Higgs Centre Workshop: Physics of Biological Systems

27-29 May 2025, University of Edinburgh

Abstracts
(Invited talks, contributed talks and posters)

Invited talks

Ada Altieri - Moment-matching inference for gut microbial communities.

The remarkable biodiversity observed in natural ecosystems has recently attracted increasing attention [1], particularly among theoretical physicists and mathematicians. In this talk, I will address timely questions in theoretical ecology by discussing a Generalized Lotka-Volterra (GLV) model with random species interactions and noise fluctuations [2].
By applying methods from disordered systems and random matrix theory, I will uncover a rich and ultimately hierarchical, organization of the equilibria to be associated with glass-like features and dynamical slowdowns.
I will then propose a *proof of concept* showing how this disordered framework can effectively capture the complexity of large microbial communities, with a particular focus on the human gut. Analyzing metagenomic data from both healthy individuals and patients suffering from inflammatory bowel diseases, I will map distinct physiological states to different disorder- and noise-driven regimes within the GLV model [3].

References:

[1] I. Hatton, O. Mazzarisi, **A. Altieri**, M. Smerlak, *Science* 383 (2024)
[2] **A. Altieri**, F. Roy, C. Cammarota, G. Biroli, *Phys. Rev. Lett.* 126 (2021)
[3] J. Pasqualini, A. Maritan, A. Rinaldo, S. Facchin, E. V. Savarino, **A. Altieri*** & S. Suweis*, eLife (2025) https://doi.org/10.7554/eLife.105948.1

Peter Bieling - Biochemical principles of Rho GTPase patterning.

Rho GTPases form plasma membrane-associated patterns that control the cytoskeleton during cell division, morphogenesis, migration, and wound repair. Their patterning involves transitions between inactive cytosolic and active membrane-bound states, regulated by guanine nucleotide exchange factors (GEFs), GTPase-activating proteins (GAPs), and guanine nucleotide dissociation inhibitors (GDIs). However, the relationships between these transitions and role of different regulators remain unclear. We developed a novel reconstitution approach to study Rho GTPase patterning with all major GTPase regulators in a biochemically defined system. We show that Rho GTPase dissociation from RhoGDI is rate-limiting for its membrane association. Rho GTPase activation occurs after membrane insertion, which is unaffected by GEF activity. Once activated, Rho GTPases are retained at the membrane through effector interactions, essential for their enrichment at activation sites. Thus, high cytosolic levels of RhoGDI-bound GTPases ensure a constant supply of

inactive GTPases for the membrane, where GEF-mediated activation and effector binding stabilize them. These results delineate the route by which Rho GTPase patterns are established and define stage-dependent roles of its regulators."

Chris Brackley - From order to disorder in chromatin fibres

Chromatin is the substrate for all DNA-associated processes, and understanding its structural and dynamical properties is crucial for our understanding of gene regulation and other nuclear processes. It was once thought that chromatin would adopt very regular structures, for example, the 30-nm diameter solenoid-like fibres which were often presented in textbooks. But there is now much evidence which suggests that chromatin actually adopts a broad range of different structures within cells, and that these different structures play an important role in function. However, we do not have a clear understanding of what controls fibre structure and properties. I will present results from recent work which combines experiments and computer simulations to study the properties of artificial chromatin fibre constructs which mimic different types of chromatin. This shows that irregularity in nucleosome positioning can lead to broad and dynamic variation of many features of the resulting fibres, which, for example, could be the source of noise, cell-to-cell variability and plasticity in gene expression.

Michael Chiang - Understanding Orientational Order in Cell Monolayers with Multiphase Field Modelling

Cells in biological tissues often move collectively and form dynamic spatial patterns that are important in processes such as embryonic development and cancer progression. Recent research suggests that different kinds of orientational order can exist within a tissue and that they can be interrelated, though the mechanisms coupling them remain ill-understood. In this talk, I will discuss how one can use multiphase field models to study orientational order in cell monolayers by incorporating different biomechanical forces acting on cells, such as intercellular friction and self-motility. I will show that variations in friction and motility lead to a transition from solid-like to fluid-like behaviour, during which local nematic order in cell shapes arises, driven by shear-induced alignment. This nematic order is strongly coupled to local hexatic order in cell positions, with +1/2 topological defects aligning with 5–7 disclination pairs—the hallmark defects of the hexatic phase. I will provide a mechanical-geometric argument to explain this coupling and how it is related to cellular extrusion events. The work highlights intercellular friction is a key contributing factor in regulating nematic and hexatic ordering in multicellular systems

Nathan Goering - Cell cycle oscillations balance responsiveness and stability in a developmental cell polarity network.

Early in the development of *C. elegans*, the conserved PAR cell polarity network patterns asymmetric cell division of germline blastomeres and thereby guides lineage specification. During this process, blastomeres must adapt to dramatic shifts in cellular context, discriminate among competing cues, and respond to changing developmental signals to ensure that they polarize at the correct time, in the right place, and with the correct

orientation. Thus, polarization of blastomeres must be both highly sensitive to cues but also yield a polarised state that is sufficiently robust to provide reliable control over downstream pathways. This need to balance signal-sensitivity with output-stability poses a paradox as theoretical work suggests that the same molecular feedback that stabilizes outcomes against perturbations or stochastic variation can also reduce sensitivity, potentially hindering the blastomeres' ability to adapt to changes. How cells resolve this conflict is poorly understood. I will discuss our recent identification of a cell cycle dependent oscillation in network feedback as a key requirement for proper cue-dependent polarization. Specifically, we show that blastomeres are born in a low-feedback regime that allows developmental cues to induce and orient molecular asymmetries. At mitotic entry, increased CDK-1 activity shifts cells into a high-feedback regime that consolidates asymmetries into stable, well-defined PAR domains. Critically, acute perturbation of either the high- or low-feedback phase compromised polarization: inhibition of CDK-1 activity during the high-feedback phase undermined stable polarity maintenance, whereas perturbing the oscillatory transition into the low-CDK-1 state led to failures in symmetry breaking and polarity reorientation. We propose that such oscillations are a general mechanism for cells to sample distinct feedback regimes, allowing dynamic optimization of network behaviour.

Stephan Grill - Chiral Morphogenesis

Abstract: One of the most remarkable examples of self-organized structure formation is the development of a complex organism from a single fertilized egg. With the identification of molecules that participate in this process of morphogenesis, attention has now turned to capturing the physical principles that govern the emergence of biological form. What are the physical laws that govern the dynamics and the formation of structure in living matter? Much of the force generation that drives morphogenesis stems from the actomyosin cortical layer of cells just underneath the cell surface, which endows the surface with the ability to generate active stresses and active torques that can drive reshaping. We combine theory and experiment and investigate how the actomyosin cell surface deforms and how it supports chiral rotations, and how these events together participate in chiral morphogenesis and the establishment of a left-right principal body axis in both the nematode worm and the Japanese quail.

