ASTBURY CENTRE

UNIVERSITY OF LEEDS

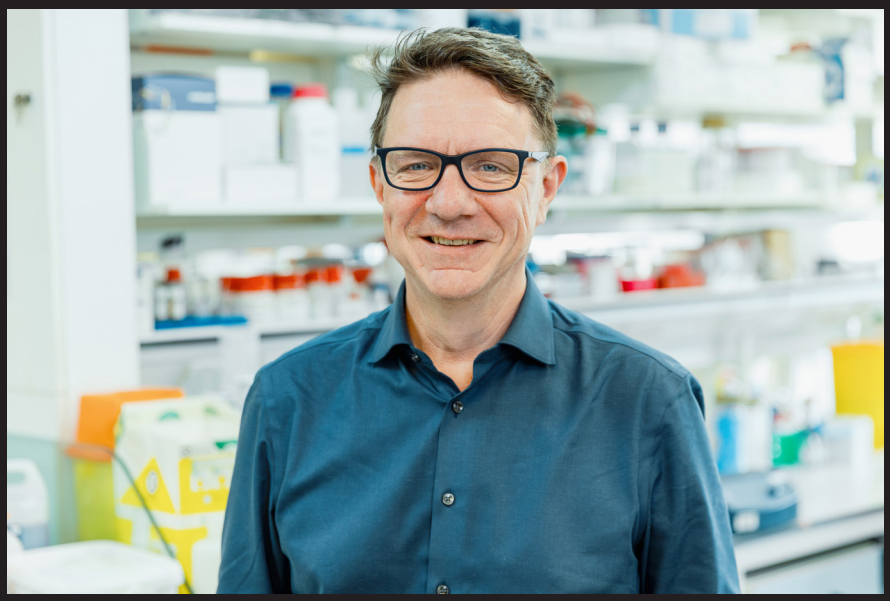
The Astbury Centre

April 2026

Welcome from the Director

Professor Neil Ranson

Welcome to our biennial Astbury Centre brochure. In it, we describe some of our most exciting science over the last two years, alongside major developments that will shape our future.



Professor Neil Ranson, Director of the Astbury Centre

The Astbury Centre for Structural Molecular Biology exists to understand life in molecular detail. It brings together more than 400 researchers, primarily from biology, chemistry, medicine and physics, joined by a common vision to understand how molecules behave, harness this knowledge to better tackle health and disease, and understand fundamental processes in nature to engineer biology. However, Astbury is much more than just world-leading research. It is a vibrant, inclusive community where we empower each other to tackle the toughest problems.

The environment in which Astbury works is changing. At a University level, the alignment of Biology and Medicine to build a faculty of Health and Life Sciences represents an unprecedented opportunity to better embed clinical relevance in our discovery research. Supported by new University structures around interdisciplinary research centres, and our colleagues in the physical sciences, I'm convinced the Astbury Centre will continue to thrive.

Beyond Leeds, changes in the approach to curiosity-driven research by UKRI are shaking up the sector, but the Centre is working to support its members to excel in new fellowship and grant schemes. I want to congratulate members on the unprecedented numbers of major programme-level applications in the last two years. There are now six Wellcome Discovery Awards in the Centre - a real validation of the quality of the science being done here by every single person doing every experiment! This is also reflected in the amazing successes of our early career members detailed in these pages. I know from talking to members, and to collaborators in academia and industry, that many more stellar applications are in the pipeline. We wish everyone well with those!

Finally, I wanted to thank everyone who makes the Centre such a great place to work and such wonderful organisation to lead. Everyone who attends a function, proofreads a paper, mentors a colleague or helps organise an event is critical to our ongoing successes. Thank you all!

Molecular Glues: Drugging the Undruggable

Molecular glues offer a new approach to controlling inflammation.

Scientists at the Astbury Centre have discovered a new class of "molecular glues" that selectively inhibit the BRISC enzyme complex (BRISC molecular glues, BLUEs). The discovery addresses a long-standing challenge in drug development.

"Some ideal targets do not have a clearly defined druggable site, making it incredibly difficult to design drugs against them, so we need to find another way"

explains Professor Elton Zeqiraj, lead author from the School of Molecular and Cellular Biology.

Unlike traditional drugs that block active sites, BLUEs work by locking two BRISC complexes together in an inactive state.

This reduces BRISC's ability to stabilise immune receptors, dampening Type I interferon-driven inflammation—a potential new approach for treating autoimmune diseases.

What makes BLUEs particularly promising is their ability to "normalize" rather than completely block interferon activity.

Collaborator Professor Francesco Del Galdo, Susan Cheney Professor of Experimental Medicine, notes:

"I was particularly excited to see that BLUEs do not switch off entirely the activity of interferon but they simply 'normalise' it. This means derived drugs could dial down abnormal cellular activation to healthy levels, rather than shutting it off completely and leaving patients vulnerable to infections."

Funding & Publication

This work, ‘Molecular glues that inhibit deubiquitylase activity and inflammatory signaling’, published in Nature Structural Molecular Biology, 32, p1812 (2025), resulted from a collaborative effort with the Wistar Institute and University of Pennsylvania and was funded by a Wellcome Senior Research Fellowship. The first author, Francesca Chandler, was funded by a prestigious Wellcome Trust PhD studentship.

Publication & Funding

This work ‘Excised DNA circles from V(D)J recombination promote relapsed leukaemia’, published in Nature, 645, p774 (2025), was led by Assoc. Professor Joan Boyes and funded by grants from the Little Princess Trust and Harley Staples Cancer Trust, administered via the Children’s Cancer and Leukaemia Group.

Circular DNAs as Novel Biomarkers

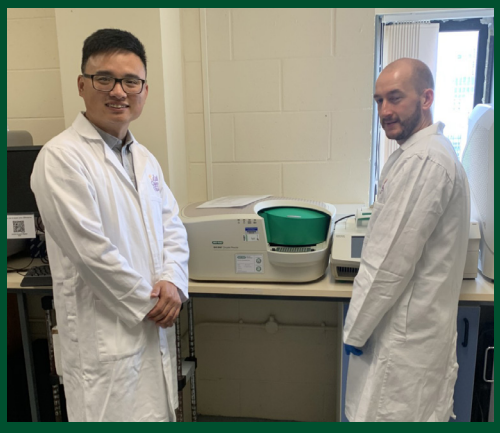
Understanding the DNA circles that influence cancer progression.

In addition to the familiar chromosomal DNA, cancer cells often contain extra circular DNA molecules that can carry genes promoting tumour growth. Patients whose cancers harbour large numbers of these circular DNAs frequently experience worse outcomes, making it vital to understand how these circles form and how they contribute to disease.

