Durham University

Biophysical Sciences Institute

Inspiring the extraordinary

BSI's Early Career Researcher's Winter Symposium

Wednesday 3rd December, John Snow College Hub, Durham University

The BSI's Early Career Researchers' Committee have organised this symposium to bring together ECRs from across biomathematics, biophysics, biological chemistry, chemical biology, and bioengineering.

Hosted by the Biophysical Sciences Institute (BSI), the event has been designed to initiate new research collaborations, inspire researchers, and celebrate the importance of interdisciplinary research.

Organising Committee:

Libbi Moon **(Chair)**	Dorothea Barnes
Dr Liz Morris	Matthew Grobbelaar
Dr Will Brittain	Katherine Deck
Ermando Canga	Giammarco Di Gregorio
William Midgley	

Programme

9:30 Arrival & Registration & Coffee

10:00 Welcome from the BSI and event overview

Session 1 Unravelling Biology Through Biophysics

10:15 **Keynote:** Mesoscale optical imaging with the Mesolens and 3D printed optics

Professor Gail McConnell (University of Strathclyde)

11:00 Oligomerisation of Ku from Mycobacterium tuberculosis promotes DNA synapsis

Dr Harriet Read (University of Sheffield)

11:15 Rheodialysis: A Platform for Real-Time Monitoring of Gelation Kinetics in Polymer Networks

Qandeel Saleem (Durham University)

11:30 Nanoscale Biophysical Regulation of Skin Regeneration

Laura Forster (Queen Mary University of London)

11:45 Biology Exploits Geometry: Impact of Aspect Ratio on Protein Networks

Dr Matt Hughes (University of Leeds)

12:00 Conference Group Photo

12.10 Lunch & Poster Session 1

Session 2 Decoding Life with AI & Computational Tools

13:00 **Keynote:** Learning (from) protein dynamics

Dr Matteo Degiacomi (University of Edinburgh)

13:45 Coarse-Grained Modelling of Protein-DNA Complexes

Kierran Falloon (University of Strathclyde)

14:00 The mechanics of crocodile head scale patterning

Dr Rory Cooper (University of Sheffield)

14:15 Modelling DNA in Complex Topologies: The Role of Gyrase

Katy Hollands (University of York)

14:30 Coffee break and poster session

Session 3 Advances in Biomolecular Discovery

15:00 **Keynote:** Breaking (is) Bad: how bacterial supercoiling machine works, how to inhibit it, and why we bother

Dr Dmitry Ghilarov (University of Oxford)

15:45 Collagen Single Fibril Mechanical Properties Measured Using Activity Microscopy

Dr Ilya M. Beskin (University of Twente)

16:00 The Synthesis of N-Substituted Hydroxamic Acids: A Critical Iron-Chelating Motif in Fungal Siderophores

Daniel Bonn (Durham University)

16:15 AccA from *Neisseria gonorrhoeae* provides a new framework for understanding periplasmic copper metallochaperones.

William Earl (Durham University)

16:30 The development of frequency-dependent mechanotransduction in auditory hair cells

Dr Samuel Webb (University of Sheffield)

16:45 From passive to active membranes: understanding how adhesion and activity shape vesicle dynamics

Natalie Richards (Durham University)

17:00 *Physics of Life Network Presentation*

17:10-17:30 *Prize ceremony and closing remarks*

Travel Information:

Location: 2 Mill Hill Lane, Merryoaks, DH1 3FP, England, United Kingdom

https://w3w.co/marble.meals.debit

If travelling by car: The Durham Howlands park and ride is not far away (map link here).

If travelling by train: The bus to the College takes around 20 minutes and there are multiple buses (from the bus station) - to walk takes around 30/40 minutes.

Catering Information:

Lunch will be provided. If you have not already and you have any allergies or special dietary requirements please fill in the form here: ECR Symposium Sessions - Special Dietary requirements – Fill in form

Hotel Information:

There are a number of hotels in Durham, all centrally located and fairly close to John Snow College:

- Premier Inn (https://www.premierinn.com/gb/en/hotels/england/county-durham/durham/durham-city-centre-walkergate.html)
- Travelodge (https://www.travelodge.co.uk/hotels/204/Durham-hotel)
- Hotel Indigo (https://www.ihg.com/hotelindigo/hotels/gb/en/durham/mmedh/hoteldetail)
- The Victoria Inn (http://www.victoriainn-durhamcity.co.uk)
- Radisson Blu (https://radissonbludurham.com)

Food and Drink:

Durham has one of the highest density of cafes in the country and there are many different excellent options for food across the city:

- Spags: a student favourite serving reasonably priced pasta and pizza
- Tangos: a burger restaurant situated on the historic Bailey
- Vennels: a hidden café serving excellent cake and breakfasts. The Durham Picnic is especially good
- Flat White: an iconic café in Durham that always has a massive queue for good reason!
- Riverview Kitchen: A café with beautiful views over the River Wear. The pancakes are truly excellent

Fun Facts about Durham:

- County Durham was the official birthplace of English mustard back in the early 1900s. It was developed by a Mrs Clements, who decided to grind up mustard seeds to get more flavour out of them.
- The Old Dun Cow is one of the oldest pubs in the county and is rumoured to be haunted
- Durham Castle is the only one built in the UK which has never suffered a breach. Together with the cathedral, it is one of the worlds first World Heritage sites. It was originally built in the 11th century and has been in constant use for over 900 years
- The founding of Durham is steeped in legend, particularly the story of the Dun Cow. According to local lore, the monks carrying St. Cuthbert's body were led to the site of Durham by a miraculous event involving a dun-coloured cow. The cow guided them to a hill overlooking the River Wear, where they decided to establish a church in St. Cuthbert's honour. This legend has been immortalized in various forms throughout the city, including statues and plaques, reminding visitors of Durham's mystical origins.

Useful Contacts:

If you have any problems before or during the event, please get in contact with the Biophysical Sciences Institute Manager, Dr Alex Probert at bsi.manager@durham.ac.uk

Oral Presentations

Session 1: Unravelling Biology Through Biophysics

Keynote: Professor Gail McConnell

University of Strathclyde

Mesoscale Optical Imaging with the Mesolene and 3D printing Optics

Since the earliest development of the microscope, optical systems have traditionally been designed around the limits of human vision. With the introduction of highly sensitive and advanced photodetectors, the eye is no longer the restricting factor, opening up fresh opportunities for imaging technologies and their application to biology.

We have created a novel objective lens, termed the Mesolens, which provides 4x magnification with a numerical aperture just under 0.5. The unusually large pupil size of this lens prevents its use with a standard microscope frame, so a dedicated imaging platform has been engineered around it. Like the original light microscope, the Mesolens proves useful across a broad spectrum of biomedical studies. In this presentation, I will outline the Mesolens technology, illustrating its implementation as both a widefield and confocal imaging system. I will also describe emerging imaging modalities adapted for the Mesolens, including mesoscale light-sheet imaging and total internal fluorescence mesoscopy, and I will demonstrate how these approaches are yielding new biological insights from large tissue specimens. I will also present our latest work on 3D printed optics and how these are informing new experiments at the mesoscale.

https://www.strath.ac.uk/staff/mcconnellgailprof

Dr Harriet Reed

University of Sheffield

Optimisation of Ku from Mycobacterium tuberculosis promotes DNA synapsis

Abstract: The bacteria, Mycobacterium tuberculosis (Mtb), causes the respiratory disease Tuberculosis (TB), which affects around 25% of the total world population[1]. Although TB is treatable with an intensive drug regime, antimicrobial drug resistance is becoming a prevalent challenge for treatment. A major driver behind for Mtb's resilience is its robust DNA repair capacity. Non-homologous end joining (NHEJ) is the major repair pathway for DNA double strand breaks (DSBs), which in Mtb is mediated by the protein Ku and the multifunctional LigD enzyme[2,3]. Despite this simplified bacterial NHEJ pathway and advancements in recent technology and methodology (particularly Cryo-EM), the Mtb NHEJ mechanism is still not well understood.

