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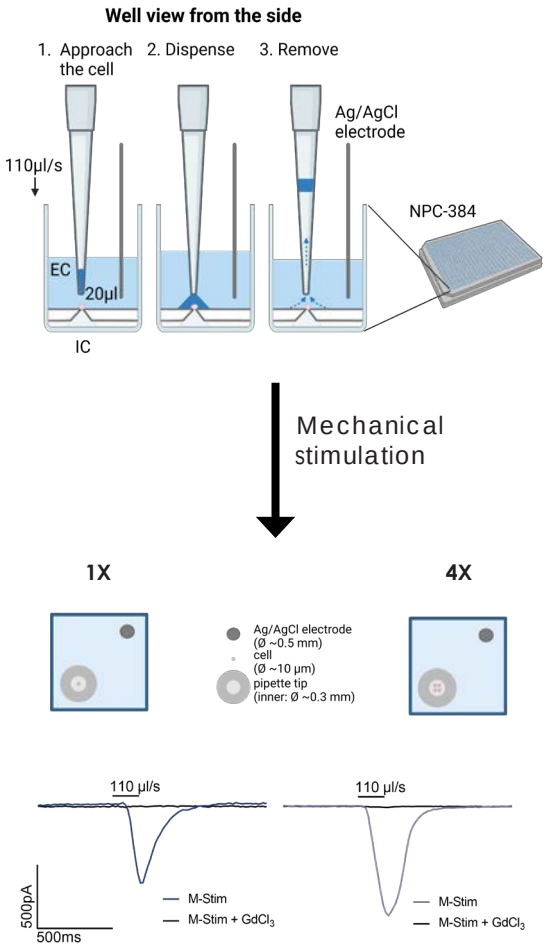


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# See biology in 4D from live dynamics to deep structure

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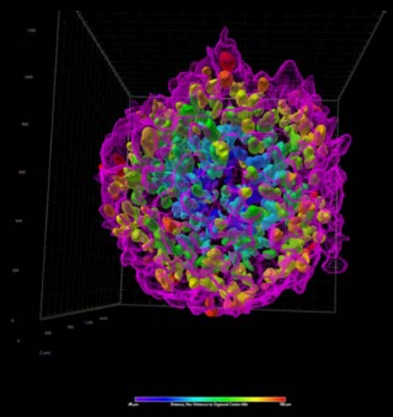

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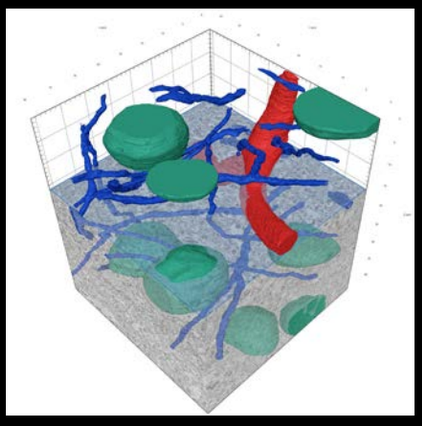
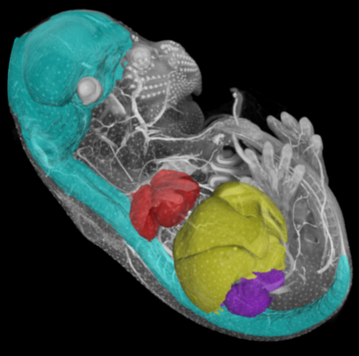


## **Volume EM,** Volutome

Automated serial block-face SEM for resin-embedded biology: unattended cutting, imaging and preprocessing for 3D ultrastructure at scale.



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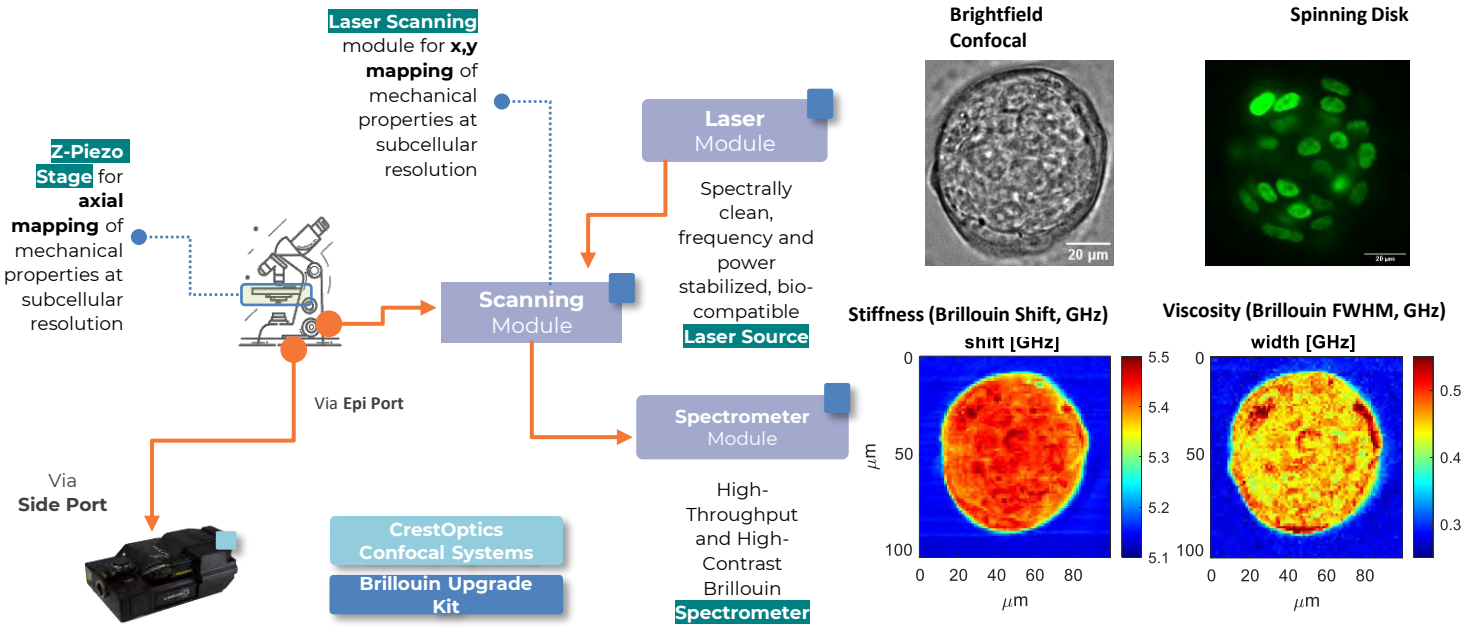


Schematic representation of the system architecture. Representative data acquired on the CrestOptics Brillouin System.

### Automated calibration routine

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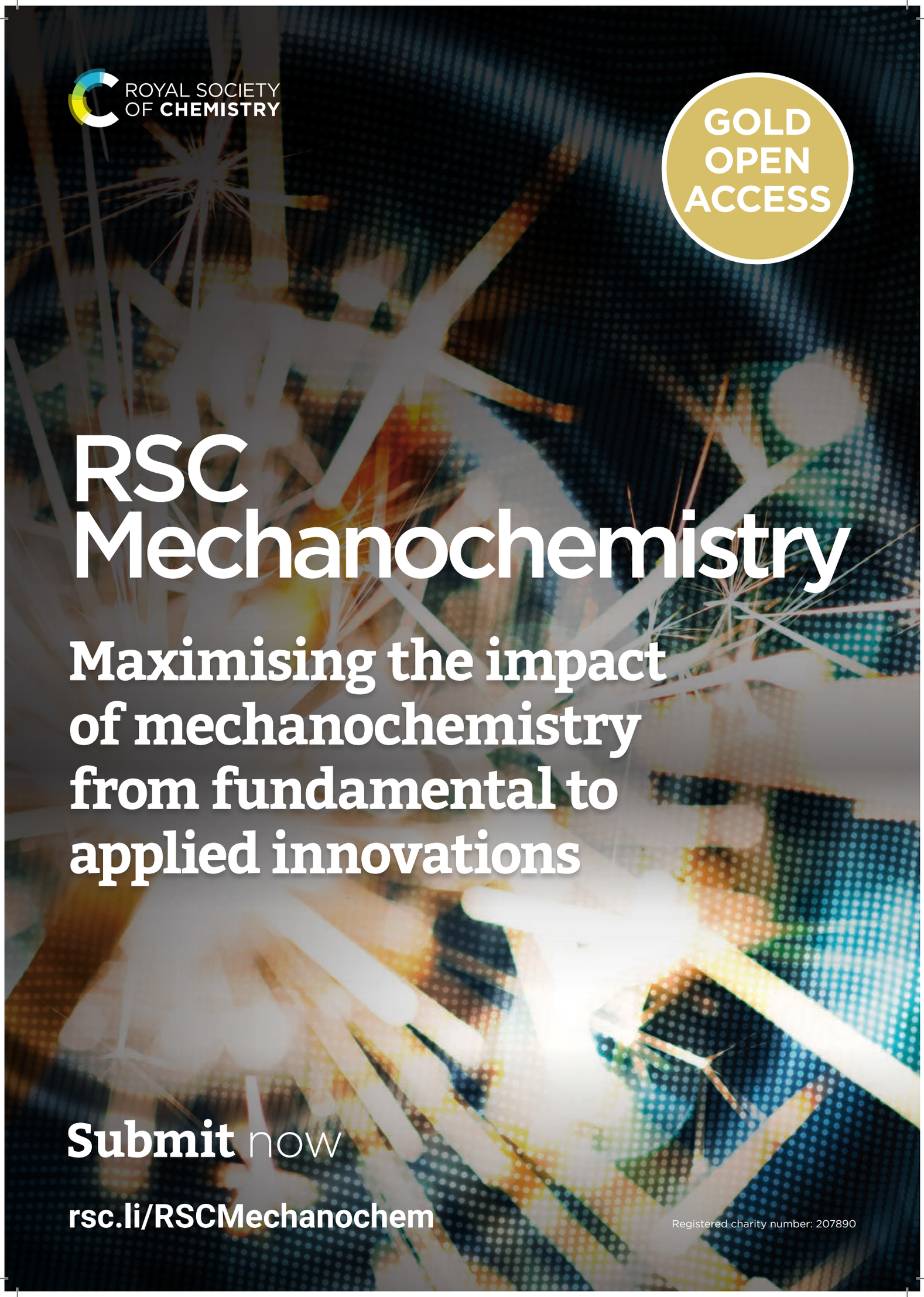
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# NON-CONTACT MECHANICAL IMAGING FOR MECHANOBIOLOGY & MATERIAL SCIENCE

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### ORGANOIDS AND 3D CULTURE MODELS

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Visualize 3D mechanical gradients in tumours, stroma and extracellular matrix to study invasion, heterogeneity and response to treatment.

### MULTILAYERED/NATIVE TISSUES

Add mechanical contrast to tissue imaging for fibrosis, cardiovascular disease, ageing, regeneration and mechanomedicine studies.

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# Plenary Speakers

## Innovation for global justice

Patricia Osseweijer[1]
[1]Delft University of Technology, Netherlands

Plenary Session: Patricia Osseweijer, July 13, 2026, 11:00 - 11:45

The transition from a fossil- to a bioeconomy has long been promoted as a way to mitigate climate change by reducing carbon emissions. However, progress has been slow. At the same time, competing uses of biomass - for food, feed, plastics, fuels and chemicals - became the subject of intense public and political debate. The sustainability of biomass production was increasingly questioned, feedstock availability became a major concern, and the renewable products proved often more costly than the fossil products they aimed to replace. These criticisms weakened support for the bioeconomy and shifted attention towards alternative technological pathways. While science and innovation in the bioeconomy domain continued to improve biomass conversion technologies, logistics and market development, transition agendas became increasingly dominated by wind and solar energy and renewed interest in nuclear power with large enthusiasm for hydrogen as novel energy storage system.
This shift risks overlooking the broader societal contributions of research and innovation for the bioeconomy. Sustainable agriculture, including soil and water management and biodiversity conservation, is essential for health, for food and water security, while the responsible use of biomass and waste streams can simultaneously strengthen energy security, rural development and social resilience. Wind, solar and nuclear energy based transitions cannot provide these wider benefits, while hydrogen remains only an energy carrier.
The bioeconomy can therefore be considered to be much more than a substitute for fossil resources. It spans the entire innovation chain, from fundamental research in biological processes and biotechnology to sustainable production systems and circular value chains. Providing valuable insight in life itself and the complex ecological system on our globe. Importantly, biomass utilisation uniquely provides opportunities for improving livelihood and social development for rural communities. However, reaching such objectives requires other design principles and integration with social sciences.
This places an important responsibility on scientists and innovators. Rather than focusing solely on technological performance or carbon reduction, research should be designed from the outset with societal objectives such as human wellbeing, resilience and global justice in mind.
In this lecture, I will examine the assumptions underlying the bioeconomy debate and reflect on lessons from public communication and stakeholder engagement around genetic modification (GM). I argue that scientists have an essential role not only in developing new technologies, but also in considering the societal directions in which they evolve. This requires integrating moral questions ex ante into research and innovation, while engaging more proactively with society, policy and industry. Drawing on several interdisciplinary projects, I will show how scientific research can be organised to maximise technological performance while simultaneously advancing sustainability, social development and global justice.

# May the Force be with you!  Piezo channels in mechanosensory biology

Ardem Patapoutian[1]
[1]Howard Hughes Medical Institute, Scripps Research, United States

Plenary Session: Ardem Patapoutian, July 13, 2026, 09:00 - 09:45

Mechanotransduction was perhaps the last major sensory modality not understood at the molecular level. Proteins/ion channels that sense mechanical force are postulated to play critical roles in sensing touch/pain (somatosensation), sound (hearing), shear stress (cardiovascular function), etc.; however, the identity of ion channels involved in sensing mechanical force had remained elusive. The Patapoutian lab identified PIEZO1 and PIEZO2, mechanically activated cation channels that are expressed in many mechanosensitive cell types. Genetic studies established that PIEZO2 is the principal mechanical transducer for touch, proprioception, baroreception, bladder, and lung stretch, and that PIEZO1 mediates blood-flow sensing, which impacts vascular development and iron homeostasis. Clinical investigations have confirmed the importance of these channels in human physiology. Current work in Patapoutian continues to explore the role of mechanosensation and interoception in physiology and disease.

# The human organ atlas as a resource for open biomedical research

Claire Walsh[1]
[1]University College London, United Kingdom

Plenary Session: Claire Walsh, July 13, 2026, 09:45 - 10:30

Understanding the human body across scales remains one of the central challenges in biomedical research. Clinical imaging can visualise whole organs but lacks microscopic detail, while histology reveals cellular structure but only within small, physically sectioned samples. The Human Organ Atlas was formed to bridge this gap: to create an open, multiscale, three-dimensional reference of intact human organs in health, ageing and disease.
The Atlas grew from the development of Hierarchical Phase-Contrast Tomography, a synchrotron-based imaging approach established through an international collaboration between clinicians, imaging scientists, engineers and data specialists. Initially driven by the urgent need to understand organ-level pathology during the COVID-19 pandemic, the project rapidly evolved into a broader open-science effort. By imaging intact organs non-destructively, while retaining the ability to zoom into selected regions at near-cellular resolution, the Atlas preserves the spatial context that is often lost when organs are reduced to small samples or two-dimensional sections.
This talk will describe the history of how the Human Organ Atlas was formed: from method development and early biological discoveries, to the creation of an open-access data and visualisation platform, and the building of a wider community around this technique. I will discuss how technical work in large-scale data formats, metadata, web-based visualisation and reusable analysis pipelines has made these complex datasets accessible beyond the original imaging teams. I will also highlight how clinical and biological collaborations are turning the Atlas into a resource for health impact, supporting anatomical discovery, disease research, validation of clinical imaging, education, and the development of AI models trained on high-quality, spatially contextualised human data.

# Cardiac mechanics to cure cancer

Serena Zacchigna[1]
[1]International Centre for Genetic Engineering and Biotechnology, Italy

Plenary Session: Serena Zacchigna, July 13, 2026, 11:45 - 12:30

The talk will focus on the mechanisms that prevent the spontaneous regeneration of the heart after damage and discuss mechanistic link with the rarity of cardiac cancers, to eventually move to therapeutic solutions to both promote cardiac repair and treat cancer.

# BBS and DGfB Invited Speakers

## Makers, thinkers, creators: reimagining public engagement with biophysics

Lorna Dougan[1]
[1]University of Leeds, United Kingdom

BBS Elspeth Garman Prize for Public Engagement Lectures, July 14, 2026, 11:00 - 12:30

In this talk I will present the ‘Maker Kit’ project at the University of Leeds which explores how tactile, creative tools can transform public interaction with complex scientific ideas. The project centres on the development and deployment of portable “maker kits” designed to translate biophysical concepts, such as molecular forces, protein folding, and nanoscale interactions, into hands-on, accessible activities.
Grounded in principles of participatory engagement and informal learning, the Maker Kit initiative invites diverse audiences to actively construct, experiment, and reflect, rather than passively receive information. Workshops delivered in community, educational, and outreach settings are used to evaluate how making-based approaches influence engagement, understanding, and confidence in discussing science. Qualitative observations and participant feedback demonstrate that physical interaction and creative exploration foster deeper conceptual understanding and promote curiosity.
The findings highlight the effectiveness of combining scientific accuracy with playful, design-led methods to break down perceived barriers to biophysics. Importantly, the project encourages dialogue between researchers and the public, supporting more inclusive and reciprocal science communication. The Maker Kit project is a team effort and contributes a scalable and adaptable model for public engagement, demonstrating how maker-based approaches can broaden participation and reframe biophysics as an accessible, creative, and socially relevant discipline.

# Development of sensitive and selective biosensors using SERS

B. Clark[1], S. Sloan-Dennison[1], K. Scullion[2], P. Fineran[3], J. Mair[3], D. Creasey[4], C. Rathmell[4], J. Faircloth[4], C. Weir[5], J. Dear[2], D. Bingemann[3], D. Graham[1], Karen Faulds
[1]Department of Pure and Applied Chemistry, Technology and Innovation Centre, University of Strathclyde, United Kingdom, [2]Centre for Cardiovascular Science, University of Edinburgh, The Queen's Medical Research Institute, United Kingdom, [3]Centre for Inflammation Research, Translational Healthcare Technologies Group, Institute for Regeneration and Repair, United Kingdom, [4]Wasatch Photonics, United States, [5]Usher Institute – University of Edinburgh, United Kingdom

Biophysics in Health and Disease, July 14, 2026, 09:00 - 10:00

Surface enhanced Raman scattering (SERS) is an analytical technique with several advantages over competitive techniques in terms of improved sensitivity and multiplexing. We have made great progress in the development of SERS as a quantitative analytical method. Many bioanalytical detection methods exist, with fluorescence spectroscopy tending to dominate, however SERS has the advantage that it is both sensitive and has the ability to multiplex which is limited when using techniques such as fluorescence. We have developed approaches to both identify and quantify the presence of multiple analytes within a mixture e.g. pathogenic DNA sequences, bacteria using SERS combined with data analysis techniques.
Acute liver failure (ALF) poses a significant mortality risk, with acetaminophen overdose representing its leading cause. Despite its widespread availability for minor ailments, approximately 40% of self-harm patients in the UK ingest acetaminophen in overdose, resulting in approximately 100,000 hospital presentations annually. To address this critical health concern, cytokeratin-18 (K-18) has emerged as a promising biomarker for diagnosing drug-induced liver injury (DILI) following paracetamol overdose. Unlike alanine transaminase (ALT), K-18 exhibits elevated levels at an earlier stage of DILI onset, rendering it an ideal candidate for a rapid point-of-care test (POC).
This study focuses on the development of a surface-enhanced Raman scattering (SERS)-based lateral flow immunoassay (LFIA) diagnostic test for quantifying K-18 associated with the early onset of DILI in combination with stable SERS active functionalized nanoparticles. The integration of SERS and LFIA technologies enables efficient and sensitive detection of K-18, facilitating rapid diagnosis and patient stratification. By employing a purpose-built portable Raman spectrometer for device interrogation, quantitative detection of K-18 is achieved within 30 minutes from clinical samples. This has potential for the triaging of patients for treatment after paracetamol/acetaminophen overdose.

# From method to mechanism: SLAM-FRET enables single-molecule views of dynamic human RNA machineries

Dina Grohmann[1]
[1]University of Regensburg, Germany

BBS-DGfB Joint Session: Single Molecule Methodologies, July 15, 2026, 15:35 - 17:35

Human cells are complex entities in which molecular recognition and selection drive cellular processes, often via structural changes and dynamic interactions. Human proteins exist in multiple chemical states, and posttranslational modifications such as phosphorylation critically affect their function. Therefore, studying proteins in their chemically native state is essential to understand how protein dynamics shape molecular function. Single-molecule FRET (smFRET) enables detailed exploration of biomolecular structure, function, and dynamics, but its application to the human proteome is limited by the lack of methods for site-specific coupling of organic dyes to native, non-recombinant mammalian proteins. Here, I present SLAM-FRET, a method based on bioorthogonal chemistry that enables site-specific labeling of fluorescent dyes into native human proteins. I will demonstrate its applicability for studying functional and posttranslationally modified proteins on the single-molecule level, including the hitherto inaccessible human Argonaute 2 (hAgo2), the catalytic core of the RNA-induced silencing machinery. Using SLAM-FRET we solved central mysteries in RNA biology gaining insights into hAgo2 structural states and conformational dynamics, its interactions with RNA substrates and Dicer during small RNA loading, and the functional consequences of disease-associated hAgo2 mutations causing the LESKRES syndrome.

# Science outreach: why so serious?

Sam Horrell[1]
[1]Imperial College London, United Kingdom
BBS Elspeth Garman Prize for Public Engagement Lectures, July 14, 2026, 11:00 - 12:30

Outreach is meant to be engaging, inspiring, and to grab your audience's attention. But this is easier said than done, especially as not all research is as attention grabbing as finding out if scaring cows makes them squirt milk1 or if Teflon can work as a zero-calorie food supplement2. But given a little effort and imagination we can make our serious science a little less serious and leave our audience with a clear message they can pass on to others. You can even do it in under 3 minutes. This talk will aim to do just that, with the most talks in a single talk ever (probably?).

1. Ely Fordyce & W. E. Petersen. Factors Involved in the Ejection of Milk, Journal of Animal Science, Vol 1939, 1, Dec 1939, Page 80, https://doi.org/10.1093/ansci/1939.1.80
2. Naftalovich R, Naftalovich D, & Greenway FL. Polytetrafluoroethylene Ingestion as a Way to Increase Food Volume and Hence Satiety Without Increasing Calorie Content. J Diabetes Sci Technol. 2016 Jun 28;10(4):971-6. doi: 10.1177/1932296815626726.

# Viewing the invisible in science and art

Rivka Isaacson[1]
[1]King's College London, United Kingdom

BBS Elspeth Garman Prize for Public Engagement Lectures, July 14, 2026, 11:00 - 12:30

Viewing the Invisible explores common ways of working between artists and scientists, demythologising preconceptions and highlighting the creativity involved in science and the technical precision of art. This BBSRC-funded, multimedia project, running since 2017 in schools, cultural spaces and online, has had measurable impact in changing thinking and practice for artists, scientists and teachers, improves uptake of science among women and minorities, and fosters open-mindedness and inter-disciplinary practice for both artists and scientists. Artists from London Fine Art Studios (LFAS) paint portraits of under-represented science 'influencers' (from politics, media, education, industry, academia and policy) with the process either filmed or in front of live audiences, with discussion between painter and sitter focussing on their ways of working, identifying common ground. The portraits, sculpture, films and objects (including a 3D printed molecular ribosome model and a display case of 'tools of the trade' which mixed up indistinguishable art and science equipment and chemicals) became a public exhibition, held in multiple locations. Associated events include science-themed drawing and painting workshops, a collaborative event with the National Portrait Gallery in which Professor Dame Janet Thornton was live-painted on stage at the NPG alongside a panel discussion, Glasgow Science Festival events and New Scientist Live. The exhibition also includes a storyboard series comparing the stages of creating a portrait with the process of solving a protein structure, with steps including optimising conditions, acquisition, processing, iteration, refinement and dissemination, demonstrating many parallels between the respective processes.

# The physiological role of alpha-synuclein at the presynapse

Yuqing Feng[1], Amberley Stephens[1], Pedro Vallejo Ramirez[1], Eugene Masharov[2,3], Alfonso De Simone[4], Giuliana Fusco[4], Stanislaw Makarchuk[1], Nino Läubli[1], Hilal Lashuel[5], Clemens F Kaminski[1], Gabriele Kaminski Schierle[1]
[1]University of Cambridge, United Kingdom, [2]Columbia University Medical Center, United States, [3]New York State Psychiatric Institute, United States, [4]University of Naples Federico II, Italy, [5]Institute of Bioengineering, Switzerland

Biophysics in Health and Disease, July 14, 2026, 09:00 - 10:00

Introduction
Alpha-Synuclein (aSyn) is a central protein in Parkinson's disease, yet its physiological role at the presynapse remains elusive. This study aims to define the native conformational states and regulatory mechanisms of aSyn in dopaminergic neurons, specifically investigating its relationship with calcium signalling and dopamine (DA) homeostasis.