A different class of circular DNA, excised signal circles (ESCs), is produced naturally by the immune system as part of normal antibody generation. For years, ESCs were considered harmless by-products. However, new research from the Astbury Centre reveals that these circles can have unexpected harmful effects.

ESCs can bind to a specific enzyme and trigger breaks within chromosomal DNA. Strikingly, these breaks occur at locations that match common mutation sites found in acute lymphoblastic leukaemia, suggesting that ESCs may play a role in the early development of this cancer.

Even more unexpectedly, the study overturned a 40-year assumption: ESCs are not lost over time. Instead, they replicate within both normal lymphocytes and leukaemia cells. Patients who later experience relapse show higher ESC levels at diagnosis, indicating that ESCs could serve as a powerful new biomarker to predict relapse risk and help guide personalised treatment decisions.



Members of the project team, Zeqian Gao (left) and Dylan Casey (right).

Myosin in motion

Swinging lever mechanism of myosin directly shown by time-resolved cryoEM.

Myosins are essential for life, acting as primary force generators for muscle contraction, cellular movement and cell division. Their dysfunction is associated with multiple disorders, including cancer and heart failure.

More than six decades ago, Professor Hugh E. Huxley articulated a bold biophysical idea: that myosin generates force through the swinging of a molecular lever arm. Although widely accepted, this mechanism had never been directly observed.

Now, scientists at the Astbury Centre, in collaboration with Professor Howard White, Old Dominion University, have directly demonstrated this long-proposed lever swing mechanism.

The historical difficulty lay in the astonishing speed of the process: once a myosin motor engages with actin, it completes its powerstroke in just milliseconds. Capturing this event required both innovation and precision.

Using a custom-built time-resolved mixing device, researchers successfully trapped the earliest actomyosin binding state and visualised its structural evolution using time-resolved cryoEM.

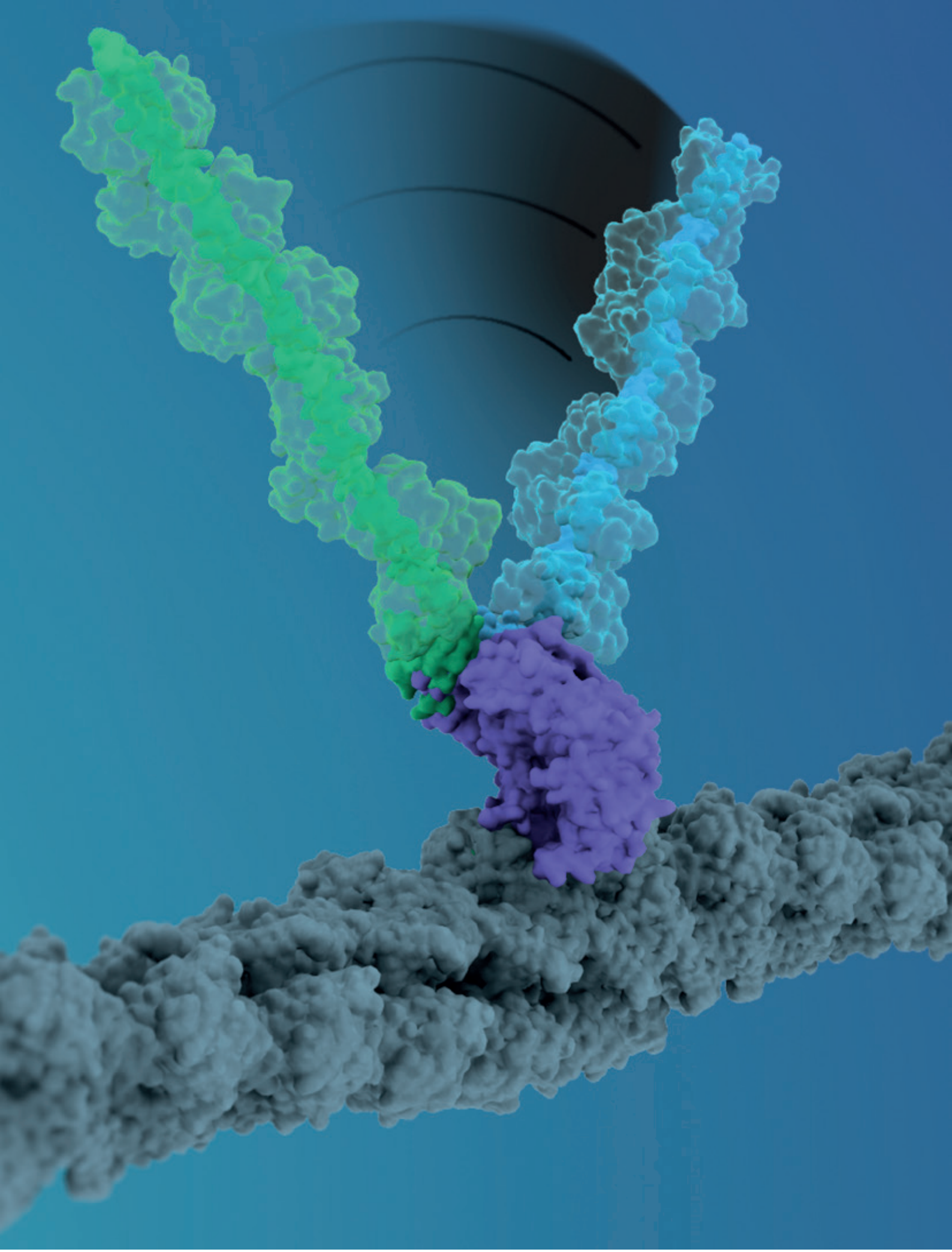
This allowed them to directly demonstrate the lever swing and show how actin activates myosin force generation.

Associate Professor Charlotte Scarff, lead author from the School of Medicine, emphasises the importance of capturing proteins in action:

"Static snapshots of proteins do not provide the full picture - we need to be able to capture them in action to fully understand function."

Publication

This work, 'Swinging lever mechanism of myosin directly shown by time-resolved cryo-EM', published in Nature, 642, p519 (2025), resulted from a collaborative effort with Old Dominion University, Rutgers University and Sheffield University.



The Astbury Community

The Astbury Centre places its members at the heart of everything we do, and we strive to develop a sense of community from which collaboration flows.

Astbury Centre members at the Be Curious Public Engagement Event

For 25 years, the Astbury Centre has tackled major challenges in biomedical discovery, contributing to breakthroughs in neurodegenerative diseases and antimicrobial resistance, paving the way for new therapies. This milestone was marked in December 2024 with a celebratory event at the University, attended by past and present Astbury members and the public.