Rhoda Hawkins - The force of molecular motor movement on filaments

Molecular motors are proteins that bind to filaments in a cell and can move along a filament. Their natural stepping movement along a filament can exert force on another object if the motor is bound to that object. Examples of such objects include vesicles or another filament. In cells, there are many motors and their collective motion can result in interesting behaviour. For example, motors often work together in teams and this increases the total force they can exert. Sometimes teams of motors work in opposite directions like in a "tug of war" game. When there are multiple parallel filaments these can be thought of as multiple lanes on a motorway with the analogy of molecular motors as motor cars. We can then consider the effect of motors changing lanes.

In this talk we will consider models of multiple motors and multiple filaments. We will discuss particular cellular examples and present some analytical results and simulations. We suggest the force of molecular motor movement on filaments can result in a varied cell processes from cargo transport to nuclear deformation and even parasite invasion.

Gijsje Koenderink - How cytoskeletal crosstalk makes cells strong

Cells are dynamic but also need to withstand large mechanical loads. This paradoxical mechanical behaviour is governed by a polymer scaffold known as the cytoskeleton. How can the cytoskeleton combine mechanical strength with the ability to dynamically adapt its structure and mechanics? I will summarize our recent insights in this question obtained via quantitative measurements on living cells coupled with experiments on cell-free model systems. I will focus on the role of mechanical crosstalk between the actin, intermediate filament, and septin cytoskeletal networks, three key determinants of cell mechanics. These filamentous systems contribute complementary structural and dynamical properties while at the same time their activities are closely coordinated via accessory proteins. I will show that combining mechanical measurements on cells and cell-free systems allows us to dissect the collaborative and individual roles of the cytoskeletal systems. Our findings may eventually be interesting to guide the search for selective anticancer drugs, since cancer cells often overexpress specific intermediate filament or septin proteins, leading to abnormal mechanical behaviours.

Martin Loose - **How Filament Mortality Drives FtsZ Self-Organization**

Treadmilling filaments grow by the addition of subunits to one end while simultaneously losing them at the other, resulting in directional motion of the filament without net movement of individual monomers. A key feature of this property is filament mortality—when growth is inhibited, filaments continue to shrink until they disappear entirely.

In this talk, I will explore how filament mortality contributes to the self-organization of treadmilling FtsZ filaments, a bacterial tubulin homolog essential for cell division. Using reconstituted systems of purified fluorescent FtsZ and its membrane anchor FtsA on supported lipid bilayers, we examined how geometric confinement shapes filament behaviour and large-scale pattern formation. Micropatterned chromium barriers enabled us to control confinement, while TIRF microscopy allowed us to track filament dynamics with high spatial and temporal resolution.

We show how confinement modulates key physical parameters such as filament length, monomer lifetime, and interactions with boundaries, all of which influence the emergence of ordered structures. These insights provide a step toward a mechanistic understanding of how treadmilling filaments self-organize into functional assemblies within the crowded, spatially constrained environment of the cell.

Satyanarayan Majumdar - **Universal dynamics of a passive particle driven by Brownian motion**

We study a simple toy model of predator-prey dynamics with non-reciprocal interaction: an overdamped ``passive" particle driven by non-reciprocal interaction with a “driver” Brownian
particle. When the interaction between them is short-ranged, the long-time behaviour of the
driven particle is remarkably universal—the mean-squared displacement (MSD) and the typical
position of the driven particle exhibit the same qualitative behaviour’s independent of the specific form of the potential. In particular, the MSD grows as $t^{1/2}$ in one dimension and $\ln t$ in two spatial dimensions. We compute the exact scaling functions for the position distribution in d = 1 and 2. These functions are universal when the interaction is short-ranged. For long-ranged interactions

decaying as a power law, the MSD of the driven particle grows as t^{ϕ} with exponent ϕ depending on the tail exponent of the interaction.

Cristina Marchetti - **Motile defects in active nematic solids as organizing centres of morphogenesis**

Motile topological defects are the hallmark of active nematic liquid crystals, where defect creation, motion and annihilation continuously remodel the texture and drive self-sustained active flows. Defects have also been shown to play an important role in the organization of epithelial tissue and in animal morphogenesis. In this talk I will describe topological defects in an active nematic elastomer – a solid-like materials where forces are generated internally by active processes. I will show that in these active solids defects can become motile through local melting of the nematic texture driven by strains induced by active stresses. Unlike in fluids, where defects are advected by active flows, this mechanism does not require flow of material as the defect move relative to the medium via local remodelling of the texture. This work provides a natural framework for understanding the restructuring of the nematic order observed in the fresh water polyp Hydra when the organism regenerates itself from an excised fragment.

Agnes Noy – **Towards modelling DNA in biological environments**

When aiming for atomic detail, DNA has typically been characterized using short, relaxed fragments (up to 50 base pairs or bp). However, inside cells, DNA is a very long polymer that is supercoiled, subjected to bending and pulling forces, and surrounded by a crowded environment. In our lab, we have developed approaches and protocols for simulating DNA at the atomic level while accounting for these mechanical stresses in order to recreate more realistic conditions. In my presentation, I will show how DNA structure and dynamics respond to supercoiling when combined with pulling and DNA-bending proteins (1-4). In addition, I will explain how sequences such as A-tracts introduce global DNA curvature on a

larger scale (5). Finally, I will provide unpublished atomistic insights into the process of target searching and binding between some of the most abundant proteins and DNA.

1. ALB Pyne *et al., Nat Commun*, **12**, 1053 (2021)
2. S Yoshua *et al., Nuc Acids Res*, **49**, 8684-8698 (2021)
3. GD Watson *et al., Comput Struct Biotech J*, **20**, 5264-5274 (2022)
4. M Burman and A Noy, *Phys Rev Lett,* **134**, 038403 (2025)
5. T Gardasevic and A Noy, *Nanoscale***, 16**, 18410 – 18420 (2024)

Juraj Szavits-Nossan - Exploring the landscape of stochastic gene expression models using queueing theory

Gene expression is a fundamental biological process in which genetic information encoded in the DNA is used to produce RNA and protein molecules. RNA molecules are typically present at low copy numbers, leading to significant molecular noise. This noise is usually modelled by Markov processes in which genes and their genetic products (RNA and proteins) "jump" between discrete states representing various molecular events. While a large body of work has been devoted to improving these models to better match reality, solving them becomes tedious and even impractical as their complexity increases. In this talk, I will show a deep connection between stochastic models of gene expression and queueing theory. By exploring this connection, I will show how decades old results from queueing theory can be employed to solve whole classes of these models in a simple and elegant way, which in turn may ease their integration with experimental data.

Xiaohua Shen - From DNA to Life: Decode the noncoding genome

Life begins with a fertilized egg and undergoes intricate developmental processes, guided by the DNA within the egg that carries essential instructions for shaping the four-dimensional patterning of an organism. The remarkable versatility of our genome enables a single genome to generate hundreds of distinct cell types. However, the specific algorithm governing cell-fate specification remains unknown. Intriguingly, the majority of mammalian genomes (about 98%) consist of noncoding sequences that produce noncoding RNA (ncRNA) transcripts, predominantly residing in the nucleus, defying the traditional dogma of protein synthesis. In this talk, I will discuss the evolving paradigm that has fundamentally transformed our understanding of gene regulation consensus.