Methods
We have utilised super-resolution imaging, NMR spectroscopy, and quantitative single-molecule analysis in dopaminergic neurons and synaptosomes. Functional assays and biochemical fractionation were employed to track DA release and vesicle association.

Results
Super-resolution imaging reveals that aSyn localises within nanometers of L-type voltage-gated calcium channels (LTCC). This proximity is enhanced by calcium and CaMKII-dependent phosphorylation. Notably, calcium and S129 phosphorylation increase aSyn's binding affinity to synaptic vesicles. Furthermore, functional data show that while evoked DA release is independent of LTCCs, spontaneous DA release is modulated by aSyn and LTCC activity. Finally, we have shown that aSyn preferentially associates with small vesicles distinct from the canonical SNARE-dependent recycling pool.

Conclusion
aSyn acts as a calcium-regulated modulator of spontaneous DA release, operating through pathways independent of full-collapse fusion. Crucially, pS129 aSyn is a physiological regulator, not merely a pathological marker.

# Targeted nucleic acid analysis with RNA:DNA nanotechnology

Ulrich Keyser[1]
[1]University of Cambridge, United Kingdom
BBS-DGfB Joint Session: Single Molecule Methodologies, July 15, 2026, 15:35 - 17:35

Rapid identification of nucleic acid molecules with as little bias as possible is a major challenge in biotechnology. Here we design three-dimensional nucleic acid constructs that enable the identification of short and long DNA and RNA molecules with single-molecule resolution.[1]

First, we show how both RNA and DNA molecules can be reshaped into nucleic acid nanostructures that can be detected with solid-state nanopore biosensing. We describe the identification of RNA transcript isoforms at the single-molecule level using solid-state nanopore microscopy. We refold target RNA and DNA into identifiers (IDs) with designed sets of complementary DNA strands. Each reshaped molecule carries a unique sequence of structural (pseudo)colours. The sequence of structural colours of RNA identifiers enables simultaneous identification and relative quantification of multiple RNA targets without prior amplification. RNA IDs discriminate circular and linear transcript isoforms in a one-step, enzyme-free reaction in a complex human transcriptome using single-molecule read-out [1]. We adapted the technique for the detection of RNA modifications (5mC, Inosine, MeC) in ribosomal RNA (rRNA) using RNA nanotechnology to detect pathogenic bacteria like A. baumannii [2]. At the end of the talk, we show how low temperature enhances the resolution of the nanopore readout to a few ten base pairs along the nanostructures.

References:
1. F. Bošković and U. F. Keyser. Nanopore microscope identifies RNA isoforms with structural colors.
Nature Chemistry, 14:1258-1264, 2022.

2. Y. Li, S. C. Meng, Y. Wang, C. M. Platnich, M. K. Earle, E. Mylona, P. Naydenova, S. Baker, J. Zhu, and U. F. Keyser1. Nanopore-based programmable nanolatches enable single-nucleotide detection of RNA mutations and modifications.
Nature Nanotechnology, 20:1473–1481, 2025

# Resolving Hidden Dynamics Using Single-Molecule Imaging

Eugene Kim[1]
[1]Max Planck Institute of Biophysics, Germany

BBS-DGfB Joint Session: Protein-Nucleic Acid Systems, July 16, 2026, 09:00 - 10:30

Many biological processes cannot be fully understood from static structures or ensemble measurements because their function emerges from dynamic molecular behavior. We develop and apply quantitative imaging and biophysical approaches to resolve these hidden dynamics and uncover the molecular mechanisms that govern biological function.
In this talk, I will present recent work from my laboratory on chromosome organization by SMC complexes. By combining quantitative single-molecule approaches with biochemical, structural, and computational studies, we uncover the principles governing DNA loop extrusion, its regulation, and its functional specialization across diverse SMC systems.
Beyond chromosome organization, I will present our recent efforts to develop quantitative imaging approaches that probe new dimensions of intracellular dynamics. By simultaneously measuring the translational and rotational motion of anisotropic gold nanorods in living cells, we uncover complementary information about the local physical environment that is inaccessible to conventional single-particle tracking alone.

# Probing the potential of the plant cell wall to restrict ice growth at freezing temperatures

Heather Knight[1]
[1]Durham University, United Kingdom

Climate Change and Sustainability, July 13, 2026, 15:30 - 16:30

The planet's plants vary widely in their ability to tolerate freezing winter conditions. Many temperate plant species can improve their freezing tolerance by acclimating gradually to low temperatures during cool periods typical of autumn. Molecular and physiological changes that occur during this period enhance the plant's chances of surviving over winter. However, climate change has increased the incidence of late spring frosts that often hit after warm spring weather, leaving crops unprepared and vulnerable to devastating damage.
Whilst low temperatures generally pose challenges for many organisms, the formation of ice crystals is particularly problematic for plants. Whilst we know a great deal about the genetic mechanisms plants use to protect themselves against the consequences of ice, our understanding of how plants might restrict ice formation lags behind. Ice forms initially within water-conducting vessels and outside of plant cells, within and between their carbohydrate-rich cell walls. With collaborators across biology, physics and chemistry we have demonstrated that the structural composition of this extracellular environment impacts upon the spread of ice within the plant and the extent of the damage it causes. Our data add to a growing body of evidence that the cell wall is an important factor in defence against freezing. We observe that when plants acclimate to low temperatures, the cell wall alters in a way that restricts ice growth. This knowledge may act as a starting point for optimising plants' ice defences in a landscape of unpredictable weather patterns, where natural early warning systems can no longer operate

# Native outer membrane features control OMP folding and function

Jonathan Machin
[1]University of Leeds, United Kingdom

The Single Cell, July 14, 2026, 16:30 - 17:30

The outer membrane (OM) of diderm bacteria is a unique membrane, characterised by the asymmetric (outer leaflet) presence of lipopolysaccharide (LPS), a high outer membrane protein (OMP) concentration dominated by a few protein species, (partial) protein-lipid phase separation and a low lateral diffusion rate. Understanding the OM is critical in tackling the challenges and opportunities posed by antibiotic resistance and developing biotechnologies. However, much remains unclear about how the organisation, composition and interactions between components modulate the OM. Here, native features of the OM are recapitulated in vitro and their consequences for OMP folding and function characterised. Generation of charge asymmetric liposomes mimicking the OM's bilayer dipole revealed that the insertion and folding of OmpA and BamA is accelerated compared to symmetric liposomes (and impeded in liposomes with an inverted charge dipole). Further, a conserved patch of extracellular positive charge in OMPs is identified and shown for OmpA to play a critical role in folding. OMP-OMP interactions are poorly understood, but here it is found that the natively abundant OMP OmpA can specifically interact with and enhance OmpT (an extracelluarly facing protease) and inhibit PagP (an OMP palmitoyltransferase) activity. An in-silico screen of OMP-OMP interactions further identifies a broad diversity of interactions. Together, these results yield new insights into the mechanisms that drive OMP assembly and function, both in vitro and in vivo, pointing to the underappreciated role of native OM asymmetry and OMP-OMP interactions to modulate the OM's form and function.

# Towards modelling DNA in biological environments

Agnes Noy[1]
[1]University of York, United Kingdom

In Silico Biophysics, July 14, 2026, 14:00 - 15:00

When aiming for atomic detail, DNA has typically been characterized using short, relaxed fragments (up to 50 base pairs or bp). However, inside cells, DNA is a very long polymer that is supercoiled, subjected to bending and pulling forces, and surrounded by a crowded environment. In our lab, we have developed approaches and protocols for simulating DNA at the atomic level while accounting for these mechanical stresses in order to recreate more realistic conditions. We also pursue the development of novel software tools that enable direct comparison between computational and experimental data like atomic force microscopy. In my presentation, I will show how DNA structure and dynamics respond to supercoiling when combined with pulling and DNA-bending proteins (1-4). I will also provide atomistic insights into the process of target searching and binding between some of the most abundant proteins and DNA (5). Finally, I will describe recent simulations that reveal the key mechanisms underlying the homologous condensation of two DNA duplexes mediated by divalent ions (6).

1. ALB Pyne et al., Nat Commun, 12, 1053 (2021)
2. S Yoshua et al., Nuc Acids Res, 49, 8684-8698 (2021)
3. GD Watson et al., Comput Struct Biotech J, 20, 5264-5274 (2022)
4. M Burman and A Noy, Phys Rev Lett, 134, 038403 (2025)
5. EW Chan, MC Leake, A Noy, JACS Au, 5, 4870-78 (2025)
6. V Velasco-Berrelleza et al. BioRxiv (2025)

# Sequence-independent imaging and mechanical manipulation of single-strand nucleic acids using chimeric SSBs

Carlos Penedo[1]
[1]University of St. Andrews, United Kingdom

BBS-DGfB Joint Session: Protein-Nucleic Acid Systems, July 16, 2026, 09:00 - 10:30

Imaging single stranded DNA and RNA in cells generally requires sequence specific probes or genetic and metabolic intervention, which limits the molecules that can be followed. Single stranded DNA binding proteins (SSBs) offer an appealing alternative, recognising single strands through a conserved OB fold in a sequence-independent manner. We previously showed that the minimal single OB fold SSB from Sulfolobus solfataricus coats ssDNA dynamically and binds ssRNA with near identical affinity from a single compact domain, giving it a markedly smaller footprint than the trimeric eukaryotic RPA used as the standard cellular ssDNA marker. Building on this minimal recognition element, we engineered chimeric SSBs (cSSB) in which thermophilic OB folds are covalently linked to increase residence time while preserving sequence independence and a compact footprint. Unlike the parental monomers, cSSB dissociates far more slowly and remains stably bound to force exposed ssDNAs under extreme conditions, including high ionic strength and elevated temperature. Fluorophore-labelled cSSB stains single strands in real time, illuminating ssDNA generated by mechanically unzipping λ DNA under the optical tweezers, while cSSB coated microspheres act as generic handles that grip bare single-strand nucleic acids to apply piconewton forces without engineered attachment chemistry. In this talk, I will present these single molecule results and our first steps towards sequence independent imaging of single stranded nucleic acids in cells.

# Assessing the performance of plastic-degrading enzymes using calorimetry

Andy Pickford[1]
[1]University of Portsmouth, United Kingdom

Climate Change and Sustainability, July 13, 2026, 15:30 - 16:30

Poly(ethylene terephthalate) (PET) is one of the most widely used synthetic polymers, with applications ranging from food and beverage packaging to textiles and engineering materials. While mechanical recycling remains the dominant route for PET waste management, enzymatic recycling has emerged as a promising complementary technology capable of depolymerising PET into its constituent monomers, terephthalic acid (TPA) and ethylene glycol. Following depolymerisation, these monomers can be purified and reused to manufacture virgin-quality PET, supporting a more circular plastics economy.
Industrial enzymatic recycling processes operate under demanding conditions, typically requiring elevated temperatures and high solids loadings to achieve economically viable reaction rates and product concentrations. Consequently, PET-degrading enzymes must combine high thermal stability with sustained catalytic activity and resistance to product inhibition. Although substantial progress has been made in engineering PET hydrolases, these enzymes often produce mixtures of mono-aromatic products, including the desired TPA and its monoester intermediate, mono(2-hydroxyethyl) terephthalate (MHET). Efficient conversion of MHET to TPA therefore requires robust and thermostable MHET hydrolases.
In this study, we employ differential scanning calorimetry (DSC) and isothermal titration calorimetry (ITC) to characterise the thermal stability and catalytic performance of MHET hydrolases, including the enzyme IsMHETase from the PET-degrading bacterium Ideonella sakaiensis. DSC measurements demonstrate that these enzymes undergo irreversible thermal denaturation that can be described by a simple native-to-denatured transition model. ITC is used to quantify Michaelis–Menten kinetics for MHET hydrolysis, identify and measure product inhibition, and determine enzyme half-lives under operational conditions. Together, these calorimetric approaches provide a powerful framework for evaluating and optimising engineered MHET hydrolases for industrial PET recycling applications.

# Tracking and tracing complex DNA structures critical to human health

Alice Pyne[1]
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Frontiers in Biophysics, July 13, 2026, 14:10 - 15:10

Complexity in DNA structures, from defects and damage to the formation of alternative structures, plays a critical role in maintaining, regulating and disrupting the flow of cellular information within the genome. Technological developments in high-resolution Atomic Force Microscopy (AFM) now enable us to routinely visualise single DNA molecules with sub-molecular resolution. However, AFM is still not routinely used to help solve problems inaccessible to the traditional tools of structural biology, due in part to a lack of software for quantitative structural characterisation. We have developed a single-molecule pipeline combining high-resolution AFM and deep-learning image analysis methodologies to identify and quantify complex DNA structures with nanometre resolution.

We use our pipeline to determine the extent of replication progression by tracing the structure of replication intermediates from Xenopus egg extracts. We identify stalled complexes as theta structures, separating and quantifying replicated and unreplicated DNA length. In ~7% of complexes, we observe reversed forks of ~20 nm, providing new insights into the likelihood of complex DNA structures forming in response to replication stress. Beyond replication, we can also assess the effect of complex DNA structures on transcription. We determine that single nick sites can drive up a large increase in R-loop formation, which present in a range of conformations, depending on defects in the template strand. Finally, we extend our pipeline to identify proteins bound to DNA to understand the effect of complexity in DNA structure on protein recognition, from Cas-9 to topoisomerases.

# Building the wall: How do bacteria do it

Sheena Radford[1]
[1]University of Leeds, United Kingdom

BBS-DGfB Joint Session: Single Molecule Dynamics, July 16, 2026, 11:00 - 12:30

Gram negative bacteria are surrounded by a robust outer membrane that is essential for cell growth and virulence. This amazingly complex structure is packed with outer membrane proteins (OMPs) that have to fold and assemble in the highly crowded OM to build a functional cell wall. The OMP biogenesis pathway thus represents a target for the generation of new antibacterial agents. It contains a fascinating protein complex - the beta-barrel assembly machinery (BAM) - that is essential for OMP assembly. Folding is also assisted by dedicated molecular chaperones in the bacterial periplasm. Despite identification all of the proteins involved in OM biogenesis, how they function and coordinate together remain mysterious. In this talk I will describe our recent structural, kinetic and biochemical data that aim to elucidate how the sequences of OMPs have evolved to enable their folding into the OM and how assembly is assisted by the molecular chaperones SurA and BAM to accomplish the feat of building the bacterial cell wall. The insights could reveal the Achilles heel in bacterial resistance mechanisms, and open the door to new strategies to develop new antimicrobial agents.

# Unlocking cellular ultrastructure with super-resolution expansion microscopy

Markus Sauer[1]
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BBS-DGfB Joint Session: High Resolution Imaging, July 15, 2026, 14:05 - 15:05

Over the past decade, super-resolution fluorescence imaging by single-molecule localization has evolved as a powerful method for subdiffraction-resolution fluorescence imaging of cells and structural investigations of subcellular structures. However, although refined single-molecule localization microscopy (SMLM) methods can now provide a spatial resolution in the one-digit nanometer range on isolated molecules, that is, well below the diffraction limit of light microscopy, translation of such high spatial resolutions to sub-10 nm imaging in cells or tissues remains challenging. This is mainly caused by the insufficient labeling density and linkage error achieved using standard labeling methods. Furthermore, even if high density labeling can be realized fluorophore communication via different energy pathways can prevent reliable molecular resolution fluorescence imaging in cells. In my contribution I will introduce and discuss different methods to bypass these limitations. One is based on physical expansion of the cellular structure by linking a protein of interest into a dense, cross-linked network of a swellable polyelectrolyte hydrogel. By combining ~8-fold Expansion Microscopy (ExM) with direct stochastic optical reconstruction microscopy (dSTORM) on post-expansion immunolabeled samples we resolve the 8-nm periodicity of a,ß-heterodimers in microtubules and the polyhedral lattice in clathrin-coated pits with nanometer resolution in intact cells. Furthermore, I will demonstrate that 2-color Ex-dSTORM reveals the molecular organization of endogeneous RIM scaffolding proteins and Munc13-1, an essential synaptic vesicle priming protein, in ring-like structures with diameters of ~40 nm at the presynapse in hippocampal neurons. Finally, I will introduce Mega-ExM, a method that enables subnanometer-scale imaging of whole cells using standard confocal microscopes, while maintaining high signal retention and ultrastructure preservation. Mega-ExM relies on iterative cycles of re-embedding expanded specimens in a cleavable neutral hydrogel followed by a swellable hydrogel, yielding tunable expansion factors of up to 250-fold. I will show that Mega-ExM resolves molecular features of mitochondria, centrioles, and the synaptonemal complex with high fidelity using both molecule-specific immunolabeling and NHS-dye staining. Imaging of respiratory chain super-complexes within mitochondrial cristae and nuclear pore complexes (NPCs) in intact cells reveal structural details approaching that of cryo-electron tomography. By enabling ultrastructural visualization of cellular architecture with conventional light microscopy, Mega-ExM establishes a framework for in situ structural biology in whole cells without the need for specialized instrumentation.

# Biophysics of the Pyrenoid

Charley Schaefer[1]
[1]University of Leed, United Kingdom

In Silico Biophysics, July 14, 2026, 14:00 - 15:00

Phase-separated liquid droplets organize molecules within cells, yet the physical principles governing this organization in living systems differ fundamentally from those of abiotic liquid mixtures. While qualitative frameworks for biomolecular condensates are well established, quantitative rules in cellular contexts remain poorly understood. The pyrenoid — a membraneless, liquid-like organelle found in photosynthetic algae and simple plants — provides a powerful model system for addressing this gap. This talk reviews recent successes of reaction–diffusion models in describing the catalytic functionality of condensates, and of the sticker-and-spacer framework in explaining their molecular self-organization. We then build on these approaches to ask how catalytic functionality is maintained under fluctuating molecular supply, and discuss mean-field Flory–Huggins analyses supporting a mechanism in which thylakoid networks act as nucleating scaffolds for condensate formation.

# How to control intracellular transporters

Anne Straube[1]
[1]University of Warwick, United Kingdom

BBS-DGfB Joint Session: Single Molecule Dynamics, July 16, 2026, 11:00 - 12:30

Intracellular transport is essential to organise the inner contents of cells, including the delivery of lipids, RNAs and proteins to the cell periphery and the positioning of organelles. Long-distance transport occurs along microtubules, long polar polymers that span the entire cellular space. Molecular motors dynein and kinesins step along microtubules and haul cargoes, with dynein moving towards the minus end of microtubules that are usually pointing towards the cell centre and most kinesins moving towards the microtubule plus ends. To limit futile energy consumption and blocking of transport tracks, motors are switched off when they are not loaded onto cargoes. Furthermore, cargoes often recruit motors of opposite polarity to enable bidirectional movement, avoid oncoming traffic and other obstacles. I will describe our recent progress in understanding the phenomenon of co-dependence of opposite polarity motors, whereby the depletion or inhibition of one motor, results in a decrease in transport towards both ends of the microtubule. Using in vitro reconstitution of complexes that contain both the kinesin-3 KIF1C and cytoplasmic dynein, fast long-distance transporters with opposite polarity, we showed that the motors mutually activate each other via the shared cargo adapter Hook3. Furthermore, KIF1C engages weakly with the microtubule during minus end directed motility and acts as a processivity factor, extending dynein-driven transport. Because many cargo adapters bind both dynein and kinesins, this mechanism could be generalized to other bidirectional complexes.

# Super-resolution for structural insights into DNA-protein interactions

Philip Tinnefeld

BBS-DGfB Joint Session: High Resolution Imaging, July 15, 2026, 14:05 - 15:05

Fluorescence techniques are little invasive and offer insights under physiologically relevant conditions. Superresolution microscopy, however, faces the challenge that Brownian motion is fast compared to the timescale of imaging. This reduces superresolution applications to immobilized (via fixation) or well-aligned objects such as filaments or nuclear pores. With the recent discovery that double-stranded DNA can be vertically oriented on graphene coverslips,[1] a new window for studying protein-DNA interactions is opened with exquisite axial (by graphene energy transfer) and lateral (by pMINFLUX) resolution.[2] Here, we present recent result of proteins acting on DNA and how DNA structural changes are visualized in 3D. In addition, approaches for fast imaging of small region are discussed.

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# Mechanical regulation of cell division in health and disease

Sarah Woolner[1]
[1]University of Manchester, United Kingdom

The Single Cell, July 14, 2026, 16:30 - 17:30

Cell division is acutely sensitive to mechanical force, in terms of both division rate and division orientation. For example, stretching an epithelial tissue increases the number of divisions and reorients divisions along the stretch axis. Mechanoregulation of division is critical in embryos to help form tissues and organs, in adults to maintain tissue homeostasis and is subverted in diseases such as cancer. However, a key gap in our understanding is across the temporal framework: how does the speed of force change impact the cellular response? This is important as most studies in this area use instantaneous applications of force to test mechanoresponse and yet in vivo strains occur over a wide variety of time frames, for example seconds for tissue wounding, minutes to hours for tissue morphogenesis and months to years for disease progression. In the Woolner Lab, we have developed novel methods to stretch and image multi-layered embryonic epithelial tissue and combine these with mathematical models for inferring mechanical stress across a tissue. In my talk I will describe new work where we uncover differential cellular responses to tissue stretch depending on the speed of stretch. While fast stretch elicits a dramatic increase in mitotic entry, a slow stretch of the same magnitude does not. We are using a combination of live imaging, mathematical analysis and phosphoproteomics to reveal how fast stretch drives entry into mitosis and why slow stretch does not.

# BBS Oral Presenters

## Investigating the effects of ceramide variation on lipid organisation in the stratum corneum from molecular dynamics simulations

Shubham Deshpande[1], Chloe Frame[2], Lingfeng Gui[1], Annette Bunge[3], Clare McCabe[1,2]
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In Silico Biophysics, July 14, 2026, 14:00 - 15:00

The stratum corneum (SC) is the outermost layer of human skin and serves as the primary barrier against water loss and external damage. The barrier function of skin arises primarily from the highly ordered lipid matrix between skin (corneocyte) cells. While the composition of the lipid matrix is known, how individual lipids contribute to lipid organisation and barrier function remains poorly understood. Molecular dynamics (MD) simulations can help address this by providing a molecular-level view of skin lipid organisation, allowing the structural roles of individual lipid components to be investigated in model systems (1).

In this work, MD simulations are used to investigate the structural organisation of SC lipids (ceramides (CERs), cholesterol (CHOL), and free fatty acids (FFAs) using a multiscale modelling approach. Multilayer lipid systems are first self-assembled using coarse-grained (CG) simulations and subsequently reverse-mapped to atomistic resolution to allow for detailed structural and hydrogen boning analysis. The final atomistic systems consist of six leaflets (three bilayers) and provide a practical representation of the short periodicity phase of the SC. Both pure CER systems and mixtures containing CERs with CHOL and free fatty acids in a 1:0.5:1 molar ratio are examined and metrics such as area per lipid (APL), bilayer height, hydrogen order parameters (SCH), and hydrogen bonding networks determined (2). The results demonstrate how slight differences in CER headgroup and tail structure can influence lipid packing and organisation, along with highlighting the capability of the multiscale approach used to complement and explain experimental observations.

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# Combining PIXE (Particle Induced X-ray Emission), the anomalous diffraction signal and XRF measurements to enhance metalloprotein biochemistry

Professor Elspeth Garman[1], Geoff Grime[2], Edward Snell[3]
[1]University of Oxford, , United Kingdom, [1]Univesrity of Surrey, United Kingdom, [3]SUNY UNiversity at Buffalo, United States
Engineering Biology - Joint with International Society for Mechanobiology, July 14, 2026, 15:30 - 16:30

The Protein Data Bank (PDB) contains information on over 200,000 proteins. Of these around 60,000 are metalloproteins, being either proteins in which a small number of metal atoms define the three-dimensional shape (and hence function), or those involved in metal transport or metabolism. For most PDB metalloprotein entries, the metal atom identity has been inferred indirectly from the X-ray diffraction data or by other methods, including the presence of an anomalous signal.
In the 1990s, we developed a method for unambiguously identifying and quantifying protein metal atom stoichiometry (+/-10%) using microbeam Particle Induced X-ray Emission (PIXE) and proton Rutherford Backscattering [1, 2, 3]. µPIXE has since informed many metalloproteins studies, but although allowing identification of different metals present, it does not give any positional information.
We have now automated the PIXE pipeline, permitting analysis/day of up to 100 aqueous protein samples deposited on a prolene film as a spot array using a non-contact inkjet printer, allowing substantially faster throughput. We have analysed 32 [4], and subsequently another 70 PDB deposited metalloproteins, with the surprising result that >30% of the PDB deposited models had misidentified metals and another 30% contained additional metals. In one of the former cases, we used the experimental and theoretical anomalous signal ratios to position the 3 different metals detected by PIXE and re-refined the deposited structure, revealing a previously missed active site ligand and thus new biological information. We have cross checked our PIXE analyses using the identical samples for XRF (X-ray fluorescence) measurements, with good agreement [5].
This contribution will review our latest results: using the correct metal in the metalloprotein structure allows improvement of the PDB models, so revealing previously unknown biological functions of the proteins studied.