In this work, we studied the necessity of Ku for Mtbs' resilience under DNA damaging conditions[4]. We designed and imaged short DNA filaments, one with a single stranded overhang, and another with a blunt double stranded end, to examine how Ku interacts with these two types of DNA damage. These constructs are only a few tens of nanometres in length and interact with small globular proteins. We therefore use high-resolution microscopy techniques to visualise and quantify the effects of these proteins on DNA structure to provide new insights into NHEJ processes in Mtb.

Using both CryoEM and AFM, we observed that Ku-Mtb forms higher-order filament structures in the presence of DNA with a single stranded overhang. These large fibrillar and heterogeneous assemblies form when Ku-Mtb interacts with DNA under a range of conditions, forming oligomeric complexes much larger than the individual proteins and DNA. Furthermore, it has been shown that human Ku cannot form such protein-protein interacting filaments on DNA. This highlights that targeting the NHEJ pathway, or Ku proteins themselves in Mtb and possibly in other bacteria, could be a route to development of novel antimicrobials to combat rising antimicrobial resistance.

References

[1] Bagcchi, S. Lancet Microbe 4, e20, (2023)
[2] Zhao, B., Rothenberg, E., Ramsden, D. A. & Lieber, M. R. Nat Rev Mol Cell Biol 21, 765-781, (2020)
[3] Pitcher, R. S., Brissett, N. C. & Doherty, A. J. Annu Rev Microbiol 61, 259-282, (2007)
[4] Zahid, S., Baconnais, S., Smith, S., Atwal, S., Bates, L., Read, H., Chadda, A., Morati, F., Bedwell, T., Stende, E. G. P., Walter, J., Hardwick, S. W., Westerlund, F., Galburt, E., Le Cam, E., Pyne, A., Mukamolova, G. V., Chaplin, A. K., (In Press) Nat Comms

Qandeel Saleen

Durham University

Rheodialysis: a platform for real-time monitoring of Gelation Kinetics in Polymer Networks

Abstract: This work presents Rheodialysis, a novel experimental platform that enables real-time monitoring of gelation kinetics in fast-gelling polymer systems. It addresses long-standing challenges in biofabrication, food science, and tissue engineering. Conventional ex-situ rheological methods often fail to capture rapid crosslinking events due to their closed-system design and the disturbance of fragile gels during sample loading. Our customized setup overcomes these limitations by allowing simultaneous rheological measurement and active control of the sample's chemical environment, making it ideally suited for studying dynamic gelation processes.

As a proof of concept, Rheodialysis was used to investigate alginate gelation in the presence of calcium ions, focusing on diffusion and crosslinking events occurring within 0.1–1 second. The setup integrates a parallel-plate geometry with an in-house designed dialysis cell that enables calcium ions to diffuse through a semi-permeable membrane into the alginate solution. This configuration allows precise control over ion diffusion length and gelation rate, offering new insights into how diffusion distance, adjusted by plate separation, influences crosslinking density and network structure.

The platform is now being extended to mimic fibrin clot formation triggered by thrombin, a key process in blood coagulation. By exploring the interplay between mechanical shear and enzymatic activity during clotting, Rheodialysis provides a framework for understanding fibrin network formation with implications for biomaterials design and the study of clotting disorders.

Overall, Rheodialysis represents a versatile and powerful tool for probing gelation mechanisms, offering in situ control and real-time insight into the structural evolution of soft materials under coupled chemical and mechanical stimuli

Laura Foster

Queen Mary University

Nanoscale Biophysical Regulation of Skin Regeneration

Abstract: Introduction and Aim: Skin scarring and chronic wounds remain a major clinical challenge[1], underpinned by disrupted extracellular matrix (ECM) organisation and persistent fibroblast activation[2]. Previous studies have shown that during impaired healing excessive connective-tissue deposition[3] and dermal thickening occur, but the underlying matrix mechanisms regulating repair remain poorly understood. This study integrates small-angle X-ray scattering (SAXS), nanoindentation, and Raman spectroscopy to reveal how molecular, structural and mechanical[4-6] changes in the ECM modulate the wound environment during regeneration.

Methods: Full-thickness 2mm punch wounds or injections of bleomycin (fibrosis induction) were performed on adult (C57BL/6) mice dorsal region. Wounds were analysed at days 4, 7, 10, 14 and 21 post-wounding, and fibrosis at 2- and 4-weeks. Excised tissue was OCT embedded and cryosectioned. 12µm sections were slide-mounted for nanoindentation (Optics11 Chiaro; 25µm 0.5N/m spherical tip) and Raman (Renishaw inVia confocal; 442nm laser) and 500µm sections were Ultralene-mounted for SAXS (I22 Diamond Light Source; 20µm2 beamsize, 1s exposure).

Results: Early-stage wounds (days 4-7) showed low, uniform collagen fibril pre-strain, reduced stiffness and decreased fibril alignment, whereas, late-stage (day 21) wounds exhibited high collagen pre-strain and stiffness, and a high degree of fibril alignment forming mechanical gradients indicative of enhanced fibroblast proliferation and scarring. These profiles resembled late-stage fibrotic tissue, suggesting impaired healing responses. Raman spectra revealed elevated lipid composition shifting amide bands associated with collagen remodelling. Multimodal correlation across the three techniques identified nanoscale signatures of ECM remodelling that directly link molecular structure to biomechanical function.

Conclusion: This work establishes a quantitative framework to understand how mediated signalling shapes the mechanical and ultrastructural landscape of healing skin. By integrating multiscale biophysical measurements, we provide insight into how nanoscale ECM regulation governs tissue regeneration and scarring—highlighting future therapeutic opportunities to promote regenerative healing through biophysical modulation.

References

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[2]. E. Rognoni et al, Development (2016)
[3]. A. Stellato et al Comm Biol (2023)
[4]. OG. Andriotis et al J Mech Behav Biomed Mater. (2014)
[5]. A. Smith et al J Synch Rad (2021)
[6]. S. Inamdar et al, Acta Biomater (2019)

Dr Matt Hughes

University of Leeds

Biology Exploits Geometry: Impact of Aspect Ratio on Protein Networks

Abstract: Interconnected networks of high aspect ratio (AR) bio-polymers provide crucial structural and mechanical support to living systems and are ubiquitous in nature. Despite this ubiquity the functional advantage of high AR network building blocks is not understood. To answer this, we engineer proteinaceous building blocks with varying numbers of protein L (pL) domains, creating seven building blocks with ARs from one to seven. Using, shear rheology and small angle neutron scattering (SANS) to characterise the mechanical and structural properties of photochemically crosslinked pL networks, we show that AR is a crucial property that defines network architecture and mechanics. Networks constructed from higher AR building blocks exhibit more homogeneous structures and higher storage moduli due to a shift from translational diffusion limited (TDL) to rotationally diffusion limited (RDL) network formation because building blocks with increased AR lack the space to rotate freely[1]. For comparison, we study a fibrin network and observe the same transition from TDL to RDL formation, confirming that living systems exploit AR for their network assembly.

High AR bio-polymer building blocks confer significant functional advantages, which work to minimise the number of building blocks required to form an effective network. These include; increased mechanical strength at equivalent protein concentrations; and the rapid assembly of homogenous networks, above a critical concentration, crucial for in vivo biological processes e.g. blood clotting. In addition to uncovering the function advantages of filamentous proteins for hydrogel formation in vivo, manipulating AR also provides a novel parameter in the design of new biomaterials [1].

References:

[1]. Hughes, M. D. G. et al. Building block aspect ratio controls assembly, architecture, and mechanics of synthetic and natural protein networks. Nat Commun 14, 5593 (2023).

