Oral Presentations

Alternative mode of cell division in MRSA

Dr Abimbola Feyisara Adedeji-Olulana[1]
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Emerging Areas in the Physics of Life, March 26, 2025, 10:15-12:15

In Staphylococcus aureus, peptidoglycan (PG) is a 3D mesh-like macromolecule that surrounds the cell, playing an essential role in cell survival, maintaining the shape during cell division, and protecting the cell against its internal turgor pressure. Its biosynthesis proteins known as penicillin-binding proteins (PBPs) are the targets of ß-lactams antibiotics. High-resolution atomic force microscopy (AFM) has recently revealed S. aureus PG to be a porous, heterogeneous hydrogel [1]. Its mature surface is an open, disordered mesh with pores that penetrate deep into the wall, whereas the inner surface, where PG is synthesized, is a much denser mesh [1]. Another feature of the PG is an outer architecture of concentric rings consisting of long glycan strands revealed upon cell division and characteristic of the newly exposed septum [1].

In this study, we focus on the peptidoglycan associated with methicillin-resistant S. aureus (MRSA) and explore the following questions: 1) Are there differences in PG architecture when MRSA cell is treated with antibiotics? 2) Are these differences observable in clinical strains? To this end, we utilized AFM to capture the nanoscopic phenotype induced by antibiotic treatment on the MRSA peptidoglycan. Our findings reveal that, in the presence of antibiotics, MRSA adopts an alternative mode of cell division and shows an altered peptidoglycan architecture at the division septum [2].

References
[1] L. Pasquina-Lemonche et al., “The architecture of the Gram-positive bacterial cell wall,” Nature, vol. 582, (2020).
[2] A. F. Adedeji-Olulana et al., “Two codependent routes lead to high-level MRSA,” Science, vol. 386, (2024).

A General Framework for Designing Evolutionary Experiments to Select Specific Phage Phenotypes Using Neural Networks, Statistical Simulations, and Symbolic Regression

Hassan Alam[1], Dr Diana Fusco[1]
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Evolution, Ecology and Epidemiology, March 24, 2025, 15:30-17:30

Understanding how environmental conditions shape the evolution of bacteriophages (phages) is critical for designing correct evolutionary experiments that select specific phage traits. This study provides a general mathematical framework that integrates physics-informed neural networks, agent-based statistical simulations, and symbolic regression machine learning techniques to design evolutionary experiments targeting specific phage traits such as high variability in phage phenotypes.

In the study, we used agent-based statistical simulations to generate synthetic time series data for evolutionary scenarios with diverse phenotypic outcomes. Subsequently, we trained Physics-informed neural networks (PINNs) embedded in differential equations on the synthetic time series to reveal possible environments that select given phage traits and uncovered hidden interactions in the system [1].

Lastly, by using symbolic regression techniques, including Sparse Identification of Nonlinear Dynamical Systems (SINDy) and genetic algorithm-based methods, on the synthetic time series data, we derived governing differential equations that identified key environmental conditions and interaction pathways driving the evolution of specific phage traits in well-mixed and spatiotemporal microbial systems. These equations serve as a foundation for predicting the correct evolutionary experiment to select for the given phage traits.

This approach provides a scalable and adaptable framework for designing evolutionary experiments to select specific phage phenotypes. It highlights the power of integrating physics-informed neural networks, agent-based simulations, and symbolic regression techniques to offer new insights into the mechanisms underlying complex microbial ecosystems.

Reference:
[1] Grigorian, G., George, S.V. and Arridge, S., 2024. Learning Governing Equations of Unobserved States in Dynamical Systems. arXiv preprint arXiv:2404.18572.

Using Whispering Gallery Modes to Monitor Single-Enzyme turnover events of NanoLuc

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Imaging and Single Molecule Biology, March 25, 2025, 10:15-12:15

Whispering Gallery Mode (WGM) sensing is an optoplasmonic technique capable of detecting the binding and movement of single molecules with Angstrom-scale precision and millisecond time resolution, without requiring fluorescent tags [1]. This universal, label-free platform provides a powerful alternative to fluorescence-based methods, enabling the direct study of enzyme kinetics and molecular interactions in real-time [2]. However, a key challenge in enzymology is the ability to directly monitor enzymatic turnover at the single-molecule level on such platforms while simultaneously verifying the production of reaction products.
This study addresses this challenge by integrating WGM sensing with a bioluminescent enzyme, NanoLuc (NLuc), whose turnover produces detectable photons as reaction products. Using Furimazine as a substrate, we demonstrate that WGM sensing can detect both single-enzyme binding events to plasmonic gold nanorods and real-time enzyme turnover. Moreover, these results produced a unique signal pattern, contributing to a new area of investigation which will provide new insights into NLuc kinetics. These WGM single molecule results provide a first step in developing a photosensitive WGM hybrid sensor, which will establish a framework to correlate enzymatic activity with product formation, providing conclusive insights into reaction mechanisms.

This approach represents a significant start toward the direct, label-free monitoring of enzymatic turnover events, opening new avenues for studying single-molecule biological systems and advancing the understanding of widely used enzymes like NLuc, which have numerous industrial applications.

[1] M.D. Baaske, et. al. Nature Photonics 10, 733-739 (2016).
[2] M.C. Houghton, et. al. Advanced Science 11(35) (2024).

Investigating the Influence of Mechanical Stresses on Ciliary Dynamics Using Advanced In Vitro Airway Models.

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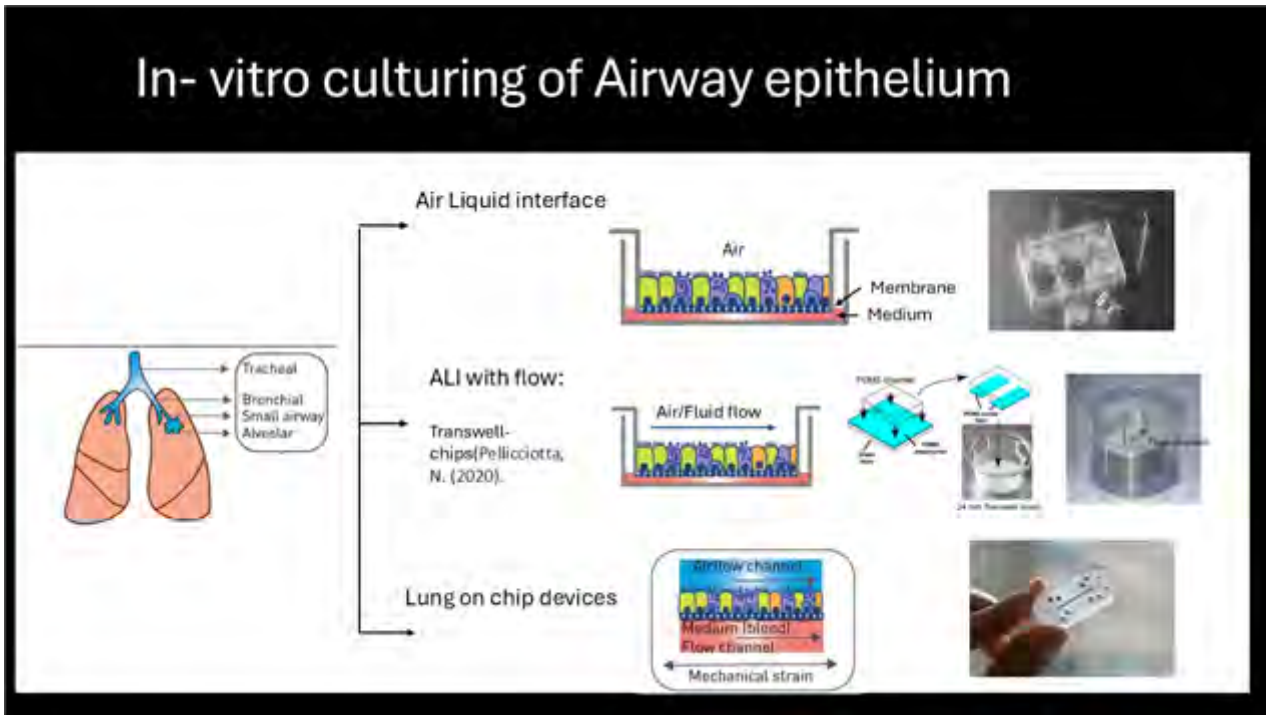
[1]Cavendish Laboratory, University of Cambridge, United Kingdom, [2]The Victor Phillip Dahdaleh Heart & Lung Research Institute, University of Cambridge, United Kingdom, [3]Department of Veterinary Medicine, University of Cambridge, United Kingdom, [4]University of Edinburgh, United Kingdom

Engineering Tissues and Organoids and Biohybrids, March 25, 2025, 14:15-16:15

Motile cilia on the epithelial surface of the respiratory tract play a critical role in mucociliary clearance, a key defense mechanism that supports respiratory health by moving mucus and entrapped pathogens out of the airways. Effective mucociliary transport relies on the coordinated beating of cilia, which collectively transport mucus away from the lungs. Mechanical stresses—including pressure gradients from breathing, compressive stresses, and shear forces from fluid flow—are known to influence ciliary activity by modulating beat frequency, coordination, and pattern. Disruptions in these dynamics are implicated in diseases like chronic obstructive pulmonary disease (COPD), asthma, and cystic fibrosis, where impaired mucus clearance leads to mucus accumulation and worsened symptoms.

In our lab, we examine how mechanical stresses influence ciliary dynamics using a combination of commercially available and custom-built in vitro systems that replicate airway conditions. These include Air-liquid interface (ALI) cultures on transwells to mimic the natural exposure of airway epithelial cells, microfluidic channels positioned above these transwell inserts (TransChips) to simulate controlled fluid flow, and dual-channel ALI setups (Lung-On-Chip devices), which regulate flow in both top and bottom channels to closely approximate physiological conditions. These advanced models enable us to systematically examine how variations in external flow conditions, boundary conditions, and varying mucus loads affect ciliary motion and coordination, providing detailed insights into the mechanobiology of airway cilia.



Shedding Light on Lipid Order in Frozen COVID-19 Vaccines Using Fluorescence Spectroscopy

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Physics of Disease, March 27, 2025, 09:00-11:00

Lipid nanoparticles (LNPs) represent a promising avenue of research in the field of drug delivery systems, with particular relevance to the development of RNA-based vaccines and therapeutics. However, a deeper understanding of the formulation concepts behind LNPs is essential for their focused optimization and overcoming obstacles such as storage instability. We aim to make a substantial contribution to this field of study by directing our research towards a detailed examination of the lipids.

The use of solvatochromic dyes, such as Laurdan, enables the precise measurement of lipid order. Laurdan is a unique probe that integrates into membranes and lipid systems, where its fluorescence properties are highly sensitive to the polarity of the surrounding environment. This allows for the examination of packing density and lipid order. By employing fluorescence spectroscopic measurements with the Lipid State Observer (LISO), we quantify the lipid order through the calculation of the generalised polarisation (GP) based on fluorescence emission spectra [1].

Notably, this approach allows us, for the first time, to analyse the lipid order of LNP-formulations like the COVID-19 vaccine at sub-zero temperatures in the frozen state. The phase transition temperatures of LNP formulations can further be estimated by measuring GP as a function of temperature, providing an additional valuable characterisation of these systems. At present, we are engaged in an investigation into the potential correlations between the lipid order and other critical properties of LNP, including encapsulation efficiency, transfection efficiency, and storage stability.

[1] Färber, Nicolas and Westerhausen, Christoph. DOI: 10.1016/j.bbamem.2021.183794.

Untangling plant cell walls biophysics and the regulation of intercellular communication

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Cell Metabolism and Growth, March 27, 2025, 09:00-11:00

A key property of all living systems is intercellular communication which coordinates growth in response to external cues. Communication in plants is far from simple as they are restricted by rigid walls. Plasmodesmata evolved as a route for the symplastic (cytoplasm-to-cytoplasm) transport of small and large molecules including signalling proteins and RNAs, metabolites and hormones. These are small pores that appear in cell wall domains enriched in the β-1,3 glucan polysaccharide callose. We studied the mechano-physical properties of callose underpinning its function in the regulation of the plasmodesmata [1]. Applying computer simulations and experimental approaches, the properties of callose in improving cellulose hygroscopicity and visco-elasticity were identified [2]. We also developed molecular probes and identified proteins that modify callose accumulation in cell walls [3]. These tools allowed us to uncover the structural properties of these cell walls microdomains that can be exploited in plant biotechnology and in biomaterial development.

I will share how we build on this knowledge and discuss potential applications in tackling environmental sustainability challenges.

References:
[1] Abou-Saleh RH, Hernandez-Gomez MC, Amsbury S, Paniagua C, et al: Interactions between callose and cellulose revealed through the analysis of biopolymer mixtures. Nat Commun 2018, 9(1):4538.
[2] Kumari P, Ballone P, Paniagua C, Abou-Saleh RH, Benitez-Alfonso Y: Cellulose-Callose Hydrogels: Computational Exploration of Their Nanostructure and Mechanical Properties. Biomacromolecules 2024, 25(3):1989-2006.
[3] Amsbury S, al. el Benitez-Alfonso Y: Structural heterogeneity in β-1,3-glucans reveals distinct calloses in plant cell wall microdomains. Biorxv 2024.

In vivo targeted and deterministic single cell cancer induction

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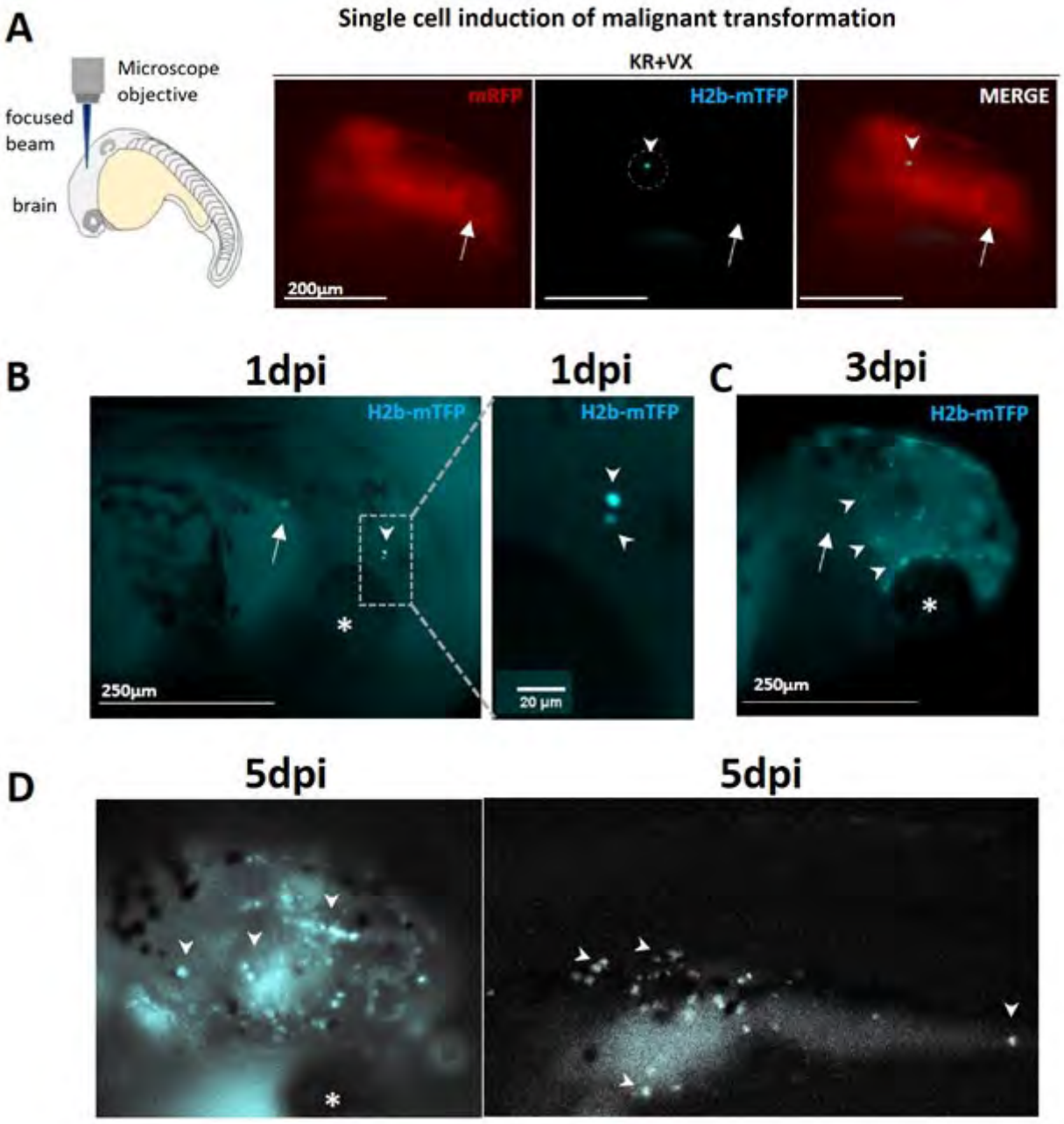
Physics of Disease, March 27, 2025, 09:00-11:00

How cancer arises from a single normal cell is still the subject of active debate, affecting intervention strategies. While many cells may harbor oncogenic mutations, only a few unpredictably end-up developing a full-blown tumour. Various theories have been proposed to explain that transition, but none has been tested in vivo at the single cell level.

Here using an optogenetic approach we permanently turn on an oncogene (KRASG12V) in a single cell of a zebrafish brain (Fig.1A) that, only in synergy with the transient co-activation of a reprogramming factor (VENTX/NANOG/OCT4), undergoes a deterministic malignant transition and robustly and reproducibly develops within 6 days into a full-blown cancer (Fig.1B-D). The controlled way in which a single cell can thus be manipulated to give rise to cancer lends support to the “ground state theory of cancer initiation” through “short-range dispersal” of the first malignant cells preceding tumour growth.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Single cell induction of malignant transformation
Microscope objective
focused beam
brain
KR+VX
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C
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Interactions between HES1 and HES5 give rise to dynamic diversity in spinal cord neural progenitors

Dr Veronica Biga[1], Dr Anzy Miller[1], Dr Cerys Manning[1], Prof. Nancy Papalopulu[1], Prof. Paul Francois[2]
[1]The University of Manchester, United Kingdom, [2]The University of Montreal, Canada

Clocks, Timers and Cell Cycle Dynamics, March 25, 2025, 14:15-16:15

Gene expression oscillations are an exciting model system for understanding complex dynamic activity and how it impacts cell fate decisions. The Hairy and enhancer of split (HES) 1 and 5 are regulated through self-repression (with protein periodically repressing mRNA production) thereby generating oscillations, i.e. periodic fluctuations in the level of HES every few hours. We showed that HES1 and HES5 transcription factors (TFs) oscillate in live neural tissue (mouse HES5: Manning et al. (2019); Her6 zebrafish ortholog: Soto, Biga et al. (2020)). However, HES1 and HES5 dynamics have never been compared in in the same cell.

We used dual reporters to observe a variety of dynamic types converging towards cells co-expressing HES1 and HES5 with synchronous oscillations in the 3-4h range. Using a coupled HES1-HES5 differential equations model parameterised for known values of protein, mRNA half-life, we confirmed that synchronisation can emerge at 3-4h matching with our single cell observations, thus indicating that the HES1 period is elongated by interaction with HES5. Differences in the protein half-life (HES5 being 4x more stable compared to HES1) appear to elongate the HES1 duration through entrainment. Our theoretical predictions, supported by in-vitro observations suggest that gene-gene interactions can enable a TF with short half-life (HES1) to operate outside of its characteristic dynamic regime through in-phase coupling to a TF with longer half-life (HES5) thus giving rise to new dynamic regimes. Our work emphasizes the need to study gene regulation in a dynamic context and in more than one gene at the same time.

Single-Cell Bacterial Patterning to Dissect Interspecies Interactions in a Minimal Nose Microbiome that Inhibits Staphylococcus aureus

Cameron Boggon[1], Jeruscha Baum[2], Dr Eleonora Secchi[1], Prof Silvio Brugger[2], Prof Lucio Isa[1]
[1]ETH Zurich, Switzerland, [2]University Hospital Zurich, Switzerland

Immunity, Resistance and Host/Pathogen Dynamics, March 26, 2025, 15:30-17:30

The human nose and upper respiratory tract (URT) is a hostile environment for colonising bacteria. Saline and nutrient-scarce, the microbiome colonising this niche is characterised by low diversity and low biomass, while strong antagonistic interactions have been reported between various URT microbes. Typical approaches to study bacteria colonising this niche rely on mono-species cultures, grown to high concentrations in nutrient rich conditions and thus often ignore both inter-species interactions and phenotypic heterogeneity within the population. Though such approaches may overlook important aspects of microbial biology as a consequence, technologies to study bacterial communities in controlled, high-resolution, high throughput conditions are largely lacking.

I will present an approach, based on Capillary-Assembly, for patterning microorganisms on a template in well-defined geometries with large scale and single-cell precision. I will demonstrate how this can be extended to pattern multiple organisms, thus allowing us to 'design' minimal microbial communities with well-defined spatial structure. By combining both 'macroscopic-scale' agar plating techniques together with our 'microscopic-scale' patterning methodology, I will show ongoing work characterising the synergistic and antagonistic interactions between three members of the URT: the commensal organisms Dolosigranulum pigrum and Corynebacterium pseudodiphtheriticum, and the pathogen Staphylococcus aureus. As prior colonisation by S. aureus is a known risk factor for post-surgical infections, our work explores potential probiotic strategies to permanently eradicate S. aureus from the URT. I will demonstrate some of the complex, multi-species interactions taking place within this three-member community and what can be learned by comparing macroscopic and microscopic approaches to study community interactions.

Evolutionary optimization of gene regulation

Réka Borbély[1], Michal Hledík[1], Gašper Tkačik[1]
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Evolution, Ecology and Epidemiology, March 24, 2025, 15:30-17:30

Cis-regulatory elements, such as enhancers and promoters, control gene expression by binding regulatory proteins. In contrast to their bacterial counterparts, eukaryotic CREs typically bind transcription factors with short recognition motifs across multiple functional yet often weak binding sites. The evolutionary origin of this architecture remains unclear. Here we study adaptive evolution of entire CREs under selection for regulatory phenotypes. In a biophysical toy model that recapitulates the essential nonlinearities of eukaryotic regulation, a regulatory phenotype requires a gene to be active when its CRE binds cognate TFs, yet inactive in the presence of noncognate TFs that can cause deleterious crosstalk.

We explore CRE evolutionary outcomes assuming an "optimize-to-adapt" approach. In this approach, CRE evolution is simulated explicitly at the sequence level, while the parameters of the biophysical model itself -- i.e., the properties of the genotype-phenotype map -- are numerically optimized for evolvability of CREs. In the optimal regime, selection navigates the tradeoff between slowly evolving strong and long binding sites (which guarantee low crosstalk) and rapidly evolving multiple short and weak binding sites (which necessitate diffuse selection against noncognate binding across the entire CRE). When we further explore various scenarios for cooperative regulation, we find that the optimal regime predicts a diversity of strong and weak short binding sites and favors "synergistic activation" of transcription, as reported in empirical studies.

These results showcase how information theory can link evolutionary dynamics with biophysical constraints to rationalize -- and possibly even predict -- optimal regulatory architectures.

Complement-mediated killing of Escherichia coli by mechanical destabilisation of the cell envelope

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[1]National Physical Laboratory, United Kingdom, [2]University College London, United Kingdom, [3]Princeton University, Princeton, USA, [4]University of Warwick, United Kingdom, [5]University of Sheffield, United Kingdom

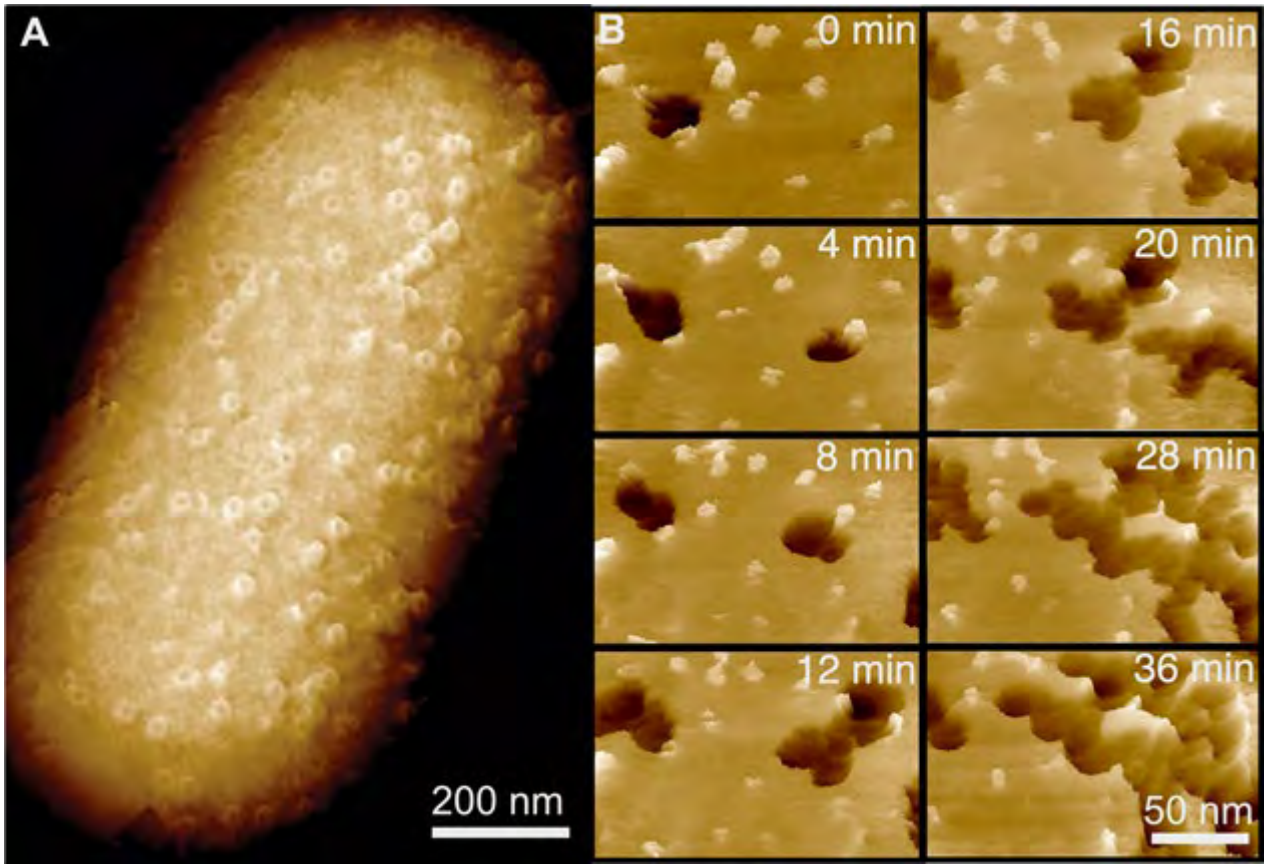
Imaging and Single Molecule Biology, March 25, 2025, 10:15-12:15

The complement system is a key part of our innate immune defence. When activated by pathogens like bacteria, it triggers an irreversible enzymatic cascade that results in the formation of membrane attack complex (MAC) pores on microbial membranes, ultimately causing cell death. Although the bactericidal role of complement proteins has been recognized for over a century, the exact mechanism has not been fully understood.

Using a combination of atomic force microscopy (AFM) and live-dead fluorescent staining, we can observe MAC formation on these bacteria and link cell death to changes on the bacterial surface caused by MAC pores. This approach allows us to detect structural and mechanical changes at the bacterial cell surface with nanometre resolution, while simultaneously tracking when each cell dies.

These experiments have allowed us to directly connect structural and mechanical alterations at the bacterial surface with subsequent cell death. They reveal the pathway of bacterial killing by the complement system's terminal pathway, showing significant outer membrane damage from complement exposure. The findings suggest that the ultimate cause of bacterial death is related to changes in the cell envelope's mechanical stability, rather than simply pore formation.

We conclude that bacterial cell lysis is a secondary effect of MAC formation; outer membrane poration leads to mechanical destabilization of the cell envelope, reducing its capacity to contain turgor pressure, which then results in inner membrane permeability and cell death. This previously unknown mechanism of bacterial cell death may provide insights for developing new antibiotic treatments.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Engineering Gene Regulatory Networks to Design Disease Resistant Crops

Amy Briffa[1], Feixue Liao[2], Juanjuan Wang[3], Ana Almeida[3], Luisa Valencia Riascos[2], Katherine Denby[2], Richard Morris[1], Nicola Patron[3]
[1]John Innes Centre, United Kingdom, [2]University of York, United Kingdom, [3]University of Cambridge, United Kingdom

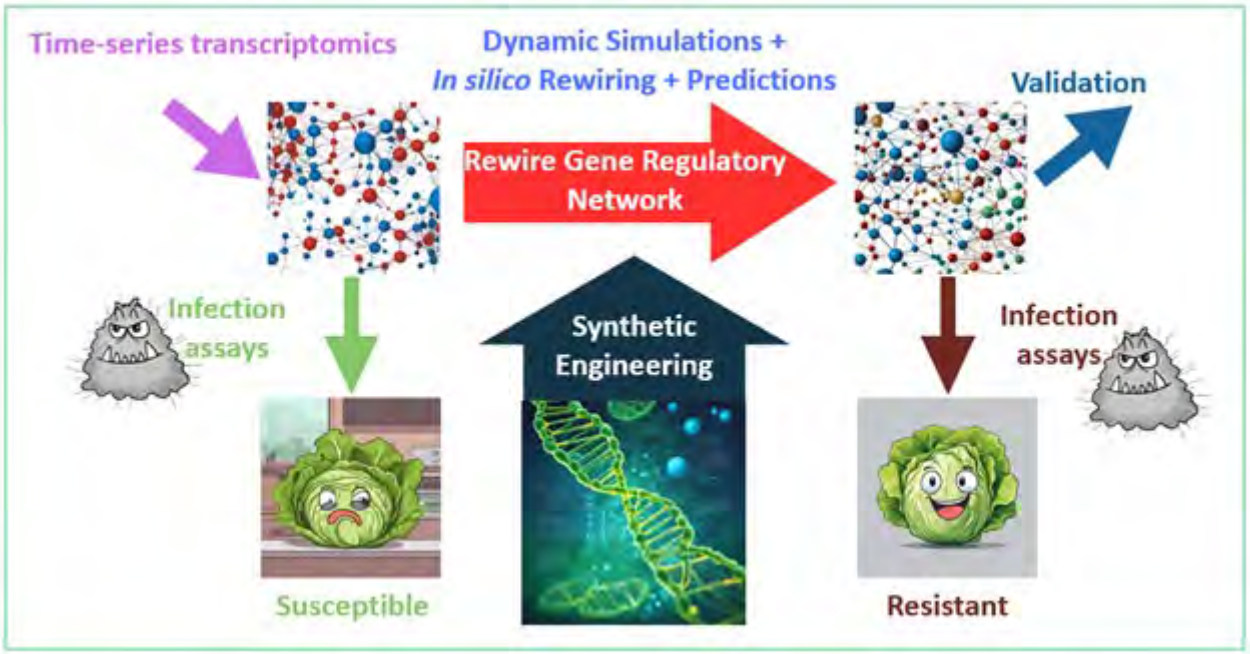
Immunity, Resistance and Host/Pathogen Dynamics, March 26, 2025, 15:30-17:30

Genetic technologies can be used to enhance pathogen resistance in crops, promoting sustainable agriculture. The responses of plants to environmental stresses are controlled by multiple genes, coordinated by complex, interconnected regulatory networks. Here, we focus on the immune response of lettuce to Botrytis, a fungal pathogen that infects a broad range plant species, including many fruits and vegetables.

Our interdisciplinary collaboration is working to uncover and validate sub-networks of transcription factors that regulate pathogen-induced plant defence responses. We will use computational simulations to guide targeted gene editing of connections to re-wire the regulatory network for enhanced disease resistance.

Here, I focus on in silico dynamical simulations. Firstly, to refine and validate the proposed networks against RNA-seq time-courses [1] of infected vs mock treated plants. Secondly, to computationally explore different re-wiring options, to identify candidates that provide robust transcriptional enhancement of the target down-stream defence genes.

[1] Harry Pink et al. (2023) bioRxiv DOI: 10.1101/2023.07.19.549542.



How is the swimming of exogenous microorganisms affected by the beating of cilia?

Viridiana Carmona Sosa[1], Pietro Cicuta[1], Jurij Kotar[1]
[1]*University of Cambridge, United Kingdom*

Patterns, Waves, Transport, Collective Phenomena and Microswimmers, March 25, 2025, 10:15-12:15

In the respiratory system, micrometric whipe-like structures work collectively to keep the airways free from pathogens. Mucociliary clearing is the term for the process by which these structures, known as cilia, move in a coordinated way.

In patients with conditions such as primary ciliary dyskinesia, or chronic obstructive pulmonary disease, dysfunctional cilia fail in generating a coordinated sweeping of the mucus, exacerbating severe infections and chronic inflammatory conditions. Because of this, here we want to understand the flow produced by the cilia in the airways from a hydrodynamic point of view, which might help explain how the initial phase of an infection arises. To do so, we use optical tweezers to study the influence of the ciliary movement on a passive agent, which is used as a simplified model of a real infection.

RNA virus genome structure determination by X-Ray Footprinting

Dr Rebecca Chandler-Bostock[1], Dr Lekshmi B. G. Nair[2], Dr Nikesh Patel[1], Prof. Reidun Twarock[2], Prof Peter Stockley[1]
[1]Astbury Centre for Structural Molecular Biology, University of Leeds, United Kingdom, [2]Departments of Mathematics and Biology, University of York, United Kingdom

Biomolecular Assemblies and Condensates, March 25, 2025, 10:15-12:15

X-Ray Footprinting (XRF) cleaves viral RNAs trapped by rapid freezing in defined conformational states via hydroxyl radical modification of the nucleotide sugar residues. Modification and subsequent backbone cleavage events occur in a flexibility-dependent fashion, i.e. most frequently where RNA is single stranded, not bound to itself or in contact with capsid protein. We used XRF to map RNA structure in the genome of the bacteriophage MS2, as both a transcript and when encapsidated in infectious phage. This revealed that viral assembly is principally due to alterations in RNA tertiary structure, since the protein-free genome contains stem-loops, displaying a specific loop sequence motif. These packaging signals (PSs) form complexes with coat protein dimers helping to define the A/B conformers that surround five-fold axes in the virion. Interestingly post-assembly many of these RNA-coat protein contacts appear to dissociate facilitating subsequent infection. This revealed many RNA-protein interactions and provided novel insights into viral assembly.

We have also used XRF to determine the viral genome structure of Satellite Tobacco Necrosis Virus (STNV). This data complements a previous work which confirmed that multiple PSs across the 5´ two-thirds of the genome make sequence-specific contacts to the viral coat protein, helping to nucleate formation of its T = 1 virus-like particle (VLP). These contacts explain why natural virions only package their positive-sense genomes. The high degree of conservation between the coat protein fold of STNV-1 and those of many other viruses suggests that these aspects of genome function will be widely shared.

Ab initio molecular dynamics of phospholipid-mineral interactions suggest a critical role for organic material in the growth of kidney stones

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[1]*University of Leeds, United Kingdom*

Physics of Disease, March 27, 2025, 09:00-11:00

Kidney stones affect around 10% of the world's population, although this figure is higher in the USA (15%) and Middle East (25%). Secondary episodes happen in 40-50% of cases, resulting in a high economic and healthcare burden. While the primary causes of kidney stones are established – high levels of calcium or oxalate in the urine for example – less is understood about the structure and chemistry of their formation. This gap in our understanding has significant implications for our ability to successfully treat this condition.

It is known that kidney stones are largely composed of mineral but they also contain small amounts of organic material such as lipids and proteins. In this work [1] we examine, using ab initio molecular dynamics, the interactions of calcium oxalate mineral with phosphocholine, one of the most prevalent organic substances identified in kidney stones and a critical part of the epithelial cell membrane, where stones can nucleate.

We show that phosphocholine binds favourably to calcium oxalate surfaces, such that it can promote further mineral deposition. Additionally, 'sandwich' simulations highlight that this phospholipid is extremely good at bringing together smaller crystallites, which accounts for its encapsulation within the stone, and highlights how the organic material can promote further stone growth. We suggest that pharmaceutical interventions that could reduce free-floating phospholipids within the urine, could be effective alternative treatments for reducing the burden of kidney stones.

1. Morris, R., Chappell, H. F., Scott, A. J., Borissova, A., Smith, J. 2024. Crystal Growth & Design, https://doi.org/10.1021/acs.cgd.4c01032.

Phototaming of Bacterial Bioelectricity

Professor Giuseppe Maria Paternò[1,2], Edoardo Cianflone[1,2]
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Bioelectricity Across Scales, March 26, 2025, 15:30-17:30

The goal of engineering living matter is to modify biological attributes to leverage the unique capabilities of living organisms. One prevalent method involves rendering living matter responsive to specific stimuli through either synthetic biology techniques or functional materials, aiming to modulate the electrophysiology and activity of cells and organisms. This method applies to bacteria as well, despite the fact that the connections between their electrophysiology, bioelectricity, bioenergetics, and behavior have only recently started to be elucidated. Recent studies have revealed that bacterial membrane potential is a dynamic, rather than static, parameter and plays a significant bioelectric signaling role. Such a communication paradigm governs their metabolism, behavior, and functions within microbial communities. Given that membrane potential dynamics mediate this language, manipulating this parameter represents a promising and intriguing strategy for bacterial engineering.

Here, I show that precise optical modulation of bacterial membrane potential can be achieved through a materials-based approach. Specifically, we found that the isomerization reaction at the membrane location induces either hyperpolarisation or depolarisation of the potential depending on the excited state deactivation pathways, within a bio-mimetic mechanism reproducing the initial fate of retinal. This can trigger neuron-like bioelectric signalling and can highlight the role of previously uncharacterized ion channels in bacteria electrophysiology. Finally, I also show perspectives on the light-modulation of antibiotic uptake, as well as on the photocontrol of bacterial motion and assembly behavior in consortia and multispecies ecosystems

Single-Molecule Visualisation of Human Topoisomerase 2A Decatenation Reveals Substrate Requirements

Erin Cutts[1], David Rueda[3], Luis Aragon[2]
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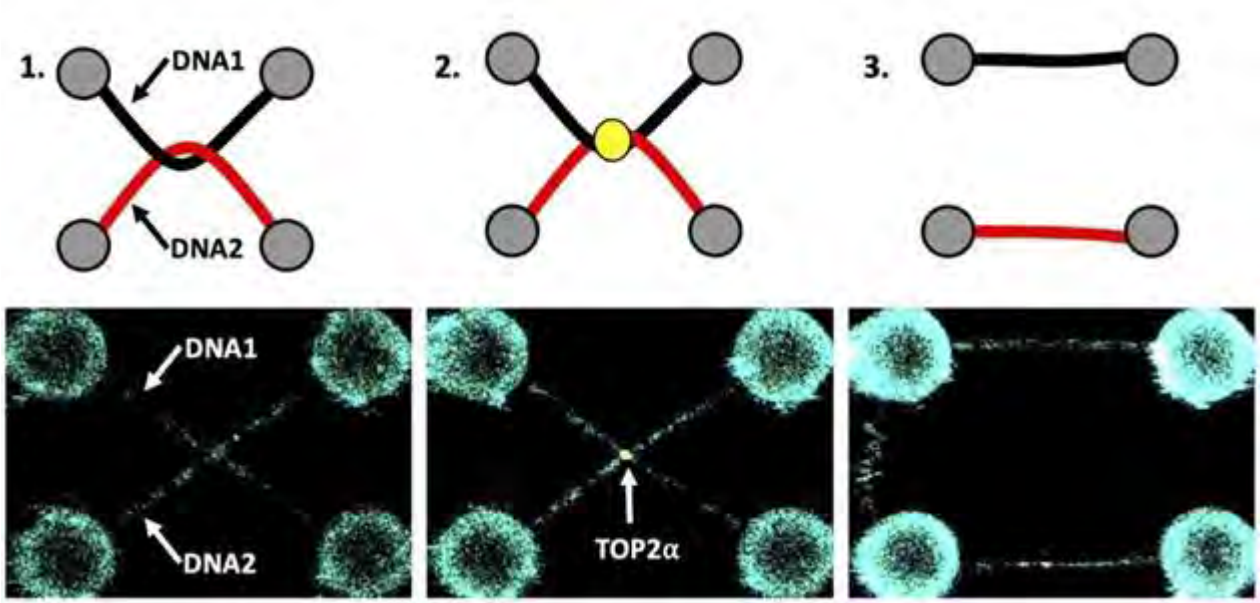
Imaging and Single Molecule Biology, March 25, 2025, 10:15-12:15

DNA replication introduces double-stranded DNA entanglements, which if unresolved, pose a challenge to cell division and faithful segregation of the genome. When cells divide in mitosis, the enzyme, Topoisomerase 2A (TOP2A), binds and resolves DNA entanglements by producing a double strand break via nucleophilic attack and then passing the other strand through the break. TOP2A is an essential protein and an important drug target, hence has been extensively studied, but until now the resolution process has not been directly visualised. In this work, I develop an assay for visualising TOP2A activity, mimicking forces that could be applied in a mitotic context, by employing optical tweezers to manually entangle two pieces of DNA. I demonstrate that TOP2A DNA resolution is inhibited at high forces, with sharp transition at the half-force of 28 pN.

My experiments indicate TOP2A readily binds DNA, consistent with cell-based experiments demonstrating large amounts of TOP2A associated with DNA during mitosis, however, I find resolution is most efficient when TOP2A associates directly at the site of a DNA entanglement, where it can act processively. During early mitosis the action of TOP2A chromosome resolution is countered by cohesin, which holds chromosomes together until late mitosis. I demonstrate that cohesin readily associated with entangled DNA, and inhibits TOP2A resolution, implicating TOP2A in regulating chromatid cohesion. Collectively, this approach provides novel insights into the important therapeutic target, TOP2A [1].

[1] Cutts, E.E., et al (2023). Substrate accessibility regulation of human TopIIa decatenation by cohesin. Biorxiv, https://doi.org/10.1101/2023.11.20.567865.



Learning (from) protein dynamics

Dr Matteo Degiacomi[1]
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Protein Structure, Dynamics and Interactions, March 24, 2025, 15:30-17:30

Determining the different conformational states of a protein and the transition paths between them is key to fully understanding the relationship between biomolecular structure and function.

I will discuss how a convolutional neural network can learn a continuous conformational space representation from example structures produced by molecular dynamics simulations, and knowledge of physical laws dictating atomic interactions. I will then show how such representation, obtained via our open-source software molearn, can be leveraged to predict putative protein transition states, or to generate conformations useful in the context of flexible protein-protein docking.

Direct experimental measurement of conformational interconversion in protein kinases and its modification by phosphorylation and ligand binding

Dr James Gilburt[1], Dr Tamsin Wilcock[2], Dr Paul Girvan[1], Ms Hajrah Sarkar[1], Dr Peter Sheldrake[3], Prof. Julian Blagg[3], Dr Liming Ying[1], Dr Charlotte Dodson[1,2]
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Protein Structure, Dynamics and Interactions, March 24, 2025, 15:30-17:30

The DFG-in and DFG-out conformations of protein kinases have been characterised by X-ray crystallography for decades. Despite this, we have only recently been able to quantify heterogeneity within protein samples in solution. Using single molecule fluorescence quenching experiments, the Dodson lab is proud to have made the first direct experimental measurement of kinase molecules interconverting between DFG-in and DFG-out conformations in solution. Our experiments have enabled us to determine the microscopic rate constants of the DFG-flip equilibrium in Aurora-A kinase and the effect of kinase ligands on the position of equilibrium in both Aurora-A and MET kinase.

In Aurora-A, phosphorylation of the kinase changes the position of conformation equilibrium, but not the effect of an inhibitor on this equilibrium. In MET kinase, the clinical inhibitor crizotinib modifies the DFG conformational equilibrium in WT but not in D1228V or Y1230H inhibitor-resistant clinical mutants. Our measurements are unbiased by sample orientation and represent the entire population of molecules present in solution. They can inform both inhibitor discovery (particularly mechanism of action) and our understanding of allostery in protein-protein signalling.

Published work:
J A H Gilburt, H Sarkar, P Sheldrake, J Blagg, L Ying & C A Dodson (2017). Dynamic equilibrium of Aurora-A kinase activation loop revealed by single molecule spectroscopy. Angew Chem Int Ed Engl 56(38) p11409-11414.

J A H Gilburt, P Girvan, J Blagg, L Ying & C A Dodson (2019). Ligand discrimination between active and inactive activation loop conformations of Aurora-A kinase is unmodified by phosphorylation. Chemical Science 10(14) p4069-4076.

Ultrastructure of protein complexes in the nucleus of human sperm cells revealed by cryo-ET

Dr Alia Dos Santos[1], Mr Oliver Knowles[1], Dr Tom Dendooven[1], Mr Thomas Hale[1], Dr Victoria Hale[1], Dr Alister Burt[2], Dr Piotr Kolata[1], Dr Giuseppe Cannone[1], Dr Dom Bellini[1], Dr David Barford[1], Dr Matteo Allegretti[1]

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Physics of the Nucleus, March 25, 2025, 14:15-16:15

During spermatogenesis, cells undergo key morphological changes which are essential for male fertility. Here, we used an integrative approach combining electron-cryo-tomography, optical microscopy and biochemical analysis, to reveal the in-situ structure of the human sperm Nuclear Pore Complex (NPC) and the presence of proteasome clusters in the nucleus of these cells.

The somatic NPC scaffold consists of three stacked rings: the cytoplasmic (CR), the nucleoplasmic (NR), and the inner ring (IR), which define a 55nm-wide central channel. We show that the human sperm NPC is composed exclusively by the IR and adopts a highly constricted conformation, with a central channel smaller than 40nm-wide. This is accompanied by a six-fold reduction in nuclear diffusion rates and mis-localization of active transport components, such as Ran and Importinβ1. We also identify a network of septin filaments interconnecting NPCs within the inter-membrane space of the nuclear envelope, suggesting a potential mechanical role in NPC constriction. Our human tissue data indicate meiotic exit as a pivotal differentiation stage driving these architectural changes.

Interestingly, we also reveal the presence of large proteasome clusters in the nucleus of human sperm cells. In-situ and single-particle structural approaches show that these clusters contain mixed populations of 20S and 20S-PA200 proteasomes, with testis-specific PSMA8 subunit. Our human tissue data also show that nuclear clustering correlates with protamine expression, and the nuclear presence of PA200, a specific adaptor that allows histone degradation.

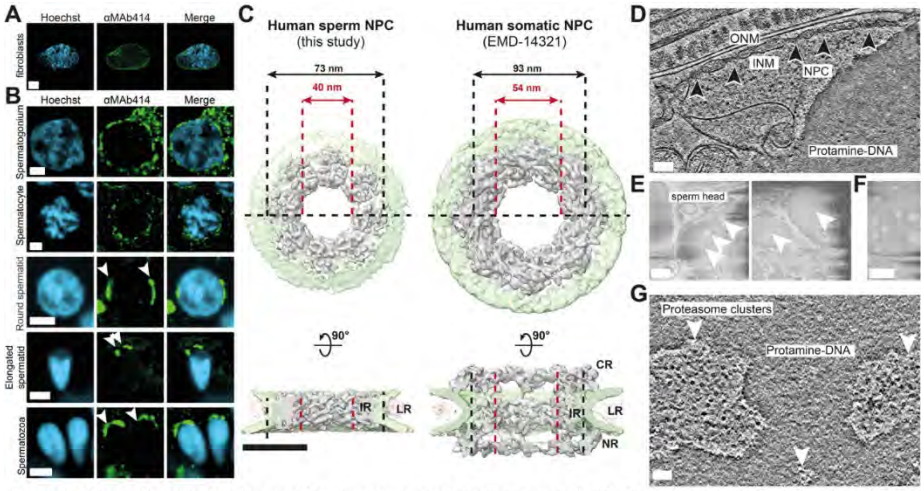

Figure 1 - Organisation and ultrastructure of nuclear complexes in human sperm cells. (A) Distribution of Nuclar Pore Complexes (NPCs) around the nucleus of a somatic cell (human fibroblast), using MAb414 (green) as a marker for NPCs. DNA is shown in cyan (Hoechst). Scale bar=5μm. **(B)** Spermatogenic cells at different stages of differentiation in human primary tissue (testis). MAb414 (green) shows NPC distribution and clustering and arrowheads indicate changes in localisation of NPCs in post-meiotic cells. Scale bar=5μm. **(C)** *In-situ* structure of the human sperm NPC (this study) and comparison with the previously published *in-situ* structure of the NPC of HEK cells (EMD-14321). Cytoplasmic ing (CR); inner ring (IR); nuclear ring (NR) and luminal ring (LR) indicated. Black dotted lines represent NPC diameter from membrane-to-membrane and red dotted lines represent diameter of central channel. Scale bar = 50nm. **(D)** Cryo-electron tomoagraphy data showing distribution of NPCs at the nuclear envelope of human sperm cells (arrowheads). Protamine-DNA and inner and outer nuclear membranes (INM and ONM, respectively) are also shown. Scale bar=100nm. **(E)** Human sperm cells. Slice-and-view data using cryo-focused ion beam and scanning electron microscopy. Large pockets highlighted with arrowheads can be observed inside the nucleus. Scale bar=500nm. **(F)** Zoom-in of nuclear pockets in a human sperm nucleus. Scale bar=500nm. **(G)** Cryo-electron tomography data of pockets present in the nucleus of human sperm cells (arrowheads) with visible proteasome particles present and surrounded by protamine-DNA. Scale bar=100nm.

Surface-Immobilized, pH-Responsive DNA Nanoswitches for Electronic Actuation

Miss Francisca D'Rozario[1], Dr. Callum Silver[1], Professor Christoph Walti[2], Dr Steven Quinn[1], Professor Steven Johnson[1]
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Natural and Synthetic Molecular Machines, March 27, 2025, 09:00-11:00

Dynamic DNA machines exploit the specificity of DNA base pairing and/or sensitivity to the local environment to fuel the reversible switching of DNA constructs between conformational states. One such example are pH-sensitive DNA nanoswitches that can be actuated by proton-mediated Hoogsteen interactions within a DNA triplex domain. To date, studies of pH-sensitive DNA nanoswitches have largely focused on DNA machines that are freely diffusing in the solution phase. For many applications, it is advantageous to integrate these dynamic DNA machines with solid-state devices, requiring immobilization on surfaces.

Here, we explore switching of a pH-sensitive DNA triplex immobilized on a surface as a dense, 2-dimensional DNA monolayer. DNA nanoswitches were examined using quartz crystal microbalance with dissipation monitoring (QCM-D) and single-molecular Förster resonance energy transfer techniques. These experiments indicate that despite the high density of DNA (10^12 molecules/cm^3) within the monolayer, pH-switching between open and closed states is retained following immobilization. Moreover, conformational switching of DNA constructs within the monolayer remains highly reversible and repeatable, with no reduction in switching efficiency observed over 20 switching cycles.

Finally, we demonstrate electrically driven, localised, and addressable switching of the DNA triplex by employing electrochemical reduction and oxidation of water at an electrode surface, further demonstrating the potential of technology for surface-immobilized dynamic DNA machines. This study not only provides insight into the actuation of DNA machines on-surface but also supports the development of new technologies such as hybrid electronic-DNA technologies able to store and process information using both molecular and electronic inputs.

Active control of focal adhesions and contractility in cells and tissues: understanding the role of mechanical coupling

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Tissue Growth, Mechanics and Mechanosensing, March 26, 2025, 15:30 - 17:30

Mechanobiological signals direct and coordinate cell behaviours across tissue types, with cell adhesion and contractility playing key roles. In individual cells, it is observed that focal adhesions and cytoskeletal contractility are both mechanosensitive, changing their magnitude and spatial distribution in response to microenvironment stiffness. Within tissues, such adaption is made more complex by the introduction of cell-cell attachments. Here, we develop a theoretical model for cell contractility coupled actively to the microenvironment enabling a whole systems perspective. In single cells, we show that experimentally observed changes in adhesion distribution and the upregulation of cellular contractility are fully explained by a consideration of the strain energy of the system. With Dr N. Tapon, Francis Crick Institute and Dr J.R. Davis, University of Manchester, we apply the framework to experimental observations of tissue layers, micropatterned to control adhesion. Here, our theoretical model predicts mechanical contractility and indeed correctly predicts specific regions of peak mechanical activity.

Furthermore, we discover that increasing gel stiffness promotes uniform contractility activity in all cells in fully adhered layers. However, for tissues with adhesion restricted to the layer edges, increasing stiffness does not have this effect, rather there is an observed (and predicted) concentration of contractile activity to the tissue edge. These results show that adhesion and contractility cannot be considered separately but must be studied as integrated components within an active coupled system.

[1] J.Solowiej-Wedderburn, C.Dunlop. Biophys. J. 121(9), (2022).
[2] J.Solowiej-Wedderburn, C.Dunlop. Phys Rev E, 107(6), (2023).
[3] J.R.Davis, J.Solowiej-Wedderburn, S.L.Vega, J.A.Burdick, C.Dunlop, N.Tapon. bioRxiv, 2024.04.10.588783.

Mechanics of entropic biopolymer networks from the thermodynamics of molecular motors

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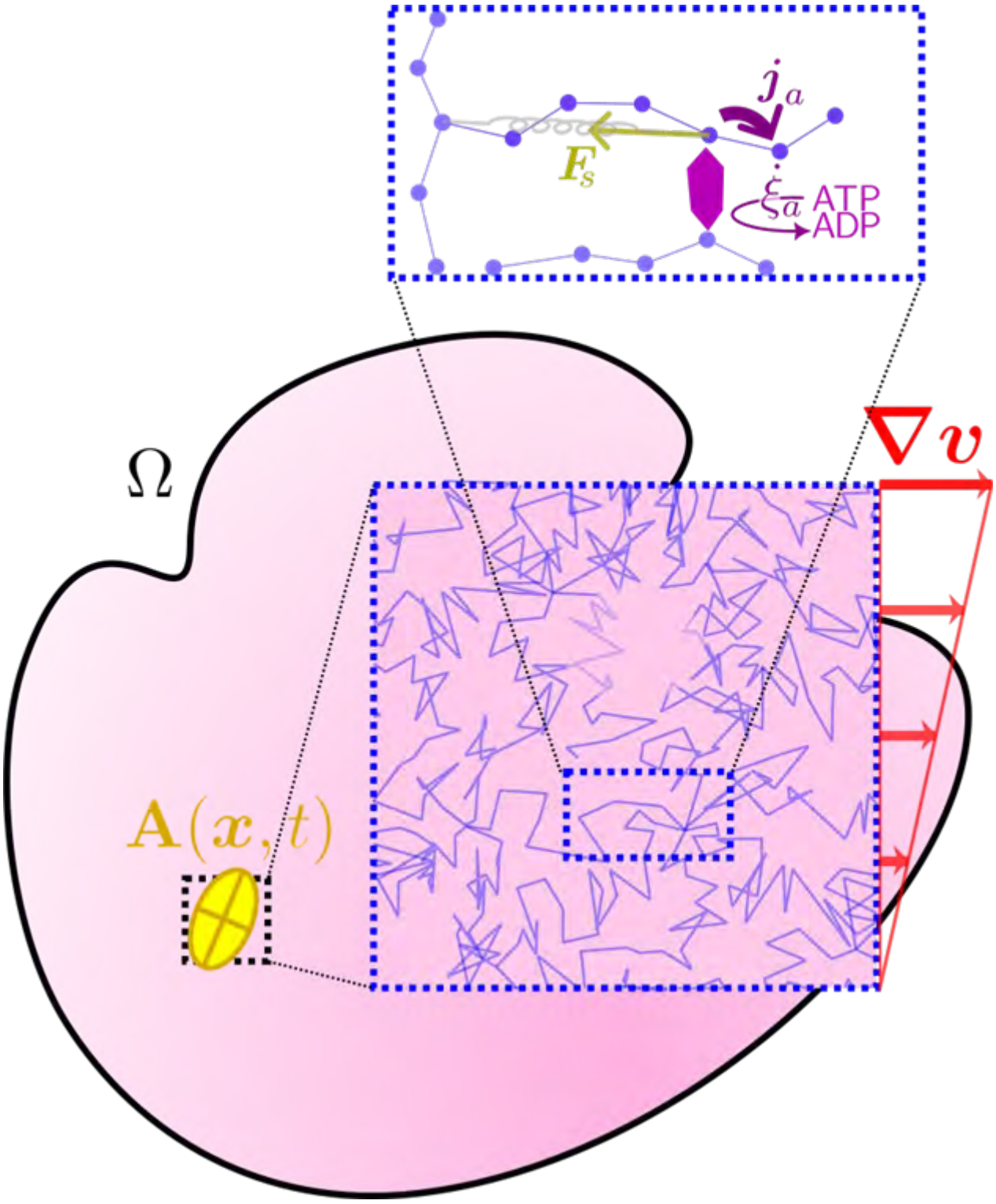
Natural and Synthetic Molecular Machines, March 27, 2025, 09:00-11:00

Contractile biopolymer networks, such as the actomyosin meshwork of animal cells, are ubiquitous in living organisms and contribute in a large part to their function such as muscle contraction or embryonic morphogenesis.

Their contractility relies on the active behaviour of molecular motors which crosslink the biopolymer of the network and can transduce at the molecular scale chemical energy into mechanical work (Jülicher et al, Rev Mod Phys, 1997).

The active gel theory (Kruse et al, Eur Phys J E, 2005), which provides a thermodynamic framework for these materials, has been mostly used in conjunction with the assumption that the microstructure of the biopolymer network is based on rigid rods (Liverpool and Marchetti, Phys Rev Lett, 2006). However, experimentally, crossed-linked actin networks exhibit entropic elasticity (Gardel et al, Science, 2004). Here we combine an entropic elasticity kinetic theory, in the spirit of the Green and Tobolsky model (J Chem Phys, 1946) of transiently crosslinked networks, with an active flux modelling motor activity (arXiv:2405.07287).

We determine this active flux using Onsager reciprocal relations applied at the microscopic scale of individual motors. We derive the macroscopic active stress that arises from the resulting dynamics and obtain a closed-form model of the macroscopic mechanical behaviour. Although similar to models commonly chosen in the active gel theory, the choice of entropic elasticity provides it with specific features of quantitative importance (Etienne et al, PNAS, 2015). Additionally, the analytical clarity of the derivation allows us to give microscopic interpretation of macroscopic active behaviours of contractile networks.


j_a
F_s
ξ_a
ATP
ADP
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Modelling evolution of risk-aversion and extreme altruism

Dr Mike Evans[1]
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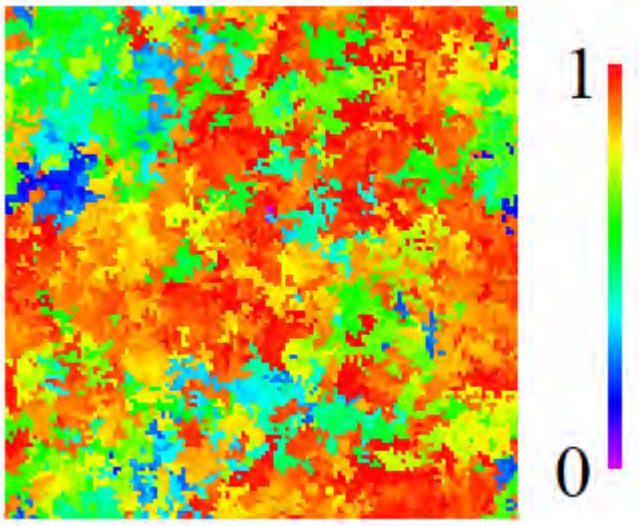
Evolution, Ecology and Epidemiology, March 24, 2025, 15:30-17:30

All organisms descend from populations with limited resources, so it is clear why evolution should select strategies that win resources at the expense of competitors. Less obvious is how altruistic behaviours evolve, whereby an individual helps others despite expense to itself. A number of evolutionary mechanisms are known to give rise to moderate levels of altruism under certain conditions.

I will demonstrate a newly discovered mechanism, whereby Evolutionary Game Theory predicts that extreme altruism can evolve when payoffs are very rare compared with death [1]. In these states, agents (representing organisms) give away most of their wealth (representing natural resources).

More generally, I will explain a new theorem for evolutionary models, showing that, when pay-offs are rare, evolution no longer selects strategies to maximize income (average pay-off), but to minimize the risk of missing-out entirely on a rare resource. Principles revealed by the theorem are widely applicable, where the game represents rare life-changing events: disasters or gluts.

[1] Pay-off scarcity causes evolution of risk-aversion and extreme altruism, R M L Evans, Sci. Rep 8:16074 (2018).



Enhancing immunotherapies: Insights from the mathematical modelling of a microfluidic device

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Physics of Disease, March 27, 2025, 09:00-11:00

A pivotal aspect of producing effective immunotherapies for solid tumours is the robust testing of product efficacy inside in vitro platforms. Collaborating with an experimental team that developed a novel microfluidic device at Children's National Hospital (CNH), we developed a mathematical model to investigate immune cell migration and cytotoxicity within the device. We study specifically Chimeric antigen receptor (CAR) T-cell migration inside the channels with the cell as a moving boundary, driven by a chemoattractant concentration gradient. We investigate the motion of the cell as a function of its occlusion of the channel and validate our findings against experimental data provided by CNH. Specifically, we identify parameter regimes under which cells clog the channel, impairing their movement.

We integrate our model results into a more general model of the device. It provides a tool for disentangling experimental artefacts from genuine CAR T-cell behaviour. This collaboration enabled the team at CNH to refine experimental conditions and uncover mechanisms enhancing CAR T-cell efficacy.

[1] D Irimia, G Charras, N Agrawal, T Mitchison, M Toner, Polar stimulation and constrained cell migration in microfluidic channels, Lab on a Chip 7 (12), 1783-1790

Investigating the relationship between chromatin structure and dynamics

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Physics of the Nucleus, March 25, 2025, 14:15 - 16:15

In living cells, the 3D structure of gene loci is dynamic, but this is not revealed by 3C and FISH experiments in fixed samples, leaving a notable gap in our understanding. To overcome these limitations, we applied the highly predictive heteromorphic polymer (HiP-HoP) model to determine chromatin fiber mobility at the Pax6 locus in three mouse cell lines with different transcription states. While transcriptional activity minimally affects movement of 40-kbp regions, we observed that motion of smaller 1-kbp regions depends strongly on local disruption to chromatin fiber structure marked by H3K27 acetylation. This also substantially influenced locus configuration dynamics by modulating protein-mediated promoter-enhancer loops.

Importantly, these simulations indicate that chromatin dynamics are sufficiently fast to sample all possible locus conformations within minutes, generating wide dynamic variability within single cells. This combination of simulation and experimental validation provides insight into how transcriptional activity influences chromatin structure and gene dynamics.

Mesoscale properties of biomolecular condensates emerge from nanoscale dynamics

Nicola Galvanetto[1], Miloš Ivanović[1], Simone Del Grosso[1], Aritra Chowdhury[1], Andrea Sottini[1], Daniel Nettels[1], Robert Best[2], Ben Schuler[1]
[1]University of Zurich, Switzerland, [2]National Institutes of Health, USA

Biomolecular Assemblies and Condensates, March 25, 2025, 10:15-12:15

Biomolecular condensates are droplets-like structures originating from the phase-separation of biomolecules. The functions of condensates within living cells span many length scales: from the modulation of chemical reactions at the molecular scale to the compartmentalization of the cell at the mesoscale. We employ single-molecule fluorescence spectroscopy to study the conformations and dynamics of intrinsically disordered proteins within single droplets (1), combined with microrheology approaches to assess mesoscale properties. By tuning the strength of the interactions among the constituent proteins, we produced condensates spanning almost two orders of magnitude in viscosity. We find that the nanoscale chain dynamics on the nano- to microsecond timescale can be accurately related to both translational diffusion and mesoscale condensate viscosity by analytical relations from polymer physics (2).

Atomistic simulations reveal that the differences in friction — a key quantity underlying these relations — are caused by differences in inter-residue contact lifetimes, thereby leading to the vastly different dynamics among the condensates. The rapid exchange of inter-residue contacts we observe may be a general mechanism for preventing dynamic arrest in compartments densely packed with polyelectrolytes, such as the cell nucleus.

(1) N. Galvanetto, et al., Extreme dynamics in a biomolecular condensate. Nature 619, 876–883 (2023).
(2) N. Galvanetto, et al., Mesoscale properties of biomolecular condensates emerging from protein chain dynamics. arXiv:2407.19202 (2024).

RNA plasticity emerges as an evolutionary response to fluctuating environments

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[1]Department of Chemical Engineering and Biotechnology, University of Cambridge, United Kingdom, [2]The Alan Turing Institute, United Kingdom

Evolution, Ecology and Epidemiology, March 24, 2025, 15:30-17:30

Phenotypic plasticity, the ability of a single genotype to produce multiple distinct phenotypes, can be studied effectively using RNA. RNA is a dynamic macromolecule that probabilistically shifts its structure due to thermal fluctuations at the molecular scale. To model the evolution of RNA plasticity, we use the RNA sequence- to-structure non-deterministic mapping, a computationally tractable genotype-phenotype (GP) map where probabilistic phenotypes are derived from the Boltzmann distribution of structures for each RNA sequence.

Through evolutionary simulations with periodic environmental switching on the GP map, we observe that RNA phenotypes adapt to these fluctuations by evolving toward optimal plasticity. These optimal phenotypes are defined by nearly equal Boltzmann probabilities for distinct structures, each representing the most advantageous configuration for alternating environments. Our findings demonstrate that phenotypic plasticity, a widespread biological phenomenon, is a fundamental evolutionary adaptation to fluctuating environments.

Legionella regulation of biofilm growth through a unique protein conformational switching mechanism

Leanne Cleaver[1], Anna Katarina Antonovic[2], Carlton Adams[3], Mark Freeley[2], Saima Rehman[1], Chris White[3], Theo Portlock[1], Sara B Whittaker[4], Matteo Palma[2], Arianna Fornili[2], Nicholas Cianciotto[3], James Garnett[1]

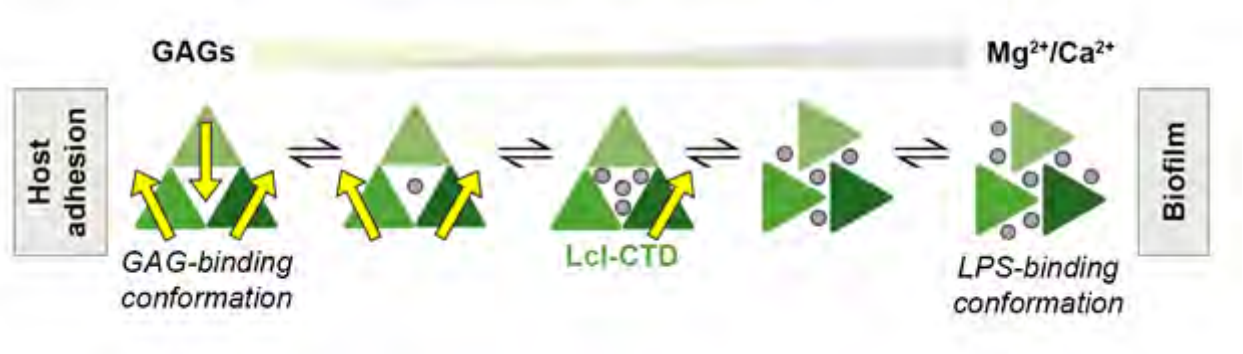
[1]King's College London, United Kingdom, [2]Queen Mary University of London, United Kingdom, [3]Northwestern University, USA, [4]University of Birmingham, United Kingdom

Protein Structure, Dynamics and Interactions, March 24, 2025, 15:30-17:30

Biofilm formation is an important survival strategy commonly employed by bacteria, which are embedded in an extracellular matrix comprising proteins, carbohydrates, lipids, and DNA. This provides protection against environmental pressures such as shear flow, host immune/inflammatory responses, and antimicrobial agents. Legionella pneumophila is a Gram-negative bacterium that inhabits natural/artificial freshwater systems within multispecies biofilms. It replicates within amoebae but also infects the human lung and causes Legionellosis. The Legionella collagen-like (Lcl) protein is an extracellular peripheral membrane protein, with a fundamental role in ecology and infection of lung tissue, through mediating biofilm formation and adhesion/entry into host cells, respectively.

In our recent work (1) we revealed how Lcl has a “lollipop-shaped” structure with a globular head and a stalk, consistent with a trimer of C-terminal domains (CTD) and a triple helical collagen-like region. Moreover, we determined the structure of the CTD and demonstrated how it recognises glycosaminoglycans and mediates host adhesion through a unique fuzzy binding mechanism. Using X-ray crystallography, molecular dynamics simulations and other biophysical approaches we now show how Mg2+ ions bind within a negatively charged internal cavity, and this results in CTD trimer rearrangement. In this state, rather than binding glycosaminoglycans, the CTD interacts with the lipopolysaccharide of L. pneumophila, and other Gram-negative bacteria commonly associated with these biofilms. Our study establishes a novel conformational switching mechanism where local concentrations of lipopolysaccharide and divalent cations, and glycosaminoglycans, select for initiation of biofilm growth or infection of eukaryotic hosts.

1) Rehman et al. (2024) Nature Communications, 15, 4912.



Evolutionary Implications of Self-Assembling Cybernetic Materials with Collective Problem-Solving Intelligence at Multiple Scales

Dr. Benedikt Hartl[1,2], Dr. Sebastian Risi[3], Dr. Michael Levin[1,4]
[1]Allen Discovery Center at Tufts University, USA, [2]TU Wien, Vienna, Austria, [3]Digital Design, IT University of Copenhagen, Copenhagen, Denmark, [4]Wyss Institute for Biologically Inspired Engineering, Harvard University, Boston, USA

Engineering Tissues and Organoids and Biohybrids, March 25, 2025, 14:15-16:15

The complex multi-scale competency architecture (MCA) of biological systems [1] - comprising nested layers of interwoven agential components - provides inspiration for advancing biomedical engineering and truly bio-inspired AI. Understanding how such architectures emerge and function is an ongoing challenge in both evolutionary developmental biology and bioengineering [2].

Here [3], we explore the influence of decision-making competencies within an MCA framework using in-silico morphogenesis experiments. We specifically model organismal development with neural cellular automata (NCAs) and evolve the functional parameters of unicellular agents to collectively self-assemble a two-dimensional cybernetic target tissue via locally-interactive self-regulatory pathways. By systematically varying the reliability of cell-type regulation, we examine how different levels of agent competency - ranging from a direct encoding scheme to an MCA - impact the developmental- and governing evolutionary processes.

Our simulations reveal that higher levels of unicellular competency and, in turn, higher noise conditions during evolutionary training, facilitate more efficient and robust pattern formation and yield NCAs with increased adaptability to changing objectives and parameter variations. While further work is needed to translate these insights to physical systems, our findings underscore the potential of leveraging MCA principles to advance the engineering of intrinsically intelligent, self-organizing materials.

1. M. Levin, Cell. Mol. Life Sci., 80, 1420-9071 (2023).
2. M. Levin, Front. Syst. Neurosci. 16, 768201 (2022).
3. B. Hartl, S. Risi, M. Levin, Entropy, 26, 532 (2024).

How does a finger get its knuckles? Reaction diffusion models in the tetrapod limb and beyond

Emmanuelle Grall[2], Daniel Muzatko[1], Jake Cornwall Scoones[3], Bijoy Daga[1], Christian Feregrino[2], Sabrina Fischer[2], Aline de Courten[2], Fabio Sacher[2], Patrick Tschopp[2], **Tom Hiscock**[1]
[1]University of Aberdeen, United Kingdom, [2]University of Basel, Switzerland, [3]University of Cambridge (present address: Francis Crick Institute)

Differentiation and Development, March 24, 2025, 15:30-17:30

The formation of periodic patterns is an essential process in the development of most organisms, generating identical/similar structures (e.g., teeth, hair, leaves) that repeat within a tissue at regular spatial intervals. Here, we investigate the repeating pattern of joints that form in tetrapod digits, which allow our fingers/toes to bend, and thus enable a diversity of limb functions across species (e.g., walking, grasping, flying). Whilst many relevant genes and cell behaviours have been identified, it remains unclear how these key players coordinately control the location, number, and orientation (i.e., the patterning) of joints within each digit.

We have developed dynamical models (PDEs) to describe the spatiotemporal dynamics of this periodic patterning mechanism. Drawing on decades of molecular genetics, we have identified a reaction-diffusion system – involving BMP signalling – that can self-organize joint-like patterns in silico. We find that our mathematical model closely recapitulates quantitative expression dynamics measured in vivo. Moreover, we can phenocopy skeletal malformations seen across a range of BMP mutants/perturbations, as well as congenital joint disorders of the hand. Our model also predicts some rather unusual patterns that are observed in certain mouse mutants, e.g., the formation of an extra joint along the digit, i.e., rotated 90 degrees to its usual orientation.

This BMP-based reaction-diffusion system is more complex, and significantly more robust, than standard Turing models. Inspired by the digits, we are now investigating more general limits on pattern formation involving complex, biologically-aligned reaction-diffusion circuits, looking for novel self-organizing mechanisms fundamentally beyond classic Turing patterns.

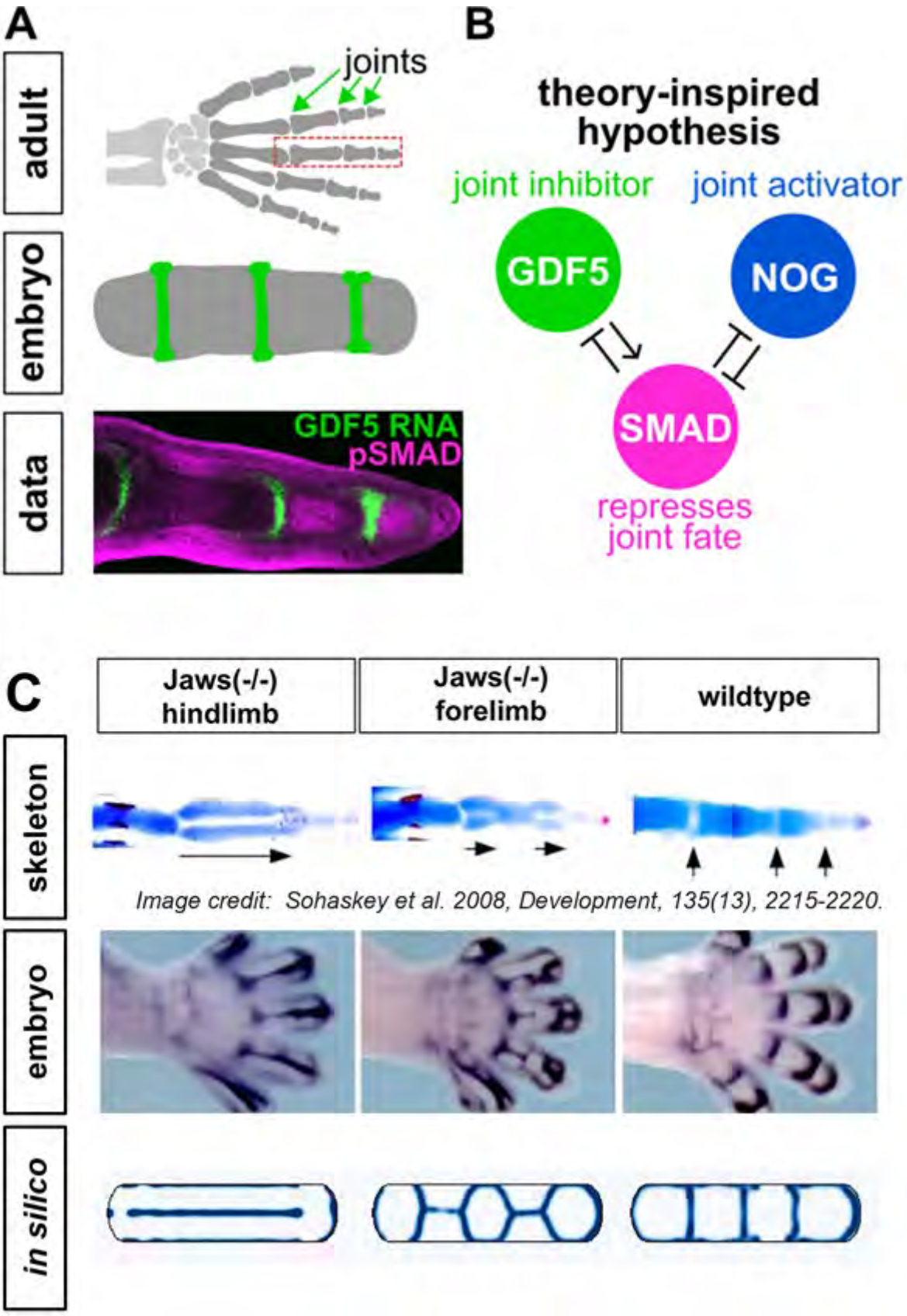

A
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Image credit: Sohaskey et al. 2008, Development, 135(13), 2215-2220.
embryo
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Stem cell density regulation in mouse skin homeostasis

Joel Hochstetter[1,2], Dan Engelman[3], Anais Baudin[3], Qiuyu Lian[2], Adrien Hallou[4], Cedric Blanpain[3], Benjamin Simons[1,2]

[1]DAMTP, University of Cambridge, United Kingdom, [2]Gurdon Institute, University of Cambridge, United Kingdom, [3]Laboratory of Stem Cells and Cancer, Université Libre de Bruxelles, Belgium, [4]Kennedy Institute, University of Oxford, United Kingdom

Differentiation and Development, March 24, 2025, 15:30-17:30

Stem cells tightly balance cell division and differentiation to maintain tissue homeostasis. Squamous tissues (e.g., skin, oesophagus) have stem cells arranged in a spatially extended quasi-2D layer with their more differentiated progeny. This raises the question of what strategies and feedback mechanisms ensure a robust density and cell-type proportions over time. In mouse skin interfollicular epidermis, we interrogate strategies of homeostatic maintenance through long-term time-lapse imaging of clonal dynamics. To decipher the data, we introduce a spatial Voronoi model with loss and replacement allowing us to contrast different paradigms for stem cell dynamics. We find that widely supported one-progenitor models fail to capture fine-grained static and temporal features of clonal dynamics. Our analysis reveals a proliferative hierarchy with differentiation occurring via a transit amplifying progenitor population which mostly execute one round of division. We infer a tight coordination in divisions and delamination between neighbouring sisters, leading to the robust features in the clonal data.

We find that the ratio of the combined progenitor populations and differentiated cells is more controlled than a random organisation at short length-scales. Comparing with our spatial model, our results support that stem cell fate decisions are influenced by the proportion of cell-types, not just the local cell density. The finding of multiple proliferative populations executing coordinated divisions and delaminations is valuable in moving towards the formidable challenge of understanding how molecular mechanisms lead to emergent feedback rules at the cell to tissue scale to maintain homeostasis.

Cellular prediction during variation in carbon availability

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[1]University of Edinburgh, United Kingdom, [2]AMOLF, Netherlands

Cell Metabolism and Growth, March 27, 2025, 09:00-11:00

When sugar runs out, cells of budding yeast that shift their metabolism from fermentation to respiration exhibit faster growth and improved adaptation. Those cells capable of predicting this scarcity by sensing both the concentration and variation of nutrients have little lag in growth.

We characterised this decision-making process using microfluidics and the dynamic relocation of transcription factors between the cytoplasm and nucleus. To achieve controlled but time-varying concentrations of sugar, we developed a novel microfluidic device. This device incorporates a serpentine micro-mixer and single-cell ALCATRAS traps to enable high-resolution, single-cell images in linearly changing sugar concentrations. To quantify transcription factor relocation from the resulting bright-field images, which previously has been ad hoc, we developed a universal convolutional neural network that enables efficient, accurate analysis, facilitating high-throughput studies.

Together, the new convolutional neural network and microfluidic device offer a powerful, integrated approach for studying how cells predict in dynamic environments. We demonstrate that yeast cells robustly anticipate low glucose levels by synchronously translocating multiple transcription factors, highlighting the remarkable adaptability of cells to changing environments.

A nuclear jamming transition in embryonic tissues

Professor Sangwoo Kim[1], Rana Amini[2], Shuo-Ting Yen[2], Petr Pospisil[2], Arthur Boutillon[2], Ilker Ali Deniz[2], Otger Campas[2]
[1]Epfl, Switzerland, [2]Cluster of Excellence Physics of Life, TU Dresden, Germany

Tissue Growth, Mechanics and Mechanosensing, March 26, 2025, 15:30-17:30

Tissue physical states are tightly regulated during embryonic development and tissue morphogenesis. While distinct cellular properties such as cell packing density and cell-cell contact mechanics are known to control tissue mechanics and rigidity transitions, the role of sub-cellular organelles remains largely unexplored. Through a combination of theoretical modeling and in-vivo experiments, we identify a novel rigidity transition, nuclear jamming transition, governed by nuclear volume fraction and nuclear aspect ratio. To study how nuclei affect tissue structure and dynamics, we implement nuclei as stiff particles, interacting repulsively with cell junctions in the Active Foam Model. For isotropic nuclei, tissue dynamics progressively slow down as nuclear volume fraction increases, a signature of fluid-solid transitions.

The nuclear jamming transition also induces crystalline ordering in tissue structures for isotropic nuclei. When the nuclear aspect ratio increases, jamming occurs at lower nuclear volume fractions because anisotropic nuclei start to interact with cell junctions at lower nuclear volume fraction, slowing down tissue dynamics. At high nuclear volume fractions and nuclear aspect ratios, nuclei significantly deform cell shapes, resulting in the formation of nematic domains and enhanced cell motility. Analysis of tissue structures, nuclear movements, and mechanical properties of developing retinal tissues in zebrafish embryos reveals that these tissues undergo nuclear jamming transition. Our result highlights a novel rigidity transition governed by nuclei, which may play a crucial role in mechanical regulation during embryonic development.

The physics of a microbial railway network

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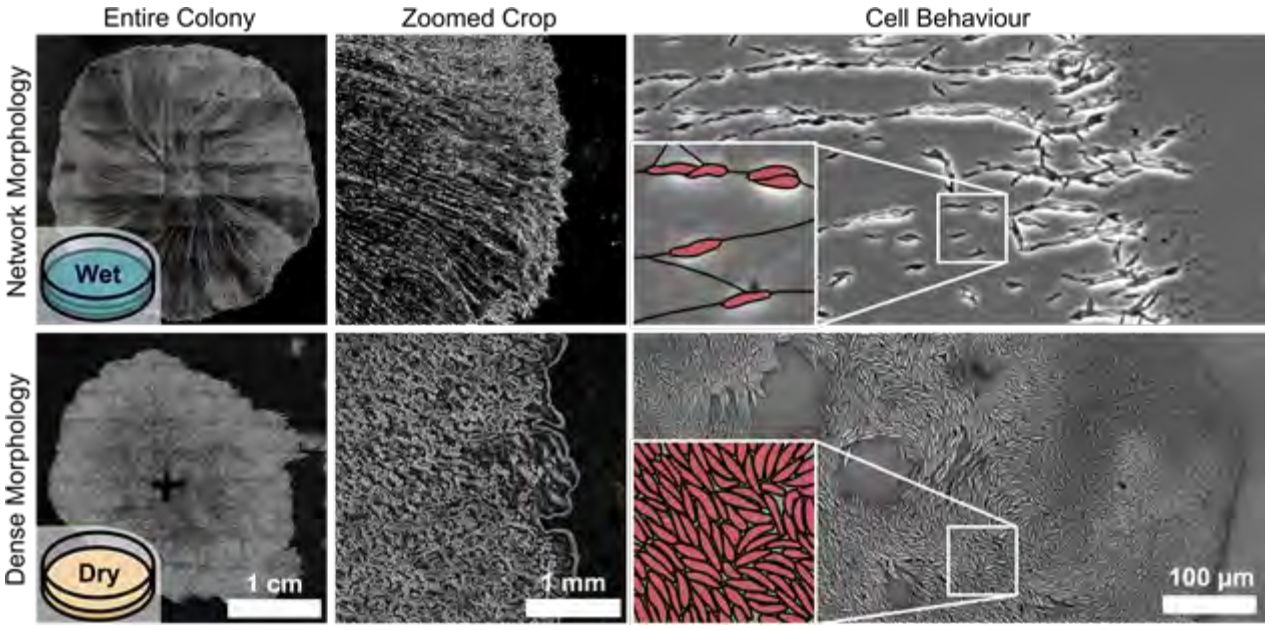
Patterns, Waves, Transport, Collective Phenomena and Microswimmers, March 25, 2025, 10:15-12:15

Labyrinthula species are protist 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 classify the behaviour of growing network colonies. We further show that the network morphology requires colony submersion beneath a seawater layer. For colonies exposed directly to air, we detail a densely packed morphology. We systematically add and remove this seawater layer to mimic the environment of an intertidal seagrass meadow, showing that Labyrinthula can switch between these two colony morphologies.



