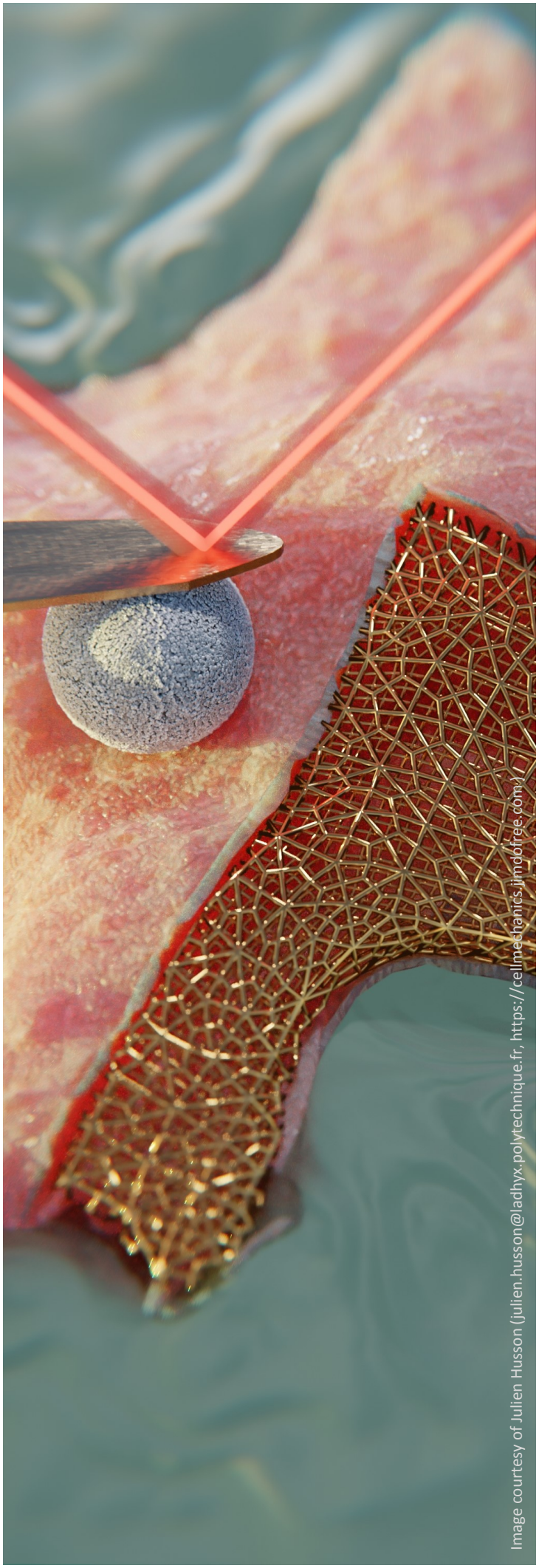

5th International Conference on

Physics & Biological Systems 2021

June 22-25 2021, Online

Invited speakers:

Markus Basan (Harvard U., USA)
Nicolas Chevalier (U. de Paris, France)
Bianxiao Cui (Stanford University, USA)
Stefan Diez (T.U. Dresden, Germany)
Alba Diz-Muñoz (EMBL, Germany)
Auguste Genovesio (ENS Paris, France)
Jean-Léon Maître (Institut Curie, France)
Paul Martin (U. of Bristol, UK)
Yasmine Meroz (Tel Aviv University, Israel)
Bruno Moulia (INRA Clermont-Ferrand, France)
Celeste Nelson (Princeton U., USA)
Aleksandra Radenovic (EPFL, Switzerland)
Ozgur Sahin (Columbia U., USA)
Khalid Salaita (Emory U., USA)
Andela Saric (University College London, UK)
Giorgio Scita (IFOM, Italy)
Christian Wagner (Saarland University, Germany)
Claire Wyart (Paris Brain Institute, France)

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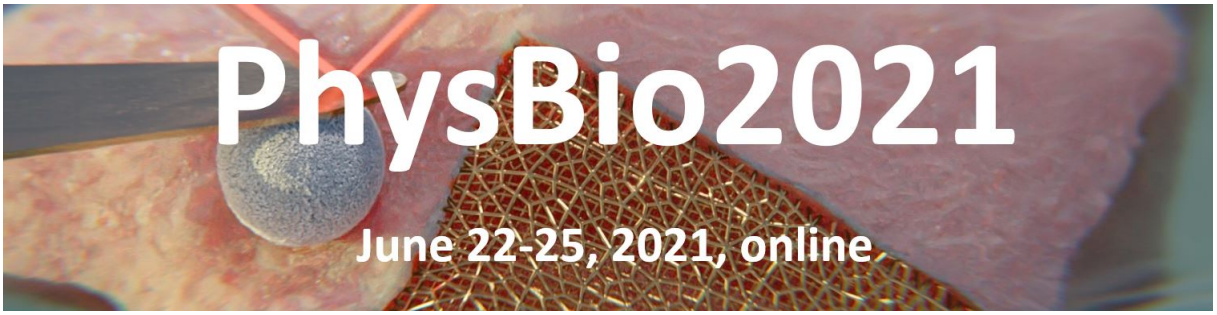

5th International Conference on

Physics & Biological Systems 2021

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CONFERENCE BOOK

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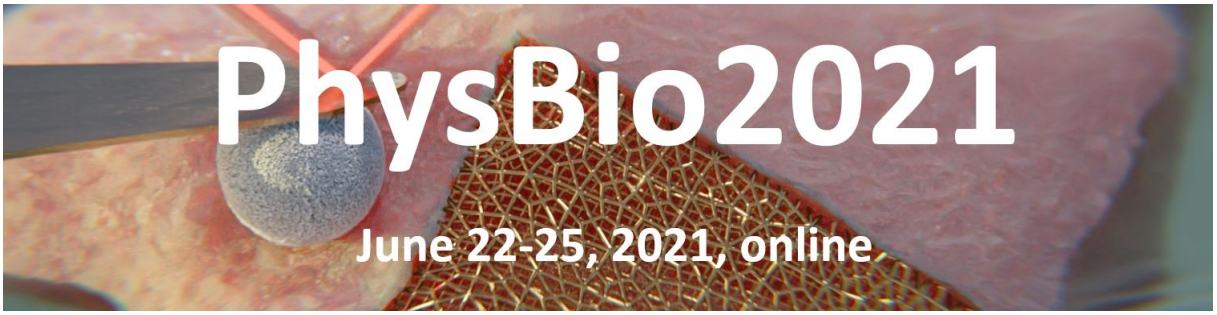