Session 2: Decoding Life with AI & Computational Tools

Keynote: Dr Matteo Degiacomi

University of Edinburgh

Learning (from) Protein Dynamics

Determining the different conformational states of a protein and the transition pathways between them is key to understanding the relationship between biomolecular structure and function. I will discuss how machine learning can be integrated with molecular dynamics simulations to characterise rare events that are inaccessible to conventional experimental and computational approaches.

https://edwebprofiles.ed.ac.uk/profile/dr-matteo-degiacomi

Kierran Falloon

University of Strathclyde

Coarse-Grained Modelling of Protein-DNA Complexes

Abstract: 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 structural movement and conformation of DNA, particularly major-minor grooving, which is crucial in many protein interactions. 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 protein-protein interactions when no experimental structures are available. This work develops both the theoretical concepts of a coupling for these models, and a high-performance software implementation leveraging tools available in LAMMPS (Large-scale Atomic/Molecular Massively Parallel Simulator)[3], a global open-source classical molecular dynamics codebase, to allow

biophysically sensible probing into the dynamics of hybrid protein-DNA structures.

References
[1] B. E. Snodin, F. Randisi, M. Mosayebi, P. Šulc, J. S. Schreck, F. Romano, T. E. Ouldridge, R. Tsukanov, E. Nir, A.A. Louis, et al. Introducing improved structural properties and salt dependence into a coarse-grained model of DNA. The Journal of Chemical Physics, 142(23), 2015.
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[3] A. P. Thompson, H. M. Aktulga, R. Berger, D. S. Bolintineanu, W. M. Brown, P. S. Crozier, P. J. In't Veld, A. Kohlmeyer, S. G. Moore, T. D. Nguyen, et al. LAMMPS—a flexible simulation tool for particle-based materials modeling at the atomic, meso, and continuum scales. Computer Physics Communications, 271: 108171, 2022.

Dr Rory Cooper

University of Sheffield

Coarse-Grained Modelling of Protein-DNA Complexes

Amniote integumentary appendages constitute a diverse group of micro-organs, including feathers, hair and scales. These structures typically develop as genetically controlled units, the spatial patterning of which emerges from a self-organized chemical Turing system with integrated mechanical feedback. The seemingly purely mechanical patterning of polygonal crocodile head scales provides an exception to this paradigm. However, the nature and origin of the mechanical stress field driving this patterning remain unclear. Here, using precise in ovo intravenous injections of epidermal growth factor protein, we generate Nile crocodile embryos with substantially convoluted head skin, as well as hatchlings with smaller polygonal head scales resembling those of caimans. We then use light-sheet fluorescence microscopy to quantify embryonic tissue-layer geometry, collagen architecture and the spatial distribution of proliferating cells. Using these data, we build a phenomenological three-dimensional mechanical growth model that recapitulates both normal and experimentally modified patterning of crocodile head scales. Our experiments and numerical simulations demonstrate that crocodile head scales self-organize through compressive folding, originating from near-homogeneous skin growth with differential stiffness of the dermis versus the epidermis. Our experiments and theoretical morphospace analyses indicate that variation in embryonic growth and material properties of skin layers provides a simple evolutionary mechanism that produces a diversity of head-scale patterns among crocodilian species.

Katy Hollands

University of York

Modelling DNA In Complex Topologies: The role of gyrase

DNA gyrase is a type IIA topoisomerase, which is an enzyme that can relax and induce supercoils in DNA through the strand passage of the double helix. It primarily occurs in bacteria and is key in the DNA replication and transcription processes, as it relaxes superhelical tension caused by DNA polymerase. It is also uniquely capable of inducing negative supercoils through the hydrolysis of adenosine triphosphate (ATP). Due to its importance in the survival of the cell, they are a common target for antibiotics, such as fluoroquinolones.

Experiments have not been able to elucidate the exact workings of the enzyme, such as strand passage and energy coupling. To find out more, we are using all-atom Molecular Dynamics (MD) simulations, which enable us to observe dynamic transitions and interactions not seen from experimental structures. By modelling the most recent structure[1], I will show how ATP facilitates ATPase domain transitions, and how other factors, like mutations, influence this process. I will also present protein-protein docking calculations that explain single-molecule results for how GyrA and GyrB subunits cluster inside the cell and the potential influence of their in vivo functioning.

[1] E. Michalczyk, Z. Pakosz-Stępień, J.D. Liston, O. Gittins, M. Pabis, J.G. Heddle, D. Ghilarov, Structural basis of chiral wrap and T-segment capture by Escherichia coli DNA gyrase, Proc. Natl. Acad. Sci. U.S.A. 121 (49) e2407398121, https://doi.org/10.1073/pnas.2407398121 (2024).

Session 3: Advances in Biomolecular Discovery

Keynote: Dr Dmitry Ghilarov

University of Oxford

Breaking (is) Bad: how bacterial supercoiling machine works, how to inhibit it, and why we bother

Bacterial type II topoisomerases are essential enzymes and critical targets for developing new generation of drugs capable of tackling resistant

Gram-negative bacteria. At the same time, they are fascinating molecular machines informing about the fundamentals of energy transfer in these systems. I will summarise some recent work in our lab devoted to the mechanism of action of gyrase-targeting antibiotics, resistance proteins, and our advances in understanding DNA capture and strand passage by type II enzymes.

Briefly, I will introduce the functions of type II topoisomerases in bacterial and eukaryotic cells followed by description of our work on characterizing mode of action and binding of novel gyrase inhibitors, albicidin[1] and LEI-800[2]. While natural product albicidin stabilizes gyrase complex with cleaved DNA, a synthetic drug LEI-800 prevents DNA cleavage by an allosteric interaction. I will introduce topoisomerase protection factors responsible for host protection against albicidin and for transmissible resistance to fluoroquinolones, AlbG and Qnr[3]. I will explain how these proteins interact with gyrase and use energy of ATP hydrolysis to remove the bound drug and share some unpublished structural data into mode of action of these proteins.

Finally, I will talk about repair of topoisomerase-induced breaks in bacteria, and our unpublished work on characterization of this process in E.coli including live-cell microscopy and structural studies of Exonuclease VII complex.

References:
1.Michalczyk, E., Hommernick, K., Behroz, I. et al. Molecular mechanism of topoisomerase poisoning by the peptide antibiotic albicidin. Nat Catal 6, 52–67 (2023). https://doi.org/10.1038/s41929-022-00904-1
2.Bakker, A.T., Kotsogianni, I., Avalos, M. et al. Discovery of isoquinoline sulfonamides as allosteric gyrase inhibitors with activity against fluoroquinolone-resistant bacteria. Nat. Chem. 16, 1462–1472 (2024). https://doi.org/10.1038/s41557-024-01516-x
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https://www.bioch.ox.ac.uk/research/ghilarov

Dr Ilya M. Beskin

University of Twente

Collagen Single Fibril Mechanical Properties Measured Using Activity Microscopy

Abstract: Filaments serve vital mechanical functions both inside and outside the cell. Outside the cell, the extracellular matrix (ECM) provides rigidity to connective tissue and creates the mechanical environment with which cells actively interact. Collagen fibrils are the main structural component of the ECM. Cell behavior, such as cell motility, or stem cell differentiation, is dictated by interactions between the cell and individual neighboring collagen fibrils. While macroscopic mechanical properties can be studied with techniques like rheology, studying properties on the single fibril level requires new tools. Activity microscopy, an optical-tweezer-based technique developed by our lab, allows one to visualize the locations, thickness, and thermal fluctuations of individual fibrils. This information can be used for measuring single fibril mechanical properties and label-free microrheology. As a first test of the technique, we measure the Young's modulus of individual collagen fibrils. Published measurements of single-fibril Young's moduli under physiological conditions vary by two orders of magnitude. This large variation is likely the result of strain-stiffening, different crosslinking within the collagen fibril, and inconsistency in the fibril's radius profile. Activity microscopy uniquely measures the Young's modulus of collagen in the extremely low strain regime by using thermal fluctuations rather than applying an external force. By measuring the thickness profile of each fibril simultaneously with the fibril's fluctuations, we account for inconsistent thickness. This makes activity microscopy an excellent tool for testing the effects of cross-linking on fibril mechanical properties. Furthermore, activity microscopy can be used within filament networks to measure the connectivity as well as their response to strain and rearrangement. Activity microscopy is a powerful new tool for studying biological single filament and network properties.

