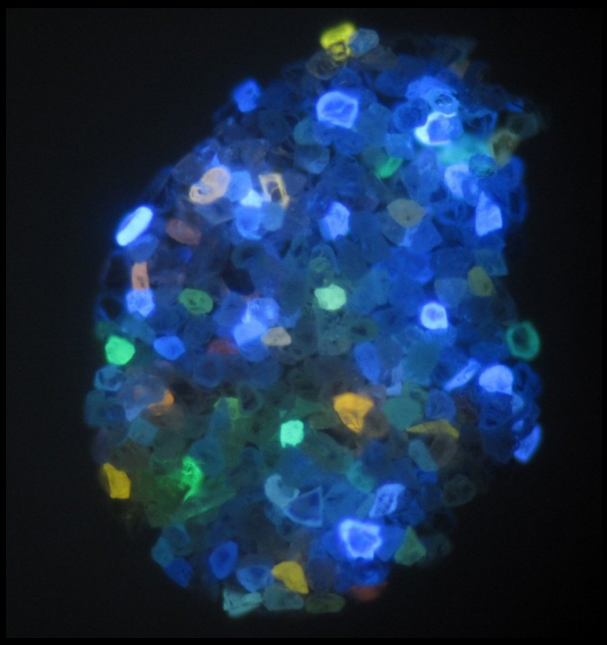

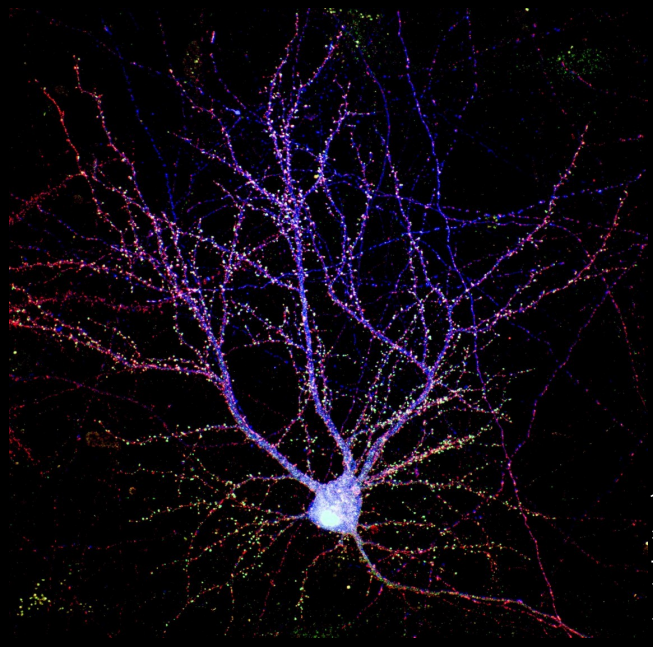

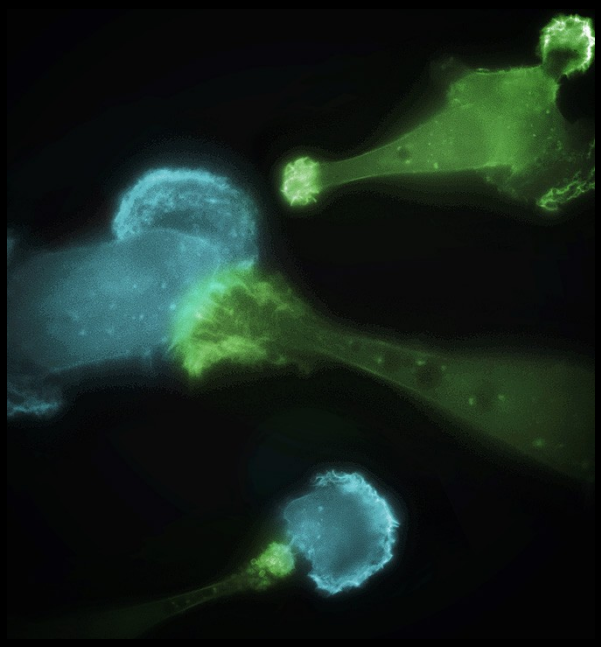

Image courtesy of Ronald WALSWORTH, Cécile CHARRIER, Chase BROEDERSZ (from top to bottom)

7th International Conference on

Physics & Biological Systems 2024

June 26-28 2024

Ecole Polytechnique, France
Amphitheater Gay-Lussac

Invited speakers:

Jean-Christophe Baret (U. Bordeaux, France)
Chase Broedersz (Vrije U., the Netherlands)
Laure Buhry (U. Lorraine, France)
Cécile Charrier (ENS Paris, France)
Peter Dedecker (U. Leuven, Belgium)
Roberto Di Leonardo (Sapienza U. di Roma, Italy)
Thomas Gregor (Princeton U., USA)
Jonathon Howard (Yale U., USA)
Benoît Landrein (ENS Lyon, France)
Séverine Le Gac (U. Twente, the Netherlands)
Manuel Maestre-Reyna (Natl Taiwan U., Taiwan)
Andreas Möglich (U. Bayreuth, Germany)
Miguel Munoz (U. Granada, Spain)
Naomi Nakayama (Imperial College London, UK)
Teuta Pilizota (U. Edinburgh, UK)
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Program

Physics and Biological Systems 2024 | Program

June 26-28 2014, Palaiseau, France

All talks will take place in amphithéatre Gay-Lussac at Ecole Polytechnique, Palaiseau, France

Wednesday, June 26

WELCOME COFFEE AND OPENING (9:45-10:15)

Session chair: Cédric Bouzigues

10:15	Andreas Möglich	Leveraging Phytochromes for Regulating Biological Processes by Light
11:00	Dominik Bucher	Towards single-cell NMR spectroscopy with quantum sensors in diamond
11:45	Severine Le Gac	Organ-on-chip platforms for biological and medical applications

LUNCH (12:30-13:30)

Session chair: Vincent Ouazan-Reboul

13:30	Mathilde Louçã	Functional impacts of Huntingtin lowering on human cortical synapses
13:45	Caroline Giuglaris	Hydrodynamics of active cells migrating under mesoscopic confinement
14:00	Marie-Charlotte Emperauger	Real time tracking of single nanoparticles motion and orientation in neurons
14:15	Lara Koehler	From waves to chaotic flows in the cytoplasm

POSTER SESSION (14:45-15:30)

Session chair: Harold Auradou

15:30	Chase Broedersz	Learning the statistical folding of bacterial chromosomes

COFFEE BREAK (16:15-16:30)

16:30	Roberto di Leonardo	Programming bacterial dynamics with light
17:15	Thomas Gregor	Precise and scalable self-organization in mammalian pseudo-embryos

Thursday, June 27

Session chair: Pavel Muller

9:00	Tony Stöcker	Structural and quantitative whole-brain MRI at 7 Tesla
9:45	Manuel Maestre-Reyna	3D molecular movies of flavins at work

COFFEE BREAK (10:30-11:00)

11:00	Peter Dedecker	Information-enhanced fluorescence imaging using smart probes and novel instrumentation

POSTER SESSION (11:45-12:30)

LUNCH (12:30-13:30)

Session chair: Xavier Serfaty

13:30	Samuel S. Gomez	Diffusion, viscosity, and linear rheology of valence-limited disordered fluids
13:45	Romain Rollin	Mechanics of Cell Nuclei under Large Deformations
14:00	Ivana Rondon	Integrative gene networks predict stromal changes in human prostate cancer upon PTEN protein loss
14:15	Dounia Zamiati	From Fluorescence Signals to Molecular Insights: FRET-Based Techniques for Investigating ER-Phagosome Membrane Associations

POSTER SESSION (14:45-15:30)

Session chair: Magda Magiera

15:30	Miguel Munoz	Scaling of brain activity and optimal functionality: from real neurons to artificial intelligence.