Astbury researchers engaged widely with the local community through Be Curious, which attracted 1,800 visitors to the University of Leeds for a day of creativity and research exploration. They also contributed to Pint of Science, an annual festival bringing science to pubs and cafés, selling over 600 tickets last year.

The biennial Astbury Lecture in June 2025 featured Professor Karen Vousden, Francis Crick Institute, presenting her works on ‘Metabolic crosstalk between tumours and hosts’, followed by the popular Summer Quiz hosted by Professor Alan Berry. In September 2024 and 2025, the Astbury Research Conference welcomed over 150 members and will expand to a two day event in 2026.

Looking ahead, the Astbury Conversation returns in April 2026 as a two-day international event themed ‘Designing Biology’- exploring synthetic biology, designer biomacromolecules, and emerging technologies shaping the field.

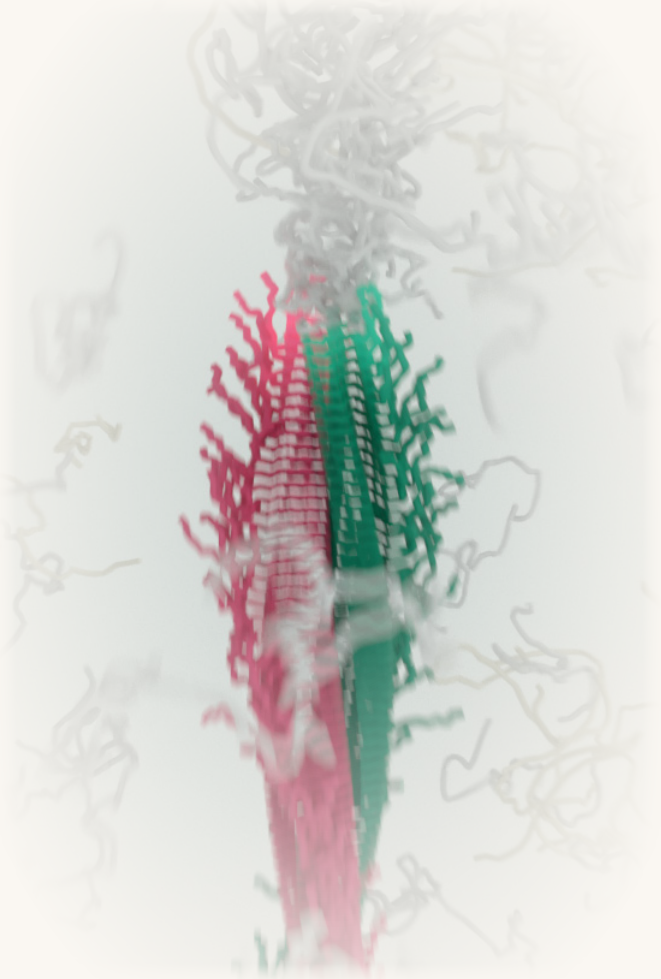
Astbury Centre members at Pint of Science Public Engagement Event

Sustainability remains central to our mission. Dr Yvonne Nyathi was appointed Sustainability Lead to drive initiatives such as achieving LEAF (Lab Environmental Assessment Framework) accreditation across all labs. Currently, over 70% of members hold LEAF status, with 35% achieving Gold, reflecting strong progress toward reducing environmental impact.

Through research excellence, public engagement, and sustainability leadership, the Astbury Centre continues to shape the future of structural and chemical biology, biophysics, and biotechnology.

ASTBURY CENTRE

Wellcome Discovery Awards



Astbury Centre researchers have secured six Wellcome Discovery Awards, providing £12.5 million to support research into life at the molecular level.

The successful awards are:

- Characterisation of a novel role for PKR in inhibiting virus assembly, Professor Mark Harris, £988k
- Paraspeckle Modification, a Potential Route to Novel Antivirals, Professor Ade Whitehouse, £2.4M
- Seeing inside the brain: the in-tissue structure of living and postmortem Alzheimer's disease human donor brain by high-resolution cryo-electron tomography, Assoc. Professor Rene Frank in collaboration with Assoc. Professor Ryan Mathew, £3.5M
- How are Bunyavirus replication factories built? Associate Professor John Barr, in collaboration with Assoc. Professors Juan Fontana and Martin Stacey, £2.2M
- From test tube to tissue: understanding amyloid polymorphism, Professors Sheena Radford and Neil Ranson, £2.9M
- Translation-associated quality control of protein secretion, Professors Liz Miller and Yogesh Kulathu, University of Dundee, in collaboration with Professor Elton Zeqiraj, £551k

Wellcome Discovery Award holders, (left to right) Professors Elton Zeqiraj, Sheena Radford and Neil Ranson.

Professors Radford and Ranson will investigate amyloid fibrils, protein structures found in the brain and other tissues that are linked to diseases such as Alzheimer's, Parkinson's and Type 2 diabetes. Their six-year project aims to uncover how these fibrils form and interact with cells, using some of the most advanced imaging and biochemical techniques available.

Professor Radford said:

"We'll identify new pathways, develop dyes that can distinguish between fibril types and recreate disease-linked structures in the lab."

Professor Zeqiraj, who currently holds a Wellcome Senior Research Fellowship, will embark on a seven-and-a-half-year project to explore how cells rescue stalled ribosomes, the molecular machines responsible for making proteins.

Working with partners in Dundee, the team will use Leeds' world-class cryo-electron microscopy facilities to capture images of ribosomes, providing new insights into how they recover from stress and what happens when these systems fail in disease.

Our Early Career Fellows

Our Early Career Fellows are research leaders of the future.

Here we highlight the research journeys and achievements of two new Astbury Members.

Dr Timea Feller earned her PhD in 2019 studying fibrin network formation and breakdown using Atomic Force Microscopy (AFM). In 2020, she joined Leeds on a British Heart Foundation-funded postdoctoral position with Professor Robert Ariëns and Dr Simon Connell to explore fibrin clot architecture and thrombus stability.

During her postdoc years, she worked on the development of two innovative methodologies: an AFM-based lateral fibre pulling technique and a magnetic microrheometer. Her work on fibrin fibres revealed mechanical behaviours unexplained by existing models, leading to a new concept of fibre organization involving dynamic protofibril connections.

To advance this research, Timea secured a Wellcome Early Career Fellowship in 2024, supporting a five-year project that includes a postdoctoral researcher. She values the Astbury Centre for fostering collaborations and access to advanced methodologies.