Daniel Bonn

Durham University

The Synthesis of N-Substituted hydroxamic acids: a critical iron-chelating motif in fungal siderophores

Abstract: The ability to make esters, amides and other carbonyl-based functionality through activated carboxylic acid analogues is highly prized including the use of highly fluorinated ester intermediates.[1] Previously, we have developed methodology for accessing similar functional groups via acyl fluorides through a deoxyfluorination process mediated by pentafluoropyridine (PFP).[2,3] Our work has since focused on using this as a new coupling agent for N-substituted hydroxamic acid formation. This unusual amide-like functional group is present in several natural products including hydroxamate siderophores. These microbial iron chelators contain

hydroxamic acid functionality distributed throughout, providing multiple key bidentate binding sites. Their high affinity towards Fe ions plays a key role in the regulation of iron through uptake, transport and storage.[4,5,6] We believe that the PFP methodology provides an improvement to previous N-substituted hydroxamic acid formation strategies also allowing for the use of 19F NMR tracking to quantify conversion to the activated intermediate. Hence, this has been applied to a range of carboxylic acids including alkyl, electron-poor & electron-rich aromatic, heteroaromatic as well as the coupling to medicinally relevant acids.

References:
[1] D. E. Bonn and W. D. G. Brittain, Chem. Commun., 2025, 61, 17060-17071; [2] W. D. G. Brittain and S. L. Cobb, Org. Lett., 2021, 23, 5793–5798; [3] L. N. D. Beardmore, S. L. Cobb and W. D. G. Brittain, Org. Biomol. Chem., 2022, 20, 8059-8064; [4] H. Haas, M. Eisendle and B. G. Turgeon, Annu. Rev. Phytopathol., 2008, 46, 149–187; [5] H. Haas, Nat. Prod. Rep., 2014, 31, 1266-1276; [6] R. C. Hider and X. Kong, Nat. Prod. Rep., 2010, 27, 637–657

William Earl

Durham University

Abstract: The bacterium Neisseria gonorrhoeae infects the human genitourinary tract and causes >82 million cases of the sexually-transmitted infection each year[1]. Like many organisms, copper (Cu) is an essential nutrient in N. gonorrhoeae, required for the function of redox-active enzymes that are central to its physiology. For example, the Cu-dependent nitrite reductase, AniA, allows N. gonorrhoeae to respire using nitrite as the terminal electron acceptor in the O2-limited host niche[2].

Many Cu-dependent enzymes require an accessory protein, namely a Cu-binding metallochaperone, to receive Cu[3-6]. The literature consensus is that metallochaperones deliver Cu along a favourable thermodynamic gradient, from a weaker binding site in the cellular Cu source to a stronger binding site in the target enzyme[3]. However, this does not explain why Cu cannot be transferred directly from the cellular Cu source to the target enzyme, without a metallochaperone.

We have now shown that a metallochaperone AccA is essential for the delivery of Cu to AniA in N. gonorrhoeae. Loss of a functional accA gene disrupts microaerobic growth and nitrite respiration, particularly under Cu-limited conditions. Purified AccA protein binds 1 Cu(I) and 1 Cu(II) ions in two separate binding sites, but only the Cu(I)-binding site is essential for Cu delivery in N. gonorrhoeae. Contrary to the established paradigm, we found that Cu delivery occurs along an unfavourable thermodynamic gradient, as the Cu(I)-binding affinity of AniA is ~40X weaker than that of AccA.

We propose that the target enzyme AniA cannot compete directly with the cellular Cu source for binding Cu(I). Therefore, the metallochaperone AccA is needed to overcome the unfavourable thermodynamic gradient for Cu transfer. These findings potentially reshape understanding of Cu trafficking in cells and the fundamental role of metallochaperones.

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2. Boulanger, M. J. & Murphy, M. E. P. Crystal structure of the soluble domain of the major anaerobically induced outer membrane protein (AniA) from pathogenic Neisseria: a new class of copper-containing nitrite reductases1. J. Mol. Biol. 315, 1111–1127 (2002).
3. Stewart, L. J. et al. Handling of nutrient copper in the bacterial envelope. Metallomics 11, 50–63 (2019).
4. Osman, D. et al. Copper Homeostasis in Salmonella Is Atypical and Copper-CueP Is a Major Periplasmic Metal Complex*. J. Biol. Chem. 285, 25259–25268 (2010).
5. Bennett, S. P. et al. NosL is a dedicated copper chaperone for assembly of the CuZ center of nitrous oxide reductase †Electronic supplementary information (ESI) available. See DOI: 10.1039/c9sc01053j. Chem. Sci. 10, 4985–4993 (2019).
6. Robinson, N. J. & Winge, D. R. Copper Metallochaperones. Annu. Rev. Biochem. 79, 537–562 (2010).

Dr Samuel Webb

University of Sheffield

The development of frequency-dependent mechanotransduction in auditory hair cells

Abstract: The conversion of mechanical vibrations into electrical signals is a fundamental feature of hearing and relies on the ability of inner hair cells (IHCs) to transduce sound-induced deflections of their stereocilia via mechanotransduction (MET) channels. While MET channel properties have been extensively characterised in pre-hearing mice, it remains unclear how these properties manifest after the onset of hearing. Determining how MET function matures is essential to understanding how sound signals are processed by the auditory system.

In this study, we compared MET properties in IHCs from pre-hearing (postnatal day 9 to 10) and adult (around postnatal day 30) mice from a normal-hearing strain. We used fluid-jet stimulation to deflect stereocilia and whole-cell patch-clamp electrophysiology to measure the resulting MET currents. During sustained mechanical deflection, we found that adult IHCs exhibited a large, rapidly adapting component in the MET current, consistent

with channels closing despite continued hair bundle displacement. This rapid adaptation was absent in immature IHCs, indicating a developmental transition in channel regulation.

To assess whether this adaptation contributes to frequency-dependent processing, we applied sinusoidal hair bundle deflections across a range of frequencies (50–1000 Hz). In immature IHCs, MET current amplitudes remained relatively constant across frequencies, indicating a lack of frequency tuning. In contrast, mature IHCs exhibited a robust frequency-dependent increase in MET current amplitude, with nearly a threefold enhancement at higher frequencies.

To better understand the contribution of single MET channels to this frequency response, we performed non-stationary noise analysis. The results revealed that single-channel conductance was unchanged across frequencies, indicating that the increased current arose from the recruitment of additional MET channels rather than changes in individual channel properties.

Together, these results reveal that MET channel adaptation emerges at hearing onset and suggest that frequency-dependent MET properties contribute to sound frequency discrimination.

Natalie Richards

Durham University

From passive to active membranes: understanding how adhesion and activity shape vesicle dynamics

Abstract: The shape of lipid membranes is determined by a balance between membrane tension, bending rigidity, and adhesion forces. While these passive mechanics are well understood, much less is known about how internally generated forces, such as those from living, motile cargo, reshape membranes[1-3]. Here, we bridge this gap using biohybrid vesicles that encapsulate motile bacteria, providing a controllable model to directly compare passive and active membrane deformations[4].

Using giant unilamellar vesicles (GUVs), micron-sized, cell-like membrane bubbles, we systematically study how adhesion and membrane tension shape vesicle morphology. By allowing GUVs to adhere to supported lipid bilayers (which mimic biological surfaces) through controlled polymer-mediated interactions, we quantify how contact area, shape, and tension evolve during osmotic deflation. Osmotic shocks produce reproducible transitions from weak to strong adhesion, accompanied by distinct shape remodelling events such as spreading and tube formation[1,2].

These passive vesicle systems provide a mechanical baseline for introducing biological activity. Encapsulating motile Escherichia coli within the vesicles shows that internal motion can dynamically stress and reshape the membrane, with outcomes dependent on both adhesion strength and bacterial activity[4]. Comparing adhered and freely suspended biohybrid vesicles reveals how confinement and adhesion jointly regulate active membrane shape changes, offering new insights for designing self-organising, motile vesicles in synthetic biology and soft robotics.

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Poster Presentations

All poster abstracts have been included in alphabetical order.