Julien Tailleur - Motility-regulation across scales in bacterial mixtures

In this talk, I will discuss how bacterial mixtures self-organize thanks to mediated interactions like quorum-sensing and chemotaxis that regulate their swimming gait. By explicitly relating microscopic and macroscopic dynamics, I will show how to account quantitatively for the rich behaviours observed in microscopic simulations including phase separation, demixing, as well as a wealth of dynamical patterns. Finally, I will show how random motility regulation in complex bacterial mixtures generically induces community formation, eventually leading to the fragmentation of the ecosystem.

Raphael Voituriez – Cellular footprints : examples of emergent memory effects in cell migration

Living cells actively migrate in their environment to perform key biological functions—from unicellular organisms looking for food to single cells such as fibroblasts, leukocytes or cancer cells that can shape, patrol or invade tissues. Cell migration results from complex intracellular processes that enable cell self-propulsion, and has been shown to also integrate various chemical or physical extracellular signals. While it is established that cells can modify their environment by depositing biochemical signals or mechanically remodelling the extracellular matrix, the impact of such self-induced environmental perturbations on cell trajectories at various scales remains broadly unexplored. I will discuss examples where such interactions with the environment can have deep consequences on the large scale cell dynamics, and show that they can effectively endow cells with a memory of their past trajectory.

Kirsty Wan - Perspectives on multiciliary coordination across scales.

Cilia are hair-like protrusions found on cells that facilitate various physiological flows, whether external (outside the organism) or internal (such as feeding or mucociliary clearance). When multiple cilia are in close proximity, they interact, leading many types of local and global coordination patterns. These interactions, which can occur through fluid or via elastic/cytoskeletal linkages, are often complex and system-dependent. This talk will explore different strategies of ciliary coordination and propulsion across diverse organisms, from single-celled protists to marine invertebrate larvae. We'll discuss how cilia can move in synchrony, maintain specific synchronization patterns, or beat metachronously on topologically interesting structures. Additionally, we'll explore how organisms use bioelectrical signalling to control ciliary activity, and the implications of this for navigating through complex environments

Christoph Weber - Theory for bottom-up sequence selection and evolution.

Non-equilibrium selection pressures were proposed for the formation of oligonucleotides with rich functionalities encoded in their sequences, such as catalysis. Since phase separation was shown to direct various chemical processes, we ask whether condensed phases can provide mechanisms for sequence selection and evolution. To answer this question, we use non-equilibrium thermodynamics and describe the reversible oligomerization of different monomers to sequences at non-dilute conditions prone to phase separation.

We find that when sequences oligomerize, their interactions give rise to phase separation, boosting specific sequences' enrichment and depletion. Our key result is that phase separation gives rise to a selection pressure for the oligomerization of specific sequence patterns when fragmentation maintains the system away from equilibrium. Specifically, slow fragmentation favours alternating sequences that interact well with their environment (more cooperative), while fast fragmentation selects sequences with extended motifs capable of specific sequence interactions (less cooperative). Our results highlight that out-of-equilibrium condensed phases could provide versatile hubs for Darwinian-like evolution toward functional sequences, both relevant for the molecular origin of life and de novo life.

Contributed Talks

Nicolas Cuny - Biomechanical determinants of shape diversity in cnidarian larvae

The study of morphological evolution has traditionally emphasized the genetic underpinnings of diversity. However, the development of form results from a complex interplay between gene expression defining cell identity, and the mechanics at supracellular scale that shapes the tissue. Yet, a significant gap remains in understanding how genetic diversity translates into biomechanical processes that sculpt species-specific shapes, and whether general biophysical principles govern shape evolution across species. Cnidarians - a family of sea animals including sea anemones, corals and jellyfish - provide an ideal system to tackle this challenge as most of them go through a larval stage in their development with a simple axisymmetric bilayer structure exhibiting species-specific variations in shape.

In this talk, I will introduce an active surface model in which the larva is described as an axisymmetric active viscoelastic shell. In addition to passive tensions and bending moments arising from surface area elasticity and bending rigidity, the tissue can exhibit active tensions and bending moments generated by the cells actomyosin complex. I will show how using this model together with quantitative imaging of different cnidarian species allowed us to identify three biomechanical modules controlling the larval shape and whose species-specific variations explain shape diversity. Basally aligned stress fibres drive axial elongation, while oral geometry and aboral rigidity control shape axisymmetry. Biological perturbations of those modules confirmed the causal relationship between module variation and shape diversity. These findings provide a general framework for how molecular complexity funnels into mesoscale mechanical determinants shaping morphological diversity.

Mathieu Dedenon - An agent-based model for active nematics and beyond.

Biological cellular tissues often exhibit large domains of orientational order, separated by topological defects where orientation is ill-defined. Those regions concentrate active stresses generated by individual cell force dipoles and give rise to spontaneous flows. This interplay of nematic order and activity has been explored based on two-dimensional continuum theory. More complex geometries and phenomena, like three-dimensional growing tissues of active and growing cells, remain largely unexplored theoretically.

Based on the two-particle growth model, we propose an agent-based model that describes cells as multi-particle filaments with controllable aspect ratio. Generic rules are introduced to capture cell division and death, and we incorporate mechanical activity in terms of individual cell force dipoles, either contractile or extensile, giving rise to an active nematic stress. This framework naturally accounts for cell-cell interactions as the main source of dissipation in three-dimensions and is designed to capture hydrodynamic modes at large scales.

We first perform a two-dimensional calibration for a non-growing tissue and recapitulate the active flow transition with extensile active stress, in agreement with the hydrodynamic theory of active nematics. In addition, we confirm the influence of mechanical activity on the onset of nematic order and recapitulate the self-propulsion of +1/2-defects. With this versatile framework, we plan to explore active nematics in complex three-dimensional geometries in the future, studying the interplay of mechanical and growth-based activity.

Jeffrey Everts - Odd viscosity in chiral active fluids.

Viscosity is a property that tells us how easy it is to cause flow in a fluid. For incompressible isotropic systems, the most well-known type of viscosity is the shear viscosity, which quantifies how much of the fluid's available energy dissipates when a symmetric velocity gradient is induced into the system. However, the situation differs in so-called chiral active fluids, which are manifestly out-of-equilibrium systems with expected realisations in biological systems. Here, the fluid particles are set into motion by activity or uniform rotation of the system and are, therefore, characterised by a non-trivial intrinsic angular momentum density. Consequently, the flow properties of such a fluid are not just described by the shear viscosity. There are additional so-called odd viscosity coefficients that do not contribute to viscous dissipation in a direct manner.

Because of the fundamental interest in this problem and recent experiments, we study such chiral active fluids in the creeping flow regime in more detail. By constructing the fundamental solution of the generalised stationary Stokes equations, we analytically solve the problem of a particle undergoing solid-body motion in an odd viscous fluid. Furthermore, we will then explicitly demonstrate that odd viscosity can contribute to viscous dissipation via alteration of the fluid flow.

Jeremy Guntoro - Information thermodynamics of genotype-phenotype maps.