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# Visualising Reaction Complexes in Amino Acid Based Unloaded and CO2 Loaded Carbon Capture Solutions

Dr Harrison Laurent[1], Daniel Sault[1], Thomas F. Headen[2], Terri-Louise Hughes[2], James E. Wheatley[3], Christopher M. Rayner[1,3], Lorna Dougan[1]
[1]University Of Leeds, United Kingdom, [2]ISIS Neutron and Muon Source, United Kingdom, [3]C-Capture Ltd., United Kingdom

Climate Change and Sustainability, July 13, 2026, 15:30 - 16:30

In power generation and industries where CO2 emissions are unavoidable, carbon capture, utilisation, and storage is an important tool to offset climate change[1]. Here CO2 from waste gas streams is removed and utilised in an industrial process or geologically stored, This occurs by bringing waste gas streams into direct contact with carbon capture agents, which react with the CO2 to store it safely until release. Many carbon capture agents are blends of aqueous amines which absorb CO2 by the formation of stable carbamates and are then thermally regenerated. However, many investigated carbon capture solvents suffer from environemental toxicity and high regeneration costs, hindering their practical application. The physical interactions between solutes in solution play a crucial role in understanding their reactivity and energy requirements for regeneration. Atomically resolved, experimentally derived information about the structure of carbon capture solutions however has yet to be reported. In this work we report the structure of two model amino acid based carbon capture solvents[2] as environementaly friendly and efficient carbon capture agents: aqueous sodium and potassium glycinate. We observe the atomistic structure of these solutions in the unloaded and CO2 loaded state by performing computational modelling refined against expermental hydrogen/deuterium isotopically varied neutron diffraction data[3]. This allows us to quantify the structure, frequency, and energetic stability of intermolecular interactions present. We use this approach to comment on likely reaction pathways and the crucial physical interactions governing CO2 loading and unloading in these solutions. Such methodology can be readily applied to other carbon capture solutions, providing unparalleled insight, and facilitating their large-scale modelling and rational design.

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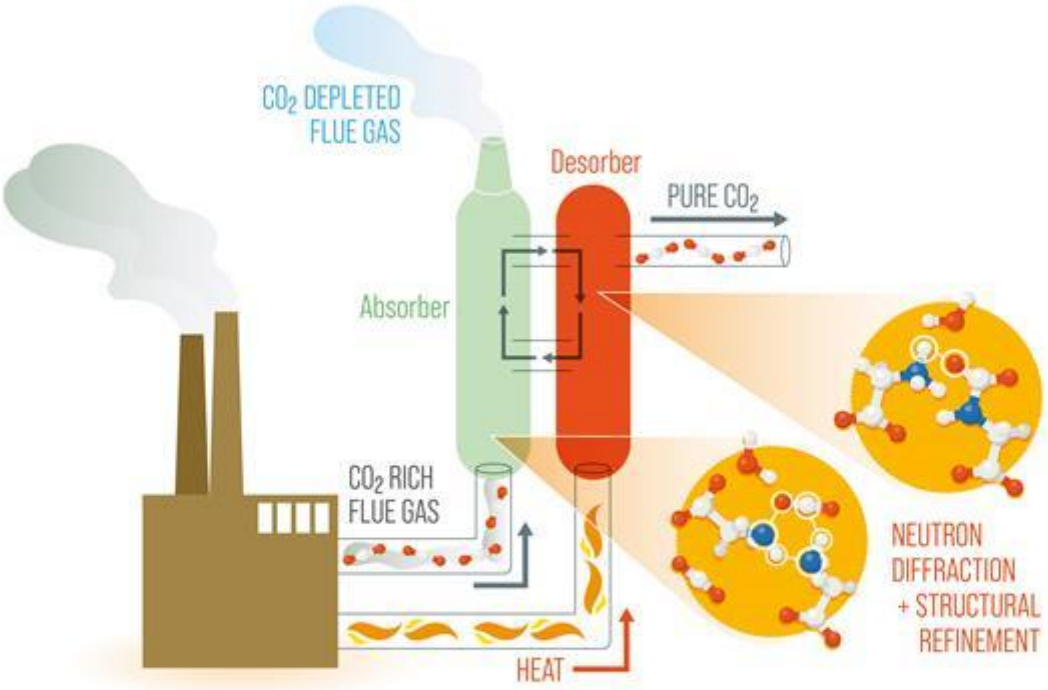


$CO_2$ is absorbed from a flue gas using amino acid salt solution in an absorber and released as a pure stream suitable for storage or utilisation on heating in the desorber. Neutron diffraction has been used to provide fundamental information on the complex solution chemistry of these processes.

# Real-time tracking of nanoparticle extravasation across the blood–brain barrier in zebrafish

Guoying Wang[1], Yueying Cao[1], Marco Morsch[1], Bingyang Shi[1,2], **Yiqing Lu**[1]
[1]Macquarie University, Australia, [2]University of Technology Sydney, Australia

Biophysics in Health and Disease, July 14, 2026, 09:00 - 10:00

Altered vascular integrity is a hallmark for many diseases. In Alzheimer's disease for instance, disrupted integrity of the blood–brain barrier (BBB) is one of the earliest markers and contributes to subsequent cognitive decline, whereas repairing BBB is regarded as a promising therapeutic strategy. Moreover, differentiation between transcellular and paracellular transport is deemed crucial in addition to the extent of permeability, as emerging evidence indicates these mechanisms play distinct roles in the progression of brain pathology such as stroke and ageing. However, targeted studies have been hampered by the lack of suitable methodologies capable of unveiling minute changes to the BBB permeability along with the exact microscopic pathways in vivo.

We report using lanthanide-based upconversion nanoparticles (UCNP) as contrast agents for fluorescence imaging to monitor BBB penetration in live zebrafish. Single particle sensitivity is achieved at 20 full frames per second on a purpose-built microscopy platform, so that any subtle leakage can be traced by visualising UCNP extravasation as it happens. Furthermore, the dynamic behaviours of individual nanoparticles reveal unprecedented information about the microscopic extravasation pathway, which is successfully resolved to differentiate paracellular versus transcellular passage. By separating the anti-Stokes upconversion luminescence from Stokes-shifted normal fluorescence, vasculature imaging is simultaneously performed for the same field-of-view to provide the spatial context of the nanoparticle movement, and the nanoparticles after extravasation can be continuously tracked to uncover their behaviours and fates in the brain parenchyma. We apply the technique to evaluate the BBB integrity in zebrafish larvae at different developmental stages as well as potential perturbation strategies, showing 36-fold increase in BBB penetration with UCNPs functionalised with polysorbate. The technique is expected to generate new insight into the BBB as well as vascular biology elsewhere in the body, facilitating the development of innovative therapeutic and diagnostic nanomedicine in the future.

# 3D Human Spheroid Systems for Studying the Impact of Mechanobiology on Adipose Tissue Development and Function

Dr. Ed Sander[1]
[1]University Of Iowa, United States

Engineering Biology - Joint with International Society for Mechanobiology, July 14, 2026, 15:30 - 16:30

Among the many cell types present in adipose tissues, preadipocytes and fibroblasts, in particular, are thought to play an instrumental role in coordinating changes to the ECM that accommodate dramatic shifts in adipose tissue size. These cells remodel the ECM to mechanically support expanding or shrinking adipocytes as they store or release lipids. This process becomes impaired in unhealthy adipose tissues and is associated with accumulation of ECM proteins and matrix stiffening (i.e., fibrosis). Fibrotic adipose tissues have reduced capacity to accommodate adipocyte hypertrophy, which results in ectopic fat deposits in peripheral tissues, insulin insensitivity, and long-term metabolic dysfunction. Furthermore, adipocyte hyperplasia (i.e., formation of new adipocytes via preadipocyte differentiation into adipocytes) is an ECM guided process associated with metabolically healthy adipose tissue that also becomes impaired in fibrotic tissues. Exactly how ECM composition and changes in stiffness relates to adipocyte hypertrophy and hyperplasia, however, remains unclear. To begin to understand these issues, we employ 3D human spheroid systems in order investigate how different ratios of fibroblasts, preadipocytes, and adipocytes impact adipose tissue ECM remodeling and mechanical environment. We find that mechanical cues impact adipokine secretion profiles, lipid content, ECM composition, and spheroid mechanical properties.

# In vitro investigations of the E coli LLPS organelle the aggresome reveal solid-like properties

Dr Jack Shepherd[1], Lewis Frame[1], Jamieson Howard[1], Aisha Syeda[1], Mark Leake[1]
[1]University Of York, United Kingdom

The Single Cell, July 14, 2026, 16:30 - 17:30

All of us experience stress, and E. coli are no different, needing to overcome lack of food, heat, antibiotics and other threats. Some stressed E. coli do not die but become “persistor” cells which seed a new colony after the threat passes. One mechanism persistor cells use is the formation of an aggresome: a liquid-liquid phase separated organelle which protects important mRNAs and proteins such as ATPases and can be disassembled so that these key biomolecules can be used for a speedy recovery, but the exact mechanism of this rapid and controlled disassembly remains is a key open question in E. coli biophysics. More generally, liquid-liquid phase separation is a common mechanism for forming membraneless organelles, but the physicochemical conditions within these droplets remains unclear. As well as posing its own specific questions, the E coli aggresome is an ideal model organelle for studying LLPS conditions because, unlike eukaryotic stress granules, it is easily purified and stable in buffers.

In this work, we have studied the internal physical conditions through disassembly dynamics and single molecule tracking. We found that in PBS the aggresomes are resistant against 1 M NaCl and 5% Hexanediol, similar to the solid-like cores characteristic of the eukaryotic stress granules. We therefore hypothesise that the E. coli aggresome consists of multiple phases within an overall LLPS schema: one more liquid-like and one more solid-like – the disassembly of which is reliant on active processes rather than passive changes in the local physicochemical environment. Identifying the proteins, molecular machines, and signalling involved in this process will shed considerable light on prokaryotic survival mechanisms, and inform future antibiotic development.

# DGfB Oral Presenters

## Building the wall, one protein at a time: Single-molecule views of OMP biogenesis

Joel Crossley[1]
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BBS-DGfB Joint Session: Single Molecule Dynamics, July 16, 2026, 11:00 - 12:30

The outer membrane of Gram-negative bacteria is a highly selective barrier whose biogenesis depends on coordinated protein trafficking across the cell envelope. This includes inner-membrane translocation, chaperone-assisted handling in the cytoplasm and periplasm, and final folding and insertion by the outer-membrane beta-barrel assembly machinery. Although the major components of these pathways are known, many critical steps are transient and highly dynamic, making their coupling and regulation difficult to resolve with ensemble approaches.

In this talk, I will show how single-molecule fluorescence can reveal the conformational landscapes and dynamic transitions that underpin outer membrane protein (OMP) biogenesis. Together, these results support a unifying principle: envelope biogenesis is carried out by dynamic, allosterically tuneable machines, and single-molecule measurements provide a direct route to connect molecular motions with biological function.

# The P3018S disease variant reveals how dynein's trailing motor sets ensemble velocity

Prof. Dr. Arne Gennerich[1]
[1]Albert Einstein College of Medicine, United States

BBS-DGfB Joint Session: Single Molecule Methodologies, July 15, 2026, 15:35 - 17:35

Mutations in the cytoplasmic dynein heavy chain (DYNC1H1) underlie a range of neurodevelopmental disorders yet how individual variants perturb dynein regulation remains poorly understood. We characterize the disease-associated P3018S mutation, located in the AAA4 module and within the Lis1-interacting region of the motor. Dynein–dynactin–BicD2 (DDB) complexes containing P3018S dynein move at half the wild-type velocity and generate reduced stall forces but retain the ability to assume the inhibitory phi conformation that Lis1 suppresses, respond to Lis1, and assemble into higher-order force-generating states. Several Schizosaccharomyces species, which lack Lis1, naturally encode a serine at this position, suggesting evolutionary relevance for dynein activation. Using mixed wild-type–mutant assemblies, we find that the dynein occupying the trailing position on dynactin dictates ensemble velocity, and that the leading dynein's LIC enhances trailing-motor velocity by ~130%, revealing a mechanism for leading-to-trailing motor stimulation within multi-dynein assemblies.

# Synergy of Topoisomerase and Condensin in regulating genome topology

Prof Davide Michieletto[1]
[1]University Of Edinburgh, United Kingdom

BBS-DGfB Joint Session: Single Molecule Methodologies, July 15, 2026, 15:35 - 17:35

Topoisomerase and SMC proteins, such as condensin and cohesin, are vital proteins that manage and regulate genome structure and topology. There is increasing evidence suggesting that they act synergistically to lower the complexity of genome's entanglement and topology.

In this talk, I will first present recent data from bulk topological relaxation assays strongly suggesting that yeast condensin enhances the topological simplification of DNA by Topoisomerase. I will also present evidence that, on the contrary, MukBEF (a bacterial SMC) inhibits topological simplification of DNA by Topo IV (a bacterial type 2 Topoisomerase).

To rationalise the observations from bulk assays, I will present single molecule evidence, i.e. optical tweezers and AFM, that help us to better understand the allosteric and cooperative behaviour of Topoisomerase and SMC proteins on DNA substrates and the differences between yeast and bacterial SMC.

Finally, I will present current state-of-the-art computational models to understand the action of Topoisomerase and SMC on DNA.

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# The ultrafine-bridge-associated endonuclease ANKLE1 is stimulated by tension in DNA to process branch-points

Dr Korak Kumar Ray[1,2], Artur Kaczmarczyk[1,2], Alasdair Freeman[3], Faith Leow[3], Timothy Wilson[3], David Rueda[1,2], David Lilley[3]
[1]MRC Laboratory of Medical Sciences, United Kingdom, [2]Department of Infectious Diseases, Imperial College London, United Kingdom, [3]School of Life Sciences, University of Dundee, United Kingdom

BBS-DGfB Joint Session: Single Molecule Dynamics, July 16, 2026, 11:00 - 12:30

Covalent linkages between chromosomes form naturally as a result of recombination or DNA replication. These can persist until late mitosis, resulting in the formation of ultrafine bridges, preventing cell division and causing genome instability through mechanical DNA rupture. The endonuclease ANKLE1, selective for DNA branchpoints during cytokinesis and localising at the cell midbody, is ideally poised to act as the ‘enzyme-of-last-resort’ in processing interchromosomal bridges, thereby allowing cell division. How ANKLE1 catalyses DNA cleavage under the high tension that exists in interchromosomal bridges during mitosis remains unexplored. Using optical tweezers, we show that ANKLE1 is a mechanosensitive endonuclease whose catalytic activity is stimulated by tension in its DNA substrate. At high tension, we observe that the rate with which ANKLE1 catalyses the cleavage of DNA junctions increases continuously with applied tension, with a twenty-fold increase in the cleavage rate at 60 pN. This indicates that the endonuclease has evolved to detect and respond to tension-induced changes to the DNA structure in a manner that facilitates nucleolytic activity. This mechano-enzymological response of ANKLE1 to tension within its DNA substrate is novel and reveals how this enzyme is well-suited to its suggested biological role as an ultrafine-bridge processing enzyme during late mitosis.

# BBS Flash Presentations

## Expression and Purification of Bacterial Membrane Receptor Domains: The case of the Heme receptor HasR from Pseudomonas aeruginosa

Federico Bosetto[1], Maria Zacharopoulou[1], Mark Bycroft[1], Giovanna Zinzalla[1], Monika Kish[2], Pamela J. Rowling[1], Jonathan J. Phillips[2], Laura S. Itzhaki[1], Ioanna Mela[1]
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Poster Flash Talks 1, July 13, 2026, 16:30 - 16:55

Iron is an essential micronutrient that is crucial for the survival and the pathogenicity of Gram-negative bacteria. Pseudomonas aeruginosa is an opportunistic pathogen which can use heme as source of iron. One of the mechanisms, in P. aeruginosa, involved in the iron acquisition relies on the extracellular hemophore (HasA) that transfers the heme to the receptor (HasR) and together form the heme assimilation system. In this work we expressed and characterized a portion of the N-terminal side of HasR which includes the N-terminal plug and the Secretin/TonB domains. The former carries the His-221 residue, fundamental for the heme coordination binding. The protein secondary structure was analysed by Circular Dichroism (CD), reporting a composition of 20% α-helices, 27% antiparallel β-strands and 53% disordered. The proper folding of the protein was assessed using NMR and hydrogen/deuterium-exchange mass spectrometry (HDX-MS) techniques. The 1D 1H spectrum of HasR showed good dispersion of the NMR signals, which was indicative of the presence of a folded structure. The spectrum also contained a significant number of amide protons with chemical shifts typical of disorder regions, which was consistent with the CD data. Altogether, the data supported that the protein contained a folded HasR domain with the rest of the protein regions being unstructured. HDX-MS analysis identified the Secretin/TonB domain as fully folded and stable, whilst the N-terminal plug domain was found to be weakly stable due to the loop regions, which are presumed to be highly flexible, and β-strands that conferred a certain degree of stability upon it. We describe a toolkit for the purification of extracellular parts of bacterial outer membrane proteins and establish such proteins as targets for DNA aptamer selection, with the aim to develop innovative therapeutic tools to efficiently target antibiotic resistant bacteria.

# Capturing dynamic conformational change in proteins during gel network formation

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Poster Flash Talks 2, July 13, 2026, 17:05 - 17:30

Protein gels are highly versatile systems that notably have multi-lengthscale behaviour and can be rationally designed. Through selection of their constituent protein building blocks they can be adapted to wound healing, tissue engineering and biosensing. There is a complex interplay between the behaviour of the individual building block and the bulk gel: when a protein in the gel undergoes conformational change, the bulk gel's structural and mechanical properties change. The converse is also true: bulk deformation can induce protein unfolding and presents a potentially complex mechanical response.

Though in-vitro experiments can map out individual protein and bulk gel characteristics well, the generic mesoscale formation and behaviour of a gel is less understood [1]. In-silico experiments have previously studied the force-lability of a few proteins or the network formation of a colloidal protein gel, but thus far there is no predictive, scalable mesoscale simulation that includes dynamic protein unfolding to our knowledge. We present a dynamic trimer model to represent protein unfolding and incorporate this into network formation simulations of over $10^4$ proteins – this simple coarse-grained model bridges both scalability and dynamic unfolding in protein gel simulations. By varying protein concentration and energy barrier for protein unfolding, the force distribution in the network can be localised and a greater understanding can be developed of how conformational change affects a protein gel's structure and mechanical properties. Real-space data analysis allows us to locate precisely where unfolding is taking place and in what proportions. This gives us unprecedented access to the physical mechanisms underlying protein gel response and highlights the relevant parameters to control to produce bespoke gels for applications.

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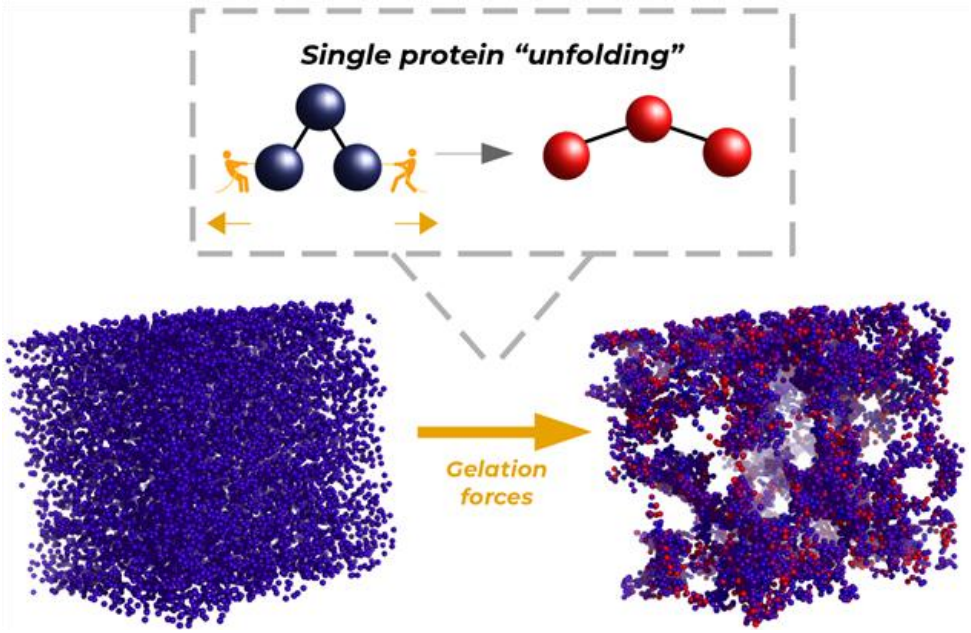

# Human diseases and fungal adaptation - applications of solid-state NMR to probe extracellular matrices

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Poster Flash Talks 2, July 13, 2026, 17:05 - 17:30

The extracellular matrix (ECM) is a complex and heterogeneous material that supports and enables life. Building on previous work on using solid-state NMR to probe collagen proteins in the ECM in bone and cartilage, we are using a similar approach to investigate Ehlers-Danlos syndrome (EDS). In patients suffering from EDS, a common symptom is hypermobility: overly mobile joints and stretchy skin. Using $^{13}$C-labelling of EDS fibroblast culture, we aim to uncover the molecular basis underlying the key symptoms of this disease, with the eventual aim of improving diagnosis and treatment. A second novel area of application involves the fission yeast Schizosaccharomyces pombe, which, like all fungi, has a glycan-based cell wall. S. pombe is not a pathogenic fungus; however, as a model organism, it is open to genetic manipulation and vast number of strains have been generated and characterised. Using solid-state NMR, we have quantified the cell wall components and also quantified the extent to which spectral differences can be reproduced [1]. Using the approach we have developed, we investigated the cell wall produced by three strains with mutations in key glucan synthases, and quantified cell wall composition changes that can explain the observed changes in morphology. Our approach enables a mechanistic understanding of fungal cell wall formation that can drive the development of new antifungal drugs and improve our understanding of fungal adaptation. [1] https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/chem.71081

# Band pattern formation of erythrocytes in density gradients is due to competing aggregation and net buoyancy: A possible diagnostic tool for haemopathologies?

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Poster Flash Talks 2, July 13, 2026, 17:05 - 17:30

Many blood disorders alter the shape, rigidity, and aggregation behaviour of red blood cells (RBCs), yet current diagnostic methods struggle to characterise these physical changes rapidly, robustly, and at low cost across representative sample size. A potentially inexpensive and convenient diagnostic readout recently proposed is the band pattern that appears when erythrocytes are centrifuged in self-forming continuous Percoll density gradients. Although this technique is widely used to sort RBCs by age, the cells do not form a smooth continuum: instead, they consistently organise into discrete bands. Early studies suggested that cell aggregation might influence spatial distribution, but it remains debated whether a continuous density population can form discrete bands. We developed a continuity equation incorporating cell aggregation to describe the macroscopic evolution of RBC volume fraction in a density gradient, considering a continuous RBC density distribution. Numerical solutions demonstrate that the competition between net buoyancy and aggregation is sufficient to create band patterns. Our model reproduces the temporal evolution observed in experiments, but also predicts several types of bifurcation-like behaviours for the steady-state patterns inconstant gradients, depending on RBC volume fraction and aggregation energy. This demonstrates that the competition between RBC aggregation and net buoyancy is a mechanism driving pattern formation. This newly identified mechanism opens the possibility of mapping band patterns to RBC physical properties, drawing on a fundamental understanding of their relationship.

# Coarse-grained modelling of protein-DNA complexes

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Poster Flash Talks 2, July 13, 2026, 17:05 - 17:30

Proteins are essential to biological function, taking on many active and passive roles in the regulation of cell function and forming many complexes with other macromolecules, such as DNA. It can be quite difficult to probe the dynamics and kinetics of these structures and their formation. This is one use of computational modelling, which has seen large improvements - both in hardware, theory, and software - over recent years.

The oxDNA(2) model [1] has emerged as one of the leading coarse-grained models of DNA and is capable of simulating DNA on much longer length and time scales than atomistic models. It is successful in analysing the structural movement and conformation of DNA, such as major/minor grooving, which is crucial in interactions with protein. Similarly, AWSEM-MD [2] is a highly successful coarse-grained protein model, combining physically motivated potentials with bioinformatics to enable de novo prediction of protein structure and simulation of protein dynamics.

Developed here are the theoretical concepts of a coupling for these models, and a high-performance software implementation leveraging tools available in LAMMPS [3], an open-source classical molecular dynamics codebase, to allow biophysically sensible probing into the dynamics of hybrid protein-DNA structures - with initial focus on nucleosomal structures, such as the nucleosome core particle (PDB 1KX5). A model output is seen in the figure.