Exploring DNA Linkers for Biomimetic Cell Adhesion of Red Blood Cells

Sebastian W. Krauss[1], Roger Rubio-Sánchez[1], Bortolo M. Mognetti[2], Lorenzo Di Michele[1], Pietro Cicuta[3]

[1]Department of Chemical Engineering and Biotechnology, University of Cambridge, United Kingdom, [2]Department of Physics, ULB, Belgium, [3]Department of Physics, University of Cambridge, United Kingdom

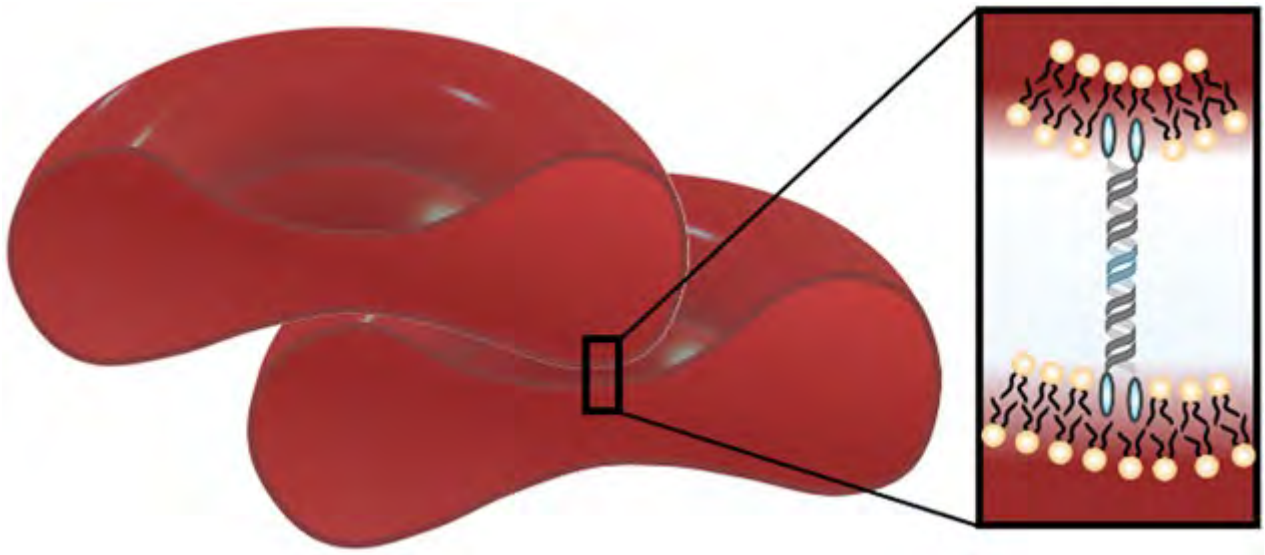
Engineering Tissues and Organoids and Biohybrids, March 25, 2025, 14:15-16:15

Ligand-receptor interactions are fundamental to cellular membrane dynamics, influencing a range of processes like cell-cell signaling, wound healing, and viral infections. The affinity and specificity of these molecular interactions govern how adjacent membranes recognize, bind, and respond to one another, ultimately determining the strength and stability of membrane contacts. To better understand these mechanisms, we developed a biomimetic approach that grants precise control over the strength of interactions between complementary receptors in opposing membranes. Our strategy employs short membrane-anchored amphiphilic DNA nanostructures featuring single-stranded 'sticky-ends', which through complementary sequences, are designed to bind labelled objects, providing a programmable platform for membrane-membrane interactions [1].

We implemented our method to functionalize the surface of red blood cells (RBCs) with complementary DNA, resulting in the formation of cellular aggregates, with tunable morphologies, ranging from doublets to star-like geometries, depending on mixing ratios and cell density. Additionally, we used DNA-functionalized particles to selectively bind RBCs. By tuning the length of the DNA sticky-ends, we precisely controlled interaction strength, enabling RBCs to progressively envelop beads. Furthermore, we employed optical tweezers to observe the rapid formation of strong bonds in situ [manuscripts in preparation].

This model system offers a versatile platform to understand the forces and dynamics of RBC aggregation and their interactions with pathogens, such as Plasmodium species responsible for malaria. Moreover, the ability to fine-tune interaction strengths opens new possibilities for developing synthetic tissues with programmable adhesion properties.

1. Chem. Comm. 57, 12725-12740 (2021).



Bionanomachine Networks: Development of Functional All-Enzyme Hydrogels for Responsive Biomaterials in Healthcare

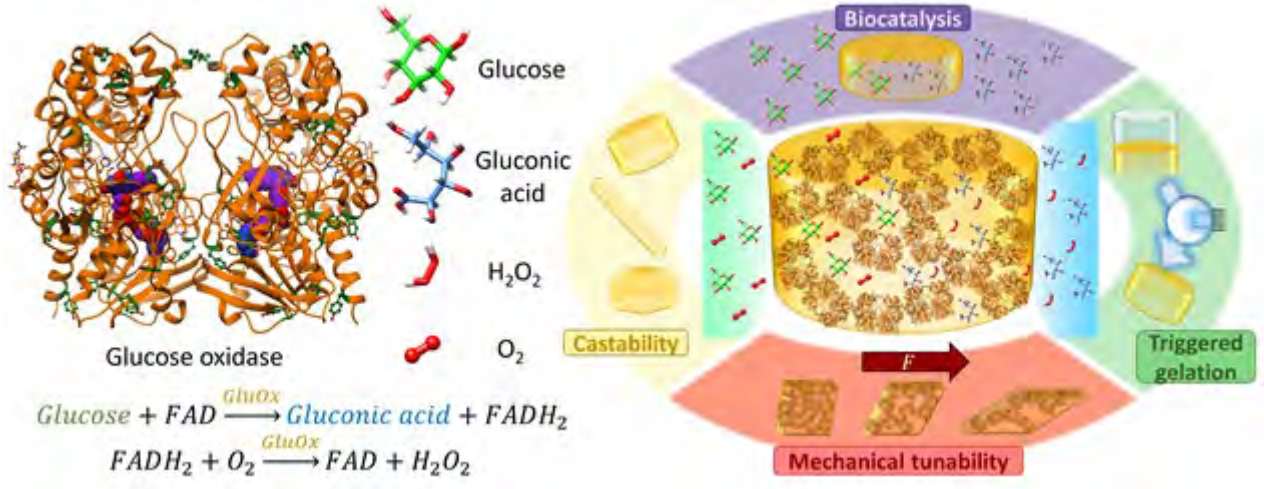
Dr Harrison Laurent[1], Dr Matt Hughes[1], Dr Najet Mahmoudi[2], Professor David Brockwell[1], Professor Lorna Dougan[1]
[1]University of Leeds, Leeds, United Kingdom, [2]ISIS Neutron and Muon Source, United Kingdom

Natural and Synthetic Molecular Machines, March 27, 2025, 09:00-11:00

The catalytic biomachines of life, enzymes, have attractive properties as catalysts due to their substrate specificity and biocompatibility, however their use in industrial and biomedical applications is limited by stability and ease of recovery. A popular solution is immobilisation of enzymes within hydrogel matrices, however the volumetric productivity of these materials is not optimised, since the hydrogel matrix is often noncatalytic. Here we present a facile approach for nanoscale engineering of all-enzyme hydrogels through photochemical covalent cross-linking of the homodimeric oxidoreductase enzyme glucose oxidase (EC 1.1.3.4) into a functional network[1]. This allows the enzyme to be both structural and catalytic in its function. Here we present an important demonstration of the potential of all-enzyme hydrogels for responsive and functional biomaterials.

We use oscillatory shear rheology to measure the mechanical robustness of the enzyme hydrogels, small angle neutron scattering to investigate their microstructure, use an established Tinder assay to quantify their catalytic activity and apply a 1D modelling approach to these data to determine enzyme-substrate affinity. This approach provides enormous potential producing functional biocatalytic materials with tuneable mechanical properties and high volumetric productivity which may find application in glucose sensing and medical device manufacture for diabetes[2] and industrial catalysis for the synthesis of pharmaceuticals[3].

[1] Laurent, H.; Brockwell, D. J.; Dougan, L. Biomacromolecules 2024, Under Review.
[2] Song, J. et al; npj Flex. Electron. 2021, 5 (1).
[3] Sun, H. et al; Bioorganic Med. Chem. 2018, 26 (7), 1275–1284.



A simple four archetype model of infection space

Yael Lebel[1], David Samuel Schneider[2]
[1]Department of Molecular Cell Biology, Weizmann Institute of Science, Israel, [2]Department of Microbiology and Immunology, Stanford University, USA

Immunity, Resistance and Host/Pathogen Dynamics, March 26, 2025, 15:30-17:30

What can an individual's response to one pathogen reveal about their reaction to other immune challenges? By comparing malaria outcomes in diverse mice infected with Plasmodium chabaudi to published data on other pathogens, we found that mice resilient to P. chabaudi exhibited poor outcomes when challenged with influenza, SARS-CoV-1, or Mycobacterium tuberculosis, and vice versa. This supports the hypothesis that the immune system's interconnectedness creates tradeoffs, where resilience to one pathogen reduces resilience to others.

We identified distinct archetypes of responses based on microbial load, immune activity, and host damage. To better understand the nature of these archetypes, we developed a mathematical model of a generalized host-pathogen system. This model characterizes the number, shapes, and distribution of response archetypes across a population of diverse hosts, integrating concepts from disease tolerance, the damage-response framework, and histrionic inflammation into a unified description of infections within a health-microbe-immunity space. Our findings suggest that understanding a host's response to one pathogen serves as a stress test, revealing insights not only about the first pathogen but also enabling predictions of outcomes for subsequent infections.

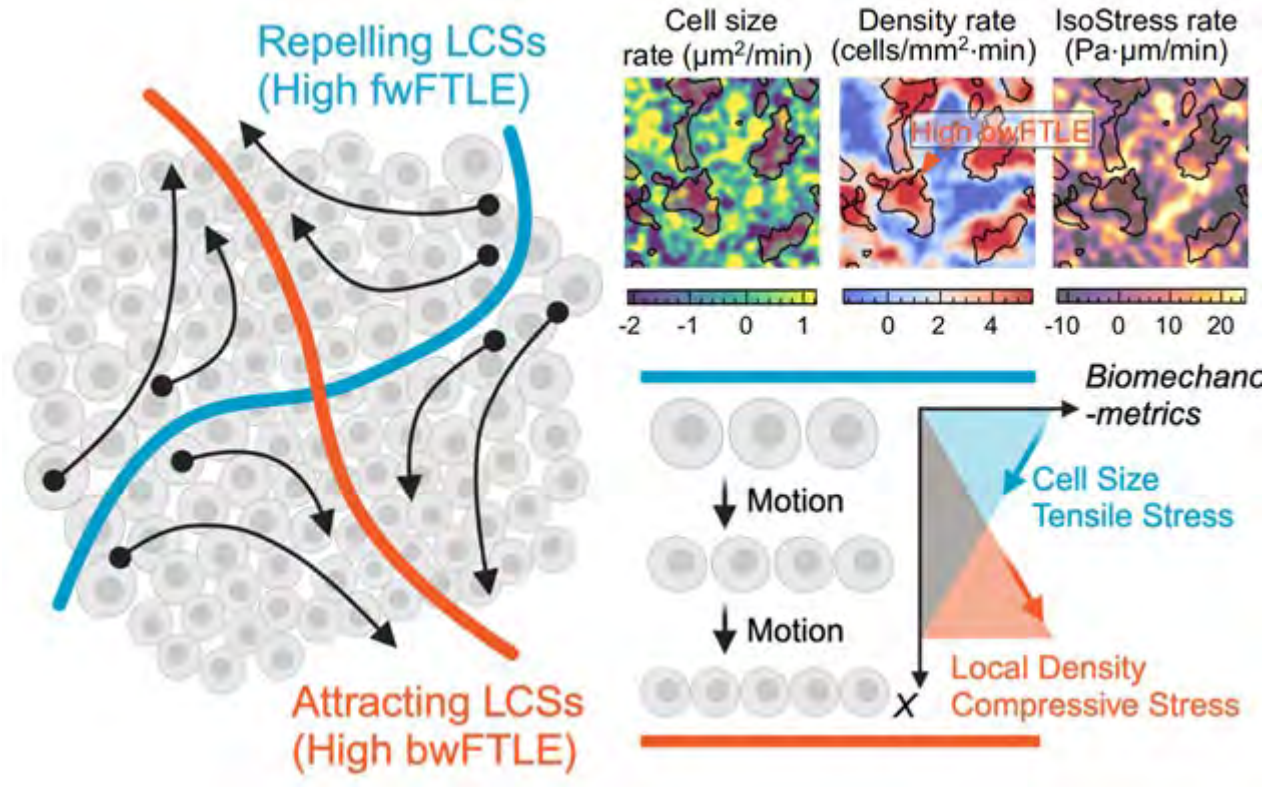
Hidden Spatiotemporal Biomechanics underlying Multicellular Coherent Motions

Tianxiang Ma[1], Valeriia Grudtsyna[1], Robin Bölsterli[1], Amin Doostmohammadi[1]
[1]*Niels Bohr Institute, University of Copenhagen, Denmark*

Patterns, Waves, Transport, Collective Phenomena and Microswimmers, March 25, 2025, 10:15-12:15

Biomechanical reorganization is crucial for fundamental biological processes such as morphogenesis and development. Key biomechanical metrics—including cell shape, local density, and stresses—govern multicellular mechanotransduction and regulate cellular functions. However, assessing these metrics often requires additional measurements and specialized techniques, posing significant challenges. Here, we introduce a unified framework that predicts diverse biomechanical metrics using only cell trajectory data by identifying Lagrangian Coherent Structures (LCSs)—robust multicellular attractors and repellers.

We reveal strong correlations between LCSs and biomechanical metrics, showcasing their ability to bridge the scale mismatch between microscopic cell motion and mesoscopic biomechanics, thereby surpassing the limitations of conventional Eulerian descriptions of cell motion. Repelling LCSs, characterized by forward Finite-Time Lyapunov Exponents (fwFTLE), are associated with increased cell size, decreased local density, and elevated tensile stress, while attracting LCSs, indicated by backward FTLE (bwFTLE), exhibit opposite trends. Notably, we demonstrate that the formation of LCSs precedes cellular stress reorganization, enabling short-term FTLE data to predict long-term, persistent changes in stress. Ultimately, these results establish a simple yet transformative framework for predicting biomechanical factors solely from cell motion, offering potential for forecasting a wide array of mechanosensitive cellular behaviors.



Lung-like spatial limits and mechanical forces enable C. albicans survival in a pathogenic polymicrobial community

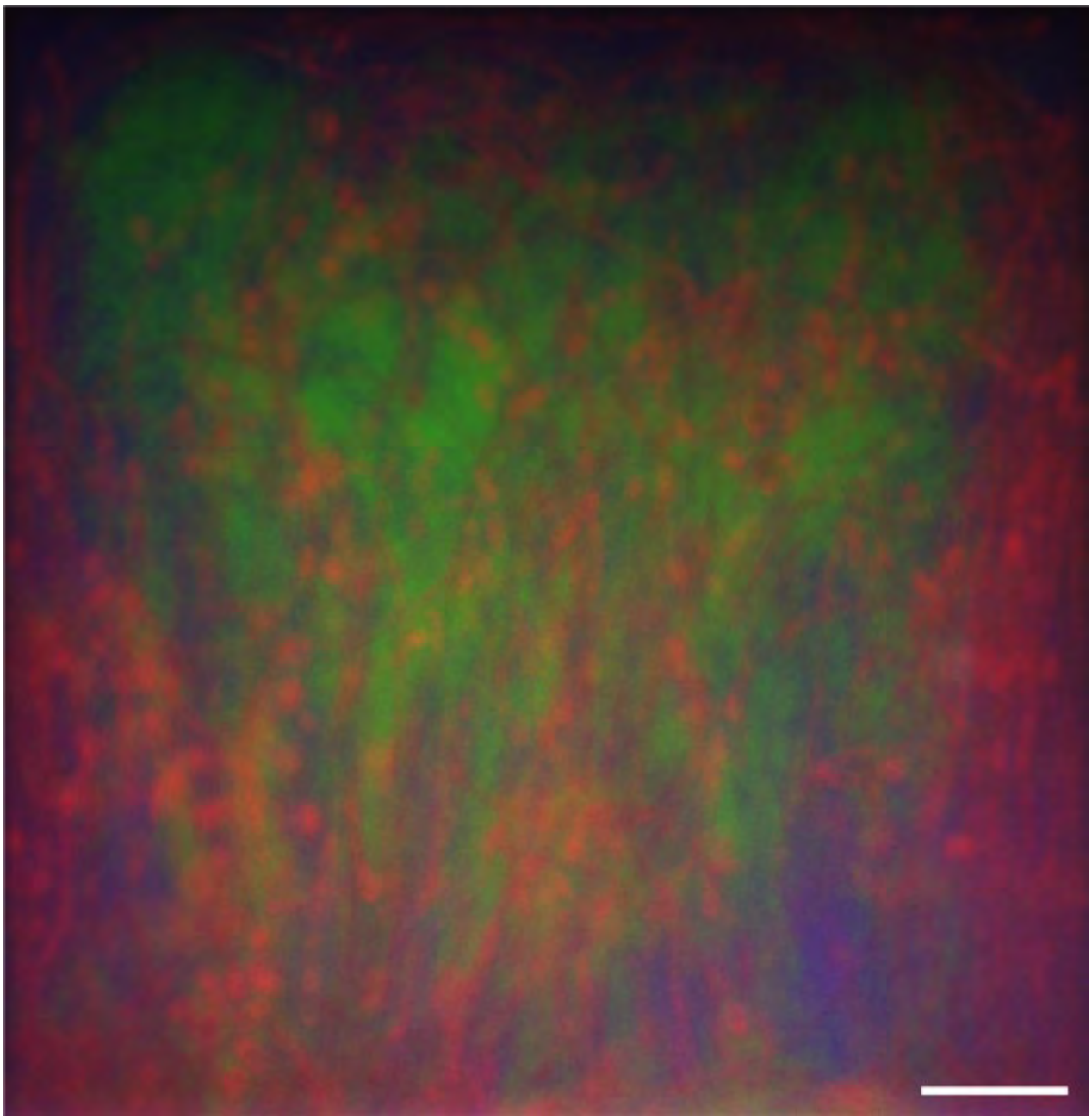
Leonardo Mancini[1], Eva Benyei[1], Martin Welch[1], Pietro Cicuta[1]
[1]*University of Cambridge, United Kingdom*

Microbes Across Length Scales, March 26, 2025, 10:15-12:15

The bodies of macroorganisms host microbes living in multi-species communities. Sequencing approaches have revealed that different organs host different microbiota and tend to be infected by different pathogens, drawing correlations between environment and microbial compositions on the scale of meters and centimeters.

Laboratory studies that have access to the microscale have thus far mostly focused on isolated species with the result that many of the mechanisms leading to infections in the polymicrobial context remain obscure. In this study, we model a lung polymicrobial infection using C. albicans, S. aureus and P. aeruginosa, and we quantify its behaviour and ecology across different scales. We find that while P. aeruginosa and S. aureus quickly outcompete C. albicans in shake flasks and on large surfaces, microfluidic microchambers that mimic the spatial and nutritional characteristics of the distal lung draw a completely different picture.

Despite its slower total growth rate, C. albicans is able to leverage fast eccentric hyphal growth to conquer the edges of the microenvironments where it establishes itself excluding the other pathogens. Such behaviour gives rise to robust spatial patterning of the community, enabling coexistence and, because the edges represent the epithelium, potentially determining infection severity and outcomes.



Transcriptional control mechanisms with different dynamical characteristics combine to enable flexible response to complex environmental signals

Dr Govind Menon[1], Mathias Nielsen[1], Yusheng Zhao[1], Eduardo Mateo-Bonmatí[1], Philip Wolff[1], Shaoly Zhou[1], Martin Howard[1], Caroline Dean[1]
[1]John Innes Centre, United Kingdom

Clocks, Timers and Cell Cycle Dynamics, March 25, 2025, 14:15-16:15

Transcription of protein-coding genes by RNA polymerase II is a fundamental nuclear process determining eukaryotic gene expression. In metazoans, the expression of key developmental and stress response genes must respond to complex environmental signals. To achieve precise timing of developmental transitions and physiological changes in response to such signals, the transcriptional regulation of these genes must be able to decode different dynamical features of these signals.

Such regulation can be achieved by having multiple molecular switching mechanisms, each having different dynamical characteristics, working together at the same gene. We elucidate how such flexible transcriptional regulation is realised at the Arabidopsis thaliana FLC gene, a key regulator of plant reproductive strategy. By combining mechanistic mathematical modelling with genetic, molecular, and imaging experiments, we dissect how two distinct molecular mechanisms with different dynamical characteristics [1,2] – one driven by non-coding transcription and the other mediated by the Polycomb repressive complex 2 – concurrently target FLC transcription. We show how this combined targeting allows FLC transcription to respond to temperature changes on a fast timescale over hours and a slow timescale over weeks, with only the slow timescale response having long-term memory capability.

References:
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2. Menon, Mateo-Bonmatí, et al., Molecular Cell, 84 (12), 2024.

Mechanics of asymmetric cell division

Prof. Alexander Mietke[1], Dr Alicia Daeden[2], Dr Emmanuel Derivery[3], Dr Carole Seum[2], Prof. Frank Jülicher[4], Prof. Marcos Gonzalez-Gaitan[2]
[1]University of Oxford, United Kingdom, [2]University of Geneva, Switzerland, [3]MRC Laboratory of Molecular Biology, United Kingdom, [4]Max Planck Institute for the Physics of Complex Systems, Germany

Cell Architecture and Forces, March 26, 2025, 10:15-12:15

The control of cell shape during cytokinesis requires a precise regulation of mechanical properties of the cell cortex. Only a few studies have addressed the mechanisms underlying the robust production of unequal-sized daughters during asymmetric cell division and, in particular, the mechanisms that ensure cell division is a mechanically stable process. Inside the dividing cell, Laplace pressure gradients generally tend to destabilize the cell surface, an effect that will be even more pronounced when cells divide in an asymmetric fashion. Experiments with asymmetrically dividing sensory organ precursor (SOP) cells in Drosophila show that modifications of relative amounts of branched Actin in the two daughter cells during division are sufficient to engineer essentially arbitrary daughter-size asymmetries.

Following this observation, we introduce a minimal model of the division process that reveals cortical bending rigidity as a crucial ingredient to quantitatively explain both the observed size asymmetries in SOP daughter cells, as well as the mechanical stability of the underlying division process.

Refined Collision Statistics Support a Force-based Model of Cortical Microtubule Organisation

Dr Francois Nedelec[1], Dr Maud Formanek, Dr Carlos Lugo, Dr Vivek Ambastha, Dr Dixit Ram
[1]*University of Cambridge, United Kingdom*

Cell Architecture and Forces, March 26, 2025, 10:15-12:15

The organisation of cortical microtubules within plant cells governs cellular expansion and thus the morphology of all plants. About 20 years ago, it was observed that cortical microtubules would collide with each other, leading to the elimination of misaligned microtubules, but this phenomena remained crudely characterized. We report here extensive statistics in hypocotyl epidermal and leaf pavement cells of A. thaliana, and, surprisingly, they appear undifferentiated. We show that microtubule collisions can be recapitulated by a Brownian model including bending elasticity and steric hindrance.

With this model, hundreds of microtubules remain disorganized as seen in pavement cells. However, when severing is added, following the observed phenomenology of Katanin, microtubules align rapidly as seen in hypocotyl cells. Our simulations support the idea that with common microtubule collisions dynamics in both cell types, the order of the resulting collective systems is directly under cellular control through activation of specific microtubule-associated enzymes.

Fast electrical signals trigger proliferation underlying organ regeneration

Dr Elisa Nerli[1,3], Dr. Jinghui Liu[1,2,5], Dr. Amit Vishen Singh[2], Prof. Dr. Charlie Duclut[4], Naomi Berbée[1], Sylvia Kaufmann[1], César Ponce Diego[1], Prof. Dr. Frank Jülicher[2], Dr. Rita Mateus[1,3]
[1]Max Planck Institute of Molecular Cell Biology and Genetics, Germany, [2]Max Planck Institute for the Physics of Complex Systems, Germany, [3]Cluster of Excellence Physics of Life, Germany, [4]Sorbonne Université, France, [5]Center for Systems Biology Dresden, Germany

Bioelectricity Across Scales, March 26, 2025, 15:30-17:30

Membrane potential changes are featured in all cells, and can be used for cell-cell communication and to instruct cell behaviours as cell migration during development and wound healing. Whether such signals, which are established at the millisecond to second timescale, can influence processes that occur at slower timescales as proliferation and growth is still scarcely explored.

We combine laser and mechanical ablation with sub second live imaging, long term imaging and theoretical modelling to understand how electrical signals kick-start fin regeneration in the zebrafish embryo.

We uncover a molecular mechanism that organs use to sense and translate electrical signals, at the subsecond to second timescale, into proliferative signals that act at the hour timescale. We observe a tissue-wide membrane depolarisation, followed by an intracellular Calcium wave and by the activation of a voltage-sensing phosphatase, VSP, in a spatiotemporally regulated manner. VSP activation triggers proliferation as soon as 1h after injury and such mechanism is necessary and sufficient to ensure successful tissue regeneration.

Our findings suggest that tissue-scale depolarization represents the earliest signal essential for successful organ regeneration.

Punching Holes and Pulling Threads: Cell Wall, The Most Complex Tapestry of Nature

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[1]University of Leeds, School of Biology, United Kingdom, [2]University of Leeds, School of Physics and Astronomy, United Kingdom

Cell Architecture and Forces, March 26, 2025, 10:15-12:15

Tomato is one of the major crop plants in the world. It is estimated that almost 25-42% of global yield of tomato is lost even before reaching shops and markets due to fungal pathogens. Primary point of attack of plant pathogenic fungi is the cell wall, polysaccharide matrix which covers all plant cells giving them shape, mechanical support and enabling growth and morphogenesis. Understanding mechanical properties of the cell wall during the fruit development and relationship between structure and mechanics of tomato fruit cell wall will enable identifying the desirable traits of tomato fruits, helping to decrease post-harvest tomato yield losses.

Application of atomic force microscopy has showed that cellulose microfibril bundles in tomato fruit cell walls are getting thinner during growth and fruit ripening over 6 weeks period, with one-week-old fruits having the thickest and six-week-old fruits the thinnest cellulose microfibril bundles. Elastic modulus of the cell wall is showing trend which is not following changes in cellulose fibrils thickness nor abundance of other cell wall components, such as different pectins and hemicelluloses, as well as callose during the fruit growth and ripening, showing that softening of the cell wall is indeed not the same as loosening. This implies much more complex relationship between cell wall mechanical properties and its biochemical composition and structure than the current understanding of this problematic.

Correlated cryo-EM and cryo-FIB-SIMS enables spatial and chemical imaging of biological specimens

Hannah Ochner[1]
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Microbes Across Length Scales, March 26, 2025, 10:15-12:15

Electron cryomicroscopy (cryo-EM) provides high-resolution images detailing the spatial structure of biological samples [1], however, there is no direct way of inferring the chemical composition of objects observed in an electron micrograph. As such information is highly relevant for the identification and localization of specific components within cells, a correlative approach providing both chemical and spatial information is needed [2]. To integrate spatial and chemical analysis into a single workflow at cryogenic temperatures, we combine spatial imaging by cryo-EM with focused ion beam (FIB) milling and chemical imaging by time-of-flight secondary ion mass spectrometry (ToF-SIMS) of the ions created during the FIB milling process [3]. Using bacterial cells as a test system, we were able to correlate and overlay cryo-EM and FIB-SIMS data, showing that the technique allows the mapping of elemental and small-molecule ions within a cellular sample prepared in a near-native state by vitrification.

Specifically, we could show that the method can be used to study the uptake of fluorinated compounds by bacterial cells. To target larger molecules of biological interest, such as specific proteins, we are employing metal-based labelling strategies of cellular macromolecules to aid localisation in SIMS imaging. As the technique provides access to the three-dimensional sample volume and is widely applicable to a variety of samples, ranging from single cells to tissue-like samples such as FIB-milled lamellae, it is a promising approach for studying the spatial and chemical properties of biological specimens within an integrated workflow.

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[3] Pillatsch, L. et al. (2019), Progress in Crystal Growth and Characterization of Materials 65: 1–19.

Microscopic transport powered by swimming bacteria and applications in biohybrid micro-robotics

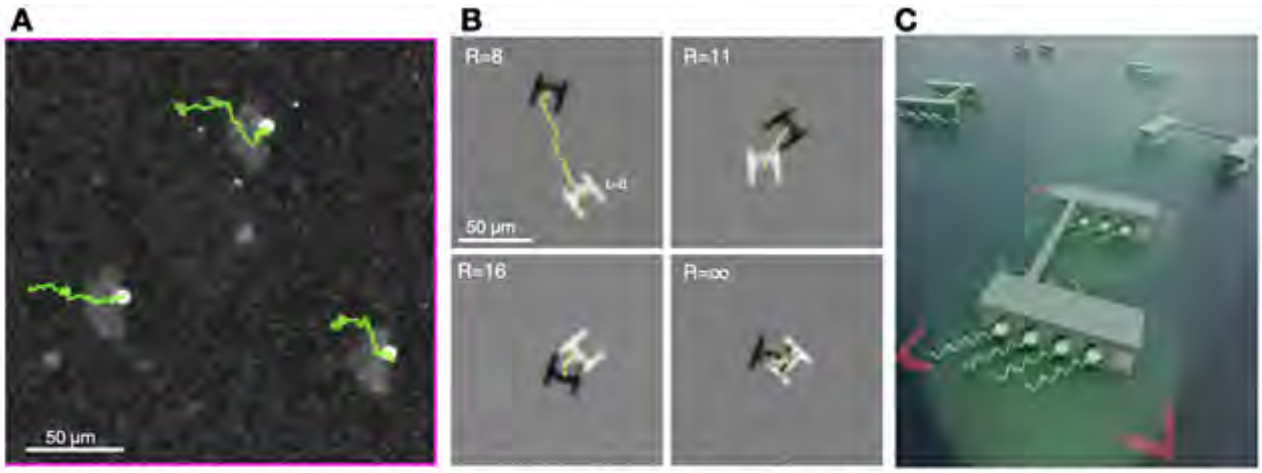
Nicola Pellicciotta[1,2], Ojus Bagal[2], Viridiana Carmona Sosa[2,3], Maria Cristina Cannarsa[2], Giacomo Frangipane[2], Silvio Bianchi[1,2], Roberto Di Leonardo[1,2]
[1]CNR - NANOTEC, Italy, [2]University of Rome La Sapienza, Italy, [3]University of Cambridge, United Kingdom

Engineering Tissues and Organoids and Biohybrids, March 25, 2025, 14:15-16:15

When a fluid contains self-propelled components that actively consume energy to move, such as swimming bacteria, the pressure around a suspended object can become non-uniform, leading to rectified transport. We investigated this phenomenon in two scenarios: (i) when the active fluid surrounding the object exhibits non-uniform activity, studied by spatially modulating bacterial motility with light [1]; and (ii) when the object has an asymmetric shape, investigated by measuring the forces exerted by swimming bacteria on microfabricated curved structures with parametrically varied radii of curvature. For the latter, we found that curved microstructures are propelled with a speed that scales linearly with curvature and is directed from the concave to the convex side.

Combining modulated activity with shape-driven actuation, we developed a 3D-printed micro-robot featuring strong concave, chevron-like regions where bacteria become trapped, enabling propulsion of the micro-robot forward [2]. Using light-driven bacteria, this "microbot" can be steered by unbalancing light intensity across different regions of its surface and guided to transport colloids through a series of spatially distributed control points.

[1] Pellicciotta, Nicola, et al. "Colloidal transport by light induced gradients of active pressure." Nature Communications 14.1 (2023): 4191
[2] Pellicciotta, Nicola, et al. "Light controlled biohybrid microbots." Advanced Functional Materials 33.39 (2023): 2214801.



(A) Dark-field microscopy snapshots showing bacteria and a colloidal bead (in white). Bacterial speed is controlled to be slower on the left side and faster on the right side of the bead, causing bacteria to accumulate on the slower side and the colloidal bead to drift systematically toward the faster side (green trajectory). (B) Post-processed bright-field images showing the initial (white) and final (black) positions of curved microstructures with different radius of curvature immersed in a bacterial bath, with their trajectories highlighted in green. (C) Illustration of the bio-hybrid microbot powered by light-driven bacteria.

Optimising the signal in cell cycle analysis by dual labelling experiments

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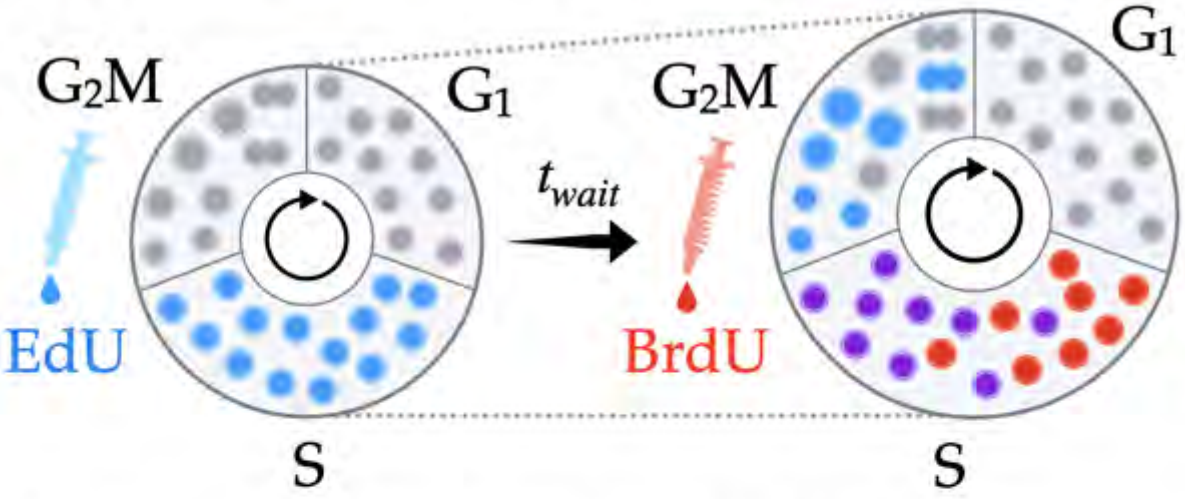
[1]Department of Bioengineering, Imperial College London, United Kingdom, [2]Department of Life Sciences, Imperial College London, United Kingdom, [3]Francis Crick Institute, United Kingdom

Clocks, Timers and Cell Cycle Dynamics, March 25, 2025, 14:15-16:15

Tightly regulated cell divisions are crucial to the development and maintenance of all organisms. Before a cell can divide, it must go through multiple phases with carefully controlled checkpoints. A quantitative understanding of how much time a cell spends in the distinct phases is fundamental to our understanding of basic cellular functions, from DNA replication to organelle duplications. Given the importance of understanding cell cycle dynamics, diverse experimental techniques have been developed to quantify the process, among these the use of nucleoside analogue substitution during the DNA Synthesis cycle phase is particularly popular due to its ease of use and high sensitivity. Detecting the amount of these modified nucleosides in cells has been a gold standard way to quantify the number of cells in the Synthesis phase.

Further increasing the accuracy of this method, a sequential substitution of nucleosides using two distinct labels has been developed, dramatically increasing the information output of the experiment. A clear control parameter in this dual-labelling method is the waiting time t_wait between the introductions of the two labels. However, how to choose t_wait to optimise the information output has thus far not received any attention. Here, we perform such a task by demonstrating, using simulation of a simple model of cell cycle, how to find the t_wait that optimises the signal-to-noise ratio of the measurements. Our work thus provides a proof of principle in how to use simple modelling to further optimise a powerful experimental method in the study of cell cycle dynamics.

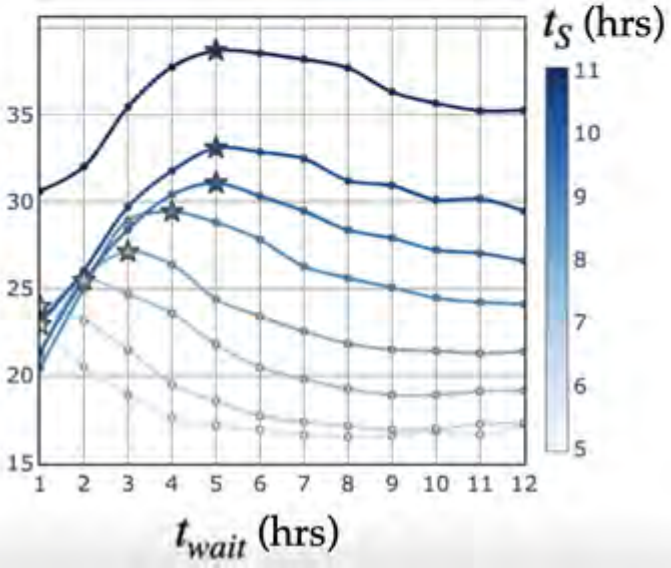
Dual pulse nucleoside labelling



t_{wait} is a free parameter controlled by the experimenter

Signal-to-Noise Ratio of inferred S phase rate

Peaks, marked by ☆, shift according to S phase duration



Visualizing chromatin accessibility spatially during early stages of embryogenesis

Blanca Pijuan-Sala[1], Katharina Bender[1], Christoph Schaub[1], Eileen Furlong[1]
[1]EMBL Heidelberg, Germany

Differentiation and Development, March 24, 2025, 15:30-17:30

During early embryogenesis, the genome undergoes a process of activation, where chromatin gradually becomes accessible and transcription factors bind to specific genomic regions, contributing to transcription initiation. How this event, known as Zygotic Genome Activation (ZGA), is triggered and unfolds is not fully understood. To date, chromatin accessibility in embryos has only been assessed by sequencing techniques, which in both bulk and single-cell experiments lose positional information within the embryo, and provide no details on how accessibility is organized in 3D within nuclei. To overcome these limitations, we have developed an imaging technique, stemming from the already existing ATAC-see, to observe chromatin accessibility in Drosophila embryos in situ. Compared to the original ATAC-see, which was performed in isolated cells, our ATAC-see protocol, called modular ATAC-see, has significantly increased signal-to-noise ratio, which is key for its success in a multicellular tissue or embryo.

Using modular ATAC-see, we quantified the gradual increase in chromatin accessibility and its organization within single nuclei of intact embryos during ZGA, and examined how this change is coupled to the levels of histones and RNA Polymerase II in the same nucleus. Applying modular ATAC-see on embryos subject to perturbations is allowing us to dissect the underlying pathways influencing global chromatin accessibility patterns. More broadly, modular ATAC-see represents a step forward in our understanding of molecular processes occurring within nuclei of multicellular systems; it enables taking the 3D nuclear context into account to interpret events that have been widely studied in a linear DNA fashion through sequencing.

Golden Signals: Transforming Blood-Based Biomarker Detection with Next-Generation Photonic Biosensors

Dr Katie Morris[1], Guilherme Simoneti de Arruda[1,2], Dr Augusto Martins[1], Serafina Coupe[1], Professor Emiliano Martins[2], Thomas Krauss[1], Dr Steven Quinn[1]
[1]University of York, United Kingdom, [2]University of Sao Paolo, Brazil

Emerging Areas in the Physics of Life, March 26, 2025, 10:15-12:15

The detection and characterization of blood-based biomarkers is critical for enabling timely treatment interventions and for advancing personalized therapeutic strategies. In the context of dementia, the development of new technologies capable of assessing small (a few kDa) peptides at extremely low (pg/mL) concentrations in blood is now an urgent and global challenge. Here, we present a next-generation biosensing platform that leverages major advances in photonics to transform biomarker detection. Using a handheld chirped guided mode resonance (cGMR) biosensor, we combine refractive-index sensing with gold nanoparticle-enhanced signal amplification to simultaneously detect key biomarkers of dementia with sensitivity in the clinically-relevant range. Our chirped resonator structure employs precision-engineered photonic structures to translate spectral information into spatial outputs detectable with a low-cost, camera-based setup.

Our platform supports multiplexed detection, mitigates non-specific binding, and ensures high specificity for isoforms of β-amyloid (Aβ) and tau, which are key biomarkers of Alzheimer's disease. We demonstrate detection limits of sub pg/mL in vitro and the detection of pg/mL peptide concentrations in diluted serum, highlighting the potential of the cGMR for early-stage diagnosis. Beyond dementia, our versatile technology is scalable, cost-effective, adaptable to diverse applications in biomarker-driven diseases and for environmental sensing. Our results demonstrate the potential of the nanoparticle-enhanced cGMR biosensor to enable rapid, sensitive, and specific biomarker readouts, paving the way for early-stage, point-of-care diagnostics and broader translation. By bridging physics, material science, and clinical demand, our work exemplifies how emergent photonic innovations can address pressing challenges in the life sciences.

Electroreceptive Sensitivity Analysis of Mechanosensory Hair Arrays

Anna Radjenovic[1]
[1]*University of Bristol, United Kingdom*

Bioelectricity Across Scales, March 26, 2025, 15:30-17:30

Arthropods use many environmental cues while foraging (e.g. for nectar), finding prey, and avoiding predators; bees, for example, seek flowers abundant in nectar. These cues include olfactory signals, colour, petal patterns and textures and, in particular, weak electric fields. Electric fields cause filiform hairs on arthropods to deflect due to Coulomb's Law. By interpreting such hair deflections, arthropods can learn the electrical properties of their environments to optimise pollination of navigation. In this model, we represent each of two hairs as stiff inverted pendulums attached to a hair socket 'spring' with spring constant S. Considering coupled forces induced by a concentrated charge at the tip of each hair, a quasi-static equilibrium is found for the system. We model the hairs' deflections due to electrostatic forces as the arthropod moves relative to external charge sources, neglecting higher-order inertial and resistive terms. In nature, we observe mechanosensory hair sockets with a preferred plane of deflection. The electroreceptive sensory capacity of an arthropod via filiform hair deflection interpretation is largely dependent on these planes. By varying the direction each hair deflection is restricted to, we analyse the effect on the overall and directional sensitivity of the arthropod. We investigate hair array morphologies and geometric configurations, including suggestions for the biomimetic design of mechanosensory hair systems to optimise the sensitivity of the system.

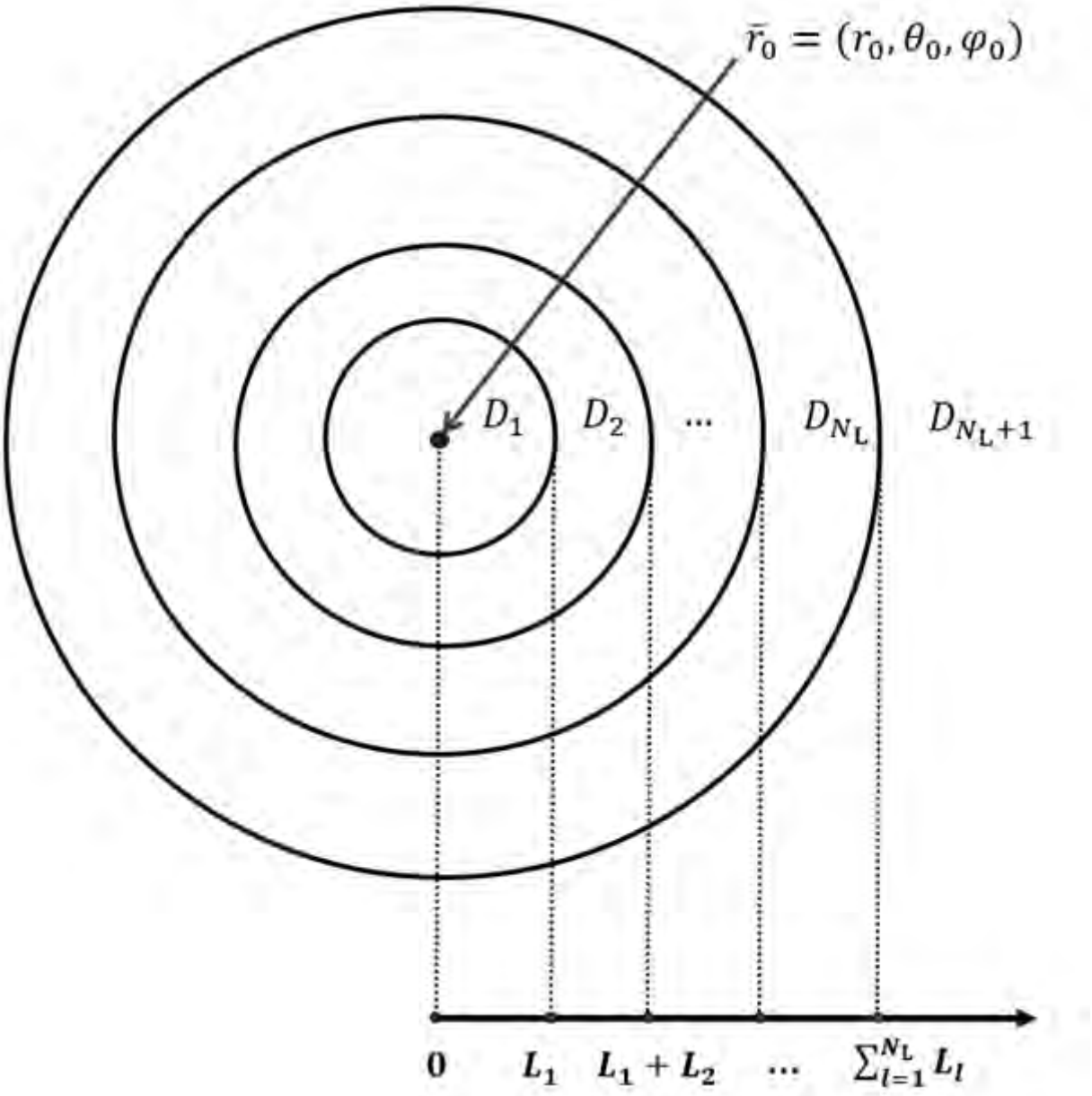
General Molecular Communication Model in Multi-Layered Spherical Channels

Mitra Rezaei[1], Michael Chappell[1], Adam Noel[1]
[1]*University of Warwick, United Kingdom*

Emerging Areas in the Physics of Life, March 26, 2025, 10:15-12:15

Spherical multi-layered structures are prevalent in numerous biological systems and engineered applications, including tumour spheroids, layered tissues, and multi-shell nanoparticles for targeted drug delivery. Despite their widespread occurrence, there remains a gap in modelling particle propagation through these complex structures from a molecular communication (MC) perspective. This abstract introduces a generalized analytical framework for modelling diffusion-based molecular communication in multi-layered spherical environments. The framework is capable of supporting an arbitrary number of layers and flexible transmitter-receiver positioning. The versatility of our approach facilitates its application to various diffusion-dominated mass transfer problems.

However, our focus in this study is on MC systems within large spheroids -- 3-D cellular aggregations in a spherical shape -- which are fundamental components in organ-on-chip systems. Large spheroids are ideal examples due to their complex, multi-layered structure: an outer layer of loosely-attached cells surrounds intermediate layers with tighter cell packing and a denser extracellular matrix. This arrangement hinders oxygen diffusion to the core, potentially causing necrosis (death) of the cells in the centre. We provide a detailed mathematical presentation of a three-layer model, given its prevalence in applications such as tumour modelling and drug delivery systems. The analytical results are validated using particle-based simulation (PBS) in scenarios that have short inter-layer distances. The findings reveal that the characteristics of each layer significantly impact molecule propagation throughout the entire structure, making their consideration crucial for designing targeted therapies and optimizing drug delivery systems.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Lipid membrane biophysics and bioengineering with DNA nanostructures

Dr Roger Rubio Sanchez[1], Prof. Bortolo Mognetti[2], Prof. Pietro Cicuta[3], Prof. Lorenzo Di Michele[1]
[1]Department of Chemical Engineering and Biotechnology, University of Cambridge, United Kingdom, [2]Université Libre de Bruxelles, Belgium, [3]Cavendish Laboratory, University of Cambridge, United Kingdom

Natural and Synthetic Molecular Machines, March 27, 2025, 09:00-11:00

Biological membranes tightly regulate the spatio-temporal organisation and interactions of membrane-bound proteins to facilitate a range of pathways critical to life, from signal transduction to motility and division. Cell-like objects, routinely referred to as “synthetic cells”, are ideal model platforms through which we deepen our understanding of biological processes in isolation from physiological complexity [1]. Exploiting the tools of DNA nanotechnology [2], my work designs and applies nano-scaled devices to interrogate the biophysical principles governing the spatio-temporal organisation of membrane inclusions.

Here, we developed DNA-Origami Line-Actants (DOLAs) to study and regulate membrane re-structuring pathways in synthetic lipid bilayers. Leveraging our ability to control the distribution of membrane inclusions within liquid-ordered (Lo) and liquid-disordered domains (Ld) [3], we engineer DOLAs to selectively accumulate the line-interface between co-existing phases in lipid bilayers. DOLAs are shown to reversibly stabilise lipid domains against coalescence, generating two-dimensional Pickering emulsions on the membrane of Giant Unilamellar Vesicles. Finally, we apply our DOLA toolkit to construct a proof-of-concept biomimetic pathway for fission of lipid domains [4], demonstrating control over three-dimensional membrane morphological restructuring events. Besides fundamental contributions to our understanding of line-active membrane inclusions and their influence on lateral cell-membrane organisation, the development of these bio-inspired responses paves the way for next-generation sensing, communication, and division pathways in synthetic cellular systems.

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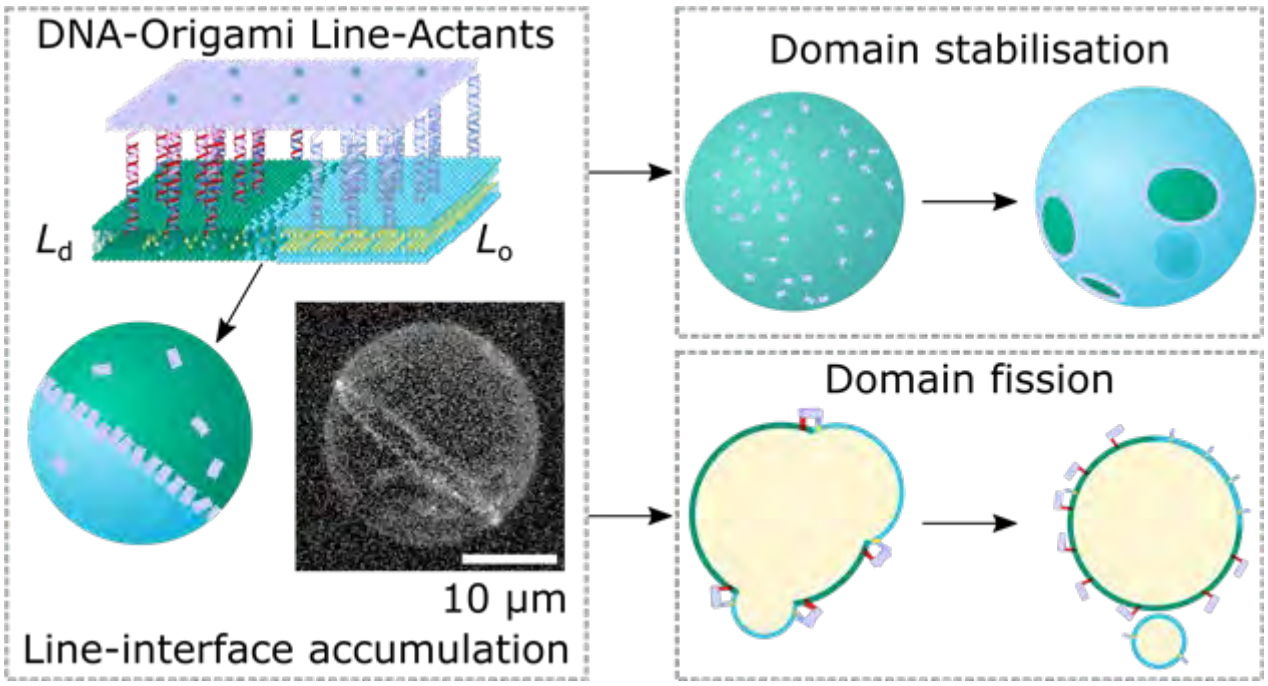
[1] Acc. Chem. Res. 2014, 47, 1807-1815.
[2] Chem. Commun, 2021, 57, 12725 – 12740.
[3] Nano Lett, 2021, 21, 2800 – 2808.
[4] J. Am. Chem. Soc., 2023, 145, 11265–11275.


DNA-Origami Line-Actants
L_d
L_o
10 μm
Line-interface accumulation
Domain stabilisation
Domain fission

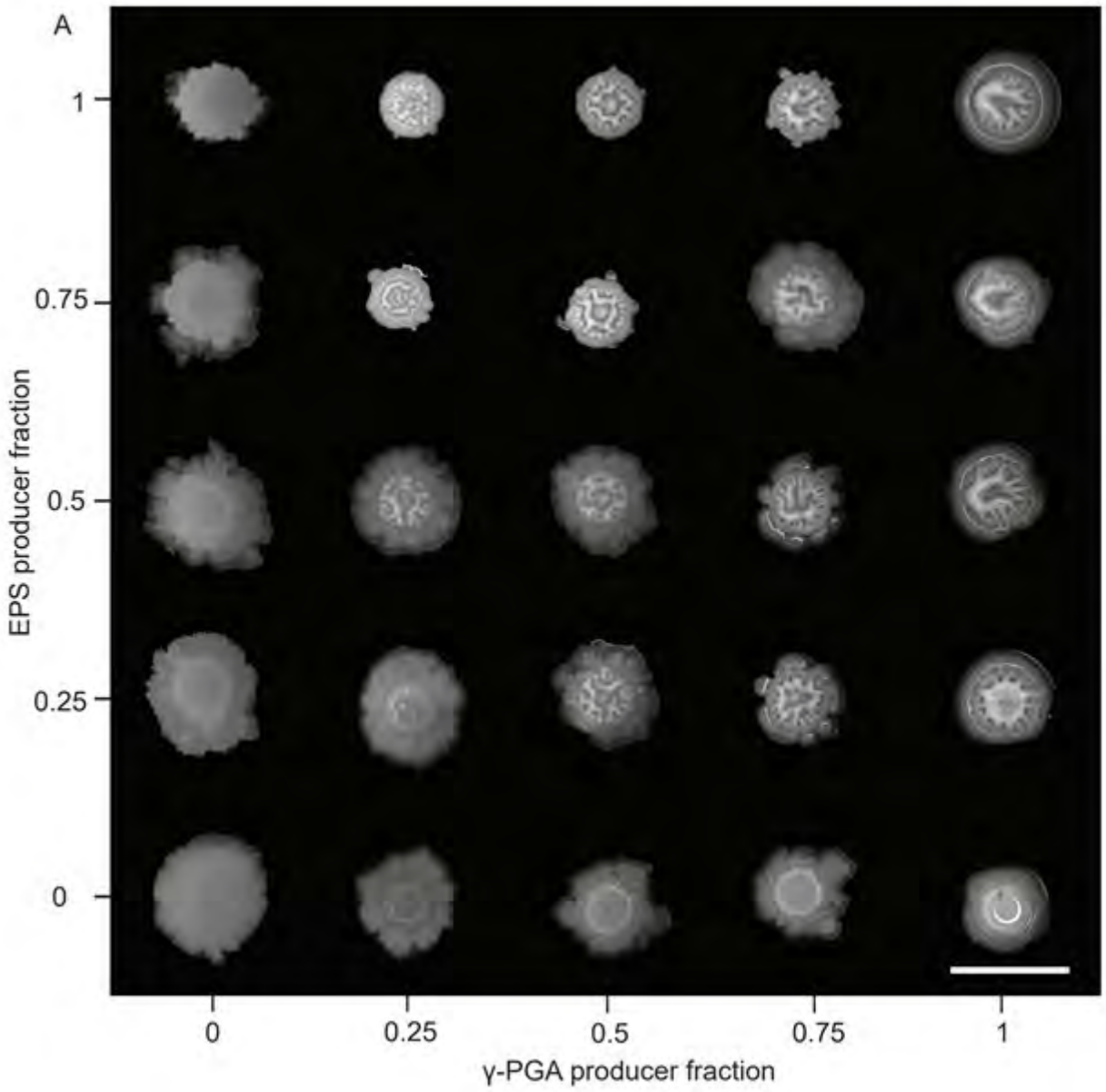
Phase Transition Induced Wrinkling in Bacillus Subtilis biofilm: The Role of γ-PGA and EPS

Ayantika Saha[1], Dr. Joseph Larkin[1]
[1]*Boston University, USA*

Microbes Across Length Scales, March 26, 2025, 10:15-12:15

A delicate interplay between physio-chemical properties and genetic programs, such as cell division and extracellular matrix production, governs the emergence of three-dimensional morphologies in living tissues. It remains an open question how cellular matrix production rates determine tissues' material physics and how large-scale morphology emerges from those physics. We investigate this question by examining the formation of wrinkles in mature Bacillus subtilis biofilms. We find that two distinct self-secreted polymers—poly-γ-glutamic acid (γ−PGA) and exopolysaccharide (EPS)—play complementary roles in the evolution of wrinkled biofilm morphology. γ−PGA fraction absorbs fluid from the substrate, halting radial expansion while promoting vertical swelling, whereas EPS provides structural integrity by forming an extensive scaffolding structure. Using FRAP and phase imaging, we image the fluidization in the γ−PGA-producing biofilms by tracking cellular motion in the fluidized region. We verify the swelling by taking OCT side profile images, showing biofilm height increases linearly with γ−PGA fraction.

The ability of EPS to provide architectural support to the biofilm structure is verified by measuring the bulk modulus of EPS-producing biofilms and observing its reduction in value with decreasing fractions of EPS producers. By varying the production rates of these polymers, we find a phase transition from thin, flat biofilms to thick, wrinkled biofilms. Using a percolation model, we propose that this transition qualitatively resembles a gelation phase transition, linked to wrinkle formation above a bulk modulus threshold. Our results offer new insights into how phase transitions govern the morphology of bacterial communities, with implications for microbial ecology and biofilm-related applications.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EPS producer fraction
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0.25
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γ-PGA producer fraction

Self-Assembly of Topological Networks of Intrinsically Disordered Proteins

Charley Schaefer[1]
[1]*University of Leeds, United Kingdom*

Protein Structure, Dynamics and Interactions, March 24, 2025, 15:30-17:30

The theoretical prediction of macroscopic properties of biopolymer networks from the constitutive protein sequence is greatly challenged by intrinsic disorder. In particular, the accessible time- and lengthscales in molecular dynamics simulations is limited by the short vibrational timescales of the interactive regions. We present a topological network model where the associations and dissociations between such regions are treated as strain-dependent elementary processes, similar to the creation and destruction of entanglements are treated in so-called sliplink models for entangled polymer melts.

We show how this model can be parametrised using single-molecule microscopy and surface plasmon resonance, and how it provides meaningful quantitative predictions on the liquid-liquid phase separation of two-component liquid-liquid phase separated biomolecular condensates [1]. Beyond these structural predictions, we will discuss how the mechanochemical properties of the interactive regions affect the dynamical properties, such as single-molecule diffusion and the non-linear rheology.

[1] Payne-Dwyer et al, Phys Rev Lett 2024.

Generating and measuring DNA plectonemes with COMBI-Tweez

Jack Shepherd[1], Sebastien Guilbaud[2], Zhaokun Zhou[3], Jamieson Howard[1], Matthew Burman[1], Charley Schaefer[4], Adam Kerrigan[1], Clare Steele-King[1], Agnes Noy[1], Mark Leake[1]
[1]University of York, United Kingdom, [2]Cairns Research, United Kingdom, [3]Guangdong Provincial Key Lab of Robotics and Intelligent System, China, [4]University of Leeds, United Kingdom

Physics of the Nucleus, March 25, 2025, 14:15-16:15

Molecular machines change DNA supercoiling, resolve knots, and package chromosomes, and large-scale structural changes contribute to gene regulation. Far from a passive information store, DNA is an active participant through its wide-ranging mechanical properties. Supercoiling produces a range of axial force-dependent responses including melting and plectoneme formation, where DNA winds around itself. Probing these properties is generally done with optical or magnetic tweezers: optical tweezing allows high force and fluorescence imaging, while magnetic tweezers provide torsional control. We present COMBI-Tweez, a combined optical and magnetic tweezing microscope which applies axial force and supercoiling while imaging with HILO microscopy. We detail properties for a magnetic bead to be optically trapped and show COMBI-Tweez accurately measures key mechanical properties like persistence length and force dependence of plectoneme formation.

We present the first images of controllably, reversibly formed DNA plectonemes, whose size and diffusive behaviour we estimate using a modified version of our particle tracking code PySTACHIO. Diffusion is low for negatively supercoiled plectonemes, explained by structural motifs identified with MD simulations: in undertwisted DNA plectonemes a melting bubble localises at the tip, forming an energy barrier for diffusion; the locations of these bubbles and hence plectoneme formation is sequence-dependent and predictable. As bacterial DNA is generally negatively supercoiled, we hypothesise that melting bubbles act as “structural staples” providing spatial organisation. Finally, we braid multiple DNA molecules into ropes, which display complex behaviour beyond that of single molecules. Our open-source design and software, alongside full results, are published in Nature Communications.

Cell-level modelling of active forces in early-stage development

Professor Rastko Sknepnek[1]
[1]*University of Dundee, United Kingdom*

Tissue Growth, Mechanics and Mechanosensing, March 26, 2025, 15:30-17:30

Gastrulation is an essential, highly conserved process in the development of all vertebrate embryos, including humans. It involves large-scale cell and tissue movements. When not executed properly, it can lead to a wide range of congenital defects, or, in more extreme cases, cause abortion of development. Gastrulation requires the integration of critical cell behaviours such as cell differentiation, division, and movement through chemical and mechanical cell-cell signalling, to achieve the morphogenesis essential for proper functions. These interactions between signalling and cell behaviours create complex feedback loops between tissue, cell, and molecular length- and timescales that have evolved to enable the robust formation of complex multi-cellular structures.

In this talk, using the vertex model for cell-level description of epithelial tissues, we will discuss how various forms of active processes, such as mechano-chemical feedback, cell growth, division, ingression, etc. couple to cell mechanics and lead to pattern formation and flows in model tissues. We will also make qualitative comparisons to the primitive steak formation (i.e., the gastrulation) in chick embryos.

An agent-based model of the bacteriophage lytic cycle to understand the evolutionary impact of stochasticity in life history parameters

Aaron Smith[1], Dr Michael Hunter[2], Dr Somenath Bakshi[1], Dr Diana Fusco[1]
[1]University of Cambridge, United Kingdom, [2]University of British Columbia, Canada

Immunity, Resistance and Host/Pathogen Dynamics, March 26, 2025, 15:30-17:30

Bacteriophages (phages) play a critical role in controlling bacterial populations, both in natural ecosystems and as potential therapeutic agents. Their success in eliminating target cells and proliferating depends on key 'life history parameters', including burst size (the number of virions produced per infected cell) and lysis time (the time taken to lyse the host cell). Life history parameters are constrained by biology, which imposes both absolute and relative limits on the values these parameters may take, leading to an environment-dependent system of evolutionary trade-offs.

Historical study of bacteriophage life history parameters has focused on population-average values. While illuminating, this approach fails to account for the fact that phage-bacteria interactions are intrinsically stochastic in nature, owing to variability in host-cell physiology as well as biochemical noise interacting with the phage's own gene expression. Importantly, the susceptibility of a bacteriophage strain to such noise may itself be heritable, with evolutionary pressure to either suppress or amplify cell-to-cell variation.

In this study, we aim to explore how variability in two bacteriophage life history parameters, burst size and lysis time, affects the function and competitive fitness of lytic phages. We use computer simulations to investigate three experimental set-ups corresponding to established laboratory protocols: the 'killing curve', 'serial transfer' and 'plaque expansion' assays. We observe unexpectedly rich competitive dynamics with implications for future evolution experiments, as well as strong connections between the adaptive value of noise and particular features of the environment.

Measuring homologous pairing using synthetic DNA scissors

Dr Andrew Stannard[1,2], Dr Ehud Haimov[1], Dr Claudia Danilowicz[3], Prof Mara Prentiss[3], Dr Yuval Elani[1], Dr Marco Di Antonio[1], Prof Lorenzo Di Michele[1,2], Prof Alexei Kornyshev[1]
[1]Imperial College London, United Kingdom, [2]University of Cambridge, United Kingdom, [3]Harvard University, USA

Physics of the Nucleus, March 25, 2025, 14:15-16:15

In homologous recombination, DNA segments are exchanged between chromosomes, a process critical to establishing genetic variation and healing DNA damage. To avoid detrimental effects, cells must ensure that homologous, not heterologous, segments are exchanged. Prior to exchange, however, pairing must occur; in the chaos of the cell nucleus, how do homologous segments find each other? [1]. The potential for homologous pairing to occur in protein-free environments has been previously demonstrated [2,3]; here, by measuring dsDNA pairing in synthetic constructs, we test the hypothesis that homologous pairing is electrostatically-driven [4] and elucidate the physiological factors that facilitate homologous recognition.

Since the electrostatic-pairing theory predicts homologous recognition to be weak, here we tether duplexes together to entropically-bias their pairwise interactions, creating so-called DNA ‘scissors’; FRET markers integrated into these constructs report on duplex-duplex separation. The physiologically-relevant, divalent cations of magnesium and calcium are known to specifically adsorb on anionic dsDNA, the resulting charge compensation reduces dsDNA-dsDNA electrostatic repulsion. Accordingly, for our DNA scissors, coaligned duplexes are observed for sufficient concentrations of these cations, an effect that disappears when duplex tethering is absent. By varying the nucleotide sequences of the duplexes-of-interest, the magnitude of divalent-cation-induced interactions between homologous and heterologous duplexes can be compared and the effect of electrostatically-driven homologous recognition can be quantified.

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Substrate geometry affects population dynamics in a bacterial biofilm

Witold Postek[1], Klaudia Staśkiewicz[2], Elin Lilja[2], Bartłomiej Wacław[2,3]
[1]Department of Infectious Disease, Imperial College London, United Kingdom, [2]Dioscuri Centre for Physics and Chemistry of Bacteria, Institute of Physical Chemistry, Polish Academy of Sciences, Poland, [3]School of Physics and Astronomy, University of Edinburgh, United Kingdom

Microbes Across Length Scales, March 26, 2025, 10:15-12:15

Biofilms inhabit diverse environments such as dental plaques or soil micropores, often characterized by non-even surfaces. While physical interactions between bacteria and the surface have been shown to play a major role for biofilm growth and evolution, the impact of surface irregularities remains elusive, as most experiments are conducted on flat surfaces. Here we show that surface texture can significantly influence genetic drift and selection within the biofilm. We culture Escherichia coli biofilms in microwells with a corrugated bottom and observe the emergence of stable clonal sectors whose size corresponds to that of the corrugations, despite no physical barrier separating different areas of the biofilm (see the figure).

Using image analysis and computer modelling, we demonstrate how this effect emerges from the physics of biofilm growth, which leads to a certain velocity field within the biofilm that hinders mixing and clonal expansion. A microscopically detailed computer model highlights the role of mechanical interactions such as adhesion and friction in microbial evolution. The model also predicts limited clonal expansion even for clones with a significant growth advantage, which we confirm experimentally using a mixture of antibiotic-sensitive and antibiotic-resistant mutants in the presence of sublethal concentrations of the antibiotic rifampicin. The strong suppression of selection contrasts sharply with the behaviour seen in range expansion experiments in bacterial colonies on agar. Our results show how a better understanding of the physics of bacterial growth can be used to control microbial evolution [1].

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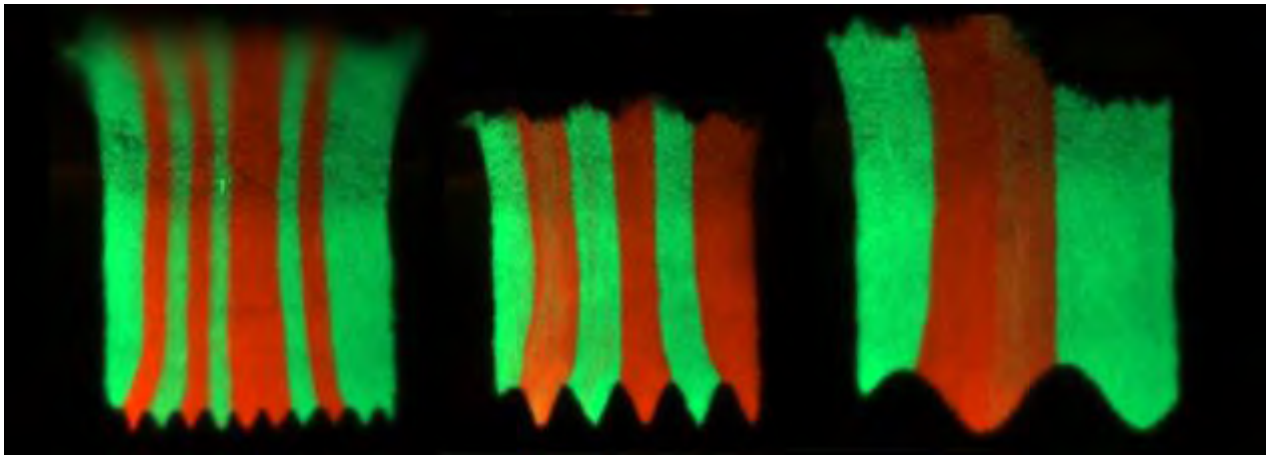

Interstitial hydrodynamic instabilities sculpt cell adhesion contacts

Margarita Staykova[1]
[1]*Durham University, United Kingdom*

Cell Architecture and Forces, March 26, 2025, 10:15-12:15

Linker dynamics is not the only parameter that controls cell adhesion. Using biomimetic experiments and theoretical modelling, we show that hydrodynamic instabilities in the thin interstitial fluid layer can lead to patterning of the membrane adhesion and to the formation of membrane blisters in two very different biological contexts. In the first system, we show that increased hydraulic pressure arising from osmotic disbalance across the lipid membrane induces membrane blistering that plays a crucial role in the lumen formation of embryos [1]. In the second system, we show that conformational changes in the glycocalyx arising from membrane area compression trigger similar hydrodynamic instabilities and membrane blistering in the adhesion zone.

Our work points to the universal, yet under-appreciated role of interstitial hydrodynamics in regulating cell adhesion.

1. Dinet, C. et al. Patterning and dynamics of membrane adhesion under hydraulic stress. Nature Communications, 14(1) (2023).

Mesoscopic multiphoton calcium imaging reveals a confluence of overlapping avalanches with varying distance to criticality and distinct roles

Dr Cedric Stefens[1], Dr Hardik Rajpal[1], Joseph Canzano[2], Dr Meghdad Saeedian[1], Prof. Lucilla De Arcangelis[3], Prof Henrik J Jensen[1], Prof Mauricio Barahona[1], Prof. Spencer L Smith[2], Prof. Simon R Schultz[1]

[1]Imperial College London, United Kingdom, [2]University of California Santa Barbara, USA, [3]University of Campania, Italy

Patterns, Waves, Transport, Collective Phenomena and Microswimmers, March 25, 2025, 10:15-12:15

The hypothesis that information processing properties emerge at this critical point has been of interest in neuroscience, inspiring a phenomenological framework for analysis of “neural avalanches” of activity that propagate with power-law distributions of size and duration. Previous studies assumed that at most a single avalanche at any time. Yet, in a system as large as the brain, it is highly likely that multiple avalanches co-exist, intersecting in space or time. Here we investigate neural avalanches with mesoscale, single-cell resolution optical imaging, finding that as neural recording technology scales up, this assumption is no longer viable.

We recorded the activity of ~7,000 layer 2/3 neurons from a 3×3 mm2 field of view centered around visual cortical areas in awake, head-fixed mice, using a Diesel2p mesoscope. The mice were presented with randomised visual stimuli, and an infrared camera recorded pupil diameter. We used the seqNMF algorithm to decompose spatiotemporal patterns of neural activity into components which we found to contain individual propagating neural avalanches, for which we calculated criticality and information metrics. seqNMF demixed 23 sets of co-occurring avalanches that displayed a range of distances to criticality, and differing information content. Pupil-related avalanches appeared to behave closer to criticality than the stimulus-related. The former tended to propagate along the antero-posterior axis, while the latter typically localised in V1 then diffused into higher visual areas.

Overall, our study suggests that the interplay of co-occurring, near-critical avalanches may play an important role in information processing across cortical circuits.

NREM-REM cycle model with incorporation of thermodynamics

Haeun Sun[1], Prof. Alexey Zaikin[2,3]
[1]Queen Square Institute of Neurology, University College London, United Kingdom, [2]Institute for Cognitive Neuroscience, University Higher School of Economics, Russia, [3]Department of Mathematics and Institute for Women's Health, University College London, United Kingdom

Clocks, Timers and Cell Cycle Dynamics, March 25, 2025, 14:15-16:15

Circadian rhythmicity includes subtler ultradian rhythmicity of Rapid-Eye-Moving (REM) states and non-REM (NREM) states, and its mechanism and role have been active topic of theoretical biology. However, there is emerging evidence of temperature dependence of vigilance state and neuronal excitability, which might be explained with physics principle of thermodynamics. In this project, we made a theory to explain REM-NREM cycle based on thermodynamic interaction of brain [1]. Synchronised stochastic heat generation from slow wave activity and deterministic heat dissipation from brain into body and ambient environment could explain the spontaneous cycle of sleep stage and temperature. We simulated it with local slow wave sleep model with addition of temperature dependent neuronal excitability and multi-segmented thermoregulatory model. The model was validated with rats' empirical data drawn from the Buzsaki Lab Databank [2]. Additionally, other temperature dependent sleep properties could be reproduced with the simulation. This can be potential theoretical base to develop thermo-engineering therapy for sleep disorders.

[1] Sun, H., Yurii Ishbulatov, Anatoly Karavaev, Zakharov, D. and Alexey Zaikin (2024). A thermodynamic model of the REM–NREM sleep cycle. Chaos Solitons & Fractals, 190, pp.115732–115732. doi:https://doi.org/10.1016/j.chaos.2024.115732.
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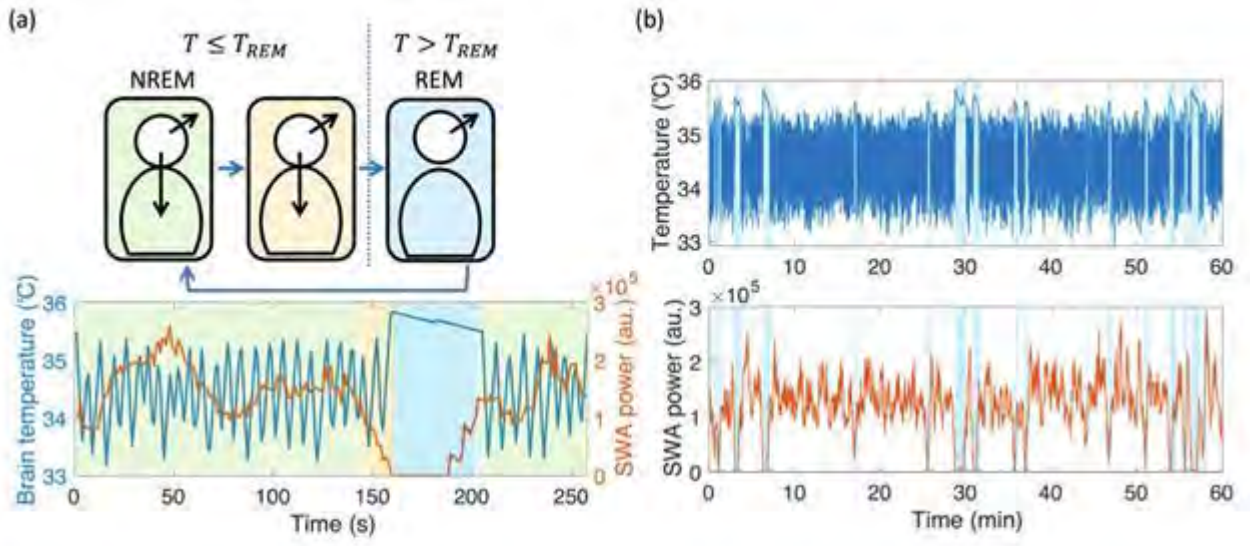

Figure 1 Concept of the model. (a) The main concept of the model (top) and plot (bottom) for brain temperature (blue line in bottom panel) and SWA power (orange line in bottom panel) during a cycle. First, in the NREM state, the brain emits heat within the body and into the ambient environment, decreasing its temperature (green shades). At the same time, heat generation from SWA in the brain increases due to temperature dependent neuronal excitability, increasing brain temperature over the threshold of the REM state (yellow shades). Third, in high brain temperature of the REM state, neural heat generation decreases, but heat dissipation into the body decreased due to sympathetic activation in REM state (blue shades). Stochastically, brain temperature decreases again, and it goes back into the REM stage. (b) Simulated brain temperature (top) and SWA power (bottom) in a series of NREM-REM cycles in 60 minutes. REM state is marked with blue shades.

Modelling of aberrant phase transitions in biomolecular condensates via multiscale molecular simulations

Dr Andres Tejedor[1], Dr Ignacio Sanchez-Burgos, Mr Alejandro Feito, Prof. Jorge Ramirez, Prof. Rosana Collepardo, Dr Jorge R. Espinosa[1]
[1]University Complutense of Madrid, Spain

Biomolecular Assemblies and Condensates, March 25, 2025, 10:15-12:15

Ageing of functional liquid-like biomolecular condensates into solid-like aggregates has been linked to the onset of several neurodegenerative disorders. Low-complexity aromatic-rich kinked segments (LARKS) contained in numerous RNA-binding proteins can promote the aggregation process by forming inter-protein β-sheet fibrils that accumulate over time, ultimately driving the liquid-to-solid transition of condensates.

In this study, we will combine atomistic Molecular Dynamics simulations with sequence-dependent coarse-grained models of various resolutions to unravel: i) the role of LARKS location within the amino acid sequence in the ageing of condensates [1]; ii) how a small number of mutations across the protein sequence can drastically modulate its ageing propensity; iii) the impact of RNA in decelerating the emergence of inter-protein β-sheets [2]; and iv) how single-component condensates that are initially homogeneous and liquid-like can transform over time into multiphase condensates as they age [3,4]. Moreover, we will compare the performance of different state-of-the-art residue-resolution models in predicting the phase diagram and material properties of condensates formed by intrinsically disordered proteins, multi-domain proteins, RNAs, or charge-rich complex coacervates [5,6].

Overall, we will show how residue-resolution coarse-grained models have surfaced as a powerful tool for studying protein/RNA interactions and providing valuable insights into the physicochemical factors governing biomolecular phase separation.

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Quantifying 3D cell shape and cell organisation during myotome formation

Dr Sophie Theis[1], Dr Mario Mendieta-Serrano[1], Dr Timothy Saunders[1]
[1]*University of Warwick, United Kingdom*

Imaging and Single Molecule Biology, March 25, 2025, 10:15-12:15

Cell and tissue morphogenesis is crucial for forming the organs that define the shape of an organism. In tightly packed tissues, cell rearrangements, divisions, apoptosis, and shape changes drive these morphological transformations, coordinated by mechanical forces and chemical signals. While significant research has focused on 2D systems like the Drosophila wing disc, recent studies emphasise the need to understand 3D cell morphology, including complex 3D shapes such as scutoids. Although significant advances in 3D imaging and segmentation have facilitated these studies, it remains difficult to obtain complete quantitative measurements beyond baseline morphological descriptors, such as volume and surface area in dense tissue.

We introduce CellMet, a Python-based tool designed for extracting detailed 3D cell shape metrics from densely packed tissues. This package provides critical cell-scale data from 3D segmentations, including cell face properties, cell twist, and spatial rearrangements. We demonstrate the utility of Cellmet to elucidate how complex cell organisation emerges during skeletal muscle formation in zebrafish. We observed that elongating and fusing muscle precursors form a polarised array displaying a helical organisation and topological chirality by 36hpf.

CellMet significantly improves the efficiency of 3D cell shape analysis, which is essential for uncovering how cell organisation within tissues drives specific morphologies. We show that muscle formation potentially relies on topology transitions, modulated by local boundary constraints, to create ordered tissue structures.

Rethinking stomatal mechanics: Insights from a new model of onion stomata

Melissa Tomkins[1], Matthew Wilson[2], Clinton Durney[1], Jodie Armand[2], Julie Gray[2], Richard Morris[1], Richard Smith[1], Andrew Fleming[2]
[1]John Innes Centre, United Kingdom, [2]University of Sheffield, United Kingdom

Tissue Growth, Mechanics and Mechanosensing, March 26, 2025, 15:30-17:30

Plant stomata are essential for regulating gas exchange between plants and their environment, influencing both photosynthesis and water balance. Despite their seemingly simple structure—a pore formed by two guard cells—stomata display remarkable morphological diversity across plant species. Previous studies on non-grass stomatal systems consisting of two kidney-shaped guard cells, have highlighted the importance of mechanical properties such as radial stiffening and pectin-based pinning of polar ends in facilitating stomatal opening.

In this talk, we present a novel finite element method (FEM) model of onion stomata, offering fresh insights into the relationship between guard cell morphology and function. We demonstrate how the flattened geometry of onion guard cells enhances the efficiency of turgor pressure in opening and closing their pores. Using the 3D modelling software MorphoDynamX, we inflate and deflate both 2.5D and fully 3D mesh representations of stomatal guard cells derived from confocal microscopy images. This approach allows for a comprehensive examination of how realistic cell geometries influence stomatal function and behaviour. Understanding the interplay between morphology and function holds the key for unravelling the mysteries of the evolutionary diversification of stomatal shapes across plant species.

Controlled liquid-liquid phase separation via the simulation-guided, targeted engineering of the RNA-binding protein PARCL

Dr Ruth Veevers[1], Dr Steffen Ostendorp[2], Dr Anna Ostendorp[2], Prof. Dr. Julia Kehr[2], Prof. Richard Morris[1]
[1]John Innes Centre, United Kingdom, [2]Universität Hamburg, Germany

Biomolecular Assemblies and Condensates, March 25, 2025, 10:15-12:15

PARCL is a plant-specific RNA-binding protein (RBP) that is highly abundant in the phloem. It has been observed to form large biomolecular condensates that move within the phloem stream, potentially being involved in RNA transport. Here we present results on unravelling which molecular properties drive PARCL's phase separation. We used coarse-grained molecular dynamics simulations to compute a residue interaction map that identifies candidate residues involved in phase separation. Subsequent simulations with mutations of candidate residues resulted in disrupted condensation, supporting their involvement in phase separation. We performed in vitro and in vivo experiments to validate these predictions. To match the experiments, we produced versions of the simulations that included eYFP tags, which we compared to the untagged simulations to find changes in the condensates' network structure.

To investigate the RNA-binding of PARCL, we added microRNA to the simulations and find a short region of PARCL consistently making contact with the miRNA, in agreement with bioinformatics predictions and experiments.

TORCphysics: A physical model of supercoiling mediated regulation in synthetic gene circuits

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Emerging Areas in the Physics of Life, March 26, 2025, 10:15-12:15

Current synthetic gene circuits are designed to perform logical functions, mimicking those in electronic circuits. These designs ignore DNA supercoiling, which can affect gene expression as it is intimately related to transcription, capable of both up- and down-regulating the expression of distal genes. Our goal is to understand, characterize, and harness the potential of supercoiling in regulating transcription in synthetic gene circuits as a novel and powerful component of the next generation of synthetic gene circuits.

In this work, we introduce TORCPhysics, a fast and computationally efficient physical model designed to predict the expression profiles of gene circuits in bacteria by simulating transcription-dependent supercoiling under various biological conditions. These expression profiles are directly comparable with experimental data. Combined with wet-lab experiments on basic plasmid-based genetic circuits in various bacterial strains and backgrounds, our results provide insights into the underlying mechanisms driving the correlated gene expression of multiple genes. They reveal the interplay between transcription, genomic architecture, and topoisomerase activity, highlighting the significance of factors such as gene orientation, topological barriers, and promoter strength.

The insights gained with TORCPhysics, in combination with experimental data, will contribute to the development of a computational toolkit called TORC. This toolkit will facilitate the design of genetic circuits that exploit transcription-dependent supercoiling, and can be used to debug circuits by proposing alternative designs that achieve the same functionality with improved efficiency. The practical implications of this work are broad, potentially enabling the creation of supercoiling-based gene circuits.

Optimising information transmission in the canonical Wnt pathway

Olivier Witteveen[1], Samuel Rosen[2], Ryan Lach[2], Maxwell Wilson[2], Marianne Bauer[1]
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Differentiation and Development, March 24, 2025, 15:30-17:30

Cells often rely on signalling molecules to make cell-fate decisions during development, which convey information through abundance and temporal dynamics. However, these signals can be noisy, and this poses a challenge for cells to make reliable decisions. One example of a signaling pathway is the canonical Wnt pathway, essential for embryonic development in many organisms. In this theoretical work, we use experimental data for cells in a tissue culture responding to optogenetic Wnt signals to quantify the precision in their response. For the range of opto-genetic signals we study, we find that the cellular response can be precise enough to allow reliable differentiation into two distinct states, but only if signals are chosen appropriately.

We use decoding maps to quantify the improvement in information processing when neighbouring cells can exchange their output gene expression. We show that as precision in the pathway improves, more distinct states can be reliably distinguished, which means that the optimal input signal protocol changes from one involving only a few distinct signals to a continuous use of signals. Finally, we suggest that both neighbourhood averaging and discretisation should play a role to allow differentiation based on the Wnt pathway.

Poster Presentations

Unravelling the effect of divalent salt on the structure of negatively supercoiled DNA

Dorothy Aboagye-Mensah[1], Aleksander Klimczyk[1], Dr Graeme King[1]
[1]*University College London, United Kingdom*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

DNA in vivo is frequently under torsional stress, which can lead to either positive supercoiling (overwinding) or negative supercoiling (underwinding) of the DNA. Negative supercoiling helps to promote DNA compaction, and plays a vital role in regulating gene expression. It is known that negatively supercoiled DNA can adopt a range of conformations, including writhed structures (plectonemes) and underwound forms (including bubble-melted DNA, L-DNA and Z-DNA). However, the influence of environmental factors, such as ionic strength, on the structure of negatively supercoiled DNA is still not well understood. Obtaining this knowledge is crucial for understanding the physiological function of negatively supercoiled DNA. Here, we develop a novel analytical strategy to quantify the mechanical properties of negatively supercoiled DNA, based on measured force-distance curves generated using optical tweezers.

We then apply this approach to explore the effect of divalent cations on the structure of underwound DNA. We demonstrate that even modest concentrations (≥2 mM) of divalent cations can substantially increase the bending stiffness of underwound DNA, consistent with the formation of a Z-DNA-like structure. Strikingly, in the presence of >5 mM divalent salt, we observe unexpected and extensive saw-tooth-like behaviour in the force-distance curves of underwound DNA, most notably at higher supercoiling densities.

This suggests that divalent cations can also substantially increase the stability of writhed structures (plectonemes). Together, our findings reveal that the structure and stability of underwound DNA is highly sensitive to the concentration of divalent cations, which has implications for the biological interactions of supercoiled DNA.