COFFEE BREAK (16:15-16:30)

16:30	Laure Buhry	Computational modeling of electrophysiological signals in neurology and psychiatry: towards the identification of new therapeutic targets
17:15	Cécile Charrier	Molecular mechanisms of synaptic development: insights from human-specific genes

POSTER SESSION (18:00-18:45)

CONFERENCE DINNER (18:45-21:00)

Friday, June 28

Session chair: Pauline Durand

9:00	Sarah Robinson	The relationship between cell division and mechanical properties
9:45	Naomi Nakayama	Future-proofing plant forms

COFFEE BREAK (10:30-11:00)

11:00	Benoît Landrein	Mechanics of seed morphogenesis
11:45	Jean-Christophe Baret	Botton-up construction of life-like synthetic cells

LUNCH (12:30-13:30)

Session chair: Stella Dees

13:30	Tom Burkart	Function Follows Form: Geometrical Guidance of Intracellular Self-Organization
13:45	Laure Mancini	Control of the spiral phyllotaxis from a single stem cell in the moss Physcomitrium patens
14:00	Thomas Bugea	Visualising the self-assembly dynamics of icosahedral viruses through fluorescence microscopy at the single particle level

COFFEE BREAK (14:30-14:45)

Session chair: Meriem Elkaroui

14:45	Joe Howard	Biophysics of branched cells: growth, scaling laws and the supply of metabolic demand
15:30	Teuta Pilizota	On the most important thing you likely know little about: the ion motive force(s)

CONFERENCE CLOSING (16:15-16:30)

Poster abstracts

This list was generated automatically from the authors' submissions. Our apologies for any formatting imperfections.

Poster #1, presented by Julien Husson

Stiffening cells with light

Eva Gonzalez (1), Julien Husson (1) (1) Laboratoire d'Hydrodynamique (LadHyX), CNRS, Ecole polytechnique, Institut Polytechnique de Paris, Palaiseau, France

Fluorescence imaging is at the core of cell biology. However, excessive illumination can result in the production of reactive oxy-gen species (ROS), leading to phototoxicity. ROS are known to destabilize cytoskeleton fibers in vitro, so that the generation of intracellular ROS could soften cells. We addressed this question using profile microindentation [1] and showed that the outcome was the exact opposite: fluorophore-loaded cells stiffen dramatically upon fluorophore excitation. This is consistent with an alternative mechanism, in which light-induced ROS induce crosslinking of their surrounding proteins and DNA. We used profile microindentation to quantify cell stiffness and demonstrated that upon loading with various fluorescent probes and 10-s exposure to light, several types of cells including T lymphocytes, endothelial cells, and neutrophil-like PLB cells became up to ten times stiffer (Fig. 1). To demonstrate a dose effect, we showed that consecutive shorter flashes stiffen the cells at a rate that increases with lamp intensity. In addition to cells becoming stiffer, their function was impaired: T lymphocytes loaded with the calcium probe Fluo-4 cease activation within seconds of probe excitation. Cell stiffening correlates with increased fluorescence of a ROS sensor, supporting the hypothesis that light-induced intracellular ROS mediate stiffening. Cells treated with cytoskeletal inhibitors still stiffened massively, consistent with ROS affecting more molecules than cytoskeletal structures. Our results show that cell stiffening is a new indicator of phototoxicity and opens avenues for exploring how cells cope with ROS, especially leukocytes such as neutrophils, which are accustomed to managing high ROS levels.

Poster #2, presented by Lukas Kalvoda

Particle Anisotropy Promotes Aggregate Order in Geometrically Frustrated Self-Assembly

Lukas Kalvoda (LMU Munich, Germany); Martin Lenz (LPTMS, Université Paris-Saclay, France)

While living cells rely on protein self-assembly to form large functional structures "by evolutionary design", a lack of regulation gives rise to pathological fibers in numerous diseases like Alzheimers, Type II Diabetes and sickle cell anemia. However, how complex and anisotropic components can robustly form well-defined large-scale morphologies is largely unknown. We propose geometrical frustration as a possible underlying physical principle of self-assembly that favors slim and porous aggregates. Geometrical Frustration arises when complex anisotropic particles are incapable of establishing favorable interactions with multiple nearest neighbors in assembly simultaneously. We investigate its small scale effects using a lattice gas model on a treelike graph. The rich variety of resulting aggregate morphologies can be classified based on 3 observables that are easily accessible within our model. Remarkably, as anisotropy and hence complexity of particles is increased, ordered aggregates emerge and dominate the state space. In this regime, geometrical frustration strongly favors slimmer aggregates like fibers and fiber networks, while its absence is characteristic of ordered space-filling morphologies like crystals.

Poster #3, presented by Andrey Zelenskiy

Morphology of Aggregates in Frustrated Self-Assembly

Andrey Zelenskiy (LPTMS, Université Paris-Saclay); Lara Koehler (Max Planck Institute for the Physics of Complex Systems); Pierre Ronceray (Turing Center for Living Systems); Martin Lenz (LPTMS, Université Paris-Saclay)

Biomolecular self-assembly lies at the very heart of the function of living cells, where it organizes individual components into functional biological machines. The macromolecular sub-units typically correspond to proteins, whose shapes have been optimized over millions of years of evolution to ensure a proper functionality of the self-assembled structures. However, in pathological cases, proteins fail to achieve the optimal folding, which often leads to complex ill-fitting shapes. This produces geometrical incompatibility, which leads to frustrated interactions between the sub-units. Surprisingly, despite a huge variability in protein structure, such misfolded units tend to robustly self-assemble into aggregates with well-defined morphologies. Interestingly, these structures display a clear preference for slimmer topologies, such as fiber aggregates. This emergent principle of dimensionality reduction suggests that the aggregation of irregular components derives from the generic physical principles, rather than the microscopic details of the interactions.

Inspired by this idea, we model the frustrated self-assembly of ill-shaped proteins as coarse-grained anisotropic particles, whose interactions depend on their relative orientations and positions in space. This simple model successfully reproduces a hierarchy of aggregate morphologies and gives pointers to the origins of dimensionality reduction.