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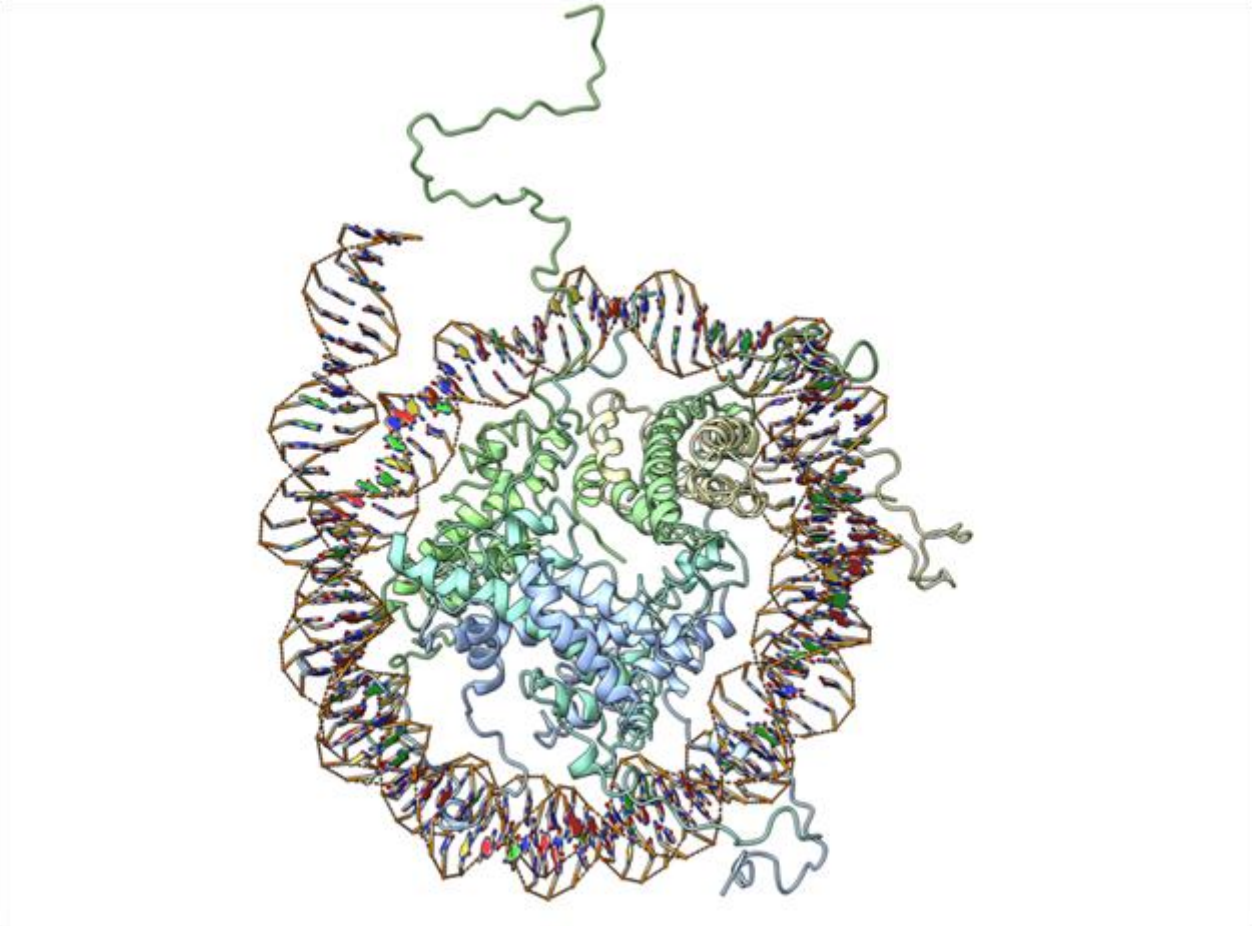

# Direct observation of ionising radiation induced DNA damage by high-resolution atomic-force microscopy

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Poster Flash Talks 1, July 13, 2026, 16:30 - 16:55

The use of radiotherapy to induce DNA damage has been a mainstay of cancer treatment for nearly a century. However, whilst routinely used in the clinic, the specific damage caused to DNA by ionising radiation (IR) remains poorly understood. Among the available IR modalities, the most common are high-energy photons, such as X-rays and gamma rays, which are used to treat breast and brain tumours respectively.

Traditional cell-based and biochemical approaches rely on indirect markers of damage, and ensemble averaging techniques obscure structural heterogeneity and potentially rare but significant biological events.

Here we show that single molecule techniques such as high-resolution Atomic Force Microscopy (AFM) combined with advanced analysis tools, enable direct visualisation and quantification of individual damaged DNA molecules at sub-nanometer resolution.

In this work we combine agarose gel electrophoresis and AFM to measure changes in DNA topology and structure in response to increasing doses of gamma radiation. Using bulk gel electrophoresis we observe an accumulation of damage with increasing dose, with plasmids transitioning from supercoiled to nicked - however, this was the limit of its resolution. Quantitative AFM measurements revealed a more heterogeneous damage landscape, demonstrated by local changes in writhe, curvature and height defects, indicative of single-stranded breaks, that are otherwise hidden in bulk assays.

We show that AFM can enhance existing methods of investigating DNA damage by providing a deeper insight into the damage mechanisms at a submolecular level. These results reveal previously unknown details of gamma ray induced DNA damage, with implications for understanding how healthy cells and cancer cells respond to radiotherapy through activation of downstream DNA damage repair mechanisms.

# oxDNA3 – Introducing Sequence-Specific Curvature and Elasticity into a Coarse-Grained DNA Model

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Poster Flash Talks 1, July 13, 2026, 16:30 - 16:55

Coarse-grained modelling of DNA [1] is not only an efficient alternative to atomistic approaches. It is indispensable for the modelling of DNA on timescales in the millisecond range and beyond, or when long DNA strands of tens of thousands of base pairs or more must be considered, for instance to study the dynamics of DNA supercoiling, which is important for gene regulation and expression.

In this regard the oxDNA2 model [2] is one of the most successful coarse-grained models of DNA to date. While it features the correct thermodynamic behaviour of duplex formation as well as a good average representation of both single and double stranded DNA, it lacks crucial aspects such as sequence-specific curvature and elasticity.

To address this shortcoming, we recently developed the third-generation oxDNA3 model, whose design and properties we will present. oxDNA3 has been trained on state-of-the-art atomistic DNA simulations [3] and has the correct local and global sequence-dependent geometry. In terms of sequence-dependent elasticity oxDNA3 combines the best of both nano- and mesoscopic world. While it retains the variations of elasticity with sequence from all-atom simulations, oxDNA3 mitigates the tendency of atomistic models to exhibit longitudinal and torsional persistence lengths that are too large.

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# High-Speed Laser-Scanning Photothermal Submicron Infrared (O-PTIR) and Stimulated Raman (PT-SRS) Platform for Real-Time Label-Free Chemical Imaging

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Poster Flash Talks 3, July 14, 2026, 10:00 - 10:30

We describe a new laser-scanning microscope developed for real-time, label-free vibrational chemical imaging, integrating Submicron IR (Optical Photothermal Infrared, O-PTIR and Photothermal Stimulated Raman Scattering (PT-SRS) also known as Stimulated Raman Photothermal (SRP), modalities into a single multimodal, correlative platform.

The platform enables true sub-micron spatial resolution and high-speed chemical imaging across a range of biological and materials science applications. High-speed synchronized IR and probe beam laser scanning supports efficient large-area imaging, with full hyperspectral data cubes acquired in minutes. The system also supports three-dimensional depth-resolved chemical imaging. To accommodate a broad range of sample types, the instrument supports both co-propagating and counter-propagating beam geometries, enabling measurements on IR-transparent and IR-opaque substrates. The combination of OPTIR and PT-SRS provides complementary vibrational contrast within one system, enhancing chemical specificity and enabling broader applicability to complex samples. The platform also includes multi-line widefield and laser-scanning confocal fluorescence, enabling fluorescence-guided infrared and Raman measurements. This facilitates correlative imaging in cellular biology, pathology, and functional materials research. We will present representative datasets from O-PTIR and PT-SRS imaging, including mixed polymer standards, subcellular structures (e.g., lipid dynamics in live cells), brain tissue sections, and microplastic mapping. These examples demonstrate the system's ability to support both high-resolution imaging and efficient analysis over extended areas.

# Triggered cell-microenvironment interactions by rapid integrin endocytosis in ovarian cancer

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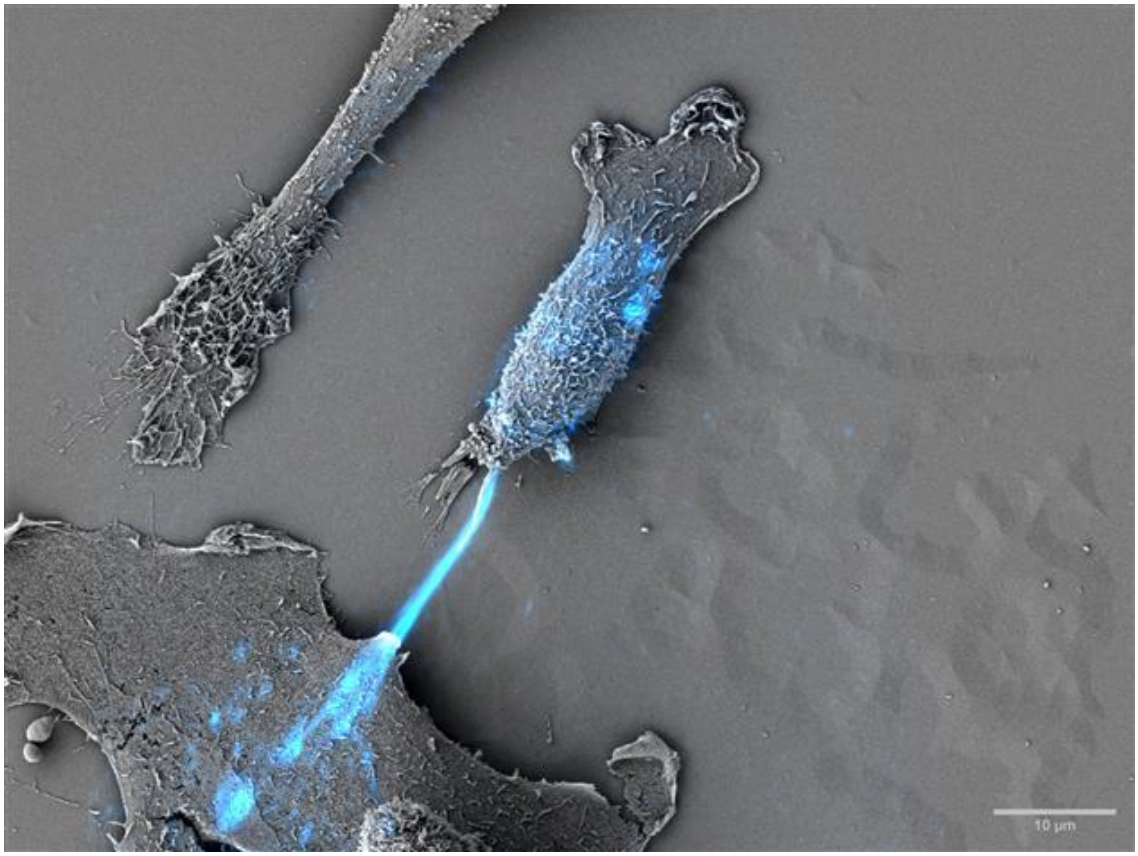
Poster Flash Talks 1, July 13, 2026, 16:30 - 16:55

Integrins, a family of transmembrane heterodimeric receptors, are indispensable for cell interactions. They influence multiscale processes such as, cell migration, extracellular matrix remodeling and tissue integrity. These processes are rooted in different timescales from milliseconds to days. In ovarian cancer, α5β1 and αvβ3 integrins, both binding fibronectin in the extracellular matrix, are pivotal to cancer dissemination, from invasion at the primary site to migration and implantation. Being able to modulate α5β1 and αvβ3 will give a better understanding of the dynamics of cellular interactions at different stages of the tumour process. While methods already exist to modulate integrins, they are either long-term or external. We extend toolbox by rapidly modulating integrin levels using cell endocytosis. We have developed chemogenetic tool, that allows rapid modulation of integrin surface levels by triggering their endocytosis. We are now in a position to use this tool to experimentally manipulate integrin trafficking on a rapid timescale and test the role of integrin-microenvironment interactions on cancer cell behaviors dynamically and the consequences of integrin intracellular trafficking.



# Bacterial electrophysiology for AMR diagnostics and modulation of cell vitality

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Poster Flash Talks 3, July 14, 2026, 10:00 - 10:30

The rapid global rise of AMR and a slowdown in the development of new antimicrobials require maximisation in the effective use of existing antibiotics. This can only be achieved with reliable and rapid antimicrobial susceptibility testing; however, current gold-standard methods require at least 24 h to produce a conclusive result, harming clinical outcomes. We examine the effectiveness of a novel antimicrobial susceptibility testing method based upon an optical electrophysiology technique, using bacterial populations treated with antibiotics from across several classes and mechanisms of action. Using voltage indicator dye thioflavin T with fluorescence time-lapse microscopy and the application of a well-defined electrical field, we demonstrate that 1 hour of exposure to meropenem, chloramphenicol, or tetracycline is sufficient to distinguish treated and untreated populations based on their membrane potential dynamics, using a 90-second test. In addition, we elaborate on advances made in image processing, and present a quantitative measure for cell vitality derived from membrane potential dynamics. This work provides a solid foundation for an expansion of the dataset to include validation with antibiotics of great clinical relevance (e.g., ciprofloxacin, colistin) for the ultimate purpose of widespread method adoption.

# Energy-Entropy Analysis of Protein-Ligand Interactions

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Poster Flash Talks 1, July 13, 2026, 16:30 - 16:55

As non-covalent association processes are ubiquitous in biology, their quantification is crucial. One approach for calculating binding free energies consists of energy-entropy methods. Entropy relates to dynamics within the system but is more difficult to calculate in a computationally efficient and accurate manner. However, assessing entropy is important as protein and solvent dynamics have been established to play a significant role in governing whether binding occurs. Multiscale cell correlation (MCC) yields the entropy of a system by discretizing configuration space into different length scales, giving rise to lower dimensional terms which are easier to compute. This approach allows for detailed insights into entropy changes occurring upon binding, as well as for scalability and fast convergence. Another advantage of this method is that it treats all molecules equivalently and hence, can be used for a complete analysis of the system. [1,2,3] The thermodynamics of the streptavidin-biotin system, widely studied due to its very high binding affinity [4], have been investigated. MCC has allowed a detailed breakdown of changes in entropy terms of the protein complex, ligands and solvation water molecules. Furthermore, the different length scales have allowed for assessing local entropy changes and gaining insights into residues' individual contributions to binding.

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# Dearth, damage and desiccation: How DNA origami can help us create drought resistant crops.

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Poster Flash Talks 1, July 13, 2026, 16:30 - 16:55

DNA origami enables the rational design of nanoscale DNA architectures by combining a long scaffold strand with short, sequence defined oligonucleotides that direct folding into a defined shape. These DNA origami tiles (DOTs) provide a structurally precise and tuneable platform in which perturbations to the DNA sequence or backbone manifest as measurable nanoscale deformations. As a result, DOTs act as sensitive reporters of DNA damage.
In this work, we design and compare several DOT geometries that enhance sensitivity to specific lesion types, enabling us to quantify structural disruption caused by UVC irradiation. Using a combination of bulk assays and single molecule Atomic Force Microscopy (AFM), we distinguish between chemical adduct formation and strand break events, observing distinct architectural signatures that correlate with increasing UVC dose. These AFM resolved structural changes allow us to probe lesion formation at the single molecule level with nanometre precision.
We further explore how dehydration influences DNA stability within DOTs. Controlled dehydration experiments reveal enhanced susceptibility to damage pathways that differ from those observed under hydrated conditions, providing insight into how DNA responds to extreme environmental stress. By coupling rational DOT design with quantitative structural readouts, we aim to build a mechanistic understanding of dehydration induced DNA damage.
Ultimately, this work demonstrates the potential of DNA origami as a modular, engineerable platform for studying environmental stressors on nucleic acids. Understanding how dehydration alters damage pathways may offer new biological insight into the remarkable resilience of organisms that survive desiccation and, more broadly, guide the development of biotechnological strategies relevant to crop robustness under drought conditions.

# Hydration and Association in Extraterrestrial Environments: Mapping Glycine Interactions in Ammonia-Water Mixtures

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Poster Flash Talks 2, July 13, 2026, 17:05 - 17:30

Investigating the behaviour of prebiotic molecules in extraterrestrial environments is essential for understanding the origins of life. Water has been found beyond earth such as in subsurface lakes on Mars [1]. These lakes are proposed to contain mixtures of volatiles and prebiotic molecules such as amino acids and nucleotides. This study investigates the interactions of glycine, the simplest amino acid, in ammonia–water mixtures, which are thought to be prevalent in frozen subsurface oceans on Titan and Enceladus [2]. Ammonia significantly perturbs the hydrogen-bonded network of water and depresses its freezing temperature, creating a unique solvent environment for potential molecular self-assembly [3].
Using neutron diffraction with isotopic substitution (NDIS) combined with structural refinement techniques (Dissolve) we probe glycine hydration, hydrogen bonding, and assembly at the atomic scale and find that ammonia hinders glycine association drastically. This important finding suggests that ammonia-glycine mixtures may require confinement, crowding or pressure to favour assembly of prebiotic molecules. This research provides insight into the potential for biomolecular association in non-terrestrial environments, as well as providing an insight into the potential early steps of biomolecular complexity in extreme environments on Earth.

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# DNA gyrase in live bacteria forms liquid condensates stabilised through weak multivalent bonding of excess GyrB

Dr Aisha Syeda[1], Lewis Frame[1], Katy Hollands[1], Jack Shepherd[1], Alex Payne-Dwyer[1], Nicholas Burton[2], Agnes Noy[1], Anthony Maxwell[2], Mark Leake[1]
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Poster Flash Talks 2, July 13, 2026, 17:05 - 17:30

Type IIA bacterial topoisomerase DNA gyrase has crucial roles maintaining transcription and DNA replication by relaxing positive DNA supercoils through introducing negative supercoils. Structural and biochemical data indicate that protein complex GyrA2:GyrB2 performs this catalysis, however, measured rates in vitro cannot explain the high rates required in vivo. To address this puzzle, we used high-speed single-molecule fluorescence imaging of GyrA/GyrB reporters in live Escherichia coli. We find that cells contain ~40% more GyrB than GyrA expressed in either a diffuse pool or in clusters whose mobility depends on whether they are bound to DNA. Unexpectedly, we discovered that clusters are non-stoichiometric containing a mean of ~150% more GyrB than GyrA, significantly greater than the cellular average, with fluorescence recovery after photobleaching revealing that clustered GyrA and GyrB behave as a liquid whose abundance can be increased by applying gyrase targeting antibiotics. Structural docking indicates that the liquid state is stabilised through excess GyrB progressively binding to existing clusters via weak, multivalent interactions. By operating in liquid condensates, GyrA2:GyrB2 that dissociates from DNA can rebind rapidly instead of diffusing away, increasing enzyme processivity to enable multiple rounds of catalysis that can keep pace with transcription and DNA replication in vivo.

# Accelerating GPCR drug discovery through Fluorescence correlation spectroscopy

Georgia Taylor-vine[1], Paris Avgoustou[1], Anna Geere[1], Zanib Maqsood[1], Gareth Richards[1], Joseph Harrity[1], Timothy Craggs[1]
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Poster Flash Talks 3, July 14, 2026, 10:00 - 10:30

Current biophysical approaches for hit identification assays in drug screening are incompatible with more challenging protein families, such as G-protein coupled receptors (GPCRs), hindering the drug discovery pipeline. Popular techniques including Forster resonance energy transfer (FRET), secondary messenger functional assays and surface plasmon resonance (SPR) are expensive, requiring protein modifications and immobilisation in addition to having long preparation and data acquisition times. A promising alternative to these is fluorescence correlation spectroscopy (FCS), an in solution, diffusion-based approach with rapid data acquisition. In combination with advancing technologies in pharmacology such as the use of native nanodiscs, FCS shows potential to unlock the drug discovery pipeline for diverse protein families such as GPCRs. We have been able to demonstrate that functional GPCR complexes (EC50=9.8 nM) can be isolated and purified in SMA200 nanodiscs to high purity, confirming a complex retention >20%. FCS can subsequently be employed for drug screening, with the use of fluorescently labelled peptides and small molecules giving Kd values of 0.04 and ~500 nM respectively. Competitive binding through non-labelled ligands provides the determination of Ki values, with displacement by compounds in high throughput assays indicating hits against the targets to be carried through in further screening. This demonstrates a methodology for novel GPCR hit identification, initially quantifying protein interactions in the absence of detergent, followed by high-throughput FCS to identify potential hits. This highlights the accessibility of FCS to be applied more widely for accelerated GPCR characterisation and drug screening, providing advancements over alternative biophysical approaches.

# The role of filopodia in the activation of cell signalling cascades involved in the regulation of cell motility and the stability of cell adhesion complexes

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Poster Flash Talks 3, July 14, 2026, 10:00 - 10:30

Cellular mechanosensing of extracellular matrix (ECM) properties is essential for physiological and pathological processes. Filopodia, actin-rich mechanosensory protrusions, enable cells to probe ECM stiffness and initiate the formation of cell adhesions. It was previously shown that mechanical stretching of filopodia triggers Ca2+ influx, generating bursts that often precede activation of lamellipodia propagation in the direction of force, suggesting a feedback loop linking force sensing to cytoskeletal remodeling. However, the regulatory mechanisms of this process remain unknown and the relationship between filopodia mechanotransduction and cell migration is still poorly understood. To bridge this gap, we developed an experimental approach based on the use of optogenetically-controlled Ca2+ channels and filopodial manipulation using optical tweezers, which combined together with TIRF imaging of changes in the Ca2+ level and maturation of focal adhesions, was used to delineate the effects of force and $Ca^{2+}$ influx on the focal adhesion dynamics and remodeling of actin cytoskeleton elements, such as the myosin II filaments. Combining this approach with mathematical modelling describing, we aim to clarify the potential role of filopodia mechanotransduction processes in guiding cell migration, establishing a multiscale framework linking molecular protein mechanics to cell-level decision-making processes.

# BBS Poster Presentations

## The Interaction of Permeation Enhancers and the Skin Barrier

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

The stratum corneum (SC), the outermost layer of the skin, acts as an effective barrier to permeation of chemicals both into and out of the skin. Topical drug formulations often include permeation enhancers such as propylene glycol (PG) and isopropanol (IPA) to improve delivery of the active ingredient through the skin barrier. To understand how PEs interact with and influence the structure and organisation of the lipid lamella observed in the SC, molecular dynamics simulations have been conducted to examine the effects of PG and IPA.
Model SC bilayers containing Ceramide Non-hydroxy fatty acid/Sphingosine (Cer[NS]24), lignoceric acid (C24), and cholesterol in a 1:1:0.5 molar ratio have been studied in contact with water containing different concentrations of PG (0–100 weight %) and IPA (0–20 %). PG/water mixtures caused measurable structural changes, including increased area per lipid and reduced bilayer thickness, indicating disruption of lipid packing but limited broadening of the interfacial region. In contrast, IPA was found to have a limited effect on lipid packing but significantly disrupted interfacial order, broadening the interface and increasing lipid mobility. Solvents containing mixtures of PG and IPA exhibited non-additive effects: the significant interfacial disruption seen with IPA alone was diminished in the presence of PG, while the systems became more structurally heterogeneous. These findings demonstrate that permeation enhancers operate through distinct yet interconnected mechanisms, emphasising how their combined presence modifies bilayer organisation beyond the effects of each component individually. This work adds to a mechanistic framework for understanding enhancer-lipid interactions in the skin barrier.

# Ultrasound stimulation to modulate focal adhesion properties of human mesenchymal stem cells

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BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

Mechanobiology influences cellular mechanisms, mesenchymal stem cell differentiation, tissue regeneration, and ageing. Focal adhesions transmit mechanical forces from the extracellular matrix to the actin cytoskeleton, activating mechanotransduction, but these processes and biological responses are not fully understood. Bone marrow derived MSCs were seeded into three culture well plates, contacting water. Each plate is stimulated with ultrasound at 1.11MHz, 2.5W for 0, 20, 60, and 180 minutes in separate experiments, once per day over the course of three days, followed by a day without stimulation. Area, orientation, quantity, focal adhesion angle, and other focal adhesion properties were collected from these experiments. Results were inconclusive and did not show significant differences or strong correlations between transducers or stimulation times against focal adhesion properties when standard deviations were assumed non-equal. Of note, these results became significantly different when this assumption was omitted. Focal adhesions are important in the activation of mechanotransduction, making these results unexpected. These experiments were constrained by focal adhesion imaging resolution, non-isolated cell imaging, inhomogeneous mechanical stimulation, and time limitations. However, these results lay the foundation for improved experiments and allow for comparisons to be made with other focal adhesion experiments to produce more defined conclusions between focal adhesions and mechanical stimulation.