Amy Wiseman

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Abstract: Bacteriophages (viruses that infect bacteria) are Earth's most abundant and diverse biological entities, as well as a largely untapped source of novel enzymes that function under extreme conditions[1]. Among these, endolysins – phage-encoded peptidoglycan hydrolases – are of significant interest as eco-friendly antimicrobial agents. Endolysins can be utilised in the food, agricultural and sanitation industries as alternatives to harsh chemicals and detergents, owing to their antimicrobial activities over a range of conditions[2]. Cold-adapted endolysins could enable energy-saving low-temperature cleaning, whilst thermophilic variants have potential use in fermentation, food processing and as low-resistance alternatives to antibiotics[3].

In this project, large-scale metagenomic mining, sequence alignment and structural prediction were used to select putative cold-adapted and thermophilic endolysins from sources such as Arctic seawater and Icelandic hot springs. Eleven candidates were selected for heterologous expression, five of these have been successfully produced and characterised using biophysical/chemical methods. Activities of these enzymes against various bacterial substrates and thermal stability have been tested, with a spectrum of activities and thermal stabilities identified (Tm = 29 to 91 °C). Structural analysis using AlphaFold and X-ray crystallography revealed unexpected and novel structural features within the enzyme class. These findings expand upon the known structural/functional discovery of endolysins, which could open new opportunities for active site engineering. This project is now being extended to the characterisation of a set of AI generated de novoenzymes, preliminary results on this will also be presented.

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Alex Pembery

University of York

Abstract: Protein toxins are weapons secreted by cells in a hostile battle against other organisms. A family of toxins, termed A/B toxins, include notable examples known to impact human health, such as cholera, anthrax, and ricin. A/B toxins are defined by a bipartite structure of active (A) and binding (B) sections. They manipulate the cell's own trafficking pathways after gaining access to the cell by binding to sugars and entering through endocytosis. The two parts then dissociate, allowing for targeted attack on organelles, such as causing cell cycle arrest.

One such example of an A/B toxin is that of the virally encoded killer toxin 28 (K28), which is secreted by infected yeast to kill other susceptible yeast. Recently, a killer toxin defence factor (Ktd1) that acts against K28 was discovered through genomic approaches comparing naturally occurring sensitive and resistant strains. Until this, the KTD1 gene was completely uncharacterised in yeast. Initial work has localised Ktd1 to the endolysosomal system, but the mechanism by which it protects cells from the A/B toxin is not yet understood. We hypothesise that Ktd1 forms oligomers in early endolysosomal compartments to target the internalised toxin for sequestration to the lysosome. To explore this hypothesis, we will employ a variety of physical and biological approaches, such as slimfield microscopy and analysis of select deletion mutants.

Benjamin Devenish

Durham University

Abstract: Biofouling is a well-documented problem on marine structures, with fouling of these surfaces increasing costs as well as reducing the operational lifetime of structures. Common antifouling strategies rely on biocides, killing fouling organisms coming in close contact with the coated surfaces during the early stages of biofouling, however these are known to have detrimental impacts on marine ecology. One

alternative entails physical methods, where the coating's varying surface energies prevent binding of fouling organisms. Herein, we investigate a promising new strategy for a polymer-based antifouling coating that combines particular mechanical properties together with nanoscale control of the surface amphilicity. This strategy can easily be scaled up for industrial use, however its specific mode of action and evolution after aging are not fully understood. Using Atomic Force Microscopy in solution and Energy Dispersive X-ray analysis (SEM-EDX), we characterise differences between candidate coatings, quantifying nanoscale structural and viscoelastic properties after aging in seawater to reveal changes in these coatings' characteristics over time.

Debajit Dey

University of Leeds

Abstract: The spike (S) protein of coronavirusesis a key determinant of virion assembly, fusogenicity,and immune recognition, yet the molecular details governing its intracellular trafficking remain incompletely understood. In SARS-CoV-2,the S protein is delivered to the virion assembly site in the ER-Golgi Intermediate Compartment (ERGIC) via coatomer-dependent trafficking from the ER and cis Golgi. Structural and functional analyses reveal that S incorporation into virus-like particles (VLPs) and their subsequent fusogenic capacity are determined by coatomer-mediated delivery from the cisGolgi and restricted by regulated S-coatomer dissociation. Mimicry of a host coatomer-binding dibasic motif (K-x-H-x-x) ensures retrograde trafficking to the RGIC. At the same time, avoiding a host-like C-terminal acidic residue enables efficient S-coatomer dissociation, facilitating virion incorporation or export for cell-cell fusion. Extending these insights, comparative studies of human embecoviruses such as HKU1, OC43, and the model murine hepatitis virus (MHV) uncover a conserved His-x-Asp (HxD) motif that substitutes for the conventional dibasic coatomer-binding signal. Structural and biochemical analyses demonstratethat the HxD motif engages coatomer subunits through unique conformations, directing S to assembly sites with the viral M-protein. Disruption of HxD-coatomer interactions leads to impaired S incorporation, compensatory viral adaptations, and notable changes in virion surface morphology. Together, these findings reveal the co-existence of canonical and unconventional coatomer-targeting motifs in coronavirus S proteins, underscoring the evolutionary flexibility of their assembly pathways. Moreover, they identify the S protein's C-terminal residues and coatomer interacting motifs as critical determinants of virion formation, fusogenic potential, and vaccine antigen design, providing a structural and mechanistic framework for anipulating S trafficking to optimise immune presentation and antiviral strategies.

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Emanualla Fiandra

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Abstract: The increasing presence of synthetic garments in consumer wash loads has made polyester soil-release polymers (SRPs) highly sought-after additives in fabric care formulations. These polymers enhance cleaning efficiency and provide environmental benefits by enabling effective cleaning at low wash temperatures and shorter cycles, thus reducing energy and water consumption. Conventional polyester SRPs comprise of hydrophobic poly(alkylene terephthalate) subunits which facilitate the deposition of SRPs onto the synthetic fibre surface, and hydrophilic poly(ethylene glycol) subunits which render the surface hydrophilic. The terephthalate structural units in conventional polyester SRPs are derived from terephthalic acid, which is primarily produced through the catalytic oxidation of petroleum-sourced p-xylene. To further improve their sustainability profile, a novel class of SRPs has been synthesised using carbohydrate-based monomers derived from lignocellulosic biomass. The potential of these biosourced polymers as replacements for conventional SRPs was evaluated through soil-release and anti-redeposition

performance tests. Additional insights into polymer behaviour were obtained using dynamic light scattering, contact angle measurements, and scanning electron microscopy.

Giulia D'avino

Durham University

Abstract: A tired infant is fussy, emotionally unstable and, most importantly, lacking in attention. This inattention ultimately impedes infant learning. A key skill developed in infancy is word learning as it builds the foundation for future language development. Infants are constantly learning new words from the environment around them and a disruption (i.e., tiredness) to this learning process may hinder language acquisition. Parents first complete the Durham Infant Tiredness Questionnaire (DITQ), a purpose-developed questionnaire designed to capture tiredness. Then infants, aged 10 to 24 months, complete a novel word learning task while their looking is captured with eye tracking. The task shows an adult gesturing to and labelling two different novel objects, infants are then tested to see whether they have learnt the word. To capture brain activity, we utilise LUMO from Gowerlabs, a high-density fNIRS system with LED lights. Eye tracking results indicate tired infants look less at the target object during the test phase. However, this is affected by gesture. If a gesture is presented during the learning phase, the looking in the test phase is higher despite the infant's tiredness. This suggests that tiredness affects word learning, but gesture may serve as an attentional aid. This is supported by the neural results. Infants with high tiredness show higher activation in the left IFG and left DLPFC; two key regions for attention. This suggests that tired infants are overcompensating for inattention due to tiredness and the use of gestures guides infant attention allowing them to overcome tiredness. Our findings suggest that while tired infants will struggle more with higher-level tasks such as word learning, overt cues such as gestures might help ameliorate these difficulties. This highlights both the importance of understanding the infant's current attentional state, and the importance of considering the multimodality of language in early language learning.

