

## Biophysics, Medical Physics and Soft Matter

*Thursday, 07.09.2023, Room 117*

Time	ID	<b>BIOPHYSICS, MEDICAL PHYSICS AND SOFT MATTER I: COLLECTIVE PHENOMENA</b> <i>Chair: Christof Aegerter, Universität Zürich</i>
14:00	901	<p style="text-align: center;"><b>Topology and geometry organize the morphogenesis of active nematic surfaces</b></p> <p style="text-align: center;"><i>Claire Dessalles<sup>1</sup>, Tzer Han Tan<sup>2</sup>, Aurélien Roux<sup>1</sup></i>  <sup>1</sup> University of Geneva, <sup>2</sup> Max Planck Institute of Molecular Cell Biology and Genetics</p> <p>Morphogenesis, the process by which tissues acquire their shape, hinges on a finely orchestrated collective motion of cells autonomously choreographing themselves to a well-defined final position. The goal of my project is to understand how geometry and topology controls the spontaneous organization of cells that drives morphogenesis, i.e. the growth from a 3D surface to tissues with complex shapes. To investigate this phenomenon, I grow cells on the surface of deformable capsules and monitor the nematic field, cellular flows, and tissue growth. We show that the collective motion of cells is controlled by the nematic order, and topological defects act as morphogenic organizers via active stresses.</p>
14:15	902	<p style="text-align: center;"><b>Determining how physical constraints shape organism behaviour</b></p> <p style="text-align: center;"><i>Daphne Laan, Guillermina Rochelle Ramirez-San-Juan, EPFL</i></p> <p>Ciliates are free swimming single-celled organisms that execute complex behaviours such as obstacle avoidance and hunting. These organisms are covered by arrays of thousands of active filaments, known as cilia, that beat to generate flows. To understand if behaviour can be encoded by cilia organization and the trade-offs between locomotion and predation risk, we analyze the interactions between the ciliates <i>Didinium nasutum</i> and <i>Paramecium multimicronucleatum</i>, a well-known predator-prey system. By studying the dynamic of these cells we aim to determine how physical constraints shape an organism's behavioural landscape.</p>
14:30	903	<p style="text-align: center;"><b>Signalling-dependent refinement of cell fate choice during tissue remodelling</b></p> <p style="text-align: center;"><i>Simone Cicolini<sup>1</sup>, Sophie Herszterg, Guillaume Salbreux<sup>1</sup>, Jean-Paul Vincent<sup>2</sup>, Marc de Gennes<sup>1</sup></i>  <sup>1</sup> University of Geneva, <sup>2</sup> The Francis Crick Institute</p> <p>How biological form emerges from cell fate decisions and tissue remodelling is a fundamental question in development biology. We investigate this interplay during the process of vein refinement in <i>Drosophila</i> pupal wing. By following reporters of signalling activity dynamically, together with tissue flows, we show that vein refinement arises from cell fate adjustments controlled by a signalling network involving Notch, Dpp, and EGFR. Perturbing large-scale convergent-extension flows does not affect vein refinement, showing that pre-patterned vein domains are able to intrinsically refine to the correct width. A reaction-diffusion model of cell fate changes recapitulates the intrinsic tissue ability to establish a thin, regular vein independently of large-scale tissue flows.</p>
14:45	904	<p style="text-align: center;"><b>Density-dependent active flow transition of biological tissues</b></p> <p style="text-align: center;"><i>Mathieu Dedenon<sup>1</sup>, Carles Blanch-Mercader<sup>2</sup>, Karsten Kruse<sup>1</sup></i>  <sup>1</sup> University of Geneva, <sup>2</sup> Curie Institute</p> <p>Biological tissues generate active mechanical stress, originating from cellular force dipoles. Active fluid theory predicts this active stress to drive a spontaneous flow transition in a confined geometry. Indeed, polar cells on a confining disc are observed to rotate with spiral orientation. However at a later stage, tissue growth induces cell reorientation into a static aster.</p> <p>To explain this transition, we introduce a passive theoretical coupling between cell density and polarity. Such coupling can lead to patterning effects, allowing spiral-aster coexistence on a disc. This work shows that cell density gradients can compete with activity to stabilize out-of-equilibrium spatial structures that may be relevant to tissue morphogenetic events.</p>