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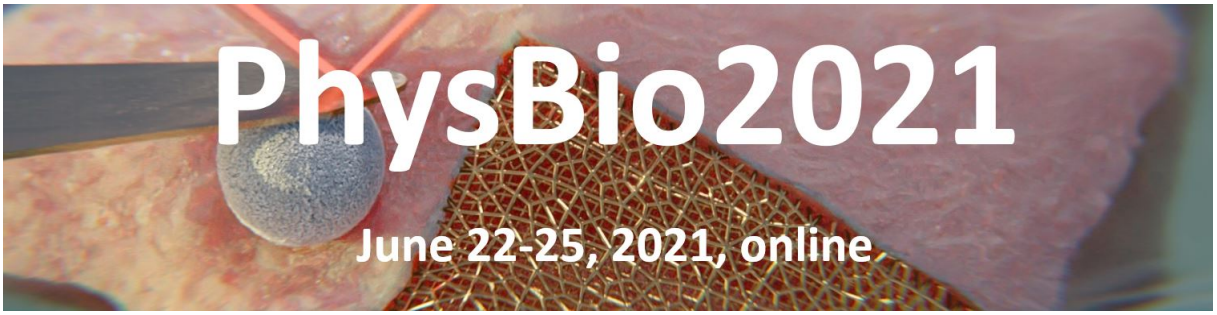


Program

	Tuesday, June 22	Wednesday, June 23	Thursday, June 24	Friday, June 25
11:20 - 11:30	**Opening**			
11:30 - 12:00	Andela Saric	Paul Martin	Alba Diz-Muñoz	Stefan Diez
12:00 - 12:30	Auguste Genovesio	Giorgio Scita	Jean-Léon Maître	Christian Wagner
12:30 - 14:00	*Lunch*			
14:00 - 14:45	Lucia Vidakovic	Arthur Boutillon	Jia Hui Li	Jean de Seze
	Mareike Berger	Diane-Laure Pagès	Vasyl Mykuliak	Sara Jamali
	Chloé Roffay	Aarren Mannion	Joris Messelink	Daan de Groot
14:45- 15:00	*Coffee break*	Poster session 1 Posters 1 - 16	Poster session 2 Posters 17 – 32	Poster session 3 Posters 33 – 47
15:00 – 15:30	Bruno Moulia			
15:30 - 16:00	Yasmine Meroz			
16:00 – 16:15	*Coffee break*			
16:15 - 16:45	Markus Basan	Claire Wyart	Bianxiao Cui	Awards: talks / posters **Closing**
16:45 - 17:15	Nicolas Chevalier	Aleksandra Radenovic	Ozgur Sahin	
17:15 – 17:45		Celeste Nelson	Khalid Salaita	

Tuesday, June 22

11:20 - 11:30 Opening remarks

11:30 – 12:30 *Session chair : Martin Lenz*

11:30 - 12:00 **Andela Saric**
University College London, Department of Physics & Astronomy, MRC Laboratory for Molecular Cell Biology, London, UK
"Active elastic ESCRT-III filaments in reshaping and splitting cells across evolution"

12:00 - 12:30 **Auguste Genovesio**
Institute of Biology of ENS (IBENS), Paris
"Synthetic cellular imaging uncovers invisible phenotypes"

12:30 - 14:00 *Lunch*

14:00 - 14:45 **Student session 1**

Session chair : *Hugo Le Roy, Eric Raspaud*

14:00 - 14:15 **Lucia Vidakovic**
Max Planck Institute for Terrestrial Microbiology, Marburg, Germany
"Dynamic interaction of V. cholerae with human immune cells"

14:15 - 14:30 **Mareike Berger**
AMOLF, Amsterdam, Netherlands
"Is size all that matters? Cell cycle regulation in E. coli"

14:30 - 14:45 **Chloé Roffay**
Biochemistry Department, University of Geneva, Switzerland
"Passive coupling of membrane tension and cell volume during active response of cells to osmosis"

14:45 - 15:00 *Coffee break*

15:00 - 16:00 *Session chair : Eric Raspaud*

15:00 - 15:30 **Bruno Moulia**
Université Clermont Auvergne, INRAE, PIAF, Clermont–Ferrand, France
"The shaping of plants (including trees) by mechanical and optical directional signals"

15:30 - 16:00 **Yasmine Meroz**
School of Plant Science and Food Security, Tel Aviv University, Israel
"Temporal integration and decision-making in plant tropisms"

16:00 - 16:15 *Coffee break*

16:15 - 17:15 *Session chair : Mathilde Badoual*

16:15 - 16:45 **Markus Basan**
Department of Systems Biology, Harvard Medical School, USA
"Density homeostasis in bacteria"

16:45 - 17:15 **Nicolas Chevalier**
Laboratoire Matière et Systèmes Complexes,
Université de Paris, CNRS, France
"Physical Organogenesis of the Gut"

Wednesday, June 23

11:30 - 12:30 *Session chair : Christophe Le Clainche*

11:30 - 12:00 **Paul Martin**
Biochemistry, University of Bristol, Bristol, UK
"Live imaging and modelling of wound repair and inflammation"

12:00 - 12:30 **Giorgio Scita**
IFOM, the FIRC Institute of Molecular Oncology, Department of Oncology and Hemato-oncology, University of Milan, Italy
"Solid-to-fluid transitions in pathophysiology"