Hannah Cole

Durham University

Abstract: Leishmaniasis is a parasitic disease caused by infection of the Leishmania parasite species spread via sandfly bites and directly affects 12 million people worldwide.[1,2] Although approximately 1 billion people around the world are at risk of contracting the disease, current medications have high associated costs and severe side effects, thus making them accessible to many who need them.[1,2] Previous work in the Cobb group identified 4-phenylsulfonyl-2,3,5,6-tetrafluoropyridine, as a potential core structure for a class of novel antiparasitics and a 3rd generation library was developed focusing on small modifications to the original core.[3] This novel library of 23 compounds was then screened against L. mexicana promastigotes and axenic amastigotes as well as macrophage cells to assess toxicity. Additionally, the library was screened with L-glutathione in 19F NMR experiments to probe how these small molecules may behave in cellular environments.

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Jiajia Luo

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Abstract: Iridium(III) complexes have played an important role in catalysis and LED material areas. Recently, their potential in biomedical applications has also been explored. Octahedral iridium (III) complexes showed excellent antibacterial and anticancer properties in several papers[1]. However, their low cell selectivity and water solubility limits their applications in medicinal studies. To overcome these problems, macromolecular drug delivery systems, such as liposomes, micelles, have been widely investigated.

This work focusses on exploring octahedral cyclometalated fluorinated iridium(III) complexes as

photosensitisers in photodynamic therapy in anticancer applications. We aim to establish a versatile conjugation method between an iridium(III) complex and a polymer backbone to construct a pH-responsive micellar structure, improving the metal complexes' solubility in aqueous media. The micelles' surface was further functionalised with modified mannosides, which are able to selectively target cancer cells with overexpressed mannose receptor. Furthermore, a series of polymers were synthesised and characterised about its pH- and thermo-responsive properties. The resultant iridium(III) encapsulated micelles could present novel photo-activated drug for cancer treatment, and therapeutics for muti-drug resistance bacteria.

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Jamie Glasper

University of York

Abstract: Biodegradability of novel polymers requires meeting OECD 301-10 test guidelines on degradability in mixed microbial communities. Our industrial partner CRODA follows this practice and uses carbon removal and oxygen demand as measurement of biodegradability of polymers developed for the personal care industry. If a novel polymer can produce 70% of theoretical CO2 and have 60% of it's theoretical oxygen demand under aerobic conditions then it's classed as readily biodegradable. Polymers used in industry have the potential to be exposed to a plethora of conditions, which includes anaerobic environments like wastewater treatment plants (WWTP). These environments are important to consider and offer other metabolic routes to biodegradability. In this study we have investigated the potential performance of three different polymer classes in aerobic and anaerobic biodegradability testing using biomethane potential tests (BMP). We are interested in how differences in polymer structure such as polymer chain length affects biodegradability. During anaerobic testing the PEG-based polymer Crothix outperformed the other polymer classes by producing more methane in 40 days indicating Crothix as the most biodegradable out of the three. These anaerobic results contrast to the aerobic OECD tests that identified that another class Brij was more biodegradable than Crothix. These initial results highlight the importance to cover biodegradability in anaerobic environments. A significant factor affecting anaerobic biodegradability is the carbon chain length of constituent monomers. When a range of polyglycerol chain lengths (C2-C10) were tested % anaerobic biodegradability declined from 45% (C4) to 2% (C10). We hypothesise this is caused by steric hindrance interfering with a mixed anaerobic microbial community's ability to metabolise and hydrolyse the ester bonds of the polymer. Our work highlights the need for further research concerning polymer biodegradability under anaerobic conditions. Our future work will utilise DNA sequencing analysis to investigate the microbial community responsible for biodegradation.

Joseph Weaver

Durham University

Abstract: Anammox bacteria are energetically impoverished; their doubling times are measured in weeks, 500 times slower than E. coli. Despite this, they thrive by committing to a narrow niche: anaerobic ammonia oxidation. That pathway uses a reactive hydrazine intermediary (a.k.a. rocket fuel) to short-circuit the traditional nitrogen cycle. Ecologically, anammox bacteria are significant factors in wetland and marine sediment N cycling. Within wastewater treatment, anammox bacteria can potentially reduce aeration power consumption and prevent nitrous oxide formation, substantially reducing greenhouse gas footprints. Despite its importance, key aspects of anammox biology remain unresolved.

One puzzle is that most anammox genomes do not encode the canonical enzymes for reducing nitrite to nitric oxide, the essential first step of anammox metabolism. Although alternative enzymes have been proposed, strong evidence also suggests reliance on syntrophic partners. How anammox bacteria spatially recruit such partners is an open question.

The second mystery lies in their unusually frequent possession of a Type VI Secretion System (T6SS). The T6SS is a molecular spear tipped with a variety of toxic proteins. The crux of the mystery is that a

T6SS is energetically expensive – so why does it show up so commonly in a notoriously energy-poor set of organisms?

We suggest that anammox bacteria employ the T6SS to differentially recruit cooperative syntrophs immune to the specific toxins. When susceptible competitors are killed, they leave open spaces into which the syntrophs are 'pushed' during biofilm growth. We tested the plausibility of this system with agent-based biofilm simulations containing: anammox bacteria (with and without nitrite reduction), susceptible full denitrifiers, and immune partial denitrifiers which reduce nitrite but do not consume nitric oxide. The simulations show that T6SS-mediated exclusion can indeed enrich immune syntrophs near anammox cells, supporting a plausible role for the T6SS in fostering cooperation rather than competition.

Joseph Knight

University of Edinburgh

Abstract: Labyrinthula species are protistan organisms found predominantly in coastal marine environments, notably as residents on seagrass leaves. A fascinating characteristic of this order, observed over a century ago but little studied since, is the ability for cells to secrete an extracellular ectoplasmic net. This allows colonies to form a spatial network of interconnected extracellular filaments across a substrate. Individual Labyrinthula cells are confined within these filaments and move independently about this network. The collective and interconnected behaviour amongst moving cells and the expanding network invites a physics-based description to this biological system. In this developing project, we describe and contextualise the behaviour of growing colonies as spatial networks and probe their environmental dependence.

Kim Moutney

University of Manchester

Abstract: The mechanical properties of lipid membranes are central to a wide range of biological and technological processes, from membrane fusion and trafficking to the design of lipid-based drug and gene delivery systems.[1-3]Understanding how environmental factors, particularly ionic strength, modulate membrane stability is critical for achieving robust lipid assemblies under physiological conditions. Because lipid headgroups are intrinsically charged or polar, variations in ionic strength directly influence electrostatic interactions at the membrane interface.[4] This effect is especially relevant for cationic lipids, which are widely employed in nucleic acid delivery platforms, where charge compensation by counterions governs vesicle fusion, endosomal escape, and overall delivery efficiency.[2,3]

In this work, we explore the ion-dependent mechanical behaviour of cationic trimethylammoniumpropane (DMTAP) supported lipid bilayers using atomic force microscopy. Force spectroscopy measurements[5,6] reveal that DMTAP membranes in pure water exhibit relatively low rupture forces which increases upon addition of potassium chloride solution. Moreover, we found a steepening of the rupture force versus loading-rate relationship with increasing salt concentration. These trends indicate enhanced membrane cohesion and a reduction in activation volume with increasing ionic strength, reflecting ion-mediated stabilisation of the lipid assembly. Such mechanically tuneable behaviour underscores the sensitivity of cationic membranes to the ionic solution and provides new insight into the physical basis of lipid stability and performance in dynamic biological environment.

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Laura Kraft

Durham University

Abstract: Cardiac alternans, a beat-to-beat variation in action potential (AP) duration or amplitude, is a precursor to life-threatening arrhythmias. Computational models such as Mitchell–Schaeffer (MS) and Iyer–Mazhari–Winslow (IMW) simulate cardiac electrophysiology numerically at different

levels of fidelity. While the IMW model reproduces detailed underlying ion-channel dynamics, the simplified MS model prioritises speed over realism. This work explores data-driven augmentation of the MS model to mimic the outputs of a biophysically motivated model.

A statistical model was formed for the prediction of the Action Potential Duration (APD) and Action Potential Amplitude (APA) for the biophysically motivated model, across many basic cycle lengths (BCL) to determine the efficacy of the methods for discrete-time. The approach was extended to then affect full AP morphology reproduction with continuous-time feedback using an ordinary differential equation model.