Exploring the “concentration quenching” effect of small-molecule fluorophores and fluorescent proteins by using lipid membranes and electrophoresis

Dr Sophie Meredith[1], Dr Ashley Hancock[1], Yuka Kusunoki[2], Dr Simon Connell[1], Prof. Kenichi Morigaki[2], Prof. Stephen Evans[1], Dr Peter Adams[1]
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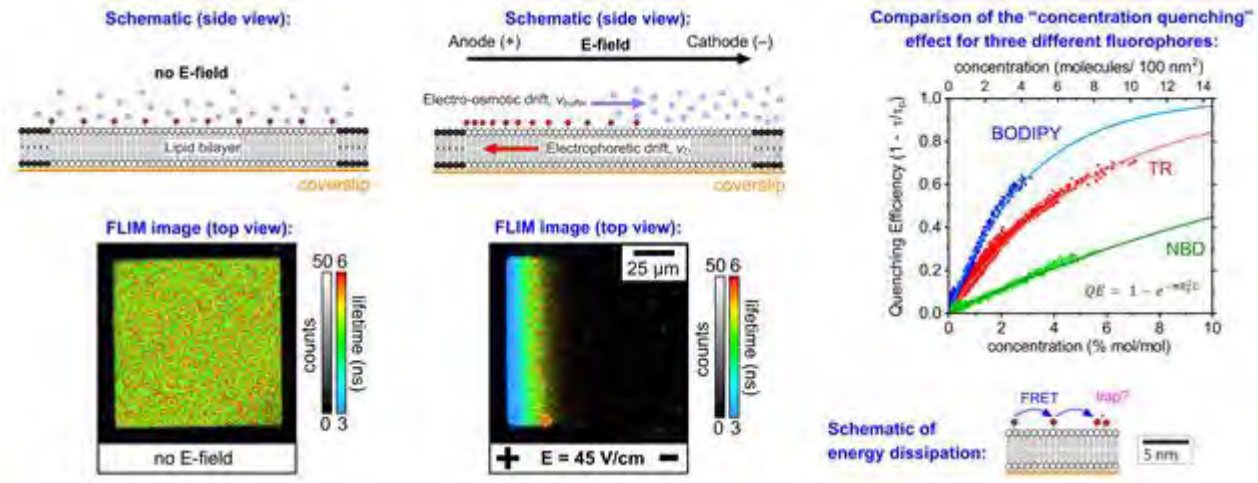
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

It is important to understand the behaviours of fluorescent molecules because, firstly, they are often utilized as probes in biophysical experiments and, secondly, they are crucial cofactors in biological processes such as photosynthesis. A phenomenon called ‘‘fluorescence quenching’’ occurs when fluorophores are present at high concentrations, but the mechanisms for quenching are debated. This presentation will describe how a technique called ‘‘in-membrane electrophoresis’’ can be used to generate concentration gradients of fluorescent lipids or fluorescent proteins within a supported lipid bilayer (SLB), from which quenching effects can be quantified. Firstly, we studied how membrane electrophoresis can be used to assess interactions between lipid-linked Texas Red (TR) fluorophores [1]. The self-quenching of TR was observed in Fluorescence Lifetime Imaging Microscopy (FLIM) images as a correlation of high concentrations of fluorophores to reductions in their fluorescence lifetime. Secondly, experimental data representing the fluorescence quenching of three different fluorophores were compared to theoretical models for quenching [2]. The analysis supported the theory that quenching takes place via a ‘‘transfer-to-trap’’ mechanism which proposes that excitation energy is transferred between fluorophores and may reach a ‘‘trap site’’ resulting in immediate energy dissipation. In ongoing research, we are studying the migration of membrane proteins from plants using electrophoresis/FLIM and their role in energy collection in photosynthesis. For the bioimaging community, our findings also highlight the fact that quenching effects must be considered and/or corrected for if the concentration of fluorophores is high.

References:
[1] Meredith et al. (2023) https://doi.org/10.1021/acs.jpcb.2c07652
[2] Meredith et al. (2024) https://doi.org/10.1016/j.bpj.2024.07.026



Biomolecular condensates mediate bending and scission of endosome membranes

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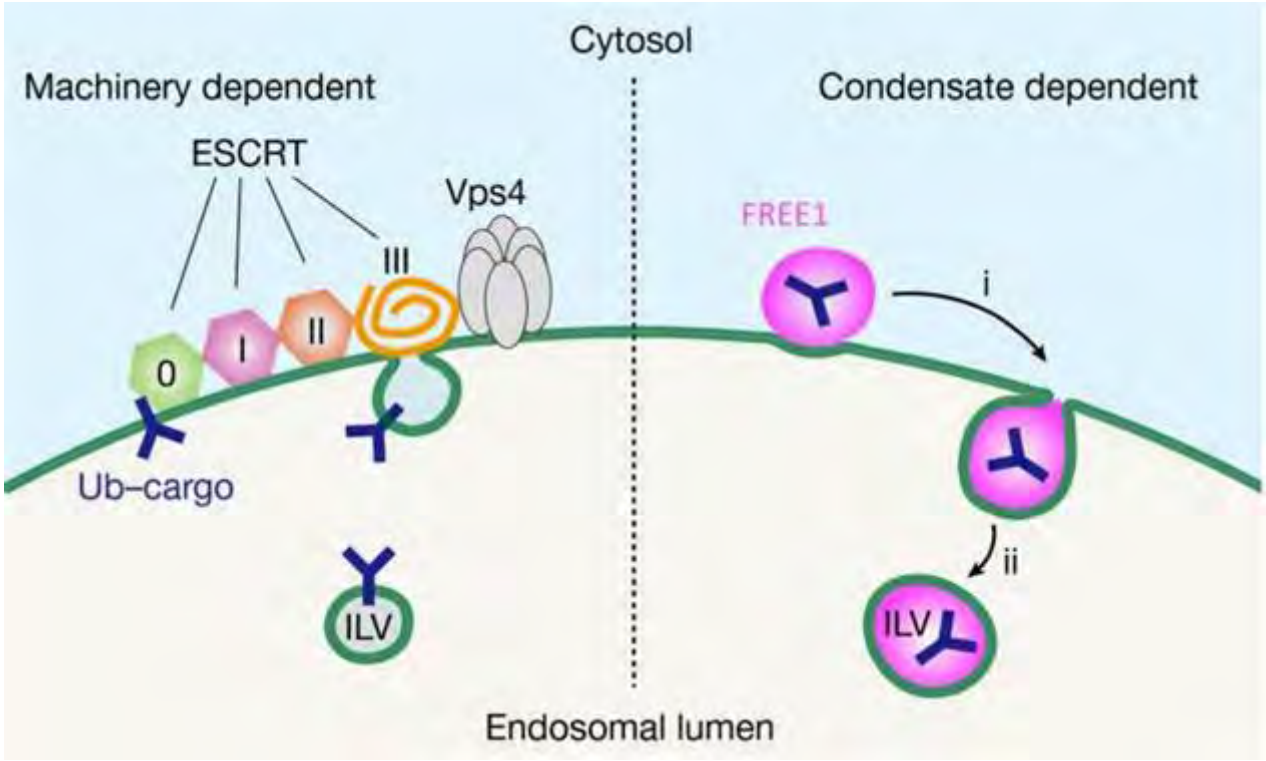
[1]UCL, United Kingdom

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Multivesicular bodies are key endosomal compartments implicated in cellular quality control through their degradation of membrane-bound cargo proteins. The ATP-consuming ESCRT protein machinery is usually thought to mediate the capture and engulfment of membrane-bound cargo proteins through invagination and scission of multivesicular-body membranes to form intraluminal vesicles. In contrast, we have recently reported that the plant ESCRT component FREE1 forms liquid-like condensates that associate with membranes to drive intraluminal vesicle formation in an ATP-independent manner [1]. I will present a minimal physical model that shows how condensate-wetting-induced line tension forces and membrane asymmetries are sufficient to mediate scission of the membrane neck without the ESCRT protein machinery or ATP consumption. We propose that condensate-mediated scission represents a previously undescribed scission mechanism that depends on the physicomolecular properties of the condensate and is involved in a range of trafficking processes. More generally, FREE1 condensate-mediated membrane scission in multivesicular-body biogenesis highlights the fundamental role of wetting in intracellular dynamics and organization.

[1] Wang, Y., Li, S., Mokbel, M, ..., J. Agudo-Canalejo, R. L. Knorr, X. Fang. Nature 634, 1204 (2024).



Complementary insights into Silicosis gained with revisit of Cytotoxic Effects of Silica

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Background: Silicosis is a notorious incurable lung disease accompanied with severe pulmonary fibrosis, which has been believed due to prolonged exposure to crystalline silica particles. However, it remains obscure or overlooked about the role of amorphous silica materials, the ubiquitous materials used even more than crystalline counterparts.
Aim: This study clarifies the highly comparable cytotoxicity between crystalline and amorphous silica particles, using A549 adenocarcinomic human alveolar basal epithelial cells as illustration.

Method: Two cytotoxicity assays employed to understand the behaviour and level of silica toxicity on A549 monolayer cells in Air-Liquid Interface (ALI) and Submerged cultures, individually. Lactate Dehydrogenase (LDH) assay to assess membrane integrity and water-soluble tetrazolium salt (WST-1) assay to study the metabolic activity of cell viability. Trans Epithelial Electrical Resistances (TEER) measurements used to evaluate epithelial barrier function of the monolayer in ALI.

Results: Our LDH findings reveal an increase in the intracellular LDH enzyme proportional to concentrations of silica particles. While the WST-1 assay revealed a reduced metabolic activity against increase the concentration and incubation time. TEER shown a decline in barrier integrity. The results indicated cellular damage to the silica-treated A549 cells.
Conclusion: These results contribute to a deeper comprehensive understanding of silica-induced pulmonary toxicity and provide insights into the cellular mechanisms of underlying the silicosis development.

Making fast decisions with phase separation

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

In recent years, the role that biomolecular condensates play in a myriad of regulatory and developmental processes has been increasingly under scrutiny. However, the process of how these condensates form, namely liquid-liquid phase separation, can also serve as a mechanism for cells to sense environmental conditions. For example, condensates can form in response to changes in temperature or pH and are sensitive to small variations in these parameters. More generally, biological agents commonly face the challenge of making fast decisions about the state of their environment with limited information. These decisions depend on mechanisms that vary greatly depending on the relevant time- and length-scales of the system.

In this work, we detail a minimal model for phase separating mixtures: building on Flory-Huggins theory, we derive dynamical descriptions for droplet nucleation and growth in ternary fluids. We explore how competition for common resources, such as building blocks for condensate formation, enhances a system's ability to measure both absolute and relative concentrations in fluid mixtures. We further demonstrate that a controlled supply of common resources improves measurement accuracy, underscoring the utility of phase separation as a tool for cellular sensing and adaption to changing environments in living systems.

Towards the modelling of chromosome movements during meiotic prophase I in Arabidopsis thaliana

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

During meiotic prophase I, chromosomes undergo rapid prophase movements and change their configuration in the nucleus. Studies in yeast showed that these movements play an important role in achieving non-erroneous meiosis, but little is known about this mechanism in plants.

Using advanced live imaging techniques and quantitative image analysis, we have recently brought to light a similar behavior in meiotic centromeres in Arabidopsis thaliana. We showed that perturbing key components of the chromosome-cytoskeleton connection (mutants of the LINC complex) abolishes centromeric movements. In the sun1sun2 mutant, for example, meiotic centromeres remain stationary, and telomere attachment to the nuclear envelope, bouquet formation and nucleolus position are all altered. One key question now is to decipher what causes rapid prophase movements of chromosomes, and how they are affected by physical constraints inside the cell nucleus.

We propose to address this question by modelling chromosome movements using polymer physics and coarse-grained molecular dynamics simulations. Our model takes into account several topological constraints specific to meiosis, such as the attachment of the telomeres to the nuclear envelope or the external cytoskeleton forces that act on the telomeres. We report here preliminary results obtained with this model and study how geometrical and topological constraints affect chromosome dynamics and can promote or impede their movements. Combining this model with experimental data will provide the means to better understand the behavior observed in movement-disruptive mutants in Arabidopsis thaliana.

Dynamics of Wound Closure in Active Nematic Epithelia

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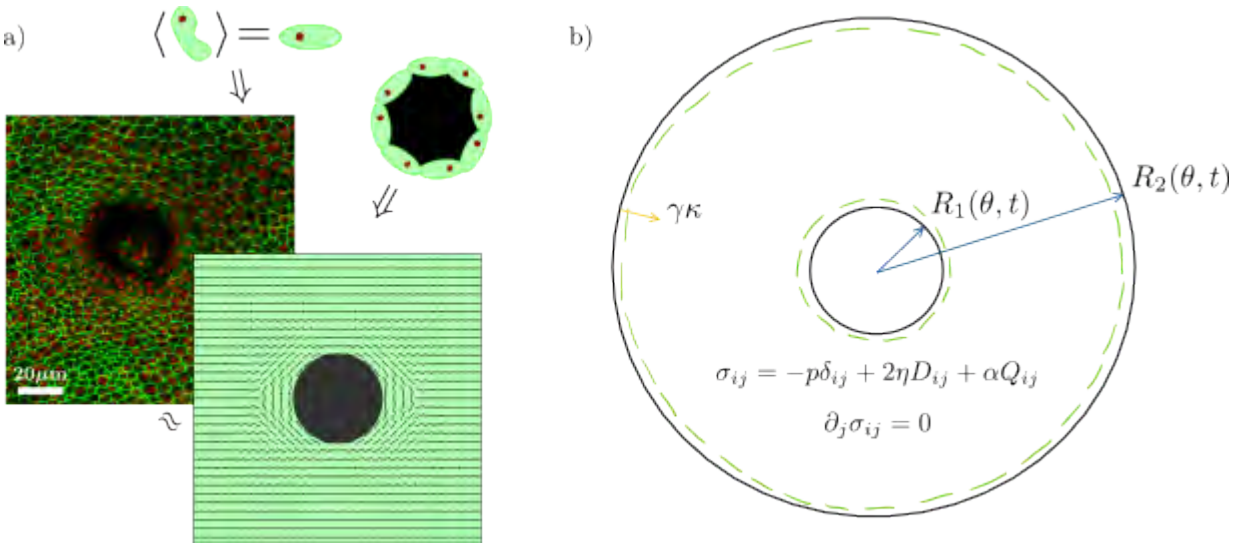
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The effective healing of external wounds is a sophisticated process essential for all organisms wishing to survive external damage. In recent years, fruit flies – Drosophila – have been used as a model organism for studying wound-healing. Drosophila are not humans, however the hope is that by studying cellular responses to wound healing, we might gain insight into mammalian healing, ultimately leading to the development of improved clinical practices.
In this work, we present a fluid dynamical model for re-epithelialisation, the process through which the epithelium extends over a wound, reinstating the outermost layer of protective tissue. Our model is inspired by two recent observations of wound closure in the wings of Drosophila pupae [1].

First, epithelial cells in healthy tissue possessed head-tail symmetry and aligned along the long axis of the wing. Second, in response to wounding, cells near the wound edge were deflected towards the tangential polar direction, parallel to the wound edge. This suggested that the tissue could be modelled as an active nematic fluid, with parallel anchoring at the wound boundary. We solve the free-boundary problem of a closing hole in a two-dimensional active nematic, finding that contractile active stresses aid wound closure and that activity will drive the wound boundary away from circular. This is exciting, as it provides an accessible measurement with which to test our model's validity.

[1]: J. Turley, et al., Deep learning reveals a damage signalling hierarchy that coordinates different cell behaviours driving wound re-epithelialisation, Development 151, dev202943 (2024).



Detergent-Induced Membrane Solubilization Monitored with Fluorescence De-Quenching

Claudia Andrews[1], Christopher Hofmair[1], Lauryn Roberts[1], Emily James[1], Katie Morris[1], Yue Wang[1], Steven Quinn[1,2]

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Detergent-induced membrane solubilization is important for several biotechnological applications including membrane protein extraction, cell lysis and virus inactivation. The thermodynamic details of detergent-induced membrane solubilization have been previously examined, but the mechanistic details remain largely underexplored owing in part, to a lack of suitable technologies capable of assessing nanoscopic disruption events. Here, we introduce fluorescence de-quenching as a tool to monitor conformational changes and dynamics in large unilamellar model-membrane vesicles containing the fluorophores, DiI and DiD.

We demonstrate using time correlated single photon counting to measure the amplitude weighted average lifetime of the fluorophore, that the assay is as sensitive as a complementary technique involving energy transfer between two membrane bound probes. Injection of the detergents Triton X-100, Tween-20 and sodium dodecyl sulfate leads to a progressive increase in the fluorescence lifetime of the probes, which we attribute to an initial vesicle swelling event followed by complete solubilization. We also probe the structure of single surface-immobilized vesicles using the de-quenching approach allowing us to unambiguously identify discrete conformational changes within in-tact vesicles. The nanoscale sensitivity of the de-quenching approach provides a platform from which to explore membrane damage induced by a wide variety of molecular disruptors including additional surfactants and proteins with important biomedical significance.

Soft matter physics of immune cell aggregates

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

T cells are a crucial subset of white blood cells that play a central role in the immune system. Once activated, T cells have the ability to bind to other cells or presented antigens. They can also form T cell aggregates when activated in vitro. The cell adhesion within such T cell aggregates provide valuable information about how different natural and artificial activation pathways work. However, probing the mechanics of these small T cell clusters is experimentally challenging.

In our study, we have developed the micropipette force sensor technique to stretch microscopically small T cell clusters and measure their mechanical properties. The technique enables force measurements at the nanonewton scale through the deflection of a slender glass cantilever. We have also developed a mechanistic model to correlate the macroscopic elastic aggregate properties with the cell-cell adhesion within the cluster. We show how the T cell adhesion strength is affected by different artificial activators and relate this to how the immune system functions. Our soft matter physics study of T cell aggregates provides insight into the coupling between mechanical forces and immune cell behavior, contributing to our understanding of the biology behind immune cell activation.

Fixation and extinction in fluctuating metapopulations subject to bottlenecks and migration

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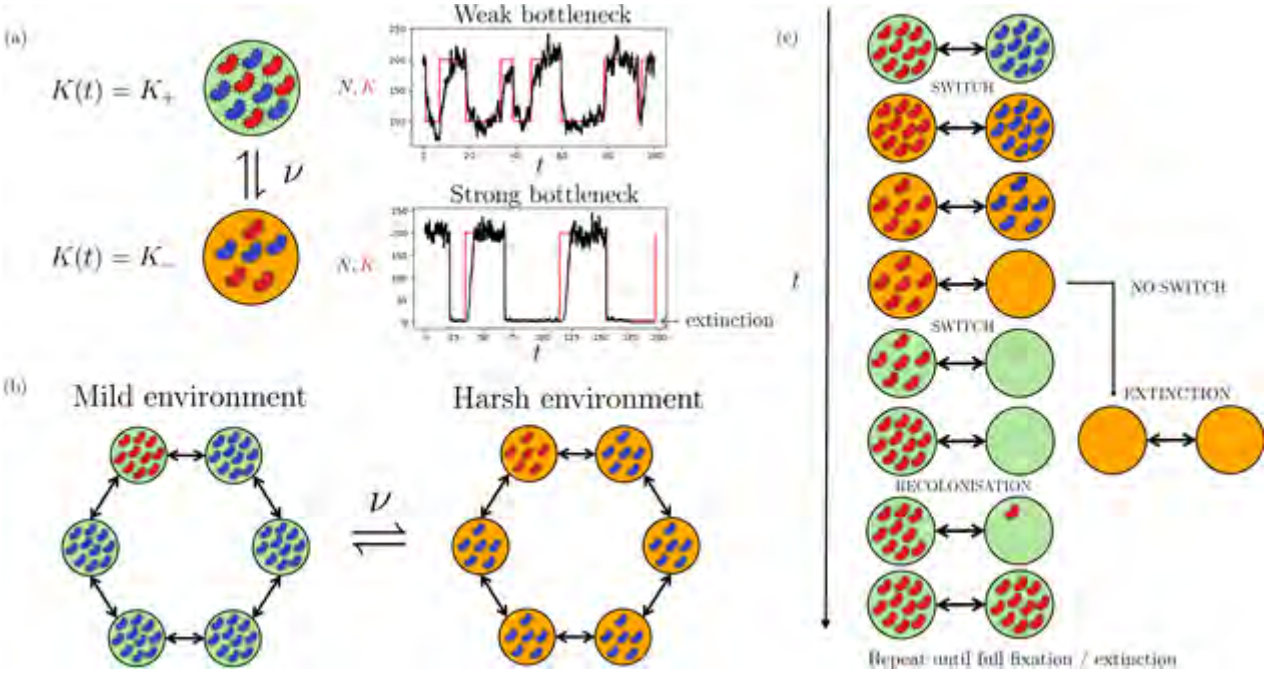
[1]University of Leeds, United Kingdom, [2]Virginia Tech, USA, [3]Stony Brook University, USA

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Microbial populations evolve within spatially structured and dynamically changing environments, a reality often overlooked by classical modelling approaches. From microbial infections spreading across host organs to environmental pollutants altering ecological niches, understanding the effects of and interplay between spatial structure and environmental change is essential for developing insights into the evolutionary dynamics of microbial communities. Here, we present a comprehensive analysis of a two-species metapopulation model, incorporating selection bias, to investigate how microbial species evolve while competing under stochastic population bottlenecks of varying strength. Our analytical framework provides insights into the long-lived behaviour of the system: will we see total extinction of all species, or will a species take over and remain, and how long does this take? We address the problem of eliminating an unwanted (advantageous) mutant in the population, and how best to do so while minimising the risk of total extinction. By combining analytical and computational methodologies, we uncover the rich dynamics underlying microbial population evolution in spatially structured and dynamically changing environments.



Cooperativity and induced oligomerization control the interaction of SARS-CoV-2 with its cellular receptor and patient-derived antibodies

Dr. Roi Asor[1], Anna Olerinyova[1], Sean Burnap[1], Manish S. Kushwah[1], Snežana Vasiljevic[1], Juliane Brun[1], Mario Hensen[1], Michelle Hill[1], Liu Chang[1], Wanwisa Dejnirattisai[1], Piyada Supasa[1], Juthathip Mongkolsapaya[1], Daming Zhou[1], David I. Stuart[1], Gavin R. Screaton[1], Nicole Zitzmann[1], Weston B. Struwe[1], Philipp Kukura1[1]
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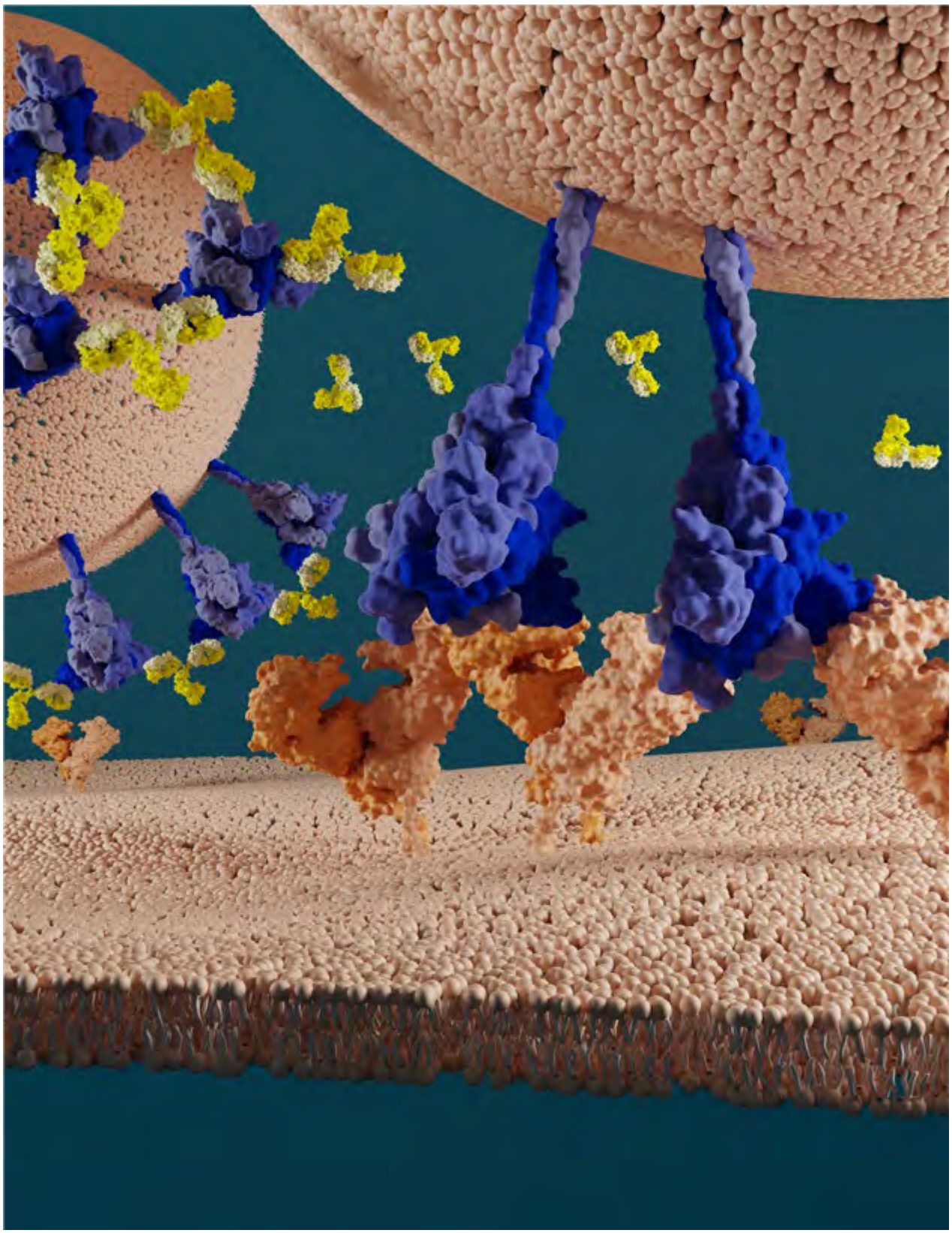
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Viral entry requires efficient engagement of the host cell receptors by viral surface proteins. Most proteins on the virus and cell surfaces are oligomeric, and therefore the interactions between them offer great scope for both the virus and the immune system to leverage the (thermo)dynamic benefits of multivalent binding.

For example, viral entry and inhibition in SARS-CoV-2 involve a trimeric spike surface protein, a dimeric angiotensin-converting enzyme 2 (ACE2) cell-surface receptor and dimeric antibodies. Although there is a growing appreciation of the importance of multivalency, its visualisation and quantification are challenging due to the resultant heterogeneity and the confinement to the membrane surface. Consequently, structural and biophysical characterisation often relies on simplifying the system by reduction to monomeric interactions, which is inadequate for describing the key molecular dynamics important to virus entry and inhibition.
Here, we use a new single-molecule tracking approach based on mass photometry to observe and quantify oligomeric interactions in solution and on lipid bilayers. We reveal that multivalency and cooperativity, rather than 1:1 affinity, correlate with infectivity and inhibition.

We find that ACE2 induces clustering of spike more strongly for more infectious variants, while exhibiting weaker 1:1 interaction. Furthermore, we find that patient-derived antibodies use induced-oligomerisation as a primary inhibition mechanism and to enhance the effects of receptor-site blocking. Our results suggest that naive affinity measurements are poor predictors of potency and introduce a novel antibody-based inhibition mechanism for oligomeric targets. More generally, they point towards a much broader role of induced oligomerisation in controlling biomolecular interactions.



Using Whispering Gallery Modes to Monitor Single-Enzyme turnover events of NanoLuc

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Whispering Gallery Mode (WGM) sensing is an optoplasmonic technique capable of detecting the binding and movement of single molecules with Angstrom-scale precision and millisecond time resolution, without requiring fluorescent tags [1]. This universal, label-free platform provides a powerful alternative to fluorescence-based methods, enabling the direct study of enzyme kinetics and molecular interactions in real-time [2]. However, a key challenge in enzymology is the ability to directly monitor enzymatic turnover at the single-molecule level on such platforms while simultaneously verifying the production of reaction products.

This study addresses this challenge by integrating WGM sensing with a bioluminescent enzyme, NanoLuc (NLuc), whose turnover produces detectable photons as reaction products. Using Furimazine as a substrate, we demonstrate that WGM sensing can detect both single-enzyme binding events to plasmonic gold nanorods and real-time enzyme turnover. Moreover, these results produced a unique signal pattern, contributing to a new area of investigation which will provide new insights into NLuc kinetics. These WGM single molecule results provide a first step in developing a photosensitive WGM hybrid sensor, which will establish a framework to correlate enzymatic activity with product formation, providing conclusive insights into reaction mechanisms.

This approach represents a significant start toward the direct, label-free monitoring of enzymatic turnover events, opening new avenues for studying single-molecule biological systems and advancing the understanding of widely used enzymes like NanoLuc, which have numerous industrial applications.

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[2] M.C. Houghton, et. al. Advanced Science 11(35) (2024)

Tuning the collective cell behavior by surface functionalization

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Active nematic systems have topological defects, which are crucial in regulating morphogenesis and tissue remodeling. Here we show that we can tune the collective behavior of cells near defects by modifying the surface functionalization. We studied the dynamics of NIH 3T3 cells on the topographic ring pattern (short micro-ridges shaped as concentric circular rings) of PDMS coated with two different chemicals fibronectin (FN) and poly-D-lysine (PDL).

The ring pattern induces +1 topological defects in the cell monolayer. The analysis of the cell dynamics reveals that the cells on the FN-coated pattern move mainly azimuthally to the ridges, and slower in the radial direction. On the other hand, the cells on the PDL-coated pattern reveal strong inward radial motion after reaching confluency. This was quantified by calculating the average tangential and radial velocities as a function of the cell density. In the case of FN, the average radial velocity of approximately 2 μm/h remains constant throughout suggesting that the cells are moving slowly inward along with the faster azimuthal movement. However, in the case of PDL, the average radial velocity starts increasing after the cells' confluency indicating a strong inward motion. The cell density rises at the +1 topological defects in both cases suggesting that the accumulation at +1 defects, which has also been observed in various biological systems, can be realized in active nematic systems through different mechanisms, and that the cell density variation at the defects can be dominated by a combination of large-scale collective migration and cell division.

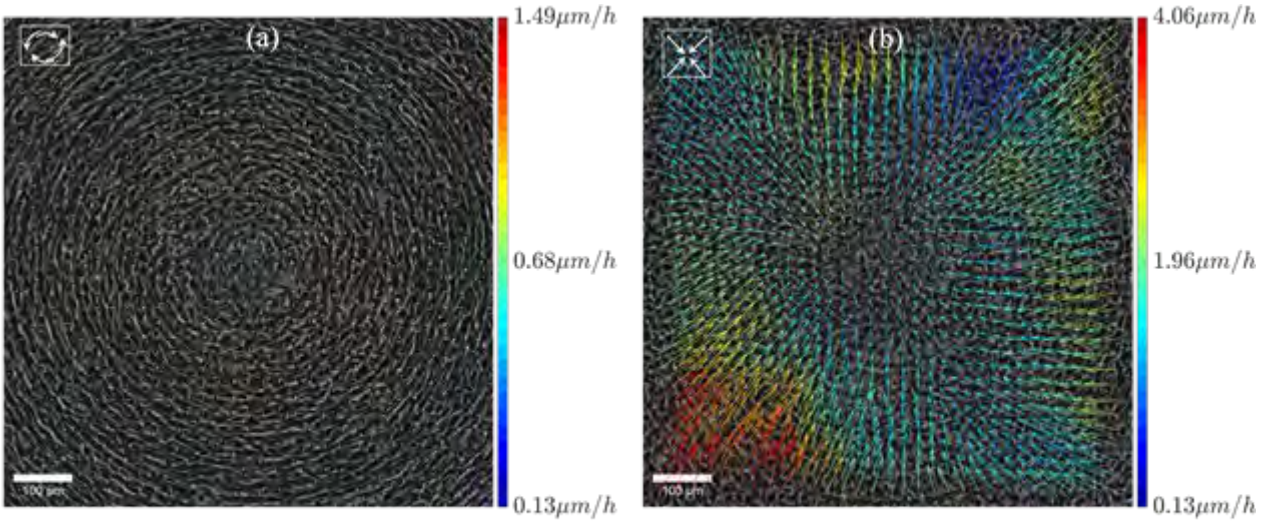

Figure 1: The pictures are showing the average velocity magnitude of fibroblasts cells on ring pattern coated with (a) fibronectin, and (b) poly-D-lysine.

Noise and global warming effects on the swimming dynamics of copepods.

Rafael Ayala Lara[1], Mohammad Doostaran[1], Matilda Backholm[1]
[1]*Aalto University, Finland*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Copepods are the most abundant multicellular organisms on the planet and are crucial to marine food webs, supporting wildlife and aquaculture. Their ability to swim efficiently is critical for their survival. However, the physiology and fitness of many aquatic animals are negatively affected by the increasing levels of noise pollution and global warming derived from human activities. The copepod Acartia tonsa is a key model organism due to its environmental sensitivity and role in marine food chains. Understanding how environmental challenges impact the motility of this species is essential for evaluating their survivability and determining their availability as a key component of the marine trophic chain.

In this work we have further developed the in-vivo micropipette force sensor technique to enable direct swimming force measurements on single copepods. Moreover, we introduce environmental variables to simulate noise pollution combined with conditions predicted under the 2100 global warming scenario, such as increased acidity, temperature, and salinity in the copepod nursing process. By characterizing the swimming dynamics and fitness of copepods under these stressors, we aim to deepen our understanding of how environmental changes affect their motility. This study highlights the implications of environmental conditions on organismal dynamics and the potential consequences for marine food webs.

Automated High-Throughput Flickering Spectroscopy for Measurements of Red Blood Cell Membrane Properties

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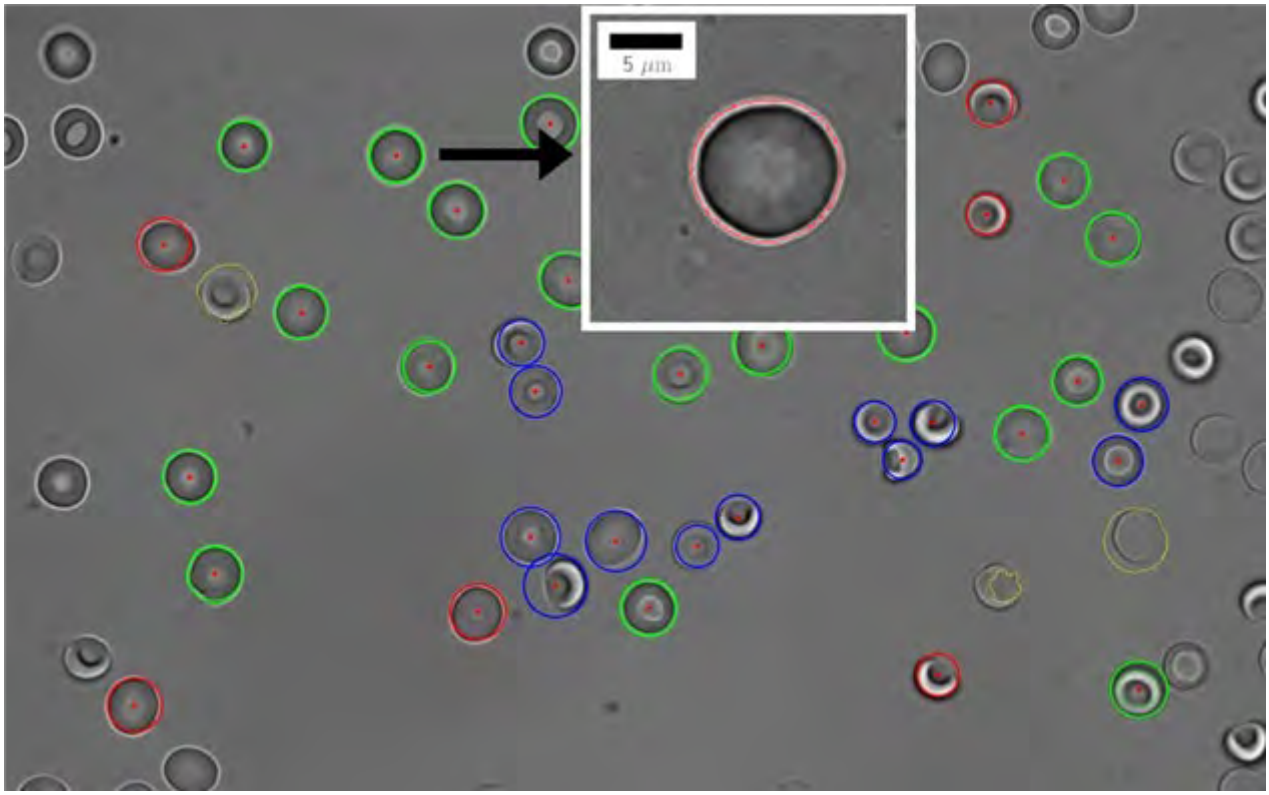
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The mechanical properties of red blood cell (RBC) membranes are critical to their function in oxygen delivery and changes to these properties have significant health effects.
The function of RBCs requires them to be very soft, which together with the small size of the cells brings the energy required for measurable deformation of the membrane into the range of typical thermal energies and the cells are seen to flicker under optical microscopy. Membrane tension and bending modulus can be obtained from spectra of these fluctuations. In this work, we address several issues with practical use of this technique. The amount of manual labour required is significantly reduced by developing a fully automated imaging system allowing the imaging of thousands of cells. A novel processing method is used to improve separation between thermal and slower non-thermal changes using high pass filtering. Several previously used methods for correcting for the effect of finite camera exposure time were tested and combined method was developed to most effectively compensate for this effect.

Supporting image shows how the automatic cell finding processed an example field of view, with cells highlighted in green chosen for further processing and an example cell with detected contour shape.



Adaptive 3D Multiphoton Microscopy for Deeper and Higher Spatial Resolution Imaging

Lu Bai[1,2], Dr K M Naga Srinivas Nadella[2], Dr Antoine Valera[2], Dr Tommy Younts[2], Dr Victoria Griffiths[2], Mr Sameer Punde[2], Dr Tomás Fernández-Alfonso[2], Dr Paul Kirkby[2], Dr Fiona Neufeldt[1,2], Prof R. Angus Silver[2]

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Multiphoton microscopy has become a major tool for studying dynamic biological processes occurring deep within live tissue. In neuroscience, it is widely used in combination with a variety of fluorescent indicators monitor the activity of synapses, individual neurons and population of neurons within neural circuits, spanning spatial scales of micrometres to millimetres in the brain of awake behaving animals. However, current galvanometer-based 2-photon microscopes are too slow to monitor fast neural activity distributed in 3D space. Besides, motion-induced artifacts, which are typically corrected using post hoc methods, are restricted to 2D correction. To address these limitations, we have developed a random-access 2-photon microscope that uses an Acousto-Optic Lens (AOL) to rapidly focus and scan a laser beam in 3D space along with a high-speed closed-loop system that tracks and corrects for 3D movement in real-time.

However, fast inertia-free AOL remote focusing through a fixed objective lens introduces optical aberrations that reduce the spatial resolution below that required for resolving synapses (<1 μm). To improve the spatial resolution and extend the achievable imaging depth while maintaining the speed and agility of random-access 3D imaging, we combined AOL 3D imaging with mirror-based adaptive optics to correct for the spherical aberration caused by remote focusing. Here we present our latest results imaging neuronal dendrites and combining AOL-based high speed 3D imaging with adaptive optics that to achieve deeper, higher spatial resolution imaging.

Funded by the EPSRC and the Wellcome Trust.

Long term evolution of spatially structured microbial communities in controlled environments

Alexander Baker[1], Dr Jordan Romeyer Dherbey[1], Dr Abhirup Mookherjee[1], Joseph Steane[1], Dr Diana Fusco[1]
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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

When growing in nature, bacteria frequently exist in aggregates or biofilms that are distributed in space with environmental cues that change over time. Experimental investigations of these complex systems are typically limited either in time, due to the limited nutrients that can be packed on a Petri dish, or in scale, due to limited dimensions of microfluidic devices where homogeneous environmental conditions can be maintained. Here, we propose a novel setup that enables the study of macroscopic biofilms over long time.

We are developing a device that allows for the flow of different substances (such as different concentrations of nutrients or antibiotics) directly into the agar. Through diffusion to the surface of the agar, a non-homogenous and time-variable chemical environment can be produced without disturbing the spatial structure of the biofilm growing on top. The setup will enable long-term studies of biofilms in environment that can vary in time and space with multiple applications, including experimental evolution of microbial and phage-bacteria communities.

A Platform for Studying Cellular Responses to Mechanical Cues

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Cells respond to various environmental stimuli, including mechanical cues transmitted through the plasma membrane[1]. This process, known as mechanotransduction, is essential for cellular function. Nano- and micro- structured arrays can be used to induce mechanical perturbations in cell membranes[2]. We present a platform for studying mechanotransduction using an array of micrometer-sized SU-8 pillars fabricated on glass coverslips via e-beam lithography. These pillars feature gold-evaporated surfaces, enabling selective protein recruitment and precise control over mechanical stimuli.

We utilize biotin-streptavidin binding for specific protein recruitment on the gold surfaces, while Biotin/OH PEGs minimize unspecific protein adsorption. This combination allows for selective membrane receptor binding through O6-Benzylguanine (BG)/SNAP-tag® chemistry[3].

Preliminary results demonstrate the success of our chemical modification technique on the micro-pillars. This was confirmed by conjugating SNAP-BG to SNAP-GFP, visualizing the specific binding events via confocal microscopy. We have further advanced our research by studying HEK cells transfected with transmembrane receptors carrying N-terminal SNAP-tag on the gold micro-pillars, enabling the observation of selective membrane receptor recruitment.

This platform offers a tool for investigating the mechanisms of cellular mechanotransduction, potentially advancing our understanding of how cells interpret and respond to mechanical cues. Next, we will conduct studies on this platform to study signalling mechanisms of specific membrane receptors such as Epidermal Growth Factor Receptor (EGFR) on these functionalized gold surfaces.

[1]Sansen, T. et al. ACS Appl Mater Interfaces 12, 29000–29012 (2020).

[2]Xie, C. et al. Proc Natl Acad Sci 108, 3894–3899 (2011).

[3]Keppler, A. et al. Nature Biotechnology 21.1, 86-89 (2003)

The Biophysics of the Main Synthase During Gram-Positive Bacterial Cell Division Using AFM

Matthew Barker[1], Dr Joshua Sutton[2], Professor Simon Foster[2], Professor Jamie Hobbs[1]
[1]The University of Sheffield, School of Mathematical and Physical Sciences, United Kingdom, [2]The University of Sheffield, School of Biosciences, United Kingdom

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

In the face of the growing threat of antimicrobial resistance, understanding how the cell wall changes during bacterial division could potentially expose vital weaknesses. We aim to do this by studying the architecture of the cell wall at the nanoscale using atomic force microscopy. This poster will show the various structures seen during the division cycle of Staphylococcus aureus and how these are affected by environmental conditions. When MRSA divides in the presence of antibiotics it employs an alternate mode of division, without its characteristic septal rings created by PBP1 [1]. Instead, PBP2a is used to form the septum as a dense mesh. From this emerges the question - is this alternate division mode possible to be triggered not just genetically, but through environmental or chemical changes? In order to test this, we first tested the viability of various mutants of PBP1 in different environmental conditions. For the mutant of ΔPBP1, the removal of the protein is catastrophic and always results in death. However, in the mutants of PBP1* and PBP1ΔPASTA, a reduction of temperature from 37℃ to 25℃ drastically increased their viability. This poster shows the architecture of the PBP1ΔPASTA mutant when grown at 25℃ and how this changes throughout its division cycle. It is hoped that by understanding how these mutants behave in various conditions, a new weakness in the defence of bacteria may be identified.

[1] Abimbola Feyisara Adedeji-Olulana et al., Two codependent routes lead to high-level MRSA. Science 386,573-580(2024). DOI:10.1126/science.adn1369

Hybrid Computational Framework for Active Polar Fluids

Mr Oleksandr Baziei[1], Dr Tyler Shendruk[1], Mr Benjamin Loewe[1]
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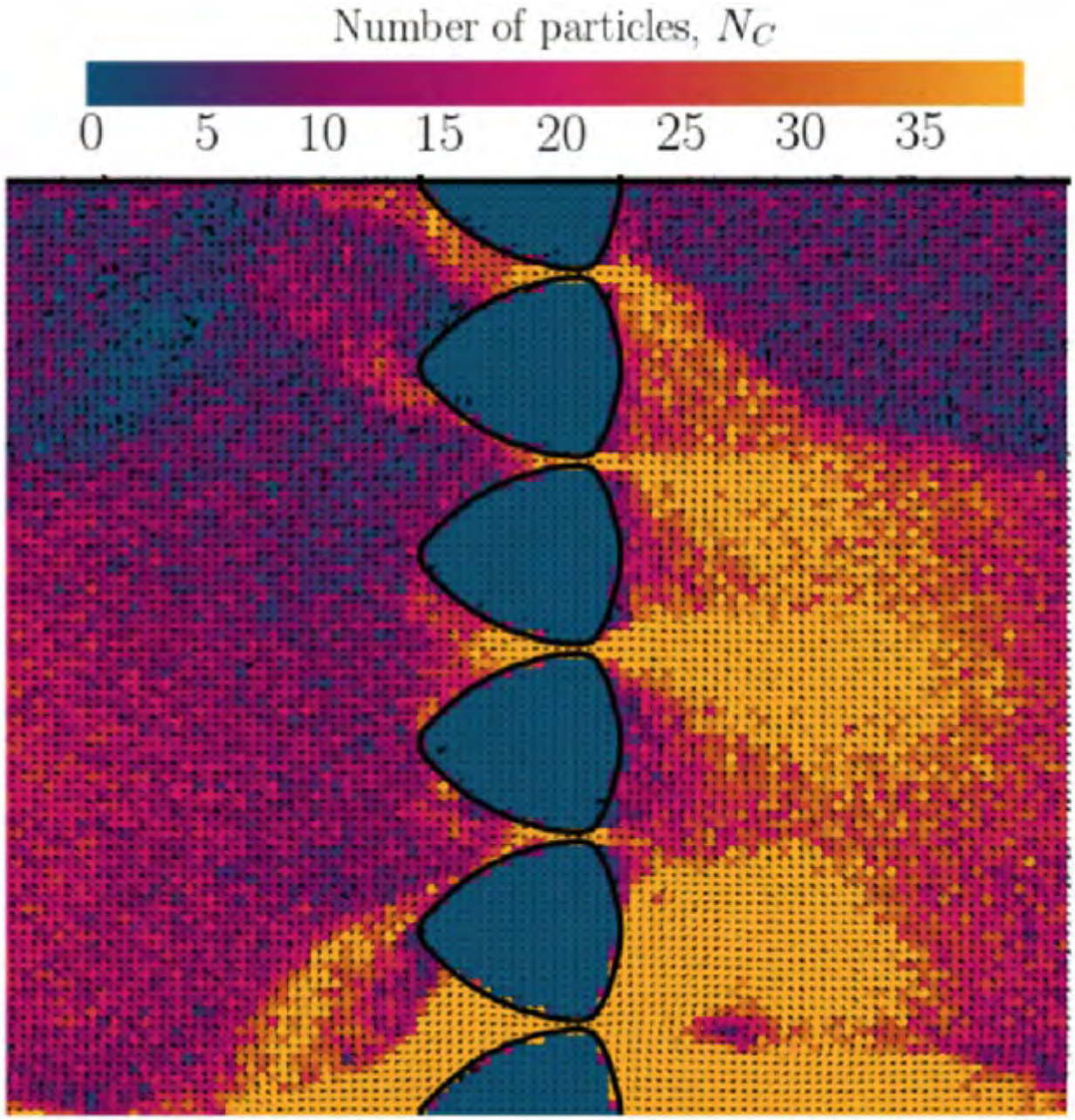
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Motility is a common defining property of living systems, with organisms from bacteria to crowds of people moving collectively in complex environments. Simple particle-based methods, such as the active Vicsek model, have successfully explored the transition from disorderly isotropic motion to ordered polar flocking but are constrained by their simplicity, are computationally costly, and have not been widely used in complex systems. We introduce three novel mesoscale algorithms for simulating active polar fluids. This poster will explain how the algorithms combine the Multi-Particle Collision Dynamics (MPCD) framework with Vicsek-like activity. MPCD is a technique for simulating fluids that does not require calculating pair-interactions, which is merged with the Vicsek model and incorporate a thermostat. These three algorithms all reveal the collective behaviour of polar active particles through a phase transition to flocking.

The simulations demonstrate critical scaling laws at low and high densities. They also reproduce coexistence of phases at the transition point through banding phenomena. The new algorithm is used to study how sufficiently strong external forces suppress banding in the system and how anisotropic geometries act as ratchets guiding the collective flock to preferentially move in one direction. These results validate the versatility of the MPCD framework for modelling active fluids, providing a robust tool for exploring complex systems. The algorithm can be extended to simulate wet bacteria swarms, which would allow us to simulate suspensions of many bacteria while avoiding solving Stokes equations for interactions between bacteria in complex geometries, including circular confinements and anisotropic boundaries.


Number of particles, N_C
0
5
10
15
20
25
30
35

Stress patterns in a model of epithelial cell sheets.

Charlotte Benney[1], Isaac Chenchiah[1], Silke Henkes[2]
[1]University Of Bristol, United Kingdom, [2]Universiteit Leiden, Netherlands

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The active dynamics of epithelial cells drives morphogenetic processes during embryonic development. Mechanical forces originating from the biological constituents of individual cells influence the global dynamics of tissues leading to collective phenomena, such as self-organisation and structure formation. The actomyosin cortex in the cytoskeleton is responsible for the active force generation of cortical tensions, along with pressure forces exerted by the cell's cytoplasm. Adherens junctions bind the cytoskeletons of neighbouring cells to form a tension network spanning the entire epithelial monolayer.

Utilising the two-dimensional approximation of a cell sheet, we model the cellular tensions and pressures as a triangular force network, similar to the planar graph tiling used in Vertex Models. Using the quasistatic argument that viscous relaxation occurs at much shorter time scales than morphogenetic processes, we assume that each vertex in the force network is in mechanical equilibrium. To investigate active stress fluctuations in this heterogeneous, discrete mechanical system, we adapt and apply a Monte Carlo simulation from statistical granular theory.

We generalise the wheel move, from the Force Network Ensemble (FNE), to irregular polygons, allowing us to calculate estimations of the global statistical properties of the cell sheet. We systematically find states of self-stress where tensions are balanced by compressive apical forces. We also find evidence of tension chains along junctions, while retaining truncated normal distributions for junctional tension and apical pressures separately. We vary the amount of anisotropy and geometric disorder in the network and show that tension chain patterns are highly sensitive to these changes.

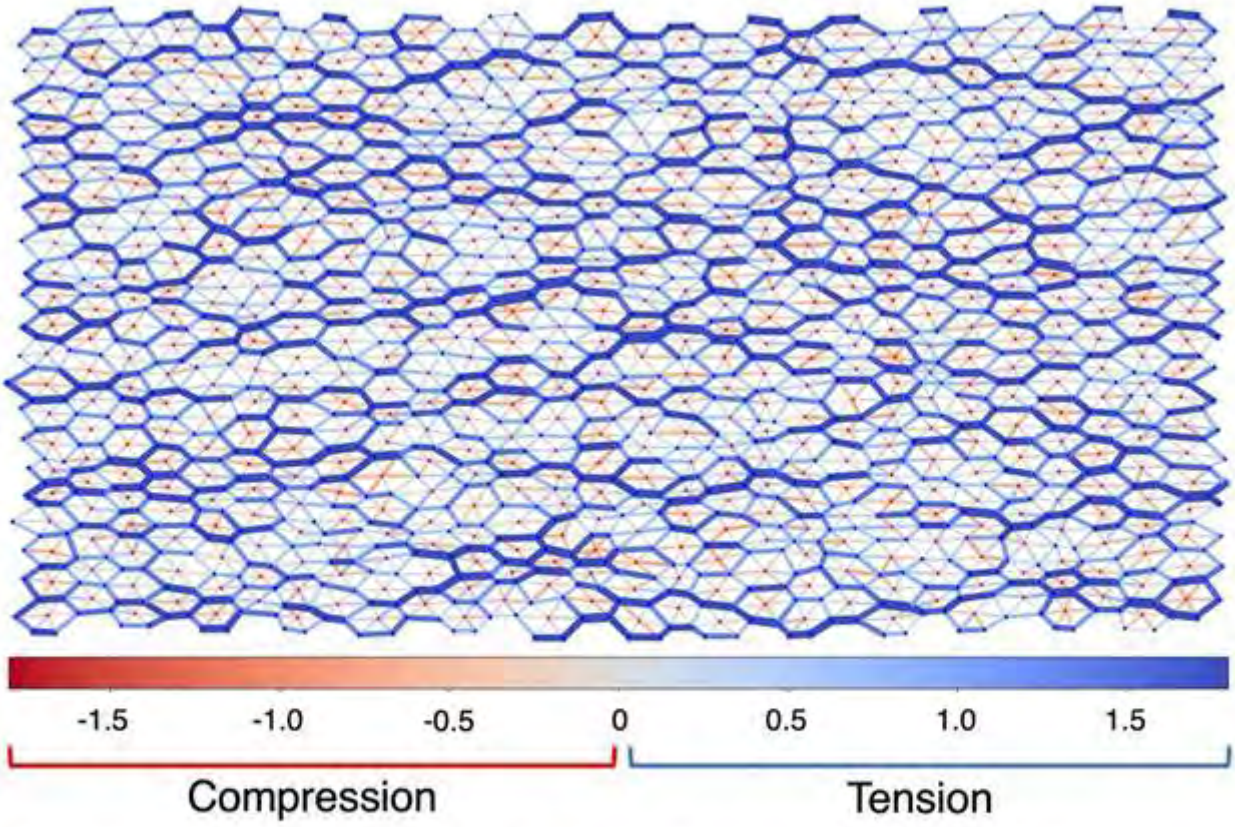


FIG 1: Force configuration plot of cell sheet model, edge thickness indicating magnitude of force with colour indicating sign.

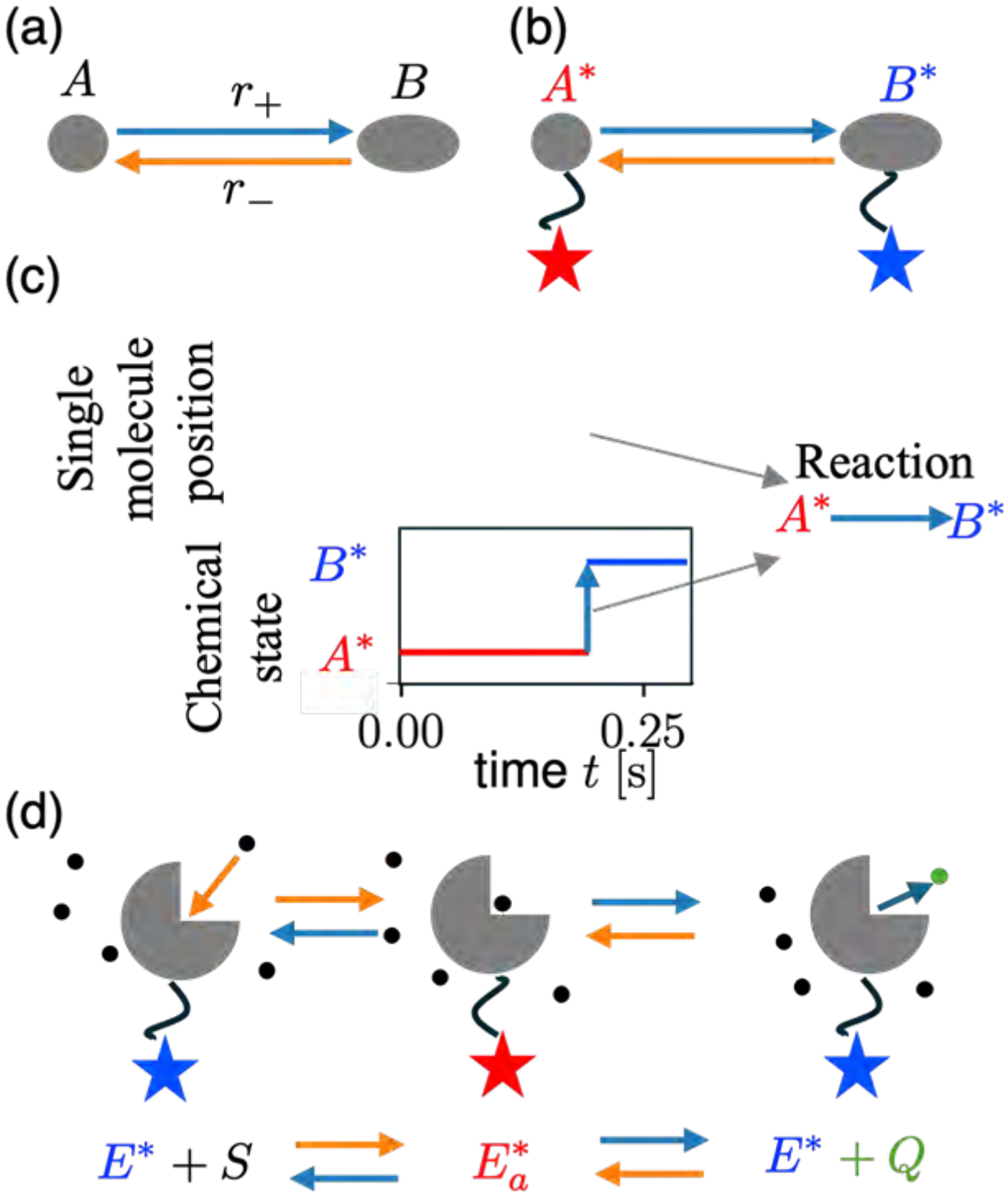
Single-molecule trajectories of reactants in chemically active condensates

Dr Stefano Bo[1], Lars Hubatsch[2], Frank Jülicher[2]
[1]King's College London, United Kingdom, [2]Max Planck Institute for the Physics of Complex Systems, Germany

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Biomolecular condensates provide distinct chemical environments, which control various cellular processes without requiring a membrane. The diffusive dynamics and chemical kinetics of individual molecules inside condensates can be studied experimentally by fluorescent labelling, offering key insights into subcellular dynamics. I will present how biomolecular condensates govern the kinetics of chemical reactions and how this is reflected in the noisy dynamics of labelled molecules.

This will allow me to discuss how the physics of phase separation influences the evolution of single-molecule trajectories and governs their statistics. I will show that, out of equilibrium, the interactions leading to phase separation induce systematic directed motion at the level of single molecules and enhance diffusion. I will discuss how this can provide an alternative explanation for the chemotaxis and enhanced diffusion of active enzymes, which has been experimentally observed. I will then present how we can use stochastic thermodynamics to quantify how far from equilibrium condensates are.


(a)
A
B
r_+
r_-
(b)
A^*
B^*
(c)
Single molecule position
Chemical state
B^*
A^*
0.00
0.25
time t [s]
Reaction
$A^* \rightarrow B^*$
(d)
$E^* + S$
E_a^*
$E^* + Q$

Communication-driven geometric bias enhances multi-agent olfactory search efficiency

Dr. Francesco Boccardo[1], Agnese Seminara[1], Simone Di Marino[1]
[1]*University Of Genoa (Machine Learning Genoa Center), Italy*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

A vital problem for many living organisms is to find the source of an odor carried by a turbulent flow, e.g., to find food or to escape from a predator. When multiple individuals perform the same olfactory search simultaneously, communication and imitation among them can potentially increase group performance.

We study the dynamics of multi-agent olfactory search using a simple swarm model inspired by moth behavior, in which each agent has access to two types of information about its surroundings: olfactory cues (i.e., odor), which are perceived at a short distance and are not shared with others, called "private information"; and visual cues (i.e., direction of neighboring agents), which are accessible to other agents within an interaction range, called "public information". In this model, agents react to the two types of information with two different behavioral responses, which are weighted by a "trust parameter". This parameter governs the degree of communication between agents.

When the olfactory signal is very sparse or even absent, the agents' private behavior involves a spatial exploration phase biased toward the opposite direction of the turbulent flow (e.g., by casting or biased random walk). With the support of numerical and analytical results, we show how varying the degree of communication between agents can amplify this bias in agents' individual search trajectories. This makes the efficiency of the swarm in multi-agent olfactory search intrinsically related to the trust parameter and the geometric constraints of the problem.

Spontaneous unidirectional loop extrusion by SMC proteins

Andrea Bonato[1], Do-Gyun Kim[2], Jae-Won Jang[2], Kyoung-Wook Moon[2], Davide Michieletto[3], Je-Kyung Ryu[2]
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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Even though DNA loop extrusion is arguably one of the most important processes underlying genome organisation, the precise mechanism by which structural maintenance of chromosome (SMC) proteins undertake it is still debated. One question still awaiting an answer is how SMCs can maintain their directional motion along DNA, without taking significant backwards steps. By using AFM, we first show that the angle the hinge domain of yeast condensing forms with the bound DNA is biased. Then, by performing computer simulations, we show that prescribing this geometric constraint during the DNA grabbing step, spontaneously rectifies loop extrusion.

Scaling Behaviour of the Mechanics and Mesoscale Structure of Folded Protein Hydrogels

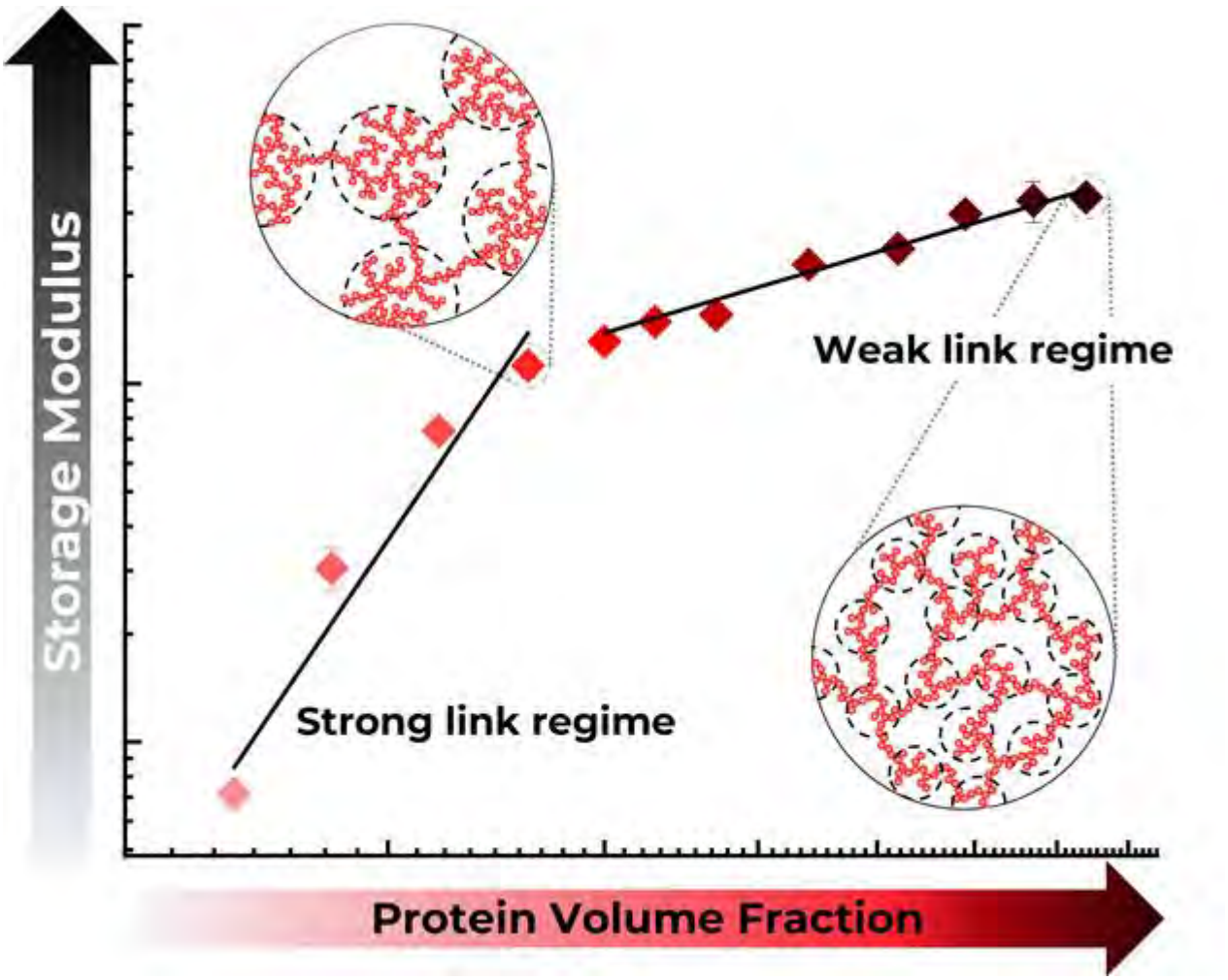
Ahmad Boroumand[1], Dr Matt Hughes[1], Sophie Cussons[2], Najet Mahmoudi[3], Dr David Head[4], Sally Peyman[5], Dr Arwen Tyler[6], Professor Lorna Dougan[1]

[1]School of Physics and Astronomy, Faculty of Engineering and Physical Sciences, University of Leeds, United Kingdom, [2]Astbury Centre for Structural Molecular Biology and School of Molecular and Cellular Biology, Faculty of Biological Sciences, University of Leeds, United Kingdom, [3]ISIS Neutron and Muon Spallation Source, STFC Rutherford Appleton Laboratory, United Kingdom, [4]School of Computer Science, Faculty of Engineering and Physical Sciences, University of Leeds, United Kingdom, [5]School of Engineering & Physical Sciences, Institute of Biological Chemistry, Biophysics and Bioengineering, Heriot-Watt University, United Kingdom, [6]School of Food Science and Nutrition, Food Colloids and Bioprocessing Group, Leeds, United Kingdom

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Folded protein hydrogels are generating significant interest for their potential as functional biomaterials with tuneable properties. A detailed understanding of the relationship between their mechanics and structure would reveal their hierarchical design principles and provide rich opportunities for the design of biomaterials for specific medical and healthcare applications. Inspired by theories from soft matter physics, we have investigated the scaling behaviour of the protein volume fraction (ϕ) and its relationship to the underlying structure and mechanics of the protein network through a combination of rheology and small-angle neutron scattering (SANS).

Using the globular protein bovine serum albumin as a model system and photoactivated chemical cross-linking to retain the colloid-like folded protein structure, we have identified a two-regime behaviour in the storage moduli as a function of ϕ which is well described by a colloidal flocculated model. SANS reveals a heterogeneous network structure with fractal-like clusters connected by intercluster regions. The fractal dimension (D) of clusters remains constant (~2.35) up to ϕ=4.4% beyond which the crowded network does not allow for further growth of mature clusters, resulting in a progressive decay in D, reaching D=2.06 at ϕ=7.4%. Network parameters such as number of proteins in an average cluster and correlation length scale with ϕ in line with predictions of both the de Gennes' blob model. Insights gained from our integrated approach will enable the design of novel biomaterials for controlled drug molecule release, with the added advantage of a building block which is responsive to mechanical and biochemical cues.


Storage Modulus
Weak link regime
Strong link regime
Protein Volume Fraction

In vitro expression and characterization of the heme binding domain of HasR from Pseudomonas aeruginosa

Dr. Federico Bosetto[1], Dr. Maria Zacharopoulou[1], Dr. Ioanna Mela[1]
[1]*University of Cambridge, United Kingdom*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

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 domain and the Secretin/TonB domains. The former carries the His-221 residue, fundamental for the heme coordination binding. The domains of interest were expressed together with a cleavable GST-tag at the N-terminal side and with a 6xHistidine-tag at the C-terminal side. The protein was first purified by GH-resin, and, after the removal of GST-tag, a second purification by affinity chromatography occurred.

The proper folding of the protein was assessed by Circular Dichroism and NMR techniques, reporting a composition of 20% α-helix, 27% antiparallel β-sheets and 53% disordered. The protein is also tested for its functionality by evaluating the capability of the purified domain for heme binding. 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.

Friction controls spatial patterning in active fluids

Douglas Brown[1], Alex Mietke[1]
[1]*University of Oxford, United Kingdom*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Mechanical stresses are known play a crucial role in a wide range of developmental processes, including cell division, gastrulation and symmetry breaking. Increasing experimental evidence suggests in addition that complex properties of the surrounding material are responsible for guiding morphogenetic processes – a feature often overlooked in theoretical models.

We consider a minimal hydrodynamic model of an active fluid in which chemically organised isotropic stresses are generated. Previous work has shown that active stresses promote the spontaneous formation of non-trivial concentration patterning [1].

To account for inhomogeneous mechanical properties of the surrounding material, we allow spatially varying patterns of external friction. We study this system by analysing non-linear mode couplings which appear as a result of inhomogeneous friction. We identify basic principles that determine how spontaneously emerging internal stress distributions orient themselves with respect to friction patterns. Numerical analysis confirms these results and reveals a rich phenomenology of non-linear steady states when inhomogeneous friction is present.

This work provides new insights into how mechanical interactions with the surrounding can guide the self-organisation of active fluids with potential applications in developmental symmetry-breaking processes and the design of synthetic active materials.

[1] Bois et al. PRL 106, no. 2 (2011)

Lymph node mechanics and its impact on immune cells

Luisa Bruno[1], Emmanuel Donnadieu[2], Jacques Fattaccioli[3], Jean François Rupprecht[4], Paolo Pierobon[1]

[1]Immune cell signaling and retroviral infection, Institut Cochin, France, [2]Cancer et réponse Immune, Institut Cochin, France, [3]Ecole Normale Supérieure, CNRS Institut Pierre-Gilles de Gennes pour la Microfluidique, France, [4]Aix Marseille Univ, Université de Toulon, France

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

B cells are crucial players in the adaptive immune response [1], primarily recognized for their ability to produce antibodies. To perform this function, naïve B cells must first be activated. This activation occurs in the lymph node, specifically within the subcapsular sinus zone. Here, B cell receptors (BCRs) engage with antigens presented by antigen-presenting cells (APCs), forming an immune synapse. The antigen is then internalized by the B cell through enzymatic or mechanical processes. Interestingly, B cells predominantly exert mechanical forces when interacting with deformable substrates [2], indicating that the mechanics of the microenvironment significantly influence B cell function.

To explore this hypothesis, we employed a system of lymph node slices. Using lipid droplets as probes, we obtained microrheological data that provided insights into tissue flow dynamics and the mechanical stress experienced by cells. A custom pipeline was developed to enable the segmentation and tracking of both droplets and cells in 3D.

This innovative approach sheds light on the mechanical properties of lymph nodes and their role in antigen presentation, offering a more physiologically relevant perspective on B cell activation

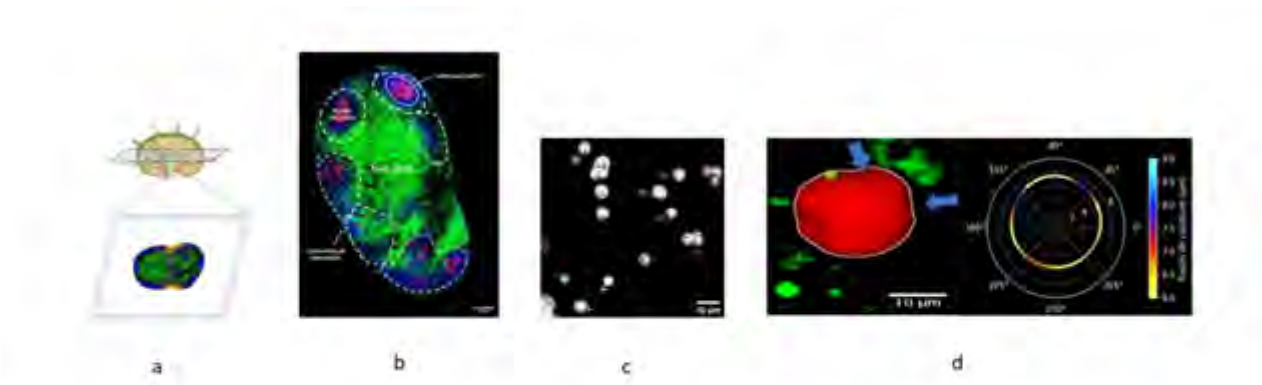


Figure 1: Schematic of the tissue slice system. (a) A schematic representation of the setup used to study lymph nodes ex vivo. (b) An image of a lymph node slice, showing the tissue structure. This system enables (c) 3D tracking of cells and lipid droplets to study their dynamics and (d) mapping of stress distribution within the tissue using lipid droplets as mechanical sensors.

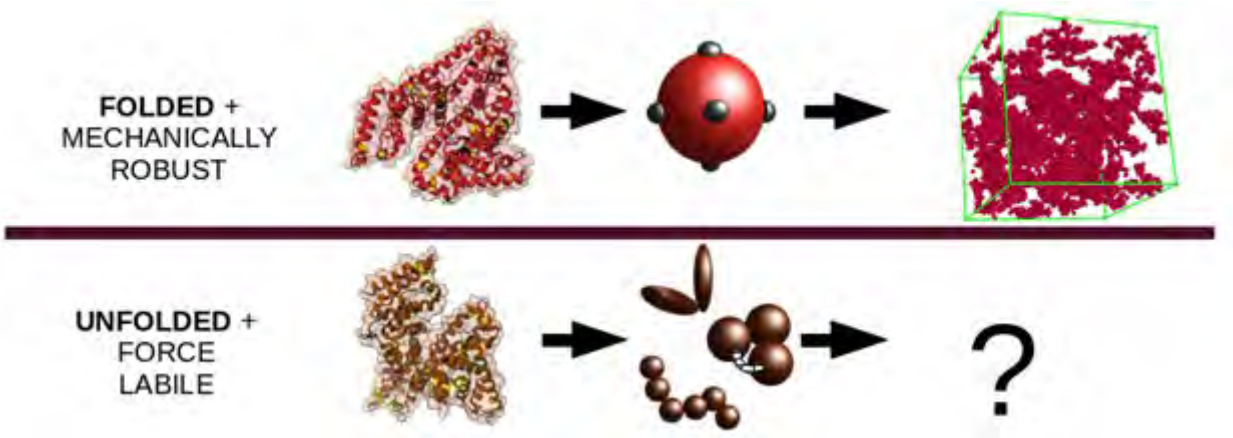
From worm-like to blobby: coarse-graining protein unfolding in hydrogel networks

Victoria Byelova[1], Dr David Head, Professor Lorna Dougan
[1]*University of Leeds, United Kingdom*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Protein hydrogels are highly biocompatible and stimuli-responsive with a capacity to be rationally designed, making them excellent candidates for applications such as tissue scaffolding and drug delivery. By suppressing the unfolding of a protein domain within a hydrogel, it is possible to take a coarse-grained approach to modelling the gel's structure and network behaviour: a mechanically robust folded protein can be represented by a globular colloidal particle. Bovine serum albumin (BSA), for instance, is mechanically robust when stapled into its folded state by disulphide bridges. Once the disulphide bridges are dissolved, the BSA molecule becomes force-labile and can unfold upon experiencing force within the network. Coarse graining makes it possible to observe wider network mechanics without being computationally expensive or infeasible.

By forming a gel from mechanically robust domains, the result is a mechanically rigid gel due to increased thermodynamic stability of individual protein domains. However, a system composed of force-labile domains has faster relaxation mechanics due to the more viscous and wormlike behaviour of the unfolded proteins. How might these features interplay with each other? There may be a complex relationship between the mesoscale and the material bulk properties to understand. As such, computationally simulating a coarse-grained network can assist in quantitatively identifying key contributions of an unfolding protein within a network. The opportunity to modulate network behaviour in-silico can mitigate the need for trial-and-error synthesis of gels and instead introduce a more methodic approach of rationally designing a protein gel.



Uncovering protein conformational dynamics within two-component viral biomolecular condensates

Alice Colyer[1], Julia Acker[2], Alexander Borodavka[2], Antonio Calabrese[1]
[1]Astbury Centre for Structural Molecular Biology, School of Molecular and Cellular Biology, Faculty of Biological Sciences, University of Leeds, United Kingdom, [2]Department of Chemical Engineering and Biotechnology, University of Cambridge, United Kingdom

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Biomolecular condensates selectively compartmentalise and organise biomolecules within the crowded cellular milieu and are instrumental in some disease mechanisms. Upon infection, many RNA viruses form biomolecular condensates that are often referred to as viral factories. The assembly mechanism of these viral factories remains poorly defined, but involves transient, non-stoichiometric protein/RNA interactions, making their structural characterisation challenging. Here, we sought to investigate the structural dynamics and intermolecular interactions of the key proteins responsible for condensate formation upon rotavirus infection, namely NSP2 (an RNA chaperone) and NSP5 (an intrinsically disordered protein [IDP]), using a combination of hydrogen-deuterium exchange mass spectrometry (HDX-MS), native MS and biophysical tools. Our data reveal key structural features of an intrinsically disordered protein NSP5 that are vital for condensate assembly.

Moreover, we demonstrate that within a condensate there are altered conformation dynamics within NSP2, which we propose represents a mechanism for allosteric regulation of RNA annealing within a biomolecular condensate. Combined, our data demonstrates that the unique environment within a biomolecular condensate can tune functionally important protein conformational dynamics, which may play a crucial role in the replication of rotaviruses.

Untangling chromatin loops: uncovering biophysical characteristics of CCCTC-binding factor (CTCF)

Colleen Caldwell[1], A Ridolfi[1], M Sá[1], A.S. Biebricher[1], G.L.J. Wuite[1]
[1]*Vrije Universiteit Amsterdam, Netherlands*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The compact, flexible 3D structure of the human genome is critical for regulation of gene expression and DNA maintenance. Dysregulation is associated with cancer and developmental disorders. CCCTC-binding factor (CTCF) acts at the mesoscopic scale of genome organization, sitting at the base of chromatin loops bordering topologically associated domains. The underlying mechanisms of CTCF in chromatin organization remain unknown.

Full-length CTCF was purified, retaining the 11 zinc fingers that drive DNA binding and the large disordered N- and C-termini. Stabilization of loops by CTCF was observed in the absence of loop extruders using atomic force microscopy (AFM) and optical tweezers. Combined optical tweezers and confocal fluorescence microscopy allowed for simultaneous observation of fluorescently-tagged CTCF binding and mechanical impacts on the tethered DNA. In these assays, CTCF sliding on non-specific DNA was observed and CTCF binding altered the force response of DNA. CTCF-dependent bridging was also observed and characterized, revealing bridges that slide readily at low force while resisting ruptures forces exceeding the stability of dsDNA.

We propose that this biophysical characterization of the dynamic CTCF:DNA complex may reveal how CTCF localizes to specific sites and promotes stable chromatin looping while allowing for dynamic flexibility. Future studies will investigate regulatory factors that target CTCF in order to alter the three-dimensional genomic structure.

Entropy production in spatially diffuse division-death dynamics.

Sam Cameron[1], Elsen Tjhung
[1]*The Open University, United Kingdom*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

We consider a generic class of stochastic particle based models whose state at an instant in time is described by a set of continuous degrees of freedom (e.g. positions), and the length of this set changes stochastically in time due to birth-death processes. Using a master equation formalism, we write down the dynamics of the corresponding (infinite) set of probability distributions: this takes the form of coupled Fokker-Planck equations with model-dependent source and sink terms. We derive the general expression of entropy production rate for this class of models in terms of path irreversibility.

To demonstrate the practical use of this framework, we present a biologically motivated model of division, death, and diffusion which includes spatial correlations through the particle division process. We compute the marginal probability distributions of this model and subsequently the marginal entropy production rate.

Active Spaghetti: Collective Organization in Filamentous Cyanobacteria

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Many active systems are capable of forming intriguing patterns at scales significantly larger than the size of their individual constituents. Cyanobacteria are one of the most ancient and important phyla of organisms that has allowed the evolution of more complex life forms. Despite its importance, the role of motility on the pattern formation of their colonies is not understood. Here, we investigate the large-scale collective effects and rich dynamics of gliding filamentous cyanobacteria colonies, while still retaining information about the individual constituents' dynamics and their interactions [1]. We investigate both the colony's transient and steady-state dynamics and find good agreement with experiments [2]. We furthermore show that the Péclet number and aligning interaction strength govern the system's topological transition from an isotropic distribution to a state of large-scale reticulate patterns. Although the system is topologically non-trivial, the parallel and perpendicular pair correlation functions provide structural information about the colony, and thus can be used to extract information about the early stages of biofilm formation. Finally, we find that the effects of the filaments' length cannot be reduced to a system of interacting points. Our model proves to reproduce both cyanobacteria colonies and systems of biofilaments where curvature is transported by motility.

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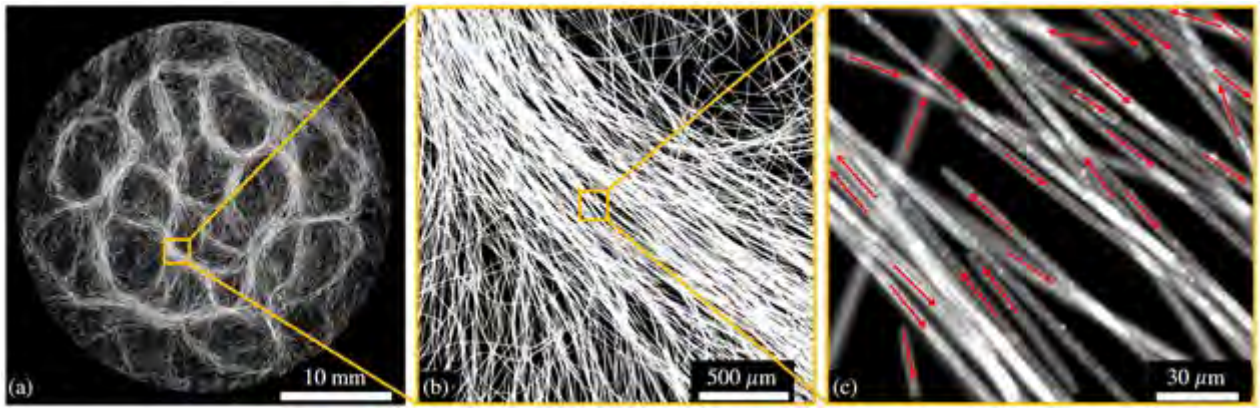

Light-driven synchronization of optogenetic clocks

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Genetic clocks keep time within living organisms in order to generate stable periodic behavior. To investigate this phenomenon, synthetic biologists have tackled the problem of designing from scratch minimal gene networks that can recreate periodic patterns of gene expression.

However, cell-to-cell variability introduces a dispersion in the characteristics of these clocks that drives the population to complete desynchronization. Here we introduce the optorepressilator, an optically controllable genetic clock that combines the repressilator, a three-node synthetic network in E. coli, with an optogenetic module enabling to reset, delay, or advance its phase using optical inputs. We demonstrate that a population of optorepressilators can be synchronized by transient green light exposure or entrained to oscillate indefinitely by a train of short pulses, through a mechanism reminiscent of natural circadian clocks. Furthermore, we investigate the system's response to detuned external stimuli observing multiple regimes of global synchronization. Integrating experiments and mathematical modeling, we show that the entrainment mechanism is robust and can be understood quantitatively from single cell to population level.

A mathematical investigation into how surfactants influence nanobubble stability in the plant xylem

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Plants transport water, nutrients and signalling molecules via their vascular system. To successfully carry out this transport, plants must overcome several physical challenges. For instance, the transportation of water from the root to the shoot is driven by transpiration and occurs in the xylem. This process operates under absolute negative pressure, which is a metastable state and can induce nanobubble (bubbles between 50 and 200nm in diameter) formation. These nanobubbles can be detrimental to the plant because they have the potential to form an embolism in the plant xylem. Plants therefore need to balance these physically dangerous conditions with their needs for water, nutrient acquisition and signalling. How plants meet these conflicting demands is currently unknown.

I will present current ideas and approaches for addressing this fascinating problem. One hypothesis is that plants utilise polar lipids (surfactants) on the nanobubble surface to induce a variable surface tension which helps to break down the bubble. However, the conditions for this break-up are unknown. We model the xylem as a Stokes flow containing the nanobubble, introduce surfactants and apply linear stability theory to the governing system of partial differential equations to examine the stability of the bubble by perturbing its radius. We then determine under what conditions the bubble will remain in a stable state or will become unstable and break up. This analysis sheds light on the process by which plants can avoid the harmful situation of embolism formation in the xylem.

Functionalising DNA Nanostructures for Lysosomal Escape and Tankyrase Inhibition

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

We are synthesising and functionalising DNA nanostructures with bioactive peptides to escape the endolysosomal pathway and inhibit human tankyrases (TNKS). TNKS are important regulators of the Wnt signalling pathway and are upregulated in many different cancer types. Peptide inhibitors that mimic native protein-protein interactions with the TNKS substrate recognition domain have been developed to overcome challenges of off-target toxicity [1]. DNA nanostructures have been explored as an effective vehicle for peptide delivery, due to their high programmability, low biotoxicity, and ease of generation. The development of the DNA origami method allows for simple and efficient assembly of 2D and 3D nanoscale DNA structures [2]. Nanostructures have been shown to uptake into mammalian cells through the endolysosomal pathway, limiting their intracellular targeting capacity [3]. To expand their potential therapeutic application to intracellular TNKS targets, 5-well frame and triangle DNA nanostructures were successfully functionalised with engineered endosomolytic peptides and tankyrase peptide inhibitors as confirmed by atomic force microscopy and agarose gels. Confocal microscopy studies revealed localisation of nanostructures to the cell surface and subsequent internalisation in a SW-480 colorectal cancer cell line.