12:30 - 14:00 *Lunch*

14:00 - 14:45	**Student session 2**
Session chair :	*Clémence Vigouroux, Christophe Le Clainche*
14:00 - 14:15	**Arthur Boutillon** *Laboratory for Optics and Biosciences,* *Ecole Polytechnique, Palaiseau, France* **"Guidance by followers ensures long-range coordination of cell migration through α-Catenin mechanoperception"**
14:15 - 14:30	**Diane-Laure Pagès** *Université Paris-Saclay, Inserm, Institut Gustave Roussy, Dynamique des Cellules Tumorales, Villejuif, France.* **"Collective amoeboid migration: a new mode of migration occuring in non-adhesive confined environments"**
14:30 - 14:45	**Aarren J. Mannion** *Department of Oncology-Pathology,* *Karolinska Institutet, Stockholm, Sweden* **"A YAP-AmotL2 vascular mechanosensory signaling axis"**
14:45 – 16:15	**Poster session 1 – Posters 1-16** (see list p.11)
16:15 - 17:45	*Session chair : Martin Lenz*
16:15 - 16:45	**Claire Wyart** *Institut du Cerveau, Paris* **"Sensing from within in the vertebrate spinal cord: an axial sensory system controls development, posture and innate immunity"**
16:45 - 17:15	**Aleksandra Radenovic** *École Polytechnique Fédérale de Lausanne (EPFL), Switzerland* **"From Cells to Ions"**
17:15 - 17:45	**Celeste M. Nelson** *Princeton University, USA* **"The biophysics of tissue folding"**

Thursday, June 24

11:30 - 12:30 *Session chair : Christophe Le Clainche*

11:30 - 12:00 **Alba Diz-Muñoz**
European Molecular Biology Laboratory (EMBL), Heidelberg, Germany
"Cortex mechanics and architecture are controlled by membrane-to-cortex attachment"

12:00 - 12:30 **Jean-Léon Maître**
Institut Curie, Paris, France
"Mechanics of blastocyst morphogenesis"

12:30 - 14:00 *Lunch*

14:00 - 14:45 **Student session 3**

Session chair : *Claire Dessalles, Mathilde Badoual*

14:00 - 14:15 **Jia Hui Li**
Institute of Biochemistry, Department of Biology, Chemistry, Pharmacy, Freie Universität Berlin.
"Magnetic manipulation of membrane molecule motion"

14:15 - 14:30 **Vasyl V. Mykuliak**
Faculty of Medicine and Health Technology,
Tampere University, Tampere, Finland
"Stable intermediates in talin rod are reached by force during unfolding"

14:30 - 14:45 **Joris Messelink**
Arnold Sommerfeld Center for Theoretical Physics, Department of Physics, Ludwig Maximilian University Munich, Munich, Germany
"Learning the distribution of single-cell chromosome conformations in bacteria reveals emergent order across genomic scales"

14:45 – 16:15 **Poster session 2 – Posters 17 – 32** (see list p.11)

16:15 - 17:45 *Session chair : Julien Husson*

16:15 - 16:45 **Bianxiao Cui**
Department of Chemistry and the Stanford Neuroscience Institute, Stanford University, USA
"Membrane curvature and cellular mechanotransduction"

16:45 - 17:15 **Ozgur Sahin**
Department of Biological Sciences, Department of Physics, Columbia University, USA
"Unexpected patterns in nanoscale cell stiffness images due to intracellular forces"

17:15 - 17:45 **Khalid Salaita**
Emory University, Department of Chemistry, Atlanta, Georgia, USA
"The force is within you: Fluorescent probes to map molecular forces in cells"

Friday, June 25

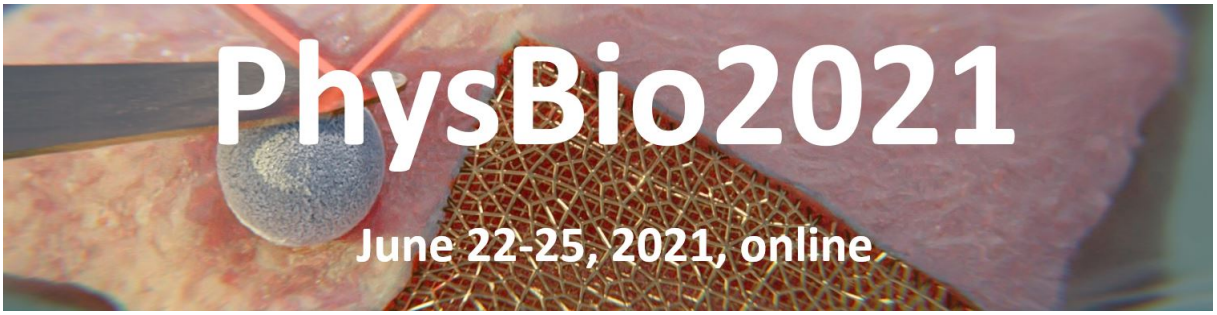
11:30 - 12:30 *Session chair : Julien Husson*

11:30 - 12:00 **Stefan Diez**
TU Dresden, B CUBE - Center for Molecular Bioengineering, Germany
"Torque generation by microtubule-crosslinking motors"

12:00 - 12:30 **Christian Wagner**
Saarland University, Experimental Physics, Saarbruecken, Germany
"Red Blood cell flow dynamic in-vivo"