Individual cells contain an ensemble of RNA and protein molecules produced from templates that specify monomer sequences. These sequences direct the folding of these molecules, which in turn plays a role in determining function. For a given molecular size, an equilibrium distribution over sequences and structures exists according to the free energy of forming specific structures from specific sequences, but the ensemble observed in a cell is generally far from equilibrium. Here, we explore how the excess free energy is channelled into creating a useful low entropy, non-equilibrium distribution over structures, selecting desired phenotypes. First, using the data processing inequality, we show that the deviation of the structural ensemble from equilibrium is upper bounded by the excess free energy stored in the sequences alone, under the assumption that folding equilibrates over structures for a given sequence, and hence a folding efficiency can be defined. On the other hand, the ability to select a low entropy distribution of structures is arguably the better metric for system performance. We show that the total stored free energy can be decomposed into an energy term, a structure entropy term, and a fold-conditioned sequence entropy term. We explore how these general results manifest in a simple, solvable helix-coli model of folding and identify different functional regimes. In general, the drop in structure entropy is lower than the free energy stored, and hence some stored free energy is wasted. We further argue that this regime applies to the ensemble of RNA molecules produced by a cell.

Elias Friman - Cohesin loop extrusion dynamics and CTCF affect long-range enhancer-driven transcription.

Enhancers drive gene transcription, and their combined effects leads to highly complex regulation. In mammals, enhancers are often located hundreds of kilobases from their target gene. One factor proposed to contribute to distal gene activation is loop extrusion by the cohesin complex, which requires NIPBL for its processivity. Extrusion can stall at CTCF-bound regions, and extruding complexes are removed from chromatin by WAPL.

To study the impact of loop extrusion dynamics on enhancer-driven activation, we combine rapid protein depletion strategies and synthetic activator recruitment to activate the polycomb-repressed Shh promoter from enhancers.

We developed a method to activate the silent Shh promoter from up to 850 kb away (the ZRS enhancer). Rapid depletion of NIPBL led to an increase in enhancer-promoter distances, consistent with loss of loop extrusion, and reduced activation from distal enhancers (>100 kb) but not proximal ones. However, activation was not fully lost in the absence of NIPBL, suggesting loop extrusion contributes to, but is not required for, distal activation. In contrast, WAPL degradation led to decreased Shh-ZRS distances and increased Shh activation from ZRS, indicating that stalled cohesin contributes to transcriptional activation. However, WAPL degradation strongly decreased the activation from enhancers without nearby CTCF sites and recruitment of CTCF dramatically boosted their activation potential.

Our results suggest that chromatin conformations driven by the dynamic loop extrusion cycle, and by CTCF, facilitate the action of enhancers at very different distances.

Lara Kruger - Uncovering molecular mechanisms driving asymmetric cell division with synthetic biology

Asymmetric cell division promotes the generation of two daughter cells with different fates, as they inherit distinct fate determinants, and is, thus, crucial for organism development and tissue homeostasis. The process critically relies on a polarized cell cortex, which controls the profound polarization of the cell cytoskeleton. We, therefore, set out to dissect the mechanisms underlying the formation of asymmetric microtubule networks during mammalian asymmetric cell division.

To do so, we developed a synthetic biology approach to artificially polarize normally unpolarized mammalian cells in culture. Capitalizing on designed 2D protein arrays allowed us to ectopically induce cortical polarity of virtually any protein of interest during mitosis in various cell types. Strikingly, cortical clustering of the conserved polarity cue, the Par complex (Par3/Par6/aPKC), is sufficient to polarize the microtubule cytoskeleton and induce key processes of asymmetric cell division: spindle orientation (via Par3) and central spindle asymmetry (via aPKC).

We further establish that molecularly, the formation of an asymmetric central spindle, where on side contains a higher microtubule density as opposed to the other, requires an asymmetric kinase activity of aPKC at the cortex. This raises the fundamental question of how a kinase at the cell cortex controls the density of central spindle microtubules in the cytosol. Strikingly, the conserved dynein-adaptor Lis1 relocalizes from the cell cortex to central spindle microtubules in an aPKC-dependent and dynein-independent manner. Importantly, the relocalisation of Lis1 appears to be required for central spindle symmetry breaking. Taken together, our work paves the way towards establishing the molecular mechanisms of cytosolic cytoskeleton symmetry breaking downstream of cortical cues.

Darius Koster - Characterisation and application of Curly, a small protein with big impact on actin filament curvature.

Single actin filaments transition from a semi-straight to a highly curved structure upon binding to an IQGAP protein, known as “Curly”, when confined to a planar membrane. These bent filaments exhibit a radius of curvature of 0.5–1 μm, with a preferred anti-clockwise bending direction. Here, we present recent experimental advances in understanding how curly binds to actin as well as a simple physical model to describe these actin shape changes, providing a quantitative explanation for the observed curvature through free energy minimization. Our analysis explains the experimentally observed curvature by proposing that Curly proteins apply an internal torque to Curly-bound segments of actin filaments, along with enhanced twist-bend coupling driven by the asymmetric binding of the protein. Considering the central role of actin in cellular mechanosensing, these findings offer insights into how mechanochemical stimuli influence and regulate the mechanical properties of actin filaments.

Shaoqian Ma - Single-cell nascent transcription is sparse and heterogenous, revealing cellular plasticity.

Single-cell nascent RNA sequencing is essential for understanding how a genome drives cell diversity. We developed scFLUENT-seq, a single-cell method that captures genome-wide transcription with brief metabolic labelling. Our analysis shows that only 3~6% of the genome is transcribed per cell in a 10-minute window, compared to over 80% in bulk, revealing significant variability in how individual cells interpret the genome. Notably, substantial transcription occurs in intergenic regions, particularly in heterochromatin, with high stochasticity. Moreover, promoter-associated antisense and genic sense transcription rarely co-occur in the same cell. Distal intergenic transcription correlates poorly with gene activity but links to increased genome-wide transcriptional diversity, which marks cellular plasticity and may precede cell-state shifts. Furthermore, mRNA synthesis and decay are uncoupled at the single-cell level, unlike intergenic ncRNA, suggesting specialized mechanisms counteracting stochastic noncoding production. In summary, scFLUENT-seq captures the full transcriptional spectrum, revealing the heterogeneity and regulatory complexity underlying cellular plasticity.

Catherine Naughton - Transcription-dependent propagation of DNA supercoiling in human cells.

DNA supercoiling refers to the process by which the DNA double helix transitions from its relaxed state to a state that is either overwound (positive supercoiling) or underwound (negative supercoiling). DNA supercoils are introduced by many fundamental cellular processes such as transcription, replication, and chromatin remodelling, and regulated by the activity of topoisomerases in order to maintain appropriate levels of DNA torsional stress. We previously developed a novel method for mapping negative DNA supercoiling and showed that transcription forms and remodels supercoiling domains. Importantly we found that these local changes in DNA topology were propagated through the chromatin fiber to unfold large-scale chromatin structures. To better understand DNA supercoil propagation we have adapted our protocol to map DNA supercoiling genome-wide. Using our high-resolution experimental data from oestrogen-responsive human MCF7 cells, we aim to determine the supercoiling flux between genes and relate this to gene orientation and local chromatin environment. This study will help elucidate whether DNA supercoiling regulates gene-gene communication and will inform an evolutionary model for genome organization.