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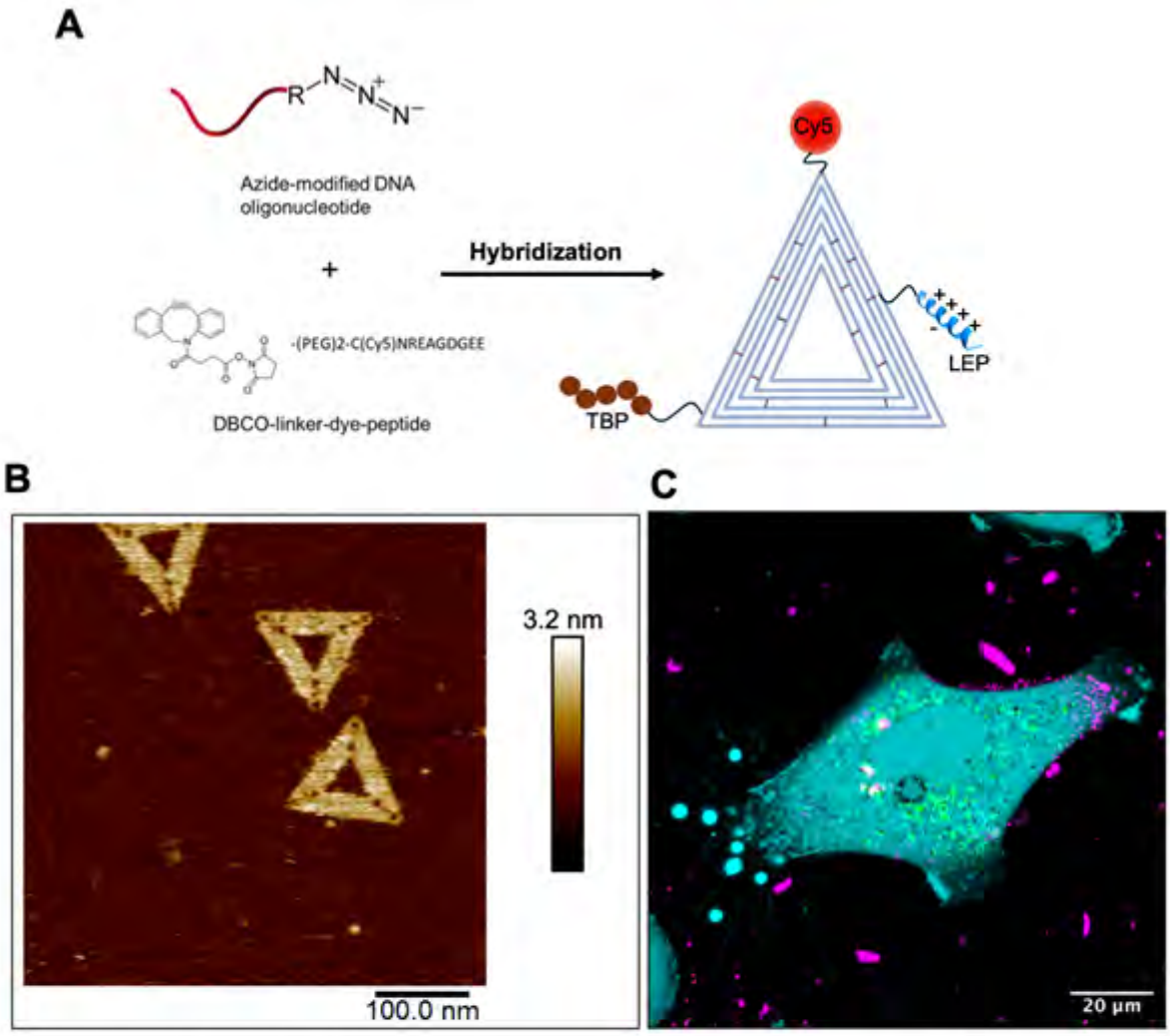

Summary of functionalized DNA nanostructures formation, functionalization, and cellular uptake. **A)** Graphical summary of click reaction used to functionalise DNA nanostructures with fluorophore Cy5, tankyrase binding peptide (TBP), and an engineered lysosomal escape peptide (LEP). **B)** Atomic force microscopy image of triangle nanostructures functionalised with TBP and LEP. **C)** Confocal microscopy image of triangle nanostructures internalized by SW480 cells following a 24h incubation. Cells expressing cytoplasmic GFP (cyan), with a fluorescent lysosomal probe (green:LysoBrite Orange), and fluorophore-hybridized nanostructures (magenta:Cy5).

Optimising hybrid vesicles for membrane protein reconstitution: applications and insights

Dr Rosa Catania[1,5], Prof Michael Rappolt[2], Prof Stephen Muench[3,5], Prof Lars Jeuken[4], Prof Paul Beales[1,5]

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Hybrid vesicles (HVs), composed of diblock copolymers like poly(butadiene-b-ethylene oxide) and phospholipids, provide a versatile platform for membrane protein (MP) reconstitution, effectively overcoming the stability challenges of liposomes. Our recent work has focused on enhancing the usability and optimisation of HVs for this purpose. We developed a detergent-free method that allows for the direct incorporation of MPs from styrene-maleic acid lipid particles (SMALPs) into HVs, significantly improving both efficiency and ease of use. Specifically, we successfully reconstituted the multi-subunit cyt bo3, a terminal oxidase from Escherichia coli, without the need for detergents. We also demonstrated that this method is applicable to complex membrane protein mixtures. In contrast, reconstitution from SMALPs into liposomes was unsuccessful.

Notably, HVs retained cyt bo3 bioelectrocatalytic activity even after being stored for over a year, as assessed by the formation of solid-supported hybrid membranes (SSHMs) that were comparable to freshly prepared samples, with cyt bo3 maintaining over 50% of its original activity. This finding confirms the longevity and stability of HV systems that we previously established.

To further understand how polymer structures influence MP reconstitution, we systematically screened various copolymer architectures, varying headgroup-to-tail ratios and polymer chain lengths. We observed significant effects on reconstitution efficiency, orientation and activity of cybo3. Our findings highlight the versatility of HVs as a biomimetic platform for MP, paving the way for advancements in artificial cell development and other applications.

Understanding the Mechanism of Novel Anticancer Drugs with Atomic Force Microscopy

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Understanding mechanism of action is crucial in the development of novel cancer treatments. Often the interactions of these drugs with DNA are studied through MD simulations, which only consider very short fragments of DNA. Given that DNA is a highly flexible molecule with dynamic structure that allows it to tightly pack the entire 2-metre-long genome into each cell, considering the wider context of the nucleic acid environment in these drug interactions is critical in understanding their effect on the whole cell. Atomic Force Microscopy (AFM) is a powerful technique that allows single molecules of DNA to be probed with submolecular resolution, which we use to localise and quantify subtle regions of damage along the DNA backbone. This can then be related to the mechanics of the DNA molecules at both an individual and global level (e.g. the levels of supercoiling or curvature), to give a clearer picture of the activity of the drugs and their downstream effects.

Here, we investigate the DNA damage activity of several novel metallodrug compounds that have distinct proposed mechanisms of action, which give them increased cancer cell specificity, ability to overcome resistant phenotypes, and reduced toxicity to healthy tissue. Further understanding metallodrug driven DNA damage is vital for the further development of new, more targeted cancer therapeutics. We have developed a new methodology for drug development and screening by developing an open-source pipeline to probe and quantify a range of drug-driven DNA conformational changes.

Counting Active Particles in Boxes to Quantify their Dynamics

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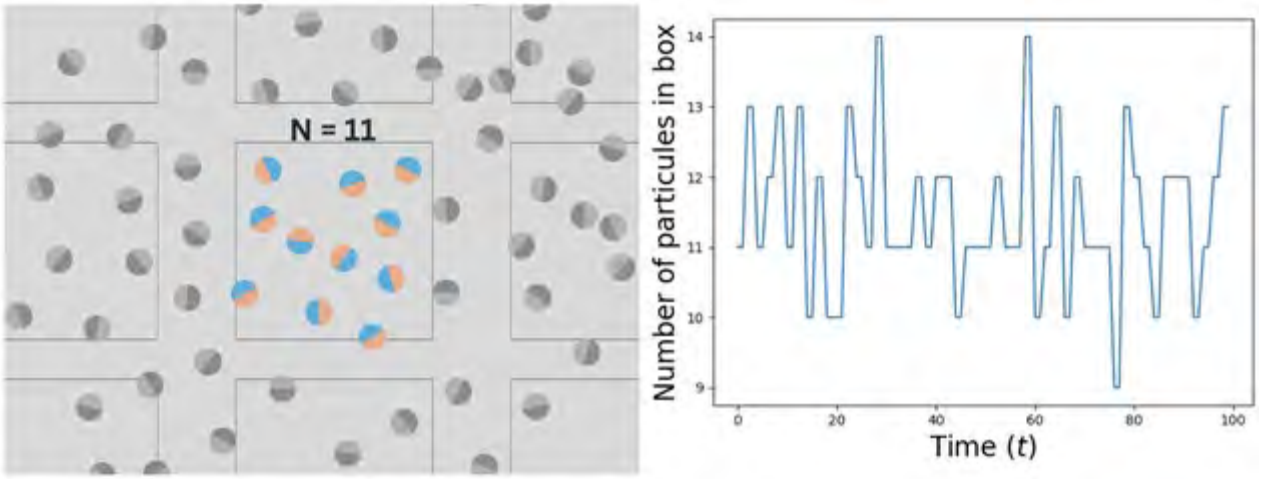
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Quantifying particle dynamics with microscopy is a great interest of the active matter community. Indeed information on motion in complex systems is essential to better understand how active particles navigate, evolve and interact with their environment: To quantify their displacement one traditionally relies on particle trajectories. Trajectories can however be difficult to obtain, especially in the presence of large concentration heterogeneities — a generic feature of active matter, canonically illustrated by MIPS (Motility Induced Phase Separation). Recent work suggests an alternative strategy to quantify dynamics, which removes the need for obtaining trajectories, simply by counting particles in virtual observation boxes. The fluctuations of the number of particles in a box can be used to infer transport parameters of passive particles. Here we develop a method to obtain the dynamic properties of active particles from fluctuating counts.

We show, using experiments and simulations on dilute Active Brownian Particle systems, that fluctuating counts are sensitive to active motion features, recovering regimes of diffusive, ballistic and long-time diffusive motion. By deriving a theory based on hydrodynamic fields, we obtain analytical laws and limiting behaviour allowing us to directly extract dynamic parameters (self propulsion speed, rotational and translational diffusion) from experiments using this counting method. These results open the possibility of rationalizing the local motion of diverse active suspensions in denser systems.



Homeostasis in confined environments

Dr. KVS Chaithanya[1,5], Jan Rozman[2], Andrej Košmrlj[3,4], Rastko Sknepnek[1,5]
[1]School of Life Sciences, University of Dundee, United Kingdom, [2]Rudolf Peierls Centre for Theoretical Physics, University of Oxford, United Kingdom, [3]Department of Mechanical and Aerospace Engineering, Princeton University, USA, [4]Princeton Materials Institute, Princeton University, USA, [5]School of Science and Engineering, University of Dundee, United Kingdom

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Epithelial tissues achieve homeostasis through a balance of cellular processes, such as division and ingression, which are influenced by mechanical properties of the tissues and their microenvironment [1]. Using a two-dimensional vertex model, we studied homeostasis in confined epithelial tissues composed of a proliferating tissue surrounded by a non-proliferating tissue fixed at the periphery [2]. Our findings show that homeostasis is maintained through a dynamic balance between cell divisions and ingressions driven solely by mechanical forces. We observed that the steady-state area and cell count of the proliferating region increase when the non-proliferating regions are more compressible, facilitating expansion of the proliferating tissue. Additionally, stronger confinement was associated with greater disorder in cell shapes and a reduction in both the proliferative area and number of cells. These insights emphasize the role of mechanical forces in regulating epithelial organization and growth in confined conditions.

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The Physics of Bacterial Survival: A Mechanical Mystery

Dr Rui Han[1], Dr Laia Pasquina-Lemonche[2], Dr Jack Dawson[1], Professor Xi-Qiao Feng[3], Professor Henk Busscher[4], Professor Waldemar Vollmer[5], **Professor Jinju Chen**[1]
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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Bacterial cell walls are essential for cell integrity and protection. Understanding the interplay between cell wall mechanics and turgor pressure is crucial for comprehending bacterial resilience. We present a novel approach that combines atomic force microscopy (AFM) with mathematical modeling to quantify these parameters. Our results reveal that while the overall 3D architecture of peptidoglycan remains relatively stable, variations in cross-linking density significantly impact bacterial mechanical properties. We demonstrate that depletion of Penicillin-binding protein 4 (PBP4), a key enzyme for high-degree crosslinking, leads to decreased cell wall stiffness and turgor pressure in Staphylococcus aureus. This compromised bacterium exhibits increased susceptibility to osmotic stress, mechanical stress, and nanostructure-mediated killing. Our findings highlight the importance of cell wall architecture in bacterial mechanics and provide insights into the development of innovative antibacterial strategies.

Impact of mRNA structures on the interaction with lipids and nanoparticle formulation properties

Miss Nga Man Cheng[1], Dr Najet Mahmoudi[3], Professor Cameron Alexander[1], Professor Zoe Waller[2], Dr James Humphrey[4], Dr Karen Alvey[1], Dr Pratik Gurnani[2], Dr Naoto Hori[1]
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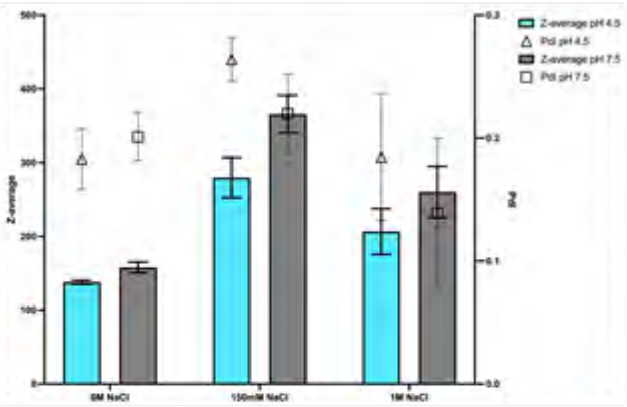
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

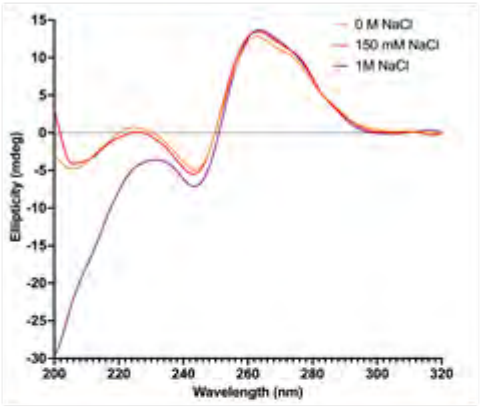
The success of COVID-19 vaccines, Comirnaty and SpikeVax, has proven the efficiency of lipid nanoparticles (LNPs) as a protective vehicle to deliver messenger RNAs (mRNAs) to express the desired antigen in the combat with an infectious disease. LNPs are made up of four main components: cationic/ionisable lipid, helper lipid, cholesterol, and PEGylated lipid, where they self-assemble into a lipid matrix. The cationic/ionisable lipids are thought to form electrostatic interactions with the negatively charged phosphate backbone, aiding the encapsulation of mRNA within the lipid matrix. However, little is known about how mRNA structure impacts the formation of LNPs and, thus, its transfection efficiency. In this project, we aimed to manipulate the mRNA structure using different formulation conditions and characterise the resulting LNPs using dynamic light scattering (DLS), circular dichroism (CD), and small-angle neutron scattering (SANS). This is also complimented by molecular dynamics simulation of LNP assembly, which helps us to understand the interaction between lipids and mRNA on a molecular level.

How does mRNA structure affect the formation of lipid nanoparticles?

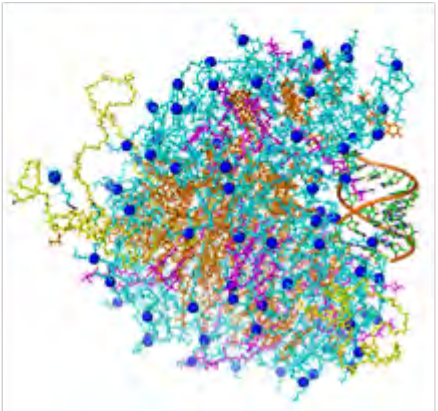
Dynamic light scattering (DLS)



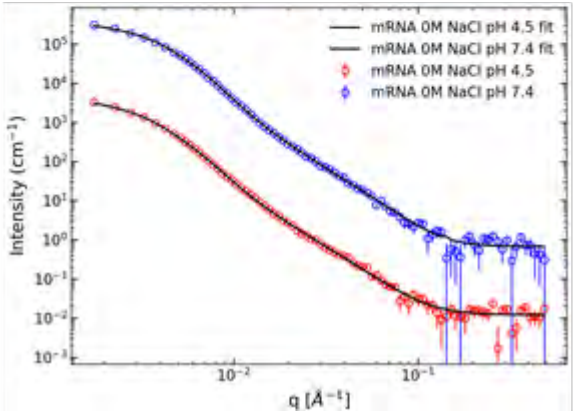
Circular dichroism (CD)



Molecular dynamics simulation



Small-angle neutron scattering (SANS)



The subtle allostery of kinesin and tubulin

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Formed of αβ tubulin heterodimers, microtubules are hollow cylindrical structures, which constitute part of cytoskeleton to facilitate intracellular transport, cell division and cell movement. Microtubules generate forces by undergoing stochastic growth and shrinkage. Motor proteins such as kinesin walk along microtubules to transport cargoes and produce forces which bend and slide microtubules.

More complex organisms tend to have many tubulin isotypes. In humans, 9 α and 10 β tubulin isotypes have been identified. Point mutations in many of these produce serious diseases, which suggests each isotype may have a non-redundant role.

Taxol is a microtubule-stabilising agent that is a critically-important therapeutic for breast cancer and lung cancers. There is evidence that taxol resistance in tumours is associated with a switch to β3 tubulin, suggesting β3 tubulin is refractory to taxol. We previously showed that human single isotype α1bβ3 and α1bβ4b microtubules exhibit different microtubule dynamics and respond to taxol differently. In particular, we found that taxol expands the lattice of α1bβ4b but not α1bβ3 microtubules, causing them to glide ~40% faster in kinesin motility assays.

The main surface-exposed sequence differences between these two β tubulins lie in their H1-S2 and H2-S3 loops, which interact with the neighbouring tubulin M-loop to link protofilaments together.

Recently, I swapped the H1-S2 and H2-S3 loops of β3 and β4 tubulins and tested the impact of this mutagenesis on microtubule dynamics and microtubule gliding. The swap potentiates the action of taxol on α1β3 microtubules, causing them to glide faster. It also influences dynamic instability.

Intercellular Friction and Motility Drive Orientational Order in Cell Monolayers

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Cells in biological tissues perform collective motion and create spatiotemporal patterns that are important in many physiological and pathological conditions, such as embryonic development and cancer. Recent studies have suggested that there can be coupling between different kinds of orientational order of tissue cells, yet the precise mechanisms underlying this are still elusive. Here, we use multiphase field simulations to examine the role played by intercellular friction in driving ordering within a motile cell monolayer. We find that varying friction and motility leads to a solid-liquid transition, and local nematic order of cell shape emerges near the transition induced by shear-aligning cellular flows. This nematic order is tightly coupled with the local hexatic order in cell positions, with +1/2 defects colocalising with 5-7 disclination pairs, the structural defects in the hexatic phase.

We propose a mechanical-geometric model to explain this coupling, and since +1/2 defects often coincide with regions of high cell-cell overlap, this may explain why these defects are correlated with cellular extrusion. Overall, our results suggest that intercellular friction is a key contributing factor in regulating nematic and hexatic ordering in multicellular collectives as seen in experiments and simulations of epithelial monolayers.

Bridging-Induced Phase Separation and Loop Extrusion Drive Noise in Chromatin Transcription

Michael Chiang[1], Cleis Battaglia[1], Giada Forte[1], Chris A. Brackley[1], Nick Gilbert[1], Davide Marenduzzo[1]
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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Single-cell studies have shown there is large cell-to-cell variation in 3D chromatin structure within a homogeneous population of cells. Concomitantly, these cells may differ in their expression profile, and such heterogeneity in transcription, or transcriptional noise, is important in development and disease. Here, we use simulations to explore how chromatin folding is related to transcriptional noise. We study a polymer model where proteins representing complexes of transcription factors (TFs) and polymerases interact multivalently with transcription units (TUs), modelling regulatory elements such as promoters and enhancers. We also incorporate loop extrusion in the model, which is important for the physiological folding of chromosomes.

We find that TF binding creates spatiotemporal clusters of TUs via the bridging-induced attraction, leading to highly variable correlation time in transcriptional dynamics that directly affects noise. Despite having minimal effect on the mean expression profile, loop extrusion also contributes to noise by further diversifying the networks of loops formed in different cells. Our results could be validated with single-cell experiments and help understand the mechanisms driving transcriptional plasticity in vivo.

Microtubule Tip-Generated Forces Drive Bipolar Spindle Organization and Chromosome Segregation

Dr. Lee-Ya Chu[1], Dr. Daniel Stedman[3], Dr. Julian Gannon[1], Dr. Susan Cox[4], Dr. Georgii Pobegalov[2], Dr. Maxim Molodtsov[2]

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The mitotic spindle is a bipolar structure essential for accurate chromosome segregation during cell division. Its size and organization are regulated by mechanical forces from molecular motors and non-motor proteins, but the contributions of individual proteins to spindle bi-orientation remain unclear.

To investigate this, we developed double-beam optical trapping tools to measure molecular forces in an artificial bipolar spindle. Our study identifies a novel mechanism where microtubule tip-trackers work synergistically with minus-end-directed motors to generate both pushing and pulling forces. Unlike the force generators that act within microtubule overlaps, this system operates at growing microtubule tips, harnessing forces from polymerization. These tip-generated forces scale differently with spindle size, providing a distinct contribution to force balance.

We demonstrated that this mechanism can independently establish and stabilize a bipolar spindle, both in vitro and in mammalian cells. By reconstituting spindles and testing in mammalian cell models, we demonstrated the system's role in organizing spindles during mitosis. These findings offer a new perspective on spindle mechanics, highlighting the importance of tip-generated forces in regulating spindle organization and chromosome segregation.

Formation and decoding of morphogen gradients in developmental space-time

Dr. Luca Cocconi[1], Anqi Huang[2], Ben Nicholls-Mindlin[2], Guillaume Salbreux[3], JP Vincent[2]
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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

In developing tissues, as well as in the context of regeneration, robust cell fate specification and pattern formation hinges upon each cell's ability to reliably estimate its position and polarity relative to other cells, as well as to keep track of developmental time to ensure coordination of tissue-scale morphogenetic processes. This spatiotemporal information is often encoded in inhomogeneous profiles of molecules known as morphogens, which are decoded by signalling machinery feeding into complex gene regulatory networks. In a series of works using the Drosophila Melanogaster wing disc as a model system [1,2,3], we have explored the formation (through an interplay of diffusive ligand transport and differential signal modulation) and decoding of such morphogen gradients. Based on these results, we discuss how the useful range of a morphogen gradient can be defined through information-theoretic measures and argue for some advantages of analysing spatiotemporally inhomogeneous developmental cues through the lens of information theory.

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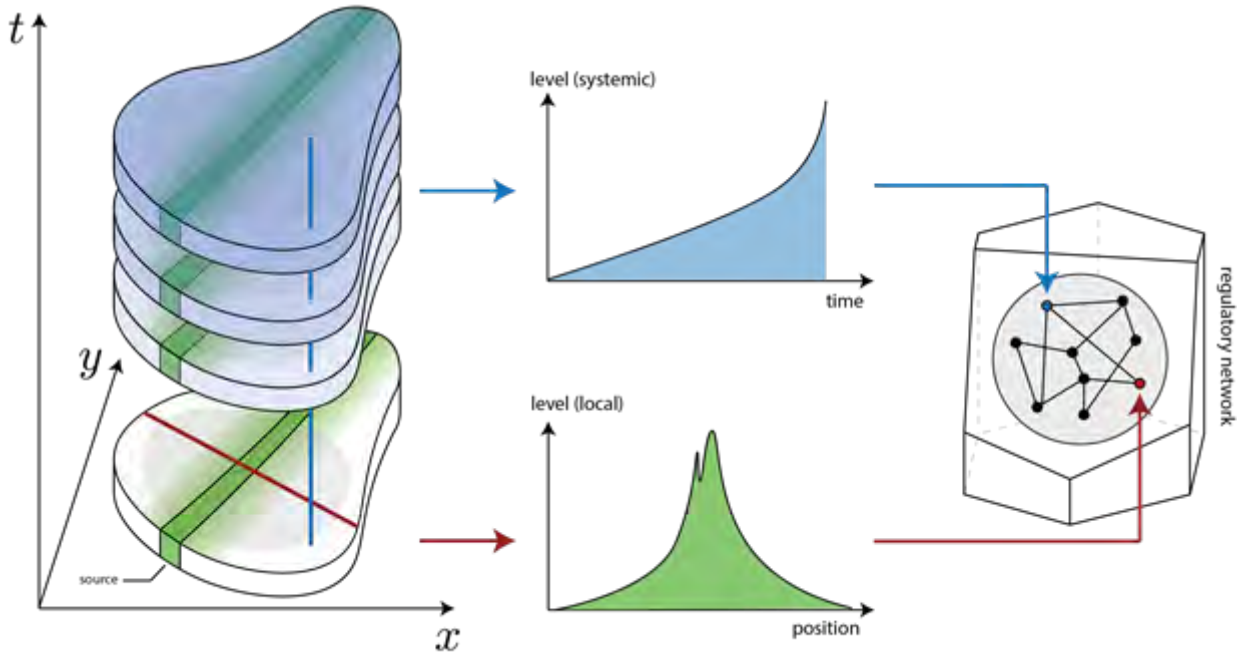

Uncovering the Fungal Cell Wall at the Nanoscale

Cameron Colclough[1,2], Eleanor Briggs[2], Abimbola Feyisara Olulanaa[1], Alexander Knight[1], Laia Pasquina-Lemonche[1], Oliver Meacock[1], Mack Durham W., Alexander Tartakovskii[1], Sam Amsbury[2], Andrew Fleming[2], K Hobbs J.[1]

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Pathogenic fungi are responsible for the most damaging diseases to plant health and crop yield. Cell walls and the mechanisms that facilitate controlled cell expansion are therefore an attractive target on which control technologies can act. Whilst previous studies have sought to understand cell wall structure largely through global polysaccharide chemistry. Here, the cell wall of the major wheat pathogen Zymoseptoria tritici is investigated using high-resolution atomic force microscopy, revealing its nanometric and location specific assembly. In situ cell walls, from live-AFM imaging, present as a furry nap, putatively a protein coat. Our data also show outer cell walls from extracted material are composed of topographic matrix of fine glycan strands (2- 5 nm wide), whereas the interior portion is overlayed by thicker microfibrils (5-15 nm).

Correlative fluorescence- AFM and complimentary nearfield techniques (sSNOM) provide chemical identification of these surfaces. The dense external mesh is formed principally from beta-1,3-linked glucans and the microfibrils, observed at several cell wall locations including cell septa and division termini, are chitin. We also find that wall of the filamentous form of growth contrasts that of the spore morphology both in size and structural arrangement, the latter having a close architectural similarity to bacteria despite the entirely different cell wall chemistry. We confirm the canonical model of cell wall structure in fungi whilst providing a completely new level of detail on the spatial and chemical variation of fungal cell walls on the nanoscale.

Optimising fixational eye movements

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

When concentrating vision on a stationary target, our eyes perform microscopic movements which we do not actively perceive. These so-called fixational eye movements (FEMs) ensure that individual receptors are subject to intensity variations which prevent adaptation to a constant light level. FEMs superficially appear like random walks but exhibit characteristic features suggesting that they are optimised for specific purposes. We present an information-based theoretical model that allows us to analytically predict the impact of FEMs on a subject's performance in simple psychophysical tests. The model incorporates retinal image motion due to FEMs, blurring due to optics and finite receptor size, uniform sampling by the receptor array, adaptation via a bandpass temporal filter, and added noise.

In particular, we study the Vernier acuity task which is concerned with assessing the horizontal offset (left or right) of a pair of vertically aligned bars. Using Bayesian estimation, we quantify the probability to make the right decision in a noisy environment as a functional of the path taken by the eye. This is closely related to the task of perceiving a single object’s position, which we also discuss. Thus, we can identify optimal eye movements and compare the average performance of different path ensembles, such as diffusive trajectories with varying levels of persistence. We obtain analytical predictions of how performance varies with model parameters such as retinal blur, adaptation time scales or contrast level. Finally, we quantify the significant variation in performance between individual trajectories within a path ensemble, identifying good and bad trajectories.

A multi-functional AOSLO for high-resolution imaging and stimulation in the living human retina

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The human retina is a directly observable part of the central nervous system and cerebrovascular system, allowing us to study the mechanisms behind visual neural processing and neurovascular coupling. Even within the retina there are neural circuits that process visual signals. Components of these circuits are differentiated through morphology and function. As such, a means to image and stimulate the human retina at single cell resolution, non-invasively, in vivo, would allow the computational principles of the retina to be elucidated.

We most recently developed a multi-functional adaptive optics scanning laser ophthalmoscope (AOSLO) that offers a unique set of functionalities to promote multi-directional research in the realm of visual neuroscience. Aberration-corrected retinal stimuli can be presented at the cellular scale to isolate, track and target single cone photoreceptors; and extended or peripheral stimuli can be delivered through a projector or liquid crystal display. A long-coherence imaging source is incorporated to record the intrinsic morphological changes in cone photoreceptors associated with phototransduction. To provide velocity samples, for dynamic processes such as blood flow, two different wavelength channels are spatially offset at the retinal plane for dual-channel imaging. Finally, both confocal and non-confocal imaging functionalities are incorporated to visualise different layers of the retina. Here, we present the core modules of this system and how they function together to support studies targeted at understanding neurological and neuropathological processes in vision.

Rab11-FIP1 interacts with Rab11-FIP5 in p53 mutant cancer cells.

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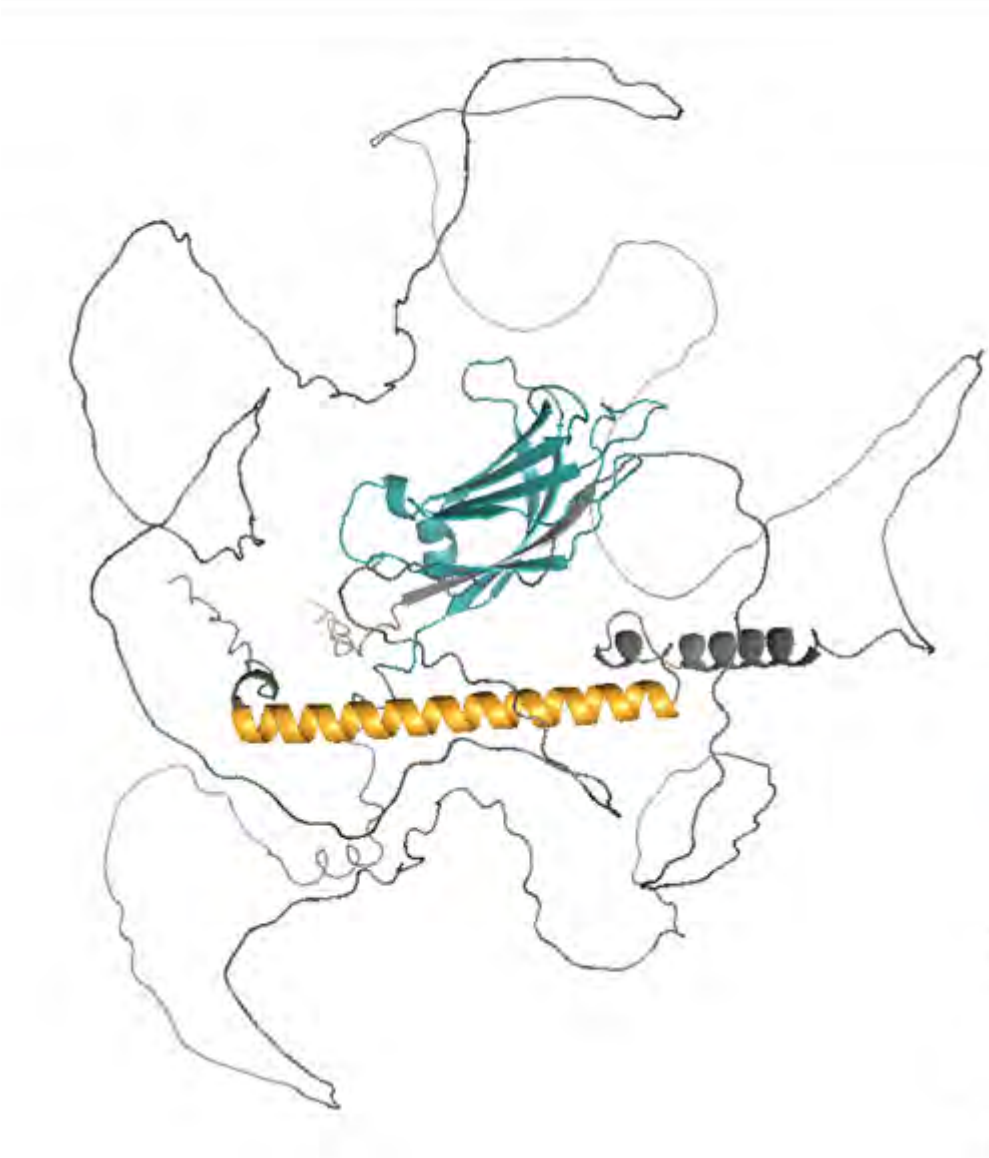
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The p53 gene (TP53) is the most commonly mutated gene in human cancers, occurring in as many as 50% of tumors [1]. These mutations result in the expression of a mutant p53 protein (mutp53), which acquires gain-of-functions (GOFs) through epigenetic regulation, altering functions of other proteins and promoting expression of new transcriptional targets [2]. These GOFs allow mutp53 to exacerbate all cancer hallmarks [3], labelling it as an oncogene with tumorigenic roles outside of loss of wild-type p53 function. Rab11-family interacting protein1 (FIP1), is able to drive the GOF effects of mutp53 by regulating endocytic recycling of proteins to the cancer cell surfaceosome [4]. Rab11-FIP1 also contributes to chemoresistance [5] and invasion [6] in p53-mutant cancer cells.

Although Rab11-FIP1 generally acts as a homodimer, we have shown that Rab11-FIP1 interacts with Rab11-FIP5, potentially forming a heterodimer. AlphaFold2 generated images of Rab11-FIP1 and Rab11-FIP5 (Figure 1) shows that their structures are highly homologous, especially at their Rab binding domains, through which Rab11-FIP1 homodimerises. Furthermore, an immunoprecipitation-mass spectrometry screen showed that Rab11-FIP5 was the most highly enriched protein in Rab11-FIP1's co-immunoprecipitate in R273H p53-mutant compared to that of p53-null H1299 cells. Additionally, confocal imaging and Western blotting have confirmed that interactions take place between Rab11-FIP1 and Rab11-FIP5. This novel heterodimer may contribute to Rab11-FIP1-mediated endosomal recycling and drive mutp53 GOF - therefore, it is critical to understanding p53 mutations in cancer cells.

Rab11FIP5



Rab11FIP1

How does chemoresistance emerge as a product of matrix stiffness in pancreatic cancer?

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Pancreatic ductal adenocarcinoma (PDAC) continues to lack targeted, curative therapies, largely due to the stiff extracellular matrix (ECM) that characterises this disease. Stiff ECM physically limits drug delivery to PDAC tumours and alters the signalling of pancreatic cancer cells. Whilst it has been observed that matrix stiffness induces chemoresistance in these cancer cells, mechanistic detail underlying how their proliferation and DNA damage response are altered to evade chemotherapy remains elusive. Consequently, three prominent questions have arisen: (1) how do standard and novel chemotherapies affect the PDAC cell cycle? (2) how does ECM stiffness alter PDAC cell cycle progression? and (3) how does ECM stiffness affect response to therapy in PDAC cells?

To answer these questions, techniques including long term time-lapse microscopy, immunofluorescence staining, mass spectrometry and the use of cell cycle targeting probes will be employed. Consequently, this project will determine how ECM stiffness induces molecular changes in the cell cycle and DNA damage response of established PDAC cell lines and how this perturbs therapeutic efficacy.

Role of Length Scales in Bacterial Swarming

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Collective swarming of bacterial swimmers is a complex behaviour, often-seen in experiments. It consists of organisms moving rapidly in a thin film while creating flow structures, such as vortices or jets, on a scale much larger than individual cells. While computational models have been successful at modelling dilute suspensions of swimming bacteria [1], they have struggled to reproduce the complexity of swarming. In particular, swarming is known to occur in sparser systems than predicted by current models, due to a near-field interaction between flagella and cell bodies.

To tackle this complexity, we introduce a new minimal model composed of three distinct length scales: the bacterial body length, the flagella length, and the screening length scale coming from the solid surface over which they swarm. This model is embedded in a thermalised hydrodynamic solver [2], and validated through single swimmer experiments and a multipole expansion. We demonstrate that this numerical approach allows for swarming to occur at a sparser packing fraction than predicted for suspensions of swimmers. Furthermore, we present the important role of the friction length scale, which modifies collective dynamics in a non-linear manner. Our results are consistent with experiments [3], and the relatively low computational costs of this approach will allow future studies to probe more complex systems than previously considered, such as swarming in the vicinity of large obstacles or in porous media.

[1] Škultety et al, https://doi.org/10.1103/PhysRevX.10.031059
[2] Howard et al, https://doi.org/10.1016/j.coche.2019.02.007
[3] Be'er et al, https://doi.org/10.1186/s40462-019-0153-9

Structural integration of integrins and cadherins at cell-cell junction sites

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Cells utilise two distinct classes of adhesive interactions to form and maintain tissues: anchorage to the extracellular matrix (ECM) through integrin-mediated focal adhesions (FAs) and hemidesmosomes, and intercellular adhesion, primarily mediated by cadherin-based adherens junctions (AJs) and desmosomes. These structures provide robust adhesion while remaining dynamic. This dynamism highlights the importance of coordination between cell-ECM and cell-cell adhesions. Notably, both FAs and AJs experience and transmit mechanical forces that are critical for intercellular communication. FAs and AJs also share certain structural and signalling components, such as vinculin. Despite these functional and structural similarities and documented instances of crosstalk, integrins and cadherins have traditionally been regarded as localised to distinct cellular sites and carrying out separate functions.
We recently demonstrated that integrins-α2β1 and α4β1 localise to cell-cell adhesions and are essential for the stabilisation of AJs [DOIs: 10.1186/s12915-021-01054-9; 10.3389/fcell.2021.750771].

These findings suggest a functional and structural integration of integrin- and cadherin-associated adhesion complexes, which we term 'integrated adhesions'. Here, to comprehensively analyse the composition of integrated adhesions, we employed a proximity labelling assay combined with tandem mass-spectrometry. TurboID biotin-ligase fused to the cytoplasmic tails of integrins-α2 and α4 were expressed in α2- and α4-knockout keratinocytes, respectively. We identified an enrichment of cadherin-binding proteins in integrin-α4-TurboID samples, including plakophilin-4, liprin-β1, and transgelin-2. We further demonstrate that loss of integrins-α2 or α4 results in accelerated migration, potentially through weakening of forces between adjacent cells. These findings suggest a structural and functional association between integrins and cadherins within integrated adhesions at intercellular interfaces.

The influence of electrostimulation and conductive surfaces on the membrane fluctuation of osteoblast-like cells with a scanning ion conductance microscope

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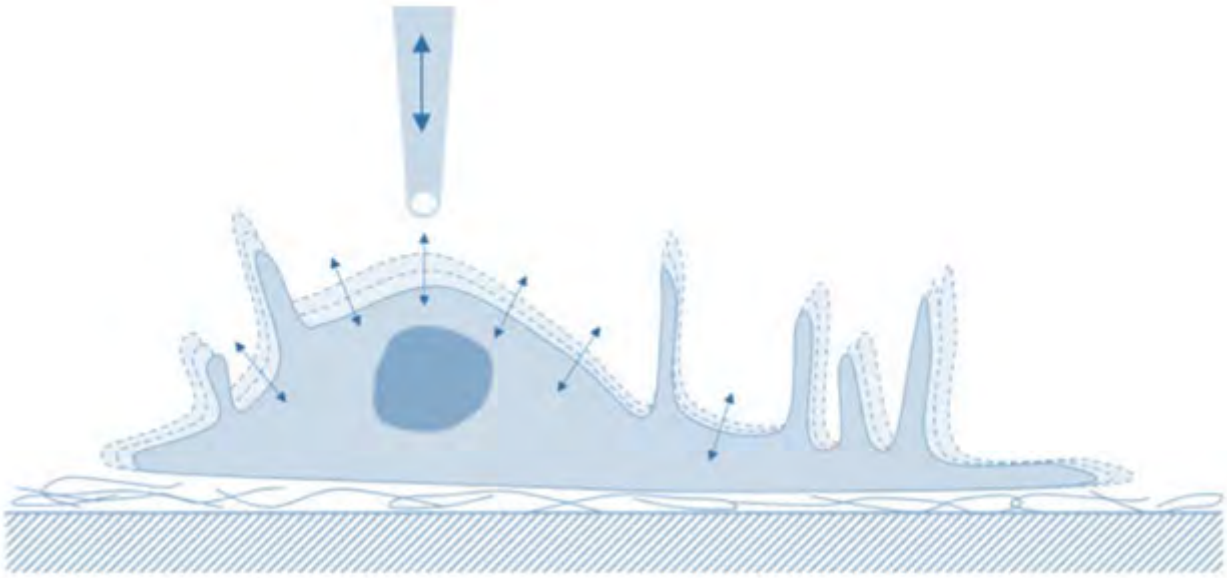
Knowledge on adhesion of osteoblasts on model implant surfaces can help to elucidate critical factors including the surface structure, electrical properties, and stimulation parameters. We develop a viability assessment based on cell membrane fluctuations. By analysing the distribution of heights, we can determine mean fluctuation amplitudes. Frequency response analysis, through power spectral density, can reveal scaling exponents, providing insights into physical excitation and damping mechanisms.

We study the effect of electrical stimulation on the membrane fluctuations of individual osteoblasts (MG63 cells). Using scanning ion conductance microscopy (SICM), we measure the vertical membrane displacements of untreated and electrically stimulated osteoblasts. Time series height data are acquired and analysed after 96h of adhesion, with a temporarily applied sinusoidal AC voltage. Thin rod-shaped platinum electrodes are used in the electrostimulation chamber. The cells are adhered on three types of substrates (glass, polyelectrolyte-carbon nanotubes, 15nm gold film).

We found fluctuation amplitudes in the range of a few tens of nanometers for both stimulated and unstimulated cells. The frequency behaviour follows a power law, f^(-m), with m denoting the scaling exponent. We discriminate three frequency regimes. Scaling exponents turn out approximately 1.7 (below ≃2Hz) and 2.7 (above ≃2Hz). Initial results suggest that our applied electrical stimulation does not significantly affect membrane fluctuations, pointing towards understimulation.

A minor response to electrostimulation may be present in the low-frequency range below 0.01Hz, but further validation is required. Additionally, membrane fluctuation analyses clearly differentiate between fixed and live cells.

Funded by the DFG (SFB1270–299150580).



Spatio-Temporal Dynamics of Gene Expression in Biofilm under Varying Environments

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Antimicrobial resistance, which currently results in 700,000 deaths each year and is expected to lead to 10 million deaths by 2050 [1], represents a critical global health challenge. A key factor driving this resistance is the formation of biofilms—structured bacterial communities encased in a protective extracellular matrix that enhances their survival under antibiotics [2]. Within a biofilm, genetically identical bacteria exhibit diverse behaviours: some remain motile, others produce the matrix, and some become dormant spores.

This study uses mathematical models and experimental data to understand whether gene-expression heterogeneity, within a biofilm, stems from cell variability that is selected by the environment, or comes from single-cell switches in response to the environment. Using dual fluorescence reporters, we tracked the spatiotemporal gene-expression dynamics of Bacillus subtilis biofilms. Time-lapse microscopy revealed dynamic ring structures: an initial matrix-dominated ring forms at the edge, followed by a peripheral motile ring after several days. These patterns were modelled using reaction-diffusion equations integrating bacterial motility, matrix production, and nutrient consumption.

Preliminary simulations successfully replicated experimental patterns, suggesting phenotypic patterns are driven by stochastic cell-state switching and selected by the environment after it switches. The model was further refined and validated through experiments under varying environmental conditions.

References:
[1] Tackling drug-resistant infections globally: final report and recommendations/ the Review on Antimicrobial Resistance chaired by Jim O'Neill.
[2] Hans-Curt Flemming, Jost Wingender, Ulrich Szewzyk, Peter Steinberg, Scott A. Rice, and Staffan Kjelleberg. Biofilms: an emergent form of bacterial life. Nature Reviews Microbiology, 14(9):563–575, September 2016. Publisher: Nature Publishing Group.

Twitching bacteria actively reverse direction to travel with their neighbours

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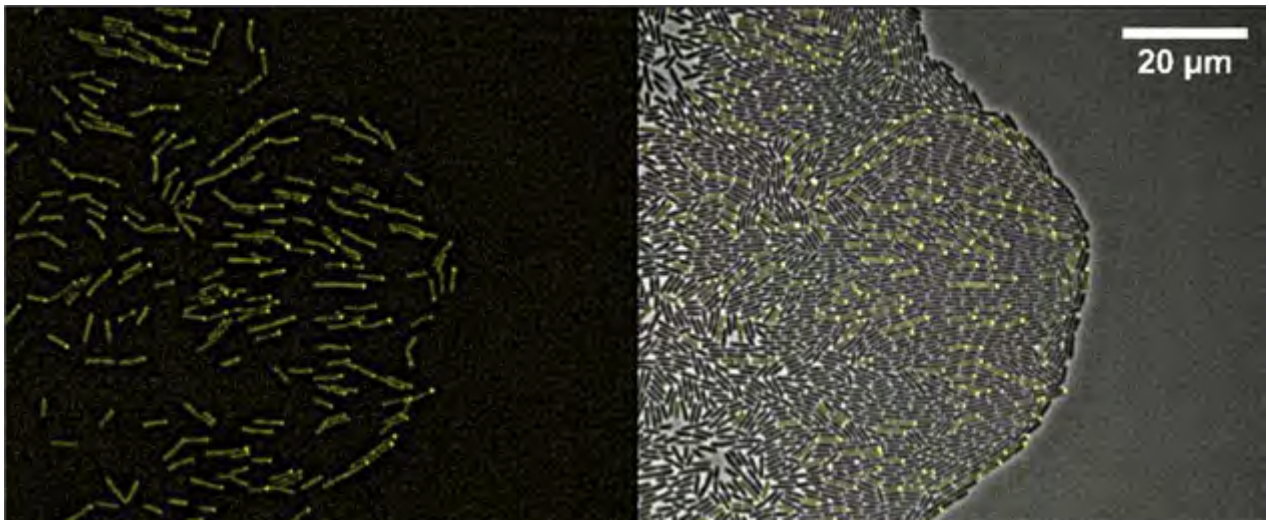
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The pathogenic bacteria Pseudomonas aeruginosa pulls itself across surfaces using tiny grappling hooks known as pili. While it is known that solitary cells regulate pili-based "twitching" motility in response to chemical and physical stimuli, it is difficult to resolve how individual cells regulate their movement within densely packed colonies where individual cell movement is strongly coupled to the movement of neighbouring cells.

Here, we follow changes in the sub-cellular localisation of proteins involved in pili-based motility in Pseudomonas aeruginosa, to quantify movement behaviour in tens of thousands of individual cells within densely packed colonies. We observe that twitching P. aeruginosa cells actively increase their reversal rate when travelling in the opposite direction to that of their neighbours. On a collective level, this active regulation of reversals tends to polarise the motility of neighbouring cells in the same direction, so that individuals work together, rather than against one another, to drive colony expansion into new territory.



Surfing one's own wave:

Initiation of motility on a compliant substrate

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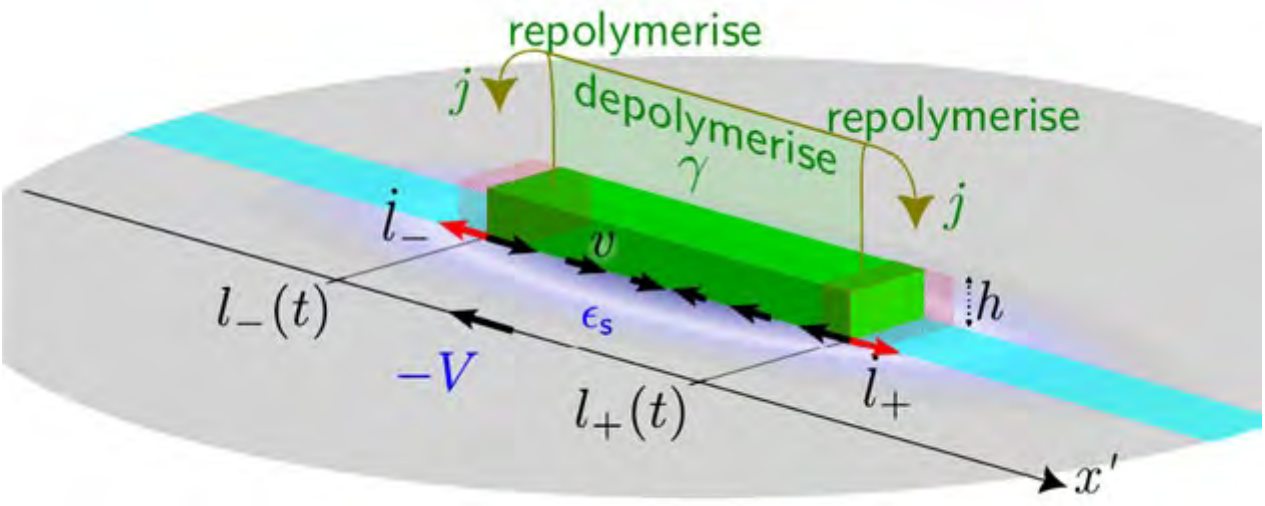
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Surfers can only dream to produce waves on the surface of the ocean and then surf them. We show that living cells are capable of this very feat, under three conditions: an ‘active’ surfboard (cytoskeleton treadmilling), a sufficiently compliant substrate, and a bimodal friction law (decreasing friction coefficient at larger velocity difference, which is observed in cell migration).

Cells crawling on the surface of elastic hydrogels meet these conditions with the correct magnitude of physical quantities. What's more, cells meet the surfing condition even when treadmilling is perfectly symmetrical: i.e., when the retrograde flow is doesn't have any bias to define a ‘front’ and a ‘back’. Then, the trivial solution to our problem is that both the ‘left’ and ‘right’ side of the cell slip on the substrate and the cell remains static.

However, if the substrate is sufficiently soft, its deformations become large and have in addition a nonlocal dependence on the traction force. If the cell moves, this makes these deformations evolve in time, creating an elastic wave which the cell can ‘surf’. We characterise this as a follower-load instability [1]. We show that the same effect is also at play in polarised cell migration, where it arises even if the friction law is linear [2]. Nonlocal feedback of the traction forces through the deformable substrate then leads to a biphasic dependence of cell velocity as a function of substrate compliance.

[1] Étienne & Recho, JMPS 183, 2024, [2] Chelly et al, IJ Nonlin Mech 139, 2022



Protein Capture using Synthetic Co-Transcriptionally Folded RNA Condensates in Mammalian cells

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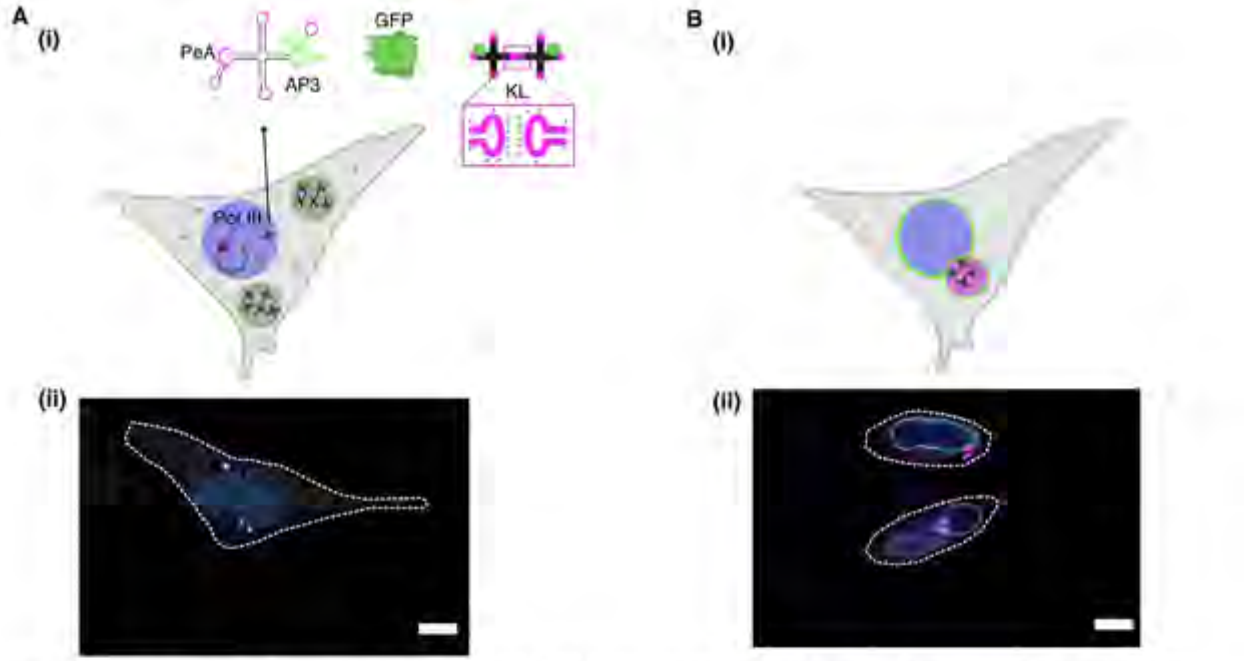
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The ability to capture, transport and manipulate protein and enzymatic machinery within living cells is a critical challenge in cell biology and biotechnology. By designing and producing co-transcriptionally assembled RNA nanostructures that form condensates through liquid-liquid phase-separation (LLPS), we are able to recruit and concentrate targeted proteins to bespoke subcellular compartments in mammalian cells. Our system is underpinned by RNA transcripts that fold into discrete nanostar geometries, which contain a Pepper aptamer to bind fluorogenic HBC620 ligands and the AP3 aptamer to capture GFP protein (PeA_AP3 in the figure).

Through Kissing Loop (KL) interactions, these nanostars are able to co-transcriptionally self-assemble from transfected plasmids into addressable condensates. With our Pe_AP3 nanostar system we have demonstrated the binding of the condensates to free cytosolic GFP protein (FigureA-ii) as well as to GFP-tagged laminA localised to the nuclear membrane (FigureB-ii) in HeLa cells. Additionally, through our system, we investigate the dynamics of condensate formation and protein association, providing insights into the fundamental principles of phase separation in the cellular environment. Beyond protein isolation, our synthetic RNA condensate platform can be modified to bind any protein of interest opening new avenues for protein engineering, drug discovery, and the development of synthetic biology tools for cellular manipulation.



GFP Capture using co-transcriptionally folded RNA condensates in HeLa cells. A) Capturing cytosolic GFP: i) Schematic of transformed HeLa cells with plasmids for cytosolic GFP expression and the transcription of an RNA nanostar (PeA_AP3) containing a Pepper aptamer to bind the HBC620 ligand (shown in magenta) as well as the AP3 aptamer to bind GFP (shown in green). The RNA nanostars contain complementary kissing loops (KL) that condense the structures within the cells. ii) Confocal fluorescenct micrograph of the RNA nanostars binding cytosolic GFP proteins within a HeLa cell. The nucleus is stained with Hoechst33342 (blue), GFP is shown in green, the RNA nanostars are visible through the bound HBC620 ligands (magenta), and the cell boundaries are indicated by the drawn dashed line. **B)** Capturing GFP-tagged laminA localised to the nuclear membrane: i) Schematic of transformed HeLa cells with plasmids for GFP-tagged laminA (green) expression of transcription of the RNA nanostar (PeA_AP3) (magenta). ii) Confocal fluorescenct micrograph of the RNA nanostars binding GFP-tagged laminA within a HeLa cell. The nucleus is stained with Hoechst33342 (blue), GFP is shown in green, and the RNA nanostars are visible through the bound HBC620 ligands (magenta). Scale bars are shown as 10μm.

High extensibility of fibrin is supported by unstructured side region, while general mechanical behaviour may arise from random backbone structure

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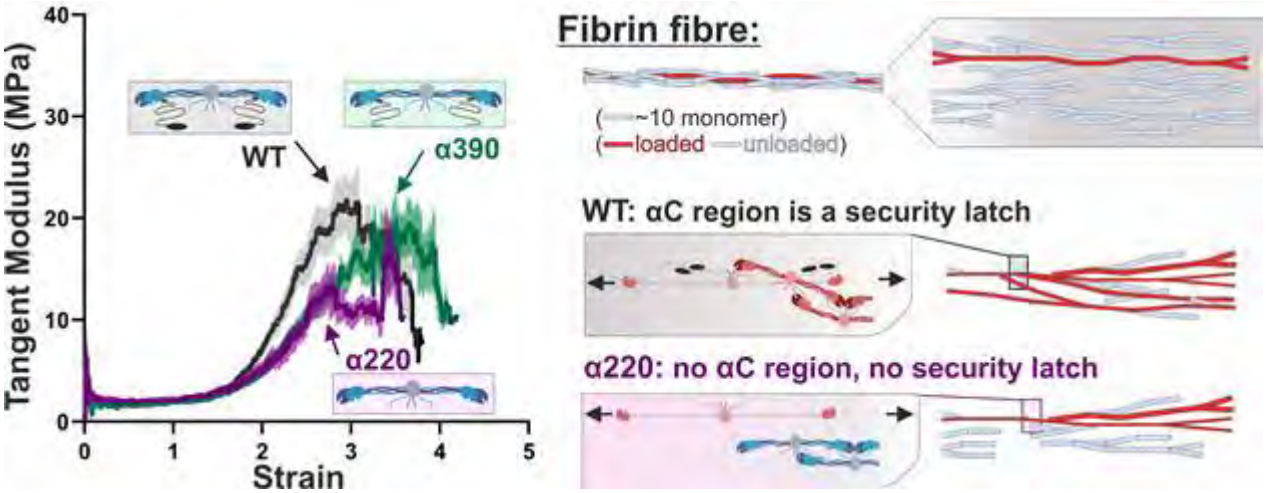
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

During blood clotting, fibrinogen is converted to fibrin, a natural biological polymer that forms the backbone of the clot. High extensibility and relatively low stiffness of fibrin fibres are both essential properties to fulfil their mechanical role as a scaffold. Fibrinogen contains two copies of a large unstructured side-region each called the αC-region. To elucidate the exact role of the αC-region in these properties, we truncated both the αC-domain (α390) and the complete αC-region (α220). Individual fibrin fibres were made, then stretched using fluorescent microscopy-combined lateral force sensing atomic force microscopy.

Absence of the αC-region did not lead to alterations in fibrin fibre stress-strain behaviour at strains<~1.5. Fibre rupture strain was only decreased when the complete αC-region (p=0.007) was truncated, showing a role of the flexible αC-region in fibre integrity. Upon stress-relaxation, decay constants and their relative contribution to the total relaxation remained similar at all strains, showing a distinct relaxation process present in all variants until fibre rupture.

These data show that the protofibril backbone, and not the αC-region is the main load-bearing structure. We present a new structural model based on protofibril branching that fully explains the unique biomechanical behaviour of fibrin fibres, while the αC-region primarily acts as a safety latch at the highest of strains (see figure). Our model includes protein unfolding and generation of new binding sites to reinforce the structure, while slippage leads to permanent deformation. Cyclic fibre pulling experiments indeed revealed permanent deformation at all strains in all variants, proving our hypothesis.



Uncoupling jamming- and adhesion-induced phase transition in embryonic tissues

Elisa Floris[1], Adrián Aguirre-Tamaral[1], Laura Rustarazo-Calvo[2], Cristina Pallares-Cartes[2], Nicoletta I. Petridou[2], Bernat Corominas-Murtra[1], Maximilian Hingerl[2], Camilla Autorino[2,3]
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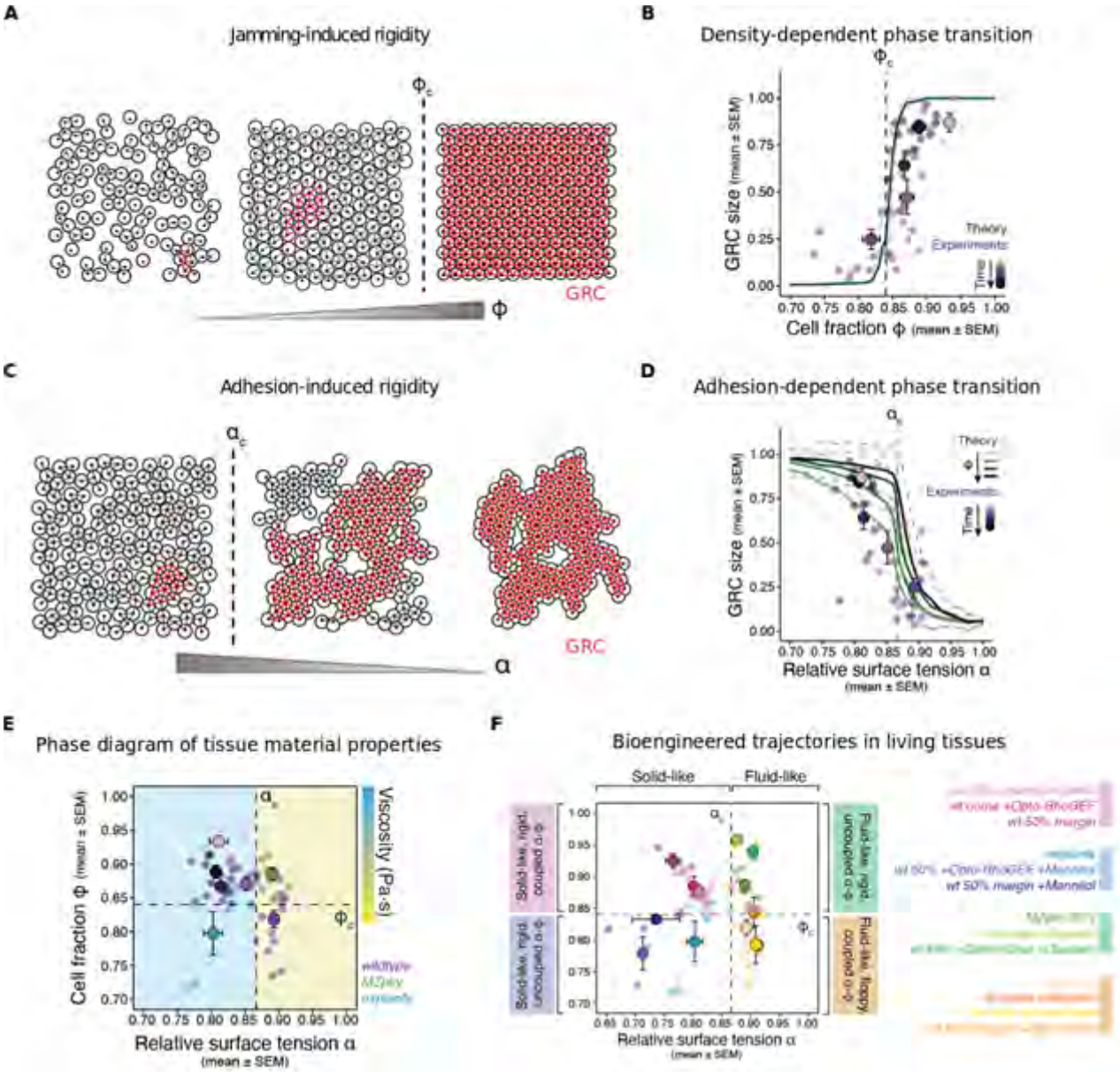
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Organism development occurs through sequences of astonishingly precise spatiotemporal changes, along which embryonic tissues switch between fluid- and solid-like states, in a way that has been characterized akin to phase transitions. Within this approach, a floppy-to-rigid transition observed in-vivo in zebrafish embryonic tissue was characterized within the theory of jamming and rigidity transitions, which predicts that at a critical point of cell fraction Φ_c, a giant rigid cluster (GRC) emerges (Fig.1A,B) where cells have no independent movements. Using genetic engineering techniques, we uncoupled the material response from the jamming properties, generating living tissues displaying solid-like or fluid-like properties although being unjammed or jammed, respectively. We explained this apparently paradoxical behaviour by analytically deriving a critical point in the relative surface tension, α, beyond which a floppy motif of soft, adhesive spheres spontaneously rigidifies.

Simulations show that arbitrary cell configurations display a sharp transition in the GRC size at the predicted α_c; a transition observed in real embryonic tissues as well (Fig.1C,D). Furthermore, experiments show that α properly predicts the material state of the tissue. Embryonic tissues are thus characterized by a phase diagram organized around a double critical point (Φ_c,α_c) (Fig.1E). Combining optogenetics and pharmacological perturbations, we “moved” living tissues around the phase diagram (Fig.1F) showing that, beyond the material response, different paths --and phase transitions therein-- instruct the formation of precursors of primary tissue types: mesenchymal, lumen-like or epithelial. Our theoretical and experimental results show how basic physical parameters have far-reaching roles in tissue architecture, properties and function.


A
Jamming-induced rigidity
Φ_c
GRC
Φ
B
Density-dependent phase transition
Φ_c
GRC size (mean ± SEM)
Theory
Experiments
Time
Cell fraction Φ (mean ± SEM)
C
Adhesion-induced rigidity
α_c
GRC
α
D
Adhesion-dependent phase transition
α_c
GRC size (mean ± SEM)
Theory
Experiments
Time
Relative surface tension α
(mean ± SEM)
E
Phase diagram of tissue material properties
Cell fraction Φ (mean ± SEM)
α_c
Φ_c
Viscosity (Pa·s)
Relative surface tension α
(mean ± SEM)
F
Bioengineered trajectories in living tissues
Solid-like
Fluid-like
Solid-like, rigid, jammed
Solid-like, rigid, unjammed
Fluid-like, rigid, uncoupled α-Φ
Fluid-like, floppy, coupled α-Φ
α_c
Φ_c
Relative surface tension α
(mean ± SEM)

Active and passive response of soft fibrous tissue in compression

Gowthamy Sivakuru[1], Thomas Charles[1], Olga Vasiljevic, Dr Léa-Laëtitia Pontani, Dr Jonathan Fouchard[1]
[1]*IBPS, Sorbonne Université, France*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Soft fibrous tissues are three-dimensional tissues which serve as scaffolds for our organs at adult age, control transport in the extra-cellular space and participate in morphogenesis during developement. In these tissues, fibroblasts cells live embedded in a porous fiber network called the extra-cellular matrix (ECM). While the ECM possesses its own dynamic mechanical properties, ECM micro-structure can also be remodeled by the fibroblasts first, through the traction forces exerted onto the ECM via specific transmembrane proteins, and second, by the synthesis and degradation of ECM constituents.

However, it remains unclear to what extent each of these mechanisms play a role in the response of soft fibrous tissue to mechanical perturbations, at what timescale they act, and how they integrate at tissue-scale. To tackle this question, we apply uni-axial compression on in vitro reconstituted soft fibrous tissue suspended between parallel rods. The suspended geometry allows the determination of tissue-scale mechanical properties and imaging of the deformations of functionalized oil droplets, used as cell-scale force sensors.

Using this system, we reveal a stiffening of the micro-tissue in response to controlled compressive deformation. This response is associated to localized densification of the ECM micro-structure permitted by poro-elastic flows and is inhibited by cell mechanical activity.

Biophysics of liquid-phase bacterial Protein-RNA droplets

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Membraneless organelles formed by liquid-liquid phase separation (LLPS) are crucial for the spatiotemporal control of cellular processes. We previously discovered that LLPS drives reversible formation of fascinating bacterial stress granules, called “aggresomes” (Jin, Lee, Schaefar, Luo 2021). Upon ATP depletion, aggresomes concentrate crucial mRNA and proteins, facilitating survival in harsh environmental conditions, including such as antibiotic treatment. Upon stress removal, aggresome disassembly allows rapid cell recovery. Here, native aggresomes expressing fluorescently-tagged biomolecules were extracted and studied using a suite of cutting-edge biophysical techniques. With “slimfield” microscopy, the motion of single constituent protein/mRNA molecules were tracked to quantify molecular mobility, providing insight into heterogeneous biomaterial properties under biological or physical perturbations.

Comparison of single particle jump distances with theoretical expectations revealed different types of diffusive motion across multiple length scales. Using atomic force microscopy, we have spatially mapped the aggresome’s force properties across its surface, showing a remarkable spatial dependence comprising a liquid layer which wets to hydrophilic surfaces surrounding a much stiffer core. The combination of these techniques provides novel insight into physical and biological interactions driving aggresome formation, how these droplets age over time and how biomaterial properties are “tuned”. The aggresome presents a potential new antibiotic target, and will inform the design of condensates with specific and controllable material properties for targeted biomolecule delivery applications.

Multi-Source Data Fusion and Dimensionality Reduction Predictive Microbial Modeling

Polina Gaindrik[1], Dr. Christian Fleck[1]
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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Bacterial communities are complex systems governed by non-linear interactions and feedback mechanisms. Mathematical modeling is an essential tool in examining how environmental factors, such as temperature, influence colony dynamics and in predicting the temporal evolution of bacterial communities. However, biological variability, diverse bacterial compositions, and unobserved variables often result in significant parameter uncertainties when modeling quantitative data obtained via traditional microbiological culturing techniques, e.g., the plate count method.

Such type of quantitative data provides the number of bacteria without distinguishing between different bacterial species and is often accompanied by significant measurement errors. To enhance prediction accuracy, it is crucial to increase model complexity and integrate additional information about the system, such as initial bacterial composition or additional environmental conditions.

Coupling bacterial composition data with classical bacterial count measurements is challenging due to differences in measurement methods, the qualitative nature of the data, and issues like high dimensionality and sparsity. We model bacterial populations with varied types of interactions based on observed total bacterial growth and two sources of bacterial diversity data: Next-Generation

Sequencing (NGS) and MALDI-ToF. Our approach involves data preprocessing, dimensionality reduction, model selection, and parameter estimation. The proposed multi-source data fusion model is applied to an industrial case study of bacterial growth in minced meat to predict product spoilage.

Exploring Dynamic Cellular Response of Erythrocytes to Rapid Deformations

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Erythrocytes (RBCs) make up more than 80% of cells in our body and are remarkable for their ability to withstand significant mechanical forces as they navigate the circulatory system, often deforming dramatically to pass through narrow capillaries. Despite their seemingly delicate structure, RBCs exhibit extraordinary resilience, maintaining functionality under these stresses. The overall goal of this study is a comprehensive exploration of the dynamic responses of erythrocytes to rapid mechanical deformation, bridging insights from biophysics and cellular mechanics. In this poster, we share our attempts to examine the behaviour of RBCs under continuous shear stress in both open flow systems and confined geometries, shedding light on the role of environmental constraints in deformation dynamics.

Molecular mechanisms of condensate membrane interaction and mutual reshaping

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Protein-condensate and biomembrane interaction is ubiquitous in both plant and animal cells [1,2]. Micron-sized protein droplets form after liquid-liquid phase segregation in plant vacuoles and reshape the vacuole membrane as they interact with it [1]. The mutual reshaping is understood by the wetting of the membrane by the liquid-like protein droplets, and the corresponding contact angle quantifies the spread of the droplets on the membrane. We devised a method to extract the contact angle directly from the fluorescent microscopy images as different protein droplets interact with supported lipid bilayers (SLBs) of various compositions. We used image analysis to segment individual droplets and determine their moments.

We find out the contact angle of the droplets by comparing the moments of the segmented droplets with that of a spherical cap. We aim to develop a 'wetosome' database cataloguing phase-separating proteins and conditions that induce wetting of the respective condensates on membranes. We observe that the wettability of a specific phase-separated protein droplet increases when the membrane charge is increased. This phenomenon might bear significant implications for different biological processes.

[1] Wetting of phase-separated droplets on plant vacuole membranes leads to a competition between tonoplast budding and nanotube formation. PNAS, volume 118, No. 36 (2021).

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Spontaneous Vortex Dynamics in Active Apolar Rods

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The emergence of collective behavior through spontaneous symmetry breaking in far-from-equilibrium active matter [1] systems – such as bacterial colonies, schools of fish, and human crowds, manifests in diverse structures and movement patterns across laboratory to geological length scales [2]. Microorganisms like bacteria and eukaryotic cells use flagella for propulsion and exhibit various collective phenomena [3]. While phenomena such as quasi-nematic ordering [4] and polar clusters [5] in active rods have been studied through numerical models, many dynamics remain unexplored. Notably, vortex arrays form in collections of rod-like organisms, such as spermatozoa [6] and microtuble filaments [7].

In this work, we present a simplified model using Langevin dynamics to investigate vortex formation in active apolar rods. Our model successfully captures vortex formation through dynamic interactions without requiring intrinsic rotation of the individual entities.

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The effects of individual nonheritable variation on fitness estimation and coexistence

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Demographic theory and data have emphasized that nonheritable variation in individual frailty enables selection within cohorts, affecting the dynamics of a population while being invisible to its evolution. Here, we include the component of individual variation in longevity or viability which is nonheritable in simple bacterial growth models and explore its ecological and evolutionary impacts.

First, we find that this variation produces consistent trends in longevity differences between bacterial genotypes when measured across stress gradients. Given that direct measurements of longevity are inevitably biased due to the presence of this variation and ongoing selection, we propose the use of the trend itself for obtaining more exact inferences of genotypic fitness. Second, we show how species or strain coexistence can be enabled by nonheritable variation in longevity or viability. These general conclusions are likely to extend beyond bacterial systems.

Exploring the Frameshifting Element in SARS-CoV-2 Using smFRET

Sarah Graham[1], Professor Mark Leake[1], Dr Chris Hill[1], Dr Steven Quinn[1]
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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

A key feature of SARS-CoV-2 and many other viruses is programmed ribosomal frameshifting, which is essential for replication. This process relies on the presence of a slippery sequence and a stimulatory RNA secondary structure, in this case, a pseudoknot. While the secondary structure of this RNA fragment has previously been evaluated, several different conformations have been proposed. We present here the first single-molecule Förster resonance energy transfer (smFRET) characterization of the pseudoknot structure labelled with donor (Cy3) and acceptor (Cy5) dyes, and using fluorescence burst analysis, we investigate the conformational landscape of the structure across a range of physiological environmental conditions.

In contrast to static Cryo-EM and X-ray crystallographic predictions, the smFRET population distributions unveil heterogeneity within the pseudoknot, indicative of a range of structures and dynamics that may be correlated with function. By revealing the structural heterogeneity of this pseudoknot we demonstrate the feasibility of smFRET studies for studying otherwise inaccessible pseudoknot interactions, and we provide a platform for obtaining further insights into the vital process of frameshifting and viral replication.

Emergent order in epithelial sheets by interplay of cell divisions and cell fate regulation

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Fundamental questions in stem cell biology are how a cell's choice to differentiate or not (cell fate choices) is regulated through communication with other cells in a tissue, and whether these choices are a one-way commitment or more plastic. However, discerning such details of cell fate choice dynamics is difficult, as it requires taking live videos inside living animals.

An alternative way to discern cell fate choice dynamics would open if different modes of cell fate choice resulted in different features of macroscopic arrangements of cells. In my talk, I discuss how the interplay between cell division, cell fate choices, and juxtacrine (cell-cell contact) signalling can affect the macroscopic ordering of cell types in self-renewing epithelial sheets (as in skin or the inner linings of organs), by studying a simple spatial cell fate model with cells being arranged on a 2D lattice, akin to spin models of statistical physics. I show that, depending on the class of regulatory interactions (mutually inhibiting vs. mutually aligning) and commitment of cell fate choice (irreversible vs reversible), different large scale features of the arrangement of cell types emerge: macroscopic clusters (with smooth or rugged boundaries), alternating (checkerboard) patterns, and random distributions, can be observed for different modes of cell fate choice and regulation.

These results can be understood theoretically by an analogy to phase transitions in spin systems: the model effectively interpolates between the Ising model and the voter model, and thus, depending on the relevant parameters, shows the features of either models.

PTSD as a Bias Toward Perceiving a Dangerous World: An Evolutionary and Mathematical Perspective

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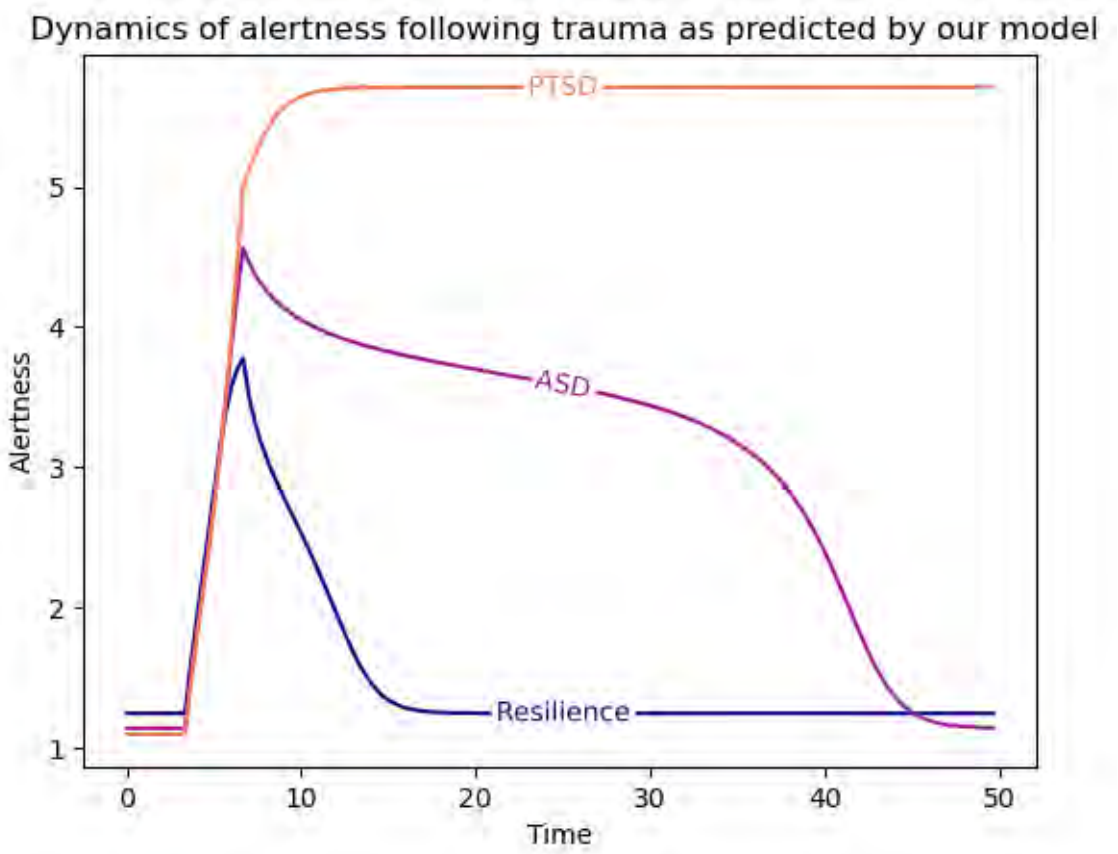
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Post-traumatic stress disorder (PTSD) is characterized by a range of symptoms arising from exposure to a traumatic event. These symptoms include hyper-vigilance, exaggerated startle responses, intrusive thoughts, avoidance behaviors, and a pervasive sense of threat. While these traits are negative in a safe world, they can be viewed through an evolutionary lens as advantageous in a constantly dangerous environment, enhancing survival by prioritizing threat detection.

We present a mathematical model to explain the dynamics of alertness and the diverse response trajectories following trauma. While most individuals return to normal within days, a minority will develop acute stress disorder (ASD), which lasts up to a month, and among them, a subset will go on to develop PTSD, which can persist, as clinically observed.

Next, we propose that heightened alertness can be linked to changes in the human stress hormone pathway the hypothalamic-pituitary-adrenal (HPA) axis. This axis shows a paradoxical hormonal imbalance in PTSD generated by lower glucocorticoid receptor (GR) affinity, observed in patients with PTSD. To test our hypothesis, we employ a mathematical model of the HPA axis, which describes the hormone level and gland size of the HPA axis over a time scale of weeks. The model demonstrates that reduced GR affinity causes a more pronounced response to identical stress inputs. These findings integrate theoretical models with biological mechanisms and clinical evidence. They offer insights into the adaptive origins of trauma responses and the dynamic pathological outcomes of PTSD.


Dynamics of alertness following trauma as predicted by our model
PTSD
ASD
Resilience
Alertness
Time
1
2
3
4
5
0
10
20
30
40
50

Local Density as a Determinant of YAP Mechanotransduction in Multicellular Assemblies

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Mechanical and biochemical cues are regulating cellular behaviour and response in epithelial monolayers. Hippo signalling pathway is modulating cellular response in terms of cell proliferation, differentiation and survival, thus having a central role in development as well as homeostasis[1]. Several groups of upstream regulators have been identified, examples of which are cell density and polarity, stress signals, soluble factors and mechanical cues[2].

We investigated the relationship between local density, YAP activation, and nuclear morphology in MDCK cell monolayers, focusing on the roles of e-cadherin-mediated force transmission, actomyosin contractility, nuclear shape and substrate stiffness. Our findings reveal a striking heterogeneity in YAP activation across local cell density gradients, independent of global cell density. Cells in low-density regions exhibit higher YAP nuclear localization, linked to larger nuclear volumes and altered shape factors. Surprisingly, perturbations of e-cadherin expression, actomyosin integrity and change of substrate stiffness did not disrupt the density-YAP activation relationship, underscoring the dominant role of local density. These results emphasize the need to account for spatial heterogeneity in tissue-scale mechanotransduction studies. Our findings highlight local cell density as a central parameter in mechanotransduction, important for understanding tissue homeostasis and disease.

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The Interplay of Heterogeneity and Product Detachment in Templated Polymer Copying

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Templated copolymerization, in which information stored in a heteropolymer template is copied into another polymer product, is the mechanism behind all known methods of genetic information transfer. In nature, this process is orchestrated by polymerases and the ribosome, and constructing minimal synthetic systems that achieve this functionality remains an open problem. A key aspect of templated copolymerization is the eventual detachment of the product from the template. A second feature of natural biochemical systems is that the template-binding free energies of both correctly-matched and incorrect monomers are heterogeneous. Previous modelling has considered the thermodynamic consequences of detachment, and the consequences of heterogeneity for polymerisation speed and accuracy, but the interplay of both separation and heterogeneity remains unexplored.

We present here our work investigating a minimal model of templated copying that incorporates both detachment from the tip of the growing copy and heterogeneous interactions (DOI:10.48550/arXiv.2410.21488). We first show that detachment from the template eliminates the sub-diffusive behaviour that arises in heterogeneous copying without detachment, thereby avoiding regimes of extremely slow copy growth. Next, we show that, in the context of models with separation, heterogeneity in correct monomer interactions tends to result in slower, less accurate copying, while the reverse occurs for heterogeneity in incorrect monomer interactions, due to an increased roughness in the free energy landscape of either correct or incorrect monomer pairs. Finally, we show that heterogeneity can improve on known thermodynamic efficiencies of homogeneous copying, but these increased thermodynamic efficiencies do not always translate to increased information transfer efficiencies.

Uncovering the coordinated nanoscale fibrillar mechanical response in the bone-cartilage unit during physiological loading

Prof. Himadri Shikhar Gupta[1], Mr. Waqas Badar[1], Prof. Nick Terrill[2], Prof. Peter Fratzl[3], Prof. Martin Knight[1], Dr. Sheetal R. Inamdar[1], Dr. Tim Snow[2]
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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The bone-cartilage layer at the end of long bones is critical in transmitting physiological loads and enabling pain-free joint articulation[1]. Structural and mechanical deterioration of the bone-cartilage unit (BCU) has been implicated in the onset of osteoarthritis, which affects over >500 million people worldwide. However, the structural biophysical deformation of the collagen-based extracellular matrix (ECM) in the BCU is challenging to measure in situ. Here, we developed a novel 3D synchrotron-based small-angle X-ray modelling and spatially correlative imaging method to quantify in situ the nanoscale deformation across the intact BCU subjected to biomechanical loading. Combined with synthetic ageing protocols, we uncovered multiple hidden mechanisms in the semicrystalline collagen fibrillar network of articular cartilage, including transitions in fibril crystallinity, pre-strain, contraction and compression, and disordering[2].

The collagen fibrils in the superficial cartilage layer have enhanced molecular disorder. Below the superficial zone, progressing toward the interface with the hard underlying bone, fibrils transition from geometric, reorientation-dependent strain at the microscale to molecular-scale kinking strain. Concurrently, fibrils are found to compress laterally much more than they contract axially, likely due to the expulsion of intrafibrillar water on loading. Cross-linking (as occurs in age-associated changes across tissues) significantly reduces fibril pre-strain, increases fibril diameter and reduces the effective resilience of the nanofibrous network by lowering the fibrillar deformability. These findings provide new insight into the nanoscale mechanobiology of this critical musculoskeletal interface and may enable future targeted structural biomarkers and therapeutic strategies.

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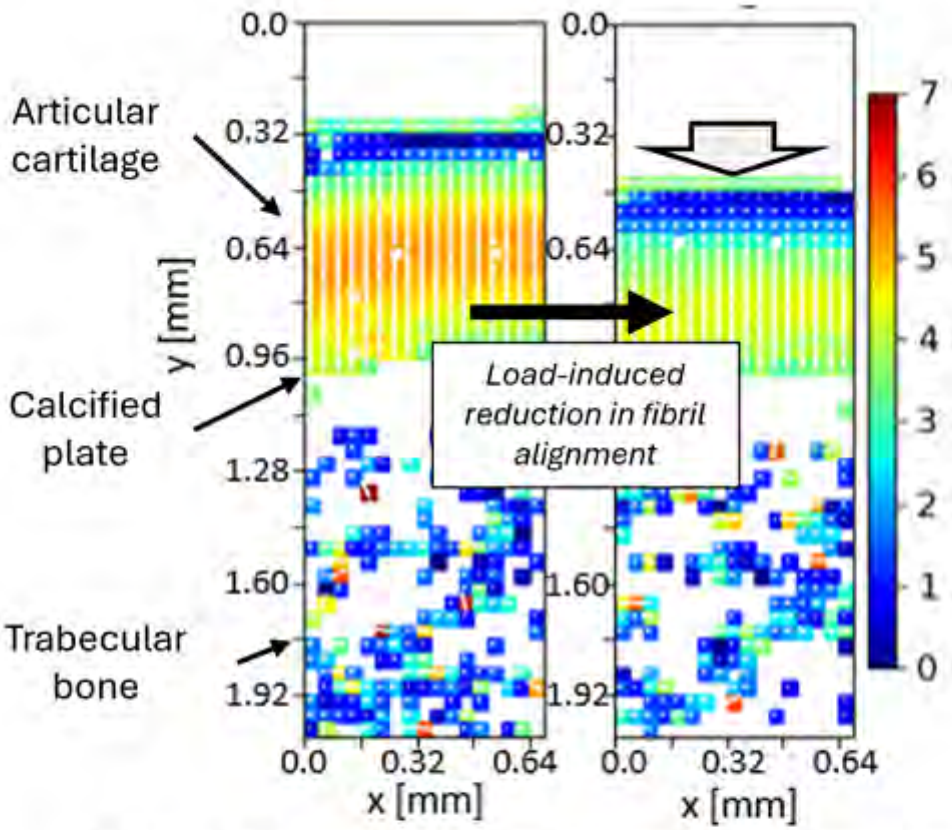

Figure 1: 2D scanning synchrotron small-angle X-ray scattering map across the bone-cartilage unit in the bovine metacarpophalangeal joint. Left: unloaded; right: under 30% compressive strain (vertical white arrow). Voxel colour = degree of collagen fibril alignment; white lines = direction of fibril orientation. Compressive loading significantly reduces fibril alignment across the entire BCU. Data from [2]

Homology recognition through intrinsic interactions - kinetics, equilibrium and stability properties

Ehud Haimov[1], Claudia Danilowicz[2], Andrew Stannard[1], Yaxuan Xiao[1], Yuval Elani[3], Marco Di Antonio[1], Lorenzo Di Michele[4], Mara Prentiss[2], Alexei Kornyshev[1]

[1]Imperial College London, Faculty of Natural Sciences, Department of Chemistry, United Kingdom, [2]Harvard University, Faculty of Arts and Sciences, Department of Physics, USA, [3]Imperial College London, Faculty of Engineering, Department of Chemical Engineering, United Kingdom, [4] University of Cambridge, Department of Chemical Engineering and Biotechnology, United Kingdom

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

One of the biggest remaining puzzles in molecular biology is how homologous genes find each other, and what drives their interaction at a distance. One key hypothesis is that dsDNA initially recognise each other through physical interactions based on charge pattern correlations along similar gene sequences [1,2].