Dr Timea Feller

Dr Martina Foglizzo

Dr Martina Foglizzo completed her PhD in 2016 and joined Leeds in 2019 to study chromatin-associated enzymes in DNA repair with Professor Elton Zeqiraj. Her research focuses on the 55LCC complex, a four-member assembly critical for protein unfolding during replication stress.

In 2024, Martina received a BBSRC Discovery Fellowship to investigate how 55LCC assembly regulates enzymatic function using structural, biochemical, and computational approaches, including AFM and CryoEM. This work aims to uncover mechanisms essential for genome stability, with implications for rare disease therapies. Martina emphasizes the Astbury Centre's world-class facilities and collaborative environment as pivotal for her career development.

Other members of the Astbury Centre with fellowships include:

Dr Sobhan Mortazavi-Derazkola – Newton International Fellow

Dr Jennifer Tomlinson - Royal Society Dorothy Hodgkin Research Fellowship

Prizes, Awards & Recognition

The Astbury Centre continues to be recognised nationally and internationally for its outstanding research, leadership, and innovation, with recent prizes and honours spanning science excellence, outreach, and entrepreneurship.

In 2024, Professor Sheena Radford was elected as an international member of the US National Academy of Sciences, one of the highest honours in science. Elected for her distinguished and continuing achievements in original research, Professor Radford is a founding member and former Director of the Astbury Centre and a world-leading biochemist. Her pioneering work on protein folding and amyloid formation has transformed understanding of diseases including Alzheimer's, Parkinson's, and Type 2 diabetes. Her many accolades include an OBE and the Biochemical Society Centenary Award.

Astbury early-career researchers awarded Best Disruptive Food and Drink Business Plan at the YES24 competition (left to right) Brian Mantilla, Darcey Ridgway-Brown, Lawrence Collins, and Amir Rahmani.

Adding to these achievements, Professor Bruce Turnbull was awarded the 2024 Royal Society of Chemistry Bader Prize, recognising his development of bioorthogonal approaches to engineer functional protein and carbohydrate systems. His interdisciplinary research, rooted in Astbury's collaborative culture, has major potential for disease diagnosis and targeted therapeutics.

In 2025, Professor Lorna Dougan was awarded the Institute of Physics Tom McLeish Biological Physics Outreach Prize, recognising her exceptional commitment to making biological physics visible, inclusive, and engaging. Through imaginative, hands-on activities and creative public engagement—such as using everyday materials to explain complex biological mechanics—Professor Dougan has inspired wide audiences while building bridges between physics and biology.

In the same year, Professor Paul Beales was awarded the Institute of Physics Biological Physics Communication Prize for his contributions to communicating biological physics to the wider public.

Finally, Astbury's early-career researchers are also making their mark. In 2025, Caffinity Biotech, a team from the Centre, won Best Disruptive Food and Drink Business Plan at the YES24 competition, showcasing innovation, entrepreneurship, and real-world impact.

Together, these honours reflect the Astbury Centre's vibrant research community and its commitment to excellence, engagement, and discovery.

Fluorinated Sugar Probes for Precision Medicine

Fluoro-sugar probes open the door to simple new diagnostic tests and safer drug discovery tools.

Sugars (glycans) coat every cell in the human body and play essential roles in health and disease. Pathogens such as *Vibrio cholerae* bacteria and influenza viruses exploit these glycans to infect cells, but as natural glycans are involved in both normal physiological processes and exploited by pathogens, it is difficult to design precise diagnostics and treatments.

In a major BBSRC-funded collaborative project involving eight universities and industry partners, Astbury Centre researchers have developed a breakthrough approach by creating artificial sugars modified with fluorine atoms.

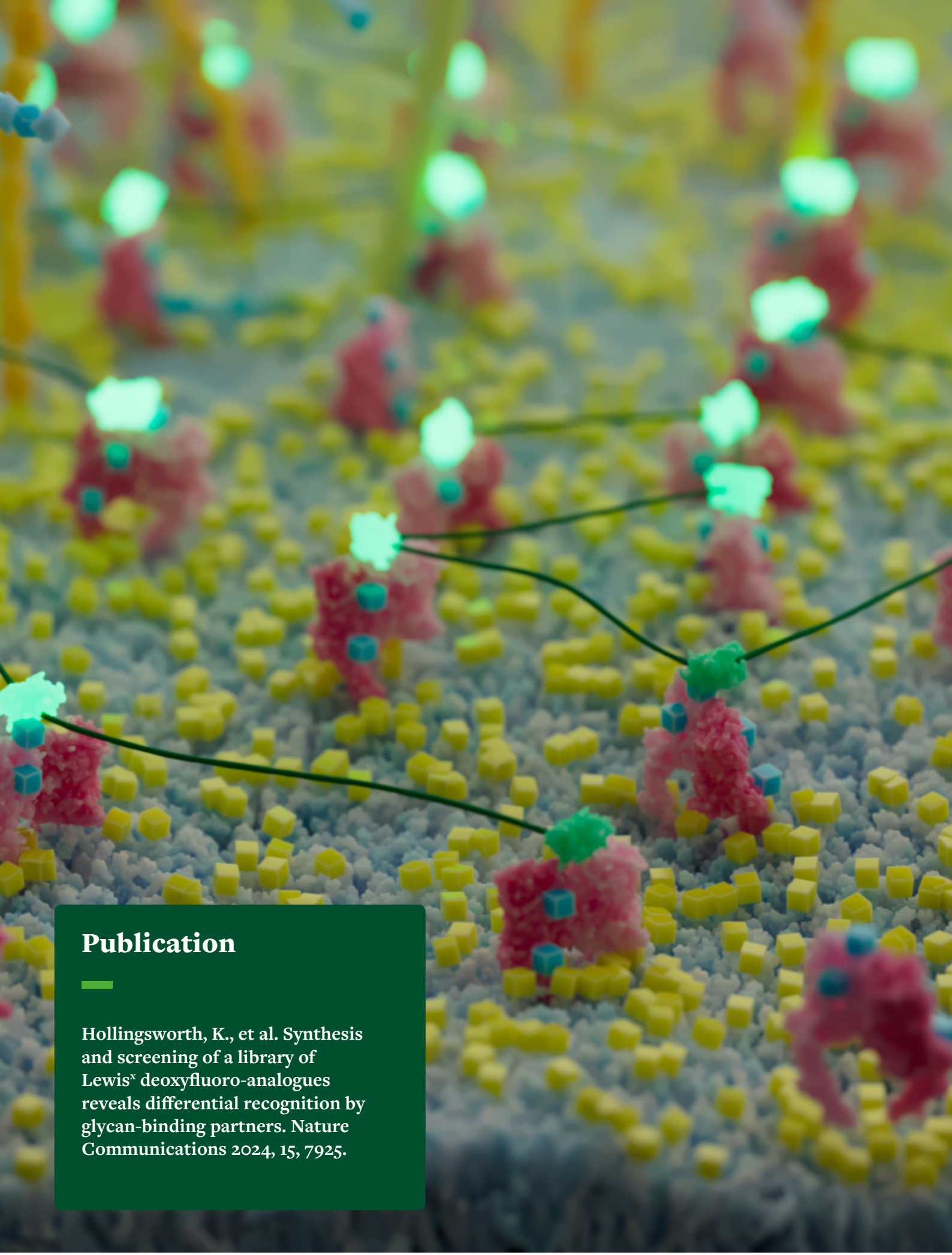
These "fluoro-sugars" retain their natural 3D structure but subtly alter protein binding, enabling scientists to distinguish between human and pathogen interactions.