# A dielectric thin-film substrate using graphene-induced energy transfer for nanoscale lipid bilayer research

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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

In recent years, super-resolution microscopy techniques have undergone a great revolution in terms of spatial details. The enhance axial resolution is necessary for studying lipid bilayers, commonly used to mimic the structure of natural membranes with a typical thickness of 4-6 nm. Graphene-Induced Energy Transfer (GIET) has emerged as a promising technique resolving axial distances of fluorescent emitters with nanometer precision. GIET relies on the distance-dependent quenching of fluorophores by a graphene sheet acting as a planar energy aceptor. The goal of our work is to design substrates suited for GIET investigations on Supported Lipid Bilayers (SLBs). In particular, we propose to deposit a graphene monolayer on glass, and subsequently an Al2O3-coated support using atomic layer deposition (ALD). With this approach, we aim to obtain the substrate suitable for SLB formation. This substrate can be used for GIET studies of membrane-protein binding and for further research in biophysics, biosensing, and elucidating the membrane-protein interactions.

# Expression and Purification of Bacterial Membrane Receptor Domains: The case of the Heme receptor HasR from Pseudomonas aeruginosa

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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

Iron is an essential micronutrient that is crucial for the survival and the pathogenicity of Gram-negative bacteria. Pseudomonas aeruginosa is an opportunistic pathogen which can use heme as source of iron. One of the mechanisms, in P. aeruginosa, involved in the iron acquisition relies on the extracellular hemophore (HasA) that transfers the heme to the receptor (HasR) and together form the heme assimilation system. In this work we expressed and characterized a portion of the N-terminal side of HasR which includes the N-terminal plug and the Secretin/TonB domains. The former carries the His-221 residue, fundamental for the heme coordination binding. The protein secondary structure was analysed by Circular Dichroism (CD), reporting a composition of 20% α-helices, 27% antiparallel β-strands and 53% disordered. The proper folding of the protein was assessed using NMR and hydrogen/deuterium-exchange mass spectrometry (HDX-MS) techniques. The 1D 1H spectrum of HasR showed good dispersion of the NMR signals, which was indicative of the presence of a folded structure. The spectrum also contained a significant number of amide protons with chemical shifts typical of disorder regions, which was consistent with the CD data. Altogether, the data supported that the protein contained a folded HasR domain with the rest of the protein regions being unstructured. HDX-MS analysis identified the Secretin/TonB domain as fully folded and stable, whilst the N-terminal plug domain was found to be weakly stable due to the loop regions, which are presumed to be highly flexible, and β-strands that conferred a certain degree of stability upon it. We describe a toolkit for the purification of extracellular parts of bacterial outer membrane proteins and establish such proteins as targets for DNA aptamer selection, with the aim to develop innovative therapeutic tools to efficiently target antibiotic resistant bacteria.

# Capturing dynamic conformational change in proteins during gel network formation

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

Protein gels are highly versatile systems that notably have multi-lengthscale behaviour and can be rationally designed. Through selection of their constituent protein building blocks they can be adapted to wound healing, tissue engineering and biosensing. There is a complex interplay between the behaviour of the individual building block and the bulk gel: when a protein in the gel undergoes conformational change, the bulk gel's structural and mechanical properties change. The converse is also true: bulk deformation can induce protein unfolding and a potentially complex mechanical response.

Though in-vitro experiments can map out individual protein and bulk gel characteristics well, the generic mesoscale formation and behaviour of a gel is less understood [1]. In-silico experiments have previously studied the force-lability of a few proteins or the network formation of a colloidal protein gel, but thus far there is no predictive, scalable mesoscale simulation that includes dynamic protein unfolding to our knowledge. We present a dynamic trimer model to represent protein unfolding and incorporate this into network formation simulations of over $10^4$ proteins – this simple coarse-grained model bridges both scalability and dynamic unfolding. By varying protein concentration and energy barrier for protein unfolding, the force distribution in the network can be localised and a greater understanding can be developed of how conformational change affects a protein gel's structure and mechanical properties. Real-space data analysis allows us to locate precisely where unfolding is taking place and in what proportions. This gives us unprecedented access to the physical mechanisms underlying protein gel response and highlights the relevant parameters to control to produce bespoke gels for applications.

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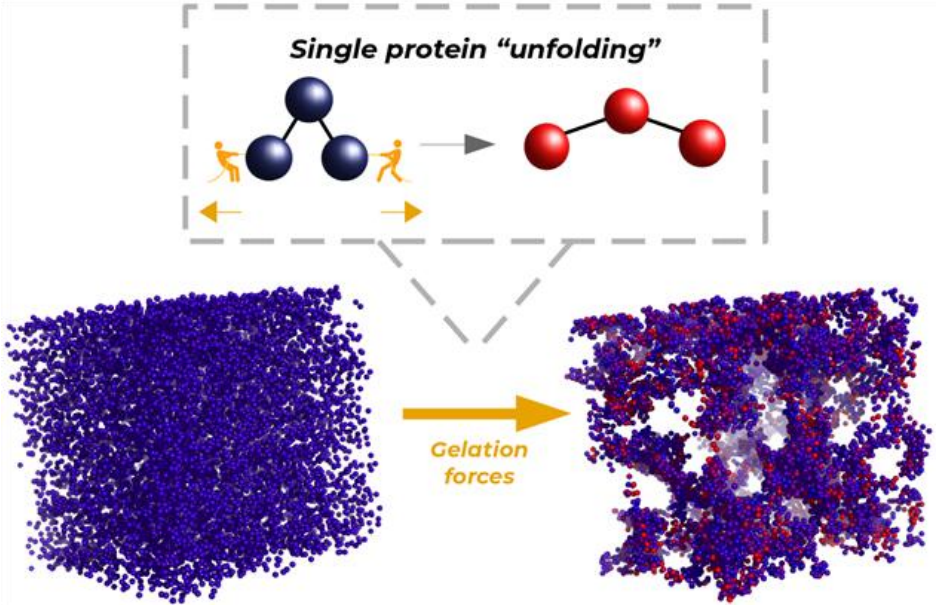

# Studying novel R-Loop formation with Atomic Force Microscopy

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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

R-loops are three-stranded nucleic acid structures that form during transcription upon re-annealing of the nascent RNA to the template DNA strand. Under physiological conditions, R-loops are well tolerated and associated with a number of adaptive processes including transcription termination and the regulation of gene expression. However, harmful R-loops have been implicated as players in a variety of maladaptive cellular processes, in particular as threats to genomic stability, as well as being linked to human diseases. Despite the growing recognition of the complex roles played by R-loops, significant gaps remain in our understanding of the fundamental principles guiding their initiation and stability.

Using a combined approach of quantitative sequencing and atomic force microscopy, we show that non-template strand DNA nicks are powerful initiators of R-loop formation, increasing R-loop frequencies by up to two orders of magnitude. We further reveal that the non-template strand in nick-initiated structures is often flayed away from the RNA:DNA hybrid and engaged in self-pairing, creating unique forked R-loop features. DNA nicks, one of the most frequent DNA lesions in cells, are therefore potential hotspots for opportunistic R-loop initiation and may cause the formation of a distinct class of R-loops. Overall, this work provides insights into how cellular factors and DNA damage influence R-loop formation, with implications for understanding genome instability in health and disease.

# Human diseases and fungal adaptation - applications of solid-state NMR to probe extracellular matrices

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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

The extracellular matrix (ECM) is a complex and heterogeneous material that supports and enables life. Building on previous work on using solid-state NMR to probe collagen proteins in the ECM in bone and cartilage, we are using a similar approach to investigate Ehlers-Danlos syndrome (EDS). In patients suffering from EDS, a common symptom is hypermobility: overly mobile joints and stretchy skin. Using $^{13}$C-labelling of EDS fibroblast culture, we aim to uncover the molecular basis underlying the key symptoms of this disease, with the eventual aim of improving diagnosis and treatment.

A second novel area of application involves the fission yeast Schizosaccharomyces pombe, which, like all fungi, has a glycan-based cell wall. S. pombe is not a pathogenic fungus; however, as a model organism, it is open to genetic manipulation and vast number of strains have been generated and characterised. Using solid-state NMR, we have quantified the cell wall components and also quantified the extent to which spectral differences can be reproduced [1]. Using the approach we have developed, we investigated the cell wall produced by three strains with mutations in key glucan synthases, and quantified cell wall composition changes that can explain the observed changes in morphology. Our approach enables a mechanistic understanding of fungal cell wall formation that can drive the development of new antifungal drugs and improve our understanding of fungal adaptation.

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# Band pattern formation of erythrocytes in density gradients is due to competing aggregation and net buoyancy: A possible diagnostic tool for haemopathologies?

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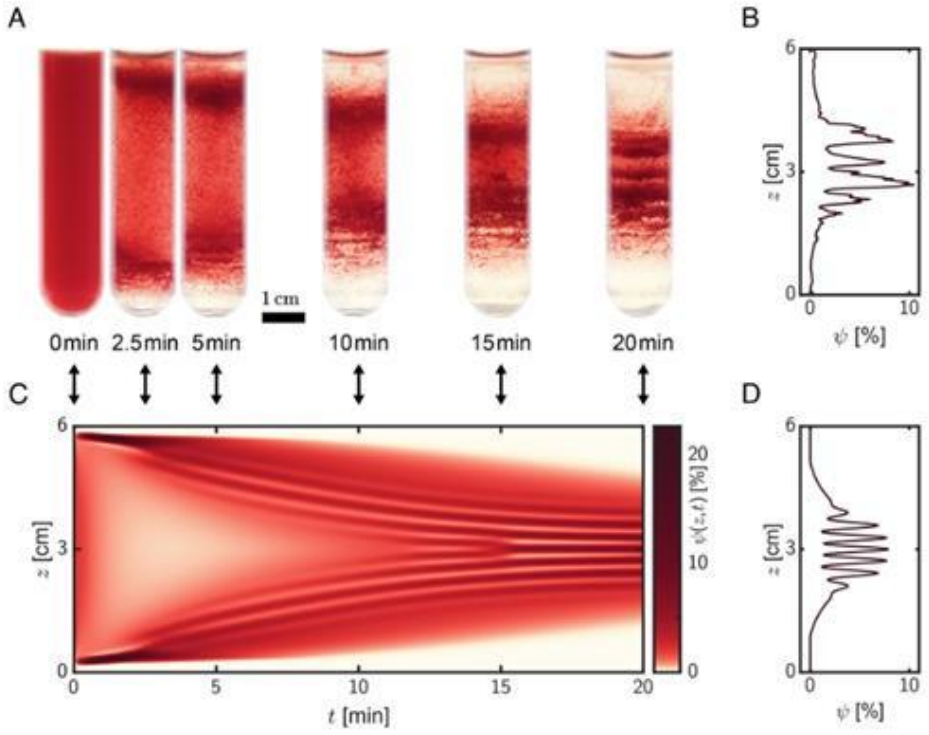
BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

Many blood disorders alter the shape, rigidity, and aggregation behaviour of red blood cells (RBCs), yet current diagnostic methods struggle to characterise these physical changes rapidly, robustly, and at low cost across representative sample size. A potentially inexpensive and convenient diagnostic readout recently proposed is the band pattern that appears when erythrocytes are centrifuged in self-forming continuous Percoll density gradients. Although this technique is widely used to sort RBCs by age, the cells do not form a smooth continuum: instead, they consistently organise into discrete bands. Early studies suggested that cell aggregation might influence spatial distribution, but it remains debated whether a continuous density population can form discrete bands. We developed a continuity equation incorporating cell aggregation to describe the macroscopic evolution of RBC volume fraction in a density gradient, considering a continuous RBC density distribution. Numerical solutions demonstrate that the competition between net buoyancy and aggregation is sufficient to create band patterns. Our model reproduces the temporal evolution observed in experiments, but also predicts several types of bifurcation-like behaviours for the steady-state patterns inconstant gradients, depending on RBC volume fraction and aggregation energy. This demonstrates that the competition between RBC aggregation and net buoyancy is a mechanism driving pattern formation. This newly identified mechanism opens the possibility of mapping band patterns to RBC physical properties, drawing on a fundamental understanding of their relationship.



# Coarse-grained modelling of protein-DNA complexes

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

Proteins are essential to biological function, taking on many active and passive roles in the regulation of cell function and forming many complexes with other macromolecules, such as DNA. It can be quite difficult to probe the dynamics and kinetics of these structures and their formation. This is one use of computational modelling, which has seen large improvements - both in hardware, theory, and software - over recent years.

The oxDNA(2) model [1] has emerged as one of the leading coarse-grained models of DNA and is capable of simulating DNA on much longer length and time scales than atomistic models. It is successful in analysing the structural movement and conformation of DNA, such as major/minor grooving, which is crucial in interactions with protein. Similarly, AWSEM-MD [2] is a highly successful coarse-grained protein model, combining physically motivated potentials with bioinformatics to enable de novo prediction of protein structure and simulation of protein dynamics.

Developed here are the theoretical concepts of a coupling for these models, and a high-performance software implementation leveraging tools available in LAMMPS [3], an open-source classical molecular dynamics codebase, to allow biophysically sensible probing into the dynamics of hybrid protein-DNA structures - with initial focus on nucleosomal structures, such as the nucleosome core particle (PDB 1KX5). A model output is seen in the figure.

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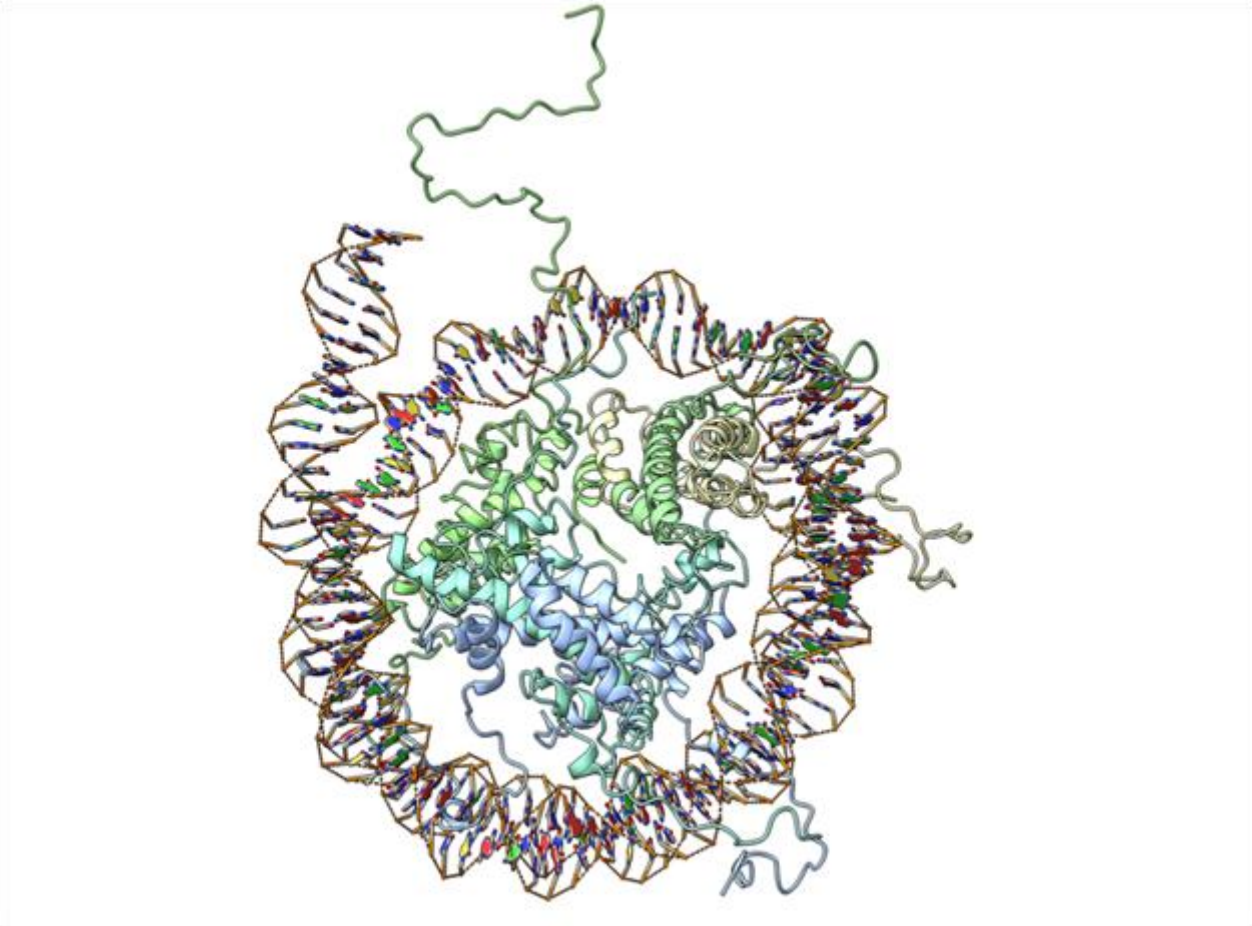

# Direct observation of ionising radiation induced DNA damage by high-resolution atomic-force microscopy

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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

The use of radiotherapy to induce DNA damage has been a mainstay of cancer treatment for nearly a century. However, whilst routinely used in the clinic, the specific damage caused to DNA by ionising radiation (IR) remains poorly understood. Among the available IR modalities, the most common are high-energy photons, such as X-rays and gamma rays, which are used to treat breast and brain tumours respectively.

Traditional cell-based and biochemical approaches rely on indirect markers of damage, and ensemble averaging techniques obscure structural heterogeneity and potentially rare but significant biological events.

Here we show that single molecule techniques such as high-resolution Atomic Force Microscopy (AFM) combined with advanced analysis tools, enable direct visualisation and quantification of individual damaged DNA molecules at sub-nanometer resolution.

In this work we combine agarose gel electrophoresis and AFM to measure changes in DNA topology and structure in response to increasing doses of gamma radiation. Using bulk gel electrophoresis we observe an accumulation of damage with increasing dose, with plasmids transitioning from supercoiled to nicked - however, this was the limit of its resolution. Quantitative AFM measurements revealed a more heterogeneous damage landscape, demonstrated by local changes in writhe, curvature and height defects, indicative of single-stranded breaks, that are otherwise hidden in bulk assays.

We show that AFM can enhance existing methods of investigating DNA damage by providing a deeper insight into the damage mechanisms at a submolecular level. These results reveal previously unknown details of gamma ray induced DNA damage, with implications for understanding how healthy cells and cancer cells respond to radiotherapy through activation of downstream DNA damage repair mechanisms.

# Large-scale DNA origami arrays for combating antimicrobial resistance

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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

Antimicrobial resistance (AMR) has largely grown as a major challenge to the efficient treatment of infectious diseases that are associated with serious implications for human health worldwide (1). Gram-negative bacteria exhibit a high level of resistance largely due to their outer membrane barrier (2). Indeed, multi-drug resistant (MDR) Gram-negative bacteria are responsible for life-threatening infections, contributing significantly to the worldwide challenge of AMR (3).

DNA origami nanotechnology involves the folding of a long-stranded scaffold strand into a predetermined shape by hundreds of short oligonucleotides called staple strands. DNA nanotechnology has reached the degree of sophistication to construct larger, higher-order DNA origami structures with complex conformations. The hierarchical self-assembly of DNA origami building blocks could produce ordered arrays capable of manipulating lipid membranes on a greater scale bioinspired by natural membrane-sculpting proteins (4).

We present a novel endeavour for programming DNA origami self-assembly into high-order, stable arrays based on sticky-end hybridisation. A two-tile design with mirrored modifications permits the hybridization of tiles whether in flipped or rotated orientation, resulting in high-order arrays. By increasing surface mobility on mica surface by the use of a monovalent salt, DNA origami triangles assemble into high-order arrays with desired specificity.

Mimicking neutrophil extracellular traps (NETs), DNA origami arrays can form a sticky web on bacterial membranes entrapping and immobilising the bacteria, altering their morphology and disrupting structural integrity. Moreover, loading such arrays with antimicrobials would target bacterial drug delivery and enhance antimicrobial permeability, a double hit strategy to overcome antimicrobial resistance.

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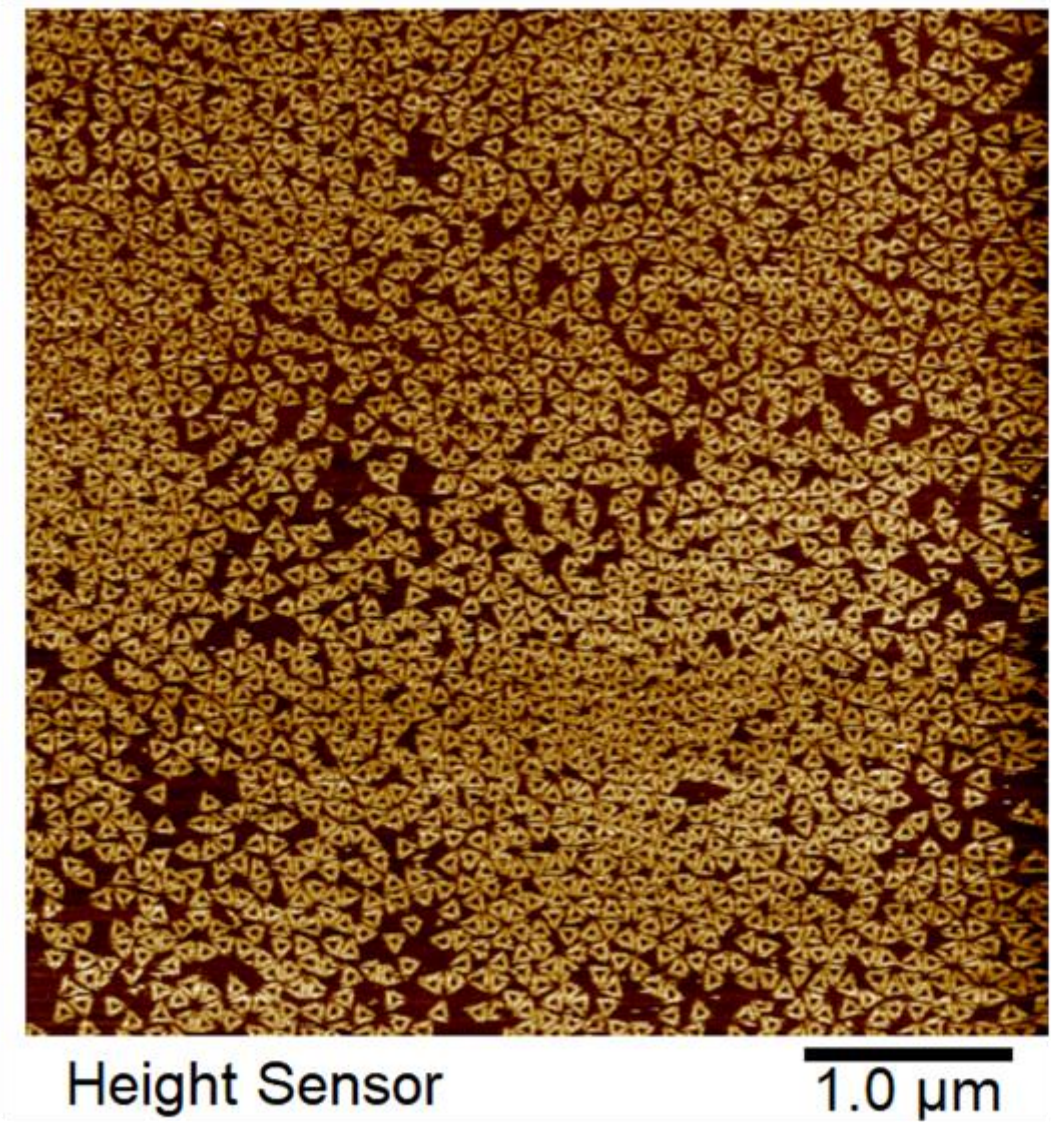


Fig. 3: AFM image of large-scale DNA origami arrays.

# Combining PIXE (Particle Induced X-ray Emission), the anomalous diffraction signal and XRF measurements to enhance metalloprotein biochemistry

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BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

The Protein Data Bank (PDB) contains information on over 200,000 proteins. Of these around 60,000 are metalloproteins, being either proteins in which a small number of metal atoms define the three-dimensional shape (and hence function), or those involved in metal transport or metabolism. For most PDB metalloprotein entries, the metal atom identity has been inferred indirectly from the X-ray diffraction data or by other methods, including the presence of an anomalous signal.
In the 1990s, we developed a method for unambiguously identifying and quantifying protein metal atom stoichiometry (+/-10%) using microbeam Particle Induced X-ray Emission (PIXE) and proton Rutherford Backscattering [1, 2, 3]. µPIXE has since informed many metalloproteins studies, but although allowing identification of different metals present, it does not give any positional information.
We have now automated the PIXE pipeline, permitting analysis/day of up to 100 aqueous protein samples deposited on a prolene film as a spot array using a non-contact inkjet printer, allowing substantially faster throughput. We have analysed 32 [4], and subsequently another 70 PDB deposited metalloproteins, with the surprising result that >30% of the PDB deposited models had misidentified metals and another 30% contained additional metals. In one of the former cases, we used the experimental and theoretical anomalous signal ratios to position the 3 different metals detected by PIXE and re-refined the deposited structure, revealing a previously missed active site ligand and thus new biological information. We have cross checked our PIXE analyses using the identical samples for XRF (X-ray fluorescence) measurements, with good agreement [5].
This contribution will review our latest results: using the correct metal in the metalloprotein structure allows improvement of the PDB models, so revealing previously unknown biological functions of the proteins studied.