Here we present theoretical predictions, verified by experiments, further substantiating this claim. Two limiting cases of dsDNA lengths were considered. The first case is a scissor-like structure ligating two short 32bp segments of homologous/heterologous sequences. A model for cation adsorption and electrostatic interaction between dsDNA constructs predicts that homologs tend to stay at closer separations from each other, compared to heterologous. This becomes apparent for physiological salt environment and was verified by FRET experiments. For the long molecules case, we adopt an Ising-type model, unravelling how complete pairing of homologous dsDNA could be. We show that homolog coils pair with ‘bubbles’, verified by experiments. In contrast, we show non-homologs cannot create a stable structure at physiological salt conditions. We analyse the time for homologs to find each other and pair and calculate the optimal confinement volume that minimises the pairing time.

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Optical trapping of active particles

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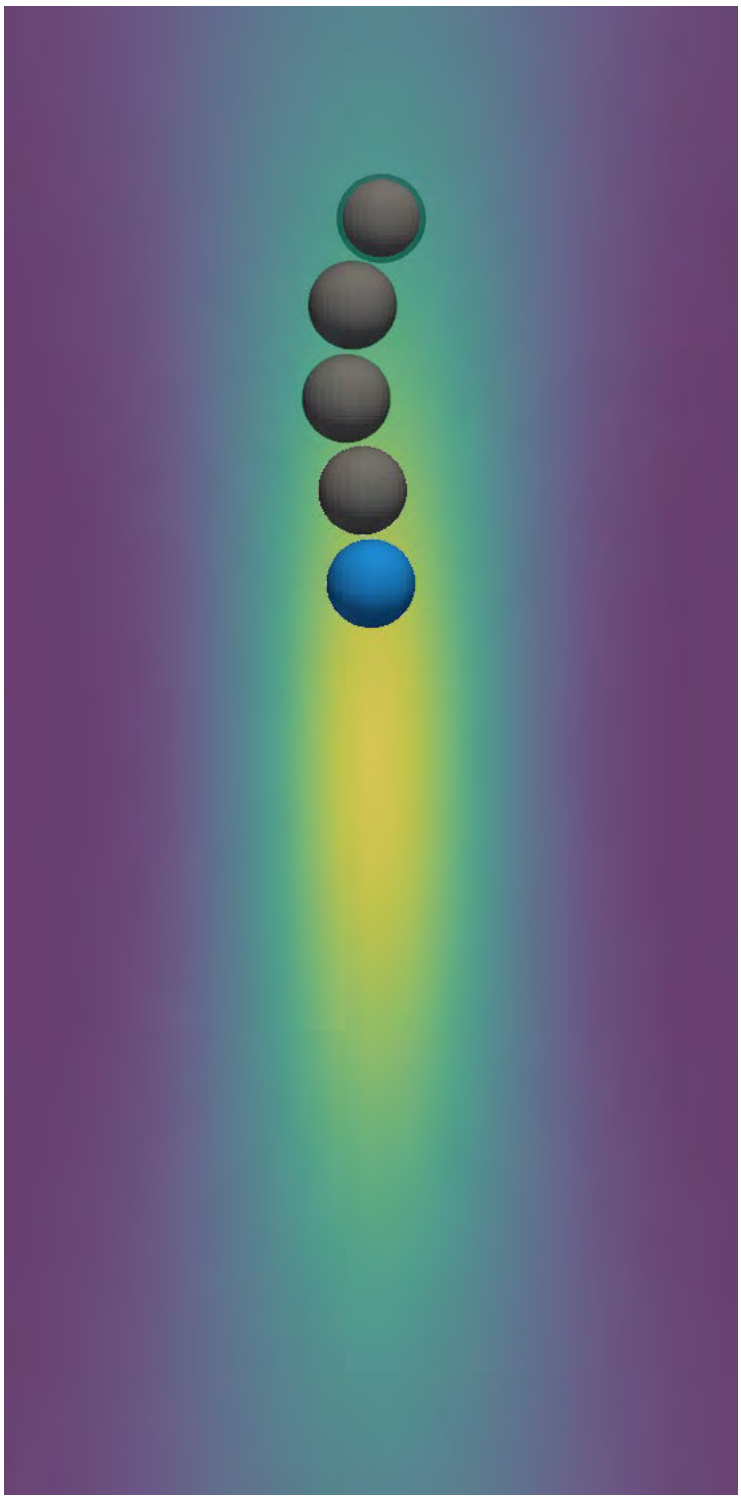
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Optical tweezers may be used to hold and manipulate active particles, including bacteria. With optical tweezers we may hold, steer and measure the forces acting on active particles. The motion of such particles in a laser trap will be similar to Brownian motion, if the particle is inactive or dead, but will be non-equilibrium if the particles is active; the Brownian motion of the particle at a given temperature can be analysed to determine both the strength of the confining potential and the power of the active swimmer.

In this paper we develop a computational model for light activated active particles. The active particles consist of dielectric beads of different refractive indices. Motion is generated on illumination due to the asymmetric scattering of light between the different refractive index regions. The dynamics of the particles is studied in a variety of complex optical fields, including combinations of Gaussian traps and optical vortices, as well as skyrmionic and random fields. The swarming behaviour of these optical Janus particles is studied in 2- and 3-dimensional random optical fields.



The roles of Ribosomal Proteins L2 and L15 in regulating Bacterial Aggresomes

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Aggresomes are a type of biomolecular condensate that form in bacterial cells through the physical process of liquid-liquid phase separation (LLPS) [1]. Some bacterial cells are able to go into dormancy when faced with potentially lethal environmental stressors. When conditions return to a more favourable state, bacterial cells resuscitate out of dormancy, and are able to continue to grow and divide [2]. Why some bacterial cells are able to persist through stressors such as antibiotic exposure, via entering dormancy, is not fully understood. However, recent research in Escherichia coli has shown that aggresomes have a key role in cell dormancy, and cell recovery from dormancy induced by stress. When E.coli is exposed to a stressor such as antibiotics, aggresomes form, and when aggresome formation is suppressed E.coli cells are unable to enter dormancy [3]. This highlights the key role of the aggresome in regulating the dormancy status of a cell. Further understanding aggresome formation, and the properties of the aggresome, is critical in unpicking why some bacteria are able to enter dormancy, and therefore tolerate antibiotic exposure.

Within this project the fate of proteins L2 and L15 in the aggresome and upon cell revival will be explored further, in order to investigate why these ribosomal proteins in particular are collected in the aggresome. Using in vivo fluorescently tagged L2 and L15 we will visualise and track these proteins in their journey in and out of the aggresome structure.

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1. DOI: 10.1126/sciadv.abh2929
2. DOI: 10.1007/s11426-014-5245-1
3. DOI: 10.1016/j.molcel.2018.10.022

Correlative light electron microscopy of individual receptor trafficking in neurons enabled by background-free four-wave mixing imaging

Miss Tess Harrison[1,2], Dr Alexandra Fletcher-Jones[2], Prof. Paul Verkade[2], Prof. Wolfgang Langbein[3], Prof. Paola Borri[1]

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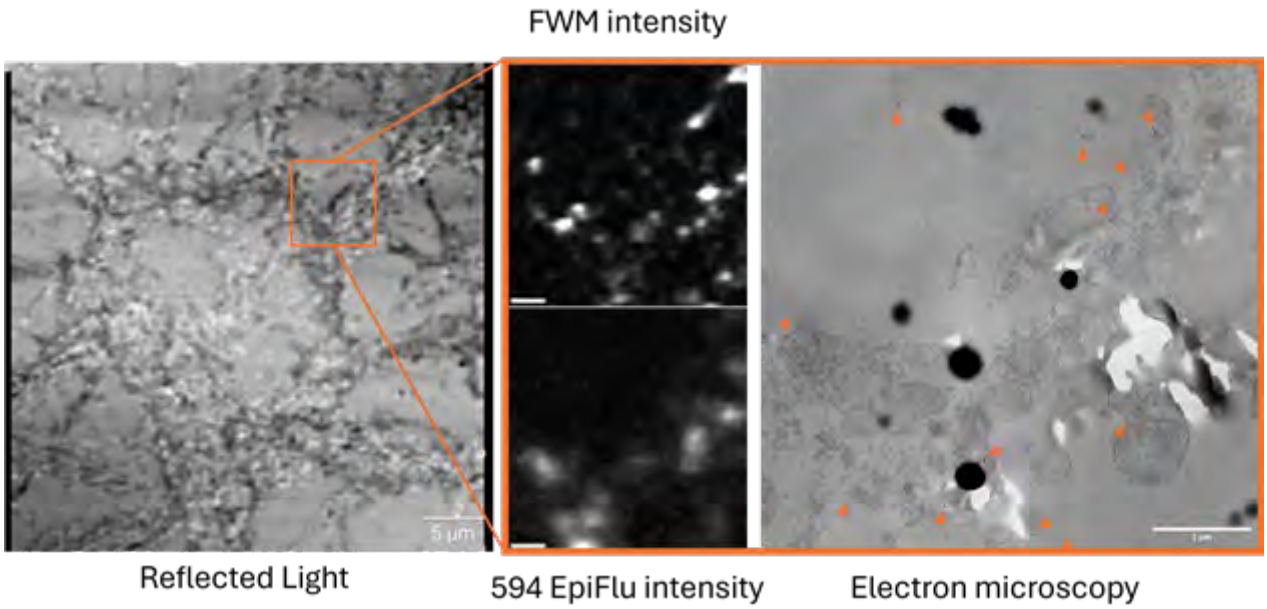
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Fluorescence microscopy (FM) is a staple of modern cellular and molecular biology, however, it is compromised by limits in resolution, contrast and photobleaching. Four-wave mixing (FWM) is an alternative light microscopy technique recently demonstrated [1]. which boasts background-free contrast down to single molecules. Unlike traditional FM, FWM exploits the nonlinear optical response of single gold nanoparticles (AuNPs) upon pulsed laser excitation, and is sensitive to the particle size, shape, and orientation. As AuNPs are electron-dense probes for electron microscopy (EM), FWM is an ideal modality for correlative light electron microscopy (CLEM), where the same probe can be imaged with FWM in living cells, and then in EM after fixation [1].

In this work, FWM-CLEM is used to investigate the trafficking responsible for the neuronal polarization of the cannabinoid receptor 1 (CB1R), a task traditional FM has been unable to complete due to the lack of precise organelle identification combined with high cytosolic background of CB1R. Our initial investigations on fixed cells suggest previously unknown trafficking routes of CB1R from the cell surface membrane to the mitochondria (see Figure). Work is ongoing to further expand this study with live-cell FWM-CLEM. Notably, owing to its high contrast, FWM features nanoscale localization precision in 3D and in turn unprecedented correlation accuracy with EM without the need for fiducial markers, placing the method at the forefront of CLEM approaches.

[1] Pope et al, Light Sci Appl 12, 80 (2023).



Neuroevolution of Decentralized Decision-Making in N-Bead Swimmers leads to Scalable and Robust Collective Locomotion

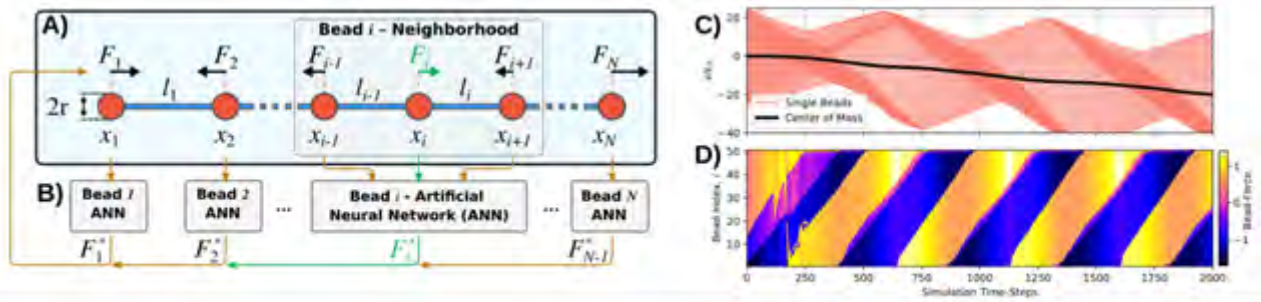
Dr. Benedikt Hartl[1,2], Dr. Michael Levin[2,3], Dr. Andreas Zöttl[4]
[1]Tu Wien, Austria, [2]Allen Discovery Center at Tufts University, USA, [3]Wyss Institute for Biologically Inspired Engineering at Harvard University, USA, [4]Computational and Soft Matter Physics at University of Vienna, Austria

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Swimming microorganisms are ubiquitous in nature and play a key role in many biological phenomena. The world of many aqueous unicellular microorganisms is governed by low Reynolds number-physics where viscous forces dominate over inertia. Noteworthy, even microorganisms are typically made of parts, which (without a centralized controller) need to be cooperatively utilized to allow them to navigate their environment. Moreover, these decentralized coordination strategies are robust and tolerant with respect to novelty or internal malfunctions, thus showing strong signs of generalizability [1].

Here [2], we investigate physical implications of decentralized decision-making of the actuators of an N-bead generalized Najafi-Golestanian microswimmer: a swimmer composed of N concentrically aligned, pair-wise linked beads immersed into a viscous hydrodynamic medium, self-propelling via coordinated non-reciprocal swimming strokes. We specifically propose a novel approach to treat each bead as an independent artificial-neural-network (ANN)-based agent that perceives information about its neighbors and whose actions induce strokes of its adjacent arms. With neuroevolution techniques, we evolve optimal policies for the single-bead decision centers such that the N-bead collective efficiently self-propels, allowing us to investigate optimal locomotion policies for increasingly large microswimmer bodies for the first time (ranging from N=3 to 100), and even identify maximally efficient microswimmer morphologies. We demonstrate that such decentralized policies are robust and tolerant concerning morphological changes or defects and facilitate cargo transport or drug delivery applications without further optimization.

[1] M Levin, Cell. Mol. Life Sci. 80, 142 (2023).
[2] B Hartl, M Levin, A Zöttl, in revision arXiv:2407.09438 (2024)



An N-bead microswimmer model (A) with bead-specific ANN controllers (B). Collective swimming trajectory (C) and bead-specific forces (D) vs. time of randomly initialized (N=50)-bead microswimmer.

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

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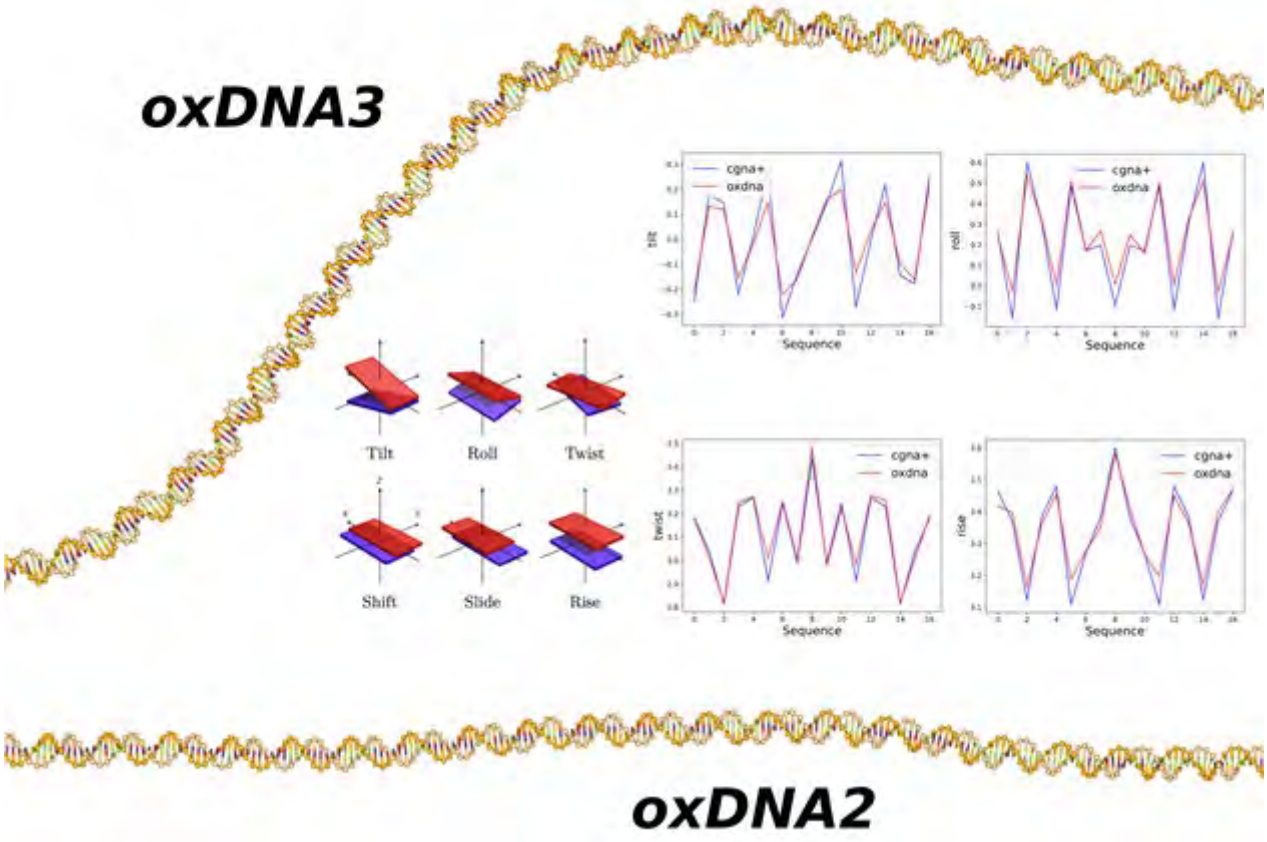
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

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.

[1] P. Dans, J. Walther, H. Gómez, M. Orozco, Curr. Opin. Struc. Biol. 37, 29 (2016).
[2] B. Snodin, F. Randisi, M. Mosayebi, et al., J. Chem. Phys. 142, 234901 (2015).
[3] R. Sharma, A. Patelli, L. De Bruin, J. Maddocks, J. Mol. Biol. 435, 167978 (2023).


oxDNA3
Tilt
Roll
Twist
Shift
Slide
Rise
cgna+
oxdna
tilt
roll
twist
rise
Sequence

oxDNA2

How small is too small: a spatio-temporal spectroscopic quantification of single-cell exchange between marine microbes

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[1]Institute of Environmental Engineering, ETH Zurich, Switzerland, [2]Department of Mechanical Engineering, UNIST, South Korea

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Chemical cues dominate marine microbial interactions, with the repercussions of these microscale interactions reverberating up through the ecosystem, ultimately dictating global-scale processes such as carbon fixation and nutrient recycling. Prominent amongst the marine primary producers are picocyanobacteria such as Synechococcus and Prochlorococcus, who contribute approximately one quarter of global oceanic primary production. Whilst previously considered effectively invisible to nearby heterotrophic bacteria, recent experimental work [1] has shown that chemotaxis does significantly increase reciprocal exchange between heterotrophic bacteria and cyanobacteria at the bulk scale, and that chemotaxis can be enhanced through the viral infection of cyanobacteria [2].

However, direct experimental measurements of single cell exchange have proven elusive to date. Here, we combine Raman spectroscopy with microfluidics to quantify for the first time the spatio-temporal flux between a single heterotrophic bacteria and an individual cyanobacteria. By measuring the exchange of heavy carbon isotopes from the marine bacteria Vibrio alginolyticus to the cyanobacteria Synechococcus, we provide the first direct quantification of the spatiotemporal extent of bacteria-cyanobacteria interactions at the single-cell scale. These results signify a substantial step forward in our understanding of marine microbial interactions, with significant implications for both experimental and modelling-driven efforts to elucidate these key microscale interactions which underpin the critical ecosystem-scale processes driving life on our planet.

[1] Raina et al., Nature Microbiology, 2023
[2] Henshaw et al., Nature Microbiology, 2024

Eco-evolutionary dynamics of cooperative antimicrobial resistance in time-varying environments with spatial structure

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Antimicrobial resistance to drugs (AMR), a global threat to human and animal health, is often regarded as a result of microbial cooperation, leading to the coexistence of drug-resistant and drug-sensitive cells in large communities and static environments. This picture is, however, greatly altered by the fluctuations arising in volatile environments, in which microbial communities commonly evolve. Motivated by the need to better understand the `eco-evolution' of cooperative AMR, we study a population of time-varying size consisting of two competing strains: resistant versus sensitive microbes. We model the time-fluctuating environment as random switches between states of nutrient abundance and scarcity, which can cause population bottlenecks.

The eco-evolutionary dynamics of cooperative AMR is thus characterised by demographic noise (microbial birth and death events) coupled to environmental fluctuations. In the first part of this work, we focus on well-mixed microbial populations. Using computational and analytical means, we discuss the environmental conditions for the long-lived coexistence or fixation of both strains, and characterise a fluctuation-driven AMR eradication mechanism where resistant microbes experience bottlenecks leading to extinction. In the second part of this study, we extend the above results to spatially structured microbial metapopulations, modelled by a 2D square lattice with migration across adjacent populations.

Modelling DNA in Complex Topologies: The Role of Gyrase

Miss Katy Hollands[1], Dr Dmitry Ghilarov[2], Prof Anthony Maxwell[2], Prof Mark Leake[1,3], Dr Agnes Noy[1]

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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 only 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.

The exact mechanisms of the enzyme, such as strand passage and energy coupling, haven't been observed with experiments [1], and so these will be investigated using all-atom Molecular Dynamics (MD) simulations. This allows us to see the system in a dynamic way, meaning key bonds and interactions, which cannot be seen from the crystal structure, can be identified, thereby making it possible for new potential targets for antibiotics to be found. The impact of varying factors, such as the length of the DNA and mutations, as well as the effect of the addition of ATP, is also being examined.

[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).

UNTANGLING HOW THE SHELTERIN COMPLEX TANGLES DNA USING ATOMIC FORCE MICROSCOPY

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

To safeguard chromosomal ends and prevent genomic instability, the Shelterin complex binds to telomeres overcoming end-protection and end-replication problems. Mutations in Shelterin are associated with premature aging disorders and familial cancer predisposition. Therefore, understanding its interaction with DNA may offer valuable insights into its cellular role and potential therapeutic interventions. However, how Shelterin remodels DNA structure and the precise mechanisms linking Shelterin's molecular structure to its protective abilities remain elusive.

To determine whether Shelterin remodels telomeric DNA, and whether this is carried out by specific proteins within the complex, we use Atomic Force Microscopy (AFM) to visualise the secondary and tertiary structure of complex DNA molecules with telomeric insertions bound by Shelterin and its components. We discovered that Shelterin could perform inter- and intra-molecular bridging between telomeric repeats, which may contribute to its mechanism of action in telomere protection. To quantify the strength of this interaction, and how it depends on the underlying DNA structure, we developed new deep-learning segmentation software in our software TopoStats.

To then determine which component of shelterin drives its bridging function, we examined the DNA binding proteins (TRF1 and TRF2) bound to the same DNA structures. It then became clear that TRF2 is the key mediator of this bridging mechanism. Our findings provide novel insights into the molecular mechanisms underlying shelterin-mediated telomere protection which may contribute to future development of therapies for age-related diseases and cancer.

Seeing through the noise: how fixational eye movements can aid the acquisition of visual information

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Fixational eye movements (FEMs) are small, apparently random motions made by the eye when fixating on a target [1]. One view of FEMs is that they represent unavoidable movement. We explore an alternative possibility: they are beneficial in overcoming retinal adaptation, in which a fixed image on the retina fades from perception. From this perspective, we can ask whether their paths are optimal.

We present a simple theoretical model for retinal processing and the acquisition of information from a visual stimulus. As well as retinal motion and adaptation, this model incorporates noise, optical blur and the potential temporal modulation of the stimulus. Taking the FEMs to be diffusive, our model reproduces the qualitative features of experimental data on contrast sensitivity for a given stimulus wavelength, and also predicts how the optimal diffusion constant relates to that wavelength.

Further, we apply our model to find the threshold amplitude for detection of a target as a function of presentation time and for targets of different sizes [2]. It has long been suggested that experimental data for these thresholds should be explained by a size-dependent visual adaptation. Our results show that this is not needed, and the data can be explained simply through the effects of retinal motion.

[1] S. Martinez-Conde, S. Macknik & D. Hubel Nat. Rev. Neurosci. 2004 5 229-240

[2] H Barlow, J. Physiol 1958 141 337-350

Towards Unraveling Nucleoprotein interactions in Supercoiled DNA: Structural Dynamics of Model Catenanes

Jamieson Howard[1], Jack Shepherd[1], Sebastien Guilbaud[3], Lewis Russell[2], Oliver Henrich[2], Mark Leake[1]

[1]University of York, United Kingdom, [2]University of Strathclyde, United Kingdom, [3]Cairn Research, United Kingdom

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

DNA undergoes interactions with a wide variety of molecules that play a critical role in gene regulation and cellular replication. Interactions range from self (via topologically active domains (TAD)) to those with helicase motor proteins and topoisomerases that can dramatically affect the 2°, 3° and 4° structure of the molecule itself. To this end, given that DNA is a torsionally constrained, the twisting forces exerted on DNA are critical to how these interactions procede. Here we build on work in which we combined optical tweezers with Helmholtz coils that allow the real time imaging of transversely oriented DNA whilst simultaneously exerting torsional and end-to-end control (Shepherd, Guilbaud, Zhou, Howard et al Nat. Comms 2024).

By ensuring two or three DNA molecules are tethered between beads we can induce intertwined DNA constructs that mimic DNA catenane structures. We find that negatively supercoiling these ‘DNA ropes’ causes them to convert twist to writhe, creating large pectoneme like structures we term hypercoils, in order to reduce torsional strain. In this work we characterize the properties of DNA hypercoils, allowing for further work investigating the interactions of DNA binding proteins and metabolisers (such as nucleosomal proteins or topoisomerases) with DNA catenanes and the resolution of these structures.

Capturing Dynamic Assembly of Protein Network Formation

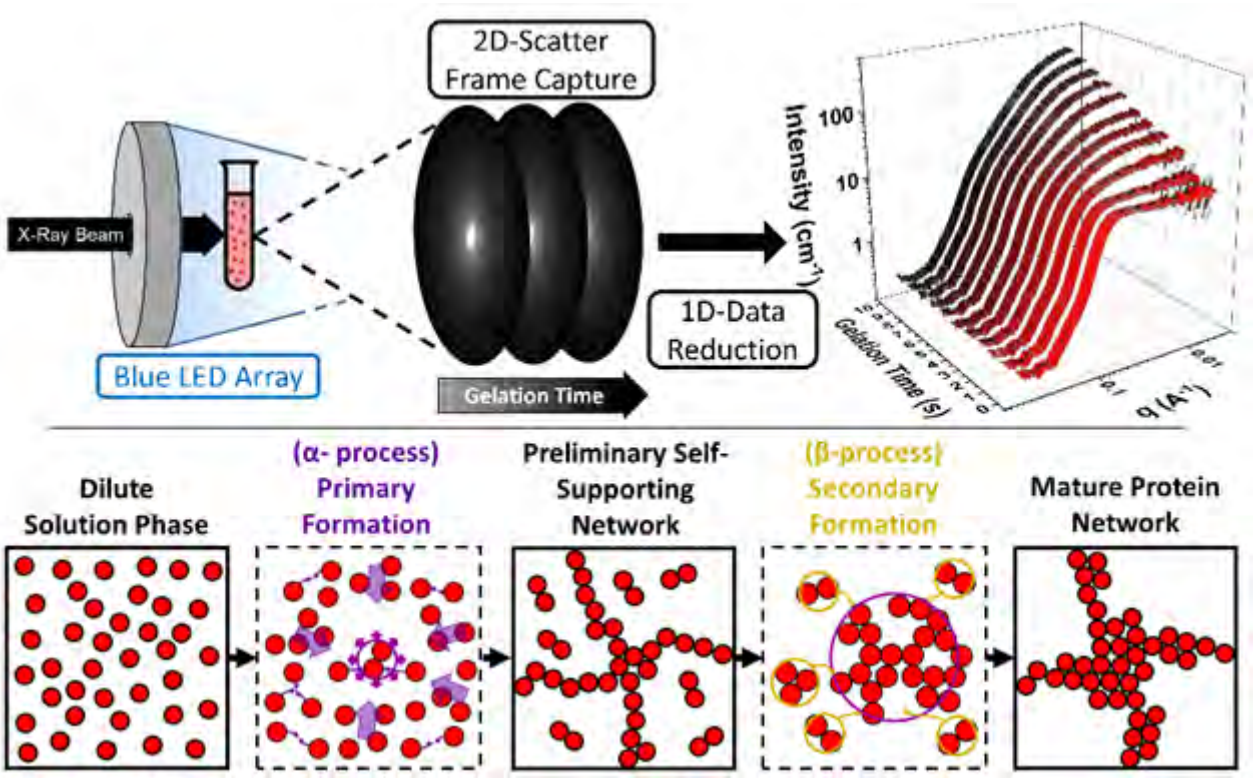
Dr Matt Hughes[1], Dr Kalila Cook[1], Ms Sophie Cussons[1], Mr Ahmad Borumand[1], Dr Arwen Tyler[1], Dr David Head[1], Prof David Brockwell[1], Prof Lorna Dougan[1]
[1]*University of Leeds, United Kingdom*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The structural evolution of hierarchical structures of nanoscale biomolecules is crucial for the construction of functional networks in vivo and in vitro. Despite the ubiquity of these networks, the physical mechanisms behind their formation and self-assembly remains poorly understood. Here, we use a combined time-resolved rheology and small-angle x-ray scattering (SAXS) approach to probe both the load-bearing structures and network architectures of protein networks. This is achieved through the development of a simple environment that allows for in situ photoactivation of chemically cross-linked folded proteins in system spanning hydrogel networks. This critical insight shows a two-stage formation mechanism. A primary formation phase, where monomeric folded proteins create the preliminary protein network scaffold; and a subsequent secondary formation phase, where both additional intra-networks crosslinks form and larger oligomers diffuse to join the preliminary network, leading to a denser more mechanically robust structure1. Identifying this as the origin of the structural and mechanical properties of protein networks creates future opportunities to understand hierarchical biomechanics in vivo and develop functional, designed-for-purpose, biomaterials2.

References:
1 Hughes,M. D. G. et al. Small(2024)
2 Mout,R. et al. Proc. Natl. Acad. Sci. 121,(2024)

Figure Caption: Time-resolved structural measurements reveal the presence of two distinct formation modes in folded protein networks: Primary Formation (purple) of the preliminary network resulting from the diffusion of protein building blocks; and Secondary Formation (dark yellow) densifying the network via the slower diffusion of high-order crosslinked protein oligomers formed during the primary formation, joining the network and the formation of ‘intra’-network crosslinks.


2D-Scatter
Frame Capture
X-Ray Beam
Blue LED Array
Gelation Time
1D-Data
Reduction
Intensity (cm-1)
100
10
1
Gelation Time (s)
q (A-1)
0.1
0.01
Dilute
Solution Phase
(α- process)
Primary
Formation
Preliminary Self-
Supporting
Network
(β-process)
Secondary
Formation
Mature Protein
Network

The Noise is the Signal: Luria-Delbruck in High Resolution

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Eighty years ago, Luria and Delbruck had a rather clever idea: simply by counting bacterial colonies on a plate, they learned something about the nature of evolution and even measured the mutation rate -- a full decade before the structure of DNA was determined. However, their particular statistical insight has not been brought into the modern age. I will present a high-throughput riff on their work -- using DNA barcodes to sample rare events in the statistics of adaptation to a new environment, resolving the so-called `Luria-Delbruck distribution' over four orders of magnitude.

At this statistical depth, the parameters underlying the evolutionary process can be determined from the shape of the distribution. I will discuss applications in the context of ongoing work on proofreading DNA polymerases, modifier loci, and protein evolvability. Overall, I hope to suggest a phenomenological, statistical approach to study the ebb and flow of genetic variation in a population.

Enhanced Enzyme Diffusion as Maxwell’s Demon: Selective Increase of Exothermal Reaction

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[1]The University of Tokyo, Japan, [2]RIKEN, Japan, [3]Institute of Science Tokyo, Japan, [4]Copenhagen University, Denmark

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

In recent years, a phenomenon known as enhanced enzyme diffusion (EED), in which the diffusion rate of enzymes increases as a result of enzymatic reactions, has been reported. Using particle simulations that incorporate this microscopic effect, we discovered that EED can alter macroscopic concentrations in the equilibrium state even in the absence of spatial organization. Furthermore, theoretical model analyses revealed that this effect allows enzymes to act as Maxwell's demons, carrying information about the type of particles they interact with and using that information to shift the balance of reactions. Additionally, we demonstrated that the conditions under which this effect operates can be derived from the relationship between the reaction rate constants, the dissipation rate of enzyme motility, and the system’s viscosity coefficient.

These findings suggest that the spatial effects of EED can influence macroscopic concentrations, potentially challenging the conventional assumptions about enzyme behavior. Specifically, we revealed the possibility that enzymatic reactions, previously thought only to accelerate reactions without altering equilibrium distributions, can have macroscopic effects on the balance of those distributions. Moreover, this study highlights the potential of enzymatic reaction systems to serve as a new subject for exploring Maxwell's demon-like phenomena.

The biophysics of transcription factor binding shapes gene regulation

Claudia Igler[1], Mato Lagator[1], Gašper Tkačik[2], Jon Bollback[3], Călin Guet[2]
[1]University of Manchester, United Kingdom, [2]IST Austria, Austria, [3]University of Liverpool, United Kingdom

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Gene regulatory networks evolve through rewiring of individual components-that is, through changes in regulatory connections. However, the mechanistic basis of regulatory rewiring is poorly understood. Using a canonical gene regulatory system, we quantify the properties of transcription factors (TFs) that determine the evolutionary potential for rewiring of regulatory connections: robustness, tunability and evolvability. In vivo repression measurements of two repressors at mutated operator sites reveal their contrasting evolutionary potential: while robustness and evolvability were positively correlated, both were in trade-off with tunability. Epistatic interactions between adjacent operators alleviated this trade-off. A thermodynamic model explains how the differences in robustness, tunability and evolvability arise from biophysical characteristics of repressor-DNA binding.

We further explore how these biophysical characteristics can lead to non-cognate TF binding across the genomic background, producing significant growth costs for bacterial cells. These growth effects depend upon (i) low-affinity TF binding to many DNA sequences, (ii) TF cooperativity, and (iii) TF concentration.

Overall, we find that biophysical determinants of TF-DNA interactions constrain gene regulatory evolution and design.

Spatiotemporal Dynamics of Bacterial Growth in Non-Well-Mixed Environments

Rita Invernizzi[1]
[1]*Humanitas University, Italy*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Bacterial growth in natural environments is influenced by complex nutrient availability, the presence of growth inhibitors (e.g. antibiotics), and the environmental physical structure, which shapes the growth dynamics. In spatially complex systems, such as biofilms, spatial constraints and fluid flow dynamics impact nutrient diffusion and the bacterial spatial organization, resulting in non-uniform colony expansion.

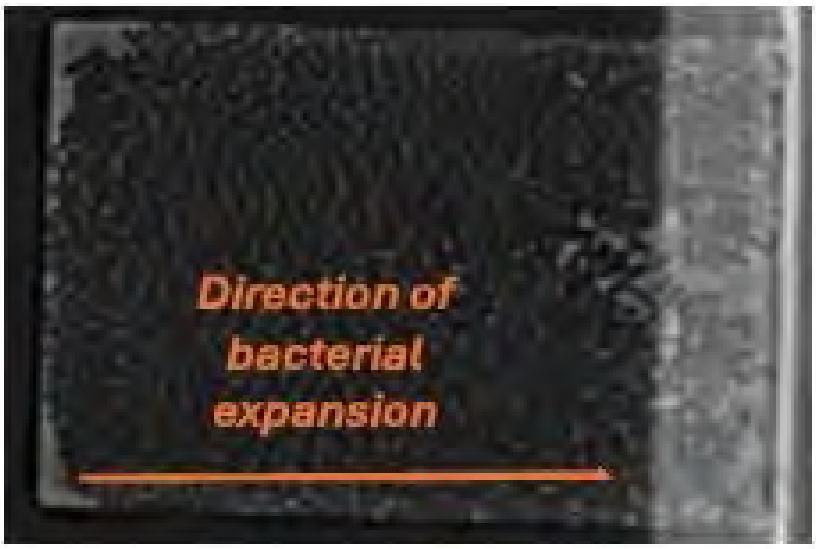
Bacteria generate micro-gradients through nutrient consumption, modulating their local environment and phenotypic responses. A key challenge is understanding how spatiotemporal dynamics, driven by nutrients uptake and environmental features, influence the growth and spatial organization of dense colonies.

Here we focus on bacteria growing on multiple carbon sources in spatially constrained systems, subjected to fluid flux. Bacteria, consuming multiple carbon sources, either co-utilize or consume them hierarchically (sequentially). Hierarchical consumption introduces lag phases: the adaptation time for catabolizing a different carbon source. Using a mathematical model, incorporating nutrients diffusion and uptake by a colony expanding with respect to the nutrient source and the fluid flux, we predict bacterial growth regimes based on spatial features and nutrient utilization strategies. Specifically, we expect a possible oscillatory behaviour in the growth rate due to the interplay between the hierarchical consumption of nutrients and the expansion of the colony.

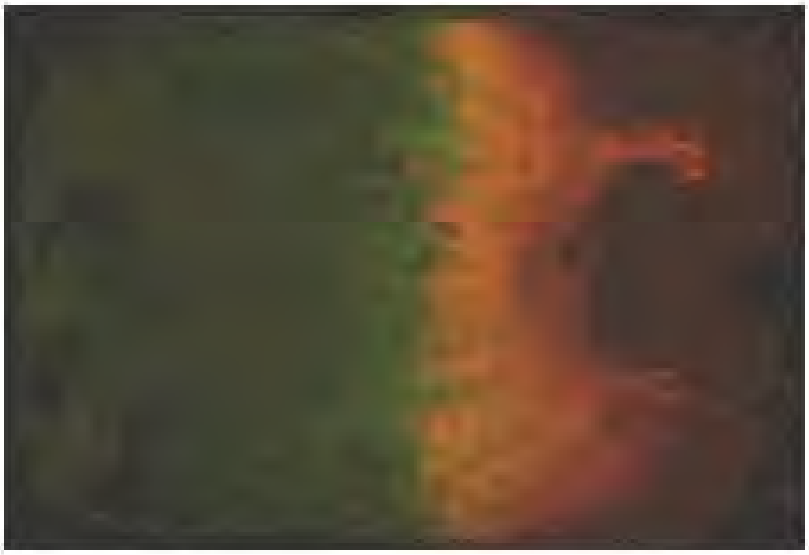
Microfluidic devices will allow us to measure the interplay between spatial complexity and lag phases shapes local nutrient adaptation within colonies, in self-generating gradients.

We aim to clarify how environmental spatiotemporal features influence bacterial growth and to reveal the role of lag phases in dynamic, non-well-mixed environments.

E. Coli in a microfluidic device

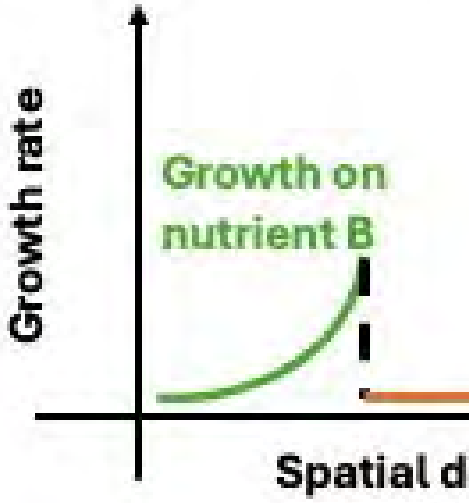


Flux of 2 nutrients entering the system



Spatial Dimension

Expectation fo



HyperGenie: A new method for predicting enzymatic gene essentiality using Hypergraph neural networks and Genome-scale metabolic models

Panayiotis Ioannou[1], Iulia Duta[1], Suraj Verma[2], Professor Pietro Cicuta[1], Professor Pietro Liò[1], Professor Claudio Angione[2]
[1]University of Cambridge, United Kingdom, [2]Teesside University, United Kingdom

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Essential genes are crucial for the survival of bacterial cells, as their removal leads to growth arrest or cell death. Identifying these genes will accelerate advancements in drug discovery, synthetic biology, and biotechnology. However, experimental methods for determining gene essentiality, such as phenotypic screening, are resource-intensive and laborious. Additionally, gene essentiality is context-dependent, varying with the environmental conditions or stressors the bacterial cell encounters.

Computational techniques for predicting gene essentiality have become more popular as a means to complement experimental efforts and accelerate the discovery of essential genes.

Bacterial metabolic networks can naturally be represented as hypergraphs, with hyper-edges corresponding to reactions and nodes representing metabolites. While traditional graphs represent relationships between objects (nodes) through pairwise interactions (edges), hypergraphs extend this concept by capturing higher-order relationships, where a single hyperedge can connect multiple nodes simultaneously. Leveraging this representation, we introduce HyperGenie, a novel computational method for predicting enzymatic gene essentiality using hypergraph neural networks and genome-scale metabolic models. Using five-fold cross-validation, HyperGenie obtains an area under the precision-recall curve (PR-AUC) of 0.95 for E. Coli growth on glucose under aerobic conditions, outperforming prior methods, which reported a PR-AUC close to 0.84 through the use of graph neural networks or random forests with genome-scale metabolic models. HyperGenie is trained on experimental gene essentiality data and incorporates metabolic fluxes from flux balance analysis as edge features, enabling robust performance under different nutrient conditions.

Tension-dependent kinetochore-microtubule interactions

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[1]*University of Dundee, United Kingdom*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Correct microtubule-chromosome attachment is paramount for the accurate segregation of chromosomes during mitosis. This connection is assured by the kinetochore, a large multi-protein complex assembled at the centromere, that binds the plus end of a microtubule. Correction of aberrant kinetochore-microtubule attachments is key to establishing proper biorientation of sister kinetochores on the mitotic spindle [1]. Tension appears to be fundamental in both this correction and in the stabilisation of correct kinetochore-microtubule interactions, reminiscent of a “catch bonds” mechanism. Several hypotheses have been formulated to rationalise the role of the tension on the kinetochore-microtubule interactions [2].

In budding yeast, Dam1 and Ndc80 complexes are key outer kinetochore components. The former encircles the microtubule, while the latter binds to the microtubule and then extends and connects to the inner kinetochore. Recently published high-resolution structures of both the Dam1 and Ndc80 complexes revealed the configuration of the kinetochore-microtubule interface in unprecedented detail [3]. Our study aims to employ a coarse-grained representation of the kinetochore-microtubule interface, to study the conformational changes when tension is applied. The consequent changes in the kinetochore structure may reveal the physical and mechanical processes underlying the tension-dependent stabilisation of the kinetochore-microtubule attachment. Computational simulations will also guide biochemical analyses to elucidate the stabilisation mechanism.

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[2] T.U. Tanaka and T. Zhang, Cells 11, 1462 (2022).
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Inertial swimmer suspensions: Instability and turbulence

Miss Purnima Jain[1], Dr. Navdeep Rana[2], Prof. Sriram Ramaswamy[3], Prof. Prasad Perlekar[4]
[1]Tata Institute of Fundamental Research, India, [2]Max Planck Institute for Dynamics and Self-Organization, Germany, [3]Indian Institute of Science, Bengaluru, India and International Centre for Theoretical Sciences, India, [4]Tata Institute of Fundamental Research, India

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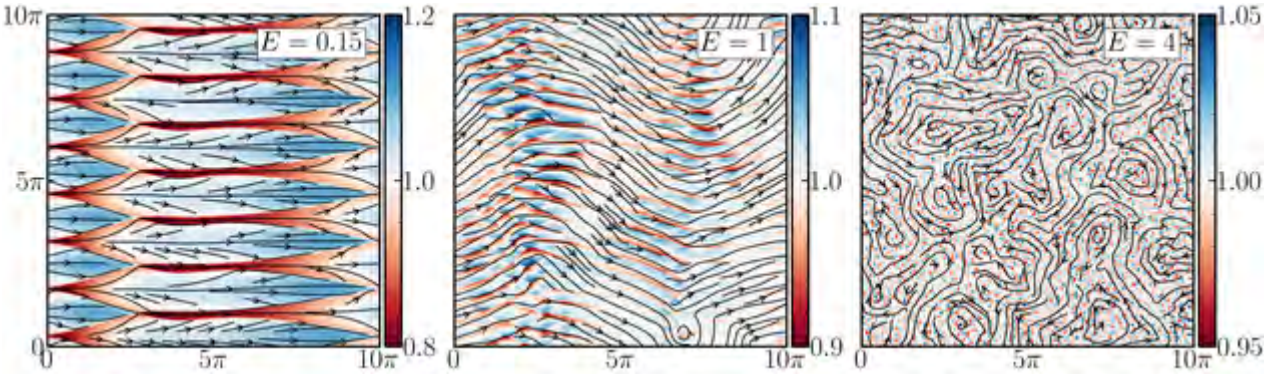
We discover an instability mechanism in suspensions of self-propelled particles that does not involve active stress. Instead, it is driven by a subtle interplay of inertia, swimmer motility, and concentration fluctuations, through a crucial time lag between the velocity and the concentration field. The resulting time-persistent state seen in our high-resolution numerical simulations consists of self-sustained waves of concentration and orientation, transiting from regular oscillations to wave turbulence [1].

We analyze the statistical features of this active turbulence, including an intriguing connection to the Batchelor spectrum of passive scalars and study the effect of concentration fluctuations on the hydrodynamic velocity field.

Reference:
[1] Phys. Rev. Lett. 133, 158302, 2024



Theory of spatial aggregation and shell formation

Mr. Pranay Jaiswal[1], Mr. Ivar Haugerud[1], Prof. Dr. Christoph Weber[1]
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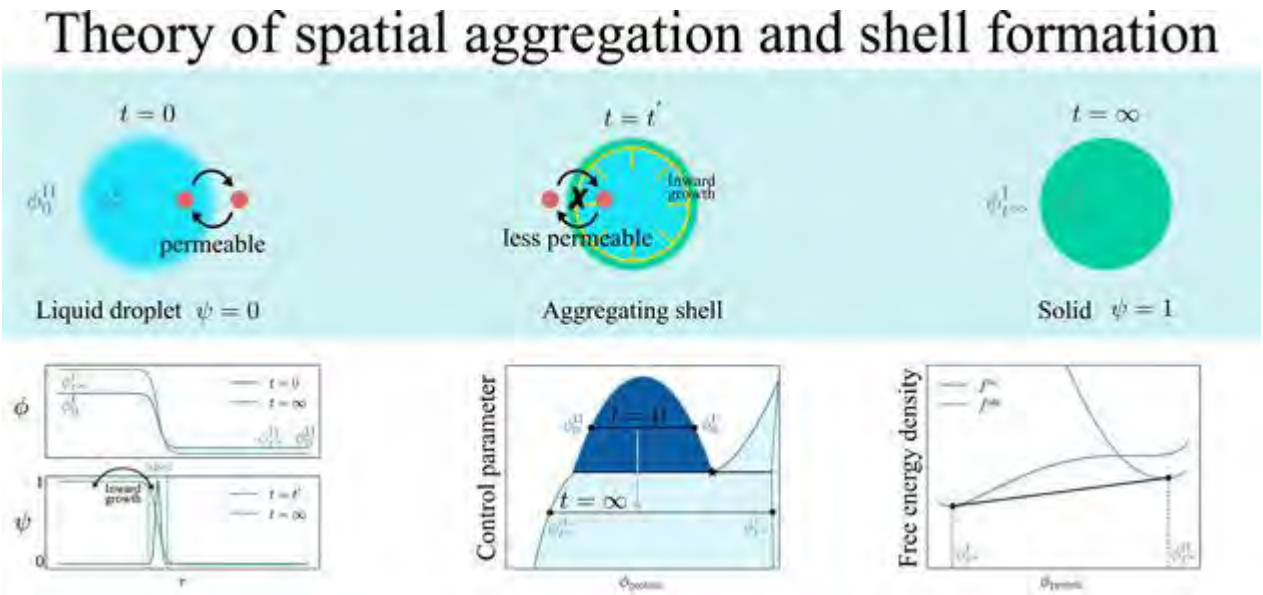
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Many biological systems use coexisting phases composed of proteins and RNA to regulate chemical processes and molecular transport. In particular, the interface can act as a nucleation site for aggregation of proteins, leading to the formation of a solid-like shell. This shell provides a physical barrier for molecular transport of further biomolecules, giving rise to molecule specific interface permeabilities. Here we propose a theoretical model for spatio-temporal protein aggregation in phase-separated systems. To this end, we use a phase-field of proteins and RNA combined with a phase-field characterising the solid-like, aggregated state.

Our key finding is that aggregation is thermodynamically favored at the interface, making aggregation shells a likely phenomenon in phase-separated systems of aggregation-prone proteins. We show how such aggregation shells control molecular transport and shell permeabilities. Our theory can be applied to experimental systems undergoing irreversible aggregation to unravel the molecular mechanism underlying ageing in protein mixtures.



Fluorescence microscopy approaches to monitor cell-to-cell heterogeneity in the regulation of cardiomyocyte contractility

Mahendra Kumar Jothi Letchumy[1,2], Dr Samantha J. Pitt[2], Prof Malte Gather[1], Dr Paolo Annibale[1]
[1]School of Physics and Astronomy, United Kingdom, [2]School of Medicine, United Kingdom

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Heterogeneity and variability are important determinants of both normal and abnormal function of the heart. One of the greatest challenges in biomedical research, drug discovery and diagnostics, is understanding how seemingly identical cells can respond differently to external cues. Investigation of the molecular mechanisms that drive heterogeneity and ultimately cardiac dysfunction is a critical challenge, towards designing strategies for the development of future therapeutics. The aim of this project is to quantify molecular determinants of cell-to-cell heterogeneity in healthy cardiac cells by means of novel microscopy and biophotonic techniques. Specifically, we are interested in the molecular mechanisms involved in the adrenergic control of inotropic response, with an increase in Ca2+ as the key driver in cardiac contraction.

We therefore began our investigation by monitoring the heterogeneity in electrical stimulated Ca2+ transients and cAMP level. Differentiated Human Induced Pluripotent Stem Cell – Cardiomyocytes (HiPSC-CMs) were loaded with the calcium indicator X-Rhodamine 1 AM and transfected with Epac1-h187 cAMP FRET biosensor. The calcium and cAMP responses between individual cells recorded, displaying large variations in Ca2+ and cAMP responses between cells within the same population. This is important, as these cell types are often used as models for heart disease to predict disease outcomes. Identification and quantification of the molecular determinants of cell-to-cell heterogeneity may therefore advance the development of more precise diagnostic tools and personalized treatment strategies, ultimately improving patient outcomes.

Single-cell analysis of the effects of cellular dormancy on the efficacy of bacteriophages

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Bacteriophages, viruses that prey on bacteria, are important regulators of microbial ecosystems in nature and have profound potential as biocontrol agents. However, as obligate parasites their effectiveness is strictly dependent on the metabolic activity of their target cells. In nature, bacterial cells often exist in dormant states and in clusters of densely packed cells, which could limit phage access and activity. Here, we use microfluidics and single-cell measurement of phage activity to investigate how the density and dormancy of cells affect the efficacy of phages.

We find that in deep-dormant E. coli cells, the model phage T7 enters the mode of pseudolysogeny where the host is refractory to lysis but not infection. However, upon resuscitation of the host cells, T7 proceeds to replicate and successfully lyse them.

By imaging varying cell densities of E. coli using microfluidic chambers with specified loading capacity, we have also found that dormant E. coli exit the stationary phase earlier when present at high cell densities, indicating possible quorum sensing between the cells.

This finding has significant implications in treating antibiotic-persistent bacterial biofilms or wounds through phage-treatment where bacteriophages can be employed in combination with antibiotics to eradicate antibiotic-resistant bacteria and combat hard-to-treat chronic infections.

Optoplasmonic single-molecule Whispering Gallery Mode (WGM) sensing platform for probing neurotransmitter-lipid membrane interactions

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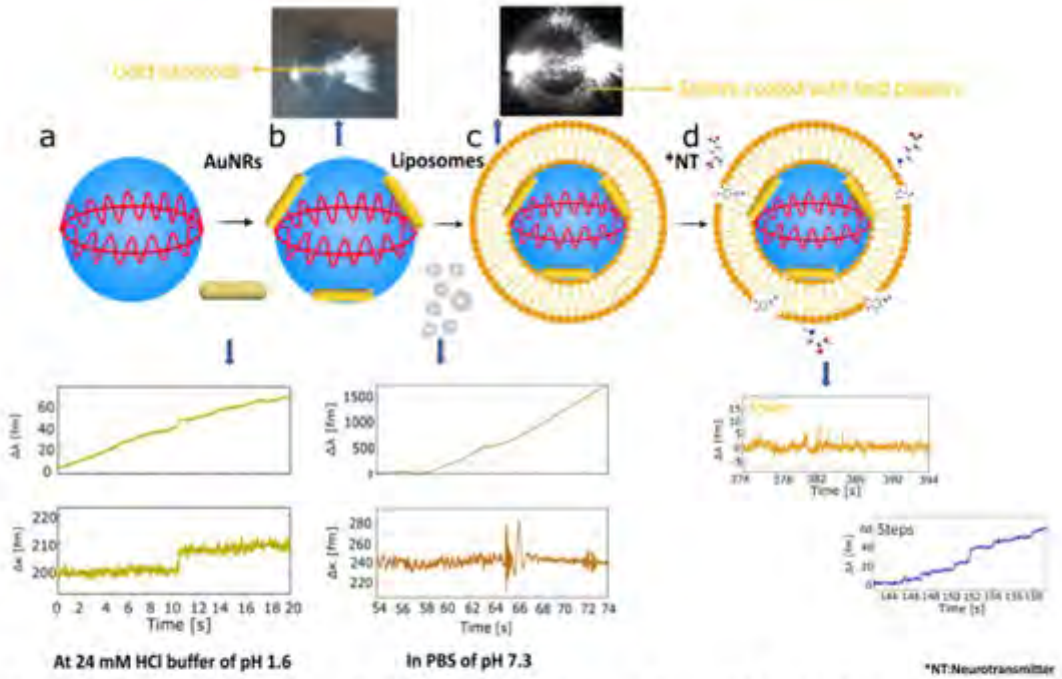
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Neurotransmitters play an important role in the effective communication of signals between neurons. Neurotransmission has been widely understood as the release of neurotransmitters from the presynaptic cell upon triggering an action potential, followed by diffusion through the synaptic cleft and eventually binding with the specific receptors embedded in the postsynaptic membrane. This leads to the opening/closing of the ion channel, thereby maintaining the membrane conductance and potential of the cell by transmitting the signal. This signal transduction plays a key role in governing neurophysiological, cardiovascular, hormonal activities and mediating cognitive functions such as heartbeat, consciousness, emotions and many more, with each neurotransmitter being unique in its function. Recent molecular dynamics (MD) studies have shown that the postsynaptic membrane can also play a significant role in neurotransmission, which accelerates the process [1], besides facilitating only receptor binding of neurotransmitters.

This study suggests that a membrane-dependent neurotransmission mechanism for signal transduction exists apart from the currently known membrane-independent mechanism. Single-molecule techniques are required to probe this neurotransmitter-lipid membrane interaction since they can deeply delve into the affinity and kinetics of individual interactions. Hence, we employ optoplasmonic single-molecule WGM sensors to study this neurotransmitter-lipid membrane interaction in ultra-low-level concentrations in a label-free manner. Our study shows that polar neurotransmitters transiently interact and amphipathic neurotransmitters predominantly bind with the lipid bilayers, supporting the MD simulations.

References:
[1] Postila, P., Vattulainen, I. and Róg, T. Selective effect of cell membrane on synaptic neurotransmission. Sci Rep 6, 19345 (2016).



Schematic of the neurotransmitter-lipid membrane intercation with optoplasmonic WGM sensors

(a) Schematic of the microsphere coupled with WGM (b) Binding of the gold nanorods to the microsphere and the binding step signal in the resonance and linewidth time traces (c) Coating of the liposomes around the microsphere forming lipid bilayers and the associated bulk shift in the resonance traces (d) Interaction of polar and amphipathic neurotransmitters forming spike and step signals with the membrane showing transient and intercalation of the neurotransmitter respectively.

Towards accurate and efficient simulations of multiphoton fluorescence microscopy in mouse brain tissue using the beam propagation method

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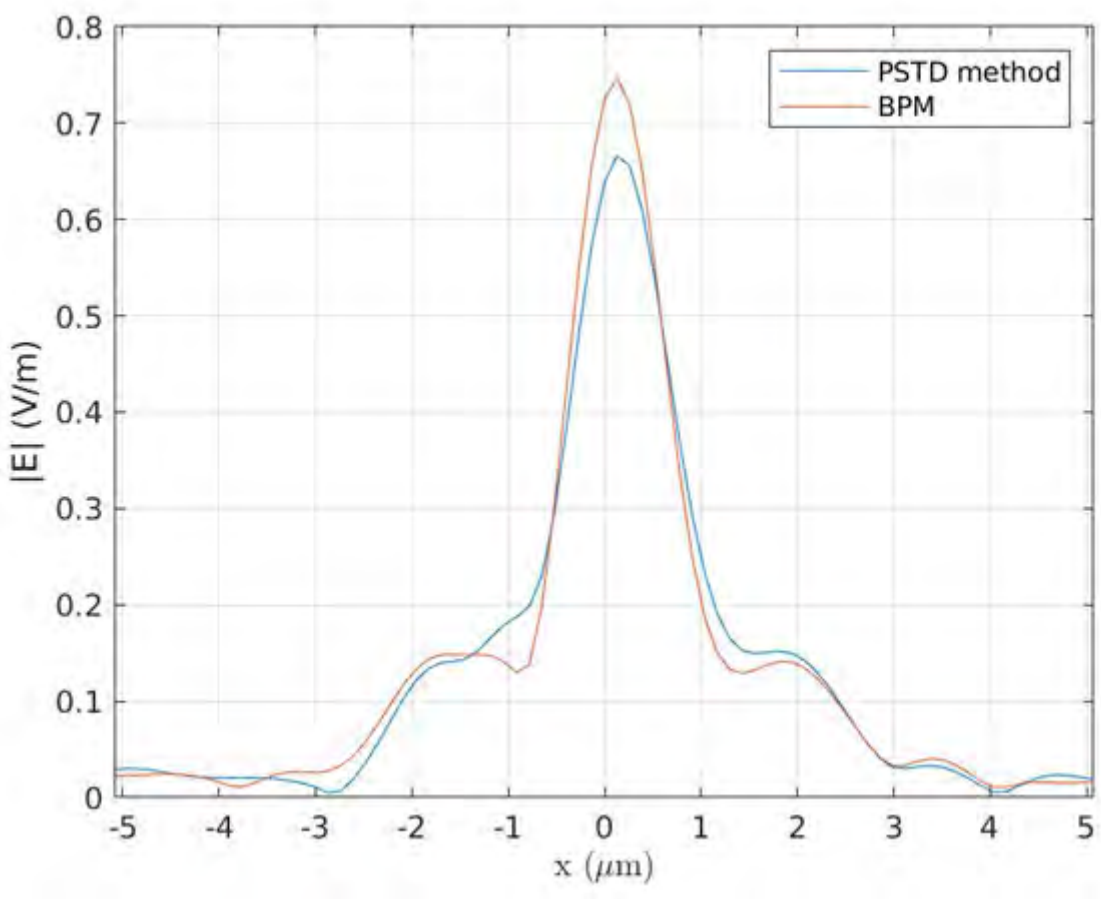
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

This work explores the potential of the Beam Propagation Method (BPM) as an efficient computational tool for simulating multiphoton fluorescence imaging in mouse brain tissue. Imaging deeper brain layers is hindered by wavefront distortions caused by tissue scattering, necessitating accurate light propagation simulations to inform the development of scattering compensation strategies. While high-accuracy methods like Finite-Difference Time-Domain (FDTD) and Pseudo-Spectral Time Domain (PSTD) are available, their computational cost restricts their scalability for large tissue volumes. We evaluate BPM's accuracy by benchmarking it against the PSTD method under conditions including plane wave and focused beam illuminations. By integrating experimentally derived refractive index data and statistical scattering models, we demonstrate BPM's unique advantages of high computational efficiency and good accuracy compared with the computationally expensive reference models. These findings underscore BPM's promise as a versatile tool for advancing high-resolution, deep-tissue imaging and optimizing optical neuroimaging techniques through improved wavefront correction strategies.



The actin cortex acts as a mechanical memory of morphology in confined migrating cells

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Cell migration in narrow microenvironments is a hallmark of numerous physiological processes, involving successive cycles of confinement and release that drive significant morphological changes. However, it remains unclear whether migrating cells can retain a memory of their past morphological states, which could potentially enhance their navigation through confined spaces.

By combining cell migration assays on standardized microsystems with biophysical modeling and biochemical perturbations, we demonstrate that local geometry governs these morphological switches, thereby facilitating cell passage through long and narrow gaps. We uncovered a long- term memory of past confinement events in migrating cells, with morphological states correlated across transitions through actin cortex remodeling. These findings suggest that mechanical memory in migrating cells plays an active role in their migratory potential in confined environments.

Link to preprint: https://www.biorxiv.org/content/10.1101/2024.08.05.606589v1.full.pdf

Unveiling the structure of protein-based hydrogels by overcoming cryo-SEM sample preparation challenges

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Protein-based hydrogels have gained significant attention for their potential use in applications such as drug delivery and tissue engineering. Their internal structure is complex, spans across multiple length scales and affects their functionality, yet is not well understood because of folded proteins sensitivity to physical and chemical perturbations and the high-water content of hydrogels. Cryo-scanning electron microscopy (cryo-SEM) has the potential to reveal such hierarchical structure when hydrated hydrogels are prepared with appropriate cryofixation. We show for photochemically cross-linked, folded globular bovine serum albumin (BSA) protein hydrogels that preparation artefacts are reduced by in-situ gelation, high pressure freezing (HPF), plasma focused ion beam (pFIB) milling, sublimation, and low dose secondary electron imaging. Cryo-SEM of folded BSA protein hydrogels prepared in this way reveals a heterogeneous network with nanoscale porosity (~60 nm pores) surrounded by high secondary electron emission regions (~30 nm diameter) interconnected by narrower, lower emission regions (~20 nm length).

This heterogeneous network structure is consistent with small angle scattering studies of folded protein hydrogels, with fractal-like clusters connected by intercluster regions. We further test the potential of cryo-SEM to detect the impact of protein unfolding on hydrogel network formation and reveal nanoscale differences in cluster sizes consistent with those derived from scattering data. Importantly, cryo-SEM directly images pores for sizing in both systems, with initial results on BSA suggesting protein unfolding induces an increase of ~10 nm in pore sizes. Our findings on cryo-SEM sample preparation challenges and solutions provide new opportunities to link hydrogel structure to function.

Advancing Biophysical Research with the C-Trap: Unveiling Molecular Mechanisms at the Single-Molecule Level

Emma Kerklingh[1], Mina Brett-Pitt[1], Andrea Candelli[1]
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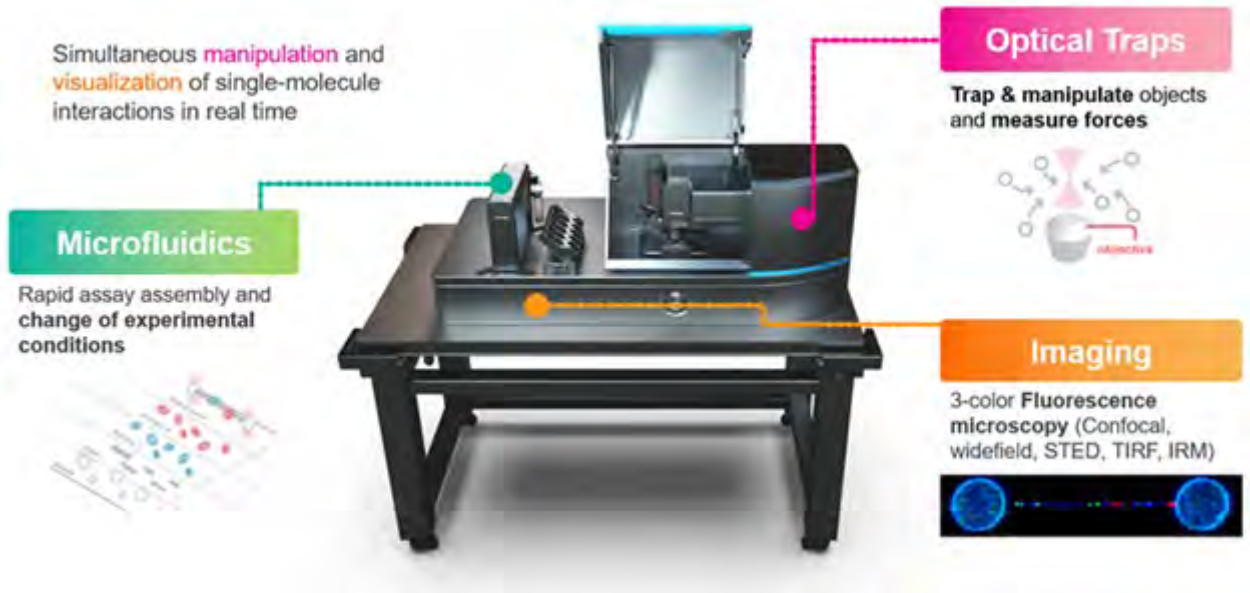
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The C-Trap, an advanced correlative optical tweezers-fluorescence microscopy platform, has transformed single-molecule biophysics by allowing direct manipulation and real-time visualization of biomolecular interactions with nanometer precision. By integrating dual optical traps, multi-color confocal microscopy, and microfluidic flow control, the C-Trap facilitates unprecedented exploration of molecular processes, including protein folding, DNA-protein interactions, and cellular mechanics.

This presentation will highlight recent breakthroughs enabled by the C-Trap, such as characterizing force-dependent dynamics in DNA repair, probing chromatin organization under tension, and studying biomolecular condensates critical for intracellular compartmentalization. The platform's capability to measure mechanical properties and monitor conformational changes at the single-molecule level has opened new avenues for understanding protein misfolding diseases, cellular stress responses, and the mechanics of biomaterials.
By making single-molecule techniques accessible across disciplines, the C-Trap fosters collaborative research, bridging physics, biology, and material science to address complex biological questions. This session will demonstrate how the C-Trap serves as a transformative tool for unravelling molecular mechanisms that underpin life, driving progress in fundamental and applied biophysical research.



Topological States in Out-of-Equilibrium Allosteric Molecular Assemblies

Mr Jan Kocka[1], Dr Kabir Husain[1], Dr Jaime Agudo-Canalejo[1]
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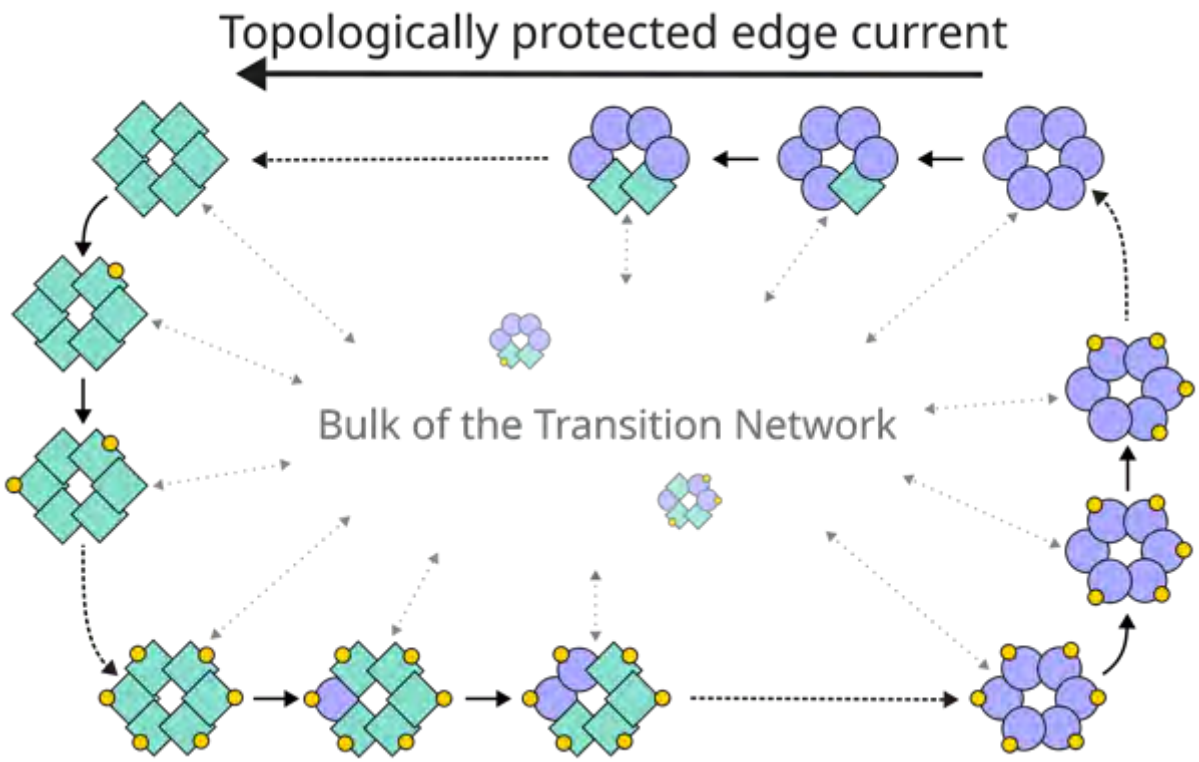
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Despite noisiness in the cellular environment, molecular systems show a high degree of robustness. A recent new direction in understanding this apparent paradox is the study of topologically protected states in stochastic systems, which robustly confine the dynamics of the system to a lower-dimensional space. However, it is unclear what the minimal biochemical ingredients are for such states to occur. Here, we study topological features in a non-equilibrium, thermodynamically-consistent model of a molecular assembly, made of subunits that undergo futile cycles of conformational changes and phosphorylation. When the subunits interact allosterically with each other, we find global, concerted cycles that emerge at the scale of the whole assembly. These involve only a small subset of all possible conformations, analogous to topological edge currents in quantum systems.

We map out the kinetics, energetics, and biochemical interactions necessary to obtain distinct classes of topological behaviour. Our results suggest that topological states can provide a minimal description of molecular coordination in protein complexes, such as circadian oscillators (e.g. KaiABC) or polymer assembly and disassembly (e.g. microtubules). More broadly, our results demonstrate that stereotyped dynamics can arise purely from non-equilibrium kinetic effects, without the need for an underlying energy landscape to channel them.



Influenza A Virion Dynamics at the Cell Surface

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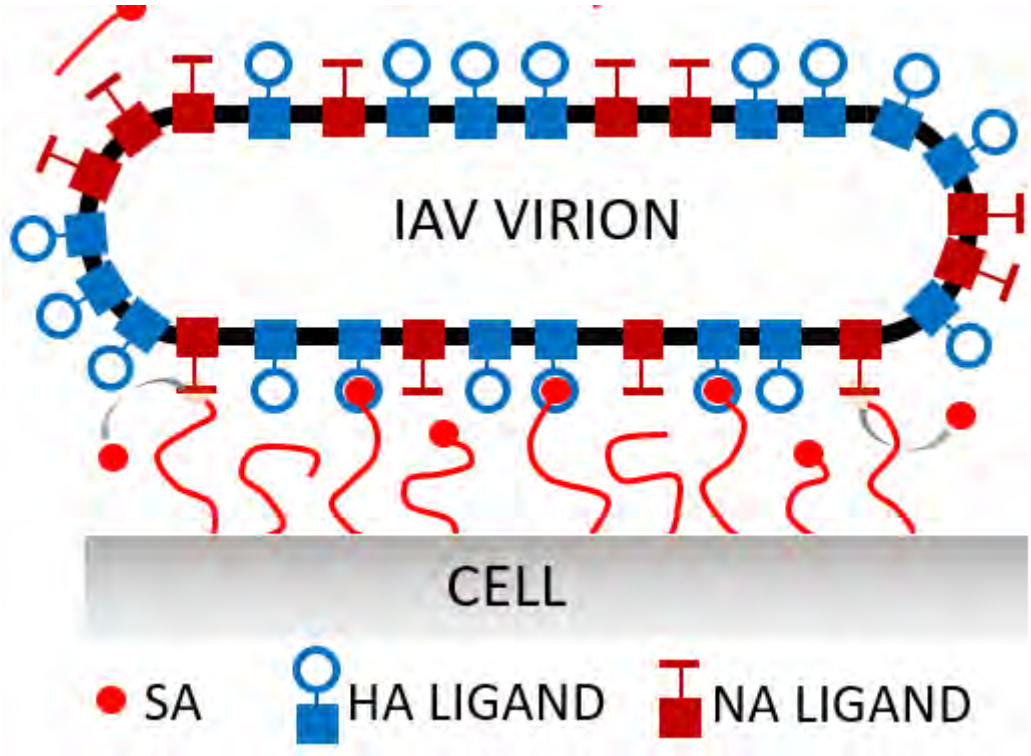
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The motility of Influenza A Viruses (IAV) within the epithelial layer is influenced by the interaction of two types of ligands on the virions' surface. Hemagglutinin (HA) binds to Sialic Acid (SA), facilitating the virus's attachment to cell surfaces, while Neuraminidase (NA) cleaves SA to prevent adhesion. The ligands' functionality, affinities, distribution, as well as their response to inhibition have been subject of frequent investigation, however a model linking these molecular details to the dynamics of the virions is still missing.

By modeling virus motion on the cell surface using a 2-dimensional reaction-diffusion system, we can closely observe motility over an extended timescale. This approach allows examining the effect of different interaction parameters and reveals how the spatial organization of ligands on the virions' surface significantly impacts motion persistence. The extension of these studies to systems with non-uniform receptor profiles demonstrates how the interplay of HA and NA enables the virus particle to explore multiple receptor clusters.



Optimisation of Electromagnetic Tweezers for Intracellular Force Application

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[1]*The Francis Crick Institute, United Kingdom*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Cellular processes like growth and division involve complex mechanical rearrangements driven by motor and non-motor proteins. While force spectroscopy has advanced our understanding of molecular mechanisms in vitro, measuring forces within living cells remains challenging. Electromagnetic tweezers have been used to apply forces in cells, but achieving forces in the tens of piconewtons requires large magnetic beads over 1 micron, limiting their use, particularly in smaller cells. Additionally, broad magnetic gradients allow manipulation of only one bead per cell.

We used physical simulations to optimise electromagnetic tip geometry, enhancing force generation to theoretical limits. Fine electromagnetic tips with controlled curvature were manufactured, enabling forces up to 10pN on particles as small as 100nm. Moreover, we developed microscale tips capable of applying independent forces in different directions on separate particles within a single cell.

Using sharp magnetic field gradients, we applied force to magnetic nanoparticles functionalised with molecular motors and manipulated particles moving along microtubules in vitro. These advancements pave the way for investigating intracellular mechanics by precisely applying torques and forces to organelles. This approach holds potential for studying critical cellular mechanisms such as spindle reorientation, mitotic division, and cytoskeletal rearrangements.

The stickers and spacers of Rubisco condensation in CO_2-fixing organelles

Dr Gaurav Kumar[1,2], Dr James Barrett[1,2], Dr Jack Shepherd[3], Dr Charley Schaefer[3], Dr Alex Payne-Dwyer[2,3], Dr Clément Dégut[2,4], Dr Michael Plevin[2,4], Prof Mark Leake[2,3], Prof Luke Mackinder[1,2]

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Pyrenoids are phase-separated CO_2-fixing organelles responsible for up to a third of global carbon fixation through the primary carbon-fixing enzyme Rubisco. Across kingdoms, Rubiscos are condensed by linker proteins that bind non-conserved interfaces using non-conserved stickers separated by disordered spacers. Despite their lack of conservation, linker proteins share common structural arrangements, with convergent numbers of stickers and properties of spacers.

Here, we study the phase separation of Rubisco by linkers from two model algal pyrenoids to probe the convergent evolution and functional importance of their properties. By studying the effects of sticker number both in vitro and in vivo, we propose a rationale for their composition that relates the phase separation efficiency of Rubisco and the energetic penalty of linker synthesis. We suggest the properties of stickers and spacers in pyrenoid linker proteins have optimally evolved to phase separate Rubisco at the lowest amino acid cost, dependent on their binding site location and interaction strength. We further demonstrate through in vivo physiology, FRAP and single molecule approaches that ensemble properties of pyrenoids are independent of linker length above a critical sticker number threshold, posing several questions about the regulation and nature of the dynamic interactions within.

Our results begin to explain the convergent evolution of linker properties in Rubisco condensates across kingdoms and provide important bioengineering parameters for ongoing efforts to transplant pyrenoids into plants to boost carbon fixation. More broadly, our results provide a framework for testing sticker and spacer properties for condensate functionality and ultimately cellular fitness.

Collective molecular dynamics behind biofilm dynamics: using anisotropic to model mixed bacterial interfaces

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[1]University of Cambridge, United Kingdom, [2]University of Miami, USA

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Bottom-up approach to biofilm modeling offers great potential for accurately describing biofilm growth and wrinkling behavior. Recent experimental work revealed that motile bacterial colonies growing against their non-motile counterparts generate intricate fractal patterns, requiring further examination of interfacial microrheology at the molecular level. While E.Coli and B.Subtilis have rod-like geometries, their dynamics are often modeled as point and spherical active particles for computational simplicity, not factoring differences from the isotropic models into account. Simulations of anisotropic particles remain computationally challenging due to the system's instability and high cost of rod-like or ellipsoidal models.

In this work, we seek to establish the constrained mapping between collective dynamics of active polar spheres and active brownian ellipsoids to identify the comparison parameters. We develop a simulation framework to encompass purely repulsive dynamics of nonspherical active particles, described by Langevin equation without hydrodynamic interactions with the interdependence on the Péclet number and packing density. The results show that such mapping exists at the restricted intermediate densities and moderate to high levels of the self-propulsion activity, also varying in prominence depending on geometry and set up of the interface. Consistent with previous studies, we observe the suppression of motility-induced phase separation (MIPS) at anisotropy degrees as low as 1.04, along with emergent polar and nematic order. This analysis provides quantitative insights into bacterial topology which has potential applications in development of predictive theoretical models and general understanding of active-passive bacterial interfaces.

Interferometric Gated Off-Axis Reflectometry (iGOR) - ultrasensitive label-free tracking of nanoparticles and suspended membranes in three dimensions

Prof Wolfgang Langbein[1], Freya Turley[1], Dr David Regan[1], Prof Paola Borri[1]
[1]*Cardiff University, United Kingdom*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

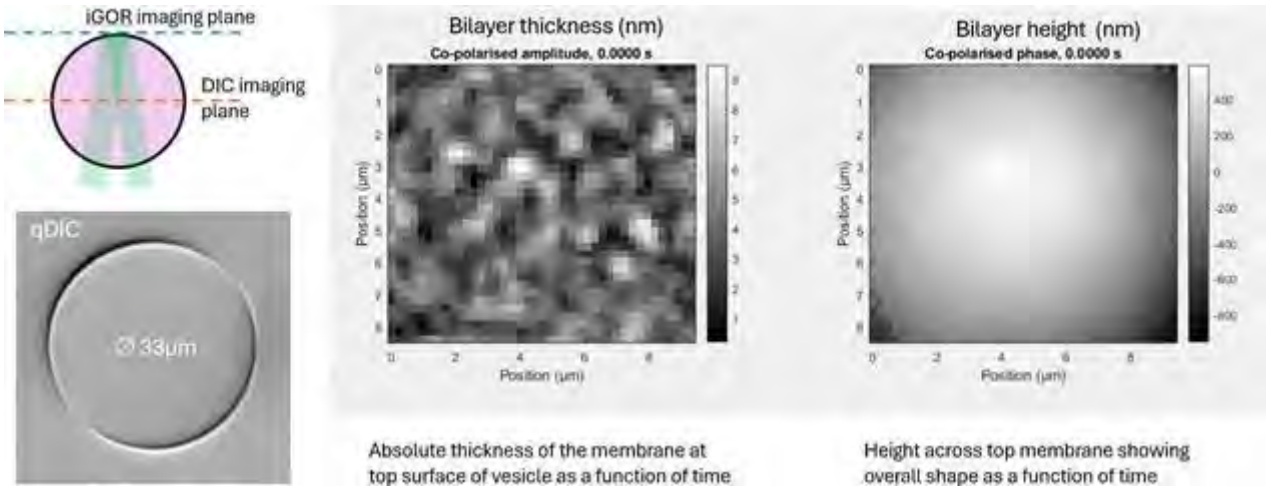
To unravel dynamic processes underpinning key functions in cell biology, it is essential to develop imaging technologies able to track the movement of individual bio-nano-objects under physiologically relevant conditions, at high speed (ms) and in 3D.

We demonstrate interferometric gated off-axis reflectometry (iGOR), suitable to investigate suspended single-membrane lipid bilayers and small nanoparticles in 3D label-free. iGOR detects the back-scattered light of samples using an external off-axis reference, to measure amplitude and phase of the detected light-field. Employing coherence gating by femtosecond pulses, the axial extension of the detected volume is controlled, and signals from other regions are suppressed. The measured field can be digitally refocused to extract the position of single particles moving in the volume. The reflection phase of the scattering provides an axial position resolution in the sub-nanometer range, an improvement of nearly two orders of magnitude compared to transmission methods.

With iGOR, we have tracked single gold nanoparticles of 10nm diameter at 3ms dwell-time. These measurements allow us to quantify the particle hydrodynamic size and its geometrical morphometry (size and non-sphericity) independently.

Moreover, we investigated the spatiotemporal dynamics of suspended single lipid bilayers, in the form of giant unilamellar vesicles as shown in the figure. We find that the membrane thickness can be measured with 0.1nm precision, and the membrane axial position with 0.5nm precision, following dynamic changes at 3ms time-resolution.

Overall, iGOR brings a new enabling capability to study e.g. single protein-lipid membrane interactions, overcoming significant existing limitations with supported membrane approaches and/or fluorophore labelling.



Absolute thickness of the membrane at top surface of vesicle as a function of time

Height across top membrane showing overall shape as a function of time

Measuring Entropy from Coarse-grained Single-molecule Statistics in Langevin Systems

Alvaro Lanza[1], Dr. Stefano Bo[1]
[1]*King's College London, United Kingdom*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

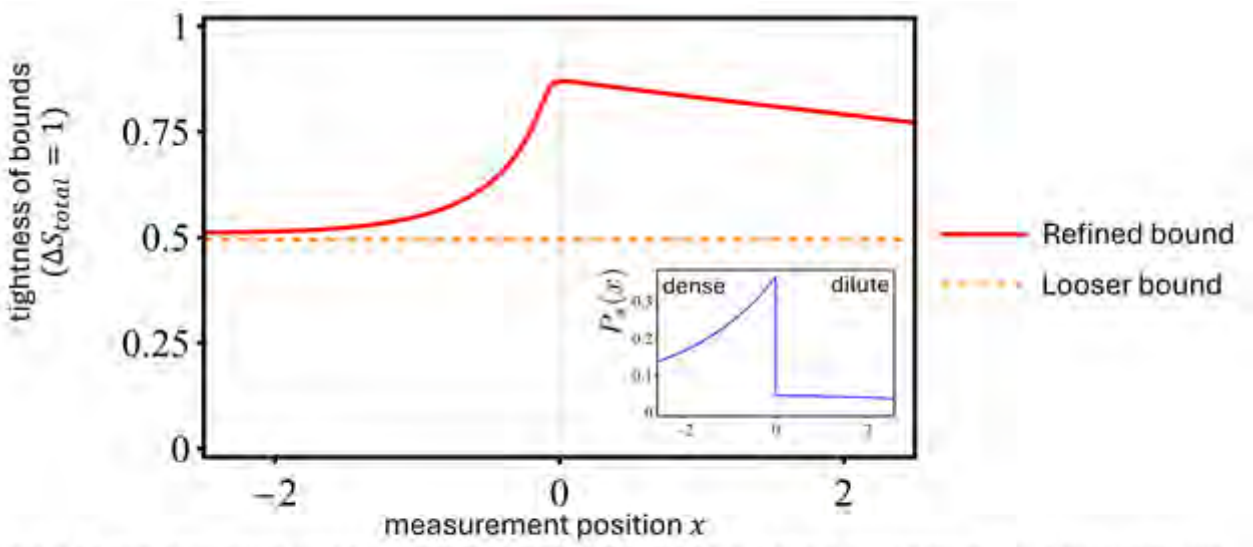
Biological processes at the subcellular level, including those pertaining to the dynamics of biomolecular condensates, often take place out of equilibrium. Establishing if, when, where and how much these processes consume and dissipate energy is made difficult by environmental thermal fluctuations. The corresponding entropy production can be calculated with complete knowledge of the molecules' stochastic trajectories, but these are typically not experimentally accessible. However, with modern single particle tracking, one can measure displacement distributions over a fixed time, which only require knowledge of the initial and final positions of molecules [1, 2].