The team assembled a library of 150 fluoro-sugar variants of the important glycan Lewis^x using a combination of enzymatic and chemical synthesis.

Their approach revealed molecules that can distinguish between different bacterial toxins and human proteins, paving the way for low-cost, diagnostic tests—similar to lateral flow devices—and offering a platform for drug discovery without relying on antibodies or animal experiments.

Professor Bruce Turnbull, who led the project at the University of Leeds, said:

"This work shows how small chemical changes can unlock big biological insights. Our work is allowing us to understand how proteins from humans and pathogens have different ways of interacting with the same glycan."

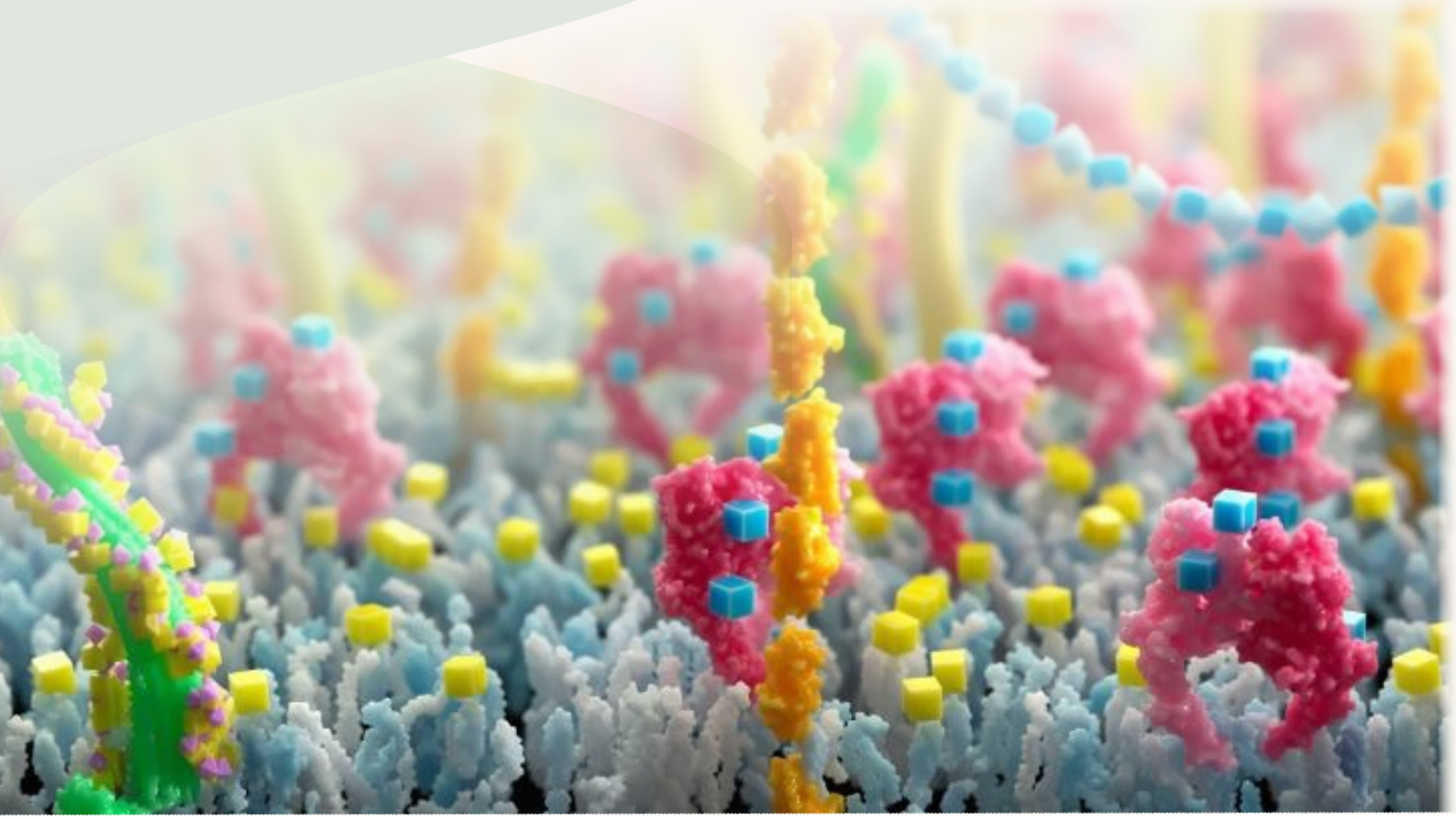


Publication

Hollingsworth, K., et al. Synthesis and screening of a library of Lewis^x deoxyfluoro-analogues reveals differential recognition by glycan-binding partners. Nature Communications 2024, 15, 7925.

Engineering Biology

The Astbury Centre has created an EngBio@Leeds network in collaboration with the Bragg Centre for Materials Research. Led by Professor Paul Beales and a dedicated steering group, the network has secured >£3M of funding.



Professor Bruce Turnbull, Dr Darren Machin and Professor Mike Webb

Engineering Biology (EngBio) is recognised by the UK Government as one of five critical technologies vital for national scientific and technological leadership.

EngBio@Leeds funding includes:

- £2.2M EngBio for Biomedicine (EB4B) Doctoral Focal Award (£740k Leeds, Professor Bruce Turnbull) led by King's College London, training future scientists to bridge biological engineering and therapeutic implementation.

- €3.5M IMProGlyco project (£879k Leeds, Professor Mike Webb), developing protocols for site-directed glycan mutagenesis in mammalian cells.

- £1.9M Artificial cells for highly sensitive and robust diagnosis of pathogen infections (ACROPATH) project (£1.04M Leeds, Professor Paul Beales) with the RIKEN and JAMSTEC Institutes in Japan, developing artificial cells for pathogen detection.

