debtors

	2020	2019
	£	£
Amounts falling due within one year:		
Trade debtors	34,688	-
Other debtors	81,846	18,997
Prepayments and accrued income	133,720	3,001,165
	250,254	3,020,162

Notes to the Financial Statements for the year ended 31 March 2020 (cont)

14 Creditors: amounts falling due within one year

	2020	2019
	£	£
Trade creditors	86,320	619,003
Other creditors	34,538	8,217
Accruals and deferred income	284,823	3,049,173
	405,681	3,676,393

15 Analysis of net assets between funds

	Restricted 2020	Unrestricted 2020	Total 2020	Total 2019
	£	£	£	£
Fund balances at 31 March 2020 are represented by:				
Tangible assets	11,905,246	59,192	11,964,438	3,614,680
Current assets/(liabilities)	4,984,323	3,575,578	8,559,901	248,231
	16,889,569	3,634,770	20,524,339	3,862,911

16 Capital commitments

At 31 March 2020 the charity had capital commitments of £13,733,114 (2019: £1,616,033) in relation to fixed asset purchases.

17 Related party transactions

Transactions with related parties

During the year the charity entered into the following transactions with related parties:

Diamond Light Source Limited

During the year, Diamond Light Source Limited contributed £20,000 (2019: £Nil) in order to enter the joint venture agreement. Income in relation to a secondment agreement amounting to £17,186 (2019: £Nil) was invoiced to the member. As at 31 March 2020, £17,186 (2019: £Nil) was outstanding and as such is included in trade debtors. Costs amounting to £29,435 (2019: £Nil) were charged by the member during the year of which £Nil (2019: £Nil) was outstanding at the year end.

The University of Oxford

During the year, the University of Oxford, a member of the joint venture, invoiced £287,756 (2019: £Nil) in relation to secondment services provided. As at 31 March 2020, £14,784 (2019: £Nil) was due to be paid to the University and as such is included in trade creditors.

In addition to this, £600 (2019: £Nil) sponsorship was paid to the University during the year.

Trustees' Expenses

During the year, two (2019: Nil) trustee was reimbursed expenditure amounting to £3,964 (2019: £Nil) in relation to travel and subsistence costs incurred.

18 Cash generated from operations

	2020 £	2019 £
Surplus for the year	16,661,428	3,862,911
Adjustments for:		
Depreciation and impairment of tangible fixed assets	298,666	1,139
Movements in working capital: Decrease/ (increase) in debtors	2,769,908	(3,020,162)
(Decrease)/increase in creditors	(3,270,712)	3,676,393
Cash generated from operations	16,459,290	4,520,281

THE ROSALIND FRANKLIN INSTITUTE STRATEGIC REPORT AND FINANCIAL STATEMENTS 2020

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