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# Chemical Landscapes in Skin: Linking pH to Lipid Organisation and Dynamics

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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

The outermost layer of the skin, the stratum corneum (SC), maintains temperature, water and solute balance, and immune response. Abnormalities in the SC lead to diseases including eczema and ichthyoses. The SC consists of corneocytes embedded within a multi-layered extracellular lipid matrix (ELM), often described as a 'brick wall'. However, this analogy oversimplifies the system; the SC instead behaves as a dynamic, hierarchically organised biomaterial whose function depends on precise chemical and physical organisation.
Recent studies reveal three distinct pH microenvironments within the SC (pH 5.4, 6.0, and 6.8), demonstrating that corneocytes differentiate under spatially structured chemical conditions. This raises the question of how these discrete pH zones influence ELM organisation and dynamics. To address this, we prepare model ELM matrices composed of fatty acids, ceramides, and cholesterol under controlled pH conditions. We use FT-IR spectroscopy with temperature control to monitor lipid chain order, phase transitions, and relaxation kinetics.
We find that increasing the pH shifts the lipid melting transition of the lipid matrix to higher temperatures, indicating enhanced stability of ordered phases under more neutral conditions. Following thermal perturbation, lipid reorganisation proceeds slowly, with both fatty acids (FAs) and ceramides (CERs) requiring nearly 18 hours at 26 °C to recover their original packing state. Notably, the lipids exhibit distinct kinetic behaviours during repeated heating–cooling cycles. For FAs, the peak position at 85 °C progressively shifts to higher wavenumbers with each cycle, indicating a cumulative increase in fluidity. In contrast, the CER peak position at 85 °C remains consistent, indicating a stable high-temperature state.
Taken together, these findings demonstrate that discrete pH stratification establishes a finely tuned chemical–physical landscape governing both the structure and dynamics of the ELM. This work establishes a mechanistic link between spatially resolved chemical environments and the dynamic processes underlying skin barrier formation and stability.

# LILACs: Looking Inside Living Algal Cell Walls

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

The macroalgae, or seaweeds, are unusually resilient organisms that deal with extreme environmental changes on a tidal cycle. The biopolymers that make up their outer coverings - their cell walls - have evolved to cope with these extreme changes. However, in comparison to land plants, we know relatively little about the composition and mechanics of marine-adapted algal cell wall polymers.
To address this gap, we are using a combination of biophysical approaches to study the marine biopolymers found in the common green 'sea lettuce', Ulva. Firstly, we are extracting and chemically characterising the protein and polysaccharide components of the Ulva cell wall using chemical analytical methods (mass spectrometry and NMR). Secondly, the biophysical properties of the extracted structural polysaccharides are being studied using novel microrheological methods to provide insight into polymer gelation across length and time scales. Further work will focus on how extracted proteins can alter these properties. Third, and finally, direct imaging of cell autofluorescence is being used to observe the impact of changing environments on polymer behaviour in vivo and we are using the extracted protein sequences to develop fluorescent molecular rotors that will allow us to image changes in local viscosity. Insights will shed light on the mechanical properties of the marine-adapted structures that support life in climate change-sensitive coastal ecosystems, while also exploring novel biopolymers with a range of tuneable structural properties that may help to develop sustainable materials, for instance in bio packaging.

# oxDNA3 – Introducing Sequence-Specific Curvature and Elasticity into a Coarse-Grained DNA Model

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

Coarse-grained modelling of DNA [1] is not only an efficient alternative to atomistic approaches. It is indispensable for the modelling of DNA on timescales in the millisecond range and beyond, or when long DNA strands of tens of thousands of base pairs or more must be considered, for instance to study the dynamics of DNA supercoiling, which is important for gene regulation and expression.

In this regard the oxDNA2 model [2] is one of the most successful coarse-grained models of DNA to date. While it features the correct thermodynamic behaviour of duplex formation as well as a good average representation of both single and double stranded DNA, it lacks crucial aspects such as sequence-specific curvature and elasticity.

To address this shortcoming, we recently developed the third-generation oxDNA3 model [3], whose design and properties we will present. oxDNA3 has been trained on state-of-the-art atomistic DNA simulations [4] and has the correct local and global sequence-dependent geometry. In terms of sequence-dependent elasticity oxDNA3 combines the best of both nano- and mesoscopic world. While it retains the variations of elasticity with sequence from all-atom simulations, oxDNA3 mitigates the tendency of atomistic models to exhibit longitudinal and torsional persistence lengths that are too large. The image shows the same sequence from Crithidia fasciculata in oxDNA2 and oxDNA3.

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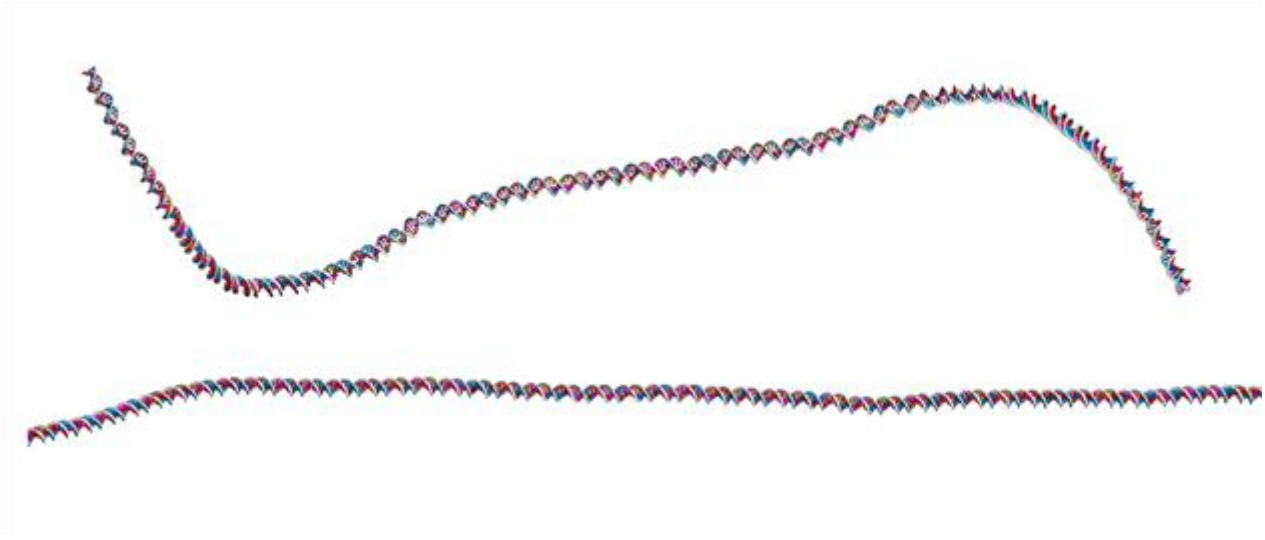

# High-Speed Laser-Scanning Photothermal Submicron Infrared (O-PTIR) and Stimulated Raman (PT-SRS) Platform for Real-Time Label-Free Chemical Imaging

Dr Mustafa Kansiz[1]
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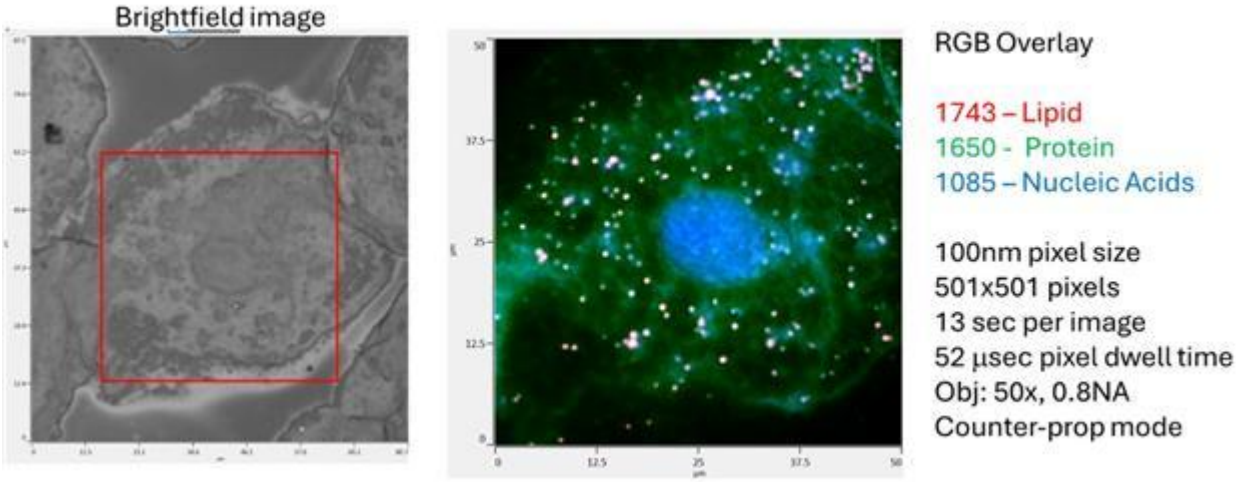
BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

We describe a new laser-scanning microscope developed for real-time, label-free vibrational chemical imaging, integrating Submicron IR (Optical Photothermal Infrared, O-PTIR and Photothermal Stimulated Raman Scattering (PT-SRS) also known as Stimulated Raman Photothermal (SRP), modalities into a single multimodal, correlative platform.

The platform enables true sub-micron spatial resolution and high-speed chemical imaging across a range of biological and materials science applications. High-speed synchronized IR and probe beam laser scanning supports efficient large-area imaging, with full hyperspectral data cubes acquired in minutes. The system also supports three-dimensional depth-resolved chemical imaging. To accommodate a broad range of sample types, the instrument supports both co-propagating and counter-propagating beam geometries, enabling measurements on IR-transparent and IR-opaque substrates. The combination of OPTIR and PT-SRS provides complementary vibrational contrast within one system, enhancing chemical specificity and enabling broader applicability to complex samples. The platform also includes multi-line widefield and laser-scanning confocal fluorescence, enabling fluorescence-guided infrared and Raman measurements. This facilitates correlative imaging in cellular biology, pathology, and functional materials research. We will present representative datasets from O-PTIR and PT-SRS imaging, including mixed polymer standards, subcellular structures (e.g., lipid dynamics in live cells), brain tissue sections, and microplastic mapping. These examples demonstrate the system's ability to support both high-resolution imaging and efficient analysis over extended areas.



# Large-Area AFM Mapping for Mechanobiology Studies in Cells and Tissues

Dr. Andre Körnig[1], Joan-Carles Escolano[1], Jordan Turney[2], Thomas Henze[1]
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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

Mechanical properties regulate mechanotransduction and transport processes, shaping signaling, molecular trafficking, and tissue organization. Atomic force microscopy (AFM) enables nanoscale characterization of stiffness, adhesion, and viscoelasticity, and is also widely used for high-resolution structural analysis – critical for understanding force-driven transport in complex biological systems. However, conventional AFM is limited by sample roughness and restricted lateral range, constraining large-scale analysis of heterogeneous specimens.

We present an advanced AFM imaging approach using SmartMapping technology, which synchronizes AFM head motors with XYZ-piezo stage movement. This innovation enables automated, high-resolution mapping across extended areas without user intervention, improving reproducibility and throughput for multi-region mechanobiological studies.

Using this technology, we analyzed Cytochalasin D-treated 3T3 fibroblasts versus controls, revealing time-dependent changes in mechanics and cytoskeletal architecture that influence intracellular transport. We also analyzed highly corrugated 3D SKOV-3 spheroids, exceeding 100 µm in height, focusing on their structural and mechanical features. Mapping mouse brain tissue along the anterior-posterior axis uncovered stiffness gradients plausibly linked to neuronal transport. Finally, 600 µm-thick neuroblastoma tumors embedded in agarose validated the performance on rough and complex tissues.

This integrated approach establishes a new standard for large-area mechanobiological imaging, enabling spatially resolved analysis of mechanical cues that govern cellular and tissue-level transport

# Triggered cell-microenvironment interactions by rapid integrin endocytosis in ovarian cancer

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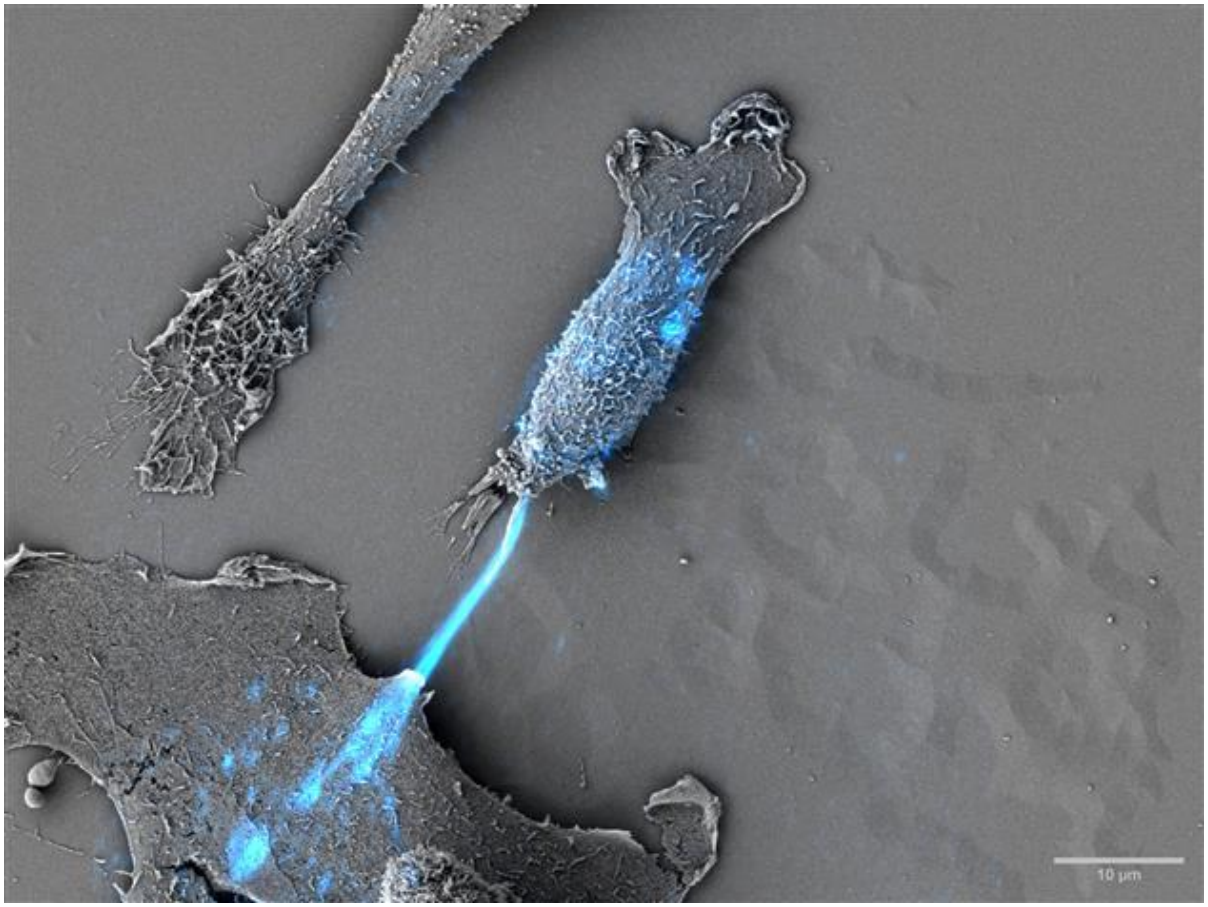
BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

Integrins, a family of transmembrane heterodimeric receptors, are indispensable for cell interactions. They influence multiscale processes such as, cell migration, extracellular matrix remodeling and tissue integrity. These processes are rooted in different timescales from milliseconds to days. In ovarian cancer, α5β1 and αvβ3 integrins, both binding fibronectin in the extracellular matrix, are pivotal to cancer dissemination, from invasion at the primary site to migration and implantation. Being able to modulate α5β1 and αvβ3 will give a better understanding of the dynamics of cellular interactions at different stages of the tumour process. While methods already exist to modulate integrins, they are either long-term or external. We extend toolbox by rapidly modulating integrin levels using cell endocytosis. We have developed chemogenetic tool, that allows rapid modulation of integrin surface levels by triggering their endocytosis. We are now in a position to use this tool to experimentally manipulate integrin trafficking on a rapid timescale and test the role of integrin-microenvironment interactions on cancer cell behaviors dynamically and the consequences of integrin intracellular trafficking.



# Thermal and pH Perturbations Disrupt Lipid Organisation in Human Stratum Corneum: Biophysical FTIR Spectroscopy Studies

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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

The outer layer of human epidermis, the stratum corneum (SC), is exposed to physical and chemical challenges which disrupt its essential bi-directional barrier function leading to penetration of external irritants and increased water loss from the body. Skin cleansing exposes the SC to surfactants, alkaline pH, high water temperatures, and mechanical stresses, all of which can compromise the skin's barrier function. These external stresses are particularly significant for individuals with diminished barrier function due to life-stage or underlying disease. Molecular vibrational spectroscopy methods, such as Fourier transform infrared (FTIR) spectroscopy and Raman spectroscopy, allow for the direct measurement of lipid organisation in the SC in a variety of experimental systems from extracted lipids to isolated SC, to in vivo studies. In the current work we exposed isolated human SC to conditions mimicking those experienced during cleansing; temperatures of 40 °C and both acidic and alkaline pH. Changes in inter- and intra-molecular organisation of SC lipids were monitored using biophysical FTIR spectroscopy. Following temperature and pH exposure alterations in SC lipid organisation were monitored via the methylene rocking modes (orthorhombic packing) and the methylene stretching modes (conformational order i.e., chain fluidity) as a function of time and temperature. Our data indicate that at ambient temperatures the restoration of lipid organisation was significantly delayed following thermal perturbation; intermolecular orthorhombic SC lipid packing had not recovered at 24 hours. Exposure to basic pH resulted in a higher SC lipid transition temperature indicating a decrease in lipids contributing to the liquid crystalline phases within the SC multi-lamellar lipid matrix. These results demonstrate that skin exposure to modest transient increased temperature or pH produces a non-transient disruption in the inter- and intra-molecular SC lipid organisation that is necessary for the barrier function of healthy skin.

# Biophysical FTIR Spectroscopy Studies of Lipid Organisation in the Outer Epidermis of the Long-Finned Pilot Whale

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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

The bi-directional permeability barrier function of mammalian skin, which is essential for life, resides in the externally facing aspect of the epidermis. In terrestrial mammals, including humans, the outer epidermis is known as the stratum corneum (SC). The barrier function of the SC is primarily determined by the composition and molecular organisation of an extracellular lipid matrix which forms a continuous multi-lamellar phase around terminally differentiated cell. Our laboratory has been involved in biophysical studies of SC organisation for over 25 years employing a range of techniques and samples. This work has demonstrated that inter- and intra-molecular SC lipid organisation determines skin barrier function. Disruption of SC organisation has a significant impact on systemic health. In the current project we extend our biophysical methods to the study of the cetacean outer epidermis, the stratum externum (SE). Using FTIR spectroscopy the thermotropic behaviour of pilot whale SE lipids has been measured at sea water temperatures. By monitoring the methylene stretching modes of SE samples we have measured the intramolecular conformational order at ocean ambient temperatures. Preliminary data indicate that lipid organisation in the SE of cetacean epidermis is much more “fluid” than the SC lipids on humans. This suggests the barrier function of SE does not result from highly crystalline lipid lamellae as in humans (and other terrestrial mammals). SE permeability barrier function is likely partly provided by its increased thickness compared to SC. As we increase our database of samples the intention is to then build confidence in understanding the SE lipid organisation of healthy cetacean skin. Future experiments will investigate the role of external stresses such as chemical waste, increased sea water temperature, and changes in sea water pH on SE lipid organisation as these are known to disrupt skin barrier function and systemic health in terrestrial mammals.

# Ultrafast Photophysics of Axitinib by Transient Absorption Spectroscopy and Femtosecond Stimulated Raman Spectroscopy

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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

Photopharmacology has emerged as a promising strategy for locally inhibiting the activity of enzymes, thereby enabling spatially confined targeting of specific enzymes and minimizing systemic side effects. Among several such initiatives axitinib ,a tyrosine kinase inhibitor, has been demonstrated to be optically switchable between active and inactive forms via light-induced isomerization. Although its steady-state optical properties have been characterized, an in-depth understanding of the underlying photophysical processes, particularly on ultrafast timescales, remains lacking. In this work, we investigate the ultrafast photophysics of the cis–trans isomerization of axitinib. Using femtosecond time-resolved spectroscopy, we identify two distinct kinetic processes associated with the cis-to-trans isomerization, with characteristic time constants of X and Y, and three kinetic processes for the trans-to-cis isomerization, with time constants of A, B, and C. These results provide a detailed mechanistic insight into the photoisomerization dynamics of axitinib, with implications for its rational design and optimization as a photopharmacological agent.

# Investigating the catalytic mechanism of a membrane-associated enzyme by EPR spectroscopy and MD simulations

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BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

Phosphatidylserine decarboxylase (PSD) is a membrane-associated enzyme conserved across all kingdoms of life.1 PSD catalyses the biosynthesis of phosphatidylethanolamine (PE) from phosphatidylserine (PS) and exists as a homodimer, with each protomer comprising one α-chain and one β-chain. Previously reported X-ray crystal structures of PSD in the apo and PE-bound states have advanced our understanding of PE biosynthesis, but the transitions PSD undertakes during enzymatic activity remains unclear.1,2,3

Here, we employ Pulsed Electron Electron Double Resonance (PELDOR) also known as Double Electron Electron Resonance (DEER) spectroscopy to investigate the conformational ensemble of the lipid bound enzyme. Using atomistic molecular dynamics (MD) simulations, we explore the conformational space of the enzyme and derive minimal conformational ensembles of PSD consistent with EPR, under different conditions.

Finally, we apply single channel electrophysiology to monitor the activity of mechanosensitive (MS) ion channels modulated by the presence of PSD, providing a link between lipid biosynthesis enzymes and MS ion channel modulation.

This work is supported by the School of Biological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester and the Biotechnology and Biological Sciences Research Council (BBSRC).

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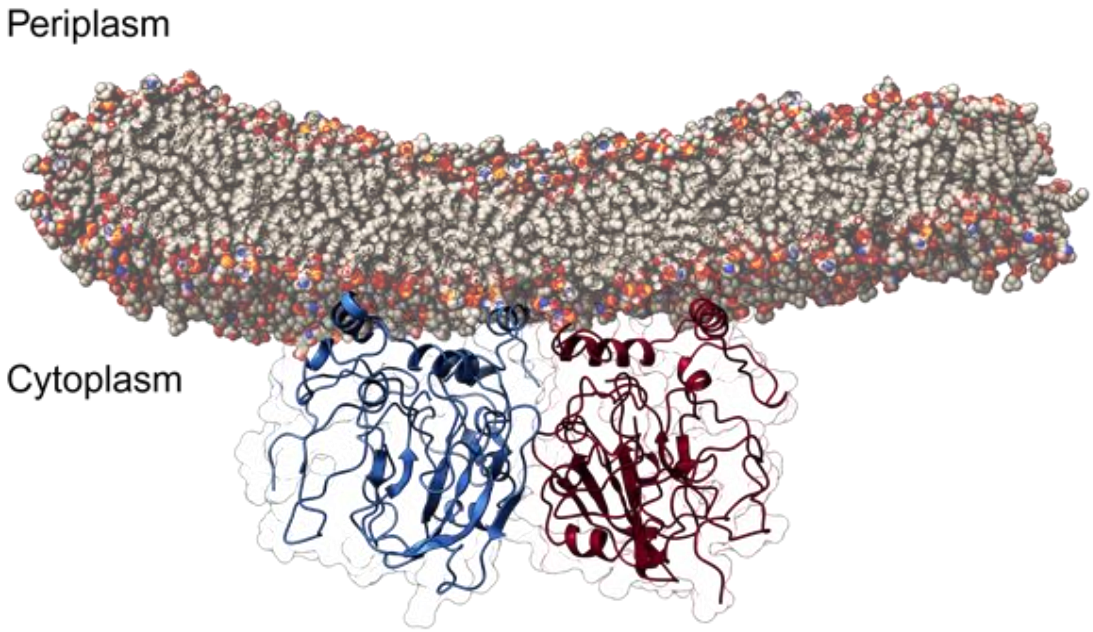

# Affinity-Based Mass Photometry for Targeted Label-Free Detection of Individual Proteins in Complex Mixtures

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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

Mass Photometry (MP) is a label-free optical method for detecting and measuring the mass of individual biomolecules in solution. It facilitates investigation of heterogeneous biomolecular systems, protein oligomerization and protein interactions. Here, we present Affinity-Based Mass Photometry (AffinMP), an implementation of MP that enables targeted detection of proteins of interest in complex mixtures that mimic the native environment. Unlike conventional MP, all non-specific protein detection is eliminated by forming a supported lipid bilayer (SLB) on the glass coverslip surface. Affinity-based protein capture complexes are inserted into the SLB to pull-down target proteins and their interaction complexes. The mass and diffusion of individual proteins are measured. We have designed a monodisperse, monovalent and adaptable nanobody-based protein capture complex for use in AffinMP assays. Every component of this capture complex is water-soluble, so it can be fully assembled in aqueous solution and inserted into any pre-formed SLB via its cholesterol base. To develop our approach, we use epidermal growth factor receptor (EGFR), a potential biomarker for various cancers including glioblastoma multiforme (GBM). EGFR is activated by dimerization and is often highly-expressed with diverse post-translational modifications and mutations. We have begun to establish an AffinMP assay to quantify wild-type EGFR abundance and dimerization in model and GBM patient-derived cell lysates. We show that this AffinMP assay enables targeted detection down to picomolar concentrations of EGFR. In addition, we have begun to extend this assay to characterise the abundance and assembly of the GBM-associated EGFRvIII mutant, using a nanobody that preferentially binds to EGFRvIII over the wild-type version. Our AffinMP framework can be broadly applied to study diverse protein interactions under physiologically or pathologically relevant conditions.