- £1.03M Data Driven Multi-scale Engineering of Cell Fate Decisions (BioEngAGE) project (£437k Leeds, Professor Richard Bayliss) with Imperial College, the Crick Institute, and Japanese institutions (Osaka, Tokyo, RIKEN) to engineer cells that respond to triggers with pre-programmed fates determined via synthetic circuits.

"We want to excite more scientists to work in this area of biology and to work internationally in the pursuit of solutions to global challenges."

said Professor Richard Bayliss.

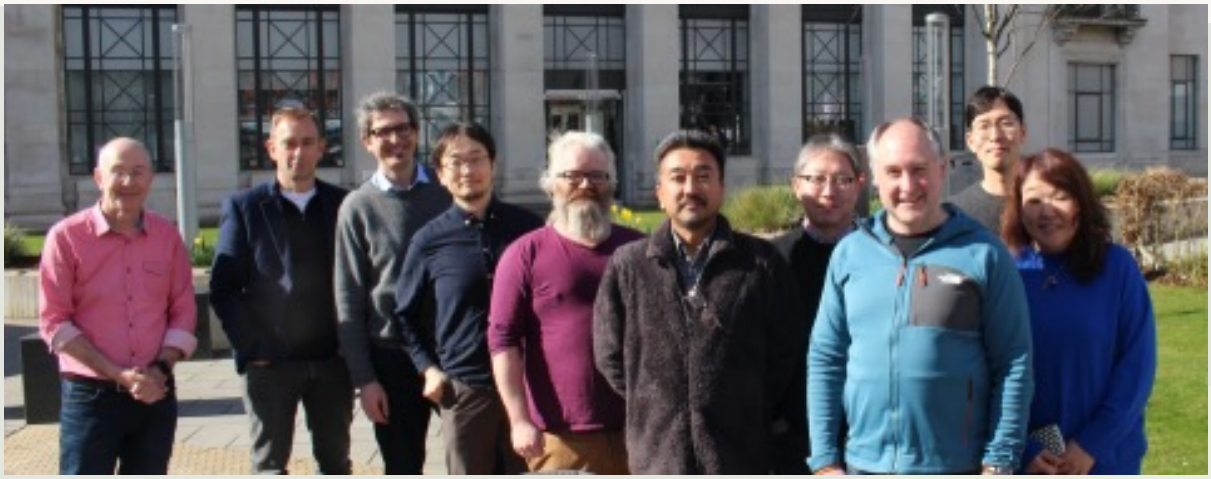
The EngBio@Leeds network continues to organise collaborative workshops, bringing its interdisciplinary community together to target new grant funding opportunities and drive innovation in Engineering Biology.

Artificial Cells to Detect Pathogens

An international team led by Professor Paul Beales (Leeds; Astbury) and Dr Yoshihiro Shimizu (RIKEN, Japan) have been funded to build artificial cells as diagnostic biosensors for pathogen infections.

Artificial cells could improve the speed and precision of clinical infection diagnosis in the future. The collaboration combines Leeds' expertise in biomolecular and membrane engineering with expertise in Japan on cell-free expression. The ACROPATH project (https://acropath.leeds.ac.uk) launched in 2025 and is funded by MRC in the UK and AMED in Japan.

One of the underpinning technologies in Leeds for engineering the ACROPATH platform is the durability of hybrid lipid-block copolymer membranes (1), which promise to enable the artificial cells to stably function in the complex biological media of patient samples, but also support the length of storage needed within a clinical laboratory environment.



Members of the ACROPATH project team at the project launch meeting (March 2025, Leeds).

Previous studies have shown that integral membrane proteins can be functionally reconstituted within a hybrid membrane environment with about a 10-fold enhancement in lifetime and stability (2). Detergent-free methods have also been developed for membrane protein reconstitution within hybrid vesicles (3). These novel, bioengineered membranes have the potential to greatly enhance membrane protein assay workflows in the pharmaceutical industry.

In the context of the ACROPATH biosensor platform, new techniques are currently being developed to fabricate artificial cells with robust hybrid membranes, internal cell-free expression systems and transmembrane communication systems that link the detection events in the external environment to internal response pathways within the artificial cell. Beyond the potential for novel diagnostics, these new tools will greatly contribute to the engineering biology toolbox for building artificial cells.

Publications

(1) **Seneviratne et al. High resolution membrane structures within hybrid lipid-polymer vesicles revealed by combining x-ray scattering and electron microscopy. Small 19, 2206267 (2023)**

(2) **Khan et al. Durable Proteo-Hybrid Vesicles for the Extended Functional Lifetime of Membrane Proteins in Bionanotechnology. Chem. Commun. 52, 11020 - 11023 (2016)**

(3) **Catania et al. Detergent-Free Functionalisation of Hybrid Vesicles with Membrane Proteins Using SMALPs. Macromolecules 55(9), 3415–3422 (2022)**