15:00	905	<p style="text-align: center;"><b>Universal thermodynamic bounds on symmetry breaking in biochemical systems: from error correction to pattern formation</b></p> <p style="text-align: center;"><i>Shiling Liang<sup>1</sup>, Daniel Maria Busiello<sup>2</sup>, Paolo de los Rios<sup>1</sup></i>  <sup>1</sup> Institute of Physics, EPFL, <sup>2</sup> Max Planck Institute for the Physics of Complex Systems</p> <p>Living systems are out-of-equilibrium and exhibit emergent selection phenomena that break equilibrium symmetries. These phenomena are possible because non-equilibrium conditions expand the non-equilibrium phase space where complex biochemical processes can lie in. We use the matrix-tree theorem to derive universal thermodynamic bounds on these symmetry-breaking features in biochemical systems. The bounds are independent of kinetics and hold for closed and open networks. We recover thermodynamic constraints in kinetic proofreading and show that reaction-diffusion patterns are bounded by the non-equilibrium driving force. Our results pave the way to understanding the role of non-equilibrium conditions in biochemical systems.</p>
15:15	906	<p style="text-align: center;"><b>Collective behaviors in bacterial colonies at curved surfaces</b></p> <p style="text-align: center;"><i>Vincent Hickl, Bruno Silva, Empa</i></p> <p>Collective behaviors at interfaces are ubiquitous in living systems and play a crucial role in guiding macroscale phenomena like tissue morphogenesis and the spread of infections. While collections of biological active particles must contend with complex environments, much remains unknown about the effects of substrate geometry on their self-organization. We use bacterial colonies at interfaces as a model active nematic to investigate how surface curvature affects collective behaviors in active matter. Using custom laser-patterned substrates and advanced microscopy, bacterial activity is quantified with high spatiotemporal resolution. The effect of curvature on orientational order in bacterial monolayers is described. These results elucidate how long-range order depends on geometry in biological systems.</p>
15:30	907	<p style="text-align: center;"><b>Symmetry breaking and number control at the onset of centriole assembly</b></p> <p style="text-align: center;"><i>Friso Douma, Pierre Gönczy, EPFL</i></p> <p>The centriole is a cylindrical organelle essential for microtubule organization. Centrioles duplicate exactly once every cell cycle through the formation of a procentriole orthogonally to an existing centriole. How the single site of procentriole formation on the cylinder is determined and what mechanisms ensure that precisely one procentriole is formed remains incompletely understood. We use super-resolution expansion microscopy to study the crucial players of procentriole formation in human cells upon varying experimental conditions. High-resolution localization patterns lead us to develop a new theoretical model, providing key insights in centriole duplication dynamics. Ultimately these insights might generalize to unifying principles of self-assembly in biology.</p>
15:45	908	<p style="text-align: center;"><b>Understanding the principles that govern cell-cycle dynamics using experimental evolution</b></p> <p style="text-align: center;"><i>Vojislav Gligorovski, Sahand Rahi</i>  <i>Laboratory of the Physics of Biological Systems, Institute of Physics, EPFL</i></p> <p>Cellular doubling time, as a crucial determinant of fitness, was optimized during the course of evolution. However, cells of different species exhibit hugely varying doubling times, ranging from a few minutes, to several days. To understand the constraints and trade-offs that dictate cell-cycle dynamics, we created a budding yeast strain in which the doubling time can be controlled exogenously, using light-activated proteins. By applying pulses of light that triggered cell division more frequently than the average cell-cycle period, we conducted an evolutionary experiment that drove the cells towards faster cycles. Cells propagated this way for 1000 generations have shorter G1 phase, are larger and more fit compared to their ancestors.</p>