12:30 - 14:00 *Lunch*

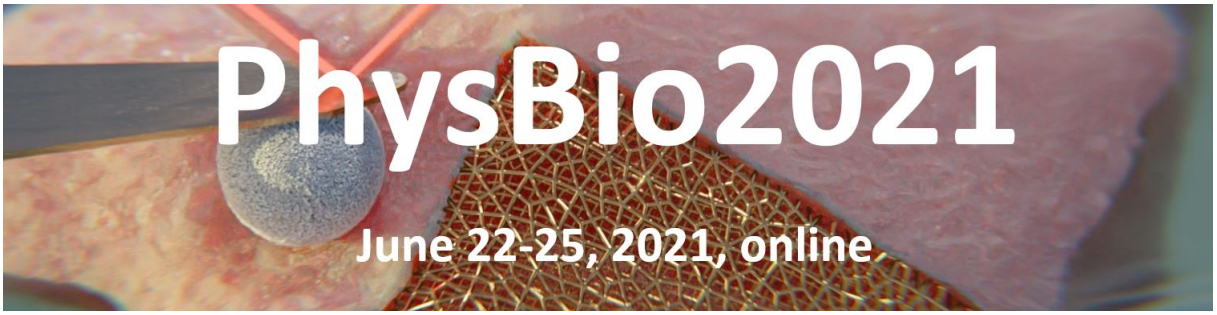
14:00 - 14:45	**Student session 4**
Session chair :	*Florian Semmer, Julien Husson*
14:00 - 14:15	**Jean de Seze** *Institut Curie, Paris, France* **"Controlling antagonist responses with a single optogenetic activator"**
14:15 - 14:30	**Sara Jamali** *Institut de l'Audition, Institut Pasteur, Paris, France* **"Coding of sequence statistics in the auditory cortex of passive vs. active mice"**
14:30 - 14:45	**Daan de Groot** *Biozentrum, Universität Basel, Switzerland* **"Coupling phenotypic stability to growth-rate overcomes limitations of bet-hedging strategies"**
14:45 – 16:15	**Poster session 3 – Posters 33 - 47** (see list p.11)
16:15 - 16:45	**Awards for best short talks and best posters** **Concluding remarks**



Posters

(see abstracts p.43-72)

Date	#	Name	Title
Wed., June 23	1	Martina Pozar	Why Should Metformin Not Be Given in Advanced Kidney Disease? Potential Leads from Computer Simulations
Wed., June 23	2	Ivo Jukić	Universal features in lifetime distribution of clusters in hydrogen bonding liquids
Wed., June 23	3	Nitin Kumar Singh	Understanding the Helical Stability of Charged Peptides
Wed., June 23	4	Carsten Schulte	The glycocalyx affects integrin adhesion complex-mediated mechanotransductive processes in the cell/microenvironment interface
Wed., June 23	5	Adam Shellard	Collective cell durotaxis along a self-generated stiffness gradient in vivo
Wed., June 23	6	Agustina Fernández Casafuz	Motor-driven transport of mitochondria in living cells
Wed., June 23	7	Tapomoy Bhattacharjee	Life in a Tight Spot: How Bacteria Swim, Disperse, and Grow in Porous Media
Wed., June 23	8	RASHMI RAMESH	ARTIFICIAL MOUSE – AN ULTRASOUND MEDIATED DRUG DELIVERY PLATFORM
Wed., June 23	9	Mehrana Raeisin Nejad	Extensile stress promotes out-of-plane flows in active layers
Wed., June 23	10	Nicolas Borghi	Persistence transitions in collective cell migration
Wed., June 23	11	Amandine Deridoux	Mechanical description of the podia in sea star locomotion
Wed., June 23	12	David Brownell	Glass nanoneedle to probe intracellular viscoelastic properties
Wed., June 23	13	Yasamin Mohebi	The Experimental Study Of The Dynamics Of A Self-propelled Rod
Wed., June 23	14	Laurent Marichal	Biophysical study of large macromolecular complexes
Wed., June 23	15	Marianna Pepona	The lymphatic pumping mechanism: A numerical study
Wed., June 23	16	Louis LAURENT	Identifying mechanisms by which cells sense multicellular density
Thu., June 24	17	Claire Lefort	Deep-3D-multiphoton imaging of whole biological structures with a computational assistance and the pipeline FAMOUS
Thu., June 24	18	Claire Valotteau	Combining Acoustic Force Spectroscopy and DNA scaffold for high throughput measurement of ligand-receptor kinetics at single molecule resolution
Thu., June 24	19	Qiao-Ling Chou	Impact of pathogenic protein assemblies in neurodegenerative diseases on mouse cortical neurons endo-lysosomal transport
Thu., June 24	20	Helena Canever	Molecular Mechanical Determinants of Collective Cell Migration
Thu., June 24	21	Elise Tourrette	The singular consequences of linkage in the infinitesimal model of an evolving population
Thu., June 24	22	Jeongeun Ryu	Physical origin of active snapping of the Venus flytrap
Thu., June 24	23	M. Mert Terzi	Collective deformation modes promote fibrous self-assembly in protein-like particles
Thu., June 24	24	Youssef OULDHNINI	Atomistic insights into the structure and elasticity of densified 45S5 Bioactive Glass
Thu., June 24	25	Valerio Sorichetti	Fluctuations control the assembly of semiflexible filaments
Thu., June 24	26	Alfredo Sciortino	Polar patterns of gliding filaments on flat and curved lipid membranes
Thu., June 24	27	Övül Eski	Electrical Fields, Cells and Their Interactions: An Overview
Thu., June 24	28	Julien Hurbain	Modelling investigation of metabolic adaptation to oxidative stress
Thu., June 24	29	Souvik Sadhukhan	Glassy Dynamics in Confluent Biological Tissue using Cellular potts Model
Thu., June 24	30	Lisa Bedin	Visual pseudotime reconstruction of a dynamic single cell process
Thu., June 24	31	Bae-Yeun Ha	Polymer physics approach to bacterial chromosomes
Thu., June 24	32	Martin Lenz	Slimming down through frustration
Fri., June 25	33	Héctor Zamora-Carreras	Sensing nuclear compaction: A fruitful model to characterize cell nucleus mechanics
Fri., June 25	34	Hoda Akl	Information transmission by heterogenous cell populations
Fri., June 25	35	Simon Hadjaje	Wing deployment in Drosophila melanogaster
Fri., June 25	36	John JAMES	Vinculin regulates collective cell behaviour by remodelling the actin cytoskeleton at cell-cell junctions
Fri., June 25	37	Olga Markova	Influence of external forces on actin-dependent T cell protrusions during immune synapse formation
Fri., June 25	38	Mouna Abdesselem	Imaging membrane contact sites in living cells with FRET-FLIM
Fri., June 25	39	Erik Maikranz	Theoretical modelling of competitive microbial range expansion with heterogeneous mechanical interactions
Fri., June 25	40	Natalia Hernando Ospina	Flickering phenomena in red blood cell membranes: differences between species
Fri., June 25	41	Clara Manesco	Label-free imaging techniques for monitoring spinal cord injury: from pathophysiology to therapeutic strategies in mice
Fri., June 25	42	Liboz Maxime	Using micro patterns to standardize cells mechanics measurements by AFM, application to cancer cells
Fri., June 25	43	Lara Koehler	Understanding fiber formation through renormalization
Fri., June 25	44	Clara Luque Rioja	Non-linear wave propagation emerged in active poroelastic media
Fri., June 25	45	Rose Bulteau	Mechanical characterization with AFM of murine oocytes to predict their fitness
Fri., June 25	46	Rogerio Lopes dos Santos	Atomic Force Microscopy-probing of phase-separated membrane nanotubes
Fri., June 25	47	Horacio Lopez-Menendez	Measurement of tumbling force and energy during swarming-like imposed by optical tweezers