Both models reproduced alternans in AP duration (APD) and amplitude (APA) under appropriate stimulus forcing. The IMW model generated physiologically realistic AP morphologies, including the phase-1 notch and prolonged plateau. Tuning timescales brought the MS model APD in line with the IMW model. APD, APA, and Diastolic Interval maps offered insights into discrepancies between the different models. Training NNs enabled robust prediction of APD and APA across BCLs. By contrast, the NN-augmented MS model predictions were less precise. The relative decrease in loss did not fully translate into accurate repolarisation dynamics, suggesting that the backpropagation error introduces problems that require further investigation. However, there was strong agreement with IMW depolarisation and early plateau phases.

These results suggest that NN-augmented low-fidelity models may provide biophysical simulation surrogates, provided augmentation targets early AP phases rather than slow repolarisation, thereby informing future studies of cardiac restitution and arrhythmogenesis.

Lauren Billet

Durham University

Abstract: Carbon-carbon bond forming reactions provide access to a plethora of pharmaceutical precursors, yet many synthetic routes require harmful organic solvents.[1,2] In nature, pyrophosphorylated vitamin B1 (ThDP) acts as a cofactor for a range of enzymes which catalyse C-C bond forming reactions through formation of an N-heterocyclic carbene (NHC) on a thiazolium scaffold.[3] Triazolium NHC species have been found to have lower pKas and higher catalytic activity in organocatalytic reactions compared to thiazolium derivatives.[4] Hence, our work aims to synthesise artificial vitamin B1 cofactors with triazolium scaffolds and analyse their catalytic activity both unassisted and in the presence of enzymes.

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Luz Rodriguez

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Abstract: Leishmaniasis is a tropical disease caused by different species of genus Leishmania, considered endemic in 92 countries or territories with an alarming increase in cases each year[7]; like a protozoan infection can course, with latency and retarded immunity phases, according to mucocutaneous, cutaneous, and visceral subtypes, each one more severe than the other[3].

The main approach of this work is the study of therapeutic activity of the compounds referred and chemical affinity -between the molecular targets and the different drugs used for leishmaniasis- through molecular docking[2] using open-source platforms. Materials and methods: A comprehensive literature review was undertaken to identify protein structures (BSA, P-glycoprotein 1 and Type 1 topoisomerase) and drugs[1,4] that form ligand-protein complexes[6] (amphotericin B, miltefosine and sodium stibogluconate). The structures obtained in the Protein Data Bank (PDB) were processed in the P2RANK site to establish grid references "xyz" for the binding with the drug structures that had been optimised in Avogadro. The docking process was conducted on the DockThor platform[5] (a complimentary resource for receptor-ligand virtual screening) employing the encoded files, which facilitated the simulation of the complexes' binding.

After this, an evaluation of their structural affinity was completed.

To summarize, the docking identified the amino acids of interest, the predominant and those stability-conferring interactions as well as those related to serum protein binding and permeability characteristics. The generation of a crystallographic data report of molecular targets by molecular docking through open platforms and open databases allows the analysis of the chemical affinity of the drug with the protein active site and its interactions responsible for the therapeutic action in drug development and more effective treatments in diseases of high impact on public health.

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Natalie Richards

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The shape of lipid membranes is determined by a balance between membrane tension, bending rigidity, and adhesion forces. While these passive mechanics are well understood, much less is known about how internally generated forces, such as those from living, motile cargo, reshape membranes[1-3]. Here, we bridge this gap using biohybrid vesicles that encapsulate motile bacteria, providing a controllable model to directly compare passive and active membrane deformations[4].

Using giant unilamellar vesicles (GUVs), micron-sized, cell-like membrane bubbles, we systematically study how adhesion and membrane tension shape vesicle morphology. By allowing GUVs to adhere to supported lipid bilayers (which mimic biological surfaces) through controlled polymer-mediated interactions, we quantify how contact area, shape, and tension evolve during osmotic deflation. Osmotic shocks produce reproducible transitions from weak to strong adhesion, accompanied by distinct shape remodelling events such as spreading and tube formation[1,2].

These passive vesicle systems provide a mechanical baseline for introducing biological activity. Encapsulating motile Escherichia coli within the vesicles shows that internal motion can dynamically stress and reshape the membrane, with outcomes dependent on both adhesion strength and bacterial activity[4]. Comparing adhered and freely suspended biohybrid vesicles reveals how confinement and adhesion jointly regulate active membrane shape changes, offering new insights for designing self-organising, motile vesicles in synthetic biology and soft robotics.

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Naomi Crabbe

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Abstract: Low molecular weight (LMW) gelators that undergo self-assembly have been extensively investigated for biomedical applications owing to their tuneable design, modular synthesis, and biocompatibility.[1-4] Among these, Fmoc-Phe-Phe-OH (9-N-fluorenylmethoxycarbonyl-diphenylalanine) has been widely studied as a model peptide gelator due to its ability to rapidly form nanofibrillar networks in response to stimuli.[5] While, peptide hydrogels offer attractive mechanical and biocompatible properties, they are limited by susceptibility to enzymatic degradation, restricting their long-term stability and use as sustained injectables and wound healing.[6-7]

N-substituted glycine oligomers, or peptoids, mimic peptide behaviour while offering enhanced stability against enzymatic and proteolytic degradation.[7] This work investigates a library of N-capped aromatic dipeptides and dipeptoids with diverse aromatic substitutions to examine how structural variation influences molecular packing, self-assembly, material properties, biostability, and antimicrobial properties. The findings aim to establish design strategies for developing biostable, antimicrobial LMW hydrogels that maintain structural integrity and functionality under physiological conditions, enabling their use as long-term injectable or wound healing materials.

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Abstract: Cell wall is polysaccharide exoskeleton deposited above plasma membrane and covering all plant cells. Plant cells are connected by plasmodesmata, channels traversing cell walls, enabling communication of neighbouring cells and directly connecting their cytoplasm. Diameter of plasmodesmata opening is regulated by polysaccharide callose. Fine tuning of callose determines size of molecules which can travel through plasmodesmata. Plasmodesmata diameter changes considerably during the growth and development of plants, affecting morphogenesis of tissues and organs. We transiently overexpressed two candidate genes for callose degrading enzymes in tomato fruits and measured elastic modulus using atomic force microscopy inside pit-fields (cell wall regions of dozens and hundreds closely clustered plasmodesmata) and far away from pit fields. Transient transgenic lines, where overexpression of callose degrading enzymes was increased, showed increase in cell wall stiffness in both pit-field and contiguous cell wall regions compared with wild type and empty-vector controls. It seems that removal of callose, although it is one of the scarcest cell wall components could be altering interactions between major cell wall components such as cellulose, pectins and hemicellulose affecting global cell wall mechanical properties such as elastic modulus. In addition to this, transgenic lines showed significant increase in cellulose microfibrils diameter, compared to wild type, as shown by high resolution AFM imaging. This study could act as a stepping stone in better understanding complex role of cell wall in fruit growth and ripening potentially opening new avenues to improve and extend shelf-life of various fruits.

Sara Plautz

Durham University

Abstract: Abstract. When included in laundry detergent formulations, Soil-Release Polymers (SRPs) serve a multitude of purposes to increase the effectiveness of a wash cycle, thereby reducing water and electricity consumption. However, the environmental benefit of many commercially available SRPs is offset by their inclusion of terephthalic acid, which is derived from petroleum and may limit the biodegradability of the resultant SRP.1 It has become essential to develop sustainable solutions without sacrificing the functions of these essential compounds. Another key function of fabric care formulations is dye transfer inhibition, or preventing the movement of dye molecules between different-coloured fabrics. Dye transfer inhibitors (DTIs) may work by several mechanisms, including preventing the initial release of dyes and capturing released molecules before they contaminate undyed fabrics.2 In this study, polymers containing aromatic acids sourced from organic matter were synthesized, one consisting of exclusively the aromatic acid (P1) as the dicarboxylate component and a copolymer with a hydrophobic unit (P2). The molecules were analysed using dynamic light scattering, contact angle analysis, and gel permeation chromatography to determine what properties give rise to favourable performance. They then underwent performance testing in simulated laundry environments. While P1 displayed low performance, copolymer P2

performed well, with comparable ability to an industry standard at preventing soil transfer. The initial promise of these compounds indicates the potential of the aromatic acid as a DTI and serves as a foundation for in-depth investigation and development, encouraging the pursuit of bio-based solutions to industry problems.