16:00	909	<p style="text-align: center;"><b>Polarity mediated self-organization in cellular aggregates</b></p> <p style="text-align: center;"><i>Mukund Krishna Kothari, Quentin Vagne, Guillaume Salbreux, University of Geneva</i></p> <p>To explore how feedback between cell polarity and mechanics guides self-organization, we develop a theoretical model of cells described as active polar beads mechanically interacting with each other. The model is motivated by the self-organization of stem cells into a rosette structure in the early stages of organoid growth. A key ingredient is the active interaction force <math>A(\vec{p}_i - \vec{p}_j)</math> arising from cells crawling over each other.</p> <p>Analysis of two beads in contact reveals 2 time scales controlling the system's transition from a unique stable steady state to degenerate oscillatory states. Numerical simulations of the aggregate show jamming-unjamming transitions, phase separation into hollow compartments, and spontaneous formation of 1D chains.</p>
16:15	910	<p style="text-align: center;"><b>Resection of DNA in response to permanent DSBs in <i>S.cerevisiae</i></b></p> <p style="text-align: center;"><i>Marco Labagnara, EPFL</i></p> <p>When double-strand breaks happens to the DNA, the cell arrests at the DNA damage checkpoint, preventing its entry into mitosis until the breaks are eventually repaired and the cell can proceed to mitosis. If the breaks persist, cells may bypass the checkpoint, this is called override. It is known that the override time depends on the number of breaks, but how the cell measure this number isn't still unknown. The most accepted model claims that cells measure the amount of resected DNA, but it was observed that mutants with less single-strand DNA take longer to override which contradicts the current model. We aim to demonstrate or deny the current model.</p>
16:30		<p><b>Coffee Break</b></p>
		<p><b>BIOPHYSICS, MEDICAL PHYSICS AND SOFT MATTER II: TECHNOLOGY DEVELOPMENT</b></p> <p><i>Chair: Christof Fattinger</i></p>
17:00	911	<p style="text-align: center;"><b>Mitochondrial structure and dynamics: Mysteries and insights</b></p> <p style="text-align: center;"><i>Suliana Manley, EPFL</i></p> <p>Mitochondria are heterogeneous organelles best known for their role in energy production through oxidative phosphorylation. Yet, they possess their own genetic material, encoding for key ox-phos proteins. Thus, they must divide to proliferate, which they do asynchronously from their host cell cycle. How do they ensure network maintenance and homeostasis? Using a customized structured illumination microscope, we discovered patterns underlying their division and genome organization, linked to biogenesis and quality control. We share new findings on the interplay between these processes and organelle trafficking within the cell. The intermittent dynamics of these processes imply that a constant imaging speed may miss important features. Thus, we also developed event-driven acquisitions, an adaptive microscope control that uses neural networks to enrich datasets for events of interest.</p>
17:30	912	<p style="text-align: center;"><b>Generative deep learning models for tracking <i>C. elegans</i></b></p> <p style="text-align: center;"><i>Sahand Rahi<sup>1</sup>, Isinsu Katircioglu<sup>1</sup>, Alice Gross<sup>1</sup>, Guillaume Obozinski<sup>2</sup></i> <i><sup>1</sup> Institute of Physics, EPFL, <sup>2</sup> SDSC, EPFL</i></p> <p>I will be describing our current efforts using generative deep learning models to create artificial training sets for tracking <i>C. elegans</i> worms using machine learning.</p>

17:45	913	<p style="text-align: center;"><b>Optogenetic control of the DNA Damage Checkpoint</b></p> <p style="text-align: center;"><i>Lorenzo Scutteri, EPFL</i></p> <p>When faced with chromosomal double-strand DNA breaks, cells activate a complex DNA Damage Checkpoint response that arrests the cell cycle and reprograms gene expression. Although the regulators of the core network have been intensively explored, the mechanism of checkpoint override remains poorly understood. To address this gap, we aim to design optogenetically-controlled checkpoint proteins by leveraging the light-sensitive LOV2 domain. By strategically integrating this optogenetic switch into specific positions of target proteins, we can dynamically and reversibly modulate their activity in response to light exposure. Through perturbation of engineered checkpoint proteins at the single-cell level, we aim to establish a quantitative model of DNA Damage Checkpoint override in <i>Saccharomyces cerevisiae</i>.</p>
18:00	914	<p style="text-align: center;"><b>Tuning colloidal interactions using random light fields</b></p> <p style="text-align: center;"><i>Augustin Muster, Luis S. Froufe-Pérez, Diego Romero Abujetas</i> <i>Department of Physics, University of Fribourg</i></p> <p>Random optical fields induce interactions between colloidal particles. Being the forces induced by the black body radiation the best known example. These fluctuation-induced interactions can be tuned by choosing an appropriate spectral energy density, hence it is possible to engineer the dynamics and equilibrium configurations. Using a coupled electric and magnetic dipoles model we present in this work how these optically induced pure pair interactions can be tuned and what are the limitations. As an application, we discuss the creation of stealth hyperuniform point patterns using such pair interactions. Moreover, we shall discuss the random fields-induced many body colloidal interactions and their properties.</p>
18:15	915	<p style="text-align: center;"><b>Predicting meiosis with a waddington landscape analogy</b></p> <p style="text-align: center;"><i>Maxime Scheder, EPFL</i></p> <p>Meiosis in <i>S. Cerevisiae</i> is a complex process which is tightly regulated by a large gene regulatory network. Such regulatory networks depend on numerous unknown parameters. Instead of modelling the gene network directly, the interest is set toward modelling the decision process through only few external measurable parameters such as the nutrient concentration. To this end, the analogy of the waddington landscape is literally put to use by fitting a two dimensional potential with experimental data.</p>
18:30	916	<p style="text-align: center;"><b>Microfluidics and imaging to understand the <i>C. elegans</i> brain development from embryo to adulthood</b></p> <p style="text-align: center;"><i>Elif Gencturk, EPFL</i></p> <p>I regard <i>Caenorhabditis elegans</i>, as a first step to understand more complex brains. I believe that microfluidics is the missing ingredient to breakthroughs. I will build microfluidic chips in which a single worm can hatch from an egg, be fed in a controlled manner with bacteria, and be imaged for whole-brain activity throughout its life while receiving stimuli to spark information processing activity. Then I will acquire in molecular biology, genetics, whole-brain imaging, and image analysis to study differences in brain activity in wild-type and mutant worms that fail to develop normally. I will test whether interventions with optogenetics or drugs can rescue brain development, generating useful hints for medicine.</p>