Eleonora Pero - The Flow-Driven Role of Red Blood Cells in Platelet Adhesion Mechanics and Thrombus Morphology.

The morphology of platelet aggregates is emerging as a key indicator of thrombotic risk and coagulation disorders, offering potential for early diagnosis and personalized antithrombotic therapies. However, current methodologies lack standardized frameworks for evaluating thrombus morphology. In particular, the interplay between hematocrit, shear forces, and platelet aggregation remains poorly understood despite its critical implications for thrombosis.

To address this, we present a standardized, quantitative framework for analysing platelet aggregate morphology, incorporating the influence of flow-driven mechanics on platelet adhesion and aggregation. Our approach integrates microfluidics with high-resolution confocal microscopy, dynamic 3D reconstruction, and Fourier-based analytical techniques. We demonstrate that shear rate governs the structural anisotropy and occlusive capacity of platelet aggregates, while red blood cells modulate thrombus stability by dynamically regulating the adhesion mechanics. Overall, our findings underscore the fundamental role of flow-driven mechanics in thrombus development, providing a robust framework for investigating the hemodynamic forces governing platelet adhesion, aggregation, and thrombus morphology.

Tuan Pham - Dynamical Theory for Adaptive Systems.

Despite their differences in terms of dynamics and structures, genetic and neural networks are similar in the sense that they both are adaptive - their connections slowly change in response to the state of their constituting elements – the nodes, such as genes or neurons so as to make the collective states functionally robust under environmental stochasticity. To address this problem, I developed an exact analytical theory for those multiple-time dynamical systems that feature a correspondence between global and local learning. In particular, I illustrated our approach within the context of adaptive evolution. Here the evolution of genotypes that control stochastic gene expression dynamics can be cast into the form of a slowly reconfiguring network of genetic regulations. The network configurations (i.e., genotypes) then are selected according to the fitness of their respective phenotypes considered as the attractor of the gene expression dynamics on them. Here we show how a trade-off between genotype and phenotype emerges due to the joint effect of fitness maximisation and frustration minimisation, giving rise to a robust phase within an intermediate level of external noise. We further discuss the thermodynamic cost of evolution, elucidating how robust energetic cost is possibly responsible for optimal information processing at criticality in biological networks.

Diogo Pinto - Mechanical stresses induced by turbulent flows can compromise epithelial tissue integrity.

Epithelial tissues form protective barriers lining organs, vessels, and cavities, making their integrity essential for proper function. However, mechanical stresses can compromise tissue structure, sometimes leading to fracture. While typically detrimental, fractures may serve functional roles in some organisms. For example, Trichoplax adhaerens generate fractures in the epithelium through their own motility, potentially facilitating asexual division. This process arises due to collective cell flows that localize stresses and strains, leading to tissue rupture.

Similar stress localization and fracture behaviour has been observed in vitro for tissues of MDCK cells, where fracture and rich hole dynamics occur as substrate stiffness decreases. To explore these phenomena, we present a continuum multi-phase field model that incorporates internal dissipation. Each cell is represented by a continuum density field, governed by free-energy minimization and overdamped force balance. Internal dissipation is captured by a viscosity-like term linked to the relative velocities of neighbouring cells, while a nematic director models an active dipolar forcing that promotes cell shape anisotropy.

Our results show that decreasing substrate friction enhances cell-cell velocity correlations, leading to active turbulence. In this regime, topological defects in the nematic director field form and annihilate dynamically, sometimes generating localized high-stress regions and spontaneous hole formation. We explore how the fate of these holes—whether they close or persist—depends on the tissue's elasticity and cell activity. Our findings highlight the interplay between epithelial tissues' elastic and viscous properties, shining light on the role of collective flows in regulating tissue integrity.

Laila Saliekh - Bacterial chaining produces multiple modes of colony buckling.

Bacterial colonies have diverse morphologies that represent essential forms of multicellular organisation. Chaining, an intercellular pole-pole adhesion, is often observed in Bacillus subtilis and is an important feature in early biofilm formation, connected to buckled colony morphologies during early proliferation. We investigate the relationship between intercellular linking and emergent colony modes. A discrete-element model simulates 2D colonies of non-motile, rod-shaped bacteria, integrating a stochastic spring-like linking to study how the

variation of the probability of linking and bending rigidity influence the transition between isotropic, aligned, and buckled colony morphologies. Increasing the likelihood of chaining drives the transition from fractured and aligned microdomains to collective and single-chain buckling, leading to the loss of order throughout these transitions. The shift between different morphological regimes

is revealed through phase diagrams, which highlight the critical threshold of colony behaviour. Chaining plays a significant effect on colony morphology, which is governed by growth and mechanical interactions, and despite the fairly simplistic model, it is able to capture the key features of the buckled chains observed in B. subtilis colonies. This model

can be extended to incorporate mechanosensitive growth, nutrient limitation, and the effect of confinement to further understand the impact of chaining on growth and buckling dynamics in more complex environments.

Mehmet Can Ucar - Space-filling optimization in branching morphogenesis.

The development of many biological structures, including vascular networks and neural tissues, rely on branching morphogenesis to optimize functions like fluid transport and sensory information processing. While self-organized branching provides an elegant mechanism to cover space, it does so at the expense of efficiency, exhibiting large spatial fluctuations and poor space-filling properties. A central question is then to clarify how growing branched networks can efficiently occupy a given territory to maximize their functional output. Here, we address this question by integrating experiments on developing lymphatic vessel networks and mathematical modelling to show that lymphatic capillaries tile space in an optimal, space-filling manner. This optimization occurs through an initial unguided invasion, followed by targeted branching into sparsely populated network regions. These findings underscore the ability of lymphatic networks to exploit local regulatory cues for tissue-scale optimization. Finally, we contrast this local guidance mechanism with alternative tiling strategies arising in the central nervous system, where morphodynamic information at the cellular scale can lead to tissue-wide collective patterning during development.

Henrik Weyer - Equilibrium-like interface laws for intracellular protein patterns.

Protein pattern formation is central to the spatiotemporal self-organization of both prokaryotic and eukaryotic cells. Operating far from equilibrium, no general theory links the microscopic reaction networks and parameters to the macroscopic pattern architecture and dynamics. Here, we show that protein patterns are generically governed by an effective interfacial tension arising from cyclic steady-state currents of attachment and detachment at the interface [1]. We develop a non-equilibrium Neumann angle law and Plateau vertex conditions for interface junctions and mesh patterns, thus introducing the concepts of “Turing mixtures” and “Turing foams”. In contrast to liquid foams and mixtures, these non-equilibrium patterns can select an intrinsic wavelength by interrupting an equilibrium-like coarsening process. Data from in vitro experiments with the E. coli Min protein system verifies the vertex conditions and supports the wavelength dynamics. Our study shows how complex equilibrium-like structures can arise from distinct physical processes in non-equilibrium systems.