In this work, we discuss how to use these measurements to infer the total entropy production. We derive a lower bound to entropy, which we study analytically by considering solvable non-equilibrium steady states of overdamped Langevin systems under phase separation. This allows us to discuss under what conditions these experimentally accessible measures capture most of the dissipation of the system, and how to spatially profile the entropy density. Our methods are benchmarked with the state-of-the-art in the field, namely, inference based on the thermodynamic uncertainty relation [3].

Our results, motivated by the physics of biomolecular condensates, promise wide applicability to other stochastic systems modelled by overdamped Langevin equations, such as molecular motors and protein pulling experiments.

A manuscript is in preparation.

[1] McSwiggen et al. eLife 2019; 8:e47098
[2] Bo et al. Phys. Rev. Res. 2021; 3:043150
[3] Manikandan et al. Phys Rev. Lett. 2020; 124:120 603



For a 1d non-equilibrium steady state distribution of a flux across a phase boundary at $x = 0$ (see inset), we take coarse measurements of entropy production with respect to a varying position of measurement. Our bound works best in this case when one measures displacements across the phase boundary.

Macrophage behavior in 3D biomaterial microenvironments

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

To participate in the host defence, macrophages must continuously probe their environment and quickly respond by translating extracellular cues into intracellular signals, leading to adaptive cellular responses or mechanotransduction. Evidence suggests that mechanotransduction in immune cells has a crucial role in promoting immune cell recruitment, activation, metabolism and inflammatory function. However, prolonged and excessive mechanical stimulation can result in pathologies, such as fibrosis, cardiovascular disease and cancer. Although the associations between mechanical cues and cell behaviour in steady-state and disease have been identified, the regulatory mechanisms among different mechanical cues are not yet comprehensively illustrated.

Here, we aim to rationalize the role of biomaterial surface topography on macrophages morphology, motility and metabolic activity. Specifically, we focused on the influence of prescribed surface topographies, fabricated by mechanical wrinkling of soft elastomeric bilayer, on macrophage remodelling, migratory potential, and proliferation.

Our results demonstrated that, depending on the wrinkles, characteristic length scales (i.e., wavelength and amplitude), macrophages adopted three different morphologies: T1 or spindle-like, T2 or egg-like, T3 or ball-like displaying differences in mechanical properties and motility.

Additionally, we observed differences in cytokines secretion in response to changes in surface topography, providing a correlation between cell immune response and material surface roughness.

Our results could pave the way to a rational design of more “immuno-compatible” biomaterials by understanding cells biomechanics in complex physiological environments, with application in the development of prosthetics and other biomedical devices.

Investigating the mechanical and adhesive properties of mitosis within a tissue, and the role of oncogenic Ras in regulating these

Rachel Lawson[1], Dr Helen Matthews[1]
[1]*University of Sheffield, United Kingdom*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Cells undergo vast architectural changes during mitosis, altering their shape, mechanical and adhesive properties to ensure successful division. Increased stiffening as a cell rounds up to enter mitosis has been described in single cells where the heightened exerted force ensures sufficient space for chromosome segregation and spindle assembly. However, it is less clear how cell shape and mechanical changes are coordinated when cells round up to divide in an epithelial monolayer where cell-cell junctions must be retained throughout to preserve tissue integrity. Using live imaging techniques, we describe how mitotic and interphase cell shapes and tensions vary when cells divide at different confluencies.

Employing Atomic Force Microscopy has allowed us to compare forces of individual and epithelial-based mitotic cells and start mapping local mechanics of mitotic and interphase cells within a monolayer. We also show that adherens junctions, tight junctions and desmosomes are maintain in epithelial cell division and have begun to examine how desmosome binding to keratin-based intermediate filaments may impact cell division mechanics. We have also examined how oncogenic h-RasG12V activation alters cell-cell adhesions, intermediate filaments, and mechanics during mitosis. Short term activation of h-RasG12V, via MEK/ERK signalling, is sufficient to alter cell stiffness, induce spindle mis-orientations and reduce cell-cell adhesion during mitosis, leading to a loss of monolayer integrity. Our ongoing investigation of the shape, force and adhesive changes that h-RasG12V activated cells exhibit when dividing within a monolayer, provide insight into how alterations to cell division can promote loss of tissue integrity during early cancer development.

Thermodynamic Consequences of Bursty Gene Expression on the Mesoscopic Dynamics of Two-Node Gene Networks in Response to an External Forcing

Mr. Crisandro Allen Lazo[1], Dr. Junie Billones[1], Dr. Paul Gerald Layague Sanchez[2]
[1]Department of Physical Sciences and Mathematics, University of the Philippines Manila, Philippines, [2]Yilan Marine Research Station, Institute of Cellular and Organismic Biology, Academia Sinica, Taiwan

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Transcriptional and translational bursting are key sources of stochasticity in gene expression. Previous works have demonstrated that bursting increases the variability in protein counts of single genes; however, these have been limited to insights from single genes at stationarity. Motivated by this gap, we analyzed how bursting shapes the behavior of the toggle switch and atkinson oscillator, key gene network motifs, when subjected to a parameter forcing simulating biological signaling.

Comparison of the epigenetic landscapes across all parameter values reveals that bursting leads to shallower attractors and lower saddle points leading to lower potential barriers. Despite these, the total quasipotentials of the attractors showed minimal changes, indicating that bursting flattens the landscape overall.

Analysis of the tipping dynamics of the promoter mesostates during and after the forcing protocol shows that the promoter dynamics are unaffected by the details of protein expression. Meanwhile, the tipping probabilities of the protein mesostates demonstrate that bursting damps sudden and large changes in gene expression.

Calculation of the thermodynamic potentials and driving forces affirm the independence of the promoter dynamics to bursting at the non-adiabatic regime. In contrast, for the protein mesoscopic dynamics, bursting lowers the magnitude of the instantaneous free energy dissipation rates as the signaling parameter is forced and during the system's relaxation period post-forcing. Decomposition of the bidirectional component reveals a greater total entropy production and housekeeping heat rate for the bursting models, implying a stronger irreversibility and breaking of detailed balance when bursty gene expression is incorporated.

Dynamical Network Remodeling of Slime Mold

Dr. Mathieu Le Verge-serandour[1], Viktor Vasilev[1], Prof. Dr. Karen Alim[1]
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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

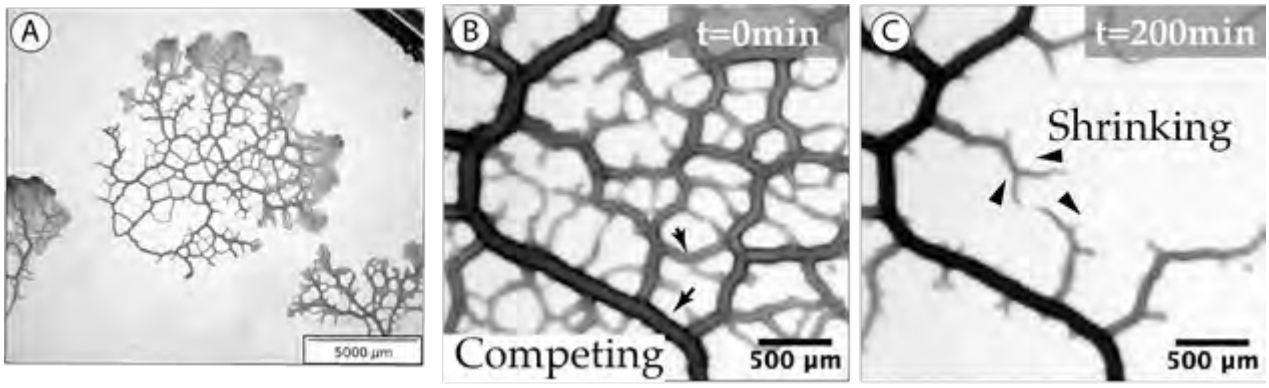
Remodeling of a network is one of the hallmarks of biological flow networks, ensuring their optimal morphology. Due to limited building costs, the removal of vessels allows these networks to reallocate matter to minimize dissipation, ensure maximum coverage, and even allow for migration.

Physarum polycephalum is a unicellular slime mold organized as a 2-dimensional tubular network (Fig. A) that evolves drastically over a few hours, evacuating a large zone of a few millimeters squared. Unfavorable competing parallel veins are first removed to form a tree-like structure (Fig B), where veins prune sequentially until complete evacuation of the zone (Fig. C).

First, we investigate the effect of sequential pruning based on the ratio of tube vs network resistance, using an analogy with power-grid networks. We analytically show that regular graphs are pruning until the average node degree is smaller than four, a result robust with simulated random networks. Including mass redistribution with pruning leads to resistance homogenization.

Second, analyzing time-lapses of the slime mold, we find an exponential decrease in the number of tubes reproduced by a toy model based on the network structure. We show the decay rate is controlled by the depth of the tree and the parallel branches dynamics that introduce a waiting time for pruning.

Our approach to flow networks may be generalized to pruning flow networks, as during embryonic development, stroke events, or evacuating networks for urban design.



Oscillations and collective behaviour in compartmentalised enzymatic reactions: Insights from numerical models

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Cells such as yeast often exhibit oscillatory behaviours and communicate through the emission of chemical species. Inspired by these natural systems, synthetic vesicles containing enzymatic reactions can mimic such behaviours, although experimental reports of oscillations in these systems remain sparse.

This work explores how the bell-shaped pH-rate profile of enzymes, coupled with compartmentalisation in membrane-bound vesicles, can lead to feedback effects and transport-induced oscillations. Through numerical modeling, we investigate the dynamics of collective vesicle systems and address the experimental challenges in detecting and reproducing oscillatory behaviours. We also propose potential strategies to enhance the likelihood of successfully detecting and reproducing such oscillatory behaviours.

Excitable systems as a design principle of the immune system

Yael Lebel[1], Uri Alon[1]
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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The immune system operates across diverse contexts, yet it appears to rely on recurring dynamic patterns to execute its functions effectively. One such pattern is excitable dynamics: transient, self-limiting spikes of activity with timescales independent of input strength. In this research, we show that excitable dynamics constitute a design motif underlying a wide variety of immune processes. Using a systematic mathematical approach, I map biological systems capable of exhibiting excitable behavior, focusing on their mathematical properties and functional implications.

Our findings suggest that excitable dynamics are not limited to autoimmune responses, such as in multiple sclerosis, but extend to other immune phenomena, including the innate response to pathogens, the complement system, and adaptive responses to cancer. By characterizing these systems, I aim to uncover how their specific features align with the demands of their biological contexts. This approach provides a unifying framework to interpret immune system behavior and suggests that excitable dynamics may be a conserved strategy employed by evolution to balance efficiency, robustness, and self-limitation.

Excitable dynamics of flares and relapses in autoimmune diseases

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Many autoimmune disorders exhibit flares in which symptoms erupt and then decline, as seen in multiple sclerosis (MS) during its relapsing-remitting phase. Existing mathematical models of MS flares often assume regular oscillations, failing to capture the unpredictable nature of flare-ups. We suggest that these flares resemble excitable dynamics triggered by random events.

Our minimal model, involving autoimmune and regulatory cells, demonstrates this concept. Autoimmune response initiates antigen-induced expansion through positive feedback, while regulatory cells counter autoimmune cells through negative feedback. The model effectively explains the decrease in MS relapses during pregnancy and the subsequent surge postpartum, based on lymphocyte dynamics. Additionally, it identifies potential therapeutic targets, indicating significant impacts from slight adjustments in regulatory T cell activity or production. These findings indicate that excitable dynamics may underlie flare-ups across various autoimmune disorders, potentially advancing treatment strategies.

Identifying Molecular Interactions through Stochastic Modelling and Optimisation

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Molecular interactions are often studied with correlation tests which are not model-specific and can be misled by correlations introduced by various noises in experimental data. Here, we present a novel approach to interaction identification. Our approach is based on stochastic modeling of the interactions and provides model-specific identification. Through optimization, our approach carries out feasibility checks to examine if the observed data can possibly be produced without the interactions of interest.

We use the miRNA-mRNA regulation as an example to demonstrate our approach with scRNA-seq data. By considering a capture efficiency model, our approach efficiently distinguishes the correlations in data from the interactions and the shared noises and hence outperforms standard correlation tests.

Host cell cycle and ribosomal resources drive phage infection outcomes

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[1]*University of Cambridge, United Kingdom*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The efficacy of bacteriophages is intrinsically linked to the physiological state of their bacterial hosts. However, identifying which physiological factors dominate and how they regulate the infection progression has been challenging. This problem stems from the inherent heterogeneity between individual cells and their dynamic physiological states. Traditionally, the field has relied on bulk interactions and measurements to infer key parameters like “average” lysis time and burst size, which obscure the dynamics of infection progression and its dependency on infected bacterial physiology.

To tackle this, we developed a microfluidic imaging assay for tracking phage infection steps in individual bacterial cells. This method enabled us to investigate how bacterial physiology shapes infection dynamics. Our findings uncovered that the burst size of phage infection is predominantly determined by the host’s translation capacity. Particularly, we identified the bacterial cell cycle as a critical factor influencing infection efficiency - something that cannot be captured through bulk assays. By perturbing the cell cycle with division inhibitors, we demonstrated how shifts in physiological states can influence phage infection dynamics.

Understanding the physiological factors governing phage infection progression opens many strategies for steering the infection kinetics by perturbing cell physiology. This insight helps to potentiate phages for their applications in biocontrol, including tackling antimicrobial resistant pathogens.

A computational model for deformation of cancer cells in microchannels

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Accurately modeling and predicting the flow-induced cancer cell deformation in microchannels is crucial for studying metastasis and developing microfluidic tools for cancer diagnosis and drug monitoring. However, the modelling has been a classical challenge, due to the complex viscoelastic structure of cancer cells and the nonlinear interactions between the cells and suspension fluid. In the present study, we develop a general computational model for the transit of cancer cells through microchannels with distinct geometries. Our cell model considers three major subcellular components: a viscoelastic membrane representing the lipid bilayer and the underlying cell cortex, a viscous cytoplasm, and a nucleus modelled as a smaller deformable capsule. The cell deformation and its interaction with the suspending fluid are solved using a well-developed immersed-boundary lattice-Boltzmann method.

To validate the model, we conduct flow experiments of prostate cancer (PC-3) and human leukemia (K-562) cells flowing through constricted and cross-slot microchannels. Extensive numerical studies have been conducted to examine the effects of the rheology of each subcellular component, and the results are compared with our experiments (see Fig. 1). We find that the classical Skalak's law can accurately describe the cells' membrane elasticity and predict their steady profiles in the straight section of the channels. However, for cell transient deformation, excellent agreements with experiments can only be achieved by carefully considering the cell membrane viscosity in the model. Interestingly, PC-3 cells showed higher membrane elasticity (3.36 mN/m) than K-562 cells (0.85 mN/m), though both exhibited comparable membrane viscosities, on the order of 10 μNs/m.

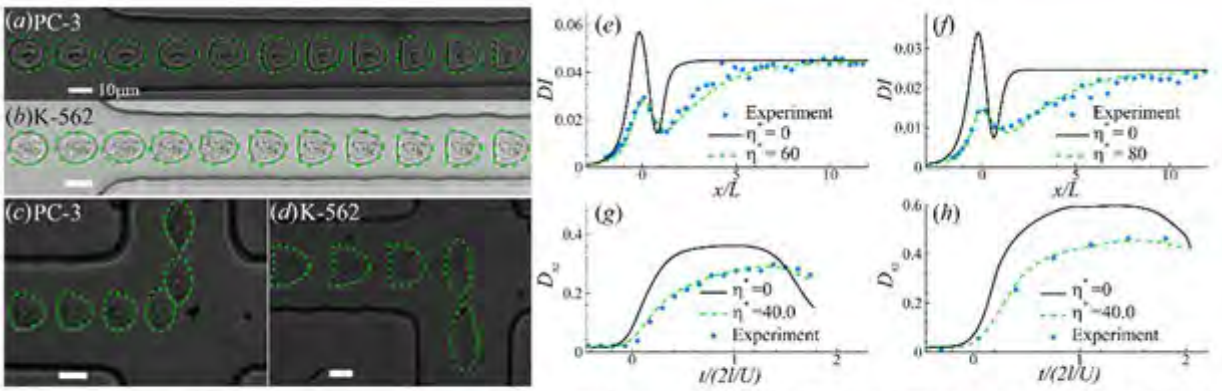

Fig 1. Comparisons of the transient deformation obtained from simulations (green dashed lines) and experiments in constricted channel (a,b) and cross-slot channel (c,d) for PC-3 and K-562 cells. The corresponding time evolutions of the deformation index (DI) for the constricted channel (e,f) and Taylor deformation parameter (D_{xy}) for cross-slot channel (g,h) are also compared respectively.

Heartbeat driven self organisation of the Endocardium during Zebrafish heart morphogenesis

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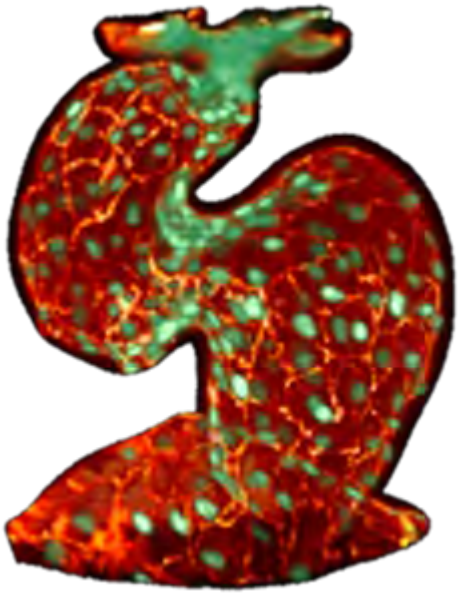
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

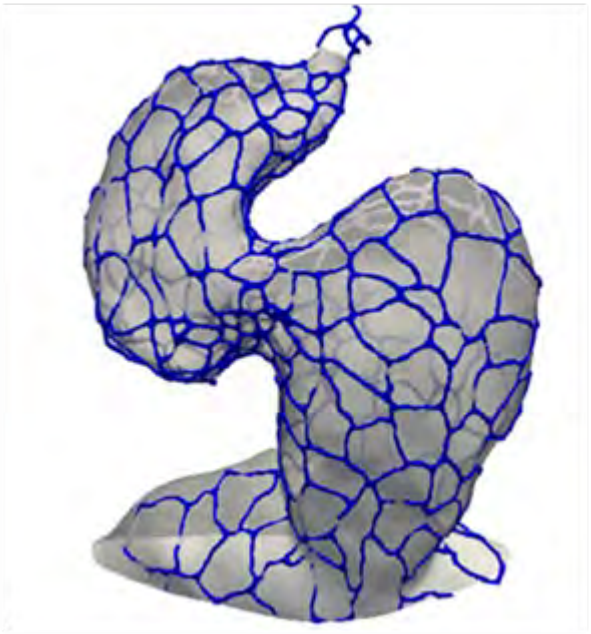
During Zebrafish heart development, the heart loops from a linear tube and expands to a two-chambered heart, involving the coordinated shape change of the myocardium and internal endocardium cell layers. How the endocardium coordinates cell shape to attune its complex tissue growth to the myocardium is an open question. We use cell-shape analysis of in-vivo imaging and biophysical modelling to describe the self-organising properties of the endocardium during chamber expansion.

During heart looping, we see a clear correlation between cell area and heart-tube radius. Treating hearts with Hydroxyurea to prevent cell division preserves this area distribution, and Hyaluronidase treated hearts with expanded chamber dimensions show equivalently local cell area increases, suggesting cell area locally adapts to chamber expansion. Furthermore, the Endocardium closely obeys a Centroidal Voronoi Tessellation (CVT), which has geometric hallmarks of in-plane, passive force balance, and strikingly this is satisfied throughout the heart across heterogeneous cell areas and elongations. In a vertex model framework, Endocardial cells are geometrically in the fluid phase, whilst shape similarities with CVTs are typically observed in uniform, solid phase cells. We propose that rhythmic stretch due to heartbeat can explain this observed behaviour; vertex modelling shows that an imposed rhythmic dilation causes cells to closely approach a CVT and solidify whilst appearing geometrically fluid in its rest position.

Together these suggest a simple self-organised picture of development, where the Endocardium is bound to the inner surface of the heart, attuning its growth to myocardial chamber expansion through local adaptations of cell area.

Cell Network Segmentation





Voronoi Comparison

Exploring Bacterial Resistance: Mechanisms of Reduced Susceptibility in Staphylococcus aureus During Stationary Phase

Calum Lloyd[1]
[1]*University of Sheffield, United Kingdom*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

For nearly 80 years, healthcare has been revolutionised by the use of antibiotics, dramatically improving treatment of infections. This wonder of the modern age however is under threat from antimicrobial resistance (AMR), significantly reducing the effectiveness of antibiotic treatments. It has been estimated that in 2021, ~4.7 million deaths were associated with AMR infections with this figure projected to increase to ~8.2 million deaths per year by 2050 [1]. While new novel treatment options are needed, further understanding of the interactions between antibiotics and bacteria is also required to improve current treatment.

Of particular interest is studying the interaction between antibiotics and the peptidoglycan (PG) layer of the cell wall of gram-positive bacteria. Antibiotics such as ß-lactams kill bacteria by disrupting synthesis of the PG layer [2]. Studies have revealed the effectiveness of antibiotics decrease as bacteria enter the stationary phase [3]. In this phase bacteria such as Staphylococcus aureus undergo a number of physiological changes in response to environmental pressures such as triggering the Stringent Response as well as potentially switching off the WalKR system, dramatically affecting growth [4][5].

This study aims to characterize the PG layer of the cell wall of S. aureus both during the exponential and stationary phase, interacting with ß-lactam antibiotics. This will be done utilising probing techniques such as Small-Angle Scattering (SAS) as well as imaging using Atomic Force Microscopy (AFM). Strains lacking the Stringent Response and WalKR system will also be utilised, investigating the role they play in resistance during the stationary phase.

A statistical theory of human lung branching morphogenesis from organ-scale imaging

Ivan Lobaskin[1], Megumi Inoue[2], Ignacio Bordeu[3], Adrien Hallou[4], Alain Chedotal[2,5], Ben Simons[1]

[1]University of Cambridge, United Kingdom, [2]Institut de la Vision, France, [3]Universidad de Chile, Chile, [4]University of Oxford, United Kingdom, [5]University of Lyon, France

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The human lung is a highly complex and ramified branched organ. How this structure is generated in development is a question that has long fascinated biologists and physicists alike. While great insight has been gained into the mechanisms that regulate tip cells at the molecular scale, how these processes integrate into the large-scale ductal organisation remains poorly understood. Here, by segmenting in three dimensions the topology of the ductal network through the early (pseudoglandular) phase of development, we use mathematical and modelling-based approaches to question whether there is a statistical basis to branching morphogenesis in the human foetal lung.

From the morphology of branch patterns, we identify two distinct branch types: the first lay the foundation of a minimally branched core network, while the second sprout from this core network, creating a forest of branching trees that fill in the available volume. Further, by quantifying the statistical distribution of duct lengths, we show that the growth dynamics of the lung tips are associated with an asymmetric branching model, rather than the conventional symmetric branching paradigm. Together, these findings reveal how a minimal set of repetitive statistical rules elaborate the complex large-scale branching organisation of the human lung.

Modelling pattern formation and self-organisation during neuruloid development

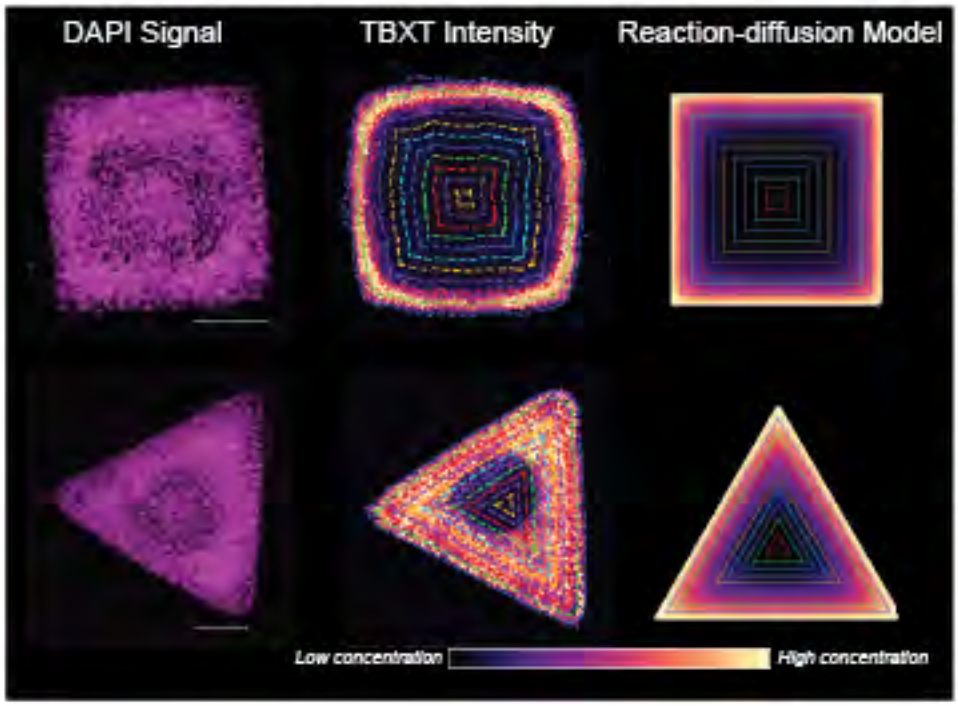
Yi Ting Loo[1], Juliet Chen[1], Ryan Harrison[1], Sophie Theis[1], James Briscoe[2], Guillaume Charras[3], Timothy Saunders[1]
[1]University of Warwick, United Kingdom, [2]The Francis Crick Institute, United Kingdom, [3]University College London, United Kingdom

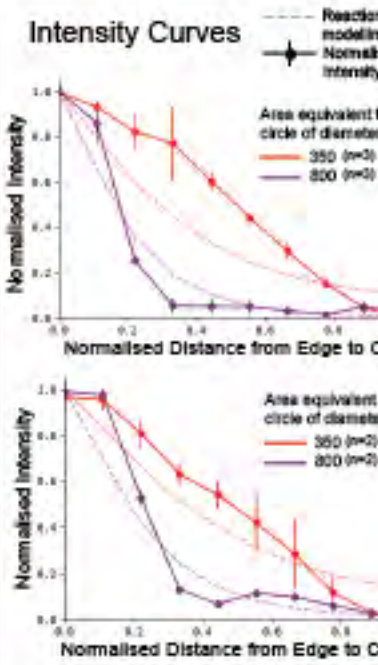
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

During organ morphogenesis, diverse cell fates robustly self-organise within spatially constrained environments. Morphogens such as Wnt and Fgf are diffusible intercellular signalling molecules which vary in concentration across the tissue, controlling cell fate patterning. However, how boundary constraints affect these patterns and are interpreted by differentiating cells remain poorly understood. To study this, we utilise an in vitro system that recapitulates vertebrate axial progenitor cells development, coined “neuruloids”, derived from human embryonic stem cells (hESCs). Our neuruloids are spatially constrained within microenvironments. Imaging reveals a distinct radial separation between differentiated mesoderm and pluripotent cells 48 hours after activation of the WNT/FGF signalling pathways.

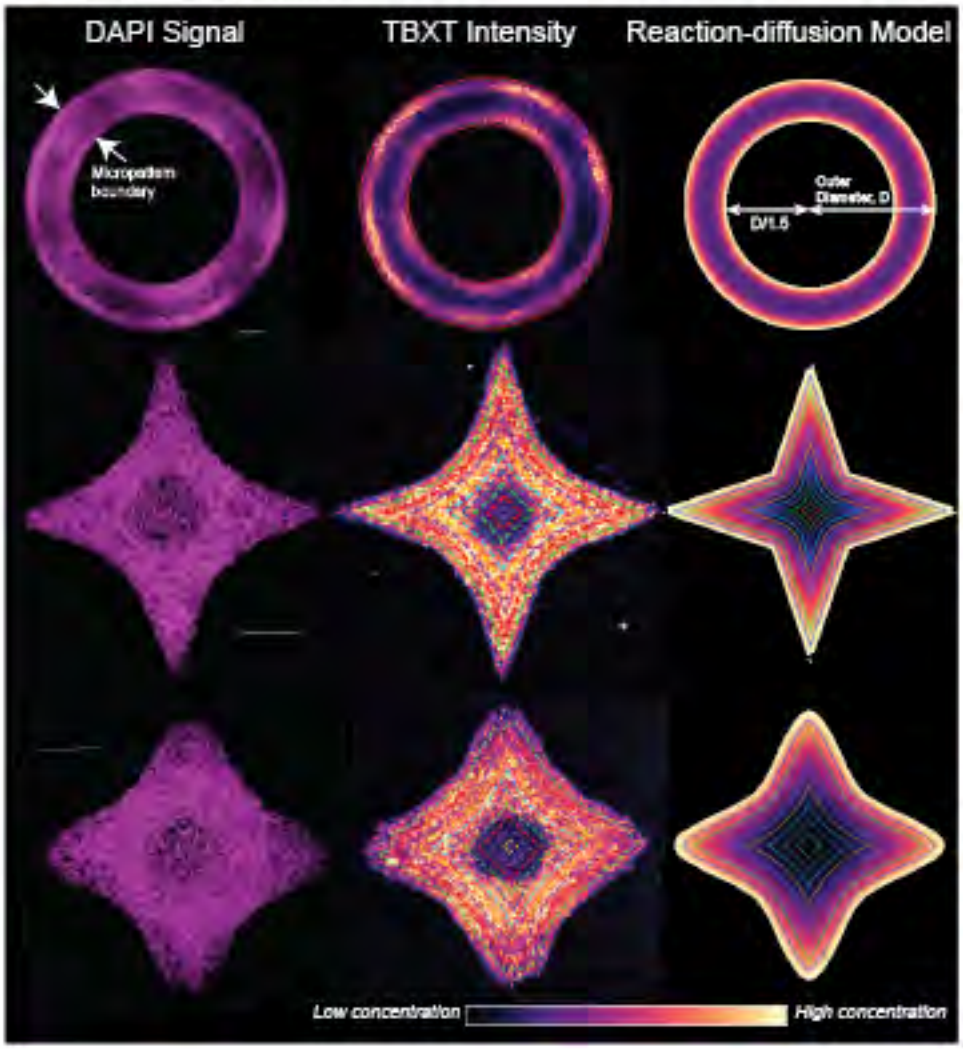
Analysis of cell fate boundaries aligns with the concept of positional information determined by the concentration profiles of diffusible morphogens. The numerous signalling pathways underlying this phenotype are complex. Therefore, to simplify the problem, we utilised reaction-diffusion equations to describe the secreted Wnt morphogen concentration which induces TBXT expression (early mesoderm cells). We considered a deterministic model for the mutually inhibiting transcription factors TBXT and SOX2. This represents a minimal model of the WNT signalling pathway. We present a sensitivity analysis of the model parameters. The modelling results align with TBXT signals observed in images across micropatterns of various sizes and predicted outcomes of experimental perturbations. The model was able to predict mesoderm specification in a range of micropattern geometries, including annuli, triangles and stars. This study highlights that self-organisation processes of axial progenitors in constrained environments may be driven by morphogen gradients established through reaction-diffusion systems.

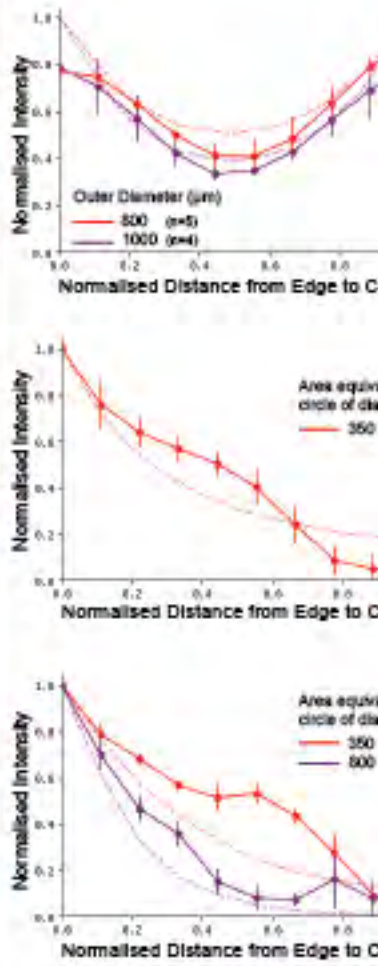
A Geometric Perturbations





B Boundary Perturbations





Quantitative Modeling of Bacterial Population Kinetics in the Gut Microbiome of Individual C. elegans

Carol Lu[1,2,3], Stanimir Tashev[1,4], Pedro Pessoa[1,4], Rory Kruithoff[4], Douglas Shepherd[1,4], Steve Pressé[1,4,5]

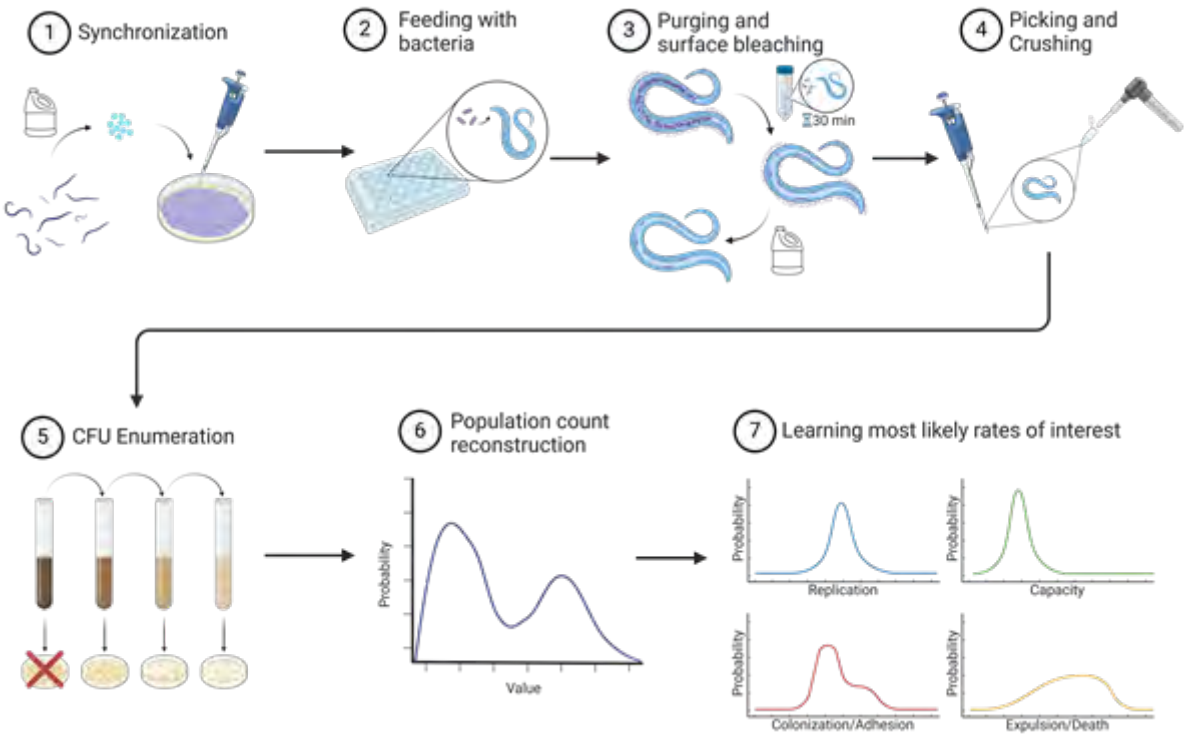
[1]Center for Biological Physics, Arizona State University, USA, [2]School of Biological and Health Systems Engineering, Arizona State University, USA, [3]School of Mathematical and Statistical Sciences, Arizona State University, USA, [4]Department of Physics, Arizona State University, USA, [5]School of Molecular Sciences, Arizona State University, USA

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The dynamics of host-pathogen interactions within the gut microbiome present a unique opportunity to investigate microbial ecology in a multi-organism system. Despite its importance, the study of intestinal population kinetics has predominantly relied on bulk quantification techniques, which provide basic estimates but fail to capture the considerable individual-to-individual variation observed in total microbiota population counts.

In this work, we focus on studying the host-pathogen dynamics in the gut microbiome by quantifying the population kinetics of Escherichia coli in individual Caenorhabditis elegans. Using experimental methods with snapshot data, such as crushing and plating the gut contents of individual worms at discrete time points throughout their lifetime, we examine key processes including colonization, multiplication, death, and expulsion rates of E. coli. The colonization process transitions from rare single-cell events in early days to bacterial populations in the millions during later stages. This necessitates a robust multiscale modeling framework that interpolates across these regimes. To address this, we introduce a Bayesian theoretical framework that quantitatively resolves the dynamics of these broad population scales.

Furthermore, we explore host-pathogen interactions by introducing a competing bacterial predator into the gut microbiome to assess its impact on the population kinetics of the primary colonizing species. Our quantitative model demonstrates the capacity to detect stochastic changes in rate parameters induced by these ecological disturbances, even within the constraints of micro-scale, space-restricted systems.


1 Synchronization
2 Feeding with bacteria
3 Purging and surface bleaching
30 min
4 Picking and Crushing
5 CFU Enumeration
6 Population count reconstruction
Probability
Value
7 Learning most likely rates of interest
Probability
Replication
Probability
Capacity
Probability
Colonization/Adhesion
Probability
Expulsion/Death

Modelling Actomyosin Oscillations in Morphogenetic Dynamics Using an Active Elastomer Framework

Mr Euan Mackay[1], Miss Aimee Bebbington[2,3,4], Prof Jens Januschke[1], Dr Jochen Kursawe[4], Dr Marcus Bischoff[2,3], Prof Rastko Sknepnek[1,5]

[1]School of Life Sciences, University of Dundee, United Kingdom, [2]Biomedical Sciences Research Complex, University of St Andrews, United Kingdom, [3]Centre of Biophotonics, University of St Andrews, United Kingdom, [4]School of Mathematics, University of St Andrews, United Kingdom, [5]School of Science and Engineering, University of Dundee, United Kingdom

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Actomyosin networks are fundamental to force generation in cells, driving processes such as migration, shape changes, and tissue remodelling. During morphogenesis in diverse organisms, these networks frequently exhibit oscillatory behaviour. To investigate how cell shape and polarity influence these dynamics, we developed a continuum active elastomer model. Using the finite element method, we performed simulations incorporating realistic geometries and boundary conditions derived from Drosophila larval epithelial cells (LECs). Our simulations captured key features of actomyosin oscillations, including spatial organisation and flow patterns, which align with experimental observations.

The model suggests that oscillations arise as emergent properties of the actomyosin network, governed by intrinsic mechanical interactions rather than external signalling. Furthermore, changes in cell polarity, geometry, and contractility during LEC development were sufficient to explain shifts in actomyosin dynamics. These findings underscore the intricate interplay between cell mechanics and geometry in self-organised morphogenetic processes.

Preprint is currently on Biorxiv:
https://www.biorxiv.org/content/10.1101/2024.10.04.616649v1.full.pdf .

Unlocking early flowering: The role of microRNAs in accelerating flowering time through small RNA transcriptomics

Miss Aileen Magilin[1], Dr Hugh Woolfenden[1], Dr Jo Hepworth[2], Prof Richard Morris[1], Dr Rachel Wells[1]
[1]John Innes Centre, United Kingdom, [2]Durham University, United Kingdom

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Sarisha-14 is an early flowering cultivar of Brassica rapa, which undergoes the floral transition a week earlier than the standard lab accession, R-o-18, while grown in identical non-vernalised conditions. We hypothesise that Sarisha-14's ability to accelerate its floral transition is through the ratio of expression of two microRNAs (miRNA), miR156 and miR172, which are key regulators of flowering time via the ageing pathway. MiR156 is a repressor of flowering while miR172 promotes flowering, and their expression patterns over time are antagonistic to each other in the model plant Arabidopsis thaliana [1,2]. In a previous study, we observed that the precursors of these miRNAs are expressed at similar levels in both Sarisha-14 and R-o-18 at the beginning of the floral transition [3].

To test our hypothesis, we conducted a time series experiment using small RNA-sequencing to profile miRNA expression from the early vegetative stage until the flowering stage, in both cultivars. In agreement with our previous findings, mature miR156 and miR172 have the same expression ratio prior to the floral transition in both cultivars, which suggests that there is a certain ratio of miR156/miR172 expression that occurs prior to the floral transition. We also identified other differentially expressed miRNAs which could potentially be associated with Sarisha-14's early flowering phenotype. This is the first study to profile miRNA expression from seedling to floral bud formation in B. rapa, which will enhance our understanding of miRNAs and their role in the control of the floral transition.

[1] https://doi.org/10.1371/journal.pgen.1006263
[2] https://doi.org/10.1371/journal.pbio.3001043
[3] https://doi.org/10.1017/qpb.2021.6

Exploring the role of class I myosins in plasma membrane organization using an in vitro reconstitution approach

Miss Bhagyashri Mahajan[1], Prof. Satyajit Mayor[1]
[1]*Ncbs, India and CMCB, University of Warwick, United Kingdom*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The plasma membrane of a cell participates in many physiological processes such as signal transduction, trafficking of molecules, cell division, cell adhesion, cell migration and cell-cell communication. Orchestration of these functions requires compartmentalization of specific proteins and lipids into distinct functional domains and their spatio-temporal regulation.
A wealth of experimental observations regarding the nature and dynamics of membrane organization, suggest that the membrane is maintained as an active composite of the membrane bilayer in conjunction with a dynamic actin cytoskeleton, and the extracellular matrix at the outside of the cell (1). To understand this complex system, Mayor laboratory has taken a bottom-up approach by reconstituting key elements of this active composite membrane system – actin and myosin, to understand the organization of molecules that are linked to dynamic actin filaments (2). In most cells, specific set of non-muscle myosins drive this organization.

Recently, experiments from the laboratory in mammalian and insect cells have shown that the motor activity of class I myosins is required for the organization of the actin-dependent nanoscale clusters of a specific membrane component, GPI-anchored proteins at the outer leaflet of the cell. In this poster, I will discuss my efforts to reconstitute a minimal system with purified Myosin I, actin filaments and supported lipid bilayers, and will present observations on myosin I and membrane organization in vitro.

References:
1. Sezgin, E., Levental, I., Mayor, S. et al. Nat Rev Mol Cell Biol (2017)
2. Koester, D. V. et al Proc National Acad Sci 113, (2016)

The role of class I myosins in plasma membrane organization

Miss Bhagyashri Mahajan[1], Prof Satyajit Mayor[1]
[1]Ncbs, India and CMCB, University of Warwick, United Kingdom

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

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A wealth of experimental observations regarding the nature and dynamics of membrane organization, suggest that the membrane is maintained as an active composite of the membrane bilayer in conjunction with a dynamic actin cytoskeleton, and the extracellular matrix at the outside of the cell (1). To understand this complex system, we have taken a bottom-up approach by reconstituting key elements of active composite membrane system - actin and myosin, to understand organization of molecules that are linked to dynamic actin filaments (2).

In all eukaryotic cells non-muscle myosin II serves as motors that drive the contractility of the actin skeleton, either as stress fibers or the actin cortex, providing potential to drive the active organization of molecules that associate with actin. However, myosin I are directly associated with the lipid membrane and could potentially serve as a key ingredient in active membrane lipid organization. Here, I discuss efforts to reconstitute a minimal system with purified class I myosin, actin filaments and supported lipid bilayers, and will present observations on myosin I and membrane organization in vitro.

References:
1. Sezgin, E., Levental, I., Mayor, S. et al. Nat Rev Mol Cell Biol (2017)
2. Koester, D. V. et al. Proc National Acad Sci 113, (2016)

Structure and stability of self-assembled multidomain peptide fibres

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[1]Rutherford Appleton Laboratory, United Kingdom

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

In this work we investigate a family of peptides that form β-sheet nanofibres and present an exceptional physical stability even after attachment of poly(ethylene glycol) (PEG). Using small-angle scattering techniques in combination with molecular dynamics simulations to probe the nanostructure, stability and molecular exchange, we show that fibres formed by KxW(QL)yKz multi-domain peptides are extraordinarily stable.[1] These findings show that robust nanostructures with little susceptibility to physical and chemical perturbations can be engineered by using relatively short β-sheet-forming peptides. Through a balance of hydrophobic interaction and hydrogen bonds, these peptide assemblies achieve superior stability as compared to regular amphiphiles. Our results clearly highlight the nanostructural stability that can be achieved by peptide assembly and further exploited in biomedical applications.

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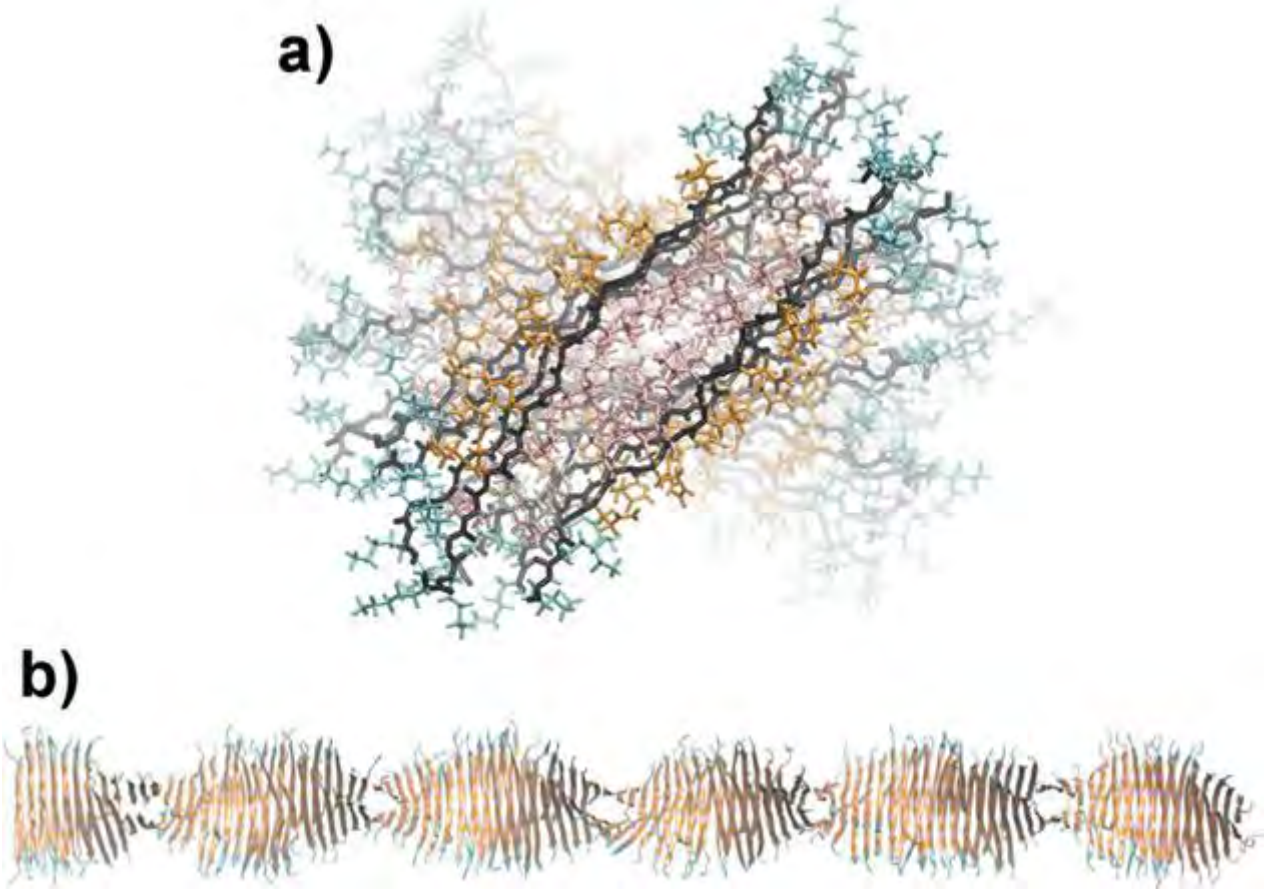

Molecular Simulations of the Pyrenoid

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

In algae, pyrenoids are biomolecular condensates that serve an important function in carbon dioxide capture. Pyrenoids are, essentially, made up of two components: the CO_2 capturing rubisco and linker proteins that link the rubisco together. Great improvement has been made in theoretically modelling these systems through the use of sticker-spacer models [1]. Using molecular simulations, these models can be parameterized more accurately.

Understanding the behaviour of pyrenoids requires the modeling of the linkers, which are highly complex, intrinsically disordered proteins (IDPs). Simulating IDPs is not a trivial task. This is due to a lack of generalisable IDP force-fields, as well as due to their high conformational variability resulting in high computational times.

In this project, through the use of CALVADOS and AMBER MD, we simulated the rubisco and linkers of Chlorella algae using novel IDP methods. We use these results to parameterize other coarse-grained models that simulate the phase separation properties of the pyrenoid, as well as to suggest linker behaviour in different physiological conditions. Most notably, we tested how the linker protein might interact with Rubisco in a more complex way than previously believed.

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Expanding the P. bursaria-algal model for endosymbiosis

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The living of one organism within another, endosymbiosis, has evolved independently multiple times across the tree of life and often includes interactions between vastly unrelated organisms. This phenomenon is central to our understanding of the evolution of emergent complexity in modern life, medicine, ecology and agriculture. In natural settings endosymbioses occur in the context of complex and diverse ecosystems. However, when studied it is often limited to overly simplistic models that revolve around one-on-one interactions between two organisms, obfuscating much of the complexity and diversity seen in natural settings. For our understanding of endosymbiosis to progress, more nuanced models need to be developed. Paramecium bursaria has emerged as a model for the study of primary and secondary endosymbiosis in eukaryotes. Its symbiosis consists of the ciliate host housing multiple species of algae and providing them with organic nitrogen (amino acids) in exchange for photosynthetic products (maltose). P. bursaria can hold multiple different species of symbiont simultaneously, the experimental opportunities this presents are yet to be explored. We propose expanding the P. bursaria-algae model to include the study of these naturally occurring tri-partite systems whereby P. bursaria plays host simultaneously to microalgae from either Chlorella or Micractiunium and the picoalga Choricystis sp. in what can be described as dual-algal systems. By increasing the number of selfish entities that simultaneously co-habit the host, we hope complexity seen in nature can be mirrored in a tractable system.

Evidence of Stochastic Resonance in Multi-Sensor Odor Source Localisation

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Biology of octopuses inspires my work. Octopuses can perform odor search using the suckers they have spread all over their body. Odor plumes convey useful information about the source that generates them and several animals use it to locate or navigate through the source. Experimental evidence shows that octopuses can perform the challenging task of finding the odor source even in a dark and turbulent environment.

I model the octopus suckers as an array of chemical sensors that collectively cooperate in locating the odor source. The main question is how many chemical sensors collectively infer a chemical source's location. In my setting, odor develops into convoluted and sparse clouds, due to turbulent transport, and each sensor measures odor concentration at its location.

Firstly, I examine the ideal case, where sensors have perfect knowledge of their relative position and combine their measures using Bayesian inference. Afterward, I insert noise in the relative positional information between sensors. In general, error affects prediction accuracy. The inference process can be enhanced under certain conditions if the error is not restored. This counterintuitive result is in accord with recent results in stochastic resonance.

Furthermore, it is possible to obtain the best of the two worlds, with and without error, if these errors are accurately accounted for.

My results set the basis for understanding whether and how imperfect proprioception may affect the olfactory behavior of animals with distributed nervous systems.

Guidelines for the development of genetic AC-DC circuits

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Gene regulatory systems such as the toggle switch and repressilator, have been extensively studied due to their ability to model key biological phenomena such as multistability and oscillations, respectively. These dynamics underpin several critical processes including cell fate decision-making and cyclical biological systems.

The AC-DC circuit [1, 2] is a multifunctional minimal gene regulatory model combining the toggle switch and repressilator into a single genetic circuit. Its ability to model both multistability and oscillatory dynamics mirrors the functionality of patterning in vertebral neural tubes [3] and the organisation of the Drosophila blastoderm [4], and opens exciting avenues for developing synthetic biological systems.

This study advances the AC-DC model initially proposed by Perez-Carrasco et al. [2], by using a thermodynamic formalism to create clear design guidelines developing experimentally viable multifunctional gene networks with tailored dynamical properties. Using Approximate Bayesian Computation with Sequential Monte Carlo (ABC-SMC) we infer parameter spaces required for multifunctionality, and we further categorise the emergent dynamics of the AC-DC into three cases (an isolated double Hopf bifurcation, saddle-node on invariant circle, and saddle-loop bifurcation) with different dynamic properties. We analyse the dynamical properties of the emergent systems, such as controlling the transition of timing between different functional states, study their sensitivity to intrinsic and extrinsic noise, and determine under which conditions one- or two-inducer models are more experimentally viable.

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AFM-based approaches for RNA structure characterization

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The secondary and tertiary structures adopted by single-stranded RNA molecules play a crucial role in determining their function in cellular processes. However, the majority of RNAs remain structurally uncharacterized. In this study, we highlight the use of Atomic Force Microscopy (AFM) to investigate RNA secondary structure, as it enables direct visualization of structural heterogeneity at the single-molecule level. Here, we developed a method for synthetizing RNA molecules with poly-A tails to tag the 3' and 5' ends. This allowed us to localize intact full-length molecules and to recognize reproducible features.

Moreover, we have established an image analysis framework to extract structural information from AFM images. As a case study, we applied this methodology to the long non-coding RNA CONCR, which is implicated in sister chromatid cohesion [1]. Our analysis reveals the structural landscape of CONCR, identifying distinct structured domains along the molecule. This work highlights the AFM advantages in deciphering the global conformation of RNAs, which in combination with other high-resolution techniques like cryo-EM and Chemical Probing can offer a deeper understanding of the functional roles of RNAs.

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Pioneering a New Era in Live Tissue Imaging with Fluorescence Lifetime Microscopy (FLIM)

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Advances in intravital and live tissue imaging have transformed our ability to study dynamic biological processes in real-time, providing unprecedented insights into cellular behaviour and molecular interactions. Among the most impactful innovations is fluorescence lifetime imaging microscopy (FLIM), a technique that measures fluorescence lifetime to assess molecular interactions, metabolic states, and cellular environments. Unlike intensity-based methods, FLIM is independent of fluorophore concentration, offering quantitative data on microenvironmental changes such as pH, ion concentrations, and protein interactions, making it ideal for in vivo tissue imaging.

Recent technological advancements, such as time-correlated single-photon counting (TCSPC) and single-photon avalanche diodes (SPADs), have made real-time, wide-field FLIM more accessible. HORIBA's FLIMera represents a breakthrough in this area, enabling high-speed, wide-field FLIM with unprecedented precision and efficiency. Its advanced sensor technology allows for simultaneous decay acquisitions at pixel level with a resolution of 50 picoseconds and acquisition speeds of up to 30 frames per second, making it one of the fastest FLIM cameras available.

When paired with HORIBA's InverTau FLIM scanning system, FLIMera becomes an even more powerful tool, providing high-resolution, real-time fluorescence lifetime imaging. InverTau supports fast acquisition with sub-millisecond per pixel speed, enabling comprehensive studies of disease progression, cellular interactions, and tissue microenvironments. Together, FLIMera and InverTau allow researchers to monitor metabolic changes, protein interactions, and therapeutic responses, paving the way for breakthroughs in cancer research, neuroscience, and precision medicine. These innovations push the boundaries of fluorescence lifetime imaging, enhancing our understanding of complex biological systems.

Active particles in nematic fluids

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Microswimmers, active particles capable of autonomous motion, exhibit remarkable collective behaviors when interacting within complex fluidic environments. In nematic liquid crystals, the interplay between microswimmer activity and the anisotropic elastic properties of the host medium introduces novel dynamics, including long-range hydrodynamic interactions and defect-mediated motility. This work investigates the cooperative dynamics of microswimmers confined within nematic liquid crystals, focusing on the role of confinement geometry, elastic anisotropy, and hydrodynamic coupling in determining emergent behaviors. Using a combination of multi-particle collision dynamics (MPCD) simulations and theoretical modeling, we explore how nematic elasticity influences particle alignment, defect formation, and collective motion.

Our findings demonstrate that confinement introduces rich spatial heterogeneity in swimmer trajectories and defect dynamics, which can be controlled by varying the system's boundary conditions and confinement scale. These results elucidate the mechanisms underpinning the self-organization of microswimmers in complex fluids and provide insights into designing synthetic active materials for applications ranging from targeted drug delivery to microfluidics. This research highlights the importance of integrating computational modeling with theoretical insights to unravel the physics governing active matter systems in anisotropic environments.

Translational impact of rapid digital holographic microscopy.

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

4D tracks (3D plus time) of motile microbes constitute a unique phenotype that can be used to identify species. Furthermore, motility itself is an indicator of the presence of viable cells and a strong biomarker in the search for life.

Digital holographic microscopy (DHM) is a high-throughput, but computationally costly tool for obtaining 4D tacks of cells, along with other characteristics such as size, shape and refractive index.

We first present recent work in methods of accelerating the processing steps I of the DHM pipeline that reduce the time needed to obtain tracks. We also discuss ongoing translational work exploring the commercial potential of DHM and these results to solve problems in microbial identification across healthcare, environmental and manufacturing sectors.

Mechanical force measurements of tandem-repeat proteins

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Tandem-repeat proteins are built from structurally identical units that stack together to form different architectures, like Lego. Through sequence alignments, consensus repeat-protein scaffolds can be designed and used in applications ranging from developing biomaterials to therapeutics. They can be further classified based on repeat type. Solenoid proteins consist of α-helical repeats and are ubiquitous in nature.

Additionally, helical repeat proteins exhibit spring-like behaviour when subjected to force [1]. This presents the possibility of using them to develop FRET-based biosensors that could detect forces at a biologically relevant pN scale. Mechanical force is an important driver and regulator of cellular processes, yet is difficult to properly track and quantify. By sandwiching a sensor between domains of a mechanosensing protein of interest, a change in FRET efficiency could provide a direct readout for when and where it experiences force [2]. Using helical repeat proteins allows customisability of sensor design, thereby allowing the development of a novel tuneable sensor toolkit. Calibration of a sensor's response under force can be achieved using a dual-trap optical tweezers setup, where a force-distance curve can be obtained by pulling a protein tethered between two beads. The unfolding behaviour of consensus helical repeat proteins can also provide a basis for understanding the complex folding and dynamics of giant repeat proteins.

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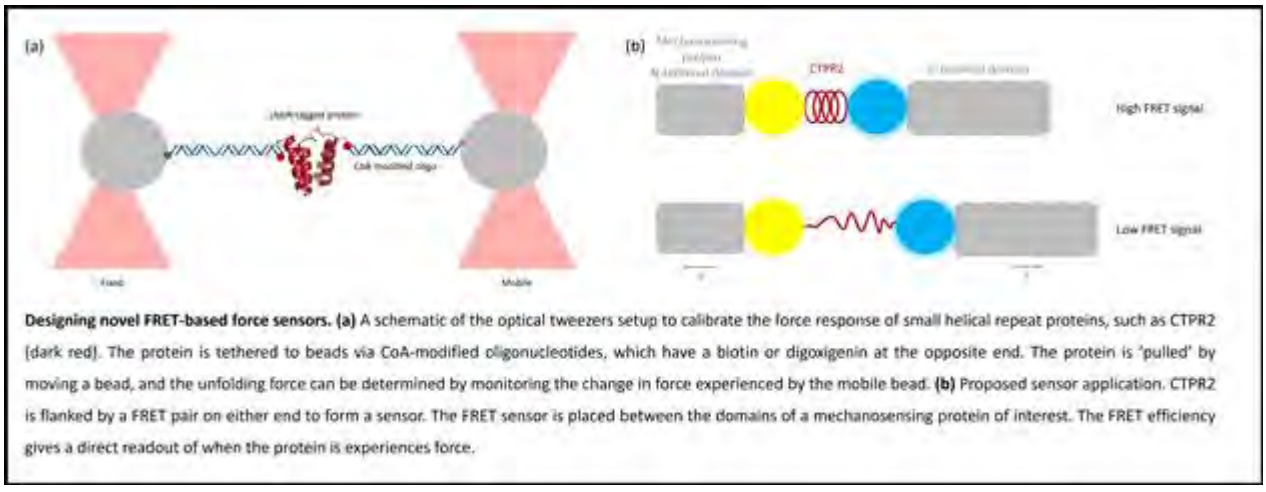

Designing novel FRET-based force sensors. (a) A schematic of the optical tweezers setup to calibrate the force response of small helical repeat proteins, such as CTPR2 (dark red). The protein is tethered to beads via CoA-modified oligonucleotides, which have a biotin or digoxigenin at the opposite end. The protein is 'pulled' by moving a bead, and the unfolding force can be determined by monitoring the change in force experienced by the mobile bead. **(b)** Proposed sensor application. CTPR2 is flanked by a FRET pair on either end to form a sensor. The FRET sensor is placed between the domains of a mechanosensing protein of interest. The FRET efficiency gives a direct readout of when the protein is experiences force.

Mechanically killing bacterial pathogens on nanostructured surfaces

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Bacterial colonisation of surfaces and antibiotic resistance are some of the biggest threats to global human health. Nanostructured surfaces (NSS) could solve both problems simultaneously, through their bactericidal properties. Previous work has proven that the bacterial killing process of NSS is largely mechanistic, making them broadly effective and likely insusceptible to resistance over time. Furthermore, eukaryotic cells are not susceptible to the killing effect of NSS, so there is potential for their use on internal medical devices, among other clinical applications. However, there are many challenges to the design and testing of NSS, including surface biofouling by dead cellular components, and specificity to microbial size/shape [1]. Most importantly, we still do not understand how bacterial pathogens are killed by NSS.

My research aims to uncover the mechanism underlying the killing effects of NSS, and optimise its efficiency for use in clinical or other settings. We will initially carry out a comparative study to directly compare the effect of each NSS parameter (nanostructure height, width, pitch, shape and stiffness), to address a lack of standardisation across the literature. NSS will be fabricated through techniques such as soft and nanoimprint lithography, and assessed with AFM/SEM. Killing efficacy will be assessed through Live/Dead staining in combination with fluorescence microscopy, as outlined in [2]. Through this research we hope to address the lack of consensus across previous studies regarding the effect of various NSS parameters on killing efficacy, and the mechanism behind the killing effect.

[1] Linklater, Ivanova (2023)
[2] Catley, Corrigan, Parnell (2023)

Odd viscous Stokes flow around a single sphere

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Understanding the flow around small particles is of essential importance in applications ranging from colloidal suspensions to biological systems. In these exemplary applications, the low-Reynolds number regime is of specific interest, which is governed by the Stokes equation.

It is well known that there is an exact analytical solution for incompressible Stokes flow around a single sphere immersed in an isotropic fluid described by a single shear viscosity. In this work, our goal is to extend this solution to anisotropic fluids. Not only does the anisotropy facilitate the presence of anisotropic shear and rotational viscosities, but also there is the possibility of having so-called odd viscosities when the anisotropy is odd under a time-reversal operation. Odd viscosities do not contribute to dissipation and can generate axial flow fields which are not present in ordinary Stokes flow. We envisage applications of our analysis to liquid crystals and chiral active fluids, which are governed by an even and odd time-reversal anisotropy, respectively.

Active self-organization of focal adhesions driving cell shape changes

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Focal adhesions (FAs) are dynamic protein complexes that mediate the interplay between the actin cytoskeleton and the extracellular matrix (ECM), enabling cells to sense and respond to mechanical forces and biochemical cues. These complexes drive essential processes such as cytoskeletal reorganization, cell shape modulation, and migration. To investigate these processes, we developed an active gel mathematical model that couples the dynamics of FAs, forces in actin-cytoskeleton, and cellular shape changes, capturing the three-way interplay between these components.

Numerical solutions of the model successfully recapitulated experimental observations, demonstrating its ability to predict how cells adapt to mechanical and topographical cues. Specifically, the model reproduced key phenomena such as the influence of substrate stiffness on FA dynamics, with stiffer substrates promoting larger, more stable FAs, aligned stress fibers, and enhanced cell motility. It also captured how anisotropic ECM features, such as aligned collagen fibers or patterned topography, direct cytoskeletal organization and cell alignment. Additionally, the model demonstrated how curvature and shear flow provide critical mechanical forces that shape cellular morphology and behavior. This work provides a novel framework for understanding the mechanistic feedback loops underlying cell-ECM interactions and highlights the central role of FAs in regulating cellular behavior.

Simulation of Monoglyceride-Induced Bilayer Deformation in Model Membrane Systems

Mr Benjamin Mitchell[1], Miss Magdalena Hudek[1], Dr Karina Kubiak-Ossowska[2], Dr Donald Kelemen[3], Dr Valerie Ferro[4], Dr Paul Mulheran[1]

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Multidrug resistance in bacteria is a topic of increasing interest as our reduced ability to treat antibiotic resistant infections is correlated with poorer prognoses and increased risk to public health. Monoglycerides show promise as an alternative molecule for overcoming multidrug resistance due to their notable antimicrobial potency and use in lipid nanoparticle formulations. The antimicrobial mechanism of monoglycerides is thought to be through significant cell membrane disruption, however the mechanism is not fully understood [1]. In this work the destabilisation of a model lipid bilayer caused by monoglyceride insertion is studied at an atomistic level using a series of all-atom molecular dynamics simulations of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine bilayers loaded with different monoglycerides at various concentrations.

From these simulations, three key aspects of the bilayer disruption mechanism of monoglycerides have been identified. Firstly, the extent of bilayer disruption is strongly correlated to the concentration of monoglyceride molecules loaded into one or both of its leaflets. Secondly, medium length monoglycerides induce bilayer disruption in similar ways, but differ from long-chain monoglyceride mechanisms. Thirdly, the extent of membrane disruption was significantly higher when the molecules were present within only one leaflet of the bilayer than when distributed symmetrically. These results align with proposed experimental hypotheses regarding membrane disruption by monoglycerides, offering further insights and opening up new avenues for further researching this mechanism.

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Physical property of the nucleoplasm revealed by creep-relaxation dynamics

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The dynamic structure of interphase chromatin occupying the nucleoplasm emerges from non-equilibrium active processes, such as motor proteins working on the cytoskeleton. Previous direct measurements have reported the elasticity of the nucleoplasm varying for more than four orders, reflecting the complicated nature of the nucleoplasm. One way to clarify such complex fluid is to compare the creep and relaxation dynamics. Creep dynamics under constant force show viscoelasticity, while post-creep relaxation reflects elasticity. Comparing elastic responses in creep and relaxation reveals structural changes during deformation.
To precisely define the creep and relaxation dynamics of the nucleoplasm, we established magnetic tweezers that can control probe forces of 10 fN - 50 pN with a temporal resolution of five milliseconds. We used 0.6 mg/ml λ-DNA solution as a reference for the measurement.

We found that, in the DNA solution, creep dynamics followed a power-law (~0.4), whereas relaxation dynamics did not. The result suggests that probe force-induced polymer disentanglement disrupts the viscoelastic structure in the DNA solution.

In contrast, interestingly, the nucleoplasm shows power-law behavior (~0.5) in both creep and relaxation. The result suggests that the nucleoplasm maintains a stable viscoelastic structure under the creep, in contrast to the passive DNA solution. We also found that under actin inhibition, the creep and relaxation dynamics of the nucleoplasm become different; the creep dynamics still followed a power law (~0.4), but the relaxation dynamics did not, resembling the DNA solution. We suggest nuclear actin-associated dynamics may help maintain chromatin’s soft yet stable structure.

Evolving Tissue Pattern Scaling and Robustness Through Spatially Heterogeneous Feedback

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The size, shape and patterning of animals varies greatly between species, despite these properties being governed by distributions of highly conserved molecules such as morphogens. Following secretion, morphogen molecules form spatial concentration gradients in developing tissues through diffusion and degradation, and control patterning by activating genes within target cells in a concentration-dependent manner. Ideally, patterning should scale with organism size during growth, while also being robust to environmental and genetic fluctuations. However, it is unclear how a single mechanism can generate morphogen gradients that are simultaneously adaptable and able to mitigate errors, or how this mechanism could have evolved.

A popular model suggested that morphogen gradient scaling can be mediated via bidirectional feedback with a population of expander molecules. Using both analytical and computational approaches, we have investigated how different types of molecular feedback mechanisms can give rise to scaling and/or robust morphogen gradients, and why position dependence of the expander gradient is vital for achieving these properties. Additionally, we have developed an evolutionary algorithm that can introduce mutations in system parameters or the form of the morphogen-expander feedback, with the aim of probing the design principles of scaling and/or robust systems. We have demonstrated that scaling and robustness can co-evolve towards a feedback state that can be predicted analytically even when only one of these properties is actively selected for.

Epigenetic variability in induced pluripotency – How much does it contribute?

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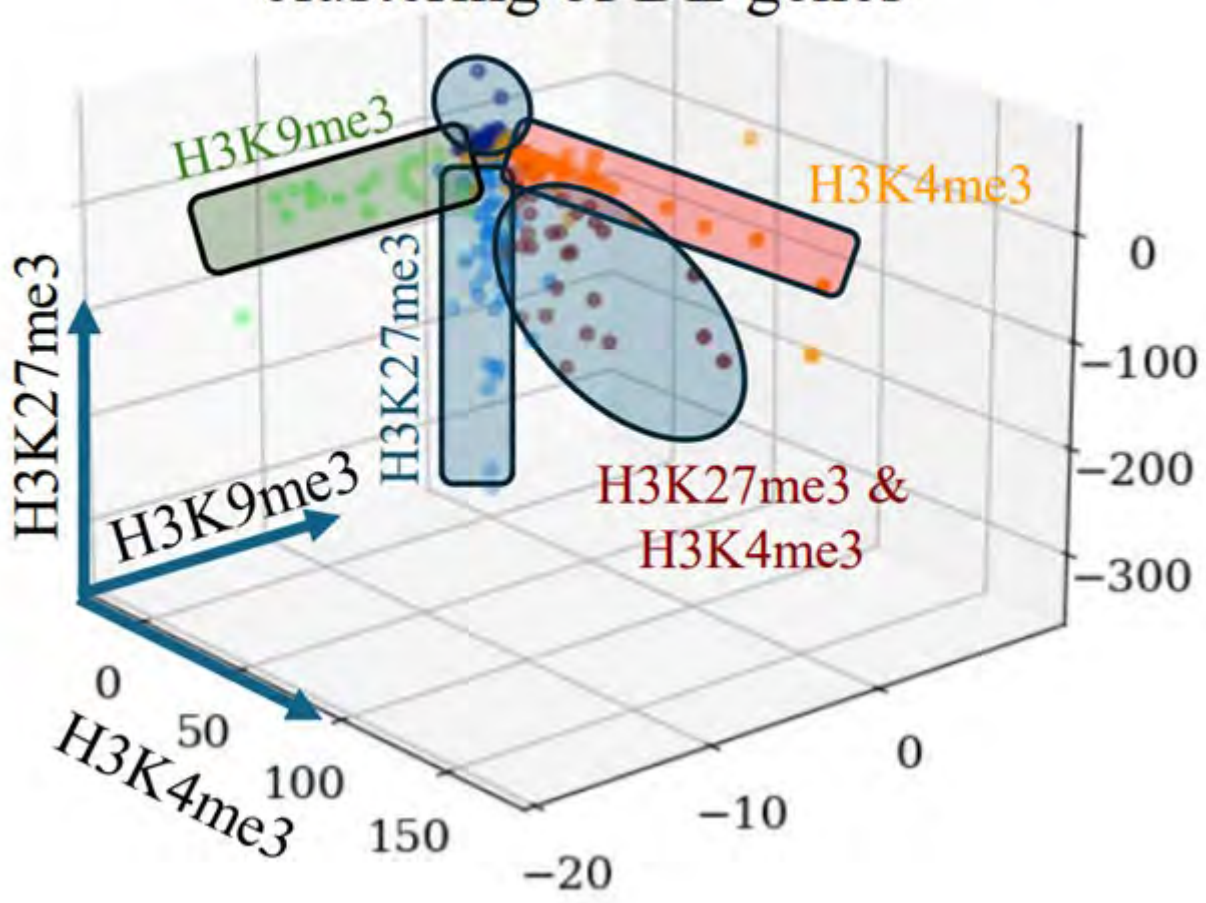
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Many human induced pluripotent stem cell (hiPSC) lines have been established, which can be differentiated in vitro into different fates. However, it is still unclear the molecular and genetic determinants that allow this, and there is a large variability in the differentiation efficiency of these cell lines (despite, in theory, being very similar, i.e., fibroblasts reprogrammed using the same protocol). To further understand this phenomenon, we teamed with experimental collaborators that assayed the transcriptome and epigenome of a panel of 10 hiPSC lines with varying differentiation efficiencies. Numerous genes are differentially expressed (DE) among these 10 hiPSC lines. To integrate the profiles of multiple histone marks into the analysis, we developed a computational method based on a support vector machine, which allowed us to understand how changes in histone marks are correlated with gene expression for each DE gene. This enabled us to cluster DE genes based on their type of epigenetic regulation (see attached figure), easing downstream analysis.

Thus, we asked which type of epigenetic regulation maintains its heterogeneity through differentiation protocols, by comparing the transcriptome of an intermediate differentiation state (precursor of mesoderm) with that of the hiPSC state, for each cluster. We found that those targets regulated by only H3K9me3, or by H3K4me3 and H3K27me3 concomitantly, are the most robust (i.e. are more likely to persist through differentiation). We also found diverse modes of H3K27me3 regulation, which, together with mathematical modelling, shed light into the role of Polycomb complexes in regulating pluripotency.


Support Vector Machine-based clustering of DE genes
H3K9me3
H3K4me3
H3K27me3
H3K27me3 & H3K4me3
H3K27me3
H3K9me3
H3K4me3
0
50
100
150
−20
−10
0
0
−100
−200
−300

Dual role of the FERONIA cell wall sensor in the regulation of plant mechanical properties and growth

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Response to mechanical stress exerted on the plant cell wall is actively mediated by wall integrity sensors. Impaired sensing has been extensively investigated and has been associated to pleiotropic defects. Nevertheless, mechanisms transducing mechanical stresses to growth control are poorly understood. We thus focus on the role of the integrity sensor FERONIA, as well as the downstream kinase MARIS, in plant morphogenesis.

We use Marchantia polymorpha as a model system. We take advantage of its low genetic redundancy and its simple organization to analyse its early morphogenesis with high-throughput thanks to a microfluidic device (Laplaud et al., J Roy Soc Interface, 2024). FERONIA is known to be a versatile growth regulator. In the context of Marchantia early morphogenesis, we found FERONIA to promote growth and to be crucial for spatial patterning of growth. Indeed, compared to wild-type, feronia loss-of-function mutant early growth is delayed and more localized to the stem cell domains.

Additionally, we probed plant mechanical properties thanks to osmotic steps, giving evidence that FERONIA maintains turgor and cell wall stiffness, as well as spatial patterns of mechanical properties. However, thanks to correlations with growth data, we concluded that mechanical regulation cannot explain the growth regulation by FERONIA.

Finally, based on osmotic treatments and modelling, we propose that FERONIA may regulate growth through the modulation of cell wall extensibility in response to mechanical stress.

Altogether, our work helps to decipher the contribution of integrity sensing to the regulation of growth.

Fundamental limits on pattern formation in Turing-like reaction-diffusion systems

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The formation of periodic patterns plays an important role in embryonic development, allowing repetitive structures (e.g., teeth, hair, leaves) to form at regular spatial intervals. Mathematical modelling – initiated by Alan Turing in the 1950s – has advanced the hypothesis that these patterns self-organize via systems of reacting and diffusing chemicals. In the canonical Turing mechanism, there are two such chemicals: an activator and its (more rapidly diffusing) inhibitor, with activator/inhibitor pairs having been identified across a range of tissues and signalling pathways.

However, whilst these 2-component models can mimic periodic patterning in silico, they do not capture the full complexity of developmental signalling in vivo, and it remains unclear to what extent the analysis of simplified activator/inhibitor systems will generalize to more realistic developmental signalling circuits.

By combining theory and simulations, we investigate more complex and biologically-realistic activator/inhibitor systems, taking into account the multi-step nature of pathway activation, transcriptional regulation and the diverse biochemical mechanisms of pathway inhibition. We find, and show rather generally, that adding intracellular complexity to our models does not significantly change their behaviour. In contrast, we predict that the ability of activator/inhibitor systems to form patterns is highly sensitive to the assumptions concerning the extracellular species in our model.

For example, we observe major differences between systems in which inhibition is achieved by receptor competition (e.g., WNT/DKK) versus ligand sequestration (e.g., GDF5/NOGGIN). Together, these results suggest that distinct extracellular interactions may play an important role in the development of periodic patterns in vivo.

Astrobiological Adaptation: Biophysical Dynamics of Life Migration in an Evolving Solar System

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

This study explores the dynamic interplay between biological systems and astrophysical changes within our solar system, focusing on the potential migration of life as the Sun evolves into a red giant over the next 5 billion years. It examines how the Sun's increasing luminosity and expansion will reshape planetary environments, impacting habitability and biochemical systems critical to sustaining life.

By integrating biological physics, planetary science, and astrobiology, this paper investigates the thermodynamic and biophysical challenges life would face on transitioning planets like Mars or icy moons such as Europa. Key aspects include an analysis of Earth's biosphere resilience, the atmospheric and chemical evolution of Venus and Mars, and the potential for subsurface oceans on moons to support life.

Furthermore, the role of orbital dynamics, tidal heating, and the asteroid belt in shaping biophysically viable habitats is assessed. This research underscores the adaptability of life and its dependence on both microenvironmental conditions and broader astrophysical processes, offering a framework for understanding life's possible future migrations within the solar system.

Direct force measurement on swimming meso-organisms

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Swimming as a mode of locomotion is ubiquitously observed in organisms over large length scale extending from the micro to macroscale and crucial for survival of organisms in nature. The propulsive strategy adopted by organisms of different length scales depends on the ratio between inertial and viscous forces, as defined by the Reynolds number (Re). The swimming dynamics of micro-swimmers in the viscosity-dominated low Re regime and the macro-swimmers in the inertia-dominated high Re regime have been extensively studied. However, there exists an intermediate mesoscale regime having both viscous and inertial force contribution. As a result, the physics behind the swimming dynamics is complicated by non-linear and time-dependant effects. This mesoscale regime consists of organisms of lengths and Reynolds numbers in the range of L≈0.1-10 cm and Re≈1-1000.

We aim to decipher the physics of mesoscale swimming by direct force measurements. We have used Artemia as a model mesoscale swimmer which has a 'butterfly-like' swimming motion. Its swimming forces are measured directly using the micropipette force sensor (MFS) technique. We have further developed this technique to correct for drag and inertial contributions arising from the dynamic motion of the micropipettes. Using advanced, deep-neural network image analysis, the Artemia's swimming motion is tracked, thereby connecting the kinematics with direct force measurements. Our results show when the low Re regime starts breaking down at the mesoscale and how a living meso-swimmer adapts to the addition of inertia. Our experimental data is beneficial for developing new mesoscale theoretical models and create bioinspired mesorobots.

Development of magnetic force biotechnology for neural regeneration

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The ability to control the growth and orientation of neurites over long distances has significant implications for regenerative therapies and the development of physiologically relevant brain tissue models. In this study, the forces generated on magnetic nanoparticles internalised within intracellular endosomes are used to direct the orientation of neuronal outgrowth in cell cultures.

We developed polymer-coated magnetic nanoparticle clusters experiencing high magnetic force from a magnetic field. Several 2D magnetic force systems based on permanent magnet arrays were designed to generate a large area of the uniform and stable magnetic force in one direction. The direction of neurite outgrowth was quantified using a 2D Fourier transform analysis, showing agreement with the derived magnetic force vectors. A bioinformatics analysis of protein expression in cells exposed to magnetic forces revealed changes to cell signalling and metabolic pathways, as well as the perturbation of processes related to cellular organisation and proliferation. The results reported will advance nanotechnology and cell therapy for neuro-regeneration where magnetic forces could help to reconnect damaged neurons or even build artificial neuronal architectures.

Presented by Dr Xue Feng and Dr Tasmin Nahar.

A computational approach to simulating a three-sphere swimmer in a viscoelastic fluid modelled via the Giesekus constitutive law

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The locomotion of microswimmers in non-Newtonian fluids is of crucial importance in many biological processes including infection, fertilisation, and biofilm formation. The behaviour of microswimmers in these media is an area with many conflicting results, with swimmers displaying varying responses depending on their morphology, actuation, and the complex properties of the surrounding fluid.

We numerically investigate the effect of shear-thinning rheology and viscoelasticity on a simple conceptual microswimmer consisting of three linked spheres. The solution of the non-linear flow problem is achieved through a hybrid computational approach utilising known Newtonian solution techniques (The Method of Regularised Stokeslets [1]) to approximate the rapidly varying flow surrounding the swimmer, with a non-Newtonian correction term obtained through solving using the finite element method. The problem is formulated such that the solution can be calculated over a coarse mesh of the fluid domain, meaning accurate results can be obtained for low computational costs.

Our results demonstrate enhancements in swimming speed and efficiency of up to 7% and 16% respectively for locomotion in non-Newtonian compared to Newtonian fluids. We discuss how this computational approach could further be used to model bio-inspired swimmers and explain the transitions between the apparently contradictory results in the literature.

[1] Cortez R. 2001. The method of regularized Stokeslets. SIAM J. Sci. Comput. 23, 1204-1225.

Co-transcriptional assembly and dissolution of computational RNA condensates

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

RNA condensates are liquid-liquid phase-separated structures formed through sequence-specific interactions between RNA molecules. A key advantage of RNA-based condensates lies in the programmability of RNA sequences, which can be easily expressed from DNA templates. Recent studies have shown that RNA condensates can assemble via a structural motif known as kissing loops—short, weakly self-complementary sequences that drive the self-assembly of RNA structures. These RNA structures can be transcribed in situ from DNA templates (1). Additionally, commercially synthesized RNA strands have been demonstrated to form condensates through similar kissing loop interactions, with potential applications such as detecting tumor-associated miRNAs (2).

Our research builds on these findings by designing and producing programmable RNA condensates through in vitro transcription from DNA templates. Specifically, these condensates were designed to disassemble upon detecting specific oligonucleotide sequences, enabling a dynamic and reversible control mechanism. To achieve this, we utilized rational design principles to create RNA sequences that form stable secondary structures driving condensate formation, while incorporating sequence-specific triggers for controlled disassembly. This approach not only advances our understanding of RNA droplet assembly but also demonstrates the potential for developing RNA-based molecular sensors and tools for synthetic biology. Future work will explore the feasibility of expressing and regulating these RNA condensates within living cells, opening avenues for applications in biomolecular sensing, therapeutic delivery, and cellular engineering.

(1) ACS Nano, 18(24), 15477-15486 (2024)
(2) Nat. Nanotechnol. 2024, 1–9 (2024)

Probing hydrodynamics of early development in C. elegans using diamond quantum sensors

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Cells must maintain a delicate balance of processes to ensure proper development, yet their dynamic nature makes subcellular measurements challenging to obtain. Quantum nanosensors, such as nitrogen-vacancy (NV) centers in nanodiamonds (NDs), provide a promising solution. These biocompatible sensors enable sensitive, simultaneous measurements of temperature and viscoelasticity [1]. Previous work in our group demonstrated ND sensing for nanoscale thermometry and rheometry in HeLa cells, identifying distinct rheological regimes in the cytoplasm [1].

This study uses NV sensing to investigate nanoscale thermal and mechanical properties in C.elegans embryos, focusing on P granules, membraneless organelles essential for germline specification. These granules form via liquid-liquid phase separation, localizing in one half of the embryo [2]. The mechanisms driving this spatial specificity, particularly the interplay between temperature and viscosity, remain unclear.

Fluorescent strains will be used to visualize P granules within C.elegans embryos. Nanoparticles will be introduced via microinjection into the gonads of adult worms, which become incorporated into the embryo cytoplasm. The rheology of the cytoplasm can be measured by monitoring the motion of these particles using confocal microscopy. This will be expanded to include the optical excitation and detection of NDs, integrating temperature sensing into the protocol to study the interplay between thermal and mechanical properties.

[1] Gu, Q., Shanahan, L., Hart, J. W., Belser, S., Shofer, N., Atatüre, M., & Knowles, H. S., "Simultaneous Nanorheometry and Nanothermometry Using Intracellular Diamond Quantum Sensors" ACS Nano, 17(20), 20034–20042,2023

[2] Wang, J. T., & Seydoux, G. (2014). P granules. Current biology, CB, 24(14), R637–R638.

Gallium ions can target chronic Pseudomonas aeruginosa biofilm infections by hijacking its ferric PQS transport system

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Cystic fibrosis (CF) is a genetic disorder in which the expression of the transporter protein CFTR within cell-surface membranes is prevented, resulting in dysregulated absorption/release of ions and water from cells. This results in a hyper-concentration of mucus within the lungs, predisposing CF patients to chronic infections that cannot be cleared by muco-ciliary movement.

Pseudomonas aeruginosa is an opportunistic pathogen that poses a significant threat to CF patients by forming biofilms. Treatments of chronic P. aeruginosa infections must therefore target the mechanisms underpinning biofilm maintenance. One such method, intravenous gallium nitrate therapy (IGNT), aims to eliminate chronic P. aeruginosa infections by providing a source of gallium ions (Ga3+) to disrupt ferric ion (Fe3+) uptake, by displacing Fe3+ from siderophore complexes.

It was, however, unknown whether Ga3+ could displace Fe3+ bound to PQS – a biofilm quorum-sensing molecule and an ancillary Fe3+ carrier. We evaluated the thermodynamic feasibility of an iron-for-gallium cation exchange into a [Fe(PQS)3] model using DFT modelling and 1H NMR. We found that Ga3+ successfully displaced Fe3+ from [Fe(PQS)3], with a formation energy of -1.92 eV. The resulting complex retained the geometry of [Fe(PQS)3], suggesting that it could facilitate Ga3+ entry into cells. 1H-NMR confirmed that only Ga-PQS complexes remained within a mixed sample of the two cations and PQS, demonstrating that [Fe(PQS)3] represents an additional target for IGNT [1].

[1] Hills OJ et al. Atomistic modelling and NMR studies reveal that gallium can target the ferric PQS uptake system in P. aeruginosa biofilms. Microbiology 2023; 169:001422. 10.1099/mic.0.001422

Structural response of microtubule and actin cytoskeletons to direct intracellular loads

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Microtubule and actin are the two major cytoskeletal polymers physically driving fundamental biological processes in the cell interior in eucaryotes. How microtubule and actin cytoskeletons respond to the loads is poorly understood. In this study, we directly applied perturbing intracellular forces to microtubule and actin cytoskeletons and quantitatively evaluated how these cytoskeletons structurally respond to the loads [1]. We established a new ferrofluid-based intracellular magnetic tweezers and observed that in a creep experiment, ~10 nN loads displaced the microtubule-nucleus complex several micrometers away from the stationary position over 10-20 seconds and revealed that rheological properties of the microtubule complex primarily determined by filamentous actin. The deformation of the microtubules was largest at the load position and decayed toward the cell periphery. The deformations of actin meshwork follow the same scaling of microtubules.