Sara Hutchings

Durham University

Abstract: AI protein structure prediction tools like Alphafold (AF) have allowed development of design tools to create of binder proteins against targets, such as Bindcraft[1]. Protein binders can be used to activate or block receptors, with a range of applications in research and therapeutics[2]. These designed proteins may be more stable, cheaper to produced and more amenable to modification compared to antibodies[1].

Here, we have designed and tested de novo binder proteins against a cell receptor, improved the binding affinity with rational design and shown that the binders are capable of activating cells via the targeted receptor.

1. Pacesa et al. Nature (2025), 2. Fox et al. BioRXiv, (2025)

Sara Graham

Durham University

Abstract: Macroalgae, or seaweeds, are unusually resilient organisms that deal with extreme environmental changes on a tidal cycle. Their outer coverings, or cell walls, have evolved to cope with these changes. In comparison to land plants, we know relatively little about algal cell walls. Through direct imaging of the cell autofluorescence we can observe the impact of changing environments however new methods must be developed in order to probe changes to the cell wall specifically. In this project we aim to address this gap in knowledge through a combination of biological, chemical and physical analysis techniques. Through the extraction and characterisation of cell wall proteins we will gain insight into their role in maintaining cell wall structure and function. In addition, we are developing methods to immobilise molecular rotors, which can detect changes in local viscosity in the cell wall, through labelling of both sugars and proteins. Rheological methods will also give further insight into the properties of cell wall polysaccharides and how these are altered by the presence of proteins. Insights gained from our study should allow us to greater understand both the fundamental biophysics of novel biopolymers that can be extracted from the cell wall and the way these organisms will be affected by changing environments.

Simone Benaglia

Durham University

Abstract: Water molecules play a major role in determining the structure and function of biomolecules.[1] Hydration layers occurring at the interface of macromolecules strongly depend on their molecular charge distribution and dielectric polarization, which in turn determine their electrostatic and electrodynamic properties.[2] Hydration layers have been demonstrated organising on the cell membrane components, and they are essential to a wide range of biological processes. For example, it is intrinsically linked to lipid thermodynamic properties, which in turn influence key cell functions such as ion permeation and protein mobility. Hence, it is of fundamental importance to understand the physical properties of interfacial water to gain information on the structure and function of bio-systems.

In this study, we used advanced Atomic Force Microscopy techniques to measure the dielectric properties and atomic-scale arrangement of the lipid-water interface. Our approach builds on recent developments of our group in which we probed the dielectric constant of water confined inside 2D nanochannels made of van der Waals crystals[3,4] and demonstrated the presence of water layers at the interface of lipid membranes with molecular scale resolution.[5] Here, we show that the interfacial water organised at the lipid interface presents a low dielectric value compared with bulk water, in agreement with our previous results for water confined between solid 2D crystals. The new experimental data presented here improve our understanding of the electrical properties of water molecules structuring near soft biological surfaces.

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William Midgley

Durham University

Abstract: PROTACs (Proteolysis Targeting Chimeras) are a new type of drug which hijack the body's protein degradation system to remove unwanted proteins. They do this by binding an E3-ligase with the “anchor” end and the protein of interest (POI) with the “warhead” end with a linker joining the two, bringing the POI close to the ligase. The ligase then ubiquitinates the POI, flagging it to be degraded by a proteasome. This unusual mechanism allows PROTACs to target previously thought to be “undruggable” proteins. Although research is limited, linker design is essential to functional PROTAC development. Linker length, content, and attachment point to the two ends can affect binding affinity and selectivity, as well as ability for the E3-ligase to ubiquitinate the POI. This project aims to develop computational methods to help direct PROTAC linker design by improving protein dynamics predictions.

We use the Cambridge Crystallographic Data Centre’s (CCDC) software suite for visualising and ranking PROTAC binding interactions with the POI and E3-ligase.

Docking is performed to obtain POI-warhead and E3-ligase-anchor poses. PROTACs are then assembled from the warhead, anchor, and a library of linkers to form 1000s of PROTACs. The CCDC’s PROTAC Conformer Generator is then used to generate and score the PROTAC conformers. Molecular dynamics simulations are then used to help determine conformer stability. This pipeline allows high throughput computational PROTAC screening prior to in-vitro testing. The pipeline under development uses established systems such as the ternary structure of SMARCA-bromodomain-VHL shown below.

We also use in-vitro techniques to determine binding affinities of PROTACs to E3 Ligases and POI to corroborate the in-silico results. The pipeline will be applied to a DNA binding protein found in the Epstein-Barr Virus as our POI. PROTACs targeting our POI could provide novel cancer treatments.

Yufang Liu

Durham University

Rhamnolipids (RLs) are bio-degradable, low-hazard anionic biosurfactants. They can be extracted from cultures of Pseudomonas and other bacteria.1 RLs can be used to adjust surface tension, as agents for environmental remediation, and as food/cosmetic additives.2 Thus, we aim to develop robust RL models to accurately predict the membrane-water partition coefficient (log Kmw), which has been shown to positively correlate with uptake into biological systems.

We are developing Martini 3 coarse-grained (CG) models to represent RLs and predict log Kmw from the equilibrated ratio of concentration between membranes and aqueous solution. Our models are designed to capture important interactions at the membrane-water interface and produce reliable trajectories of self-assembly and aggregation with oil molecules, at the CG resolution. Initial CG models were obtained from cg_param: an automated CG mapping and parameterisation software developed and maintained by our group.3,4 Then, we refined these generic models using the domain knowledge.5 Models are also applied to (1) monitor statistics of RL functional groups at interfaces between the bilayer and water regions; (2) predict relevant physical properties like osmotic pressure; (3) simulate the aggregation behaviour of RLs in mixed aqueous phase; (4) simulate membrane curvature induced by RLs interacting with POPC molecules on liposomes and rafts.

Our preliminary results show that cg_param provides sensible mapping and parameterisation for the calculation of log Kmw. RL models tuned to guidelines tend to overestimate hydrophobic interaction with the membrane. Thus, we continue to optimise the mapping, bonded and non-bonded

parameters and have made progress on simulating aggregation related to oil capture and interactions at interfacial regions. In the future, we are going to investigate the RL-induced membrane curvature to gain a better understanding of membrane-water partitioning.

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Zoy Cassidy

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The Wnt signalling pathway is a recognised driver of colorectal cancer progression and metastasis and is regulated by the enzyme tankryase. Novel tankyrase-binding peptides (TBP) show selective tankyrase inhibition and Wnt downregulation. DNA nanostructures have emerged as a highly programmable and biocompatible platform for therapeutic delivery that allow multivalent targeting of polymers such as tankyrase. However, the use of DNA nanostructures to target intracellular proteins is limited by their endo-lysosomal uptake and degradation. Agarose gel electrophoresis, atomic force microscopy, and mass photometry showed effective synthesis and functionalisation of 2D triangle and 5-well frame DNA origami with TBP and lysosomal escape peptides. The colorectal cancer SW480 and model (non-cancer) HEK-293 cell lines showed uptake of DNA nanostructures and partial lysosomal localisation. Mass photometry revealed that DNA origami functionalised with TBP can bind tankyrase *in vitro,* and Wnt luminescence assays confirmed that TBP triangles inhibit signalling more effectively than free TBP. These findings highlight the potential of DNA nanostructures for intracellular delivery and clustering of biologic drugs.

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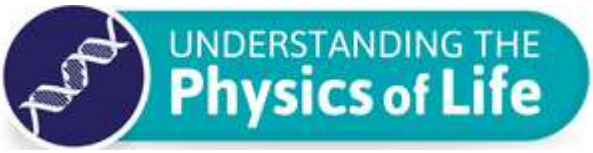

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