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Posters

Aidan Brown - Buckling instabilities in chaining bacterial colonies

Bacteria frequently grow together as colonies. Large, complex colonies, known as `biofilms', are often multi-species and exhibit cooperative behaviour reminiscent of multicellular organisms, such as signalling and controlled cell death. However, even at the early stages, colonies exhibit many different structures and morphologies, which are controlled by a dynamic interplay between cell growth and division, the shape of cells and the physical interactions between them. One type of interaction, called `chaining', consists of the maintenance of a physical, usually protein, link between sister cells following division. Chaining is common in many bacterial species, but is particularly well known in the rod-shaped Bacillus subtilis, where buckling of single chains of bacteria leads to convoluted, open colonies with many pores and channels. This contrasts with the structure of non-chaining bacteria, such as Escherichia coli, which typically fracture into multiple small, aligned domains. Here, I will present 2D discrete-element simulations of growing bacterial colonies, where we continuously tune the probability and strength of chaining between daughter cells. At the extremes, we reproduce the behaviour of B. subtilis and E. coli -like colonies, but for intermediate values of the chaining parameters, we identify a novel state, where the whole colony buckles collectively. A toy, lattice model reproduces the shape of the transition between the `aligned domains' and `collective buckling' states, and enables us to show that the impact of chaining is to modify the rate and probability with which these different mechanisms occur.

Josh Cailhau - Physical modelling of ParB droplets' fusion-defusion in E.coli.

Liqi Chen - How do cellular resources limit viral growth?

Efficient resource allocation is crucial for cellular growth and survival, particularly under constrained conditions. A well-established "growth law" shows a linear correlation between bacterial growth rates and the cellular concentration of ribosomes, the machines that make proteins. Ribosomes can be inactivated by the ribosome-targeted antibiotic chloramphenicol, leaving only a fraction capable of translating proteins, referred to as active ribosomes.

Our study extends a growth principle to bacteriophages, viruses that infect bacteria, showing that viral replication rates are directly proportional to the number of active ribosomes per cell under ribosome-limited conditions. Under the specific conditions we investigated, this suggests that ribosome availability can constrain viral growth.

Mathieu Dedenon - An agent-based model for active nematics and beyond.

Biological cellular tissues often exhibit large domains of orientational order, separated by topological defects where orientation is ill-defined. Those regions concentrate active stresses generated by individual cell force dipoles and give rise to spontaneous flows. This interplay of nematic order and activity has been explored based on two-dimensional continuum theory. More complex geometries and phenomena, like three-dimensional growing tissues of active and growing cells, remain largely unexplored theoretically.

Based on the two-particle growth model, we propose an agent-based model that describes cells as multi-particle filaments with controllable aspect ratio. Generic rules are introduced to capture cell division and death, and we incorporate mechanical activity in terms of individual cell force dipoles, either contractile or extensile, giving rise to an active nematic stress. This framework naturally accounts for cell-cell interactions as the main source of dissipation in three-dimensions and is designed to capture hydrodynamic modes at large scales.

We first perform a two-dimensional calibration for a non-growing tissue and recapitulate the active flow transition with extensile active stress, in agreement with the hydrodynamic theory of active nematics. In addition, we confirm the influence of mechanical activity on the onset of nematic order and recapitulate the self-propulsion of +1/2-defects. With this versatile framework, we plan to explore active nematics in complex three-dimensional geometries in the future, studying the interplay of mechanical and growth-based activity.

Francois El-Daher - Mechanical Principles of Brain Tissue Repair: A Combined Experimental and Computational Study of Wound Closure in Zebrafish.

Understanding how tissues repair themselves after injury requires bridging cellular behaviours with tissue-scale mechanics. We present a comprehensive analysis of wound closure dynamics in the zebrafish brain, combining high-resolution imaging with multi-agent computational modelling. Through detailed tracking of cellular dynamics, we reveal how individual cell forces collectively drive tissue-scale wound closure. Our analysis identifies key mechanical signatures during the repair process, including coordinated cell shape changes and emergent tissue-level forces. Combining high-resolution live imaging with multi-agent computational modelling, we demonstrate how local cell-cell interactions and mechanical constraints give rise to the observed wound closure patterns. These findings bridge stochastic cellular behaviours and deterministic mechanical processes, with future implications for understanding regenerative capacities across injury contexts.

Alexander Houston - Spontaneous Oscillations in Heterogeneous Active Nematics.

The framework of active nematics may be used to model many living systems, including cell layers and bacteria [1]. The study of active nematics has focused on uniform activity, but real biological systems are not homogeneous, rather they have population variance or are composed of different species. As well as arising naturally, it has been recently demonstrated that the structure of activity in a material can be controlled through modulating light intensity [2]. This provides motivation to understand the effects of activity patterning, both to gain insight into the in vivo behaviour of living systems and to enable desired dynamics to be engineered in active matter.

A central feature of active nematics is that, when confined, they exhibit a transition to a flowing state, provided their activity exceeds a critical value [3]. In this context we show that activity variation allows control of the structure of the flowing state and, most strikingly, can lead to oscillatory dynamics. We show analytically that the behaviour of the confined active nematic can be mapped onto a dynamical system, the coefficients of which are determined by the activity variation, and confirm these results numerically. We find that an activity gradient can induce oscillations, and in this case determine how the properties of the system influence the frequency of the oscillations.

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Martin James - Swimming mode determines how well mesoscale swimmers shield their odor in turbulence.

Marine organisms manipulate their surrounding flow through their swimming dynamics, which affects the transport of their own odor cues. We demonstrate by direct numerical simulations how a group of mesoscale swimmers immersed in a turbulent flow alters the shape of the odor plume they release in the water. Odor mixing is enhanced by increased velocity fluctuations and a swimmer-induced flow circulation which widen the odor plume at close range while speeding up dilution of the chemical trace. Beyond a short-range increase in the likelihood of being detected, swimming considerably reduces detections with effects that can persist at distances of the order of ten times the size of the group or more. We find that puller-like swimmers are more effective at olfactory shielding than pusher-like swimmers. We trace this difference back to the dynamics at the swimmer location, which tends to trap odor at the source for pushers and to dilute it for pullers. Olfactory shielding is robust to changes in the conditions, and is more pronounced for weak turbulent Reynolds numbers and large swimmer Reynolds numbers. Our results suggest that olfactory shielding may play a role in the emergence of different swimming modalities by marine organisms.

Hyojun Kim - Macromolecular crowding regulates RNA population dynamics under pressure.