Poster #4, presented by Giacomo Donini

Torque response in the flagellar motor of E.coli

Giacomo Donini, Silvio Bianchi, Filippo Saglimbeni, Giacomo Frangipane, Cristina Cannarsa, Roberto Di Leonardo

The bacterial flagellar motor (BFM) is a rotating nano-motor embedded in the cell membrane that rotates the flagellum, generating self-propulsion. Capable of rotating at up to hundreds of Hertz, the bacterial flagellar motor is one of the most powerful and efficient molecular motors in nature, but it still lacks a satisfactory model to explain its molecular functioning. The relevant quantity that characterises the motor is the torque delivered at different frequencies. Using rotating optical tweezers, we impose the frequency of the motor and simultaneously measure the torque. We find new experimental evidence for a discontinuity of torque across the zero-frequency stall point, reopening a debate that was thought to be closed.

Poster #5, presented by Gizem Nuran YAPICI

Towards quantum microscopy of neuron electric signals

Gizem Nuran Yapici (Université Paris-Saclay, ENS Paris-Saclay, CNRS, CentraleSupélec, LuMIn, Gif-sur-Yvette, France) Liam Hanlon (Université Paris-Saclay, ENS Paris-Saclay, CNRS, CentraleSupélec, LuMIn, Gif-sur-Yvette, France) Baptiste Grimaud (Université Paris-Saclay, ENS Paris-Saclay, CNRS, CentraleSupélec, LuMIn, Gif-sur-Yvette, France) Anton Savitsky (Faculty of Physics, Technical University Dortmund, 44227 Dortmund, Germany) Tan-Duy Ho (Université Paris-Saclay, CNRS, Centre de Nanosciences et de Nanotechnologies, 91120, Palaiseau, France) Dieter Suter (Faculty of Physics, Technical University Dortmund, 44227 Dortmund, Germany) Xavier Checoury (Université Paris-Saclay, CNRS, Centre de Nanosciences et de Nanotechnologies, 91120, Palaiseau, France) Francois Marquier (Université Paris-Saclay, ENS Paris-Saclay, CNRS, CentraleSupélec, LuMIn, Gif-sur-Yvette, France) François Treussart (Université Paris-Saclay, ENS Paris-Saclay, CNRS, CentraleSupélec, LuMIn, Gif-sur-Yvette, France)

Despite recent improvements in the brightness and speed of neuron transmembrane voltage indicators, notably the genetically encoded ones, there is a need for widefield sensors of neuron electrophysiological activity that can achieve nanoscopic spatial resolution alongside sub-millisecond temporal resolution and high sensitivity. We propose a device relying on a wide-field quantum sensor which uses the nitrogen-vacancy (NV) center.

The NV center is an atomic defect in a diamond lattice with unique quantum properties that allows for exceptionally high sensitivity measurements of electromagnetic fields in ambient conditions based on optically detected magnetic resonance. We place these defects in a diamond nanopillar array that favors the growth of neurites from one pillar to a nearby one. Doing so, we expect to achieve the closest possible contact between the membrane and the pillar sensor and therefore circumvent the Debye layer which screens neuron external electromagnetic fields [1]. To perform the measurement, we have built a diamond quantum microscope relying on a conventional fluorescence microscope and a cage incubator adapted to live cell imaging. As a first test of the sensor, we imaged AC magnetic fields with millisecond temporal resolution using a fast array detector that has a built-in pixel-wise lock-in detection process. Such a very fast array detector is instrumental to resolve individual neuronal spikes [2]. In parallel, we have cultured human neurons derived from induced pluripotent stem cells on nanopillar samples and using calcium flux imaging as a proxy to electrical activity, we have proved that they are functional. Moreover, using neuronal immunolabeling, we observed that the neurites coordinate with the nanopillars array. Future work includes evaluation of the sensitivity of our device for sensing electric fields, using a controlled source from an atomic force microscopy tip.

References: [1] Hanlon L., et al. "Diamond nanopillar arrays for quantum microscopy of neuronal signals," Neurophotonics. 7, 035002 (2020), https://doi.org/10.1117/1.NPh.7.3.035002. [2] Webb, J. L., et al. "High-Speed Wide-Field Imaging of Microcircuitry Using Nitrogen Vacancies in Diamond." Phys. Rev. Appl., 17, 064051, https://doi.org/10.1103/PhysRevApplied.17.064051

Poster #6, presented by Baptiste Grimaud

Measuring axonal transport in models of Alzheimer's disease using neurotropic fluorescent nanodiamonds

Baptiste Grimaud (Université Paris-Saclay, ENS Paris-Saclay, CNRS, CentraleSupélec, LuMIn, Gif-sur-Yvette, France) Devrim Kilinc (Université de Lille, Institut Pasteur de Lille, CHU Lille, INSERM U1167, LabEx DISTALZ, Lille 59019, France) Marcos Costa (Université de Lille, Institut Pasteur de Lille, CHU Lille, INSERM U1167, LabEx DISTALZ, Lille 59019, France and Brain Institute, Federal University of Rio Grande do Norte, Natal 59056-450, Brazil) Régis Daniel (CNRS, Université d'Évry Paris-Saclay, Cergy Paris Université, LAMBE, France) William Buchmann (CNRS, Université d'Évry Paris-Saclay, Cergy Paris Université, LAMBE, France) François Treussart (Université Paris-Saclay, ENS Paris-Saclay, CNRS, CentraleSupélec, LuMIn, Gif-sur-Yvette, France)

Defects in axonal transport at the molecular level are observed in neurodegenerative diseases, but their roles in the development of the pathology are unknown. We developed a method to measure axonal transport based on the endocytosis of fluorescent nanocrystal (nanodiamonds, FNDs) into neurons, followed by recording their movement using fast video-microscopy. The goal of this project is to extend this method to human cerebral organoids (hCO), which present a diversity of cell types closer to that of the brain. To facilitate internalization into hCOs, which are denser than two-dimensional cultures and less mature than primary mouse neurons, our strategy is to graft a neurotropic peptide (RVG29) onto the FNDs. We have generated and characterized a first batch of FND-RVG29 nanoconjugates, starting from commercial FND-PEGs (nominal size ≈40 nm)

prefunctionalized by maleimide groups, and from custom-synthesized RVG29-C. Direct characterization of the complex by MALDI-TOF mass spectrometry (MS) is challenging due to the considerable difference in molecular mass between FNDs and RVG29. We therefore opted for a chemical cleavage of the peptide, which should only release its N-terminal fragment if it is covalently bound to the FND and which is measurable by MS. To overcome the quantitative limitations of MS, we recently obtained an isotopically labelled peptide with an identical structure to RVG29 but 10 Da heavier. We thus hope to quantify the amount of peptide that reacted with FNDs. In addition to the physicochemical characterization of the conjugates, and prior to studies on hCOs, we developed neuronal cultures derived from human induced pluripotent stem cells (iPSCs). Specifically, we differentiate neural progenitors with and without mutations of the BIN1 gene (a risk factor for Alzheimer's disease). Differentiation into neurons and axonal growth (in microfluidic channels) was validated by immunofluorescence. Neurons are also functional, as evidenced by calcium influx (visualised by a genetically encoded probe) and spontaneous electrophysiological activity (detected using a high-density microelectrode array on which the culture was grown for 2 weeks).