<b>18:45</b>	<b>917</b>	<p align="center"><b>Chaperones-stabilized non-equilibrium native state of proteins</b></p> <p align="center"><i>Paolo de los Rios, Pierre Goloubinoff, Alessandro Barducci, Alberto Sassi, Satyam Tiwari, Bruno Fauvet, Salvatore Assenza</i> <i>Institute of Physics, EPFL</i></p> <p>Under favourable conditions, proteins fold autonomously, and their native state is the minimum of the free energy. Under adverse conditions, like in the presence of elevated temperatures, non-native states be the true minima of the free energy, leading to protein denaturation and subsequent protein aggregation. All cells possess a set of molecular machines, known as chaperones, that counteract protein misfolding and aggregation. We have shown that, using the energy liberated by ATP hydrolysis, they stabilise proteins in their native states even under denaturing conditions., partly challenging our view of the energy landscape of proteins.</p>
<b>19:00</b>		<b>Transfer to Dinner</b>
<b>19:30</b>		<b>Conference Dinner</b>

**Friday, 08.09.2023, Room 117**

<b>Time</b>	<b>ID</b>	<p align="center"><b>BIOPHYSICS, MEDICAL PHYSICS AND SOFT MATTER III:</b> <b>MEDICAL AND MEDICALLY RELEVANT PHYSICS</b> <i>Chair: Rainer Leitgeb, Med. Universität Wien</i></p>
<b>12:00</b>	<b>921</b>	<p align="center"><b>Ultra-fast treatment delivery to enhance the potential of proton therapy for cancer treatment</b></p> <p align="center"><i>Vivek Maradia, Paul Scherrer Institute and ETH Zürich</i></p> <p>Proton therapy is a promising cancer treatment, but uncertainties due to anatomical changes and motion limit its effectiveness. To overcome this, Ultra-fast treatments might make tumor irradiations within a single. To enable ultra-fast treatment delivery, we investigate methods to reduce beam-on and dead time. By optimizing beam optics, using a dynamic ridge filter, and employing spot-reduced planning, treatment time can be significantly reduced, allowing for effective treatment of moving targets and expanding the potential of proton therapy.</p>
<b>12:30</b>	<b>922</b>	<p align="center"><b>Protein fibrils disassembly by the HSP70 chaperone machinery</b></p> <p align="center"><i>Davide Cois, Paolo de los Rios, Institute of Physics, EPFL</i></p> <p>Molecular chaperones are ubiquitous highly conserved proteins across all domains and living systems depend on them for cellular homeostasis. The chaperone machinery is able to disassemble toxic aggregates, which are a hallmark of neurodegenerative diseases. In vitro and in vivo studies, for different species, provide experimental evidence of aggregate dispersal by chaperone activity. However, the underlying fundamental mechanisms of disassembly are still not fully understood. In our work, we build a mesoscopic model based on coarse-grained interactions, aiming at describing the experimentally-observed behaviour of these systems and paving the way for their better understanding.</p>
<b>12:45</b>	<b>923</b>	<p align="center"><b>Deep-tissue imaging via multi-photon adaptive optics</b></p> <p align="center"><i>Maximilian Sohmen <sup>1</sup>, Çağlar Ataman <sup>2</sup>, Alexander Jesacher <sup>1</sup>, Juan D. Muñoz-Bolaños <sup>1</sup>, Pouya Rajaeipour <sup>2</sup>, Monika Ritsch-Martel <sup>1</sup></i> <i><sup>1</sup> Med. Univ. Innsbruck, <sup>2</sup> Phaseform GmbH</i></p> <p>Combining adaptive optics (AO) with multi-photon techniques is a powerful approach to image deep into biological tissue. Here, we present a new, fast and robust sensorless multi-photon AO scheme. We study our scheme in numerical simulations and in experiments with a novel, optical wavefront shaping device that is transmissive, refractive, polarisation-independent, and broad-band. We demonstrate scatter correction of two-photon-excited fluorescence images of microbeads as well as brain cells. Our method and technology could open new routes for AO that were previously inaccessible to multi-photon microscopy.</p>