ASTBURY CENTRE

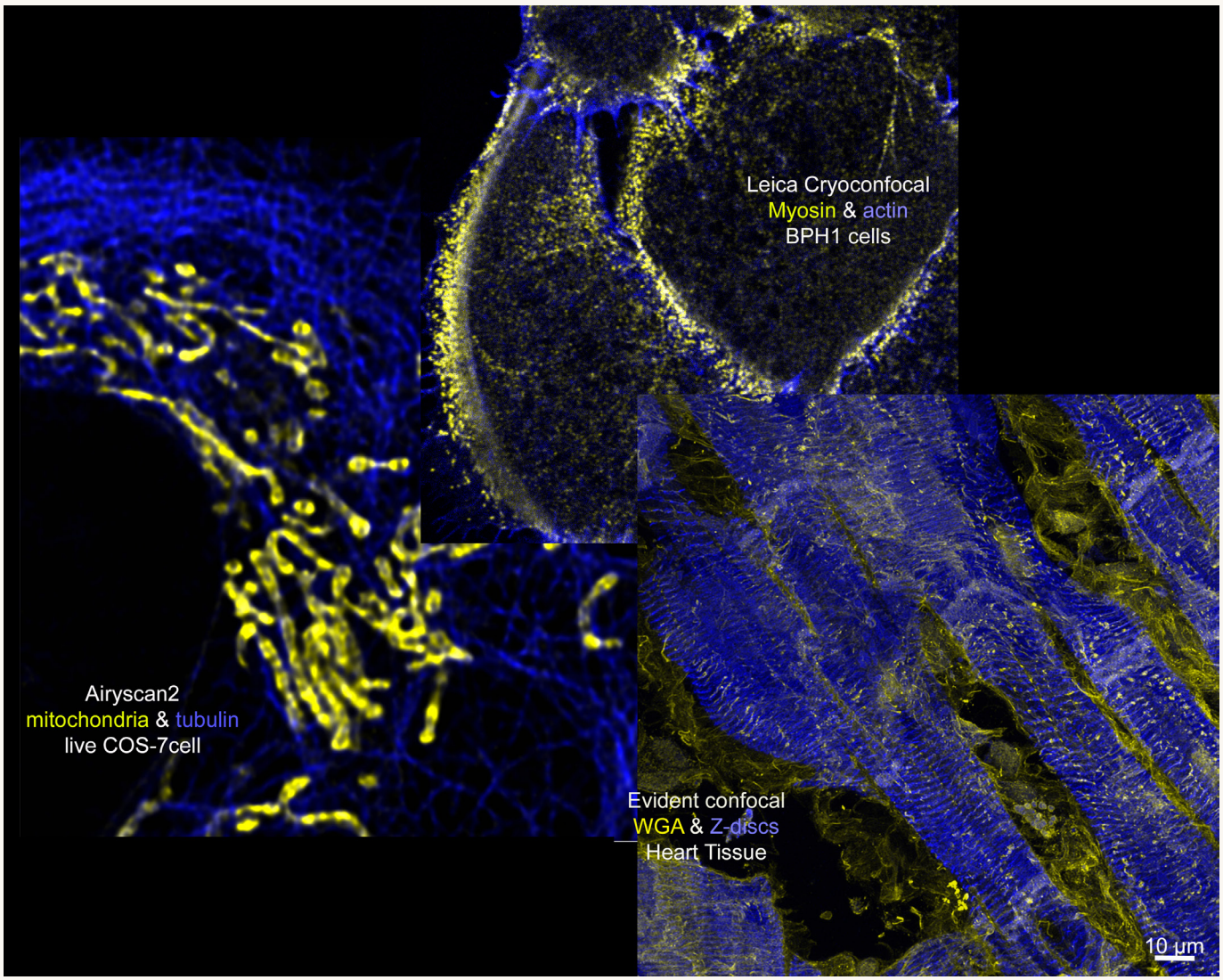
Next-Generation Bioimaging

New confocal and cryo-imaging capabilities, co-located in a new collaborative hub, enable us to accelerate discovery.

The BioImaging Facility in the Faculty of Biological Sciences has moved into its new space, in the Cheney Biomedical Accelerator, next to the Astbury Biostructure Laboratory.

This co-location has been designed to foster closer collaboration between imaging scientists working across light and electron microscopy, strengthening our interdisciplinary research environment.

Thanks to generous support from Peter and Susan Cheney and the Wolfson Foundation, the facility has recently installed three state-of-the-art confocal microscopes.



The first is a new Zeiss LSM 990 with Airyscan 2 detector; an inverted confocal microscope, which enables live and fixed cell imaging, some clever new AI features, and the combination of the Airyscan 2 detector together with image deconvolution, can achieve ~90 nm resolution.

The second, the first in the UK, is the Evident FV5000 (inverted) confocal, equipped with new SiLVR Detectors, and 10 lasers (from 405 to 785 nm). The SiLVR detectors have a linear and high dynamic range, high signal to noise ratio, and are excellent at imaging bright and dim objects next to each other in the same image, enabling high-quality imaging of complex samples.

Finally, we have a new Leica Stellaris Cryo-confocal, which is equipped with a white light laser, and ability to perform fluorescence lifetime imaging (TauSense) in addition to normal confocal modes. The main use for this microscope is to image cryo-sections, to support correlative light and EM (CLEM) workflows.

Together, these cutting-edge instruments significantly enhance the Facility's imaging capabilities, offering researchers powerful new tools for advancing biological and biomedical discovery.

Our funders

We rely on the generous support of a wide range of funders, who underpin every aspect of the Centre's research. Members of the Astbury Centre have £66M in live grant funding (with a total value of £120M to the University of Leeds).

Diagram illustrating how Centre members secure funding together and highlighting the interdisciplinary nature of our science.

In 2024 and 2025, Centre members secured £30M of new awards from a range of funders, including UKRI, the EU and charities.

Alongside our six Wellcome Discovery Awards, some major award highlights include:

- Adam Nelson, Megan Wright & Richard Bayliss' EPSRC grant: General chemical approach to covalent inhibitors of protein kinases, £1.15M
- Ralf Richter's MSCA Doctoral Network: GLYCOCALYX, £1.09M
- Neil Ranson and collaborators' BBSRC ALERT grant: A plasma focused ion beam microscope for Structural Cell Biology at the Astbury Biostructure Laboratory, £1M
- Ralf Richter and David Brockwell's BBSRC ALERT Grant: Concurrent force sensing and fluorescence imaging - Enabling the next generation of single molecule biophysics research across faculties at Leeds, £0.88M