Poster #7, presented by François Anquez

Spatial self-organization of cancer stem cell niches revealed by live single-cell imaging

Mathilde Brulé (1), Anaïs Horochowska (1), Emeline Fontaine (1), Raoul Torero-Ibad (2), Flavie Woesteland (1), Marie Denoulet (1), Jean Pesez (2), Eric Adriaenssens(1), Robert-Alain Toillon (1), Xuefen Le Bourhis(1), Benjamin Pfeuty (2), Chann Lagadec(1,3) and François Anquez(2)
[1] Canther ; Univ. Lille, CNRS, Inserm ; France [2] PhLAM ; Univ. Lille, CNRS, UMR 8523 ; France

Phenotypic plasticity is a major factor of tumor heterogeneity and treatment resistance. In particular, cancer stem cells (CSCs) represent a small subpopulation within tumors with self-renewal and tumor-forming capabilities. Understanding reprogramming, maintenance, and lineage properties of CSCs requires dedicated tools to disentangle the respective influences of phenotypic inheritance and cell-cell interactions. Here we set up ultra-wide field microscopy of breast cancer cell lines expressing a stemness fluorescent reporter for several days. The fluorescent reporter distinguishes three phenotypes : cancer stem cells (CSCs), cancer differentiated cells (CDCs) and intermediate/transiting cancer cells (iCCs). Spatial statistics indicate significant zonation, aka phenotypic niches, with CSC clustering near each other but away from CDCs. Surprisingly, single cell time series reveal spontaneous reprogramming events from CDC to CSC even in unperturbed populations. We identify that such transitions are prone to arise during the cell cycle. Moreover, lineage analysis shows that the phenotype is partially inherited from ancestor cells. However, such heredity is not sufficient to explain the spatial properties of the cell population, which also depend on cell-cell interactions. Indeed, we identified that phenotypic transitions of cancer cells are influenced by the phenotypic state of neighboring cells. Reprogramming into CSCs is respectively promoted and inhibited by the presence of CSCs and CDCs in the neighborhood. Altogether, our results disentangle how phenotypic inheritance and intercellular interactions orchestrate the spatio-temporal self-organization of cancer cell heterogeneity, maintaining a subpopulation of CSCs within niches.

Poster #8, presented by Maria Dimitra Chiotelli

Screening the swimming motility of bacterial gut commensals

Maria Dimitra Chiotelli1, Charlie Pauvert1, Thomas Clavel1, Marianne Grognot1
1 Institute of Medical Microbiology, RWTH Aachen University, Germany

Introduction An estimated half of bacterial species can swim, propelled by one or more flagella, and display a variety of swimming behaviors1. It enables them to seek out favorable environments within their ecological niche. Here, we dive into the complex ecosystem of the human gut, which houses trillions of commensal bacteria, and where elevated flagellin (a major component of the flagella) levels have been linked with intestinal inflammation2. However, direct assessment of commensals' motility is lacking beyond the model organisms E. coli. Methods & Results We present the development of a simple motility screening method, compatible with anaerobic culturing, and apply it to bacterial isolates from the Human intestinal Bacterial Collection (HiBC3). As the HiB collection has been fully sequenced, we can demonstrate a 96% true positive detection rate and provide insights bridging motility phenotype and genotype. We further characterize swimming behaviors of commensals, from the HiB collection or from fresh faecal samples, using a stain-free high-throughput 3D tracking method4. Preliminary results demonstrate elevated motile fraction in a chronic inflammation mouse model, and hint at diverse swimming behaviors other than that of E. coli. Conclusions Our work paves the way for a quantitative approach of bacterial commensals motility, and to test the long-hypothesized role of bacterial swimming motility in inflammation and subsequent gut diseases.

References 1. Grognot, M. & Taute, K. M. More than propellers: how flagella shape bacterial motility behaviors. Curr. Opin. Microbiol. 61, 73–81 (2021). 2. Tran, H. Q., Ley, R. E., Gewirtz, A. T. & Chassaing, B. Flagellin-elicited adaptive immunity suppresses flagellated microbiota and vaccinates against chronic inflammatory diseases. Nat. Commun. 10, 5650 (2019). 3. Retrieved March 2023, DOI:10.5281/zenodo.7966673 4. Taute, K. M., Gude, S., Tans, S. J. & Shimizu, T. S. High-throughput 3D tracking of bacteria on a standard phase contrast microscope. Nat. Commun. 6, 8776 (2015).

Poster #9, presented by Chiara ENRICO BENA

Real-time monitoring of replication errors' fate reveals the origin and dynamics of spontaneous mutations

Chiara Enrico Bena (Micalis Institute, Université Paris-Saclay, INRAE, AgroParisTech, Jouy-en-Josas, France), Jean Ollion (Laboratoire Jean Perrin (LJP), Sorbonne Université, CNRS, Institut de Biologie Paris-Seine (IBPS), Paris, France; SABILab, Die, France), Marianne De Paepe (Micalis Institute, Université Paris-Saclay, INRAE, AgroParisTech, Jouy-en-Josas, France), Magali Ventroux (Micalis Institute, Université Paris-Saclay, INRAE, AgroParisTech, Jouy-en-Josas, France), Lydia Robert (Micalis Institute, Université Paris-Saclay, INRAE, AgroParisTech, Jouy-en-Josas, France), Marina Elez (Micalis Institute, Université Paris-Saclay, INRAE, AgroParisTech, Jouy-en-Josas, France).

Mutations are the driving force of evolution and play an important role in health. DNA replication errors, i.e., the insertion of erroneous bases during DNA replication, are one of the major sources of spontaneous mutations in growing cells. The highly evolutionarily conserved Mismatch Repair System (MMR) corrects these errors. In rare cases (~1%), the correction fails, causing mutations to appear. It has so far been impossible to study repair efficiency at the level of individual cells and to investigate if it varies within isogenic cell populations. Indeed, the traditional techniques used to investigate mutations are based on population-level measurements, do not consider neither cell-to-cell variability nor the temporal dynamics of mutations, and assume that every cell in the population has an equal probability of undergoing mutation. However, repair efficiency may fluctuate through time and among cells due to, for example, fluctuating concentrations of repair enzymes. Moreover, the reason why some errors escape repair remains unknown. To tackle these

questions, we apply a combination of fluorescent labelling of the Escherichia coli MMR complex, microfluidics, and time-lapse microscopy, to monitor in real-time the fate of >20000 replication errors in thousands of cells growing in parallel for a hundred consecutive generations. In this way, we show that i) many mutations result from errors that are detected by MMR but inefficiently repaired, ii) this limited repair efficiency is due to a temporal constraint imposed by the transient nature of the DNA strand discrimination signal, a constraint that is likely conserved across organisms, and iii) although replication errors occur according to a Poisson process, the repair capacity varies from cell to cell resulting in a subpopulation of cells with higher mutation rate and leading to a non-Poisson dynamics. Such variations could influence the fitness and adaptability of populations, accelerating for instance the emergence of antibiotic resistance.