# Designing a Nanopore Sensing Platform for the Diagnosis of Ovarian Cancer

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BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

Extracellular vesicles (EVs) are phospholipid-bound nanoparticles released by cells across all biological organisms. Their contents and morphologies vary depending on their cell of origin, suggesting their potential role as disease biomarkers and involvement in proliferation. Specific surface markers have been detected on EVs from ovarian cancer (OC) cells, a disease notorious for its late diagnosis and poor prognosis due to nonspecific symptoms. This would be greatly improved by the development of a liquid biopsy test for OC markers on EVs derived from patient blood.

Nanopore sensing (NS) is an emerging single-molecule technique for the characterisation of analytes such as extracellular vesicles, which typically have a high polydispersity, rendering their study by bulk methods difficult. NS functions on the principles of resistive pulse sensing: a potential difference is applied across a nanopore, driving the translocation of an analyte and its detection through the characteristic resulting drop in current. NS yields large quantities of data on various physical properties such as size and zeta potential, and nanopore walls can be functionalised to detect specific markers such as surface proteins on EVs, resulting in distinct translocation signals for analytes carrying markers of interest. As a versatile and high-throughput detection technique, NS therefore shows potential for applications in medical diagnosis such as for OC.

This work describes initial results from designing a glass nanopore system for the detection of surface markers on OC-derived EVs, by first optimising the NS platform through characterisation of synthetic vesicles (liposomes). Liposomes are synthesised from various phospholipids to investigate differences in surface charge and membrane fluidity, and characterised using a combination of traditional methods such as dynamic light scattering, and NS, to evaluate the reliability of the platform designed. This will enable future experiments to detect and characterise EVs.

# Bacterial electrophysiology for AMR diagnostics and modulation of cell vitality

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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

The rapid global rise of AMR and a slowdown in the development of new antimicrobials require maximisation in the effective use of existing antibiotics. This can only be achieved with reliable and rapid antimicrobial susceptibility testing; however, current gold-standard methods require at least 24 h to produce a conclusive result, harming clinical outcomes. We examine the effectiveness of a novel antimicrobial susceptibility testing method based upon an optical electrophysiology technique, using bacterial populations treated with antibiotics from across several classes and mechanisms of action. Using voltage indicator dye thioflavin T with fluorescence time-lapse microscopy and the application of a well-defined electrical field, we demonstrate that 1 hour of exposure to meropenem, chloramphenicol, or tetracycline is sufficient to distinguish treated and untreated populations based on their membrane potential dynamics, using a 90-second test. In addition, we elaborate on advances made in image processing, and present a quantitative measure for cell vitality derived from membrane potential dynamics. This work provides a solid foundation for an expansion of the dataset to include validation with antibiotics of great clinical relevance (e.g., ciprofloxacin, colistin) for the ultimate purpose of widespread method adoption.

# Energy-Entropy Analysis of Protein-Ligand Interactions

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

As non-covalent association processes are ubiquitous in biology, their quantification is crucial. One approach for calculating binding free energies consists of energy-entropy methods. Entropy relates to dynamics within the system but is more difficult to calculate in a computationally efficient and accurate manner. However, assessing entropy is important as protein and solvent dynamics have been established to play a significant role in governing whether binding occurs. Multiscale cell correlation (MCC) yields the entropy of a system by discretizing configuration space into different length scales, giving rise to lower dimensional terms which are easier to compute. This approach allows for detailed insights into entropy changes occurring upon binding, as well as for scalability and fast convergence. Another advantage of this method is that it treats all molecules equivalently and hence, can be used for a complete analysis of the system. [1,2,3] The thermodynamics of the streptavidin-biotin system, widely studied due to its very high binding affinity [4], have been investigated. MCC has allowed a detailed breakdown of changes in entropy terms of the protein complex, ligands and solvation water molecules. Furthermore, the different length scales have allowed for assessing local entropy changes and gaining insights into residues' individual contributions to binding.

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# Discovery of a FANCD2-interacting protein motif (DIP-box) linking DNA Damage Response processes

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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

FANCD2 is a DNA clamp involved in the repair of damage to DNA, in particular interstrand crosslinks that tether two DNA strands together. Repair of interstrand crosslinks requires the coordinated action of chromatin remodelling, nucleases to cut out the crosslink, and homologous recombination. It has long been proposed that FANCD2 recruits proteins involved in several of these processes, however the molecular details remain unclear. Here we use biochemical reconstitution and cryoEM to show that FANCD2 has a conserved acidic region that recognises a nuclease and homologous recombination protein via a short linear motif (SLiMs) in these proteins. We refer to this motif as a D2-interacting protein box (DIP-box), akin to PCNA-interacting protein boxes (PIP-boxes), another DNA clamp. We use structural bioinformatics to identify additional candidate DIP-box proteins that are involved in histone modification and RNA processing. These data demonstrate FANCD2 is a hub for protein-protein interactions providing a structural explanation for FANCD2's central role in repair of DNA interstrand crosslinks.

# Structural Dynamics and Topological Properties of Supercoiled DNA Ropes/Braids

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

DNA achieves an incredible million-fold compaction within the cell nucleus by wrapping, folding and looping in a multi-hierarchical manner creating domains with varying degrees of organisation. As a result, DNA often exists in a supercoiled state, and studying it is crucial for understanding gene expression and regulation in both prokaryotes and eukaryotes.

Supercoiled DNA undergoes large structural rearrangements, leading to the formation of plectonemes (loop-like, intertwined structures). Topological properties are critical here in determining interactions within cell environments, exemplified by DNA where its response to mechanical perturbation is as important as biochemical properties to its cellular roles.

On top of supercoiling, and particularly during DNA replication, transcription and repair, DNA often presents itself in multi-stranded assemblies such as ropes and braids. While these structures are common in the cellular context, our understanding of their mechanical properties is far from complete.

Here, we present results of a combined study of DNA braids and ropes using the oxDNA coarse-grained DNA model [1,2] and the unique COMBI-Tweez experiment [3], which allows simultaneous control of DNA torque and stretch permitting directly imaging of structural changes in plectonemes. We quantify the effective spring elastic constant of DNA braids and the plectoneme size distribution, diffusivity and dynamics depending on topology and supercoiling state.

Fig 1, Attached | Left: Experimental; white spots highlight plectonemic and close proximity locations. Right: Computational; an example of plectoneme formation within the upper left blue strand.

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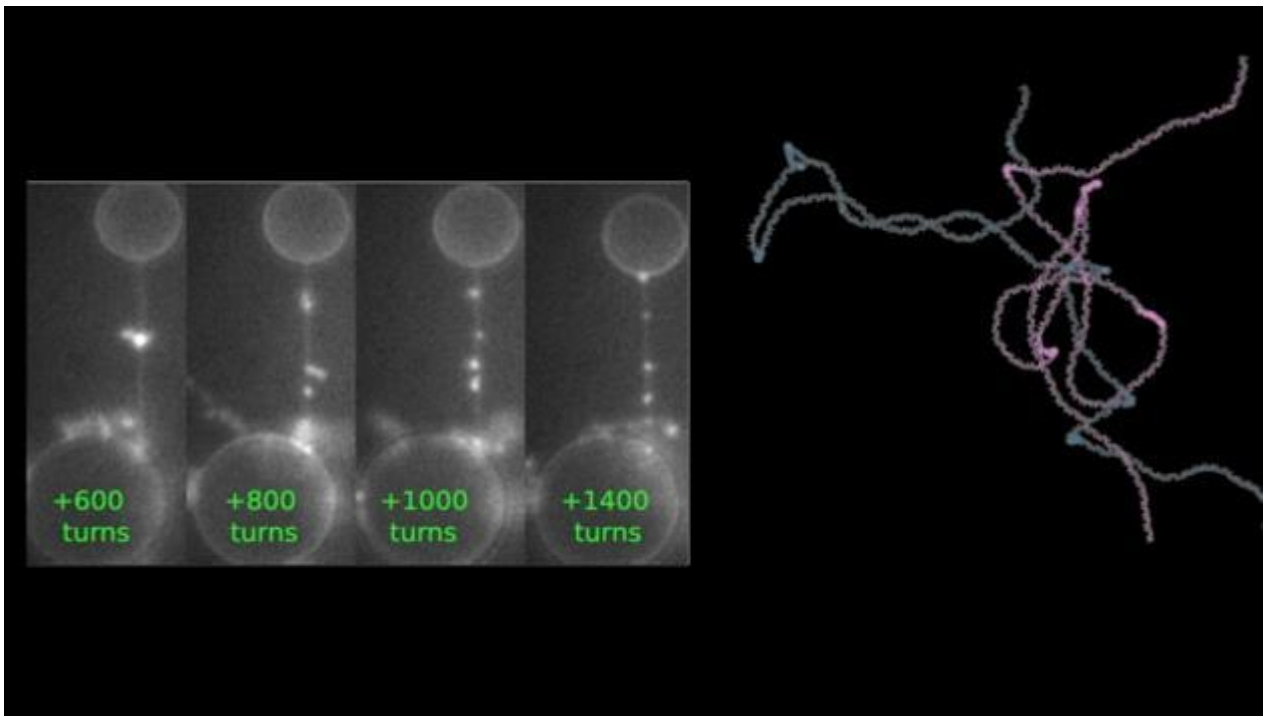
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# Lipid Nanoparticle Endosomal Escape: Insights from Vesicle-Based Model Systems

Jan Šimek[1], Radek Šachl[2]
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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

Lipid nanoparticles (LNPs) have emerged as safe and versatile systems for the delivery of therapeutic RNA into human cells. [1] Successful delivery of siRNA or mRNA enables a broad range of gene therapy applications, including treatment of cancer, genetic disorders, and vaccination. [2] However, delivery efficiency remains a major challenge – LNP endosomal escape has been identified as a key bottleneck in the delivery process and its mechanism remains poorly understood. [3]

Here, we study LNPs of different compositions under various pH conditions to identify links between formulation, chemical environment, and mechanisms of content release. Fusion of selected LNP formulations with liposomes mimicking endosomal membranes was examined using FRET-based assays, Laurdan Generalized Polarization, and Fluorescence Quenching, revealing strong dependencies on both pH and LNP composition.

To directly address cargo delivery, LNPs loaded with fluorescently labeled DNA were imaged after delivery into Giant Unilamellar Vesicles (GUVs). Comparison of DOPE and DSPC as helper lipids revealed higher delivery efficiency for DOPE-containing LNPs, especially at pH 6.0. Fluorescence Correlation Spectroscopy (FCS) showed that delivered species often correspond to oligonucleotide-sized cargo, while in some cases larger objects – potentially intact LNPs – were detected within the GUV lumen, particularly at pH 5.0.

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# Dearth, damage and desiccation: How DNA origami can help us create drought resistant crops.

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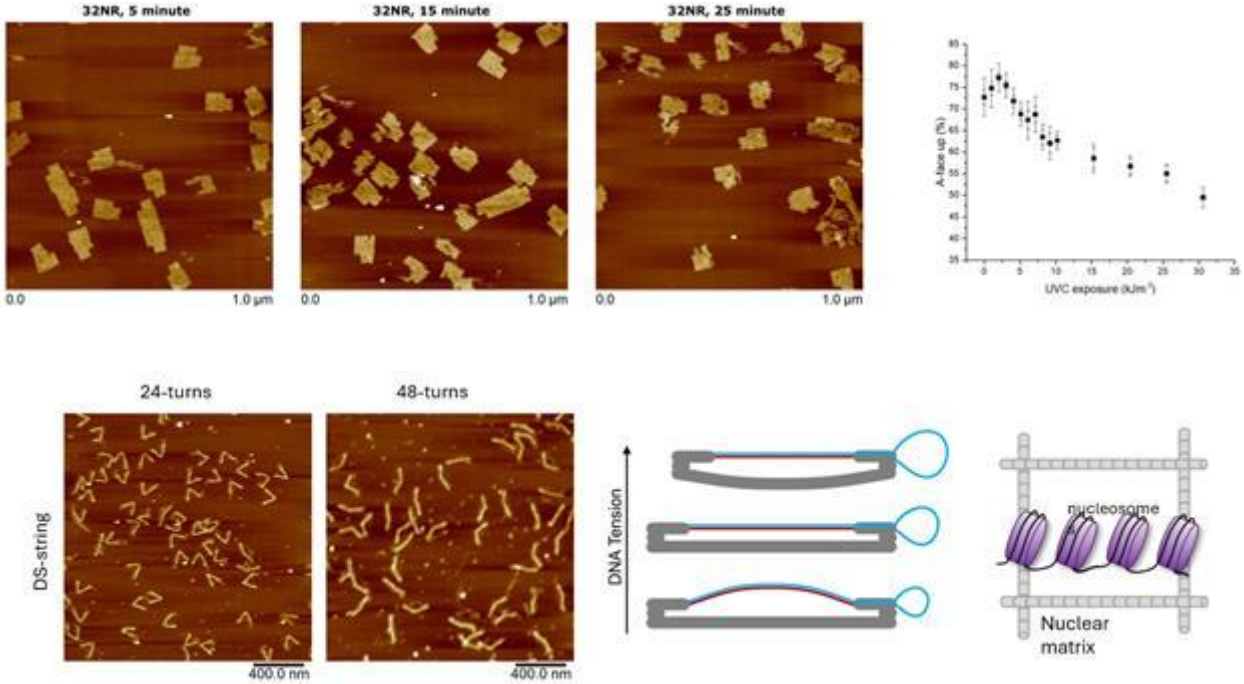
BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

DNA origami enables the rational design of nanoscale DNA architectures by combining a long scaffold strand with short, sequence defined oligonucleotides that direct folding into a defined shape. These DNA origami tiles (DOTs) provide a structurally precise and tunable platform in which perturbations to the DNA sequence or backbone manifest as measurable nanoscale deformations. As a result, DOTs act as sensitive reporters of DNA damage.
In this work, we design and compare several DOT geometries that enhance sensitivity to specific lesion types, enabling us to quantify structural disruption caused by UVC irradiation. Using a combination of bulk assays and single molecule Atomic Force Microscopy (AFM), we distinguish between chemical adduct formation and strand break events, observing distinct architectural signatures that correlate with increasing UVC dose. These AFM resolved structural changes allow us to probe lesion formation at the single molecule level with nanometre precision.
We further explore how dehydration influences DNA stability within DOTs. Controlled dehydration experiments reveal enhanced susceptibility to damage pathways that differ from those observed under hydrated conditions, providing insight into how DNA responds to extreme environmental stress. By coupling rational DOT design with quantitative structural readouts, we aim to build a mechanistic understanding of dehydration induced DNA damage.
Ultimately, this work demonstrates the potential of DNA origami as a modular, engineerable platform for studying environmental stressors on nucleic acids. Understanding how dehydration alters damage pathways may offer new biological insight into the remarkable resilience of organisms that survive desiccation and, more broadly, guide the development of biotechnological strategies relevant to crop robustness under drought conditions.



# Measuring Translocating Proteins using Mass Photometry

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BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

Exploring proteoform diversity is essential for understanding cellular processes and disease. Traditional proteomics, dependent on mass spectrometry (MS), faces challenges in resolving proteoform heterogeneity and detecting low-abundance species in complex samples, motivating the development of complementary single-molecule approaches. In this vein, we explore the combination of mass photometry (MP) and nanopore methods to address these limitations.

Nanopores are a well-established method for DNA sequencing and offer a route to probe individual proteins, where measured signals can encode information on structure and post-translational modifications. However, the complexity of these signals presents a challenge for interpretation. MP, a label-free optical technique, provides single-molecule mass measurements and could offer orthogonal constraints to support nanopore sensing.

Here, we establish an experimental platform for MP measurements in membrane systems relevant to nanopore studies by developing suspended lipid bilayers on microstructured substrates. Using CYTOP, a refractive index-matched polymer, we fabricate low-scattering structures that support stable suspended bilayer regions compatible with MP imaging. Using this platform, we demonstrate MP measurements of the nanopore protein α-hemolysin (aHL) inserted into suspended bilayers. MP reveals aHL localised within the microstructured wells, with the signal remaining spatially confined as a function of increasing aHL concentration. This localisation indicates that insertion occurs within the suspended membrane regions rather than via non-specific surface binding. The observed signals are consistent with dynamic events, likely arising from clusters of aHL pores, reflecting current limitations in resolving individual low-mass species.

To address this, we implement a mass amplification strategy based on gold nanoparticle labelling, enabling the resolution of individual nanopore insertions in MP measurements. This work establishes MP as a viable approach for probing proteins within suspended bilayer architectures and provides a practical route toward future integration with nanopore-based measurements for single-molecule proteoform analysis.

# Hydration and Association in Extraterrestrial Environments: Mapping Glycine Interactions in Ammonia-Water Mixtures

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

Investigating the behaviour of prebiotic molecules in extraterrestrial environments is essential for understanding the origins of life. Water has been found beyond earth such as in subsurface lakes on Mars [1]. These lakes are proposed to contain mixtures of volatiles and prebiotic molecules such as amino acids and nucleotides. This study investigates the interactions of glycine, the simplest amino acid, in ammonia–water mixtures, which are thought to be prevalent in frozen subsurface oceans on Titan and Enceladus [2]. Ammonia significantly perturbs the hydrogen-bonded network of water and depresses its freezing temperature, creating a unique solvent environment for potential molecular self-assembly [3].

Using neutron diffraction with isotopic substitution (NDIS) combined with structural refinement techniques (Dissolve) we probe glycine hydration, hydrogen bonding, and assembly at the atomic scale and find that ammonia hinders glycine association drastically. This important finding suggests that ammonia-glycine mixtures may require confinement, crowding or pressure to favour assembly of prebiotic molecules. This research provides insight into the potential for biomolecular association in non-terrestrial environments, as well as providing an insight into the potential early steps of biomolecular complexity in extreme environments on Earth.

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# Single-molecule live-cell imaging reveals multimeric phase-separated clustering of DNA gyrase on DNA with excess GyrB over GyrA that may facilitate rapid catalysis

Dr Aisha Syeda[1], Lewis Frame[1], Katy Hollands[1], Jack Shepherd[1], Alex Payne-Dwyer[1], Agnes Noy[1], Anthony Maxwell[2], Mark Leake[1]
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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

The type IIA bacterial topoisomerase DNA gyrase has a crucial role maintaining transcription and DNA replication by relaxing positive DNA supercoils through introducing negative supercoils. Structural and biochemical data indicate that GyrA and GyrB proteins form a catalytically active A2B2 complex that performs this function, however, the measured rates cannot explain how positive supercoiling is resolved at the high speeds of DNA replication in vivo. Here, we used rapid localisation microscopy to pinpoint genomically-encoded fluorescent reporters of GyrA and GyrB in live Escherichia coli. Single-molecule analysis indicates that cells contain phase-separated gyrase clusters comprising ~40% more GyrB than GyrA. Single particle tracking reveals high mobility clusters either freely diffusive or transiently bound to DNA, and low mobility clusters, bound to DNA. Low mobility clusters contain means of ~17 GyrA and ~41 GyrB molecules, GyrB levels increasing to ~64 molecules upon adding coumermycin which inhibits ATP binding to GyrB. Structural docking indicates that GyrB progressively binds existing clusters via weak, multivalent interactions generating assemblies that have more GyrB than GyrA. Excess GyrB may enhance gyrase processivity by suppressing cluster dissociation from DNA through forming crossbridges to heterotetramers mediated by multivalent interactions, enabling multiple rounds of catalysis to keep pace with DNA replication.

# Accelerating GPCR drug discovery through Fluorescence correlation spectroscopy

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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

Current biophysical approaches for hit identification assays in drug screening are incompatible with more challenging protein families, such as G-protein coupled receptors (GPCRs), hindering the drug discovery pipeline. Popular techniques including Forster resonance energy transfer (FRET), secondary messenger functional assays and surface plasmon resonance (SPR) are expensive, requiring protein modifications and immobilisation in addition to having long preparation and data acquisition times. A promising alternative to these is fluorescence correlation spectroscopy (FCS), an in solution, diffusion-based approach with rapid data acquisition. In combination with advancing technologies in pharmacology such as the use of native nanodiscs, FCS shows potential to unlock the drug discovery pipeline for diverse protein families such as GPCRs.

We have been able to demonstrate that functional GPCR complexes (EC50=9.8 nM) can be isolated and purified in SMA200 nanodiscs to high purity, confirming a complex retention >20%. FCS can subsequently be employed for drug screening, with the use of fluorescently labelled peptides and small molecules giving Kd values of 0.04 and ~500 nM respectively. Competitive binding through non-labelled ligands provides the determination of Ki values, with displacement by compounds in high throughput assays indicating hits against the targets to be carried through in further screening.

This demonstrates a methodology for novel GPCR hit identification, initially quantifying protein interactions in the absence of detergent, followed by high-throughput FCS to identify potential hits. This highlights the accessibility of FCS to be applied more widely for accelerated GPCR characterisation and drug screening, providing advancements over alternative biophysical approaches.

# Direct, nanoscale mapping of molecular organisation and biogenesis across the Escherichia coli outer membrane

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BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

The outer membrane (OM) of Gram-negative bacteria plays a vital role in protection against antibiotic compounds [1,2], as well as providing structural support [3] and allowing for rapid cell growth and division. Its success in performing these functions depends upon its composition, but also its organisation and biophysical properties. The former is relatively well characterised – the OM contains an asymmetric mix of lipopolysaccharides (LPS), β-barrel OM proteins (OMPs) and phospholipids, but open questions remain about their precise molecular-scale organisation and how this relates to membrane function.

Recent data have shown that the OM contains a rather immobile network of OMPs [2,4], but it must also be sufficiently fluid to allow for biosynthesis and rapid adaptation of the membrane to cell growth. To date, we lack a fundamental understanding of how the outer membrane grows in size and adapts to its environment, despite its apparently static nature.

Here, we use high-resolution atomic force microscopy (AFM) to directly map the organisation and dynamics of the outer membrane from single OMP trimers [4] up to entire cells in living Escherichia coli . By analysing such molecular-to-cellular-scale data for dividing cells, we resolve protein density and organization, as well as phase separation into OMP-enriched and LPS-enriched domains, and identify how these depend on cell growth, thereby linking outer membrane biophysics to cell cycle and the metabolic state of the bacteria.

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# Integrating MD simulations with PELDOR/DEER spectroscopy and cryoEM reveals the dynamics and energetics underlying mechanosensation

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

Mechanosensitive ion channels respond to membrane physical properties through large-scale conformational transitions that couple protein dynamics to lipid bilayer mechanics. However, the energetic and structural mechanisms governing these transitions remain poorly understood. Here, we combine molecular dynamics (MD) simulations with PELDOR/DEER spectroscopy and cryoEM to investigate the membrane-dependent conformational landscapes of two mechanosensitive ion channels: the bacterial mechanosensitive channel of large conductance (MscL) and the mammalian K2P channel TRAAK.

For EcMscL, cryoEM structures resolved closed and expanded conformations in lipid nanodiscs (1), while MD simulations in bilayers and nanodiscs revealed that membrane thickness, leaflet interdigitation, and hydrophobic mismatch strongly influence channel expansion. Simulations showed that nanodiscs facilitate MscL opening by thinning the bilayer and relieving hydrophobic mismatch, thereby stabilising expanded conformational states.