This result suggests that the two cytoskeletal systems behave as an integrated elastic body. We then investigated shape dynamics of a single microtubule under the perturbing loads. The microtubules exhibited non-Euler buckling in response to compressed loads, suggesting that microtubules are enclosed within actin meshwork at the polymer scale. Lastly, we demonstrated that a point force localized in the cytoplasm propagates in actin meshwork and deforms a microtubule at a distance. Taken together, our results suggest that microtubule and actin cytoskeletons act as an integrated continuum in the cytoplasm in response to intracellular loads.

[1] Ryota Orii, and Hirokazu Tanimoto. "Structural response of microtubule and actin cytoskeletons to direct intracellular load." Journal of Cell Biology 224.2 (2025).

Benchmarking viscosity-sensitive optical probes to quantify the structural architecture of lipid interfaces

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Biophysical properties of lipid membranes regulate cellular function and are becoming a promising biomarker of diseases including cancer or Alzheimer's. Further, they underpin some functionalities of synthetic cells and other therapeutic solutions, such as liposomal-based carriers. The activity of lipid membranes is linked to their molecular organization, which dictates their structural and biophysical properties (e.g. viscosity). Over the last two decades, the use of environmentally-sensitive fluorophores has become the gold-standard for measuring the biophysical features of lipid membranes in a parallel fashion and/or in biological settings. However, the relationship between fluorescent readouts and lipid organization remains largely unexplored, hindering the detailed understanding of the membrane's mechanical behavior.

We combine molecular rotors (MRs), fluorescent molecules capable of reporting on their microviscosity,1 fluorescence lifetime imaging microscopy (FLIM), and X-Ray diffraction (Figure 1), to investigate the relationship between the membrane's structure and its mechanical behaviour.2 Our results demonstrate that the fluorescence from MRs directly and unequivocally reports on the membrane's molecular architecture, unlike comparable commercial probes.[2] We also evidenced that certain membrane compositions lead to unexpected, non-classical behaviors including viscoelastic uncoupling,3 negative compressibility,[4] or phase-separation in single-component membranes.3

Altogether, our work establishes the first benchmark for using dyes to investigate the molecular structure of lipid membranes and presents the first experimental evidence of non-classical mechanical behaviors. These findings will contribute to the understanding of mechanotransduction and disease development and could be leveraged to engineer optimized therapeutic solutions and synthetic cells.

[1]Paez-Perez et al. Angew.ChemieInt.Ed.(2024) [2]Paez-Perez et al. Anal.Chem.(2023)[3] Paez-Perez et al.Commun.Chem.(2023)[4]Paez-Perez et al.Chem.Sci.(2021)

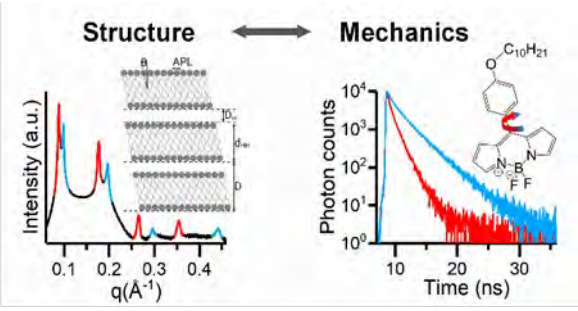

Figure 1: Relation between membrane structure and mechanical properties

Intermittent cell-cell attachments generate emergent fluid-like properties in migrating cell aggregates

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Cells migrate in response to gradients in extra-cellular chemical signals in a process known as chemotaxis. In recent work combining continuum theory with experiments on the model microorganism Dictyostelium discoideum, we have shown that dense aggregates of cells collectively undergoing chemotaxis exhibit emergent fluid-like properties such as viscosity and surface tension [1]. Here, we use simulations to explain how active interactions between cells give rise to these previously observed emergent phenomena. We propose an agent-based model for intermittent cell-cell attachments and show that it gives rise to emergent fluid-like behavior for an aggregate of cells. We generalize this model to include cell-surface attachments, and show that surface-associated aggregates display properties similar to a liquid droplet resting on a surface.

Furthermore, we study the situation where cells self-generate and respond to a chemical gradient by consuming an externally supplied chemoattractant. Our simulations reveal how individual cells move inside the swarm as the cells move as a collective; we compare our findings with the experimental data and with continuum theory. Finally, we predict some of the key cellular processes that are responsible for this collective behavior, and provide hypotheses to be tested in future experimental studies.

References:
1. Ford, et al. Pattern formation along signaling gradients driven by active droplet behavior of cell groups, bioRxiv. doi: https://doi.org/10.1101/2024.04.08.588511

Characterising the rupture, fatigue and recovery of intercellular junctions using a stochastic bond model

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Soft tissues' mechanical properties are increasingly recognized as a regulator of tissue homeostasis. When tissues become injured or damaged, a cascade of cellular, molecular and mechanical responses is triggered, thereby extending the material's lifespan and maintaining its structural integrity even under continuous stress. While it is understood that soft tissues are resilient to rupture, the mechanisms of load distribution, remodelling and healing remain unclear.

This has led to increasing interest in characterising rupture and repair in soft tissues. A well accepted theoretical framework for studying intercellular junction dynamics was proposed by Bell in 1978, which assumes that cell adhesion is mediated by reversible bonds between surface molecules. Here we use a stochastic model inspired by Bell's work, to explore the force-dissociation kinetics of junction proteins.

Our hypothesis is that cyclic loading can probe the reversible kinetics of individual bonds and predict the rupture and recovery dynamics of intercellular junctions. Our key findings indicate that (i) intercellular junctions have characteristic rupture and recovery timescales, (ii) cyclic loading perturbs these characteristic timescales and (iii) maps with universal features can be used to predict intercellular junction behaviours. Overall, this theoretical framework may be used to overcome the challenges of experimentally characterising the remodelling and recovery of active biomaterials.

Quantitative imaging of bacterial cell wall with AFM: function of PBP1a synthase

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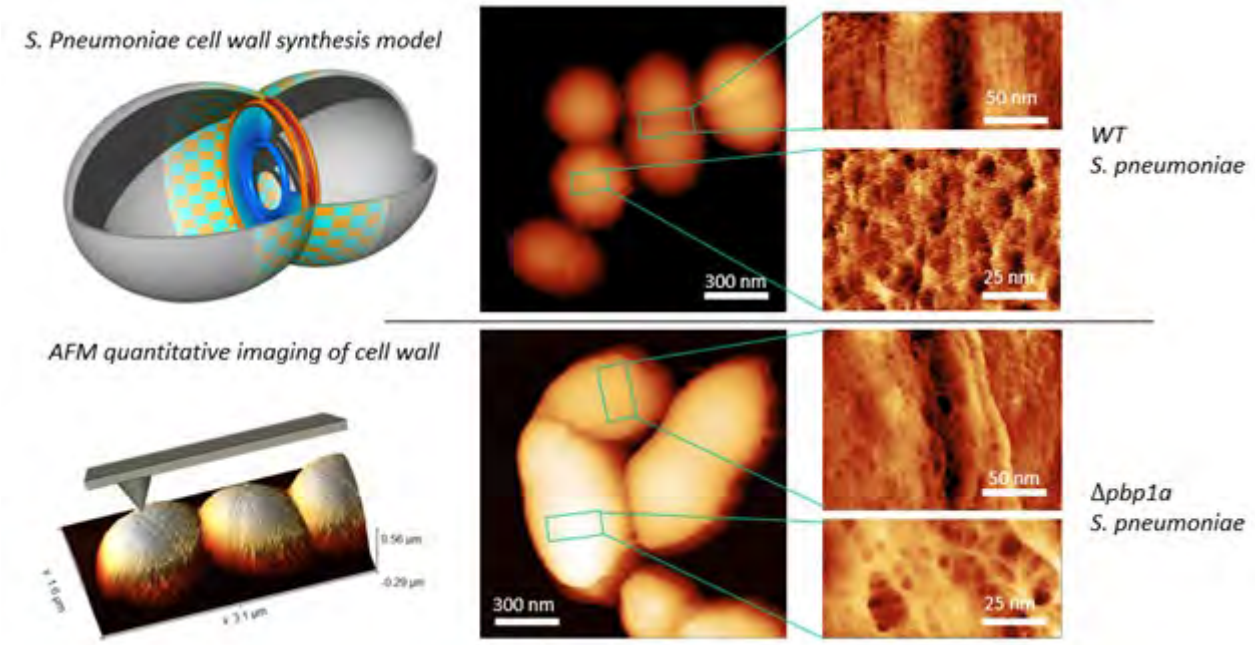
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Streptococcus pnuemoniae is the leading cause of death by Pneumonia (1M cases annually) and is becoming resistant to existing antimicrobials. We urgently need to develop long-awaited new solutions. However, we first need to understand vital components of bacteria cells: their cell-wall (peptidoglycan, PG). Here we will apply ultra-resolution microscopy [1-2] and analysis to understand the basic framework of PG.

After years of research using atomic force microscopy (AFM) on other species, the conclusion is that the cell-wall, composed mainly of PG is a highly porous heterogeneous hydrogel with four different architectures [2]. In this project, we apply similar tools to obtain the molecular architecture (on the order of 1 nm) of S. pneumoniae PG for the first time. We have previously explored spherical shaped and rod-shaped cells. However, S. pneumoniae does not fit either of these shapes, it has ovococci shape. The shape difference is driven by the coordination of the Division and Elangosome machineries [1]. They are complex assemblies of synthesis and hydrolysis enzymes working together to create new PG. Here we use high resolution AFM in liquid to image purified PG and whole cells to reveal the novel PG architecture from S. pneumoniae and compare it to a mutant lacking a synthase called PBP1a. Finally, we use custom-made image analysis tools to obtain quantitative comparison between samples (e.g. WT and the PBP1a mutant) to investigate the function of individual enzymes and how they create nanometric structures that drive the different shapes of bacteria.

[1] https://doi.org/10.1016/j.cub.2021.04.041
[2] https://doi.org/10.1038/s41586-020-2236-6



Zero-shot Adaptation of Drug Diffusion Model for Fragment Elaboration.

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Understanding how small molecules, or ligands, can bind to target proteins is crucial for drug design. Key potential intermolecular interactions can suggest new ligand growth vectors, and incorporating 3D structural information allows for efficient in-silico evaluation. One way to discover these interactions is through fragments bound to a target protein obtained from X-ray crystallography. Building on these fragments, fragment elaboration is a critical step in the design of complete molecules.

Diffusion models have emerged as a leading method for 3D molecular generation of drug-like molecules. [1] However, they do not inherently generate molecules that effectively elaborate fragment hits into complete drug-like structures. Frameworks like SILVR and MolSnapper use iterative guidance to generate molecules around a reference structure to address this issue. [2, 3] However, these methods exhibit diminished generation performance compared to the base model when reference information is incorporated.

We propose a framework, BRIDGE, that enhances the generation quality of the baseline diffusion model around a reference molecule. As a result, our protocol enables zero-shot adaptation for fragment elaboration, allowing for the generation of targeted molecules. To demonstrate this, we retrospectively investigate the performance of BRIDGE for fragment linking, targeting the enzyme IMPDH. The computational experiments with BRIDGE successfully recovered known inhibitors that were experimentally tested with improved affinity by Trapero et al. [4] In addition, potential alternative structures with improved binding could be identified and would require validation through biophysical assays. We plan to apply and validate the tool in further fragment elaboration cases.

1.arXiv:2302.09048
2.acs.jcim:3c00667
3.bioRxiv:2024.03.28.586278
4.acs.jmedchem:7b01622

The single-molecule biophysics of turbocharged, carbon-fixing condensates

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Algae actively fix >30% of the world's living carbon, thanks to specialised organelles known as pyrenoids. Pyrenoids form as characteristic biomolecular condensates, or liquid droplets, when the key carbon-fixation enzyme, Rubisco, condenses with a 'linker' protein. This droplet concentrates Rubisco together with CO_2 to accelerate its fixation into organic carbon. What then makes a 'good' linker for Rubisco? The spontaneous in vitro condensation of Rubisco by native linkers suggests that their individual binding interactions might be well described by equilibrium statistical mechanics. To test this, we not only derive a new combinatorial model for small aggregates in the dilute phase, but we also track binding events directly using single-molecule biophysical experiments.

We develop a novel single-molecule fluorescence binding assay using customised linker constructs of different lengths. Our robust pipeline extends this quantitative analysis over six decades of concentration. In combination with surface plasmon resonance data, we fit binding-titration curves for each construct. The binding energy shows a minimum aligned with the naturally occurring number of linker repeat units.

We then address the more complex process of condensation into droplets, successfully predicting the critical linker concentration within a factor of two without using any free parameters. Finally, we track molecules directly with 'SlimVar' microscopy to estimate dynamics inside droplets.

Our alignment of theory and experiment at the molecular level offers insights into how functional condensates form across convergently evolved species. We provide a biophysical foundation to engineer pyrenoids in crop plants, which would deliver transformative enhancements in agricultural yield and efficiency.

Predictive power: **a molecular model for the self-assembly of carbon-fixing biomolecular condensates**

UNIVERSITY of York

Part of the **York Physics of Pyrenoids Project**

Alex Payne-Dwyer **Gaurav Kumar** **James Barrett**
Laura Gherman Michael Hodgkinson Michael Plevin
Luke Mackinder Mark Leake **Charley Schaefer**

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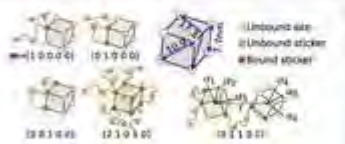
Why are algae such efficient supersinks of global carbon?

- **30%+ of all living carbon** is fixed by algae in an enzyme-rich organelle called the **pyrenoid**.
- Pyrenoids have dedicated **linker proteins** that bind and condense **Rubisco** fixation enzymes into a **dense liquid droplet.**
- As a result, **CO_2** can also be **concentrated** and consumed **~60% more efficiently** than most plants, all with similar enzymes!

How do linkers bind Rubisco? Let me count the ways...

Each linker protein has **disordered repeats** between its Rubisco binding sites, fitting a **sticker-and-spacer** description. In the model alga *C. reinhardtii*, the linker, EPYC1, has 5 sticker domains.

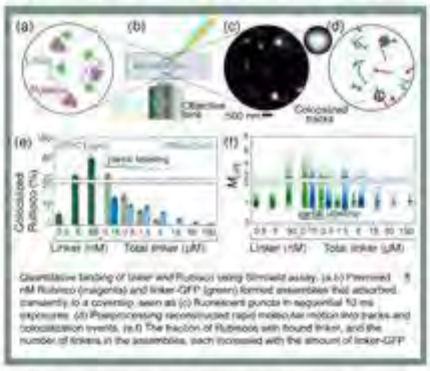
Why are 5 stickers necessary - or perhaps optimal? We attempted to answer this using statistical mechanics.



By parameterising Rubisco as a cube with binding sites at its corners, we counted the permutations of multiple linkers binding using partitions w_i and the combinations with rotations u and centre-centre distance r.

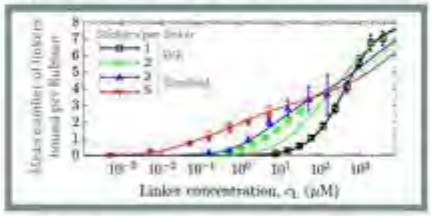
We considered small aggregates in dilute solution. Using a **freely jointed chain** statistical model, we calculated the **average number of linkers** expected to be **bound to each Rubisco**, depending on the linker's number of stickers.

- To test these predictions, we purified linker and quantified the amount bound to Rubisco by **surface plasmon resonance (SPR)**.
- Linkers of 3+ stickers formed droplets during SPR, so we developed a **single-molecule fluorescence imaging assay.**



Quantitative binding of linker and Rubisco using SPR/reflectometry assay. (a,b) Premixed 1 nM Rubisco (magenta) and linker-GFP (green) formed assemblies that adsorbed transiently to a coverslip, seen as (c) fluorescent puncta in sequential 10 ms exposures. (d) Post-processing reconstructed rapid molecular motion into tracks and colocalisation events. (e,f) The fraction of Rubisco with bound linker, and the number of linkers in the assemblies, each increased with the amount of linker-GFP.

- We tracked and counted **millions of individual binding events** *in vitro* between purified linker-GFP and **Atto594-Rubisco** molecules.
- We then fitted our model curves to all four experimental data simultaneously.



The free fit parameters tell us **three key characteristics** of linkers, independent of the number of stickers:

- sticker binding affinity: K_D ~ 400 μM
- binding energy / site: ϵ ~ −12 k_BT
- Kuhn length: l_K ~ 0.9 nm

Each sticker binds strongly, but linkers need many to bridge adjacent binding sites without a severe entropic penalty.

Molecular binding predicts stability of *μm*-sized pyrenoids!

Notably, **a minimum in the predicted binding energy per sticker** occurs at the **naturally occurring number of 5 stickers.**

Our theory also **predicts the critical concentrations** of total protein at which higher order complexes of Rubisco —and hence droplets— become stable.

We checked the lowest concentrations that proteins formed droplets *in vitro*. For 3+ stickers, our **freely jointed chain model is accurate to a factor of <2.**

- We are now working on condensing Rubisco with **designed linker constructs** from different species. We aim to help **engineer pyrenoids into crop plants for greater yield**.

Paper now in *PRL*:

Predicting Rubisco-Linker Condensation from Titration in the Dilute Phase,

Phys. Rev. Lett. 132, 218401, May 2024.

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UKRI Engineering and Physical Sciences Research Council

Reduction of bacterial adhesion on wrinkled surfaces under fluid shear

Dr Luca Pellegrino[1], Prof Roberto Rusconi[1], Dr Eleonora Secchi[2], Mr Giovanni Savorana[2]
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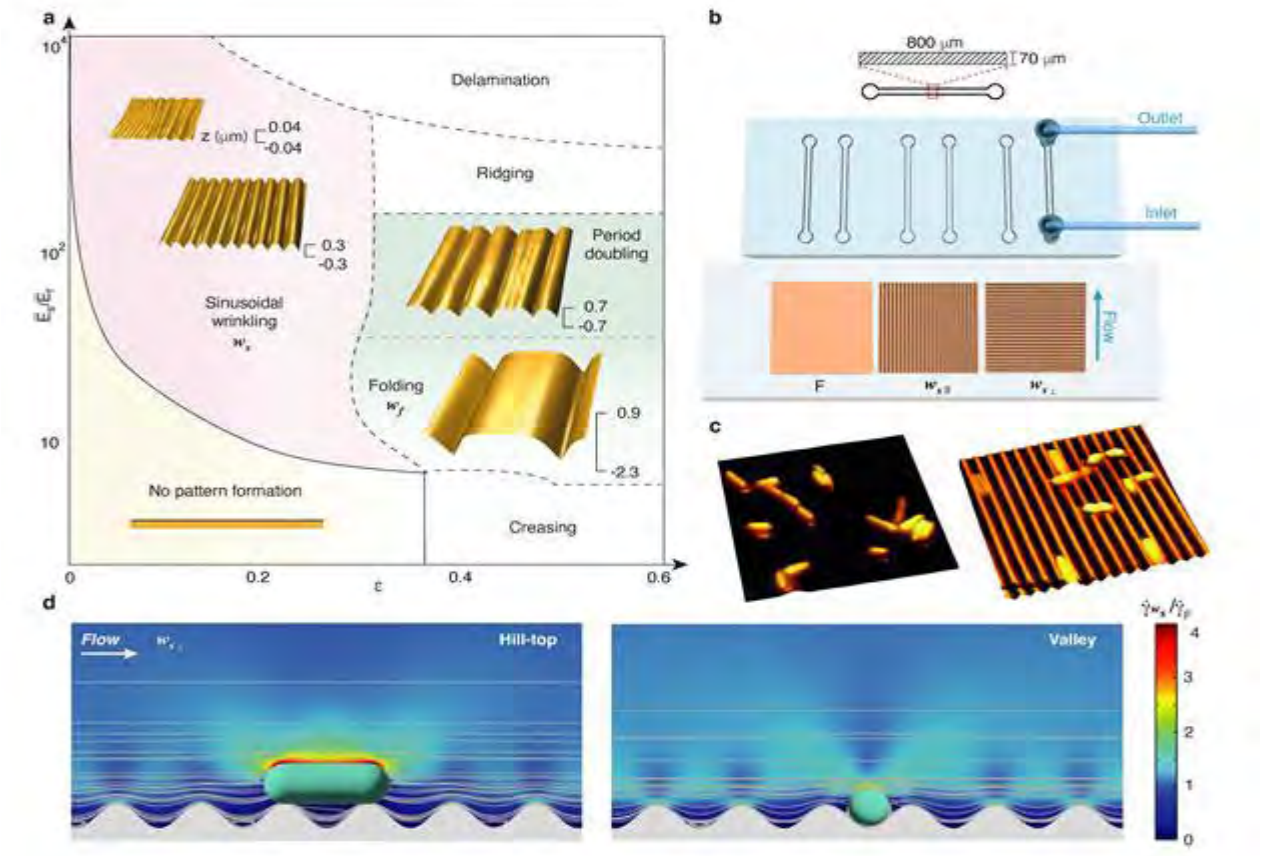
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Surface properties and fluid dynamics within confined spaces are pivotal factors influencing bacterial surface colonization and biofilm formation. Yet, the interplay between surface topography and fluid shear in microbial attachment remains inadequately understood. Here, we employ surface fabrication techniques coupled with microfluidics to investigate the adhesion of both motile and non-motile bacterial strains on wrinkled patterns and in the presence of flow, across varying shear rates. Our findings revealed that the presence of a patterned surface topography significantly impacts the local shear rate field, creating stress concentration points that hinder bacterial spatial arrangement, particularly for non-motile species. Prescribed pattern geometries and curvatures define different confinement behaviours impacting bacterial cells duplication speed and motility across different bacterial strains. In turn, as shear rates increase, we observed a `shear-detachment' effect that contrasts with what has been found in the case of flat surfaces and specifically when patterns are aligned perpendicular to the flow direction.

These results provide valuable insights into the interplay between prescribed surface topography and fluid shear forces, shedding light on strategies to delay and frustrate the early stages of biofilm formation in the context of implantable devices, where biofilm-related infections present daunting clinical challenges due to their resilience against mechanical stresses and antibiotics.



Modelling The Meristem Transitions Underlying Development of Wheat Inflorescence Architecture

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Plants display a striking diversity of floral patterning. Modified through both evolution and domestication, grasses exhibit a broad range of inflorescence architectures, yet there are many similarities, raising questions about the conserved developmental mechanisms. Wheat inflorescence (spike) architecture is an important yield determinant, as spikes determine the number of grain-producing florets. Spikes consist of repeating arrangements of spikelets, defined by vegetative and reproductive branching patterns. Meristems in developing spikes undergo a series of transitions before reaching final floral identity. This project aims to investigate gene regulatory networks that coordinate wheat spike development through meristem transitions, to describe inflorescence architecture.

Recently, Backhaus et al., (2022) showed opposing expression gradients of two interacting gene families, SEPs and SVPs. A computational model based on interactions between SEPs and SVPs suggested that formation of rudimentary basal spikelets is due to their delayed formation during the transition from vegetative to flowering. The model sufficiently explained the classic lanceolate shape of wheat spikes, but fails to recapitulate key mutants, such as vrn1ful2ful3, where altered meristem transitions are observed. Based on experimental observations, wheat inflorescences appear to be a series of initiation of [Leaf + Meristem] units. We aim to expand the current model to incorporate ideas of the [Leaf + Meristem] unit and explore the effect of known and new gene networks on meristem transitions and leaf states. We are currently exploring the use of gene regulatory network modelling and L-systems using python and cpfg (vlab) to capture gene-structure interactions and investigate different wheat spike architectures.

Mechanical coupling of tissue layers facilitates avian left-right symmetry breaking

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Consistently defining a left and a right body side is a key event during embryonic development. In avians the left-right (L/R) symmetry is broken during gastrulation, when a collection of cells in the epiblast migrates around the Hensen's node in a counterclockwise fashion and thereby sets up asymmetric gene expression. However, what drives this chiral, rotatory tissue flow and what determines its handedness remains unclear.

Here, we combine theory and experiments to better understand this process in developing quails. Theory indicates that the forces and torques required for L/R symmetry breaking are generated at Hensen’s node. We speculated that a torque dipole between the epiblast and the underlying cell layers is responsible for chiral tissue flow at the node. To test this hypothesis, we performed micro-surgery to remove the lower tissue. Indeed, this led to reduced chiral flow and a more L/R symmetric tissue architecture. Notably, chiral tissue flow could be restored by providing an artificial substrate, supporting the idea that mechanical coupling is required for rotatory cell migration.

We conclude that the tissue architecture of the Hensen's node is key to this cilia-independent mechanism that breaks L/R symmetry in birds, and potentially also in mammals.

Spontaneous flows in confined epithelial cell sheets

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Coordinated cell motion is essential for biological processes such as development, tissue repair, and disease progression. These movements drive significant morphological changes and are often guided by the surrounding microenvironment. Notably, cells frequently migrate collectively within confining tracks defined by their environment, which induces spontaneous flows. However, the link between these flows and collective migration remains poorly understood. In vitro studies of epithelial monolayers on substrates demonstrate that collective migration can arise from the coordination of mechanical forces over distances larger than individual cells.

Similarly, large-scale collective motion can occur without a solid substrate, as seen in early embryonic development (e.g., avian gastrulation). In such cases, directed self-propulsion is absent, suggesting that movement is driven by internal forces between cells, akin to simple fluids.

To better understand these processes, we propose a continuum multi-phase field model incorporating internal dissipation. This model represents each cell as a continuum density (phase) field, whose dynamics are governed by a free-energy minimization coupled to an overdamped force balance between interacting cells. A viscosity-like term, tied to the relative velocity of neighboring cells, captures internal dissipation, while an active dipolar interaction, represented by a nematic director, accounts for cell shape anisotropy. The model reproduces sustained unidirectional flows in channels without requiring self-propulsion or fixed boundary alignment. The transition from chaotic to ordered flow arises from internal dissipation, enabling long-range correlations in velocity and cell orientation. This mechanism may help explain collective cell migration across large distances, relevant to morphogenesis and embryogenesis.

RecA filament kinetics explain heterogenous SOS response induction and cell death

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The SOS response is a widely conserved bacterial stress response, responsible for regulating both high-fidelity and mutagenic DNA repair amidst many stress tolerance functions. It is well-known that single cells spontaneously induce the SOS response during normal growth and that SOS levels are highly variable across cells in a population, but the root cause and potential function of this heterogeneity remain unknown. Canonically, induction proceeds due to processing of DNA damage to form a RecA-single stranded DNA filament, which prompts self-cleavage and degradation of LexA, the regulon's master transcriptional repressor. We imaged fluorescent labelled RecA in single E. coli cells without DNA damaging treatment using mother machine microfluidics.

We uncovered that foci indicative of RecA filament events precede spontaneous, transient SOS response induction and that the duration of RecA filaments modulate SOS response heterogeneity. We find that genetic perturbations affecting RecA filament stability and LexA degradation influence RecA structures and gene induction kinetics, and that RecA filament kinetics predicts cell death events. Taken together, our results show that spontaneous SOS induction, and its heterogeneous magnitude, is in fact a precise response of single cells to prevent death from endogeneous DNA damage.

Multiscale dynamics in filamentous cyanobacteria: from filament to aggregate motility

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

In this talk we focus on the dynamics of a filamentous cyanobacteria, Fluctiforma draycotensis, at scales from individual filaments up to milli- and centimetre scale structures formed by multiple interacting filaments. Filaments suspended in bulk fluid aggregate to form motile, millimetre sized clusters of higher density. Over a few hours these clusters join together to form centimetre sized aggregates. A non-motile mutant strain of cyanobacteria does not form such aggregates, showing that aggregation is linked to individual filament motility.

We characterise the aggregation dynamics of the clusters at the macroscopic scale, and describe the gliding motility of individual filaments at the microscopic scale.

It is not clear whether aggregates form simply as an emergent property of the intrinsic motility behaviour of individual filaments, or if it requires some interaction response in the filament motility. Towards addressing this question, we present preliminary results from experiments at intermediate length scales, where we study the interaction between filaments, and between filaments and solid particles.

Dynamics of an Algae-Bacteria Inhomogeneous Active Suspension

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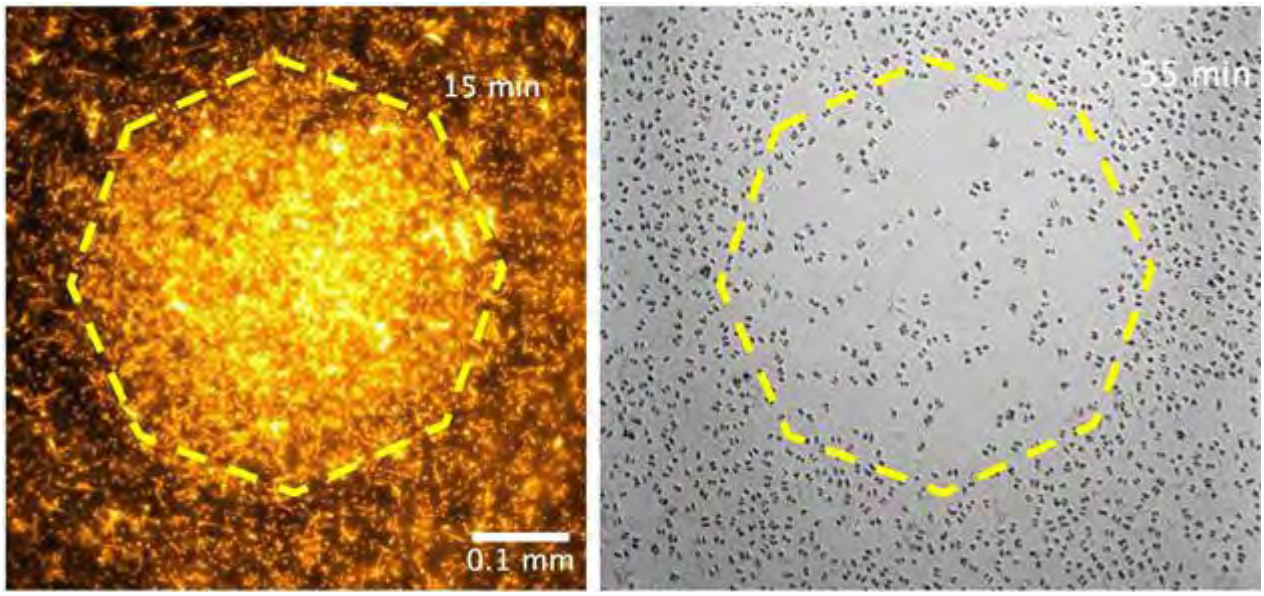
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Microorganisms inhabit highly fluctuating environments and survive in low-nutrient resource bath. It is recognized that symbiotic relationships between microbes play a vital role in their survival. The existence of such interaction raises general questions about the spatio-temporal dynamics of nutrient exchanges. Here we experimentally and theoretically examine a model system of this problem – bacteria, an obligate microbe capable of chemotactic response towards the green algae. Even in their simplest arrangement in a localized domain, we find a complex dynamics involving nutrient exchanges, enhanced algal diffusivity due to the bacteria, and a stochastic version of “flux expulsion”.



Electroreceptive Sensitivity Analysis of Mechanosensory Hair Arrays

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[1]*University of Bristol, United Kingdom*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Arthropods use many environmental cues while foraging (e.g. for nectar), finding prey, and avoiding predators; bees, for example, seek flowers abundant in nectar. These cues include olfactory signals, colour, petal patterns and textures and, in particular, weak electric fields. Electric fields cause filiform hairs on arthropods to deflect due to Coulomb's Law. By interpreting such hair deflections, arthropods can learn the electrical properties of their environments to optimise pollination of navigation. In this model, we represent each of two hairs as stiff inverted pendulums attached to a hair socket 'spring' with spring constant S. Considering coupled forces induced by a concentrated charge at the tip of each hair, a quasi-static equilibrium is found for the system. We model the hairs' deflections due to electrostatic forces as the arthropod moves relative to external charge sources, neglecting higher-order inertial and resistive terms. In nature, we observe mechanosensory hair sockets with a preferred plane of deflection. The electroreceptive sensory capacity of an arthropod via filiform hair deflection interpretation is largely dependent on these planes. By varying the direction each hair deflection is restricted to, we analyse the effect on the overall and directional sensitivity of the arthropod. We investigate hair array morphologies and geometric configurations, including suggestions for the biomimetic design of mechanosensory hair systems to optimise the sensitivity of the system.

Identifying biophysical mechanisms in health-to-disease (MASLD-MASH) transition of human HepaRG cells

Mr Callum Rafferty[1], Dr Anabel Martinez Lyons[1], Mrs Debbie Neill[1], Dr Justyna Cholewa-Waclaw[2], Dr Stephen Mitchell[3], Dr Matthieu Vermeren[2], Miss Amy Dillon[4], Dr Giacomo Russo[4], Dr Pierre Bagnaninchi[2], Dr Leonard Nelson[1,2,4,5]

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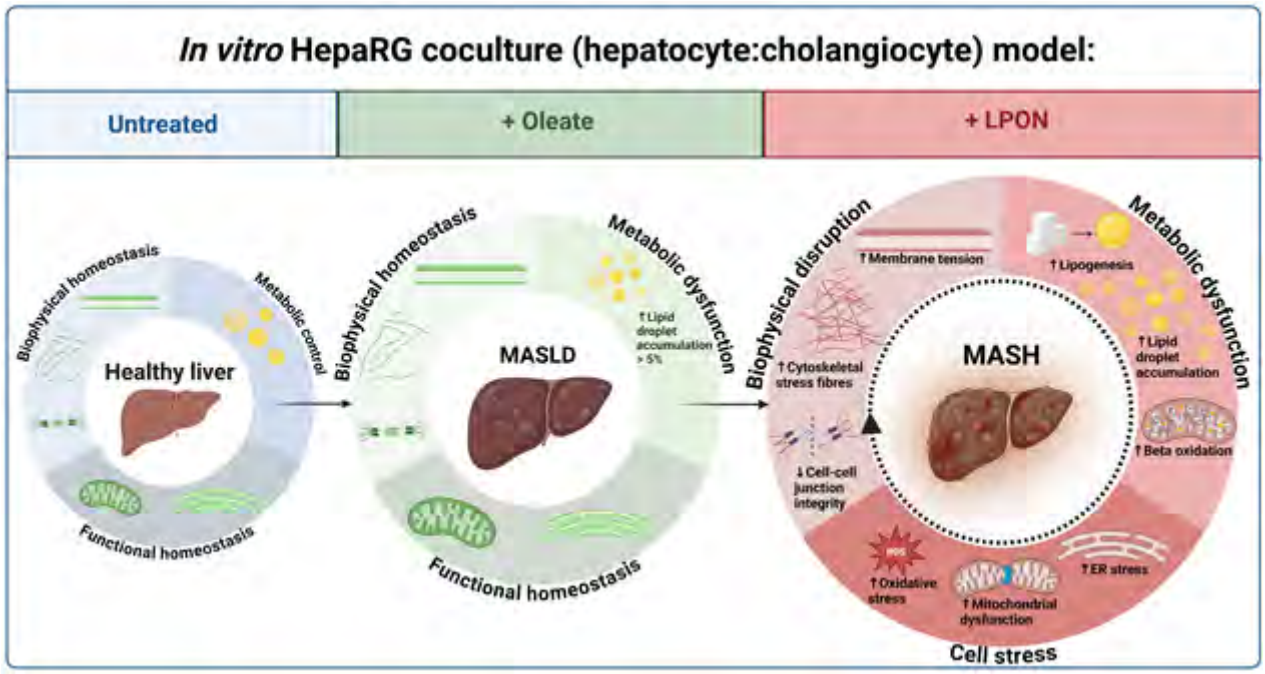
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Introduction: During the onset of metabolic dysfunction-associated steatotic liver disease (MASLD) and its progression to metabolic dysfunction-associated steatohepatitis (MASH), energy balance is disrupted by increased lipid droplet (LD) formation, de novo lipogenesis, metabolic dysfunction, and oxidative stress. These stressors impair cellular homeostasis and structural integrity, driving inflammation and disease. We aimed to identify key biophysical transitions between healthy liver, MASLD, and MASH using a novel in vitro hepatic model to explore the interplay between biophysical disruption and cellular stress to uncover biophysical-mediated pathogenic mechanisms for potential therapeutic targets.

Methods: HepaRG116 cells (hepatocyte:cholangiocyte co-culture) were treated with basal medium (healthy; controls), oleate (simple steatosis; MASLD model), or lactate, pyruvate, octanoate, and ammonia (LPON; inflammation-associated MASH model). Cell-cell junction integrity, membrane integrity, and cell adhesion were assessed by Electric Cell-substrate impedance sensing (ECIS). Confocal, electron microscopy, and protein quantification, were used to phenotype the health-disease transition, including intrahepatic lipid content, beta-oxidation, tight junction disruption, membrane tension, and ER stress. Targeted lipidomics of isolated LD was performed by GC-MS/MS.

Results: ECIS monitoring displayed significant disruption in cell-cell junction integrity in the MASH model. Confocal with image quantification revealed increased LD formation, correlating with decreased ZO-1 content. Membrane tension fluctuations and lipidomics confirmed altered LD species in MASH vs MASLD or controls; with concomitant elevated ALT, ER stress, and β-oxidation observed in the MASH-LPON model.

Discussion/Conclusion: Loss of structure in MASLD-to-MASH pathogenesis disrupts mitochondrial and ER-associated pathways. Compromised barrier function correlates with increasing lipid deposition and increased membrane tension, resulting in cellular injury (Figure).


In vitro HepaRG coculture (hepatocyte:cholangiocyte) model:
Untreated
+ Oleate
+ LPON
Biophysical homeostasis
Metabolic control
Healthy liver
Functional homeostasis
Biophysical homeostasis
Metabolic dysfunction
↑ Lipid droplet accumulation > 5%
MASLD
Functional homeostasis
Biophysical disruption
↑ Membrane tension
↑ Lipogenesis
Metabolic dysfunction
↑ Cytoskeletal stress fibres
MASH
↑ Lipid droplet accumulation
↓ Cell-cell junction integrity
↑ Beta oxidation
↑ Oxidative stress
↑ Mitochondrial dysfunction
↑ ER stress
Cell stress

Investigating IHF-DNA Interactions at Biofilm pH Using Single-Molecule Techniques

Dr Saminathan Ramakrishnan[1], Dr Davide Michieletto[1], Mr Dinesh Parthasarathy[1]
[1]*University of Edinburgh, United Kingdom*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30 - 19:30

Integration Host Factor (IHF) is a bacterial DNA-binding protein essential for biofilm formation and stability, facilitating DNA compaction and regulating adhesion and matrix production [1,2,3]. Its role in biofilm resilience and antibiotic resistance makes IHF a promising therapeutic target. However, real time observation of IHF's interaction with DNA at strong acidic conditions on a single-molecule level remains a significant technical challenge. Here we present a single molecule study on DNA-IHF interactions across a range of pH values, from neutral to highly acidic, using Optical Tweezers and Atomic Force Microscopy (AFM) [4].

Our results show that IHF binding induces a strong reduction in DNA persistence length across all pH conditions, without altering contour length, indicating increased DNA flexibility and compaction. At pH 5.5, force profiles indicative of DNA crosslinking observed in optical tweezers, along with high resolution AFM images, confirm DNA compaction, crosslinking and structural reorganization. These findings suggest that IHF binding enhances DNA compaction under acidic conditions, influencing biofilm architecture and providing insights into biofilm resilience and IHF-DNA interactions in infections.

FEMS Microbiology Letters, 195(2)
Science, 284(5418), 1318-1322
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Science, 258(5085), 1122-1126.

Using molecular dynamics simulations to understand PIEZO1 mechanosensitive ion channel in red blood cells

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Cells recognize and respond to mechanical forces via proteins in their membranes such as the PIEZO1 mechanosensitive ion channel. In red blood cells (RBCs), PIEZO1 is located to membrane with an unusually high concentration of cholesterol (50%). When PIEZO1 is altered in the RBC via gain of function mutations, osmotic fragility and haemolysis occurs. However, knowledge of PIEZO1's dynamics and interaction with lipids in the RBC membrane is elusive. In this study we used molecular dynamics simulations at the coarse-grained and atomistic resolution of the human PIEZO1 structure model inserted in a lipid membrane composition resembling a native RBC plasma membrane.

Our simulations suggest that in the closed state PIEZO1 creates a dome in the RBC membrane with a trilobed topology. This curvature is seen to be more pronounced between the protein blades in the RBC compared with the endothelial membrane. Analysis of the interactions of PIEZO1 with lipids indicated that PIEZO1 has preferential interactions with phosphatidylinositol 4,5-bisphosphate and phosphatidylcholine lipids. Simulations in which lateral pressure was applied to the bilayer showed that PIEZO1 can move from a curved state to a more flattened state. Together, our data provide novel insights into the dynamics and interactions of PIEZO1 in RBC membranes, and give opportunity for future investigation into PIEZO1 disease causing mutations located in the RBC.

Feeling piconewton forces in single-molecule biology

Dr Ankita Ray[1], Melanie Koehler[3], Joshua Simpson[2], Qingrong Zhang[5], Adolfo Poma[4], David Alsteens[2]

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The emergence and spread of a novel coronavirus, a causative agent for severe acute respiratory syndrome and has garnered considerable attention because of its ability to evade the host immune surveillance and retain its infectivity while undergoing mutagenesis. The virus infects by attaching its homotrimeric spike glycoprotein primarily to the angiotensin converting enzyme 2 (ACE2) receptor, guided by co-receptors like the DC-SIGN, and L-SIGN. [1, 2] Mutations in genetic material of CoV-2 have led to the development of 'Variants of Concern' (VoCs) with unusual epidemiological characteristics with different infectivity profiles. Mutants differing by a few amino acids are expected to display altered affinity towards the ACE2 receptors, and thereby affects its severity in a population. To understand these molecular mechanisms, we have leveraged the power of correlative atomic force microscopy (AFM) - confocal imaging along with steered molecular dynamics to map the nature and strength of interaction forces operating at the virus/cell interface. [1-5]

Additionally, we have also looked at the ability of carbohydrate recognition domains of DC- and L-SIGN receptors that helps in the initial attachment of the virus to cellular surfaces and probed the kinetics for differential recognition of sugars present on the spike. Furthermore, with height-clamp AFM spectroscopy we have showcased the importance of cholesterol, that helps in the fusion between the virus and mammalian cells and derived related kinetic and thermodynamic parameters interactions.[6] Such single-molecule studies provide detailed mechanistic understanding of the recognition interface that is of crucial importance in the development of vaccines and novel therapeutic platforms.

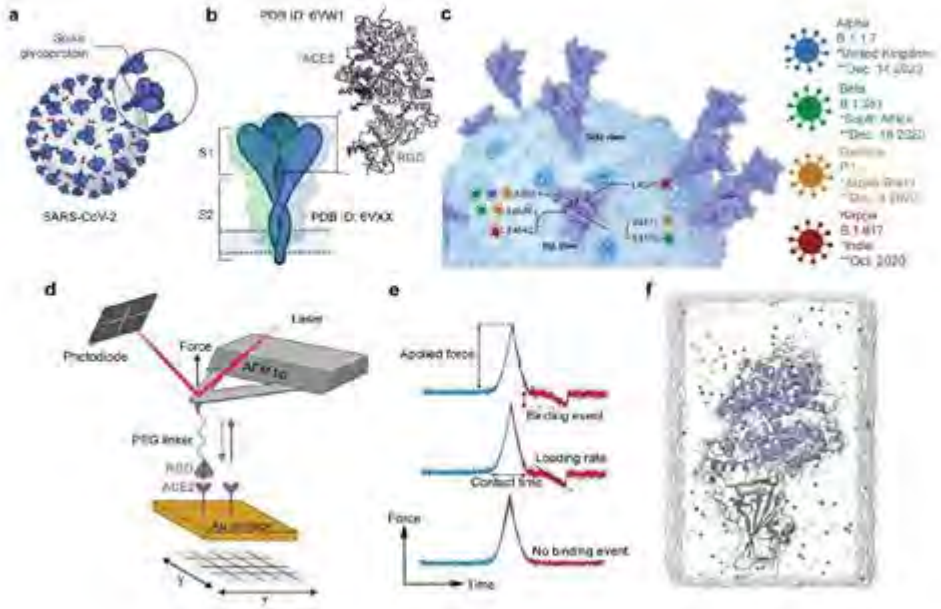

Figure.1 (a) Schematic of a SARS-CoV-2 virus particle, expressing at its surface the spike glycoprotein (S) that mediates the binding to host cells. (b) The S glycoprotein is composed of two subunits, S1 and S2, and is commonly represented as a sword-like spike. (c) Featuring a 3D rendering of SARS-CoV-2, this panel showcases the key spike protein mutations in the RBD domain on each of the studied SARS-CoV-2 variants of concern: Alpha, Beta, Gamma, and Kappa. (d) Schematic of probing RBD mutant binding to ACE2 receptors using atomic force microscopy (AFM). RBD is covalently attached to the AFM tip via a heterobifunctional PEG-linker and their binding to ACE2 receptors immobilized on a gold (Au) coated surface is probed. Pixel-for-pixel force distance (FD) curve-based AFM approaches and retracts the tip of an AFM cantilever from the sample to record interaction forces, F, over the tip-sample distance in FD curves. (e) Force–time curve from which the loading rate (LR) can be extracted from the slope of the curve just before bond rupture ($LR \approx \Delta F/\Delta t$) (upper curve). The contact time refers to the time when the tip and surface are in constant contact (middle curve). The lower curve shows no binding event. The tip approach is highlighted in blue, and tip retraction in red. (f) Representation of the RBD^{κ}/ACE2 system used in MD simulations.

References:

1 *Nat. Commun.* **2021**, *12* (1), 1–13.

2 *Nano Lett.* **2023**, *23*, 4, 1496–1504.

3 *Chem. Commun.* **2022**, *58* (33), 5073–5087.

4 *ACS Nanosci. Au* **2024**, *4*, 135–145.

5 *Nature Rev Methods Primer* **2021**, *1*, (65).

6 *Nat. Commun.* **2024** (Just accepted manuscript)

The curious case of alternative mode of cell division in Staphylococcus aureus

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The canonical mechanism for S. aureus to evolve methicillin resistance is due to the acquisition of the mecA gene that encodes for a modified penicillin binding protein (PBP2a) with low affinity for beta-lactams. High-resolution atomic force microscopy (AFM) imaging revealed that mecA acquisition, coupled with additional mutations that lead to changes in cell physiology, allow continued growth in the presence of high concentration of antibiotics, but that there are clear changes in the nanoscale architecture of peptidoglycan (PG) at the division septum.[1] AFM micrographs demonstrated the presence of a dense mesh of PG at the outer septum surface instead of concentric rings, hinting at the presence of an alternative mode of division which helps MRSA to tide over the challenge imposed by antibiotics. [1-2]

In this study, we have focused on how different conditions (temperature, high concentrations of salts, or sugars) could cause S. aureus (in the absence of beta-lactam antibiotics) to divide via this putative alternative mode of division and to probe essential division machineries that support such processes. To address this, we utilize AFM imaging to interrogate peptidoglycan of S. aureus derivatives with genetically manipulated division machinery, grown under different conditions. And secondly, we leverage AFM-infrared spectroscopy (AFM-IR), a technique which combines topographic imaging with chemical analysis, to probe changes in cell wall constituents (e.g., wall teichoic acids) to determine the distribution of constituents around the septal wall and the cell periphery.

1. Adedeji-Olulana et al., Science 386, 573–580 (2024)
2. L. Pasquina-Lemonche., Nature 582, 294-297 (2020)

Mechanics of force sensing in Piezo ion channels

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Since their discovery in 2010, Piezo proteins have been found to provide the molecular basis for many different forms of mechanosensation, including the sensation of touch in humans. Piezo proteins are mechanosensitive ion channels that locally bend the membrane into the shape of a spherical cap that can, in turn, produce a large membrane footprint. Previous work has shown that the shape of Piezo's membrane footprint can be predicted quantitatively through membrane elasticity theory, that Piezo ion channels are similarly flexible as a typical lipid bilayer membrane, and that Piezo's gating properties emerge from the interplay of Piezo structure, membrane shape, and the mechanics of the Piezo-membrane system [1]. Building on this previous work, we develop a simple analytic model of Piezo gating, which we test against fully nonlinear, numerical solutions.

This analytic model provides us with straightforward mathematical expressions describing the dominant physics of Piezo's response to lateral membrane tension. We then extend the theory of Piezo gating to account for vertical forces exerted onto the cell membrane by, for instance, the cytoskeleton. We employ this generalized theory to systematically explore the modulation of Piezo's gating response by such vertical forces. The results of this study shed light on how Piezo can be gated by a combination of vertical forces onto the membrane and membrane tension.

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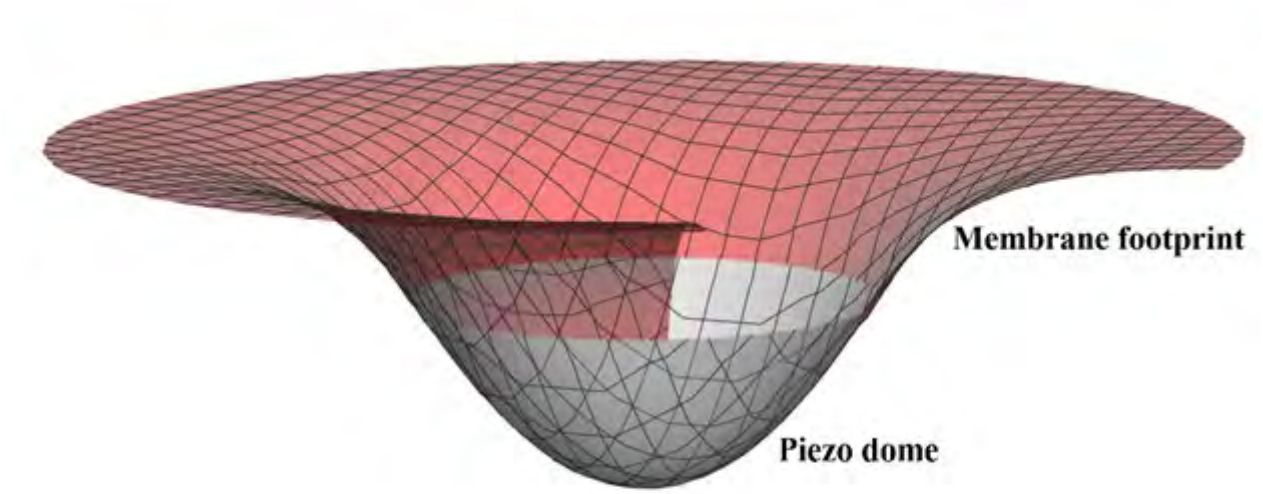

Modelling the role of the SOS response on bacterial filamentation and survival under antibiotic stress

Mr James Rayner[1], Mr Octavio Reyes-Matte[2], Dr Nikola Ojkic[1]
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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The SOS response, triggered by DNA damage, is a bacterial survival mechanism against DNA-targeting antibiotics such as ciprofloxacin. Although we know the immediate effects of ciprofloxacin, understanding the biophysical and biochemical mechanisms of how SOS facilitate bacterial survival under stress remains unclear [1]. In this study, we investigate the interplay between the SOS response, cell division timing, and antibiotic stress in Escherichia coli. We developed a mathematical model that predicts bacterial growth and cell division dynamics under antibiotic stress.

Our model integrates the roles of key molecular players such as FtsZ and FtsZ inhibitor (SulA) [2], which is only expressed during SOS response in a dose-dependent manner. By simulating bacterial growth and division dynamics under various antibiotic concentrations, we investigated cell size control mechanisms under stress. To validate our model, we compare simulation predictions of cell length distributions with real-time observations obtained from timelapse microscopy experiments. Our model successfully predicted the rate of SOS induction for various ciprofloxacin concentrations as well as in vivo binding affinities between SulA and FtsZ. Surprisingly, our model suggests that for large antibiotic concentrations, SOS induction is potentially harmful and facilitates bacterial lysis – as we experimentally observed.

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2. Ojkic & Banerjee. Bacterial cell shape control by nutrient-dependent synthesis of cell division inhibitors. Biophys J 120, (2021).

Investigating the physical underpinnings of collective function in synthetic microbial communities

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The frontiers of synthetic biology provide not only promise for industrial application, but also a fruitful testing ground for basic assumptions about the construction of life. In this work we will discuss the application of a synthetic system to investigate the link between the emergent structure of a microbial community and its collective function.

Division of labor in microbial communities is an emerging paradigm in synthetic biology and metabolic engineering. Dividing metabolic steps amongst the members of a microbial community can reduce individual metabolic load, compartmentalize redox states, and increase modularity in engineered systems. Fully harnessing the promise of these advances necessitates a deeper understanding of the biological and physical factors that promote cooperation in communities of microbes.

Recent years have yielded great strides in our understanding of the determinants of spatial structure in microbial communities. Both ecological manipulations as well as studies within the active matter paradigm have shed light on the architecture of adhered microbial communities; a hallmark of naturally occurring biofilms. However, the relationship between spatial structure and community level function remains poorly understood.

In this work we will begin to untangle how induced spatial structure modulates cooperative community function employing both an experimentally realized cooperative community and agent based simulations. Specifically, we will investigate a mutually obligate pair of S. Cerevisiae strains that together produce the dye indigo. By modulating the physical and ecological interactions between the strains we can begin to build a link between spatial structure and community function.

Supported lipid bilayer tubular network dynamics measured by quantitative differential interference contrast microscopy

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[1]*Cardiff University, United Kingdom*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Lipid bilayer tubes are ubiquitous structural motifs in nature, with diameters from tens of nanometres for the tubule networks found in cellular organelles such as the Golgi apparatus [1] and endoplasmic reticulum [2], to tens of microns for the largest axons of the nervous system [3]. While convenient model systems are well established for the study of planar and spherical membranes, tools to study tubular bilayer structures are more limited.

Here, we demonstrate the formation of stable lipid bilayer tubular networks on a glass substrate from spin-coated multilamellar films. Unlike conventional approaches which produce free standing tubes by mechanically manipulating the membrane of giant unilamellar vesicles [4], these supported tubular networks have the advantage of being amenable to study with a variety of surface sensitive techniques.

One such technique is quantitative differential interference contrast (qDIC), which generates quantitative phase maps from standard DIC images [5]. By fitting the tube phase profiles (see figure) we find the tubes have a mean diameter of (382 ± 15) nm, and we extract information on the shape of the tubes cross section. Using qDIC, we probe the biophysical properties of these tubular networks, examining the mechanism by which these networks form from multilamellar films and investigating changes in tube structure over the main (gel-liquid) bilayer phase transition.

Figure: Supported tubular networks in a) fluorescence, b) qDIC integrated phase. c) a line cut through a tube.

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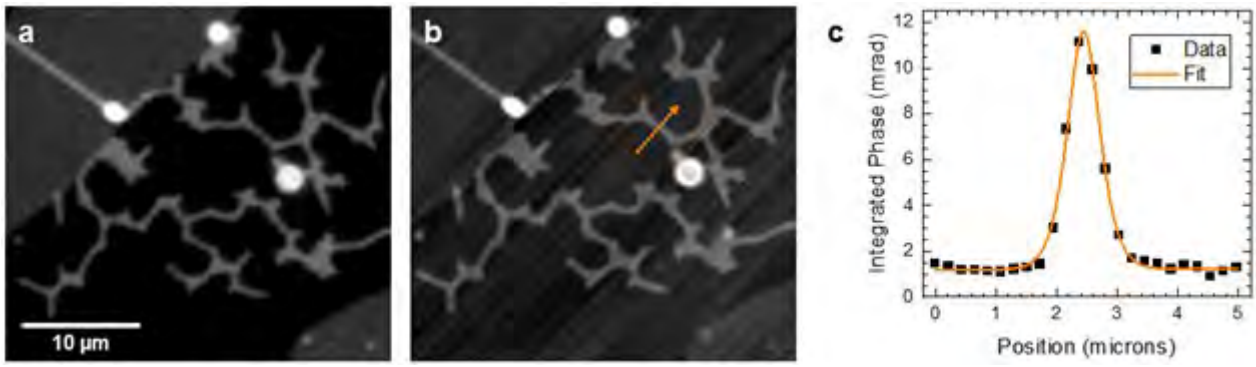

Deformation cytometry for high-throughput rheological analysis of 3D multicellular systems

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

During embryonic development, tissues undergo drastic morphogenetic changes, which suggests remarkable rheological properties [1]. Multicellular three-dimensional systems, such as organoids, have become indispensable in vitro models for studying how tissues respond to mechanical constraints. Numerous methods have been developed to characterize the behavior of these systems under compression, stretch, and shear, thus enabling fine measurements at the level of individual engineered tissues [2]. However, scalable and quantitative approaches for analyzing whole populations of multicellular systems remain limited.

Here, we present a microfluidic-based method for the high-throughput characterization of the rheological properties of large populations of multicellular systems, extending the principles of single-cell deformation cytometry to the tissue scale [3]. We apply this approach to cysts - closed spherical epithelia of human induced pluripotent stem cells that recapitulate the epiblast in vitro. By flowing cysts through constriction slits of varying geometries, we impose controlled deformations and perform time-resolved morphological analysis to extract quantitative metrics of their mechanical properties.

This scalable approach enables the systematic collection of extensive datasets, offering a statistical perspective on tissue mechanics. By enabling reproducible analysis of large populations of multicellular systems, our approach uncovers consistent patterns in tissue rheology. We anticipate that this method provides a robust platform to explore the mechanical drivers of tissue morphogenesis.

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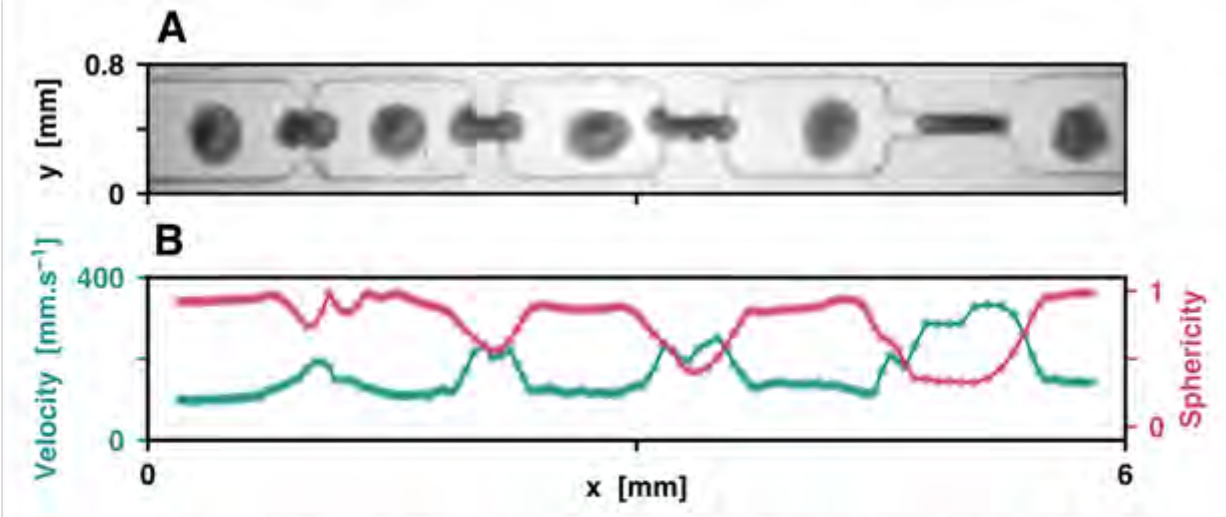

Deformation cytometry for multicellular systems. A: Flow of a lumenized tissue of human induced pluripotent stem cells through constriction slits. B: Velocity and sphericity profiles of the tissue along the slits.

pH-taxis Biohybrid Lipid Vesicles

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Biohybrid bacteria microswimmers, which combine living bacteria with synthetic components have been investigated for targeted drug delivery by reducing the exposure of healthy tissues and enabling lower drug doses. However, current systems face significant limitations, including the host immune response, inconsistent attachment of bacteria to external surfaces, and the failure to incorporate daughter bacteria after cell division.

Our research aims to overcome these challenges by developing a novel biohybrid vesicle that encapsulates living bacteria within an artificial lipid vesicle [1]. These vesicles are designed to employ bacterial chemotaxis to navigate pH gradients, mimicking the physiologically relevant microenvironment. This study investigates how bacterial-driven forces within the vesicle influence its deformation and directed propulsion in response to a pH gradient.

To enable these studies, we have developed a flow-free microfluidic system that generates stable, diffusion-based pH gradients without inducing flow-induced shear forces. Fabricated using a hydrogel, this system creates spatially consistent and temporally stable gradients, providing a controlled environment to study bacterial chemotaxis under conditions that closely replicate physiological environments. This platform enables detailed, quantitative analysis of vesicle deformation and bacterial motility over extended timescales [2].

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A Numerical Study of the Role of Hijacked Enhancers in B-Cell Cancers

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Enhancers are cis-regulatory elements that drive the expression of their companion genes. Highly expressed and cell identity controlling genes often interact with clusters of such enhancers that are usually called a super-enhancer. However, following genome rearrangements, super-enhancers can be relocated within the genome and then 'hijacked', becoming associated with a gene other than their original target. This can cause overexpression of the new gene which in some cases leads to proto-oncogene to oncogene conversion and cancer.

Using computer simulations, we investigate the particular case of B-cell cancers which are driven by the hijacking of the immunoglobulin heavy locus (IGH) super-enhancer. Fed with the coordinates of the rearrangement breakpoints and 1D epigenetic data from patient-derived samples, our polymer physics-based simulations can predict the new set of promoter-enhancer interactions and levels of gene expression. The existence and function of these interactions in vivo are then tested by targeted chromosome conformation capture and CRIPSR-dCas9 silencing experiments respectively. By simulating these hijacking events in samples from patients with different malignancies, we aim to identify and characterise sites which are common across or specific to these malignancies.

AFM to probe structural changes involved in Clostridium sporogenes germination

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Bacterial spores are the dormant and environmentally resilient forms of many infectious bacteria, such as Bacillus Anthracis, Clostridium botulinum, and Clostridiodes difficile. Through the process of germination, bacterial spores release vegetative cells that are capable of producing and releasing toxins. There is a complex interplay of proteins and structural changes that are undertaken as part of this process. Clostridium sporogenes is a non-pathogenic bacterial species with high degrees of similarity to other pathogenic clostridia and makes an ideal model organism for studies on germination.

Electron Microscopy and Atomic Force Microscopy can be used in conjugation to reveal key structures of the germinating spore. AFM also provides the possibility of imaging under a variety of different conditions and measuring local changes in mechanical properties. This project aims to exploit these possibilities to gain structural insights into Clostridium sporogenes germination.

Molecular Dynamics Simulations to Investigate Interactions Between Polymers and RNA in Polymer Nanoparticles

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

RNA therapeutics are increasingly used for the treatment of disease with a prominent example in the SARS-CoV-2 vaccines. Polymer nanoparticles are a form of delivery allowing RNA to be encapsulated and protected for delivery to tissues. Molecular dynamics is a vital tool in understanding molecular interactions between RNA and polymers. We aim to use these simulation tools to investigate structures of polymer-RNA nanoparticles. Atomistic simulations aid in investigating binding patterns but lack the scale needed to see large scale aggregation. By coarse graining the systems to include multiple atoms in single beads, far larger systems can be created and simulated to understand the organisation or formations of larger nanoparticle systems.

Atomistic results have given insight into major and minor groove binding, ion displacement, and hydrogen bonding, while coarse-grained results have shown the importance of concentration and N/P ratio, nanoparticle structure, and aggregate formation. These insights have implications for formulation as investigating these affects will be useful in designing both RNA sequences and chemical polymer structures to better aid in the delivery and therapeutic effect of the nanoparticles.

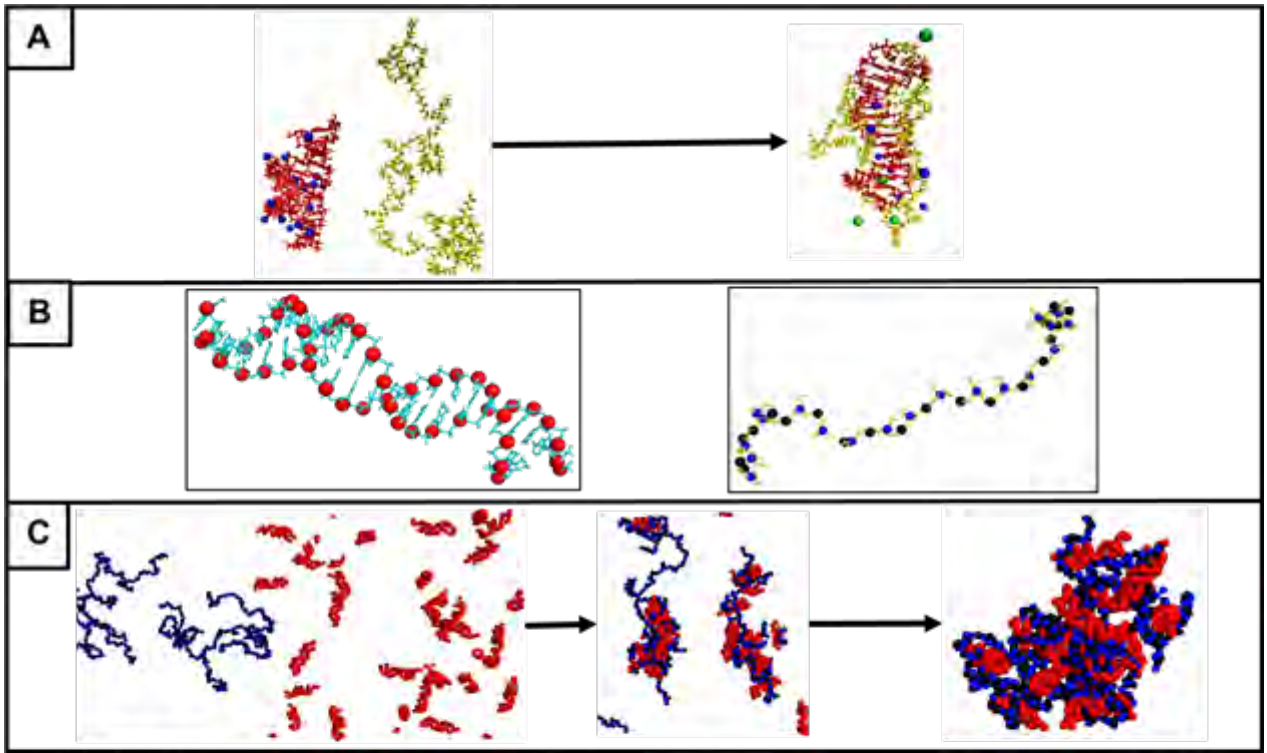

Figure 1: Molecular dynamics simulations of RNA and polymers to understanding structures of polymer nanoparticles. (A) atomistic simulations of polymers and RNA together show details of binding between the RNA and polymer at the atom level but lack the scale necessary to see larger systems. (B) The coarse graining process involves putting multiple atoms into single beads, reducing detail but allowing larger scale simulations to run. (C) Coarse-grained simulations of nanoparticle formulation allow us to view and generate systems which form larger nanoparticles and enable analysis on the structures generated to aid in the design of polymers for formulation.

The role of vibrational molecular structure in entangled two photon absorption in biomolecules

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Entangled two-photon absorption (ETPA) in molecular systems is a promising area of research for probing such systems at low photon fluxes, with applications in spectroscopy and molecular control, such as optogenetics. However, experimental measurements of ETPA cross sections in organic molecules often yield conflicting results. On the other hand, many theoretical models oversimplify the problem, neglecting critical features like the vibrational structure, which can significantly influence ETPA processes. In this work, we use second-order perturbation theory to derive an analytical expression for vibronic populations in a diatomic system excited by ultrabroadband frequency-entangled photons. Our approach agrees with numerical predictions from the full Schrödinger equation, while providing deeper physical insights into vibronic selectivity as a function of photon correlations and requiring less computational effort. We evaluate population dynamics for varying degrees of photon entanglement and demonstrate that vibronic selectivity can be achieved even with low entanglement.

The derived expression includes a term predicting enhanced vibronic selectivity based on photon entanglement, the targeted vibrational energy level, and the Franck-Condon factors encoding the molecular structure. These results emphasize the importance of incorporating vibrational structure to fully understand quantum enhancements from light-matter interactions. Additionally, our findings highlight previously unrecognized differences in vibronic excitation pathways for uncorrelated versus quantum-correlated photons, advancing our understanding of quantum light-matter interactions and their potential applications.

Phage T7-E. coli AR3110 long-term coevolution experiment in a spatially structured environment

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Bacteriophages (phages) have re-emerged as a promising approach to treat pathogenic bacteria and their biofilms. However, bacteria can easily become resistant to phage infection via various mechanisms. In response, phages may evolve and overcome the resistance. This evolutionary arms race has been extensively studied in liquid cultures, where phages are cocultured with sensitive bacteria and allowed to coevolve for several generations. While these experiments have improved our understanding of phages and bacteria adaptive dynamics, they often underestimate the diversity of available evolutionary pathways. Despite its significant interest, few studies have explored phages-bacteria adaptation under relevant natural conditions.

In this project, we investigate how a phage infects, propagates, maintains its population and coevolves with its host in macro-colony biofilms. We use E. coli K-12 AR3110, a matrix-producing strain, and its coliphage T7 as our model system. T7 has been modified previously to produce a fluorescent signal upon infection, allowing us to easily track its propagation within the biofilm using epifluorescence and confocal laser microscopy methods. Preliminary observations showed that the phage tends to infect cells present in forming wrinkles. To explore the diversity of phages-bacteria adaptive pathways in macro-colony biofilm settings, we run long-term coevolution experiments on a custom-made millifluidic device. With these combined approaches, we expect to gain a deeper understanding of the mechanisms behind the arms race between phages and bacteria in biofilm settings. This knowledge will be crucial for fully harnessing the potential of phages in human and animal medicine, agriculture, and industry in the future.

Dissipation, Flows, and Sorting in an Active Nematic Vertex Model

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

We study a vertex model extended to include active nematic stresses [1] and confined to a channel [2]. Under the usual substrate friction dissipation dynamics of the vertex model, flows in the channel are chaotic. However, if dissipation is instead internal, modelled as vertex-vertex friction, channel-wide sustained unidirectional flows emerge. The transition from chaotic to unidirectional flows takes place because internal dissipation allows the model to develop long-range velocity-velocity and director-director correlations.

We then turn to a mixture of extensile and contractile cells [3]. The two cell populations sort over time. While phase separation strengthens monotonically with an increasing magnitude of contractile activity, the dependence on extensile activity is non-monotonic, so that sufficiently high values reduce the extent of sorting. We interpret this by showing that extensile activity renders the system motile, enabling cells to undergo neighbour exchanges. Contractile cells that come into contact as a result are then more likely to stay connected due to an effective attraction arising from contractile activity.

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Multimodal characterisation of an epicardial spheroid model

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The epicardium provides progenitor cells and paracrine signals crucial for cardiac development and repair [1–3]. Although dormant in adulthood, epicardial cells are reactivated after cardiac injury to promote repair [4], however, in vitro models to study these cells are scarce.

This project engineered a multicellular spheroid model with an epicardial layer. Initially optimized with neonatal rat ventricular myocytes (NRVM) and rat fibroblasts (rFB), the model was refined using rat cardiomyoblasts (CM), human fibroblasts (hFB), and human endothelial cells (HUVECs), surrounded by adult pig epicardial cells (EPDCs) or mouse embryonic epicardial cells (MECs). Cardiac spheroids (cardioids) formed from FB, CM, and EC generated epicardioids by adding 1,000 epicardial cells. Cell ratios and media were optimized based on shape and stability. Spheroids were characterized via brightfield, OCT, and confocal microscopy, stained with markers like CD31, Mesothelin, Connexin-43, alpha-sarcomeric actinin, and ethidium-homodimer, and treated with TGF-β1 to monitor fibrosis.

OCT results revealed that MEC epicardioids showed a decrease in cell density following TGF-β1 treatment as shown qualitatively by attenuation profiles. CD31 staining showed that endothelial cells form tube-like structures. Additionally, CMs within MEC epicardioids exhibited lower viability compared to those in EPDC epicardioids and cardioids ($P \leq 0.01$). MEC epicardioids retained more HUVECs compared to cardioids ($P \leq 0.001$) and EPDC spheroids ($P \leq 0.01$). Furthermore, CM morphology in EPDC epicardioids was more elongated, indicating a maturation effect.

In conclusion, this epicardial spheroid model offers a valuable platform for studying the epicardium's role in cardiac repair, enabling high-throughput screening and label-free imaging analysis.

Optical Coherence Tomography: An Emerging Modality in Deep Tissue Imaging

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Intra-vascular ultrasound (IVUS) and angiography are one of the modalities to assess coronary tissues, however Optical Coherence Tomography (OCT) has comparatively emerged as an advanced diagnostic technique due to providing high axial resolution (in) by extending the depth of focus (DOF).

The extended DOF of OCT also finds potential applications in multitude of areas such as gynaecology, ophthalmology, oncology etc. E-DOF is achieved through designing a probe having constituents namely step-indexed-fiber, graded-indexed-fiber (GRIN) or no-core-fiber and patterning the probe using biomaterials. Microsecond Bessel-type laser is utilized as a probe beam and investigating its optical transfer function. In this proposition we investigate the utility of OCT in intervening acute myocardial infarction through monitoring of stent-embedded coronary blood vessels.

Bacterial super-exponential growth and cell wall dynamics

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Bacterial growth has been widely studied, with the exponential elongation phase during the bacterial cell cycle traditionally assumed1–5. Recently, it has been shown that in Gram-negative E. coli cells, elongation rate increases during the cell cycle implying super-exponential growth6. However, molecular and mechanistic details of super-exponential growth that governs bacterial cell growth mechanics have been missing. Here we demonstrate that super-exponential growth arises from stochastic peptidoglycan synthesis of lateral cell wall. To investigate the cell wall synthesis dynamics, we used the fluorescent D-amino acids (FDAAs) HADA and NADA which provide cell-wall synthesis patterns at a single-cell level7.

Using imaging and image analysis, we measured non-growing parts of lateral cell walls during the cell cycle, which gives rise to super-exponential growth. By growing cells in different growth conditions (different growth media and under antibiotic exposure), we show that non-growing part scales with cell width in line with single-cell measurement in the mother machine. Furthermore, by inducing cell filamentation with cell division inhibitor cephalexin, we showed that non-growing segments are constant and independent of cell length. A similar growth pattern was observed in Gram-positive B. subtilis. Together, we demonstrated that super-exponential growth arises from stochastic peptidoglycan synthesis in both Gram-positive and Gram-negative bacterial cells.

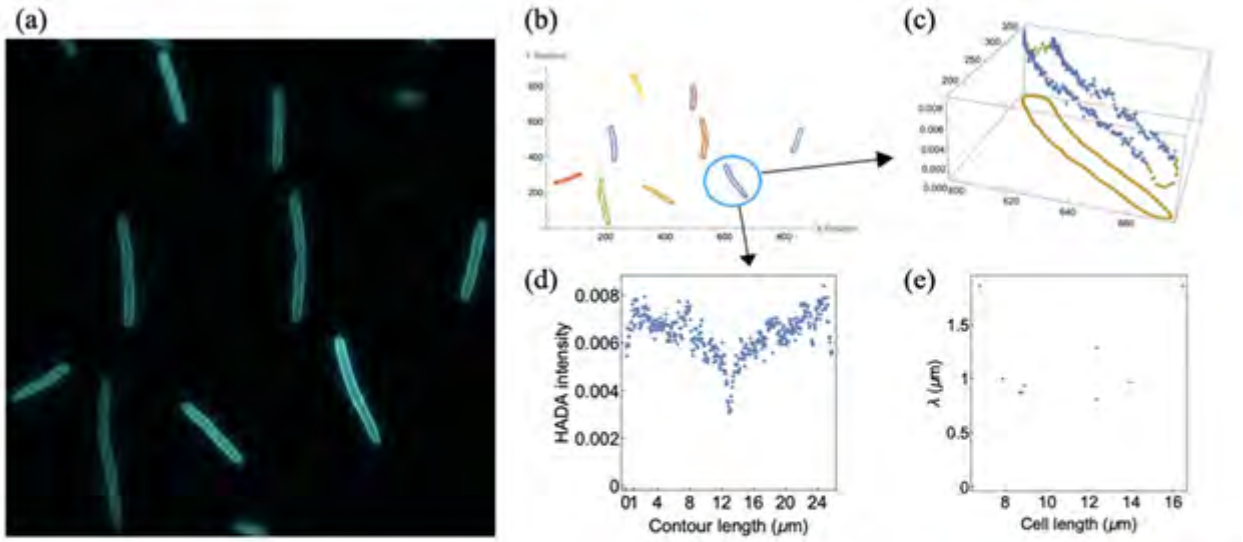

Figure 1. Analysis of cell length and non-growing regions during cell cycle under cephalexin exposure using fluorescence microscopy of E. coli stained with HADA. Image processing and quantification were performed using ImageJ, JFilament, and Mathematica

Charged peptides enriched in aromatic residues can decelerate condensate ageing

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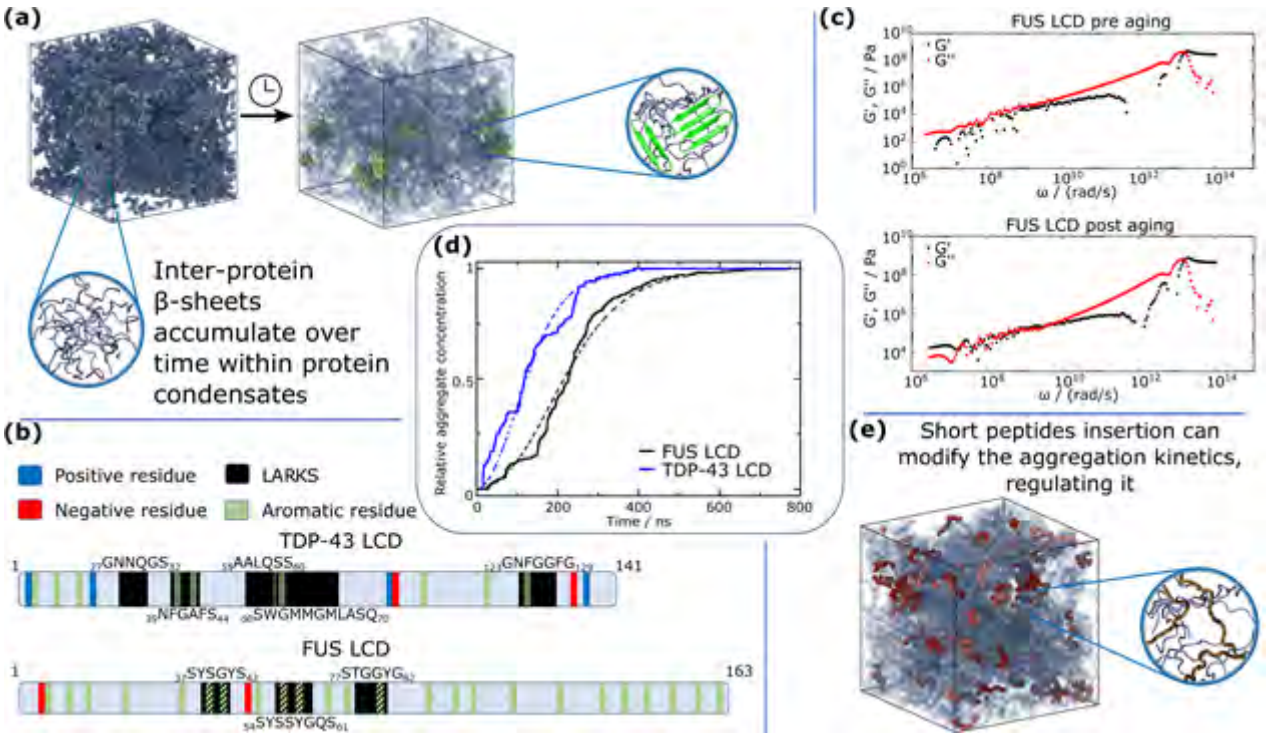
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Biomolecular condensates, formed through liquid-liquid phase separation (LLPS), play critical roles in cellular compartmentalization and biological processes. However, their aging, marked by a transition from dynamic liquid-like states to more rigid, solid-like structures, can lead to pathological aggregation associated with neurodegenerative diseases. In this study, we propose a methodology to prevent this pathological transition by exploring the potential of small peptides in the aging of biomolecular condensates formed by the intrinsically disordered proteins TDP-43 and FUS. We first systematically study phase diagrams in the absence and presence of various peptides to investigate their effects on condensate stability. We then focused on how these peptides impact aging dynamics by observing changes in the liquid-to-solid transition timescales.

To capture the molecular basis of these processes, we employed a dynamic algorithm in non-equilibrium simulations, which enables the formation of inter-protein beta-sheets. Using contact frequency maps derived from these simulations, we further identified the molecular interactions responsible for the observed deceleration in aging. Our findings reveal key insights into peptide-mediated modulation of biomolecular condensates and point towards small peptides containing moderate amounts of charged and aromatic residues as a relevant feature for a successful deceleration of aging. Our approach offers novel pathways for controlling phase transitions relevant to disease prevention.



Probing Drug Pharmacokinetics -

Can the impact of Cisplatin-like Anticancer Drugs on Protein Dynamics explain the difference in toxicity

Mona Sarter[1], C Martins[2], A.L.M. Batista de Carvalho[2], Victoria Garcia Sakai[1], Tilo Seydel[3], J Ollivier[3], L.A.E. Batista de Carvalho[2], M. P. M. Marques[2]
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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Upon the discovery of the anticancer drug cisplatin, it was discovered that polynuclear complexes such as Pd2Spm reduce the toxicity while increasing the therapeutic effect. [1,2] While DNA is the target for therapeutic effects, protein drug interactions are relevant for the pharmacological activity. Both due to parallel reactions, which are prone to elicit side effects as well as drug transport and therefore bio distribution. Human Serum Albumin (HSA) is the most prevalent protein in the blood plasma and was therefore selected as the protein of interest in this study.

The studied drugs are known to bind strongly to HSA upon intravenous administration, thus the protein drug interaction is of particular interest. In addition to the impact of the drugs on HSA dynamics we will also discuss its effects on the protein's hydration shell, which is of critical importance to the proteins normal biological function. [3] We used quasi-elastic neutron scattering (QENS), which is particularly suited to studying these interactions and will discuss how the different efficacy and side effect intensity relates to the drugs influence on HSA and HSA hydration shell dynamics with the aim of finding communalities that will aid in the development of future drugs.

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Understanding the Roles of Carotenoids in the Photophysics of Bacterial Light-Harvesting Protein Complexes

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Light-harvesting (LH) pigment-protein complexes are an integral component of photosynthesis, where they absorb light energy and transfer it to the reaction centre (RC) for conversion to chemical energy. Along with chlorophylls (Chls), carotenoids (Cars) are widely distributed pigments among LH complexes and play a critical role in regulating energy transfer and photoprotection. In this work, we aim to explore how diverse Cars lead to different energetic pathways and protective processes within the bacterial light-harvesting complex, LH2.

We used genetically modified strains of Rhodobacter sphaeroides, where each mutant LH2 protein contains only one specific type of Car pigment (conjugation length, N = 7, 9, 10, 13). To explore the role of the microenvironment on LH2 photophysics, we also studied the effect of different model membrane systems such as, in detergent (isolated LH2), in nanodiscs (only lipid-protein interaction) and proteoliposomes with different protein-lipid ratio modulating the protein clustering. We compared the BChl excited state dynamics of different LH2 mutants in detergent and proteoliposomes with a series of protein-to-lipid ratios which show that high-energy carotenoids are inefficient in dissipating the energy even in detergent due to the formation of triplet trap states which becomes more prominent in presence of protein-protein interactions in proteoliposomes. We are exploring how this triplet state formation will change in the presence of different Carotenoids.

These findings will provide a new understanding of how Cars can change the energetic state of LH complexes, to switch between light-harvesting and photoprotective (quenching) states.

Turning up the heat; mechanistic insights from thermal inactivation of influenza A virus

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Even prior to recent pandemics, viral inactivation has been crucial in the food industry for centuries[1]. Surprisingly, we lack a mechanistic understanding for even simple thermal inactivation. Using influenza A virus (IAV), we explore the limits of virus survival following heat exposure, gleaning important clues as to the inactivation mechanism from thermodynamic analysis.

IAV infectivity shows a first-order exponential decay on exposure to temperature over time, suggesting a non-cooperative process. Inactivation rates reveal Arrhenius behaviour between 40-50°C, consistent with a single, dominant inactivation mechanism. The measured activation enthalpy of 99 ± 3 kBT is similar to that of the energy barrier for haemagglutinin (HA) unfolding in simulations[2]. The activation entropy we obtained for inactivation (66 ± 3 kB) is consistent with a partially-unfolded (rather than, say, aggregated) state. A lower activation enthalpy of 42 ± 2 kBT was obtained below 40°C, suggesting an alternative mechanism may apply at lower temperatures, which are most relevant for environmental transmission.

Combining the effect of pH and temperature reveals that pH catalyses thermal inactivation; suggesting electrostatic forces are integral to the mechanism. Another temperature-independent inactivation process appears present initially at low pH, implying population heterogeneity. Furthermore, IAV HA mutants with a higher activation pH show an increased inactivation rate. Taken together, these results strongly suggest that premature HA-triggering, essential for viral entry, is key to thermostability above 40. Considering the ubiquity of such fusion proteins across enveloped viral species[3], mechanistic insights in this area will have broader implications for understanding viral stability and disinfection.

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Detecting epistasis from SARS-CoV-2 genomic data

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The COVID-19 pandemic's extensive sequencing efforts have provided an unprecedented number of high-quality viral genomes. This wealth of data can be used to characterize the viral fitness landscape. The landscape maps the genome to global fitness, encompassing phenotypes such as transmissibility, infectivity, and immune escape. Determining the fitness landscape is not only theoretically interesting but also practically useful, e.g., for vaccine design or assessing novel variants. In previous work [1], viral fitness was quantified by comparing mutation counts on the phylogenetic tree with expected neutral mutation rates. Building on these fitness estimates, our goal is to develop a method for detecting and quantifying epistasis at the protein level. Epistasis refers here to the context-dependent effects of point mutations.