Poster #10, presented by Kauffmann Lisa

How Amphipathic Helices from Proteins Allow Binding to Lipid Droplets

Lisa Kauffmann (Laboratoire de Physique de l'Ecole Normale Superieur , PSL, France) Mehdi Zouiouich (Laboratoire de Physique de l'Ecole Normale Superieur , PSL, France) Abdou Rachid Thiam (Laboratoire de Physique de l'Ecole Normale Superieur , PSL, France)

Lipid droplets serve as critical energy storage compartments within cells. These droplets are composed of a core of neutral lipids surrounded by a phospholipid monolayer(2). Proteins are also present on the surface of these droplets. The composition of neutral lipids and phospholipids is known to influence the specific recruitment of proteins to lipid droplets (3). Two pathways for protein binding to lipid droplets have been described(1). In this project, we will focus on unfolded proteins in the cytoplasm that fold upon contact with lipid droplets. These proteins typically form a secondary structure known as the amphipathic helix (1). However, how these helices sense the physicochemical properties of lipid droplets and bind specifically to them is not well understood. To achieve the project's aim, a screening of different amphipathic helices will be conducted to elucidate how these helices sense the physicochemical properties of the lipid droplets and bind specifically to them. (1) Song, J. et al. , (2022). Identification of two pathways mediating protein targeting from ER to lipid droplets, Nature cell biology (2) Thiam, A. R., & Beller, M. (2017). The why, when and how of lipid droplet diversity. Journal of Cell Science, 130(2), 315-324 (3) Chorlay, A., & Thiam, A. R. (2020). Neutral lipids regulate amphipathic helix affinity for model lipid droplets. Journal of Cell Biology

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Poster #11, presented by Maxence Arutkin

Doubly stochastic continuous time random walk

Maxence Arutkin 1,2, and Shlomi Reuveni 1,3, 1/School of Chemistry, Center for the Physics & Chemistry of Living Systems, Tel Aviv University, 6997801 Tel Aviv, Israel 2/Service d'Epidémiologie-Data-Biostatistiques, Délégation à la Recherche Clinique et à l'Innovation, Hôpital Foch, 92150 Suresnes, France 3/Sackler Center for Computational Molecular & Materials Science, Ratner Institute for Single Molecule Chemistry, Tel Aviv University, 6997801 Tel Aviv, Israel

Leveraging the foundational Montroll-Weiss continuous time random walk (CTRW), our study introduces an innovative approach to address the previously uncharted territory of "diffusing diffusivity" in random walks. This advance encompasses the conceptualization of a fluctuating jump rate, a significant leap beyond traditional models that assumed a constant rate. Our doubly stochastic model not only captures the essence of diffusing diffusivity but also extends the Montroll-Weiss framework to encompass a broader spectrum

of diffusion phenomena, including Brownian yet non-Gaussian diffusion, a behavior increasingly observed in diverse systems.

This model, by incorporating a time-dependent jump rate that randomly fluctuates, allows for a richer exploration of diffusion dynamics, showcasing versatility in modeling super, sub, and normal diffusion processes alongside elucidating the Brownian yet non-Gaussian diffusion phenomena. Such a comprehensive tool offers profound implications for understanding the intricate dynamics of diffusing systems, ranging from molecular movements in heterogeneous environments to the fluctuating nature of financial markets. Our presentation will delve into the core principles of this model, demonstrating its ability to provide novel insights into the diffusion process, backed by analytical results and simulations.

Poster #12, presented by Victoria Nicolazo-Crach

Bio-convective transport of passive particles

Victoria Nicolazo-Crach (FAST, Universite Paris-Saclay, France) Taha Laroussi (LadHyX, École polytechnique, France) Julien Bouvard (LadHyX, École polytechnique, France) Gabriel Amselem (LadHyX, École polytechnique, France) Mojtaba Jarrahi (FAST, Universite Paris-Saclay, France)

Active particles are inherently out-of-equilibrium systems, able to uptake energy from their environ- ment and convert it to motion. For example, Chlamydomonas Reinhardtii (CR) is a micro-swimmer whose orientation can be dictated by a light gradient in its environment (phototaxis). It is known that a collective motion triggered due to the phototaxis of a population of CR generates a nonlinear phenomenon: bioconvective structures that affect the fluid medium [1].

The purpose of this experimental study is to control the motion of algae swarms and resulted bio- convective vortices in order to achieve a guided transportation of microscopic objects submerged in the algal suspension. High concentrations of algae and microparticles were confined in a small square Hele-Shaw cell surrounded by a series of LED, allowing us to apply different well-controlled gradients of light stimulus in a quasi-2D horizontal domain. It was shown that the microparticles can be trans- ported to a target zone by controlling the displacement of algal bioconvective structures.

[1] J. Dervaux, M. Capellazzi Resta, and P. Brunet, Nature Phys 13, 306–312 (2017).

Poster #13, presented by Emerson Rodrigo da Silva

Cell-Penetrating Peptides from the SARS-CoV-2 Proteome: Structural Insights and Therapeutic Potential

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The high infectivity of SARS-CoV-2 makes its proteome a valuable source of new cell-penetrating peptides (CPPs), promising significant discoveries in the coming years. This study aimed to characterize the nanoscale structure of peptides derived from the SARS-CoV-2 spike protein and chimeric sequences combining fragments from SARS-CoV-2 and simian virus 40 (SV-40) proteomes. We investigated the nanoscale organization of peptide/DNA complexes based on selected sequences, studied their effect on the elastic properties of lipid vesicles, and tested their interaction with cells. A chimeric peptide was designed by combining the decameric segment YRLFRKSNLK from the recognition binding domain of the SARS-CoV-2 spike protein with the nuclear localization signal KKKRKV from the SV-40 antigen, with a linker domain WSQP. This sequence was chemically modified to create a lipidated analog by covalently linking a stearoyl tail to the N-terminus of the peptide. Using a range of biophysical approaches, including spectroscopy tools, small-angle X-ray scattering (SAXS), and cryogenic electron microscopy (cryo-EM), we showed that lipidation imparts self-assembling capabilities to the modified chimera, leading to the formation of micelles ~5 nm in size. While the chimera peptide exhibited antimicrobial activity against S. aureus and E. coli strains, with inhibitory concentrations of 27 μM and 55 μM, respectively, the lipidated version was innocuous against bacteria. Interestingly, internalization assays conducted in HeLa cells indicated that the SARS-CoV-2-derived peptides promote the uptake of 200 base pair DNA strands into cells. Importantly, lipidation endowed the sequences with the ability to reach cell nuclei, indicating an advantage for gene therapy. In conclusion, our findings highlight the potential of a new class of CPPs derived from the SARS-CoV-2 proteome and provide insights into their interactions with biomembranes, paving the way for a novel class of peptide-based vehicles for gene delivery applications.