SPEAKER ABSTRACTS

Active elastic ESCRT-III filaments in reshaping and splitting cells across evolution

Andela Saric

University College London, Department of Physics & Astronomy, MRC Laboratory for Molecular Cell Biology

The molecular machinery of life is largely created via self-organisation of individual molecules into functional larger-scaled structures. Such processes are multi-scale in nature and constantly driven far from thermodynamic equilibrium. Our group develops minimal coarse-grained computer models for non-equilibrium organisation of macromolecules into functional nanomachinery that can produce mechanical work involved in key cellular processes. Today I will discuss our recent research on physical modelling of active elastic ESCRT-III filaments that dynamically shift their geometries and mechanical properties to reshape and cut cell membranes. I will first present our model in the context of eukaryotic cell trafficking, supported by experimental data. Then I will discuss the evolutionary origins of this physical mechanism and its role in cell division in the archaeal branch of the tree of life. Finally, I will show quantitative comparison between live cell imaging of dividing archaeal cells and our simulations of the whole cell division process.

Synthetic cellular imaging uncovers invisible phenotypes

Auguste Genovesio

Institute of Biology of ENS (IBENS), 46, Rue d'Ulm, 75005 Paris

Biology, as an experimental science, heavily relies on observations. However, despite humongous progress in our ability to see and quantify biological events thanks to techniques such as super resolution microscopy, mass spectrometry or single cell sequencing, many processes and phenotypes remain out of reach, inaccessible. This is the case for instance for subtle phenotypic alterations that are hidden by biological or experimental cell variability. In this talk, I will relate research projects from our lab where synthetic imaging based on biophysical modeling or deep learning can be used to explain and even quantify subtle phenotypes, invisible to the human eye. I will illustrate the usefulness of these general approaches in the context of basic research in neuroscience and drug discovery.

Dynamic interaction of V. cholerae with human immune cells

Lucia Vidakovic[1], Knut Drescher[1,2,3,4]

1 Max Planck Institute for Terrestrial Microbiology, Marburg, Germany.
2 Department of Physics, Philipps-Universität Marburg, Marburg, Germany.
3 Center for Synthetic Microbiology (SYNMIKRO), Philipps-Universität Marburg, Marburg, Germany.
4 Biozentrum, University of Basel, Basel, Switzerland.

Biofilms, multicellular microbial communities, are recognized as a bacterial defense mechanism against various environmental threats, including antibiotics, viruses and eukaryotic predators. In particular, biofilm formation protects bacteria from predation by the human immune system and contributes to persistence of pathogenic bacteria in the human host, yet the mechanisms that determine the interactions between biofilms and immune cells are unclear. Using the biofilm-forming bacterium Vibrio cholerae, which elicits an immune response during human infection, we discovered that biofilm formation is not only a protective, but also an aggressive trait to collectively predate on immune cells. Our detailed analysis with macrophages revealed that V. cholerae forms biofilms on the eukaryotic cell surface which relies on MSHA pili, toxin co-regulated pili (TCP) and the secreted colonization factor TcpF. The multicellular bacterial structure efficiently retains Vibrio cholerae hemolysin and thereby significantly enhances killing of human macrophages. Together, these results uncover a mechanism for how biofilms invert the traditional predator-prey relationship between bacteria and the human immune system.

Is size all that matters? Cell cycle regulation in E. coli

Mareike Berger and Pieter Rein ten Wolde

AMOLF, Amsterdam, Netherlands

All living cells need to coordinate DNA replication with growth and division to generate cell cycles that are stable in time. The bacterium *Escherichia coli* initiates replication at a volume per origin that on average is independent of the growth rate. It also adds an on average constant volume per origin between successive initiation events, independent of the initiation size. Yet, a molecular model that can explain these observations has been lacking. Here, we develop a mathematical model of DNA replication initiation in *E. coli* that is consistent with a wealth of experimental data. We first show that the previously proposed initiator titration model, which is based on the accumulation of the initiator protein DnaA on chromosomal titration sites, is not consistent with the experimental data. We then present a model that is based on an ultra-sensitive switch between an inactive form of DnaA and an active form that induces replication initiation. Our model shows that at low growth rates the switch is predominantly controlled by activation of DnaA via lipids and deactivation via the chromosomal site *datA*, while at high growth rates *DARS2* and RIDA become essential. Crucially, in our mean-field model DNA replication is initiated at a constant volume per origin, qualifying our model as a sizer. Yet, we show that in a stochastic version of the same model the inevitable fluctuations in the components that control the DnaA activation switch naturally give rise to the experimentally observed adder correlations.

Passive coupling of membrane tension and cell volume during active response of cells to osmosis

Chloé Roffay

Biochemistry Department, University of Geneva, CH-1211 Geneva, Switzerland.