13:00	924	<p style="text-align: center;"><b>Rapid T1, T2 and fraction quantification in two-compartment systems using bSSFP profile asymmetries</b></p> <p style="text-align: center;"><i>Nils Plähn, Berk Açıköz, Jessica Bastiaansen, Adèle Mackowiak Department of Diagnostic, Interventional and Pediatric Radiology (DIPR), Inselspital, Bern University Hospital, University of Bern, &amp; Translation Imaging Center (TIC), Swiss Institute for Translational and Entrepreneurial Medicine, Bern</i></p> <p>A novel analytical method in magnetic resonance imaging using phase-cycled balanced steady state free precession (PC-bSSFP) was developed for multi-compartment systems. The approach exploits asymmetries in complex PC-bSSFP signal profiles and enables simultaneous quantification of proton fraction, T1 and T2 relaxation times. Monte-Carlo simulations and experiments at 3 T and 7 T in an acetone-water phantom were performed. The proposed method for multi-parameter quantification in multi-compartment singlet systems was validated with high accuracy, precision, and ultra-rapid reconstruction time. This work provides important insights for PC-bSSFP multi-parameter quantification with PC-bSSFP sequences in presence of multiple compartments and a first steps towards more complex multiple- systems such as water-fat mixtures.</p>
13:15	925	<p style="text-align: center;"><b>Secure and versatile data and computing platform for cutting-edge data science in biomedical research compliant with the new Data Protection Act</b></p> <p style="text-align: center;"><i>Peter Strassmann, ETH Zürich, LeoMed Support</i></p> <p>Leonhard Med is a scientific IT-platform to securely store, manage, and process sensitive data. The digitalization of healthcare and medical devices in everyday life allow collecting vast amounts of health-related data, e.g., clinical and -omics data, data from biobanks and from wearables. Researchers transform such data into insights and decision-making tools for precision medicine and personalized health. Yet, data related to human health is sensitive and requires protection measures to protect the integrity of individuals. What options do researchers have for securely managing sensitive data and what are best practices in the daily research with sensitive data? Leonhard Med offers such a secure and customizable platform for researchers in Switzerland.</p>
13:30	926	<p style="text-align: center;"><b>Predicting behaviour from interneuron activity in <i>C. elegans</i></b></p> <p style="text-align: center;"><i>Mahsa Barzegarkeshteli, Alisa Gross, EPFL</i></p> <p>We will focus on how <i>C. elegans</i> worm responds to sensory cues depending on its internal brain state. They can be defined as the patterns of neuronal activity that are highly predictive of behaviour. Recent technological advances have made it possible to image whole-brain calcium activity at cellular resolution in freely moving animals. From changes in behaviour and neural dynamics, internal brain states should in principle be inferrable. However, it remains unclear how to identify internal brain states, how they control behaviour, and how neurons can be manipulated to induce state transitions. We will focus on interneurons that integrate sensory information in the sensorimotor pathway to parameterize computational models.</p>
13:45	927	<p style="text-align: center;"><b>Quantitatively pin-pointing individuality at the single neuron level</b></p> <p style="text-align: center;"><i>Matthieu Schmidt, EPFL</i></p> <p>In this study, I investigate factors contributing to consistent behavior throughout an individual's lifespan in <i>C. elegans</i>. Using optogenetic stimulation, I redefine individuality by examining stimulus-induced behavioral responses. I then explore serotonin's role in maintaining behavioral consistency by optogenetically controlling serotonergic neuron NSM. A custom high-throughput setup tracks individual worms from egg to adulthood, while optogenetic stimulations are applied. An automated data analysis pipeline manages the extensive generated data. This investigation aims to deepen understanding of behavioral consistency and individuality in conspecifics.</p>
14:00	<b>END</b>	