Poster #14, presented by Robin Kuhner

Ultrasensitive detection using YVO4 luminescents nanoparticles

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The rapid identification of pathogens or biomarkers (viruses, bacteria, toxins) with high sensitivity, in the environment (bioaerosols, water, food matrices,...) or in biological media, is essential to deploy physical and medical protection measures. Existing methods are either quite sensitive but expensive and difficult to implement (SIMOA) or not sensitive enough to allow the early detection of these biomarkers (HIV-GAG-P24, inflammatory biomarker, ...). However, the use of luminescent Eu/YVO4 nanoparticles allows to reduce the limit of detection (LOD) for many targets grace of their physical properties. Indeed, rare earth doped vanadate nanoparticles combine a high absorption coefficient with a large band, a large Stokes distance and a narrow emission band.This last propertie allows an easy selection of wavelenght for the detection.these nanoparticles coupled at a homemade microplate reader allowed to have an hight sensitive results with a the same cost an ELISA.Under the optimized conditions the detection of insulin (proof of concept analyte) is 25000 times better than a commercial assay with the same antibody couples. By this good sensitivity we work to detect directly viral nucleic acid without amplification.

Poster #15, presented by Julien Le Dreff

Swimming dynamics and efficiency in diatom chain colonies

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Diatoms are among the most abundant microorganisms found in both oceanic and freshwater environments worldwide. While some species drift passively with ambient currents, others employ various strategies for movement or self-propulsion. One species in particular, called Bacillaria Paxillifer, forms colonies of stacked rectangular cells that slide along each other while remaining parallel. This unique collective motion leads to beautiful and nontrivial trajectories at the colony scale. By using a numerical method developed to simulate articulated bodies in Stokes flows, we show that the swimming speed of such microorganisms changes non-monotonically with the sliding delay between pairs of cells. The observed swimming efficiency as a function of the number of oscillations along the colony exhibits several local maxima, contrary to what is commonly observed in flagellate microorganisms. In addition, the optimal cell aspect ratio found with our simulation matches those observed in real diatom chain.

Poster #16, presented by Billoir

Investigating the Time-Dependent Response of Glioma Cells to Radiotherapy: Comparison of a Compartmental Model to Experiments

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Gliomas constitute the majority of malignant brain tumors in adults. Their ability to diffusely infiltrate neighboring brain tissue makes them very hard to treat and they are typically associated with a poor prognosis. Radiation therapy stands as a crucial cornerstone of their therapeutic strategy, entailing the delivery of fractionated doses according to a precise schedule. This approach allows surrounding non-cancerous tissues to recover between treatment fractions. Nevertheless, despite remarkable advancements in the field, there has been no definitive improvement in the long-term survival of glioma patients. A potential explanation lies in the lack of temporal description of the tumor's response to radiation of the conventional radiobiological models on which are based the planning of the therapy sessions.

To address this gap, we propose a simple, biologically motivated, compartment-based model characterizing the temporal response of glioma cells to single dose radiation therapy. To validate our model, we conducted in vitro experiments using time-resolved fluorescence microscopy to track the density of F98 glioma cells following exposure to varying radiation doses and initial cell concentrations. We show that it is possible to get an excellent agreement between the model and the data with only four free parameters. We also highlight an interesting adverse effect of the initial cell density at high doses. We now seek to integrate a spatial dependance in our model in order to compare it with minibeam radiation experiments, a new modality of irradiation that seems promising for glioma patients.

Poster #17, presented by Alexander Chervanyov

Kinetic model of the static and dynamic patterning in the system of self-propelled agents

Alexander Chervanyov (University of Münster, Germany)

The self-propelled agents (SPP) are often used as a workhorse model of the collective motion of such bio-systems as bacterial colonies, fish schools, bird flocks, to name a few. The reported work looks into the formation of steady non-equilibrium states of the SPP undergoing the competitive processes of the Turing patterning, rotational relaxation and rotational diffusion of the SPP self-propulsion velocities. The

developed kinetic model predicts several non-trivial steady (moving and resting) states of the SPP system. The transitions between these states are caused by the intricate interplay among the involved effects of the pattern formation, orientational order, and coupling between the SPP density and orientation fields. In its non-equilibrium steady state, the patterns of SPP are shown to exhibit collective motion with the constant velocity predicted by the model. As a main result of the reported study, the transition between the resting and moving non-equilibrium steady states of the SPP system are quantitatively explained by rationalizing the primary and secondary instabilities experienced by this SPP system. The obtained analytical results show excellent agreement with the performed rigorous numerical simulations.

Poster #18, presented by Nazli Demirpehlivan

Illuminating Genetic Translation

Laboratoire Charles Coulomb Nazli Demirpehlivan Jean-Charles Walter Nils-Ole Walliser Jerome Dorignac

The recent developments of live-imaging microscopy enable us to decipher the molecular mechanisms of genetic translation in order to understand how gene expression is performed at this essential step. However, a theoretical framework to turn these techniques into quantitative tools is still lacking. Our research focuses on quantifying kinetic parameters, specifically initiation and elongation rates, involved in genetic translation using the TASEP model under low-density conditions. We adapted our simulations to investigate the Suntag experimental technique, which enables the tagging of synthesized proteins with Green Fluorescence Particles (GFP), providing real-time observation through Fluorescence Signal tracking. We employ statistical tools such as autocorrelation, covariance, and fluctuations analysis to extract information about these kinetic parameters. Our aim is to enhance our understanding of the translation process in genetic expression by adding a kinetic perspective into the existing dynamical work. By integrating experimental data from live-imaging microscopy from our collaborators (IRIM, Montpellier) with our theoretical modeling, we hope to delve deeper into this process and evaluate the efficacy of the tagging method.

Poster #19, presented by Pawat Akarapipattana

1-d self-assembly of complex elastic molecules

Pawat Akarapipattana (LPTMS, Universite Paris Saclay, France); Martin Lenz (LPTMS, Universite Paris Saclay, France);

In biological systems, many different proteins can self-assemble into fiber-like aggregates. This process depends on both the complexity and elastic properties of the protein. The universality of fiber formation suggests the presence of underlying mechanisms beyond specific details of a given protein.

The aim of this work is to develop and investigate a toy model for the self-assembly of generic proteins. Generally speaking, an aggregate of frustrated particles limits its growth in space to mitigate its frustration. We study this phenomenon in a system of one dimensional complex elastic particles, where each subunit is a fully connected random spring network of an arbitrary shape. Thanks to the low dimensionality of this system, we are able to provide detailed analytical descriptions of deformations in the aggregate, as well as how these deformations control the aggregate size.

Poster #20, presented by Lixin HUANG

A microfluidic platform for studying actin-based membrane remodeling

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Cell shape changes are essential for processes such as motility or division. Their mechanisms can be deciphered in vitro using biomimetic reconstituted systems, such as giant unilamellar vesicles (GUVs) with controlled lipid composition coupled to reconstituted actin networks. These assays allow the reproduction of cell shape changes in controlled biochemical and physical environments. However, studying the dynamics of these shape changes on many GUVs, with the possibility to sequentially add proteins in the assay, is a major experimental challenge. To address these issues, we developed a microfluidic chamber that traps and filters GUVs by size and a protocol enabling the spatiotemporal monitoring of membrane and actin network evolution. We first characterize the filling of the chamber with GUVs and actin. Then, we show that we can monitor the dynamics of the actin-induced remodeling of populations of homogeneous and phase-separated GUVs. Our microfluidic setup and experimental strategy thus allow for studying actin-membranes in vitro and pave the way for studies on other membrane remodeling processes.