The simplest model incorporating epistatic interactions is the pairwise Potts model, which we use to parametrize fitness effects of mutations. By comparing mutational effects across different clades, we devise an inference framework to determine the parameters quantifying the interaction of pairs of mutations for each viral protein's fitness. This approach enhances our understanding of the fitness landscape, shedding light on the interplay of multiple mutations. Predictions can be compared to in-vitro experiments on the Spike or other proteins and understood from a structural and immune perspective. Once validated, this method allows us to unveil novel epistatic interactions, possibly guiding further experimental explorations.

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Understanding algal pyrenoid dynamics with coarse grained molecular dynamics

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Algae are the largest carbon sink on the planet, with most of this carbon fixation occurring in the liquid-liquid phase separated organelle the pyrenoid, which concentrates carbon dioxide for photosynthesis, increasing its efficiency by orders of magnitude. A key challenge in bioengineering is tuning these pyrenoids and introducing them to new plants, where they could increase crop yields and help mitigate increasing atmospheric carbon dioxide levels. However, the physics of the pyrenoid – and other LLPS systems – is currently poorly understood. Here, we present the results of coarse grained molecular dynamics simulations of a simplified pyrenoid system, consisting of globular proteins interacting with linker proteins, mimicking the Rubiso/EPYC1 system.

Key parameters for the LLPS efficiency are linker length, linker concentration, number of linker protein binding sites, position of Rubisco binding sites, and the interaction potential between the globular proteins and the linkers. Here, we focus on models of two algal pyrenoid systems, Chlorella and Chlamydamonas, which differ in size of linker protein and globular protein binding site location. We parameterise our model to state-of-the-art experimental data, and then build condensed phase Rubisco/linker systems with varying linker protein concentrations. We measure the size of the condensate and its diffusive behaviour, and compare to experimental data from the purified two-component system. We believe that in the future our physiologically relevant simulation strategy may be used to fine tune desired LLPS properties as a first start towards de novo LLPS organelle design.

Fluorescence spectroscopy of cell membranes under dynamic mechanical perturbation: investigating modulations to cell signalling

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Cells convert mechanical stimuli into biochemical signals for further downstream regulation in a process called mechanotransduction. Understanding the interplay between mechanical stress and cell response is key to uncovering the mechanisms driving important physiological processes like cell migration, tissue development and repair. Mechanosensitive membrane proteins have adopted diverse mechanisms to sense and respond to mechanical forces [1].

The combination of microscopy imaging with the application of a precisely controlled mechanical force provides a direct way to characterize mechanotransduction at the single cell level [2]. Optical tweezers is a force spectroscopy technique capable of applying precise forces in the piconewton range. We have developed a protocol that combines tether pulling experiments using optical tweezers with microscopy imaging to characterize receptor response to cell membrane deformation. We have used fluorescence recovery after photobleaching [3] to study the diffusion rate of the receptors in the tethers pulled by optical tweezers. We aim to investigate whether mechanically perturbed regions of the cell exhibit alterations in their downstream signaling pathways compared to areas that remain mechanically undisturbed.

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From model to crops: Determining the regulatory control of floral transition

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The transition from vegetative to floral is a crucial step in plant development. Research in the model plant, Arabidopsis, has shown that its genetic control is influenced by environmental cues, including response to temperature. Gene regulatory networks (GRN) offer a means of describing this control logic of genes and their interactions. Understanding these regulatory mechanisms can support the development of crops that maintain yields in changing climate conditions. Translation of this knowledge to crops, however, presents challenges. Brassica napus (Oilseed rape, OSR) is an important crop and evolutionarily among the closest relatives to Arabidopsis. However, it has undergone multiple genome duplication events (polyploidisation), the effects of which on flowering time regulation are unknown.

We sought to use machine learning tools to unravel GRN for flowering time in OSR from expression data. We collected RNA-time course datasets of apex tissue for multiple OSR cultivars, with varying lifecycle trajectories. A comparison of expression dynamics across timescales revealed that over 80% of orthologues of Arabidopsis flowering genes have conserved expression dynamics in OSR. However, we observe that the inferred GRNs split into two distinct hubs, depending on cultivar type, with one hub constituting genes incorporating cold response. Our analysis indicates that different copies of SOC1, a key floral integrator in Arabidopsis, are bridging signals from these sub-networks, evident by divergence exhibited in their expression dynamics. Interestingly, this expression divergence can be induced by subjecting cultivars to cold treatment. This study sheds light on the functional divergence of a key flowering gene following polyploidisation.

DNA nanostructure tags for electron cryotomography

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Signpost Origami Tags (SPOTs) are DNA nanostructures used as molecular markers for cryo-electron tomography (cryoET), enabling the identification of specific proteins within tomograms. SPOTs have been successfully used to identify proteins on the vesicles, viruses and the cell surface.

To address a broader range of research questions, the SPOT technology is being expanded to support multiplex labelling and intracellular applications. For multiplex labelling, several distinct nanostructure designs have been developed, alongside orthogonal labelling strategies including the use of nanobodies. This growing library of nanostructures has been successfully employed to simultaneously identify multiple proteins on the surface of viruses.

To adapt SPOTs for intracellular use, reconfigurable DNA nanostructures are being developed that undergo conformational changes upon target binding, providing an unambiguous readout. Additionally, the cellular delivery of SPOTs is being optimized using techniques to ensure efficient uptake while maintaining functionality. These advancements will enable precise labelling in crowded intracellular environments and facilitate the investigation of complex protein interactions in situ.

Together, these developments extend SPOT technology into new domains, offering a versatile toolkit for both extracellular and intracellular labelling, with broad potential applications ranging from viral assembly to cellular signalling pathways.

AI-Driven Temporal Feature Analysis for Forecasting of Alzheimer's Disease Progression

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Recent advances in machine learning methodologies, coupled with the increasing availability of large-scale medical datasets, have enabled innovative approaches for analyzing Alzheimer's disease (AD) progression. This study presents an AI-driven framework that integrates diverse biomarker features to forecast AD progression trajectories while providing scientific insights into the underlying pathology and temporal disease patterns.

The framework was evaluated using the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, which encompasses comprehensive longitudinal data including MRI scans, PET images, genetic markers, and clinical assessments. Our methodology addresses the challenges of longitudinal medical data through comparative analysis of multiple imputation techniques for pre-processing temporal sequences.

Our investigation of feature selection methodologies demonstrates the framework's capability to identify dominant predictive biomarkers affecting AD progression. Comparative analysis of random forest, mutual information, and attention-based approaches revealed superior predictive accuracy through attention-based feature selection.

The temporal dynamics of AD progression are captured through recurrent neural networks (RNN) and their variants, including Long Short-Term Memory (LSTM) and Gated Recurrent Unit (GRU) architectures, surpassing traditional machine learning approaches. The integration of attention mechanisms with RNN enables precise identification of critical temporal patterns, providing steps towards modelling disease progression from prodromal phase (pre-symptomatic stage) to clinical diagnosis.

Experimental results demonstrate the framework's effectiveness in both prediction accuracy and interpretability, offering valuable insights for clinical trial design and personalized treatment strategies. This scientific approach advances our understanding of AD progression while providing practical tools for patient care optimization.

Nematic Torques in Scalar Active Matter

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Active matter describes systems comprising elementary units able to exert non-conservative forces on their environment. Activity leads to a fascinating variety of collective behaviours unmatched in passive systems, such as the transition to collective motion. The latter is arguably the most studied phase transition in active matter and the ordered phases emerging from the interplay between self-propulsion and aligning interactions have naturally attracted a lot of attention [1].

In this talk, I will instead focus on the role of aligning interactions in the disordered phase. In particular, I will show that nematic alignment, which is ubiquitous in active systems from rod-like bacteria to cells, plays an unexpected role in the high-temperature phase: it can induce or suppress phase separation, increase particle accumulation at boundaries, and suppress demixing in systems comprising active and passive particles.

I will then show how all these phenomena can be understood by introducing a field-theoretical framework to go beyond the mean field description of the system. In the presence of nematic torques, fluctuations are then shown to enhance polar order, leading to an increase in the particle persistence length. In turn, the latter accounts quantitatively for all the phenomena reported above. To show this, I will briefly describe a new theory for motility-induced phase separation in the presence of aligning torques [2].

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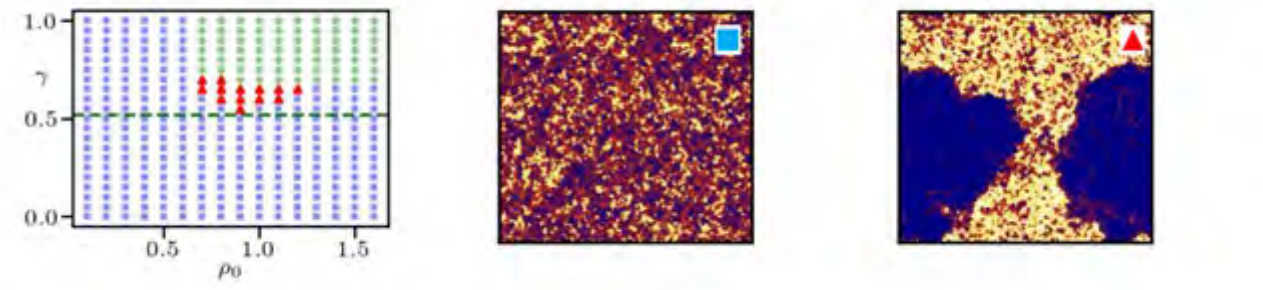

Synchronisation of chemical reactions in a population of condensates

Alisdair Stevenson[1]
[1]*Eth Zürich, Switzerland*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Collective behaviour refers to the actions and interactions of a group of individuals, which results in emergent patterns and behaviour that cannot be explained by individual actions alone. Examples of this emergent behaviour from complex systems are widespread in physics, ecology and biology and include phase transitions in materials and ant or bee colonies displaying swarm intelligence. How is this possible? A method of communication is universally required for a complex system to exhibit collective behaviour. In this project, we explore whether biomolecular condensates formed via liquid-liquid phase separation could act as a means for collective behaviour to emerge within a cellular environment to enable population-level control of chemical reactions relevant to complex biological processes.

If such processes are regulated at the cellular scale by condensates, how is communication possible between spatially distinct condensates? How does this coordinate the behaviour of multiple droplets, resulting in a more predictable and stable outcome of chemical reactions, with specific functions, at the population level? As the mechanisms by which communication and population-level regulation may be possible for in vitro/vivo systems that form droplets have not been explored, this is an exciting opportunity to generate a novel understanding of how complex processes are regulated at the cellular scale. Here we have demonstrated that communication via the dynamic exchange of materials to maintain partition concentrations between the dense phases of individual droplets and the surrounding dilute phase is able to efficiently synchronise chemical clock reactions occurring within the droplets.

Exploring the Impact of Tumour Mechanics on Immunological Synapse Formation

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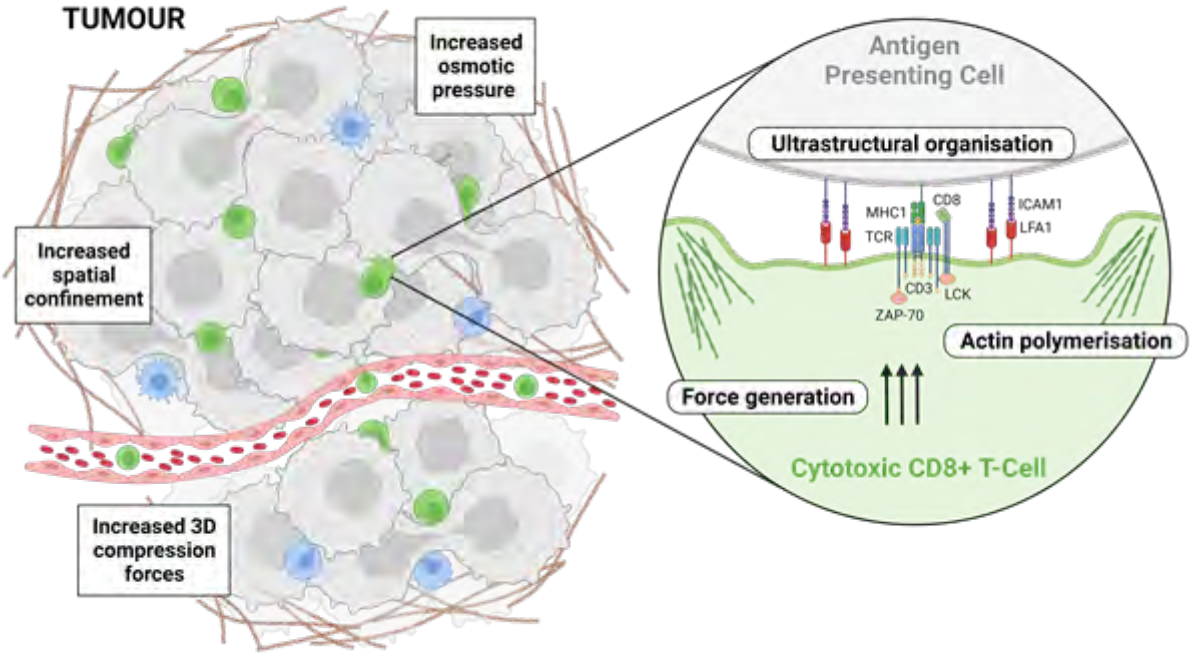
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Cytotoxic CD8+ T-cells (CTLs) are important effectors in the anti-tumour response. CTLs can navigate tumour microenvironments (TMEs) to kill cancer cells through the polarised release of cytotoxic granules via the formation of an immunological synapse (IS). The distinct mechanical properties of the TME present considerable biophysical challenges for infiltrating CTLs, hypothesised to compromise IS formation and target cell killing. The direct impact of tumour mechanics (including increased spatial confinement, three-dimensional compression forces, and osmotic pressure) on IS formation and killing remains to be investigated. Through the development of a multimodal imaging pipeline, integrating light and electron microscopy, we aim to probe how dynamic and molecular features of the IS are impacted by different biomechanical environments. This approach will reveal key features that contribute to compromised CTL cytotoxicity within the TME.

Primarily, we have established a substrate-based experiment to quantify how mechanical force generation at the IS is impacted with traction force microscopy. CTLs interact with antibody functionalised polyacrylamide hydrogels containing fiducial fluorescent beads where exerted force on the hydrogel surface is visualised by corresponding bead movement. We aim to correlate this understanding of force generation to the underlying ultrastructural organisation of the IS with in-situ cryo-electron tomography. Cryogenic sample preparation workflows have been optimised, enabling subsequent fluorescence guided focused ion beam milling at ISs for targeted lamella fabrication and tilt-series acquisition. The understanding provided by this advanced microscopy approach will be crucial in informing bioengineering strategies to improve adoptive CAR-T cell therapies for solid tumours.


TUMOUR
Increased osmotic pressure
Increased spatial confinement
Increased 3D compression forces
Antigen Presenting Cell
Ultrastructural organisation
MHC1
CD8
ICAM1
TCR
LFA1
CD3
LCK
ZAP-70
Actin polymerisation
Force generation
Cytotoxic CD8+ T-Cell

DNA nanostructures targeting activated platelets

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

DNA nanostructures can be made by combining a long single-strand DNA scaffold with more than 200 short DNA oligonucleotides (staples) that will direct the folding of the scaffold to any pre-designed shape [1]. DNA nanostructure products have numerous functions, such as studying nanoscale biological interactions and facilitating drug delivery. It has been shown that DNA nanostructures can bind platelet membranes without triggering activation [2], however, DNA nanostructures have not been explored for their potential to target activated platelets and deliver thrombolytics. In this project, we investigate the interaction of various DNA nanostructures with activated platelets, and we assess their potential for anticoagulant drug delivery. DNA nanostructures with different shapes (like triangles, tetrahedron, 5-well-frame, etc.) were synthesized and visualized using atomic force microscopy (AFM).

Flow cytometry reveals that 1 nM folded DNA nanostructures (triangular, tetrahedral, and 5-well-frame structures) specifically bind to activated platelets with high affinity in 30 minutes of incubation time, without modifications. Confocal microscopy images suggest the internalization of these structures into activated platelets, though further confirmation is needed. Future work will focus on conjugating thrombolytic agents to DNA nanostructures and evaluating their effects on platelet function and clot dissolution. This study highlights the potential of DNA nanotechnology in developing targeted anticoagulant therapies for thrombotic diseases.

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Feedback between F-actin organization and active stress govern criticality and energy localization in the cell cytoskeleton

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Self-Organized criticality (SOC) is characterized by cascading dissipative events observed across diverse natural phenomena, including earthquakes, avalanches, and landslides. During complex physical behaviors of the cell such as migration and division, the F-actin cytoskeleton undergoes dramatic changes in structure, organization, and dynamics, suggestive of large dissipative events. To drive these changes, non-equilibrium activities of molecular motors impart mechanical stresses upon the cytoskeleton. To explore criticality in the dynamics of the cytoskeleton, we reconstruct an experimental model of the cytoskeleton in vitro, composed of purified protein polymers (F-actin), motors (myosin II), and nucleating promoting factors (NPFs). We alter the connectivity and nematic order of F-actin networks through varying NPF concentrations. In ordered (nematic) and poorly percolated networks, dissipative events are exponentially distributed.

By contrast, in disordered (branched) and highly percolated networks, dissipative events are Levy-α distributed and exhibit 1/f noise, characteristic to SOC. The increased disorder attenuates the propagation of stress, distributes it amongst stiffer eigenmodes, and localizes it spatially, reminiscent of strong localization of electromagnetic waves in disordered lattices. Finally, the extent of disorder determines the magnitude of mechanical stress applied, as it determines the size and activity of myosin II filaments, demonstrating that SOC is regulated by chemical-mechanical feedback.

Crowding and Its Role in Calcium Carbonate Crystallization Processes

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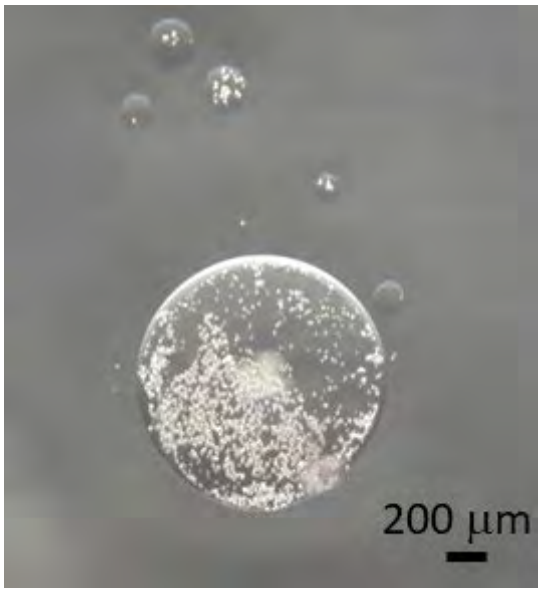
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Macromolecular crowding plays a crucial role in biomineralization by influencing nucleation and growth pathways. In this study, we explore the formation of a liquid-like mineral phase in calcium carbonate crystallization by employing polyethylene glycol (PEG) as a crowding agent and polyacrylic acid (PAA) and proteins as additives. By systematically varying the concentrations of PEG and PAA, we investigate their effects on crystal size, growth rate, and polymorphism.

To gain structural and morphological insights, we utilize a combination of optical microscopy, fluorescence microscopy, Raman spectroscopy, and scanning electron microscopy (SEM). These techniques allow us to analyze crystallization dynamics and phase transitions at both microscopic and molecular levels. A key observation in our study is the occurrence of liquid-liquid phase separation (LLPS), mediated by PEG-PAA-Ca^{2+} interactions, which leads to the formation of confined microdomains where crystallization occurs (optical microscopic image was added as supporting document).

Our findings demonstrate how macromolecular crowding can modulate mineralization pathways, providing a deeper understanding of biomimetic crystallization. This research has potential implications for designing bio-inspired materials and controlling mineralization processes in synthetic and natural systems.



Advancing Gynaecological Disease Research: A Fallopian Tube-on-a-Chip Model for STIC Progression and High-Grade Serous Ovarian Cancer Development

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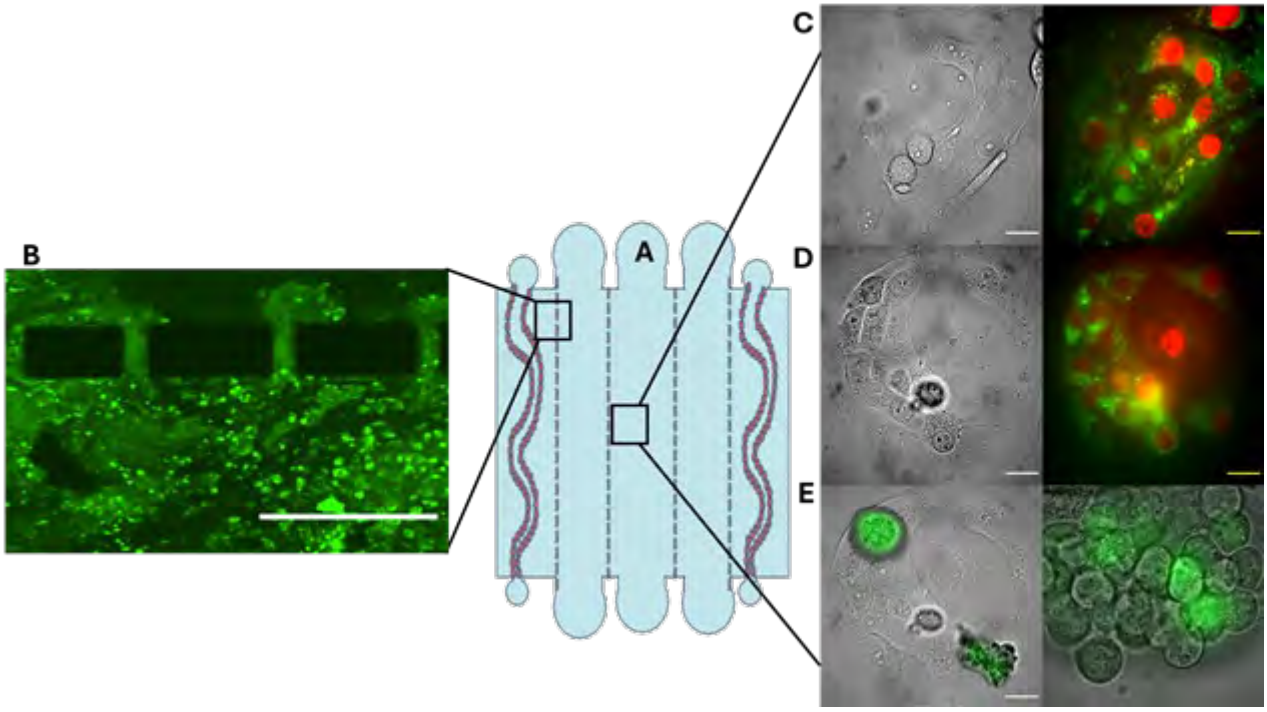
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

High-grade serous ovarian cancer (HGSOC) is the most lethal gynecological malignancy, often diagnosed at advanced stages due to a lack of early detection strategies. Emerging evidence suggests that a significant proportion of HGSOC originates from serous tubal intraepithelial carcinomas (STICs) in the fallopian tube epithelium. However, the mechanisms driving STIC lesion progression remain poorly understood. Here, we present a novel fallopian tube-on-a-chip platform that models the transition from STIC lesions to invasive ovarian cancer. This microfluidic system integrates physiologically relevant epithelial-stromal interactions within a biomimetic microenvironment, enabling real-time, high-resolution imaging of disease progression.

The platform supports live-cell tracking of key oncogenic events, including cellular transformation, invasion, and metastatic dissemination. Additionally, dynamic outflow collection facilitates multi-omic profiling—encompassing transcriptomic, proteomic, and metabolomic analyses—to identify molecular signatures associated with malignant progression. By capturing extracellular matrix remodeling, inflammatory signaling, and metabolic shifts, our system provides a powerful tool for unraveling early disease biomarkers and therapeutic vulnerabilities. This in vitro model bridges the gap between histological observations and functional disease progression, offering a scalable, high-throughput approach for drug screening and biomarker discovery. Ultimately, our technology paves the way for precision oncology strategies in early ovarian cancer intervention.

Figure 1 | (A) Microfluidic device seeded with fallopian tube (FT) organoid sheets. (B) FT sheets line the main channel, supported by pillar scaffolds and sustained by vascular flow. (C,D) Mitochondrial viability assay (green) and nuclear stain (red) highlight FT sheets. (E) Ovarian cancer cells cluster, modeling STIC lesion progression. Scale bars: 200 μm (A–D), 20 μm (E).


B
A
C
D
E

Modelling spatial competition in toxin-antitoxin producing bacterial populations

Anna Tarodi[1], Xingjian Hou[1,3], Anna Schwarzenbach[2], Professor Kevin Foster[2], Professor Diana Fusco[1]

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Bacteria often utilize toxins (bacteriocins) to kill or inhibit susceptible bacteria not only ones that belong to different species but also strains of their own [1]. Therefore, bacteriocins and biotherapeutic bacteria have been suggested as alternative methods of pathogen eradication within complex microbiomes.

Our collaborators are working on experimentally evolving such toxin-producing bacteria for increased potency and specificity against target pathogens. They are using spatially structured environments to counteract the proliferation of cheater cells and thus enhance the toxin producers. Cheater cells are resistant to the toxin, however, their killing ability is weak or non-existent and therefore, they are not hindered by the burden of toxin production and can exploit the killer cells' clearing by proliferating quicker in mixed cultures.

However, experimentally there are numerous parameters to control such as the initial cell densities, toxin strength and release rate, toxin diffusion and adsorption rates among others. It is not trivial which combination of values for these would result in colonies with maximally enhanced toxin producers, which motivates my computer simulation approach.

My research involves modelling the spatial competition of a population of toxin producers, susceptible bacteria and cheaters with the following aims. First, to optimise the experimental parameters for picking out the most potent killer cells for target bacteria. And second, to develop a mathematical framework for describing the complex dynamics of these bacterial populations.

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How to steer catalytic nanoswimmers?

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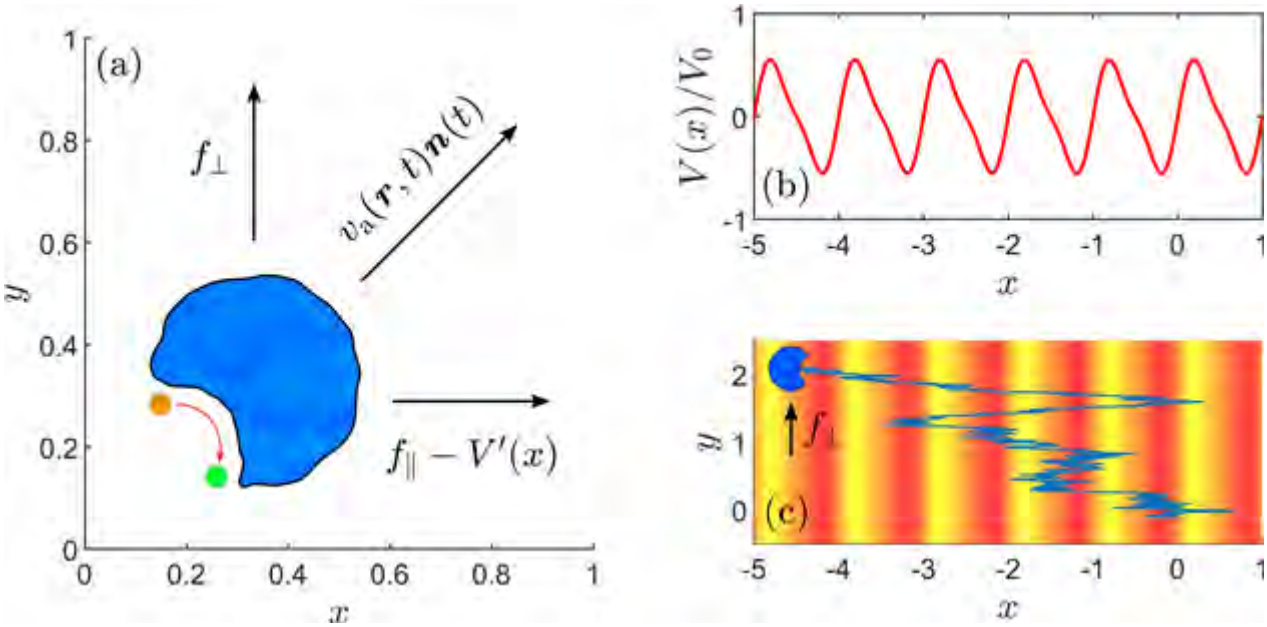
Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Self-propelled nanoparticles moving through liquids offer the possibility of creating advanced applications where such nanoswimmers can operate as artificial molecular-sized motors. Achieving control over the motion of nanoswimmers is a crucial aspect for their reliable functioning. While the directionality of micron-sized swimmers can be controlled with great precision, steering nano-sized active particles poses a real challenge. One of the reasons is the existence of large fluctuations of active velocity at the nanoscale. Here, we describe a mechanism that, in the presence of a ratchet potential, transforms these fluctuations into a net current of active nanoparticles. We demonstrate the effect using a generic model of self-propulsion powered by chemical reactions.

The net motion along the easy direction of the ratchet potential arises from the coupling of chemical and mechanical processes and is triggered by a constant, transverse to the ratchet, force. The magnitude of the rectified current sensitively depends on the amplitude and the periodicity of the ratchet potential and the strength of the transverse force. Our results highlight the importance of thermodynamically consistent modelling of chemical reactions in active matter at the nanoscale and suggest new ways of controlling dynamics in such systems.



Optimized residue-resolution coarse-grained model for electrostatic-driven biomolecular condensates

Dr Andres R. Tejedor[1], Dr Anne Aguirre Gonzalez[1], M. Julia Maristany[1], Pin Yu Chew[1], Prof. Jorge Ramirez[2], Dr Jorge R. Espinosa[3], Prof. Rosana Collepardo-Guevara[1,4]
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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Electrostatic interactions play a central role in driving biomolecular self-assembly, which is an essential mechanism for regulating the formation and stability of membraneless organelles in cells. The cooperative and many-body nature of biomolecular condensation poses a challenge to traditional predictions based on polymer physics and coarse-grained models, as these often fail to capture the nuanced attraction-repulsion balance in electrostatic interactions. In this work, we present the Mpipi-Recharged model, a residue-level coarse-grained force field specifically designed to describe highly charged protein and RNA condensates. This model stands out for the implementation of asymmetric electrostatic interactions between charged amino acids. Our atomistic potential-of-mean-force calculations demonstrate significant differences in the strength of attractive versus repulsive interactions, depending on the nature of the involved amino acids.

By introducing pairwise Yukawa interactions tailored for charged residues, the Mpipi framework effectively reproduces the electrostatically-driven phase behavior of proteins. The model has been rigorously validated using extensive experimental data, including protein radii of gyration, in vitro phase diagrams for various sequence mutations and protein lengths, and the salt-dependent phase behavior of complex coacervates reaching an excellent agreement. Furthermore, we investigate the influence of globular domains on the phase separation of multi-domain proteins and predict RNA-driven reentrant phase behavior across diverse protein sequences. With these advancements, the Mpipi-Recharged model emerges as a robust tool for studying protein and RNA interactions, offering critical insights into the physicochemical mechanisms underlying biomolecular phase separation.

Investigating the Effects of Nucleosome Positional Irregularity on Chromatin using a Nucleosome-Scale Computational Model

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

The spatial organisation of chromatin is critical for genome regulation, controlling accessibility of the DNA to transcription factors. Nucleosomes are the first level of compaction into higher order structures, and therefore understanding chromatin at the scale of nucleosomes is elucidative. While behaviour of chromatin with regular nucleosome spacing, achieved with strongly positioning Widom 601 sequences, is fairly well characterised in-vitro, the nature of chromatin in-vivo is less clear. Beyond the textbook 30nm fibre and towards more disordered states, we present the results of our molecular dynamics simulations, using a nucleosome-scale coarse grained model that allows us to vary linker lengths to the nearest base pair, and vary entry/exit angles of each nucleosome individually. We computationally replicate the results of our experimental collaborators, who use cryo-electron-microscopy and atomic-force-microscopy to image assays of irregular chromatin, using their nucleosome positioning data.

Complementing their experimental work, we are able to obtain measurements in-silico that are impossible in-vitro, including DNA accessibility per base pair and dynamic measurements of physical properties such as persistence lengths and shape parameters from the gyration tensor. Further, we correlate variance in DNA accessibility with degree of positional irregularity per chromatin fibre, and explain this through measurements of relative nucleosome orientation along the chain. Our model can also be applied to existing in-vivo data to compare different organisms (yeast vs mammals) or genomic regions (active genes vs heterochromatin).

Modelling-guided engineering and rerouting of biomolecular assemblies

Prof Damien Thompson[1]
[1]*University of Limerick, Ireland*

Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

In this talk, I will describe our work in coupling molecular simulations with crystallography and imaging experiments to understand, track and ultimately control the self-assembly of biomolecules. The design rules emerging from these works are informing (a) the discovery of novel drug targets for neurodegeneration [1] and (b) new crystalline materials for biomolecule-based energy harvesting [2].

[1] Accelerated Alzheimer's Aβ-42 secondary nucleation chronologically visualized on fibril surfaces. PN Nirmalraj, S Bhattacharya, D Thompson. Science Advances. In press for publication on 25 October 2024.

[2] The Dimensionality of Hydrogen Bond Networks Induces Diverse Physical Properties of Peptide Crystals. H Yuan, PA Cazade, D Thompson, E Gazit. ACS Materials Letters. 2024. 6, 3824.

Is the energetics of E.coli influenced by the nature of stress that stops it from growing?

Mr Keshav Todi[1], Dr Teuta Pilizota[1]
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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Recently, it was reported that bacterial cells respond differently to stress based on its intensity and duration. When cells are exposed to an acute stress strong enough to disrupt their genetic pathways without being lethal, they transition to a so-called 'disrupted state'. This disrupted state is characterized by unusually slow recovery dynamics reminiscent of ageing in physical materials. On the other hand, a gradual stress allows the cells to enter a so-called 'regulated state' which does not induce ageing-liake behaviour. To substantiate this hypothesis, we examined the energy levels of E.coli under the above-described experimental conditions. We closely observed changes in the swimming speed of cells exposed to the stress, as a proxy for the changes in the proton motive force (PMF), one of the main energy sources in living cells that also powers the swimming.

We found that under acute stress cells maintain a constant swimming speed over extended periods. Conversely, under gradual stress, cells decrease their swimming speeds and even no longer swim. The result suggests that PMF generation proceeds with resources that are available at the time of acute stress, a signature of passive response consistent with the disrupted state hypothesis. Changes in swimming speed during gradual stress suggest adaptation, either through changes in PMF or regulation of swimming itself, again consistent with the regulated state hypothesis.

Force propagation inside a living cell

Ayama Tokuyasu[1], Hirokazu Tanimoto[1]
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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Mechanical forces generated inside living cells are essential in various cell-biological processes including cell motility and division. The location of force production is widely investigated by various methods such as live-cell imaging. However, it is far less understood how the produced forces propagate inside the cell to target their functional location, and how the propagation mode is determined by internal cellular structures. In this study, we established a new approach for mapping the propagation of mechanical forces in the cytoplasm of an adherent cell.

By combining intracellular magnetic tweezers with traction force microscopy, we determined how probe forces applied to the cell nucleus propagated in the cytoplasm to the cell-substrate boundary. In this experimental system, by applying forces of ~100 nN to a cell, we detect substrate displacement of ~5 μm. We calculated traction forces from the substrate displacement and quantified the results by introducing a propagator function between probe and traction forces. The result shows that the applied probe forces are propagated in cytoplasm mostly vertically. We also quantified the relationship between intracellular stress and strain of actin meshwork. In the presentation, we will show these results and discuss the characteristics of the intracellular force propagation and the roles of cytoskeletons.

Multiphoton line-scanning FLIM for fast, dynamic 3D imaging of breast cancer spheroids.

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[1]Comprehensive Cancer Centre, School of Cancer and Pharmaceuticals, King's College London, United Kingdom, [2]Institute for Integrated Micro and Nano Systems, United Kingdom

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Fluorescence lifetime imaging (FLIM) microscopy captures local biological variations using fluorescent probes and intrinsic markers. However, traditional FLIM approaches struggle with dynamic processes due to high photon requirements for accurate lifetime fitting. Time-correlated single-photon counting (TCSPC) systems are hindered by electronic dead time and pulse pile-up, necessitating prolonged exposure and high-powered lasers, which can damage samples.

We introduce a multiphoton line-scanning FLIM system featuring a novel single-photon avalanche detector (SPAD) array with on-chip histogramming, capable of acquiring up to 16.5 Giga-photons/s. Using a cylindrical lens to focus a laser line and a single-axis scanner to sweep it across the sample, fluorescence emission is de-scanned and projected onto the linear SPAD array. The 512 x 2-pixel sensor integrates 2 x 8 SPADs per pixel, each paired with a 16-bit time-to-digital converter. Photon arrival times are histogrammed and stored on-chip for efficient image reconstruction. This parallel excitation and detection method improves acquisition speed and reduces sample damage compared to traditional single-beam scanning FLIM.

We demonstrate this system's potential through functional 3D live-cell FLIM of breast cancer spheroids. Our tumour model combines HCC-1954 carcinoma cells with fibroblasts and endothelial cells. Spheroids stably expressing Gam-mScarlet3, a marker for DNA double-strand breaks (DSBs), and a γH2AX FRET-biosensor are used to monitor DNA damage repair. Changes in fluorescence lifetime post DNA damage reveal DSB sites and repair initiation, showcasing the system’s advanced capabilities.

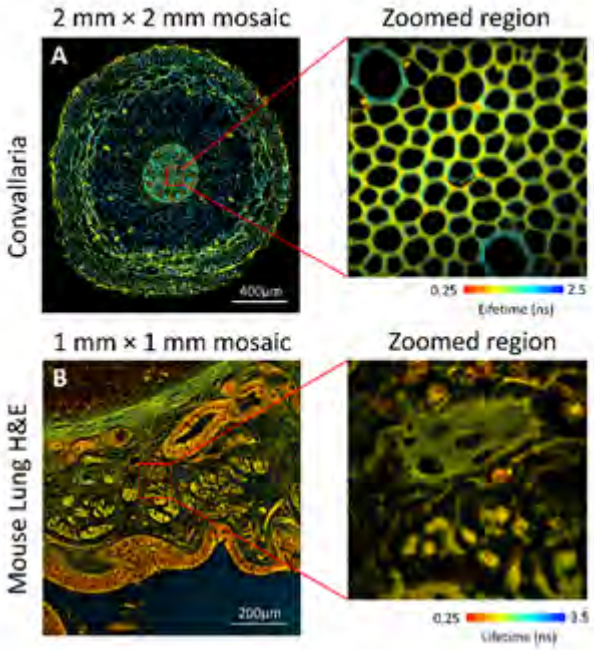

Figure 1: Macroscale FLIM composite images of: (A) Convallaria Majalis (7168 × 7168 pixels) acquired in 49 seconds and (B) Mouse pulmonary tissue section stained with H&E (3584 × 3584 pixels) acquired in 12.5 seconds. Zoomed regions of single image tiles (512 × 512 pixels) are also included.

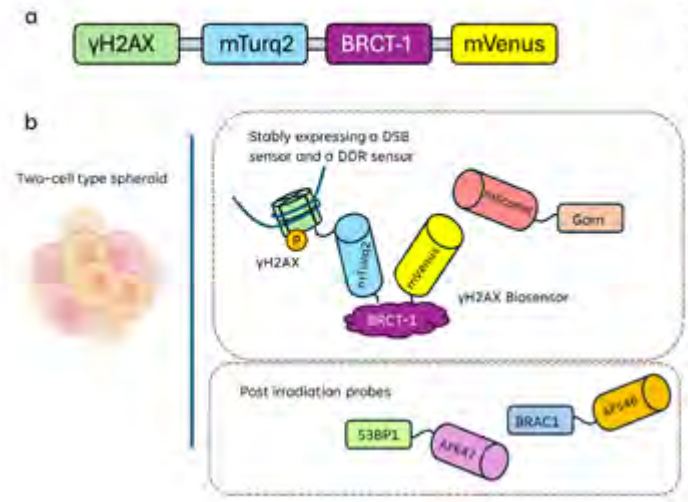

Figure 2. Experimental design and function of the γH2AX-based DNA damage repair biosensor in 3D culture. a) The biosensor consisting of full-length γH2AX linked by a 12-amino acid flexible linker (GGSGGSGGSGGS) to mTurquoise2. This is connected via the same linker to the BRCT-1 domain of MDC1, which is also joined by the same linker to the fluorescent protein mVenus. b) Multiplexed experimental design showing how Gam-mScarlet3 and the γH2AX biosensor will be used in tandem with tradition immunofluorescence to image the spheroid

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

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

The outer membrane (OM) of Gram-negative bacteria is an asymmetric cocktail of lipopolysaccharides (LPS), proteins (OMPs) and phospholipids that represents a formidable first line of defence against antibiotic compounds [1], maintains mechanical loads [2] and allows for rapid cell growth and division.

The OM must thus form a robust barricade whilst being sufficiently fluid to allow for biosynthesis and rapid adaptation of the membrane to the cell's environment. As yet, we lack a fundamental understanding of how these two apparently conflicting functions arise and are maintained. Such insight is crucial in the escalating fight against antimicrobial resistance, but is challenging to unpick, especially at the nanoscale and in living, growing cells.

Here, we use high-resolution atomic force microscopy (AFM) to directly map the organisation and dynamics of the outer membrane at the scale of single OMP trimers in live Escherichia coli cells [3]. We demonstrate that the heterogeneous interactions of OM components lead to proteinaceous networks interspersed with domains rich in LPS, each with distinct mechanical properties. The extent and connectivity of these OMP networks depends sensitively on the cells' growth phase and nutrient content, indicating a key relationship between outer membrane biophysics and the metabolic state of the bacteria.

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Self-organized guidance of mixed cell populations

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[1]University of Sheffield, United Kingdom, [2]Institute of Science and Technology Austria, Austria

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Cell and tissue movement in development, cancer invasion, and immune response relies on chemical or mechanical guidance cues. In many systems, this behavior is locally guided by self-generated signaling gradients rather than long-range, pre-patterned cues. However, how heterogeneous mixtures of cells interact and navigate through self-generated gradients remains largely unexplored. Here we introduce a theoretical framework for the self-organized chemotaxis of heterogeneous cell populations. We find that relative chemotactic sensitivity of cell populations controls their long-time coupling and co-migration dynamics, exhibiting an optimal range that leads to robust colocalized migration. Surprisingly, boundary conditions and interactions with an attractant reservoir substantially influence the migration patterns. We test our theoretical predictions with experiments on co-migration of different immune cell populations.

Finally, we compare relative influences of mechanical interactions vs. chemotactic coupling between different cell populations on their migration patterns. Our findings reveal self-generated chemotaxis as an elegant strategy for multicellular navigation beyond external signaling cues or direct intercellular interactions.

Intermittent migration of a cell cluster in a confluent tissue

Dr Rahil Valani[1], Dr Jan Rozman, Professor Julia Yeomans
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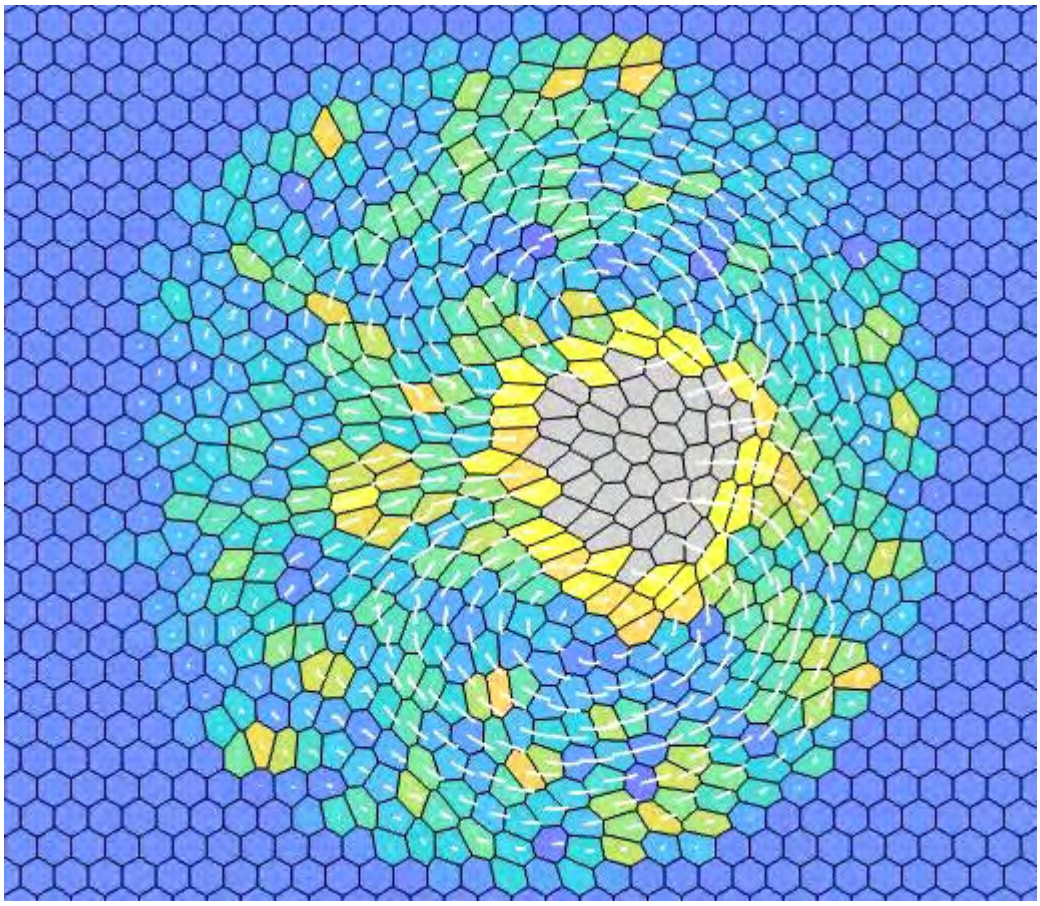
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

During early mouse embryogenesis a group of cells, the distal visceral endoderm (DVE), move through intermittent bursts of motion. Motivated by this we model the dynamics of a self-propelled (active) cell cluster within a background of passive cells in a vertex model of confluent tissue.

For small strengths of self-propulsion, the cluster comes to a halt, whereas for large strengths of self-propulsion, the cluster migrates steadily within the tissue. Interestingly, for intermediate strengths of self-propulsion, we find that the yield-stress rheology of the surrounding passive cells results in a regime of intermittent motion of the migrating cluster.



Nonlinear and chaotic dynamics of a microswimmer in confined flows

Dr Rahil Valani[1], Dr Brendan Harding[2], Professor Yvonne Stokes[3]
[1]University of Oxford, United Kingdom, [2]Victoria University of Wellington, New Zealand, [3]The University of Adelaide, Australia

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

In this talk, I will present our theoretical and numerical investigation of the nonlinear dynamics of a point-like active particle, e.g. a microswimmer, interacting with fluid flowing through a straight channel. For this particle-fluid system, we derive a constant of motion for a general unidirectional fluid flow and apply it to flows in channel with rectangular cross-sections.

We obtain a nonlinear dynamical system that displays a diverse set of active particle trajectories, both regular and chaotic, which we classify into different types of swinging, trapping, tumbling and wandering motion. Outcomes of this work may have implications for dynamics of natural and artificial microswimmers in experimental microfluidic channels that typically have rectangular cross-sections.

Signalling Molecule Detection in Liquid Cultures Using Surface-Enhanced Raman Spectroscopy

Mo Vali, Elle Wyatt, Kieran Abbott, Diana Fusco, Ashraf Zarkan, Jeremy Baumberg
[1]*University of Cambridge, United Kingdom*

Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Background: Interactions between bacteria are often mediated by extracellular bioactive metabolites. Indole is an important signalling molecule influencing biofilm formation. Surface-enhanced Raman spectroscopy (SERS) is used to detect indole in E.coli supernatant. SERS is performed on strains with and without the enzyme tryptophanase (TnaA) to understand TnaA's role in biofilm formation. TnaA is studied due to its potential to prevent E. coli biofilms in UTIs.

Methods: Two strains of E.coli BW25113 were prepared, one with a tnaA gene knockout and one wild type strain. 11 amino acids (L-Cysteine, L-Arginine, L-Alanine, L-Asparagine, L-Glutamic Acid, L-Glycine, L-Isoleucine, L-Methionine, L-Tyrosine, L-Tryptophan, L-Serine) whose effect on biofilm formation was known from existing work were added separately to M9 at 1mM concentration. SERS was performed on the supernatant. Gold nanoparticles were combined with Cucurbituril-5 molecules for the SERS substrate.

Results: Clear distinction seen in SERS spectra between wild-type and TnaA-knockout strains, primarily related to indole. Indole spiking confirmed dominant spectral peaks at Raman shifts of 600cm-1 and 760cm-1 relating to benzene and pyrrole ring modes, respectively. Unique spectral peaks were found in wild-type versus TnaA-knockout strains for most amino acids studied, suggesting a TnaA-dependent degradation pathway contributing to biofilm formation.

Conclusions: SERS is used to detect extracellular metabolites such as indole in a label-free manner. Biofilm formation was found to be partly mediated by a TnaA-amino acid degradation pathway for most amino acids studied. This work presents initial steps towards a mechanistic understanding for the role of the enzyme TnaA in biofilm formation using SERS.

UNIVERSITY OF CAMBRIDGE

UNDERSTANDING THE Physics of Life

Signalling Molecule Detection in Liquid Cultures Using SERS

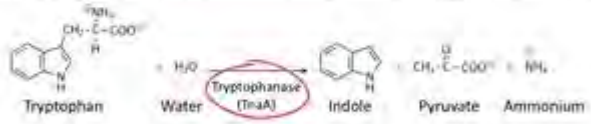
Moe Vali[1], Kieran Abbott[2], Elle Wyatt[3], Diana Fusco[1], Ashraf Zarkan[2] and Jeremy Baumberg[3]

INTRODUCTION

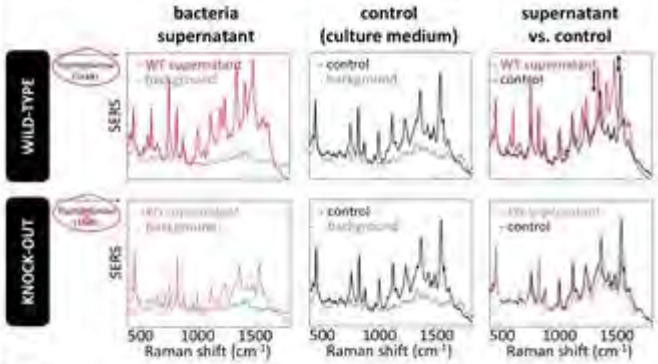
- **Interactions between bacteria** are often mediated by bioactive metabolites secreted into the environment[1].
- **Indole** is one such signalling molecule, influencing processes such as biofilm formation, antibiotic resistance and quorum sensing, present in 85+ species[2].
- **Surface-enhanced Raman spectroscopy (SERS)** is used to detect the presence of extracellular bioactive metabolites such as indole in supernatant of *E.coli* cultures.
- We also perform SERS on strains with and without the enzyme **tryptophanase (TnaA)** to explore its role in **biofilm formation** via the degradation of various amino acids.

ISOLATING INDOLE SIGNAL USING A GENE KNOCK-OUT

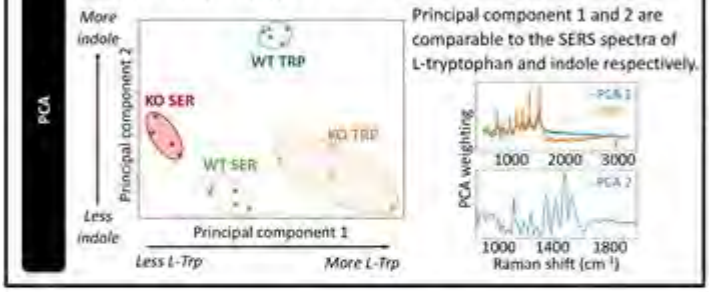
- To extract a clearer indole SERS peak from the supernatant, **the gene that produces the enzyme (TnaA)** that degrades the amino acid to indole was **knocked out**.



- SERS spectra of wild-type (WT) *E.coli* strains grown in L-Tryptophan show increased amino acid degradation compared to the knock-out (KO) strain.



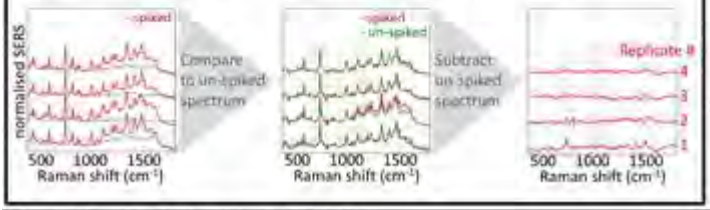
- PCA of SERS of wild-type and knock-out strains grown in different amino acids, L-Tryptophan (trp) and L-Serine (ser), shows a split between spectra.



Principal component 1 and 2 are comparable to the SERS spectra of L-tryptophan and indole respectively.

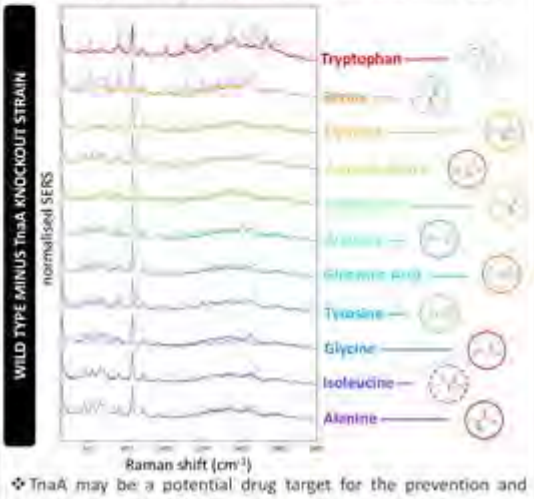
SPIKING TO DETERMINE PRESENCE OF INDOLE

- Wild-type supernatant spiked with indole to confirm indole SERS signature



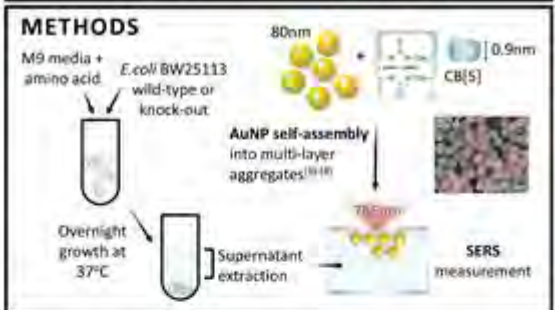
TOWARDS A MECHANISTIC APPROACH TO (PARTLY) EXPLAINING BIOFILM FORMATION

- Indole for biofilm formation has been extensively studied, but the effect of amino acids and the enzyme TnaA remains unclear[3].
- Prior work has shown several amino acids contribute to biofilm formation, mediated by the TnaA degradation pathway[4][5].
- WT and KO *E.coli* strains are cultured with different amino acids. Distinct spectra for KO and WT observed for most amino acids.



- TnaA may be a potential drug target for the prevention and treatment of *E.coli* biofilms in chronic/recurrent UTIs.

METHODS



LIMITATIONS & FUTURE WORK

- The equivalent amino acid spectra for the knock-out strain may provide a more insight into the TnaA-dependent pathway for biofilm formation versus just the wild type.
- Future work aims to purify TnaA and combine with amino acids, to verify whether this interaction is direct or indirect

CONCLUSIONS

- SERS is used to detect extracellular metabolites such as indole in a label-free manner. Biofilm formation is found to be partly mediated by a TnaA-amino acid degradation pathway.
- This work presents an initial step towards a determining a mechanistic understanding for the role of the enzyme TnaA in biofilm formation using SERS.

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Characterising the microbial composition of follicular fluid using 16srRNA sequencing and its importance for IVF outcomes

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Existing work on whether microbial communities are endogenous to follicular fluid has so far proved inconclusive. One study found decreased pregnancy, embryo transfer, and live birth rates associated with microbiota endogenous to follicular fluid, whilst another found no association. Culture-based methods have been used to detect certain microbes whilst failing to fully identify other potentially important microbes. Here we characterise the microbial composition of ovarian follicular fluid using 16srRNA sequencing and assess whether endogenous microbial species, abundance and diversity are predictive of embryo transfer outcomes during IVF treatment.

Methods: Paired follicular fluid and vaginal swab samples were collected for over 40 patients during oocyte collection from patients undergoing IVF / ICSI cycles. DNA was extracted and 16srRNA sequencing was performed. Several patient-level variables were tracked throughout the patient's IVF treatment, including embryo grading and outcomes. Microbial compositions were evaluated using standard alpha and beta diversity scores. PCA, linear regression and Shapley values were performed to assess relevance to IVF outcomes.

Results: An endogenous microbiome to follicular fluid was identified, including a broader range of microbial species beyond existing work using culture-based methods. An association with embryo transfer and pregnancy outcomes was identified, however factors such as endometrial thickness, age and collected oocytes were important in explaining outcome variation. Full results will be available at the presentation.

Conclusions: Follicular fluid is considered unsterile using 16srRNA sequencing methods on uncultured samples. Microbial compositions and abundance of certain genera are associated with IVF outcomes suggesting their potential as a biomarker for predicting IVF outcomes.

Proteins evolve structural robustness to cope with locally chaotic folding landscape as predicted by ESMfold

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

According to classical textbooks, the function of a protein derives from its structure which in turn results from the physical folding process of its amino acid sequence. Yet until recently, predicting protein structure from sequence was not feasible (unlike for RNA secondary structure), hindering large-scale investigations into evolutionary dynamics of protein structure. Now, the advent of large language models such as ESMfold allows a global exploration of the protein sequence-to-structure landscape.

We use ESMfold to predict the effect of mutations on thousands of natural proteins, including the entire yeast proteome and putative de novo proteins from several organisms, as well as random amino acid sequences. We find that established proteins have evolved high mutational robustness and inhabit a special region of phenotype space relative to random sequences whose mutational robustness is lower and decreases with their structural complexity. The robustness of de novo proteins resembles that of random proteins, even though, strikingly, some do take on globular folds that resemble those found in established proteins.

Our results paint a picture that distinguishes protein folding from other genotype-phenotype maps such as RNA folding and gene regulatory networks. In RNA, neutral networks are ubiquitous in genotype space, yielding robustness and evolvability. In contrast, there appears to be a tradeoff between robustness and evolvability in proteins. Natural proteins reside in a “flat” region of genotype space, suggesting limited evolutionary potential for duplicated genes. Conversely, de novo proteins emerge in an extremely “rugged” landscape, which may be equally hard for evolution to navigate.

From physics to vision: using ISETBio to predict visual performance from physical information

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Vision, akin to all physical systems, is limited by the presence of noise at multiple stages, and it fundamentally relies on differentiating between noisy distributions to detect or discriminate visual targets. ISETBio (https://isetbio.org/) is a computational toolbox designed to simulate the early stages of visual processing based on knowledge derived from anatomical, physiological and behavioral experiments.

Starting with an input image, ISETBio models the optical properties of the eye, the effects of eye movements, and the formation of the retinal image. It then calculates the cone photoreceptor excitations based on a realistic simulation of the cone mosaic that samples the retinal image. Both in modeling the retinal image and computing the cone responses, the modeling accounts for effects of wavelength (e.g., chromatic aberration, cone spectral sensitivities).

This framework allows predictions of visual performance based on the computed information available at the cone mosaic. ISETBio enables researchers to explore the relationship between the physical properties of the input image and visual functions across spatial and temporal dimensions.

We will demonstrate the application of ISETBio in predicting visual performance across three key behavioral tasks: 1) Vernier acuity task: detecting relative spatial offsets between nearby objects. 2) Temporal summation task: integrating light signals over time. 3) Chromatic discrimination task: discriminating between colours. Through these demonstrations, we highlight ISETBio's potential to address a wide range of questions in vision research. Our broad goal is to understand these processes through a multidisciplinary approach, bridging theoretical modelling and experiments involving human participants.

Optimised adaptive optics illumination strategies for three-photon microscopy in deep neuroimaging

Jingyu Wang[1], Qi Hu[1], Huriye Atilgan[2], Armin Lak[2], Randy Bruno[2], Martin Booth[1]
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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Multi-photon microscopy (MPM) with its advantages in optical sectioning, minimal invasion and cellular resolution has become the method of choice for intravital neuroimaging. While two-photon microscopy (2PM) techniques have been extensively used in studying cortex neuron activity in intact brains up to hundreds of micrometres deep, three-photon microscopy (3PM) extends the imaging depth well below one millimetre into subcortical regions. MPM imaging at great depth remains challenging because the focused excitation beam suffers from attenuation, scattering and wavefront distortion due to tissue medium.

Adaptive optics (AO) has been successfully adopted by both 2PM and 3PM imaging to compensate for aberrated wavefront induced by both the system and the specimen. Wavefront-sensor based AO methods, although direct in wavefront measurement, inevitably involve extra system complexity and are prone to non-common path error. Wavefront sensorless AO methods by using modal-based optimisation to estimate and correct aberrations, were shown to be simpler and more versatile. MPM typically requires femto-second lasers with ultra-short pulse-width and large pulse energy to generate nonlinear excitation to fluorescence. This requires optimisation for maximal transmission to penetrate tissue at great depths and underfilling the illumination profile at the objective lens for optimise image resolution. The strict requirement for illumination profile has not been fully considered in most current AO-MPM designs. We explored modified aberration modes for in-situ measured laser beam profiles that led to optimised AO performance in MPM imaging in deep tissue. We present the advantages of the synergy between optimised illumination strategies and an advanced machine-learning-based AO method.

Developing a modular platform of DNA-protein nanostructures for targeted protein degradation

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

DNA origami is a versatile technique by which high complexity nanostructures can be created by leveraging the self-assembly properties of DNA molecules to fold a long, single-stranded DNA scaffold into a desired shape using short oligonucleotide staple strands [1]. DNA nanostructures are soluble, biocompatible, easily programmable and amenable to functionalisation with bioactive ligands, thus making them promising candidates for next-generation therapeutic devices [2].

In this project, origami techniques were used to engineer triangle- and rectangle-shaped nanostructures functionalised with bioactive molecules targeting epidermal growth factor receptor (EGFR), a receptor tyrosine kinase frequently overexpressed in various cancer types [3]. The project aimed to induce EGFR degradation in EGFR-GFP transfected HeLa and MDA-MB-231 cells via the endo-lysosomal pathway using nanostructures hybridised to the high-affinity EGFR-targeting peptides, Ge11 and Ge22, as well as Cetuximab, an anti-EGFR monoclonal antibody (Figure 1a) [4,5,6].

The nanostructures were successfully synthesised and functionalised, as confirmed by agarose gel electrophoresis and atomic force microscopy (Figure 1b). Confocal microscopy images of HeLa cells revealed that after three hours of incubation with functionalised DNA origami, the nanostructures colocalised with the cell membrane (Figure 1c). After three hours, evidence of endocytosis of the peptide-functionalised nanostructures was observed, with this internalisation becoming more pronounced after 24 hours. Although unfunctionalised nanostructures also exhibited some internalisation after 24 hours, it was comparatively less noticeable.

[Confocal imaging and flow cytometry functional assays are currently underway to quantitively assess EGFR targeting and degradation induced by Cetuximab/Cetuximab-functionalised nanostructures in comparison with peptide-functionalised nanostructures in Hela and MDA-MB-231 cells].

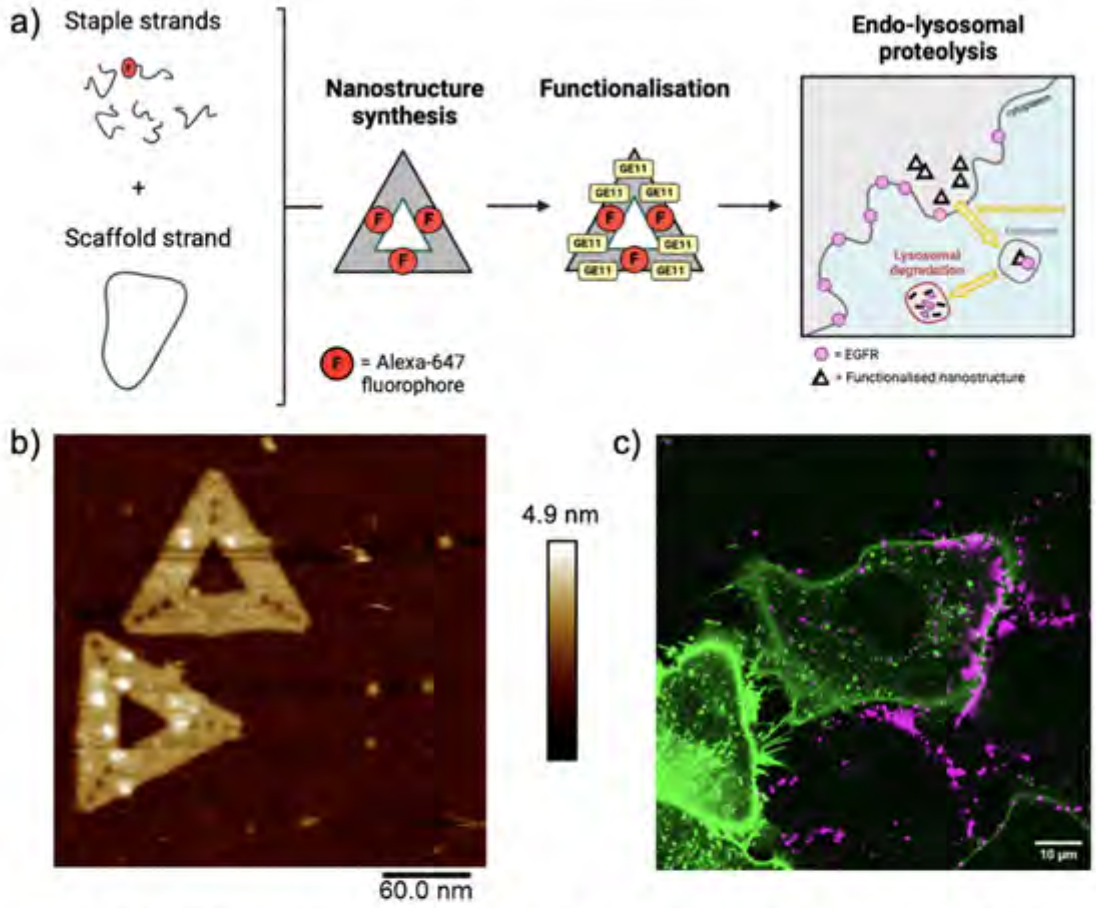

Figure 1. GE11-functionalised triangle nanostructure workflow schematic and imaging results. a) Schematic detailing nanostructure synthesis from scaffold and staple strands, functionalisation with Ge11 peptides and uptake into the endo-lysosomal pathway; **b)** Atomic force microscopy image of Ge11-functionalised triangle nanostructures, and **c)** Confocal microscopy image of EGFR-GFP (green) transfected HeLa cells after 3 hours incubation with Ge11-functionalised triangle nanostructures (magenta).

Molecular determinants of mechanics and shape changes during cell division

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Cells undergo significant shape changes during division, driven by spatiotemporal regulation of actomyosin cortex mechanics. Pre-division rounding is mediated by myosin recruitment, increasing surface tension. During anaphase, myosin accumulates at the equator while decreasing at the poles, aligning the actin cytoskeleton and enabling equatorial flattening and furrowing. While RhoA controls myosin activity and actin polymerization via RhoGEFs and RhoGAPs, it remains unclear whether F-actin nematic alignment is signal-driven or an emergent property.

We investigate the evolution of surface tension using AFM and compare it to the dynamics of myosin accumulation. Between anaphase and the onset of furrowing, myosin intensity increases fourfold at the equator while surface tension increases tenfold. This suggests that part of the tension increase is due to actin filament alignment, supported by computational simulations. One potential mechanism is an increase in F-actin density due to cortical flow driven by myosin at the equator. Myosin contractility influences furrow kinetics and stiffening. High-dose blebbistatin inhibits furrowing, while low doses slow it. Although blebbistatin reduces equatorial surface tension, it does not affect stiffening kinetics, suggesting alignment is signaling-driven, while furrow closure depends on myosin. We now explore equatorial RhoGEFs/GAPs using RNAi, mechanical measurements, and shape analysis. Interestingly, during Ect2 knockout, cells furrow slower without any myosin accumulation in the furrow.

Can AI classification of cancerous tissue yield chemical insight and prognosis?

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

A variety of AI techniques have been shown to classify cancerous tissues. However, a more difficult problem is to predict the prognosis of cancer and to combine this with chemical insight into the underlying chemical changes giving rise to classifications and that drive the progression of the disease.

This presentation will explore these issues in the well-defined case of metastatic oral squamous cell carcinoma (OSSC) which is the eighth most common form of cancer in the UK and the incidence of which is continuing to rise. For this disease AI techniques have had considerable success in identifying biomarkers that classify the disease, and the several types of benign and associated tissue, [1,2] and some success in predicting the prognosis of lesions [3,4]. However, identifying the underlying chemical differences between different types of tissue is more difficult, though progress can be made by combining insights obtained from AI techniques with other techniques such as image fusion, which has been shown to identify contributions from cytokeratin, collagen and DNA [5], and scanning near field optical microscopy [1].

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A Machine Learning Approach to Identify Carbon Dioxide Binding Proteins for Sustainability and Health

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Carbon dioxide (CO_2) has a fundamental role in biological processes throughout the biosphere. While much is known about the impact of CO_2 on the overall physiology of an organism, much less is known about how its interaction with specific biomolecules may affect their function [1, 2]. Our work focusses on carbamylation, a non-enzymatic reversible protein post-translational modification (PTM) where CO_2 binds onto the neutral lysine ε-amino groups [3]. A novel mass spectrometry-based experimental technique, TEO trapping, has been recently used to demonstrate that, for reasons yet unclear, CO_2 does not bind to every lysine [2].

While informative, this experimental technique is laborious, which limits our ability to gain a clear and comprehensive view of the interactions between CO_2 and proteins. For this reason, we are carrying out extensive molecular dynamics simulations and developing a computational method to predict which lysine, in any protein, may undergo carbamylation.

We found that standard metrics (pKa, solvent accessible surface area, and amino acid depth) are insufficient to singlehandedly explain why some lysine may be modified, but not others. Therefore, we are now exploring the usage of atomic environment vectors, commonly used in machine learning, for this classification task.

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Quantifying the Role of DNA Topology in Cas9 Activity using Atomic Force Microscopy

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR-associated proteins (Cas) arose as a bacterial defense mechanism against viral infections and are now a powerful tool used for genome editing [1], however, off-target effects, where Cas9 binds to unintended DNA sequences, remain a significant challenge [2]. Off-target structures have been captured using X-ray crystallography and Cryo-EM. DNA topology, including negative supercoiling, has been shown to strongly modulate off-target Cas9 activity [3], however the molecular basis of this remains elusive.

We have developed a new multi-class deep-learning algorithm to segment Cas9 bound to DNA minicircles in AFM images, and implement this in our open-source software TopoStats (Figure 1). Our pipeline determines that supercoiling induces defects in DNA minicircles, which causes them to collapse into a condensed form. We show that Cas9 binding is able to restore these molecules to an open state. Our methods for quantifying the effect of supercoiling on DNA structure and protein activity, could have an impact spanning genome stability, DNA topology and wider DNA-protein interactions.

Figure 1: Negative supercoiling induces structural collapse in DNA minicircles, which is rescued by Cas9 binding (A). Multi-class deep learning segmentation enables masking (B), skeletonisation (C), and quantification (D) of each molecular complex.

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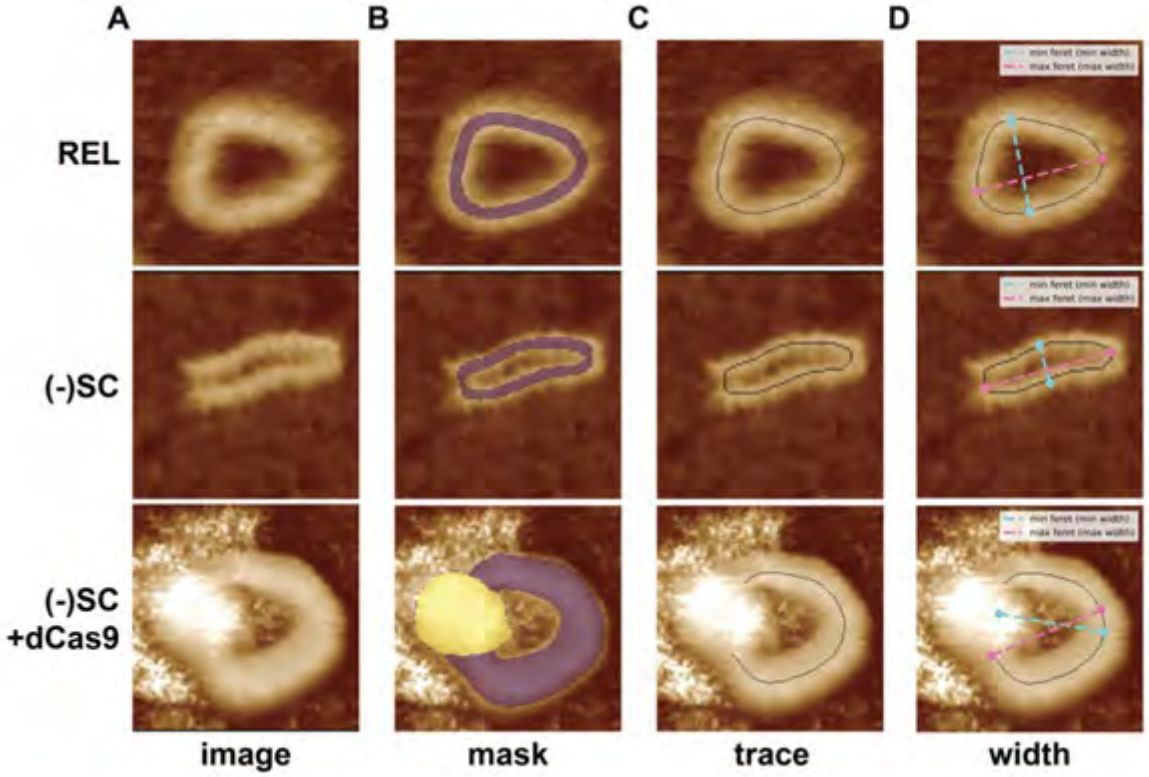
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Spore germination: what can we learn from live spore imaging?

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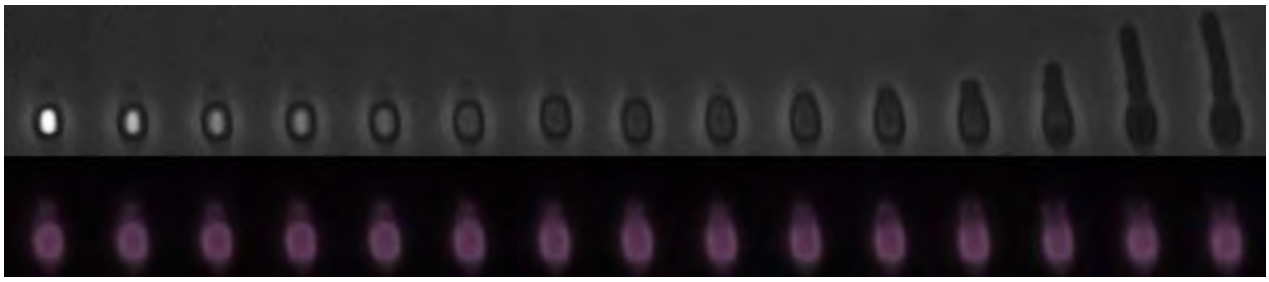
Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Clostridium sporogenes is an anaerobic, Gram positive species which produces endospores to survive unfavorable conditions. C. sporogenes is used as a surrogate to study its lethal sister species, Clostridium botulinum, and also causes costly spoilage in the food industry in its own right. Spores have many layers that work in different ways to protect the DNA and these must be breached or degraded during the germination process to allow the cell to resume growth. In this work, we focused on three cysteine rich proteins within these outer layers by comparing the behaviour of wild type cells with deletion mutants.

Using live phase and fluorescent time-lapse microscopy and automated pixel intensity tracking, we identifed defects in spore rehydration as well as differences in both individual spore morphology and how the vegetative cell exits the spore. Resolving the function of these proteins will allow us to understand the choreography of molecular processes that allow cells to germinate from spores, where they can then infect food products and cause disease.



Quantifying the Mechanical Properties of Stress Granules in Live Cells

Dr Jack Law[2], Dr Carl Jones[2], Dr Thomas Stevenson[2], Mr Thomas Williamson[1], Prof Matthew Turner[3], Prof Halim Kusumaatmaja[1], Prof Sushma Grellscheid[2]
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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Biomolecular condensates are membrane-less compartments, rich in specific biomolecules, which play many important roles in sub-cellular organisation such as regulating stress response and RNA transcription. There is growing recognition that the mechanical properties of condensates govern their macroscopic behaviour and, in turn, are determined by condensates' biomolecular composition.

However, until recently, it has been difficult to measure these properties at scale in-vivo. We demonstrate a flicker spectroscopy method for measuring two key mechanical properties of thousands of condensates in live cells, with an initial study focusing on stress granules. We find that the fluctuation spectra of stress granules in live cells cannot be adequately fitted with an interfacial tension-only model, as expected for simple Newtonian liquids. Instead, the measured fluctuation spectra require an additional contribution, which we attribute to elastic bending deformation. We then show that at the population level, surface tension and bending rigidity span several orders of magnitude so cannot be accurately determined by observing only a small number of condensates. However, the mean behaviour of these properties across a population of stress granules can be used to distinguish between granules induced by different chemicals (e.g., arsenite vs clotrimazole) or containing different ratios of constituent proteins.

Additionally, we have preliminary results which suggest that stress granules display broken detailed balance in the amplitudes of the fluctuation modes, which we believe is a signature of ageing. Taken together, these results support the view that condensates are viscoelastic droplets which age with time.

Extracellular matrix alignment regulates cellular mechanotransduction

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

During development, wound healing, and cancer invasion, the organisation of the extracellular matrix (ECM) plays a crucial role in guiding cell behaviour, suggesting that individual cells can detect ECM alignment cues and translate them into functional responses. However, the mechanisms underlying ECM sensing and its impact on intracellular signalling remain largely elusive. Here, we use a photo-patterning approach to generate single cell patterns featuring thin, uniaxial lines of fibronectin, allowing precise control over the cell shape, line gap size, and geometry.

We find that the orientation of cells relative to the ECM alignment governs the efficacy of nuclear force transmission and the localisation of the mechanosensitive transcription factor YAP. These changes are coupled with marked variation in focal adhesion morphology and actin cytoskeleton architecture depending on ECM alignment.

Additionally, we observe a gap-size dependence of these effects, where differences are abrogated at low ECM line spacing. Our results show that the spatial arrangement of the ECM is a powerful regulator of cellular mechanosignalling.

Mechanobiology of Tomato Fruit Cell Walls During Ripening: Insights into Callose and Cellulose Dynamics

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Tomatoes suffer extensive post-harvest losses due to damage and decay linked to ripening-induced softening. This softening is associated with changes in the composition and structural looseness of the cell wall, a polysaccharide matrix crucial for maintaining cell shape and providing mechanical support. Understanding the mechanobiology of cell walls during tomato development is essential for identifying traits that can reduce these losses. During fruit ripening, nutrient transport shifts from symplasmic (through plasmodesmata intercellular channels) to apoplastic mechanisms, a process regulated by callose deposition in the cell wall. This regulation by callose presents a unique target for improving fruit resilience.

Our study investigated the mechanical properties and composition of tomato fruit cell walls during development, with a focus on callose and cellulose. Using immunolocalization, we demonstrated that callose deposition undergoes distinct changes, potentially driving the transport switch. Manipulating callose metabolism through the transient overexpression of beta-1,3-glucanase genes in fruits revealed that callose significantly impacts cell wall composition. Atomic force microscopy (AFM) showed that decreased callose levels increased cell wall stiffness. Additionally, AFM revealed that cellulose microfibril bundles become progressively thinner over a six-week ripening period, while elastic modulus changes independently of cellulose thickness.

These findings highlight the complex relationship between cell wall mechanics and biochemical composition. While callose levels correspond with mechanical changes, the separation of elasticity from overall composition indicates that fruit softening involves complex biomechanical processes beyond simple loosening. This mechanobiological insight positions callose as a promising target for strategies aimed at enhancing tomato fruit quality and durability.

Design of DNA-peptide nanostructures against intracellular targets in cancer

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

A promising approach for the development of effective cancer treatments is to target specific proteins involved in cell signalling pathways and control their activity. In this project, we are designing peptide-functionalised DNA nanostructures targeting the tankyrase proteins, regulators of the Wnt signalling pathway. Changes in tankyrase expression or activity have been linked to various hard-to-treat cancers.

In recent work, a new class of highly specific peptide inhibitors of tankyrases were developed, based on modulating protein-protein interactions (PPI) by mimicking the interacting surface of the natural binding partner protein. A challenge we are addressing in this project is efficient delivery of the inhibitor peptides intracellularly to the desired site of action. To do so we are utilising DNA nanostructures, which act as an active carrier: the density and distribution of the peptide therapeutics on the nanostructures can be finely tuned, while the shape and surface properties of the nanostructures can affect their uptake by cells. We have successfully loaded DNA nanostructures of two different geometries with tankyrase-inhibiting peptides using azide-DBCO click chemistry.

We show that HeLa cells and the Wnt-active cell line SW480 readily uptake non-functionalised DNA nanostructures, as well as DNA nanostructures that carry the tankyrase binding peptide. Using super-resolution microscopy, we show that the DNA nanostructures are primarily localised within the lysosomes, indicating that they are entering the cells through the endolysosomal pathway.

Our current strategies are focused on functionalising the nanostructures with lysosomal escape peptides, to direct them to the desired site of action.

Bionics of Plant Tendrils

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Poster Session 2, Drinks Reception and Exhibition, March 25, 2025, 17:30-19:30

Connection between plant growth and mechanical stresses remains a puzzling problem, particularly in tendrils. Their coiling ability depends on the interplay between growth patterns and mechanical forces. Tendrils in plants like cucumbers, vines, and passionflowers—undergo a writhing transition after attaching to a support, forming two helices with opposite chiralities. Experiments on about 100 cucumber tendrils monitored curvature evolution over three days under controlled axial traction. Above a critical load Tc the writhing failed. Below Tc the transition to successful writhing exhibited a significant jump in the generated curvature. In a simplified geometry, differential growth in tendrils was modeled at the cell scale using the Lockhart growth model, combined with Kirchhoff rod theory. The resulting bifurcation diagram reproduces fairly the experimental data.

Moreover, it revealed that the transition between failed and successful writhing can either be subcritical or super critical, depending solely on the tendril's twist-to-bending ridigity ratio. The derived stress-dependent curvature evolution may extend to other tendril species and broader curvature generation mechanisms in plants.
The aforementioned findings constitute a solid basis for progress in the field of plant robotics and tendril-based bionics.

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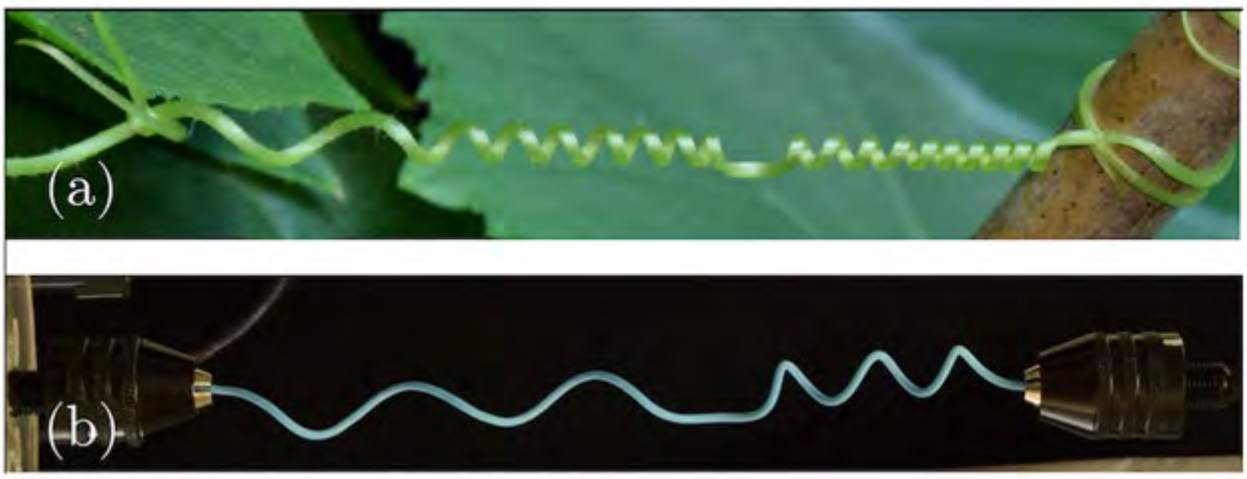

Transport Dynamics of Red Blood Cells in the Microcirculation

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Poster Session 1, Drinks Reception and Exhibition Commences, March 24, 2025, 17:30-19:30

Red blood cells (RBCs) are essential in delivering oxygen to tissues and organs across intricate networks of small vessels or narrow passages. Notwithstanding decades-long research, it remains elusive until recently how the transport dynamics of RBCs can mechanistically contribute to the pathophysiology of microcirculatory disorders, either through modulating the haematocrit distribution or wall shear stress patterning.

This talk will introduce the key findings of our recent modelling works based on hamster capillaries [1], mouse retina [2] and human placenta [3], respectively. Through combining cell-resolved mesoscopic simulations with imaging data of animal models or biological tissues, we have qualitatively and quantitatively investigated the RBC behaviour in a range of vascular/extravascular environments including capillary-level bifurcations, microvascular networks and porous media. Our studies provide potential mechanisms for hindered microcirculatory blood flow under pathological conditions where the RBC stiffness or vascular morphology have markedly altered.

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