During osmotic changes of their environment, cells actively regulate their volume and plasma membrane tension that can passively change through osmosis. How tension and volume are coupled during osmotic adaptation remains unknown, as a quantitative characterization is lacking. Here, we performed dynamic membrane tension and cell volume measurements during osmotic shocks. During the first few seconds following the shock, cell volume varied to equilibrate osmotic pressures inside and outside the cell, and membrane tension dynamically followed these changes. A theoretical model based on the passive, reversible unfolding of the membrane as it detaches from the actin cortex during volume increase, quantitatively describes our data. On top of that, mTORC2 is immediately activated after hypoosmotic shocks and desactivated after hyperosmotic shocks following the same dynamic than tension and volume. After the initial response, tension, volume and mTORC2 activity recovered from hypoosmotic shocks but not from hyperosmotic shocks. Using a new fluorescent membrane tension probe (Flipper-TR), we investigated the coupling between tension and volume during these asymmetric recoveries. Caveolae depletion, functional inhibition of exchangers, ion channel or mTOR and pharmacological disruption of the cytoskeleton all affected tension and volume responses. The coupling between them was, nonetheless, maintained in several pharmacological treatments supporting that volume and tension regulations are independent from the regulation of their coupling.

The shaping of plants (including trees) by mechanical and optical directional signals

Bruno Moulia

Université Clermont Auvergne, INRAE, PIAF, 63000 Clermont–Ferrand, France

Plant shape can be described at two levels. First, one may consider the shape of a given plant stem, described as the distribution of its curvatures and of its angular orientations. Here we show that this shaping involves an oriented growth, known as tropism (Bastien *et al.* 2013, 2015). Two orientation cues are used : i) the sensing of the angle to the gravity (thanks to intracellular granular avalanches, Berut *et al.* 2018)) and ii) the sensing of the light direction. However shape control also requires the sensing by the plant of its own curvature, that is a proprioception (Moulia *et al.* 2021). Finally elastic bending under self-weight can be involved in thin twigs (Chelakkot and Mahadevan 2017). Altogether, the shaping of the plant axes is fully controlled by three dimensionless numbers: i) the Balance number B (ratio of the sensitivities to the angle to the gravity and to the self-curvature), the Motion pointing number M (ratio of the sensitivities to the angle to the gravity and to the light) and the Elastic sagging number E (ratio of flexural stiffness and gravitational load).
Upscaling to entire trees, it is then shown that the shape of the crown of isolated trees can be understood as a kind of tropic growing droplet, which shape is also controlled by the BME triplet of morphogenetic dimensionless numbers (Duchemin et al. 2018).

Bastien R, Bohr T, Moulia B, Douady S. 2013. Unifying model of shoot gravitropism reveals proprioception as a central feature of posture control in plants. *Proceedings of the National Academy of Sciences of the United States of America* 110(2): 755-760
Bastien R, Douady S, Moulia B. 2015. A Unified Model of Shoot Tropism in Plants: Photo-, Gravi- and Propio-ception. *Plos Computational Biology* 11(2)
Berut A, Chauvet H, Legue V, Moulia B, Pouliquen O, Forterre Y. 2018. Gravisensors in plant cells behave like an active granular liquid. *Proceedings of the National Academy of Sciences of the United States of America* 115(20): 5123-5128.
Chelakkot R, Mahadevan L. 2017. On the growth and form of shoots. *Journal of the Royal Society Interface* 14(128)
Duchemin L, Eloy C, Badel E, Moulia B. 2018. Tree crowns grow into self-similar shapes controlled by gravity and light sensing. *Journal of the Royal Society Interface* 15(142).
Moulia B, Douady S, Hamant O. 2021. Fluctuations shape plants through proprioception. *Science* 372(6540): eabc6868.

Temporal integration and decision-making in plant tropisms

Mathieu Riviere, Roni Kempinski, Yasmine Meroz

School of Plant Science and Food Security, Tel Aviv University, Tel Aviv, Israel

Plants need to survive in a harsh and fluctuating environment, optimising their search for fluctuating nutrients, and predicting danger. They achieve this through complex response processes, such as decision-making, based on memory, or the capability to accumulate and compare past stimuli. For example, a plant shoot accumulates sensory information from various fluctuating light sources, decides which direction yields consistently most light for photosynthesis, and grows in that direction. Here we propose a reverse-engineering approach to investigating the underlying rules for the accumulation and integration of sensory inputs, while combining experiments with mathematical models. We then build on this understanding and suggest a theoretical and experimental framework for the study of decision-making in plant tropisms.

Meroz, Bastien and Mahadevan "Spatio-temporal integration in plant tropisms" 16 *J. R. Soc. Interface,* *http://doi.org/10.1098/rsif.2019.0038*

Density homeostasis in bacteria

Markus Basan

Department of Systems Biology, Harvard Medical School

Homeostasis of dry mass density is essential to ensure optimal function of most cellular processes by preventing molecular crowding or excessive dilution of cellular components. Bacteria must coordinate their biomass production and volume growth in order to achieve homeostasis of dry mass density across vastly different growth rates. We accurately quantified single-cell and population-level dry mass densities of *E. coli* across different growth conditions using quantitative phase microscopy. We observe that dry mass density was surprisingly constant across different growth rates. How bacteria achieve this remarkable feat is presently poorly understood. We present a mechanical simple feedback model that can explain how E. coli achieves dry mass density homeostasis and tested this model experimentally using different genetic and environmental perturbations.

Physical Organogenesis of the Gut

Nicolas Chevalier

Laboratoire Matière et Systèmes Complexes, Université de Paris / CNRS UMR 7057, 75013 Paris, France

The intestine is a pump and a biochemical reactor. Its length (7 m in the adult) provides an important absorption surface for nutrients and allows for digestion to occur in successive compartments. Autonomous movements of the bowel wall – peristalsis – are responsible for mixing and transporting the food bolus. How do these essential physiological characteristics arise during embryonic development? I will show that mechanobiological effects underpin virtually every step of gut morphogenesis. I will explain how, by examining the successive contractile regimes of the developing intestine, we can grasp the elementary reflexes that underpin complex digestive movements in the adult. I will particular outline a key role for mechanosensitive enteric neurons (the "second brain") in orchestrating gut motility. The highly dynamic phenomena investigated will be illustrated by numerous videos.