Poster #21, presented by Vincent Ouazan-Reboul

A kinetic model for fibril growth in alpha-synuclein biomolecular condensates

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Alpha-synuclein is a small protein with the ability to aggregate into fibrilar structures, a process which is strongly associated with neurodegenerative pathologies such as Parkinson's disease or Lewy body dementia. In a recent experimental study, alpha-synuclein expressed with a "scaffold" domain has been made to self-assemble into biomolecular condensates, which feature all the archetypal properties of these membraneless organelles: spontaneous formation through liquid-liquid phase separation, high concentration in alpha-synuclein monomers, and liquid-like rheological properties. Upon addition of pre-formed alpha-synuclein fibrils, these condensates undergo dramatic rheological and morphological changes, becoming more solid and growing fibril-like protrusions. While these changes are likely caused by intra-condensate fibril elongation and aggregation, the specific mechanism through which fibrils grow has not been elucidated yet. Here, we write a simple kinetic model for the elongation of alpha-synuclein fibrils in a monomer-rich condensate, and compare two kinetic scenarii: one involving seeding and growth of fibrils in the condensates, and the other involving the breakage of fibrils as they grow. By solving the associated equations, we find that these two cases lead to radically different fibril length profiles as a function of time, which we plan to compare to experimental measurements.

Poster #22, presented by Partho Sakha De

PREDIG: Modelling software to predict the enzymatic digestion of lignocellulosic biomass

Partho Sakha De, Torben Glass, Adélaïde Raguin (CCB, HHU Düsseldorf Germany)

Enzymatic digestion of lignocellulosic plant biomass is a key step in bio-refinery approaches for the production of biofuels and other valuable chemicals. However, the recalcitrance of this material in conjunction with its variability and heterogeneity significantly hampers the economic viability and profitability of biofuel production. To complement both academic and industrial experimental research in the field, we designed an advanced web application that encapsulates our in-house developed complex biophysical model of enzymatic plant cell wall degradation. PREDIG (https://predig.cs.hhu.de/) is a user-friendly, free, and fully open-source web application that allows the user to perform in silico experiments. It employs a Gillespie algorithm to run stochastic simulations of the enzymatic saccharification of a lignocellulose microfibril, at the mesoscale, in three dimensions. Such simulations can for instance be used to test the action of distinct enzyme cocktails on the substrate. Additionally, PREDIG can fit the model parameters to uploaded experimental time-course data, thereby returning values that are intrinsically difficult to measure experimentally. This gives the user the possibility to learn which factors quantitatively explain the recalcitrance to saccharification of their specific biomass material.

Poster #23, presented by Enrico Lorenzetti

Modelling and Inferring Protein Dynamics in Fission Yeast Mechanosensing

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Mechanical forces play an important role in determining the growth and the shape of a cell, yet they can also be a potential cause of damage. Indeed, cells are endowed with mechanosensors, i.e. receptors at the subcellular scale able to detect mechanical stimuli. In fission yeast, the transmembrane protein Wsc1 is such a mechanosensory. It stimulates glucan synthesis to reinforce the cell wall, the protective thin layer that surrounds the cell. Interestingly, Wsc1 clusters in the region of the cell wall where stress is applied.

This work aims at describing clustering by building a mathematical model based on reaction-diffusion equations that take into account the interactions between cell wall polysaccharides and Wsc1. To quantify the dynamical parameters of this model, we developed a new inference method for Fluorescence Recovery after Photobleaching (FRAP) experiments which only requires minimal hypotheses. Thanks to the flexibility of this method, it is possible to carry out the experiment with the Wsc1 protein as the cell wall is under compression and obtain accurate protein mobility estimations as a function of mechanical stress.

This study offers fresh methodologies for quantifying and comprehending intricate protein dynamics within cells and tissues.

Poster #24, presented by Elise Muller

The plant mechanosensor FERONIA regulates morphogenesis timing and patterning in Marchantia polymorpha.

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Plant cells and tissues are subjected to internal and external mechanical stress which impact several processes such as growth or tissue patterning (Nakayama et al., 2012; Landrein and Ingram, 2019; Cosgrove, 2016). Response to mechanical stress can be passive but is also active and mediated by mechanosensors. If impaired mechanosensing has been associated with defects as in cell wall integrity, cell-cell adhesion and tissue cohesion

(Fruleux et al., 2019), the mechanisms linking mechanical stress to morphogenesis are poorly understood. We thus focus on the role of mechanosensing and cell wall mechanics in plant morphogenesis. We use the plant Marchantia polymorpha as a model system. We take advantage of its low genetic redundancy and its simple organization to analyze its early morphogenesis in a high-throughput way thanks to a microfluidic device (Laplaud et al., 2024). We show that the transmembrane mechanosensor FERONIA (Mecchia et al., 2020), as well as a downstream kinase MARIS (Boisson-Dernier et al., 2015), affect Marchantia's early growth kinetics and spatial patterning. Indeed, compared to wilde-type, feronia loss-of-function mutant early growth is delayed and more localized to the stem-cell regions. Additionally, we probed the plant mechanical properties thanks to osmotic steps and compared those parameters with growth kinetics properties. We showed that FERONIA drives the plant into a regime we coined the "cell-wall controlled growth regime". This regime is characterized by both high cell wall stiffness and high cellular hydrostatic pressure (turgor) and by growth rate being negatively correlated with the plant stiffness. Perturbing the system with osmolyte treatments showed that the interplay of FERONIA with mechanical deformation or stress might be also at stake. Altogether, our work sheds light on the complex interplay between mechanosensing and cell mechanics during morphogenesis.

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Poster #25, presented by Xue Bing

Investigating nonlinear photodamage in multiphoton light-sheet microscopy

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Scaling up the imaging speed in multiphoton microscopy to capture fast biological processes, such as a beating heart in vivo, is a very active and promising field of research. However, its application to live imaging requires a challenging balance between image quality, signal level, induced photodamage and optical setup complexity. For example, we have shown that fast live imaging with multiphoton light-sheet microscopy requires the tunability of laser parameters, such as wavelength or pulse repetition rate, to optimize two-photon excitation with low photodamage [1]. Here, we propose to further investigate the origin of photodamage in

multiphoton light-sheet microscopy and to devise a strategy to mitigate them. By combining simulation and experiments on live zebrafish embryos, we investigate the beam propagation through biological tissue and propose a new strategy to reduce nonlinear photoadamage. [1] Maioli, V., Boniface, A., Mahou, P., Ortas, J.F., Abdeladim, L., Beaurepaire, E., and Supatto, W., Fast in vivo multiphoton light-sheet microscopy with optimal pulse frequency. Biomedical Optics Express, 2020. 11(10): p. 6012-6026.