For TRAAK, PELDOR/DEER spectroscopy revealed coexisting swapped and non-swapped extracellular cap conformations with temperature-dependent population shifts (2). MD simulations demonstrated that the associated energetic differences arise from both intrinsic conformational rearrangements and membrane deformations induced by the channel. Analysis of effective protein–membrane non-bonded interaction energies, including Lennard-Jones and electrostatic contributions, revealed how membrane mechanics and lipid-dependent interactions govern the conformational equilibrium.

Together, these studies demonstrate how multiscale MD simulations integrated with structural and spectroscopic techniques can resolve the energetic basis of mechanosensation by linking membrane physical properties to conformational dynamics and functional state transitions in ion channels.

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# A multiscale approach to study the mechanisms of filopodia mechanotransduction and their role in guiding cell migration

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BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

Cellular mechanosensing of extracellular matrix (ECM) properties is essential for physiological and pathological processes. Filopodia, actin-rich mechanosensory protrusions, enable cells to probe ECM stiffness and initiate the formation of cell adhesions. It was previously shown that mechanical stretching of filopodia triggers Ca2+ influx, generating bursts that often precede activation of lamellipodia propagation in the direction of force, suggesting a feedback loop linking force sensing to cytoskeletal remodeling. However, the regulatory mechanisms of this process remain unknown and the relationship between filopodia mechanotransduction and cell migration is still poorly understood. To bridge this gap, we developed an experimental approach based on the use of optogenetically-controlled Ca2+ channels and filopodial manipulation using optical tweezers, which combined together with TIRF imaging of changes in the Ca2+ level and maturation of focal adhesions, was used to delineate the effects of force and $Ca^{2+}$ influx on the focal adhesion dynamics and remodeling of actin cytoskeleton elements, such as the myosin II filaments. Combining this approach with mathematical modelling describing, we aim to clarify the potential role of filopodia mechanotransduction processes in guiding cell migration, establishing a multiscale framework linking molecular protein mechanics to cell-level decision-making processes.

# DESIGN OF DNA-PEPTIDE NANOSTRUCTURES AGAINST INTRACELLULAR TARGETS IN CANCER

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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

Cell signalling pathways have been shown to be disrupted in cancer cells, leading to uncontrolled growth and proliferation. One promising approach for the development of effective cancer treatments is to target specific proteins involved in these pathways and control their activity. In this project we are designing peptide-functionalised DNA nanostructures targeting the intracellular tankyrase proteins for inhibition, which are protein regulators of the Wnt signalling pathway. The DNA nanostructures act as a drug delivery vehicle for the tankyrase inhibitor peptides. They are synthesised by predictably folding a long single-stranded DNA scaffold with shorter complementary DNA strands, and are easily functionalised with fluorophores and active molecules to a high degree of multivalency. We have successfully loaded DNA nanostructures of two different geometries with peptides using azide-DBCO click chemistry. HeLa cells and the Wnt-active cell line SW480 readily uptake non-functionalised DNA nanostructures, as well as the DNA nanostructures that carry the tankyrase-binding peptide. Using super-resolution microscopy, we show that the DNA nanostructures are primarily localised within the lysosomes after 24 h incubation. Moreover, diffuse signal that does not colocalise with the lysosomes can also be detected near the periphery of the cells. The peptide-functionalised nanostructures efficiently inhibit the Wnt pathway, in a comparable degree to known small molecule tankyrase inhibitors. Our work in progress involves thoroughly characterising the endocytosis mechanism of the nanostructures.

# DGfB Poster Presentations

## Mechanochemical Regulation of Focal Adhesion Proteins

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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

Cells sense and adapt to mechanical forces imposed by their microenvironment. Mechanical cues from the extracellular matrix are detected at focal adhesions, where they are transduced into biochemical signals that drive cellular responses. At the molecular level, focal adhesion proteins are directly stretched by extracellular forces, triggering conformational changes that regulate force-dependent interactions and enable cells to interpret mechanical inputs. However, the mechanisms governing the elasticity of these proteins remain poorly understood, particularly the role of posttranslational modifications in modulating protein nanomechanics and binding interactions.

We developed a novel single-molecule magnetic tweezers instrument with enhanced resolution, force control, and stability, enabling the study of protein mechanics under physiologically-relevant forces and timescales. Here, I will present two recent studies that illustrate how targeted chemical modifications in focal adhesion proteins modulate their mechanical response and ligand binding. First, phosphorylation of a cryptic tyrosine in focal adhesion kinase renders the protein mechanically labile, thereby inhibiting paxillin binding. Second, disulfide bond formation in the talin R2 domain finely-tunes its mechanical stability, promoting vinculin binding under physiological low forces. Together, these findings demonstrate how force-dependent post-translational modifications introduce an additional regulatory layer that fine-tunes the mechanical response of focal adhesion proteins.

# Mechanical Forces Trigger the Phosphorylation of the Focal Adhesion Kinase FAT Domain to Modulate Protein Folding Dynamics and Block Paxillin Binding

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BBS-DGfB Joint Poster Session 1a, July 15, 2026, 09:00 - 09:45

The focal adhesion kinase (FAK) functions as a force-sensing kinase, anchoring to focal adhesions (FAs) via interactions between its focal adhesion targeting (FAT) domain and the LD2 and LD4 motifs of paxillin. FA disassembly depends on Src-mediated phosphorylation of Y925 in FAT, which disrupts paxillin binding. However, bulk biochemical studies have shown that Y925 phosphorylation is elusive in the native folded state of FAT, suggesting conformational changes expose the cryptic Src-binding site. Here, we employ novel ultra-stable single-molecule magnetic tweezers force spectroscopy alongside molecular dynamics (MD) simulations to investigate the hypothesis. Our experiments reveal that FAT exhibits sharp force-dependent two-state folding dynamics in response to forces of 6-7 pN. Paxillin LD2 and LD4 motifs cooperatively bind the native folded FAT, as confirmed by our MD simulations. We induced real-time FAT phosphorylation, showing that mechanical forces enable Y925 phosphorylation by unfolding FAT for Src access. Upon phosphorylation, FAT exhibits reduced mechanical stability, unfolding at forces ~1.5 pN lower than the unmodified state. This structural modification alters the folding pathway and accelerates kinetic rates, effectively outcompeting paxillin rebinding. MD simulations support this impaired interaction, demonstrating a significantly shortened lifetime for LD2 binding. Altogether, our work highlights how mechanical forces regulate protein dynamics and signaling, offering insight into cellular mechanotransduction.

# Expanding the Reach of FRET: Quantitative Quenching for Probing DNA Allostery and Sub-3 mm Distance Determination

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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

Single-molecule Förster Resonance Energy Transfer (smFRET) is widely used to monitor biomolecular conformations in the 3-10 nm range. However, the method is inherently less sensitive to distance changes below 3 nm, such as those postulated between adjacent DNA bases during allostery. To address this limitation, we introduce quantitative quenching FRET (qqFRET), a method based on distance-dependent quenching between common dye pairs including Cy3B, ATTO550, Alexa546, Atto647N, and Alexa647. Molecular dynamics simulations indicate that quenching arises from intermolecular dye-dye interactions, and we developed a predictive model based on the overlap of dye-accessible volumes mapped onto biomolecular structures. This interaction produces a continuous, quantifiable signal sensitive to sub-3 nm changes, enabling resolution beyond the Förster radius. Using DNA duplexes as nanometre-scale rulers, we designed constructs where the acceptor dye position differs by a single nucleotide (3.4 Å) in either the 3′ or 5′ direction. These subtle changes yield distinct quenching levels, validating qqFRET as a high-resolution, orientation-sensitive tool. Importantly, quenching is not binary but continuous, allowing nuanced distance measurements without specialised instrumentation. Complementary spectral shift and fluorescence anisotropy measurements characterised dye environments and rotational mobility, providing insight into orientation and local interactions. We then applied qqFRET to a biologically relevant system: ComK transcription factor and its cooperative binding to a promoter region in Bacillus subtilis. ComK binds to two promoter ‘boxes’, inducing long-range allosteric communication. The quenching signal shifts in a manner undetectable by conventional smFRET, aligning with the expected ~3 Å change and suggesting alterations in groove width and tension propagation in the spacer region. This study establishes qqFRET as a powerful extension of smFRET, enabling high-resolution insight into short-range DNA dynamics, cooperative protein-DNA interactions, and structural transitions inaccessible with traditional smFRET.

# The Molecular Contortionist: How Rep Helicase Changes Shape

Dr Jamieson Howard[1], Benjamin Ambrose[2], Mahmoud Abdelhamid[3], Lewis Frame[1], Antoinette Alevropoulos-Borrill[1], Ayesha Ejaz[4], Lara Dresser[1], Maria Dienerowitz[5], Steven Quinn[1,6], Allison Squires[7,8], Agnes Noy[1,6], Timothy Craggs[3], Mark Leake[1,6,9]
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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

Accessory DNA helicases are essential in maintaining genome stability, helping the replisome overcome nucleoprotein blocks to replication. The Escherichia coli superfamily 1A helicase Rep carrying out this function in vivo, yet how its structural dynamics regulate activity has remained unclear.
Here, we use integrated single-molecule and computational approaches to resolve Rep conformational transitions with high temporal and structural resolution. High speed confocal single-molecule FRET shows Rep populates four interconverting conformational states: open (S1), closed (S4), and two previously hidden intermediates (S2, S3). Hidden Markov modelling reveals that Rep proceeds predominantly along an S1→S2→S3→S4 pathway, with kinetics spanning microseconds to seconds.
NaCl concentration modulates both state occupancies and transition rates. Low salt favours closed conformations, whereas high salt biases Rep toward open states. Anti-Brownian ELectrokinetic trapping confirms that individual molecules reversibly access these states over extended timescales, revealing persistent dynamic heterogeneity. The addition of DNA reduces conformational variability and shifts specific transition rates, consistent with conformational “locking” upon substrate engagement.
All-atom molecular dynamics simulations support a mechanism in which closure involves a truncated swing of the 2B subdomain followed by coordinated rotations of subdomains 1B, 2A, and 2B. Together, our results support a model in which Rep employs salt-tunable conformational plasticity to explore multiple structural states prior to DNA binding.
These findings provide mechanistic insight into how accessory helicases regulate activity during replication and illustrate how integrated single-molecule biophysical, computational and biochemical approaches can uncover dynamic features that would otherwise remain hidden

# Single-Molecule Fluorescence: Conformational Heterogeneity of the BAM complex

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BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

The β-barrel assembly machinery (BAM) complex is a conserved and essential factor in Gram-negative bacteria, making it an attractive target for antibiotic development. Structural and biochemical studies have significantly advanced our understanding of how outer membrane proteins (OMPs) are folded and inserted into the outer membrane (OM). However, how conformational changes in the OM insertase, the BAM complex, are coupled to function remains unclear. To address this, we developed a single-molecule FRET (smFRET) construct to monitor the real-time dynamics of the BamA lateral gate, a key functional region of the complex. Reconstituted into E.coli polar lipid extract liposomes, this system enables detailed characterisation of BAM conformational dynamics in a native-like membrane environment and, in combination with cryo-EM and biochemical assays, may provide new mechanistic insight into how the BAM complex assembles OMPs in vitro and in vivo.

# Double-Strand Break Stabilisation by PARP Proteins

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

Poly ADP-ribosylation polymerases (PARPs) are DNA-strand-break-sensing proteins frequently targeted in treatments for BRCA mutation-associated cancers. PARP inhibitors (PARPi) bind PARP–DNA strand break complexes, trapping PARPs at DNA strand break and inhibiting the site repair otherwise triggered by PARPs. BRCA-mutant cells, with dysfunctional homologous recombination DNA repair, are particularly sensitive to PARP inhibitor treatment as unrepaired double-strand breaks (DSBs) accumulate leading to cell death. Off-target effects are common clinical issues for PARPi and may stem from lesser-understood PARP2-DSB interactions, as PARP1, being the more abundant and well-understood paralogue, is often used to characterise PARPi affinities and effects. Previous research found that PARP2-DSB affinity is highly dependent on the structural characteristics of DSBs.

In this project we used magnetic tweezers to investigate how DNA binding and stabilisation by PARP2 varies according to DSB structure. We found that reducing the overhang length of DNA flanking the DSB by only one base (4 to 3 bases) decreased the possible configurations of PARP2 on the DSB from two to one. This suggests that PARP2 stabilisation of DSBs can happen via multiple configurations and that not all PARP2 binding modes are possible at all DSB structures. PARP2 affinity for DSBs therefore appears more sensitive to DSB structure than PARP1, potentially due to PARP1's much more extensive DNA-binding domains, highlighting the complexity of effective PARPi characterisation.

To investigate PARPi-mediated trapping of PARP2 at these DSBs, I also developed a more stable technique for tethering DNA to surfaces. Replacing the typically used digoxigenin-antidigoxigenin interaction, this novel system uses covalent HaloTag protein-ligand chemistry to increase tether durability and lifetime. This high stability enabled repeated force ramps reaching 120 pN, within which we observe the overstretching of torsionally constrained B-DNA (at ~110 pN).

# Single-molecule tools to probe how transitional kinetics between "open" and "closed" enzyme structures can be tuned by salt through intermediate states

Prof Mark Leake[1], Jamieson Howard[1], Benjamin Ambrose[2], Mahmoud Abdelhamid[3], Lewis Frame[1], Antoinette Alevropoulos-Borrill[1], Ayesha Ejaz[4], Lara Dresser[1], Maria Dienerowitz[5], Steven Quinn[1], Allison Squires[6], Agnes Noy[1], Timothy Craggs[3]
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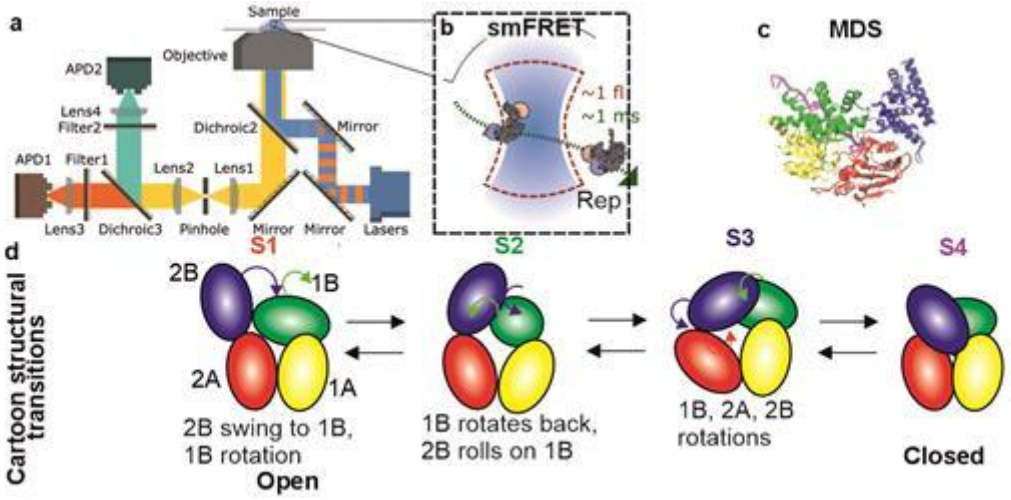
BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

DNA helicases undergo conformational changes; however, their structural dynamics are poorly understood. Here, I report findings on the superfamily 1A DNA helicase Rep, a model enzyme for studying catalytically functional structural dynamics, which undergoes conformational transitions during bacterial DNA replication, repair and recombination. We use time-correlated single-photon counting (TCSPC), fluorescence correlation spectroscopy (FCS), rapid single-molecule Förster resonance energy transfer (smFRET), Anti-Brownian ELectrokinetic (ABEL) trapping and molecular dynamics simulations (MDS) to provide unparalleled temporal and spatial resolution of Rep's domain movements. We detect four states revealing two hitherto hidden intermediates (S2, S3), between the open (S1) and closed (S4) structures, whose stability is salt dependent. Rep's open-to-closed switch involves multiple changes to all four subdomains 1A, 1B, 2A and 2B along the S1→S2→S3→S4 transitional pathway comprising an initial truncated swing of 2B which then rolls across the 1B surface, following by combined rotations of 1B, 2A and 2B. High forward and reverse rates for S1→S2 suggest that 1B may act to frustrate 2B movement to prevent premature Rep closure in the absence of DNA. These observations support a more general binding model for accessory DNA helicases that utilises conformational plasticity to explore a multiplicity of structures whose landscape can be tuned by salt prior to locking-in upon DNA binding. I will summarise the findings published earlier this year (https://doi.org/10.1093/nar/gkaf1483) and delve into recent unpublished details for the wider opportunities for developing a general single-molecule pipeline to enable inference of structural kinetics without requiring expensive traditional structural biology instrumentation.



# Shelterin generates T-loops by tethering distal telomeric DNA

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BBS-DGfB Joint Poster Session 2a, July 15, 2026, 11:00 - 11:45

Shelterin binds telomeres, regulating telomere length and protecting the ends of chromosomes by preventing mis-repair. Chromosome end-protection uniquely depends on the shelterin protein TRF2, which is required to remodel telomeres into a T-loop structure in vivo, but the mechanism by which this is achieved is unknown.

Using our recently developed reconstituted telomere system and a combination of optical-tweezers and high-resolution atomic force microscopy we can directly observe shelterin recruitment and activity on telomeric DNA at single-molecule resolution.

We have identified a novel tethering activity of shelterin, and propose that shelterin initiates T-loop formation by tethering distal telomeric DNA. Structure-function and domain swap analysis shows this tethering activity is intrinsic to TRF2 and requires, but is not limited to, its TRFH domain, which is also essential for T-loop formation in cells. We propose a model whereby TRF2 functions as a molecular Velcro, tethering distal telomeric DNA in close juxtaposition to initiate loop formation prior to invasion of the telomeric 3’ ssDNA overhang. This provides unique insight into an early step in the generation of the T-loop structure which is critical for protecting the telomere end and preventing genomic instability.

# Intricate Folding Pathways of the Bacterial Conjugation Enzyme TrwC Uncovered by Force Spectroscopy

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BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

Bacterial conjugation, the contact-dependent secretion of DNA from a donor cell to a recipient cell, is one of the main roads for horizontal gene transfer and spreading of virulence factors and antibiotic resistance genes. One crucial model enzyme for bacterial conjugation is the relaxase enzyme TrwC, a large 966 amino acids long multidomain protein with various activities. TrwC recognizes the origin of transfer within its conjugative plasmid, primes and covalently binds DNA. Likely, a second TrwC molecule unwinds the conjugative plasmid, and the covalently bound TrwC is secreted together with the single-stranded DNA towards the recipient cell. Successful secretion of the TrwC-DNA complex is a tightly controlled mechano-chemical process powered by molecular motors in the Type IV Secretion System (T4SS), which requires the unfolding of TrwC due to the constrictive nature of the secretion channel. Here, we studied the mechanical unfolding of TrwC using high resolution magnetic tweezers. We discover multiple folds with stabilities ranging from 5 pN up to 100 pN, large energy dissipation, and intricate folding pathways. Split and truncated variants of TrwC show stable folds with enriched pathways by inter-domain interactions. Refolding is surprisingly fast for the size of TrwC, which is likely enabled by independent subdomain folding. Finally, we observed how DNA regulates mechanical stability of TrwC, suggesting that mechanical stability would allow the T4SS to discriminate between TrwC and TrwC-DNA. Our findings provide novel insights on TrwC mechanobiology, which we anticipate will allow a better mechanistic understanding of bacterial conjugation crucial for our race against antimicrobial resistance.

# See your favorite protein complexes in action - Easy-to-use single-molecule fluorescence tools to observe biomolecular dynamics and interactions

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BBS-DGfB Joint Poster Session 2b, July 15, 2026, 11:45 - 12:30

Structural biology methods like cryo-electron microscopy and X-ray crystallography are enormously powerful tools to unravel biomolecular mechanisms of action. More recently, Artificial Intelligence and other computational approaches have opened new frontiers in protein design and structure determination. However, due to the largely static nature of their outputs, both types of approaches are typically unable to provide insights into the precise dynamics of biomolecular complexes, such as temporal conformational changes, binding kinetics and diffusion properties. Dynamic single-molecule techniques, such as Förster Resonance Energy Transfer (smFRET) and Fluorescence Correlation Spectroscopy (FCS) fill this gap. By revealing transient states and heterogeneous populations in real time, these approaches bridge the gap between high-resolution structures and functional dynamics, enabling a comprehensive understanding of biomolecular mechanisms. Unfortunately, so far, these methods have been inaccessible to the broader life science and drug development community.
Here, we introduce the EI-FLEX Pro, a novel benchtop instrument designed for seamless smFRET and FCS measurements, democratizing access to these powerful techniques. Its compact, user-friendly design requires minimal setup and no specialized expertise, allowing researchers in standard laboratory environments to perform experiments effortlessly, at high throughput (96- and 384-well plates). Ease-of-use is achieved through integrated calibration and correction routines and automated sample handling, supporting rapid screening of multiwell plates as well as individual samples with sub-millisecond and sub-nm spatio-temporal resolution and single molecule sensitivity. Data analysis is streamlined via intuitive software featuring automated fitting algorithms, real-time visualization, and exportable reports, minimizing post-processing time and errors.

The EI-FLEX empowers structural biologists, biochemists and drug developers to finally incorporate dynamic data on the level of individual biomolecular complexes into their workflows. It enables them to truly unravel and quantify drug-target interactions, complex formation and biomolecular conformational changes at unprecedented spatio-temporal resolution. By lowering barriers to entry, it propels the field toward faster, more complete discoveries in complex biomolecular systems.
Here, we will discuss the scientific and technical background, as well as various applications of our technology, such as: the conformational dynamics of proteins, DNA and RNA, quantification of protein-DNA and protein-RNA interactions, ternary complex formation as well as antibody, nanoparticle and vesicle characterization directly in solution.

# Solid-State Nanopore-Based Detection of Acute Kidney Injury–Related RNA Biomarkers

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BBS-DGfB Joint Poster Session 1b, July 15, 2026, 09:45 - 10:30

Cardiac surgery–associated acute kidney injury (CSA-AKI) is a frequent and serious complication after cardiopulmonary bypass, yet current diagnosis still relies on delayed bulk markers such as serum creatinine and urine output. This limits early risk stratification and fails to capture the molecular heterogeneity of injury. Here, we propose a solid-state nanopore–based single-molecule assay for rapid and multiplex detection of acute kidney injury (AKI)–associated microRNAs using an engineered 9.1 kbp λ-DNA carrier. The carrier contains two spatially encoded probe sites targeting miR-7-5p and miR-382, two candidate biomarkers relevant to AKI-related injury and repair pathways. Upon hybridisation with target miRNAs and reporter strands, each binding event generates characteristic sub-blockades during translocation through a solid-state nanopore, enabling digital identification of unbound, singly bound and doubly bound carrier states.

The project aims to construct and validate this dual-probe carrier system, optimise nanopipette geometry and measurement conditions for robust event classification, and translate the assay from buffer to Proteinase K–treated plasma spiked with known miRNA concentrations. By directly counting molecular binding states at the single-event level, the platform is expected to provide concentration-dependent and co-occurrence-resolved biomarker readout without fluorescent labelling or enzymatic amplification. Beyond improving analytical sensitivity and specificity, this strategy may offer a scalable route towards compact, information-rich diagnostics for peri-operative AKI risk stratification. More broadly, the carrier–nanopore framework could be extended to higher-order RNA or hybrid biomarker panels for multiplex molecular diagnostics in kidney disease and other complex disorders.

# Unparalleled approaches to directly visualize protein complexes regulating DNA repair, replication and transcription

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The structure, replication, and transcription of DNA are critical to cellular function. Errors in these dynamic mechanisms play a major role in diseases such as cancer. As a result, insights into transient molecular details are needed to advance our understanding and improve biological models. Dynamic single-molecule technologies offer an exciting opportunity to meet these challenges by observing protein activity in real time. Here, we present several examples of recent discoveries enabled by the combination of fluorescence microscopy with optical tweezers.

First, we introduce OT-curtains, a novel modular DNA substrate design that overcomes the traditional inaccessibility of free DNA ends in standard dumbbell assays. By combining this tethered backbone with free-ended branches, OT-curtains allow for multiplexed, low-force investigation of DNA-end interactions, enabling the direct observation of AddAB helicase-nuclease unwinding, Ku stoichiometry, and KpnI restriction activity. Second, we highlight how directly tracking replication machinery challenges the classic load-and-go model of eukaryotic sliding clamps. Recent work reveals that the RFC clamp loader forms a long-lived, co-traveling complex with PCNA and Polδ, providing a dynamic handoff mechanism critical for processive DNA synthesis. Finally, we present recent findings detailing the kinetic control of mammalian transcription elongation by RNA Polymerase II. Real-time tracking demonstrates that the elongation complex operates in distinct kinetic gears, cooperatively driven by elongation factors to adapt transcriptional output.

Importantly, these examples demonstrate how advances in dynamic single-molecule methods successfully resolve complex, transient mechanisms, unlocking new avenues for studying DNA-binding proteins and genome regulation.