Live imaging and modelling of wound repair and inflammation

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We model various aspects of tissue repair in several genetically tractable model organisms from *Drosophila* and zebrafish through to mice, (and, most recently, even Arabidopsis). We know that in animals, inflammation can be both beneficial for healing in that it fights infection and drives wound angiogenesis, but it has negative consequences also, in that it causes scarring and is aberrant in chronic wounds through release of cell damaging ROS. We use *Drosophila* and translucent zebrafish, which are both amenable to live imaging and mathematical modelling, to make movies of innate immune cell migration into the wound and to dissect the genetics of inflammatory cell recruitment towards tissue damage, and its consequences at the wound site. Most recently we have also begun to investigate how adipocytes, which "swim" towards *Drosophila* wounds utilizing biophysics-defying adhesion-independent motility, and their collaborative efforts with inflammatory cells, might also impact on wound repair.

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Solid-to-fluid transitions in pathophysiology

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During wound repair, branching morphogenesis and carcinoma dissemination, cellular rearrangements are fostered by a solid-to-liquid transition, known as unjamming. The biomolecular machinery behind unjamming, its pathophysiological relevance remains unclear. Using a combination of physical approaches, ex vivo and in vivo model systems, we will address these issues and discuss whether an endocytic-driven transition between "solid" and "liquid" states of cell collectives is a complementary gateway to cell migration in pathology, focusing specifically on the progression of early breast cancer lesions that become locally invasive. We will show how these dynamics changes featuring the coexistence of long range coordinated motion and local cell re-arrangement are sufficient to promotes matrix remodeling, local invasion and exert mechanical stress on individual cell nuclei. This is accompanied by profound transcriptional rewiring, with the unexpected activation of inflammatory response, change in cell state, and the emergence of malignant traits.

Guidance by followers ensures long-range coordination of cell migration through α-Catenin mechanoperception

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Morphogenesis, wound healing and some cancer metastases depend upon migration of cell collectives that need to be guided to their destination as well as coordinated with other cell movements. During zebrafish gastrulation, extension of the embryonic axis is led by the mesendodermal polster that migrates towards the animal pole, followed by axial mesoderm that is undergoing convergence and extension. We here investigate how polster cells are guided towards the animal pole. Using a combination of precise laser ablations, advanced transplantations and functional as well as silico approaches, we establish that the directional information guiding polster cells is mechanical, and is provided by the anteriorward migration of the following cells. This information is detected by cell-cell contact through E-Cadherin/α-Catenin mechanotransduction and propagates from cell to cell over the whole tissue. Such guidance of migrating cells by followers ensures long-range coordination of movements and developmental robustness.

Collective amoeboid migration :
a new mode of migration occuring in non-adhesive confined environments

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[#] *Equal contribution*

Migration is a key step in many biological processes, including the metastatic progression of cancers which accounts for most patient's deaths. As far as we know, cell locomotion occurs through three distinct mechanisms. In a few words, single cells can migrate via two modes, mesenchymal (adhesive, traction-based) or amoeboid (non-adhesive, propulsion-based). Cell cohorts are generally led by protrusive leaders, towing the collective through adhesion to the substrate. Here we demonstrate the existence of an undescribed mode of collective migration. We study tumour cell clusters' migration, transformed and non-transformed, in non-adherent microfabricated channels. This collective migration is independent of focal-adhesions and traction but is dependent on integrin-mediated friction to the substrate. Moreover, cell clusters display an actomyosin cortex that is polarised to the rear of clusters, proportionally to migration speed. Inhibiting ROCK and myosin activity decreases migration, while optogenetic activation of RhoA dictates directionality, demonstrating that this migration relies on actomyosin contractility. However, such migration is not driven by a sustained cell or myosin flow. Instead, we observed fluctuating cell and myosin displacements that are correlated with clusters' speed. We then demonstrate analytically that, together with friction with the substrate and myosin polarisation, this behaviour leads to migration. Our results suggest that cell clusters can use a unique mode of collective migration, that may explain the metastatic potential of these tumour intermediates. We call this new mode of migration "collective amoeboid migration", by analogy with single cell amoeboid migration.

A YAP-AmotL2 vascular mechanosensory signaling axis

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The endothelium is constantly exposed to forces of fluid shear stress, and in larger blood vessels such as the aorta, stretching of the vessel wall to accommodate pulsatile fluctuations in blood expelled from the heart. How these forces are sensed by endothelial cells and transduced, from the cell-cell junctions to the nucleus, remains an understudied aspect in the homeostatic regulation of the circulatory system and when dysregulated contributes significantly to vascular disease. The scaffold protein Angiomotin like 2 (AmotL2), is localised to endothelial cell junctions and is required for endothelial alignment and actin reorganisation under conditions of high shear stress, such as those found in the aorta. However, in the vena cava, where the endothelium is exposed to relatively low rates if shear flow, AmotL2 expression is reduced. Transcriptional control of AmotL2 is regulated by the mechanotransducer Yes-associated protein (YAP) and we hypothesised that the high shear stress of the aorta drives YAP activity to promote high AmotL2 expression. Using a proximity-ligation based assay we show increased YAP activity in the aorta compared to the vena cava. Furthermore, *in vivo* endothelial specific knockout of YAP resulted in the downregulation of AmotL2 in the aorta. Knockdown and overexpression of constitutively active YAP *in vitro*, decreased and increased AmotL2 respectively, confirming that YAP transcriptionally regulates AmotL2 in an endothelial context. The endothelial-specific deletion of AmotL2 *in vivo* impairs endothelial mechanosensing, resulting in misalignment of endothelial cells of the aorta, disrupted nuclear morphology and subsequent aneurysm formation. We investigated this phenotype and show that AmotL2 depletion leads the to the downregulation of YAP mRNA and protein levels, suggesting a positive feedback loop of regulation between AmotL2 and YAP. Functionally, this downregulation of YAP resulted in decreased proliferation when endothelial cells were subjected to mechanical forces such as stretching and shear flow. Overall, these results suggest a model in which YAP transcriptionally regulates endothelial AmotL2 expression, and AmotL2 itself is required for endothelial mechanosensing through the regulation of YAP.