Poster #26, presented by Pauline Funke

In vitro reconstitution of lipid transport mediated by the yeast flippase complex Drs2-Cdc50

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Lipid asymmetry in eukaryotic membranes is essential for cellular processes like vesicle-mediated trafficking and is maintained, among others, by flippases (P4-ATPases) that catalyse unidirectional lipid transport across membranes at the expense of ATP. Dysfunction of P4-ATPases may cause severe diseases, e.g. mutations in the human flippase ATP8B1 are directly linked to intrahepatic cholestasis. The yeast flippase Drs2, homolog to the human P4-ATPase ATPB81, transports phosphatidylserine (PS) in the trans-Golgi network (TGN). Drs2 tightly associates with a Cdc50 subunit, requires phosphatidylinositol-4-phosphate for stimulation of its activity and has long, partially unstructured N- and C-terminal extensions that keep the flippase in an autoinhibited state [1]. It has been shown that Drs2 interacts with proteins involved in trafficking at the TGN: Arl1, a small GTPase and Gea2, an activator of small GTPases. Gea2 also directly interacts with Arl1 [2]. However, the exact interaction mechanisms of Arl1 and Gea2 with Drs2 and their involvement in lipid transport remain to be elucidated. Given that Arl1 or Gea2 deletion in yeast impairs PS transport in isolated TGN membranes [2], we hypothesize that their binding to Drs2 contributes to autoinhibition relief in vivo. To study the regulatory mechanism of lipid transport we purified the various components of the flippase machinery: Drs2-Cdc50, Arl1 and Gea2. Interestingly, we found that in vitro N- and C-terminally truncated Drs2 (ΔNC Drs2) displays ATPase activity not only in presence of PS but also for other negatively charged and asymmetrically distributed phospholipids like phosphatidylglycerol (PG) or phosphatidylinositol (PI), indicating that Drs2 is not as PS-specific as initially assumed and raising the question of Drs2 substrate recognition. To directly show lipid transport we reconstituted ΔNC Drs2 in proteoliposomes and followed translocation of fluorescently labelled phospholipids. Using POPC-proteoliposomes dopped with a few mol% NBD-PS, we could detect a significant and ATP-dependent transbilayer movement of NBD-PS in Drs2-containing proteoliposomes. With this approach we studied transport of various other phospholipids like PG and PI and confirmed that Drs2 ATPase activity is indeed linked to lipid transport. We next aim to reconstitute full-length Drs2 together with Arl1 and Gea2 in proteoliposomes and investigate the involvement of Arl1 and Gea2 in Drs2 activation, lipid transport and regulation.

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[2] P.-C. Tsai, J.-W. Hsu, Y.-W. Liu, K.-Y. Chen, F.-J. S. Lee (2013). Arl1p regulates spatial membrane organization at the trans-Golgi network through interaction with Arf-GEF Gea2p and flippase Drs2p. Proc. Natl. Acad. Sci. U. S. A. 110, E668-677.

Poster #27, presented by Pablo CASTRO

Dynamical structure-function correlations provide robust and generalizable signatures of consciousness in humans

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Resting-state functional magnetic resonance imaging evolves through a repertoire of functional connectivity patterns which might reflect ongoing cognition, as well as the contents of conscious awareness. We investigated whether the dynamic exploration of these states can provide robust and generalizable markers for the state of consciousness in human participants, across loss of consciousness induced by general anaesthesia or slow wave sleep. By clustering transient states of functional connectivity, we demonstrated that brain activity during unconsciousness is dominated by a recurrent pattern primarily mediated by structural connectivity and with a reduced capacity to transition to other patterns. Our results provide evidence supporting the pronounced differences between conscious and unconscious brain states in terms of whole-brain dynamics; in particular, the maintenance of rich brain dynamics measured by entropy is a critical aspect of conscious awareness.

Poster #28, presented by Bouhet

Monitoring the ribosome dynamics at the single molecule level

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Protein synthesis is a complex multi-step process involving many factors that need to interact in a coordinated manner to properly translate the messenger RNA. As translating ribosomes cannot be synchronized over many elongation cycles, single molecule studies, mainly using total-internal-reflexion fluorescence microscopy, have been introduced to bring a deeper understanding of translation dynamics. In order to perturb as little as possible the translation machinery and to use cell extracts, we decided to monitor the passage of individual, unmodified mammalian ribosomes at specific fluorescent primers hybridized along a mRNA. Because of the ribosome helicase activity, the double strand formed by the oligonucleotide and the mRNA is opened while the ribosome translates this region of the mRNA. Two different oligonucleotides are hybridized at two different places on the mRNA. Thus, the consecutive loss of the fluorescence signal of both oligonucleotides allows us to measure the translation speed distribution of single ribosomes. We use this system to study IRES- and cap-dependent initiation, show that the IRES initiation strongly limits the rate of the first elongation step [1], and compare 3 IRES, CrPV, HCV and EMCV, in different cell extracts. We are currently developing a

magnetic tweezers assay to get complementary information on the elongation kinetics during frameshifting. Thanks to its versatility, this method is a valuable tool to investigate the role of translation machinery modifications in human diseases. [1] Bugaud et al, RNA (2017)

Poster #29, presented by Tamizhmalar Sundararajan

Phase separation kinetics of bio-inspired condensates under passive and active conditions

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In this project, we investigate the structural dynamics and kinetics of condensates made up of cationic peptides (RRASLRRASL) and poly uracil (polyU) RNAs under active and passive conditions, serving as an ideal model system for membrane-less organelles. Employing absorbance measurements at 500 nm, the critical peptide concentration is estimated to be 400 μM at a fixed polyU concentration (0.5 g/L) in a buffer containing 50 mM HEPES, pH 7.4, 4 mM MgCl2, 2.25 mM ATP, 1.6 mM dithiothreitol. Confocal microscopy images of fluorescently labelled peptide/polyU condensate at this concentration display a droplet-like morphology on the micrometer scale (1 to 5 μm). The absorbance increased rapidly (t $<$ 1s) and remained stable for 150 minutes for the sample containing 0.5 g/L polyU and 1000 μM peptide, indicating coacervation. The charge ratio was estimated to be 2.45. Preliminary experiments were carried out by performing time-resolved small-angle X-ray scattering (TR-SAXS) with a stopped-flow device for rapid mixing at 37 °C. TR-SAXS patterns revealed that with unphosphorylated peptides, the condensate size increased rapidly and reached a few hundred nanometers in less than a second (t $<$ 400 ms). Contrary to the anticipated $\alpha \approx 1/3$ for a standard coalescence process established from the scaling law R$\sim$tα, our empirical findings yielded a scaling exponent of 0.45 $\pm$ 0.03, marking a 35% deviation from the theoretical prediction. Next, we studied the dephosphorylation of double-phosphorylated peptides by Lambda Protein Phosphatase (LPP), which dephosphorylates the serine residues of the peptide, thus driving coacervation. The absorbance linearly increased by 50% within 150 minutes for the sample containing 0.5 g/L polyU, 1000 μM peptide, and 400 U/mL LPP, denoting an increase in the number and/or size of the condensates over time. When the sample concentration was doubled, the absorbance started to increase at t = 15 minutes and remained relatively stable for the subsequent 125 minutes. This could be attributed to the higher concentration of the sample, which may have increased the rate of condensation, resulting in an early equilibrium. Future experiments will be focused on studying the dissolution of condensates by Protein Kinase A (PKA) and the formation of condensates under nonequilibrium steady-state conditions.