Cells growing in confined spaces eventually build up mechanical compressive stress. Growth-induced pressure (GIP) decreases cell proliferation across all kingdoms of life. In the yeast Saccharomyces cerevisiae, we showed that the decline in proliferation is most likely due to a slowdown in protein production, coinciding with an increase in both nuclear and cytosolic macromolecular crowding, which originates from macromolecular accumulation within the cell. We hypothesize that increased intracellular macromolecular crowding could directly contribute to this slowdown in protein production. However, little is known about which steps of protein biosynthesis are limited by crowding and whether major pathways such as mTORC1 are downregulated under pressure. Here, we investigate the RNA population dynamics of Saccharomyces cerevisiae under pressure. Metabolic labeling of newly synthesized RNA with 5-ethynyl uridine (5-EU) revealed that the mean transcriptional rate of the whole transcriptome decreased threefold under 0.5 MPa of GIP, while RNA degradation was similarly delayed, suggesting the presence of feedback regulation. Next, we examined the transcriptional dynamics of an individual gene using single-molecule live-cell imaging and the PP7/MS2 system. The transcription dynamics of GAL10 showed that the ON and OFF durations of the bursting state became shorter and longer, respectively, as pressure increased. The estimated reduction in RNA production rate was consistent with the global-level results obtained through 5-EU metabolic labeling. These findings indicate that the dwell time of transcription factors (e.g., Gal4 for GAL10) was reduced, leading us to infer that nucleosome unwrapping dynamics may be disrupted by crowding under pressure.

Joseph Knight - The Physics of a Microbial Railway Network

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.

Mathieu Le Verge-Serandour - Dynamical Network Remodeling of Slime Mold.

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 that evolves drastically over a few hours, evacuating a large zone of a few millimeters squared. Unfavourable competing parallel veins are first removed to form a tree-like structure, where veins prune sequentially until complete evacuation of the zone.

First, we use an analogy with power-grid networks to investigate the effect of sequential pruning based on the ratio of tube vs network resistance. 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, analysing 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 that the decay rate is controlled by the depth of the tree and the parallel branches' dynamics, which introduces a waiting time for pruning.

Our approach to flow networks may be generalized to pruning flow networks during embryonic development, stroke events, or evacuating networks for urban design.

Siyang Li - Nuclear RNA mesh formed by Pol II transcription regulates transcription and chromatin decompaction.

The non-chromatin components occupy the majority of nuclei, yet their coordinated involvement in chromatin-associated biochemical processes remains unknown. Non-coding RNAs (ncRNAs) have been extensively implicated in nuclear activities. Through super-resolution imaging, we observed an RNA mesh surrounding chromatin domains (CDs), formed by nascent RNA transcribed by whole genome. Nuclear matrix protein hnRNPU (or SAF-A) depletion significantly affect RNA localization, causing fibrillary aggregation of the RNA mesh. Nascent RNA aggregation induces relocalisation of multiple RNA-binding proteins and core nuclear machinery components, accompanied by chromatin fibrotic coalescence. These structural perturbations significantly alter CD arrangement and induce abnormal DNA exposure. Consequently, it promptly causes transcription dysregulation, DNA damage and nuclear structure destabilization. These effects suggest that the dynamic RNA mesh serves as both a molecular transport “canel” and biochemistry reaction hub. It critically regulates chromatin properties and participates in decoding genetic information.

Manish Patel - Impact of inertia on active Brownian particles.

The active Brownian Particle (ABP) model has been extensively used to study the behavior of active agents such as bacteria, Janus particles, etc. Usually, the model is analyzed in the overdamped limit, assuming that inertia does not influence the steady-state properties. However, for larger particles such as hexbugs and vibrobots, inertial effects become significant and impact long-term behavior. Our study of inertial active Brownian particles reveals inertia-dependent steady-state observables, including kinetic temperature, diffusivity, pressure, and entropy production rate. We present a detailed phase diagram demonstrating a re-entrant transition from active to passive-like behavior in the dynamics of both position and velocity as a function of inertia.

Rodrigo Rivas Barbosa - A Computational Study of Enhancer-Promoter Interactions in B-Cell Cancers.

An enhancer is a cis-regulatory element that controls, to some extent, the level of expression of its companion gene. In fact, highly expressed genes can be often escorted with clusters of such enhancers into what is usually called a super-enhancer. However, following genome rearrangements, super-enhancers can be misplaced or 'hijacked' and associated with a gene other than the one originally intended, causing dangerously overexpressing levels of the new gene which in some cases lead to proto-oncogene to oncogene conversion.

Using computer simulations, we investigate the role of a hijacked super-enhancer for the particular case of B-cell cancers involving the continuously rearranging immunoglobulin heavy locus. Fed with the coordinates of the breakpoints and 1D epigenetic data from patient-derived samples, our polymer-model based simulations predict the new set of promoter-enhancer interactions and levels of gene expression which are then tested experimentally.

Shubhadeep Sadhukhan - Modelling how lamellipodia-driven cells maintain persistent migration and interact with external barriers.

Cell motility is fundamental to many biological processes, and cells exhibit a variety of migration patterns. Many motile cell types follow a universal law that connects their speed and persistency, a property that can originate from the intracellular transport of polarity cues due to the global actin retrograde flow. This mechanism was termed the "Universal Coupling between cell Speed and Persistency"(UCSP). Here we implemented a simplified version of the UCSP mechanism in a coarse-grained "minimal-cell" model, which is composed of a three-dimensional vesicle that contains curved active proteins. This model spontaneously forms a lamellipodia-like motile cell shape, which is however sensitive and can depolarize into a non-motile form due to random fluctuations or when interacting with external obstacles. The UCSP implementation introduces long-range inhibition, which stabilizes the motile phenotype. This allows our model to describe the robust polarity observed in cells and explain a large variety of cellular dynamics, such as the relation between cell speed and aspect ratio, cell-barrier scattering, and cellular oscillations in different types of geometric confinements.

Ludivine Sanchez Arias - How Cryptophytes swim and feed: insights into mixotrophy and locomotion.

Cryptophytes are motile microorganisms that can display phototrophic, heterotrophic, or mixotrophic feeding strategies. While motility is key to environmental adaptation and nutrient acquisition, the link between swimming behaviors and mixotrophy remains unclear. This study examines how motility correlates with bacterivory in cryptophytes.

We quantified mixotrophy using fluorescently labeled bacteria (FLB) and flow cytometry under different nutrient conditions, including phosphorus depletion. High-speed microscale imaging was used to track swimming trajectories across different growth phases. Results show species-specific variations in motility and feeding behavior. Cryptophytes with higher phagotrophic activity displayed distinct non-helical swimming behaviors, with rapid directional changes or abrupt pauses, suggesting a link between locomotion and feeding. Nutrient depletion enhanced mixotrophic activity in some species, indicating that environmental stressors can drive shifts in trophic strategy.

This study provides insight into the adaptive strategies of cryptophytes in dynamic environments and their contributions to microbial food webs and nutrient cycling. Understanding these relationships enhances our knowledge of planktonic ecosystems and the selective pressures shaping cryptophyte evolution.

Jenna Schafers - Turning up the heat; mechanistic insights from thermal inactivation of influenza A virus.

Thermal inactivation is an age-old method1 of sterilisation, but the molecular mechanisms through which this occurs remain elusive. We experimentally studied the dynamics of influenza A virus (IAV) heat inactivation, finding a simple exponential decay of infectivity over all tested temperatures. The decay rate shows an Arrhenius-like temperature dependence indicating a transition between two distinct inactivation mechanisms at approximately 40℃. Within the 40-50℃ range, a measured activation enthalpy of 99 ± 3 kBT was similar to that found in simulations of conformational change of the IAV membrane protein haemagglutinin-2 (HA2)2, and the activation entropy of 66 ± 3 kB, was consistent with such a protein unfolding process. Normally, this conformational change is triggered by progressive acidification inside a host cell's endosome. It exposes a hydrophobic peptide that fuses the viral and endosomal membranes, allowing viral entry once the genome is released by the acidic environment.