Our publications

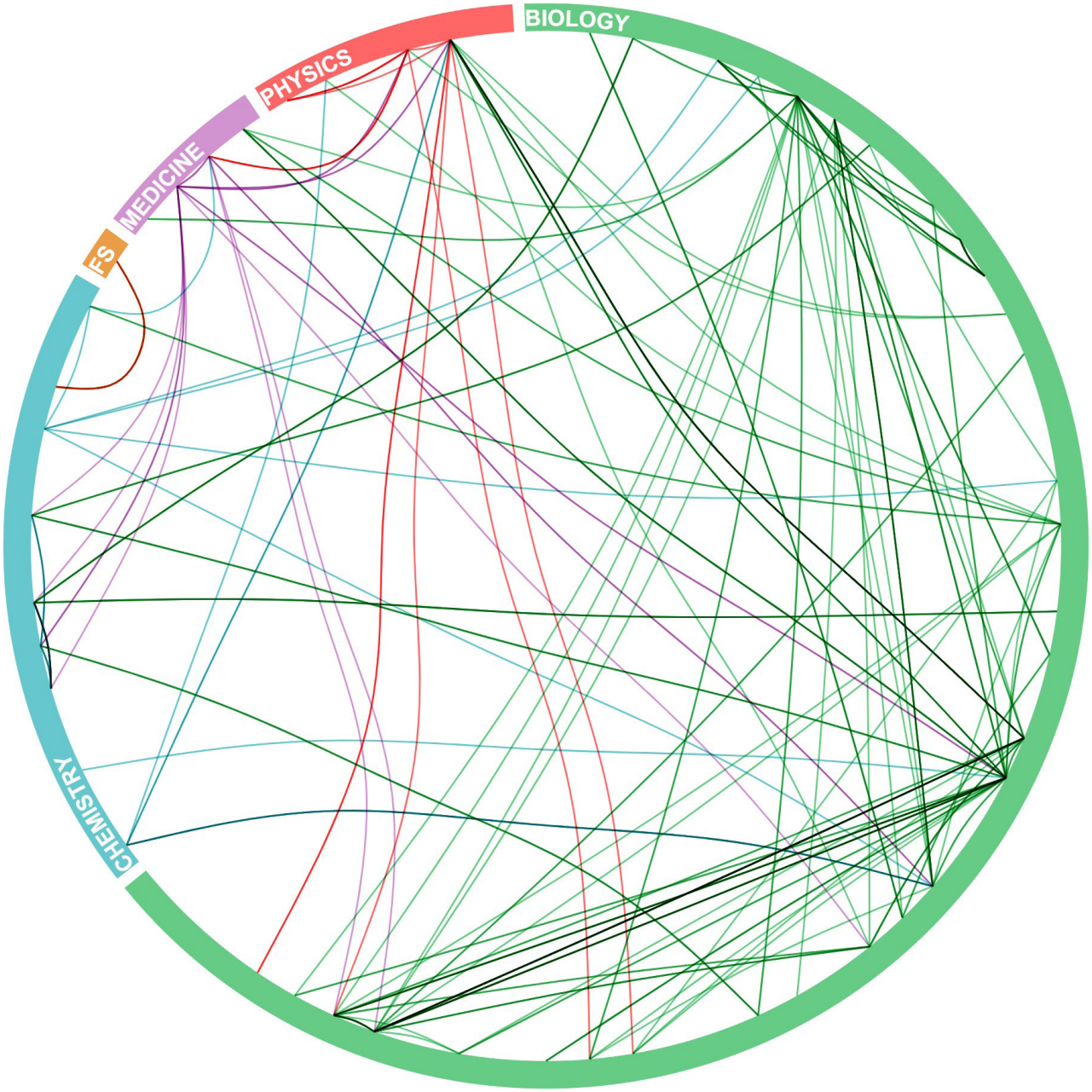


Diagram illustrating publications obtained by Centre members in collaboration in 2025.

Publications

The centre published **239** peer-reviewed publications in **2024-2025** – with some of our most popular destinations including:

- ***Nature Communications*** 17
- ***Structure*** 10
- ***PNAS*** 7
- ***Scientific Reports*** 6
- ***Journal of the American Chemical Society*** 6
- ***Science Advances*** 5
- ***Nucleic Acids Research*** 4
- ***Journal of Molecular Biology*** 4
- ***Nature*** 4
- ***EMBO Journal*** 3
- ***Science*** 2

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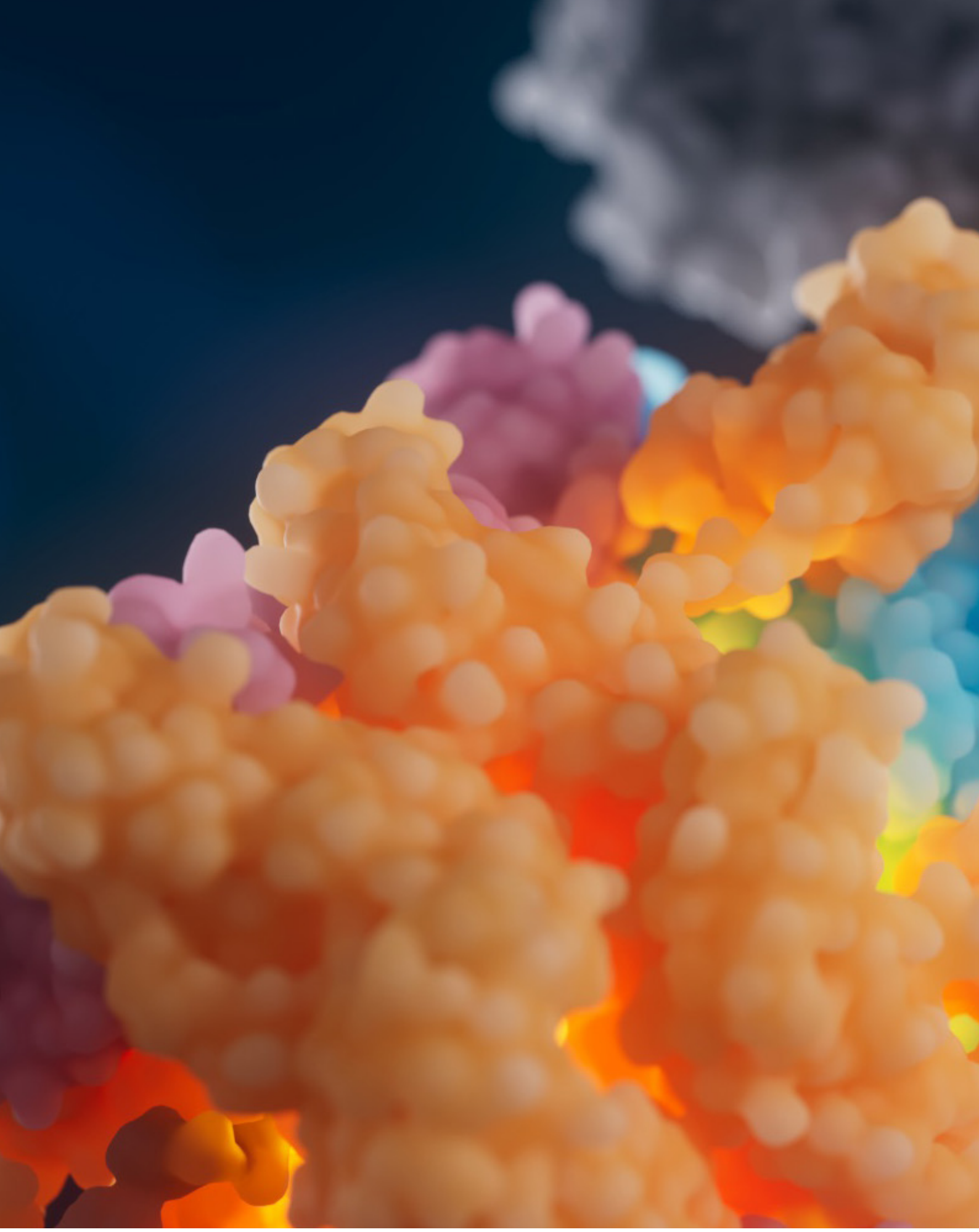
Notes



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