We confirmed the involvement of HA in viral failure by testing IAVs with mutant HA, and by lowering the pH. At low pH, virus inactivation exhibited a time-dependent (non-exponential) decay rate. We were able to reproduce both the neutral and low-pH data by using a 3-state model for HA conformation. A necessary condition of our model is that a single triggered HA can cause viral failure, perhaps by binding to the wrong cellular membrane, or interfering with genome release. This suggests a general principle, which is that the sensitive molecular triggers for viral genome release are by necessity likely points of viral failure.

Badeer Hassan Ummat - Effect of actin-modulating proteins on actin filament mechanics.

The plasma membrane wraps around animal cell to delimit it from the environment, and the underlying thin actin cortex regulates membrane morphology. Force generation by a dynamic network of actin filaments and actin-modulating proteins (AMPs) induces deformation in lipid membranes. Conversely, membrane geometry promotes specific actin filament organisations. Examples of such an interplay are filopodia (membrane tubes formed by bundles of formin-generated, linear actin filaments) or lamellipodia (membrane sheets formed by Arp2/3-generated, branched actin filament networks) formation, where each structure is associated with distinct actin organization.

In addition to these well-established actin filament geometries, we recently reported on the formation of highly bent actin filaments and actin rings by the interaction with the N-terminal part of IQGAP proteins, such as curly (S.pombe Rng2(1-189)). Here we present a semi-automated computational analysis to extract mechanical properties from images of fluorescently labelled actin filaments.

We compare the bending of actin filaments associated with 2D membrane-tethered curly in the presence of various AMPs. Estimations of bending persistence length showed us the presence of curly makes actin more flexible compared to control. And, actin flexibility can be further adjusted by adding other AMPs such as formin and myosin along with curly. In addition to persistence length, we derive curvature distribution of actin filaments, which informs our theoretical model of the curly-induced actin bending. In future, we will expand our analysis to 3D datasets to study features and mechanisms involved in morpho dynamics of lipid membrane spheres linked to dynamic actin networks.

Bruno Ventejou - A hydrodynamic toy model for fish locomotion.

The social interaction of fish has been mainly studied in 2D without hydrodynamic interactions [1,2] or with hydrodynamic interactions in the limit of the far-field [3]. As a fish swims, it affects the flow around its body in a complex manner at distances much larger than the typical fish scale. Thus, it could compete with cognitive interaction. Some efforts have been done to describe precisely the flow generated around a fish [4,5]. But, the high cost of hydrodynamic simulations prevents the use of such models to study schools of fish.

We propose a toy model[6], that is able to generate the vortex wake induced by the fish locomotion and which is light compare to solving the fish tail flapping. We describe the fish as a rigid body by a penalty method and achieve the description of the tail flapping by exerting a torque in the fluid compensated in the body. The trajectory of the fish is determined by the position of the tail in relation to the body. We perform a full characterization of the toy model and compare it to the scaling found in the animal kingdom [7].

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Kaiyuan Yan - Transcription shapes dynamic nuclear ribonucleoprotein meshwork.

Understanding intracellular hierarchical organization is the basis of studying biochemical activities in cell nucleus. However, so little do we comprehend about the physical nature of nuclear organization.

Cell nucleus is composed by chromatin and ribonucleoprotein (RNP) mesh. Based on earlier study, chromatin is regarded as a stationary component within it due to its limited dynamics, characterized by its highly compressed state as a long chain polymer. Accordingly, RNP undertakes a series of functions such as transcription, splicing, and transport in the nucleus by forming a dynamic meshwork structure. RNP mesh determines the dynamics of molecular movement and the global thermodynamics of biochemical reaction in the nucleus.

From a biophysical perspective, this study aims to depict influence of RNA transcription in the nucleus based on EDTA de-staining transmission electron microscopy (TEM), fluorescence correlation spectroscopy (FCS) and fluorescence recovery after photobleaching (FRAP), conclusively construct a physical RNA topological meshwork model and mathematical dynamics model, predicting dynamics and thermodynamics characteristics of RNP mesh in the nucleus.

Wanjia Yu - Genetically Encoded Magnetosome Biogenesis in Human SHSY-5Y Neuroblastoma Cells.

Magnetosomes are membrane-enclosed magnetic nanoparticles (MNPs) biomineralised by magnetotactic bacteria such as Magnetospirillum magneticum AMB-1. Their redox-regulated formation involves membrane invagination, iron transport, protein recruitment, and magnetite crystallisation. The conserved magnetosome island (MAI) encodes essential genes, including mms6, which regulates magnetite nucleation and crystal morphology. The amphiphilic mms6 protein facilitates iron binding and templated crystal growth, promoting the synthesis of uniform superparamagnetic nanocrystals. Building on previous demonstrations of mms6-induced MNP formation in human mesenchymal stem cells (MSCs), this study explores its biomineralisation potential in neuronal cells.

A bioengineering approach underpins the investigation of mms6-driven magnetosome formation in SHSY-5Y neuroblastoma cells. We will assess intracellular MNP biosynthesis alongside validating gene expression via RT-qPCR and Western blotting. Physicochemical properties, including size distribution, surface charge, and magnetic response, will be characterised using transmission electron microscopy (TEM) and SQUID magnetometry. To

determine the stability and intracellular fate of the synthesised MNPs, we will analyse iron trafficking dynamics, metabolic activity, cell viability, and endocytic pathway engagement via cellular assays, fluorophore-tagged mms6 tracking and co-localisation analysis with endosomal-lysosomal markers.

By elucidating the mechanisms and potential constraints of magnetosome formation in neuronal cells, this study aims to establish a foundation for bioengineered intracellular magnetism, which might offer advantageous alternative to exogenous MNPs regarding biocompatibility and dispersion- response profiles. These findings could inform the spatiotemporal positioning of bioassimilated MNPs for targeted, non-invasive, and remotely controlled neuromodulation, with potential applications in deep-penetrating magnetogenetics, pending further research.

Shiheng Zhao - A physical model of hindgut morphogenesis.

During Drosophila morphogenesis, the initially circular hindgut primordium moves from the posterior pole to the dorsal side of the embryo and deforms into a characteristic keyhole shape. We show that this symmetry breaking can be the passive mechanical consequence of active deformations of the tissues that surround it, which include the invaginating midgut and the extending germband. We develop a minimal model of this symmetry breaking in which the hindgut appears as an inextensible elastic ring in the plane. We discover that, as the area enclosed by the ring decreases (midgut invagination) while a diameter is held fixed (by the germband), the circular shape bifurcates robustly into the observed keyhole shape. Moreover, we show how embryonic curvature breaks symmetry further to select the observed orientation of the keyhole shape. This illustrates that complex shape changes can emerge passively during morphogenesis and provides a potential explanation for the diverse morphologies of blastopore equivalents across different organisms.