Sensing from within in the vertebrate spinal cord :
An axial sensory system controls development, posture and innate immunity.

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The cerebrospinal fluid (CSF) is a complex solution circulating around the brain and spinal cord. Multiple evidence indicate that the activity and the development of the nervous system can be influenced by the content and flow of the CSF. Yet, it is not known how neuronal activity changes as a function of the physico-chemical properties of the CSF.

We identify throughout vertebrate species, ciliated neurons at the interface between the CSF and the nervous system that are in ideal position to sense CSF cues, to relay information to local networks and to regulate CSF content by secretion.

By combining electrophysiology, optogenetics and calcium imaging in vivo in larval zebrafish, we demonstrate that neurons contacting the CSF detect local bending of the spinal cord and in turn feedback GABAergic inhibition to multiple interneurons driving locomotion and posture in the spinal cord and hindbrain. Such inhibitory feedback modulates neuronal target in a state-dependent manner, depending on the fact that the animal is at rest or actively moving at a define speed.

Behavioral analysis of animals deprived of this sensory pathway reveals differential effects on speed for slow and fast regimes, as well as impairments in the control of posture during active locomotion. Our work first sheds light on the cellular and network mechanisms enabling sensorimotor integration of mechanical and chemical cues from the CSF onto motor circuits controlling locomotion and posture in the spinal cord.

We will present converging evidence that this interoceptive sensory pathway is involved in guiding a straight body axis throughout life, as well as innate immunity via the detection and combat of pathogens intruding the CSF.

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From Cells to Ions

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From the plethora of correlative imaging modalities, SR techniques were most frequently combined with electron microscopy to provide protein-ultrastructure relationships at nanometer-scale resolution[1]. At the other forefront of methods development, scanning probe microscopy techniques aim to capture nanoscale topographical dynamic changes of cells under physiological conditions. To avoid membrane deformation and to provide a method that could unlock long-term monitoring of the biological processes, we recently implemented SICM[2]. The method currently experiences vast leaps in performance due to instrument developments[2] and the ability to fabricate capillaries below tens of nanometers[3] reliably. In contrast to AFM, SICM is truly non-contact, and represents the soft cell surface much more faithfully[4]. In addition to providing accurate topographic imaging with nanometer resolution[5], SICM can be used to measure membrane stiffness[6] surface charges[7] and allows local delivery of material (e.g. fluorescent probes)[8]. In parallel, the use of self-blinking dyes in SR microscopy permitted imaging conditions such as low laser excitation intensities and negligible bleaching that are ideal for live-cell imaging. In addition, the high SNR and photophysical properties of self-blinking dyes allow us to extend multiplane cross-correlation analysis to the 4th order using 8-plane volumetric imaging, achieving up to 29 (virtual) planes[9]. Finally, with a combined SICM-SR setup we demonstrate long-term correlated live-cell imaging.

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The biophysics of tissue folding

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"Our real teacher has been and still is the embryo, who is, incidentally, the only teacher who is always right." – *Viktor Hamburger*

Evolution has generated an enormous diversity of biological form. Given this diversity, it is highly likely that every tissue structure that one can imagine has been built by the embryo of one species or another. We are interested in uncovering the physical (mechanical) mechanisms by which epithelial sheets fold themselves into branching tubes in the embryo, and using those mechanisms to engineer tissues in culture. Over the past half century, developmental biologists have identified several biochemical signaling pathways and genetic control mechanisms necessary for tissue morphogenesis. In parallel, biological systems must obey Newton's laws of motion, and physical forces need to be generated in order to sculpt simple populations of cells into complex tissue forms. Inspired by the evolutionary diversity of embryonic forms, we have created microfabrication- and lithographic tissue engineering-based approaches to investigate the mechanical forces and downstream signaling pathways that are responsible for generating the airways of the lung. I will discuss how we combine these experimental techniques with computational models to uncover the physical forces that drive morphogenesis. I will also describe efforts to uncover and actuate the different physical mechanisms used to build the airways in lungs from birds, mammals, and reptiles.

Cortex mechanics and architecture are controlled by membrane-to-cortex attachment

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The plasma membrane and the underlying actomyosin cortex constitute the surface of animal cells, and their mechanical properties are key for a plethora of cell processes. Although they are often studied as independent structures, the plasma membrane and the cortex are physically tethered to each other via linker proteins, globally referred to as membrane-to-cortex attachment (MCA). MCA contributes to membrane tension and regulates biological processes such as cell migration and stem cell differentiation. Nevertheless, it remains the most elusive element of the animal cell surface. We have developed artificial signaling-inert linker proteins to specifically perturb MCA and have found it has a key and unforeseen role in the regulation of cortex mechanics. Specifically, it modulates cortical tension and stiffness in a density-dependent manner. To understand how, we have used in-situ cryo-electron tomography to decipher how MCA controls the architecture of the cortex in cells. Last, I will show the relevance of our findings for early mouse embryo cell specification.

Mechanics of blastocyst morphogenesis

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During pre-implantation development, the mammalian embryo forms the blastocyst. The architecture of the blastocyst is essential to the specification of the first mammalian lineages and to the implantation of the embryo. Consisting of an epithelium enveloping a fluid-filled lumen and the inner cell mass, the blastocyst is sculpted by a succession of morphogenetic events. These deformations result from the changes in the forces and mechanical properties of the tissue composing the embryo. Combining microscopy, image analysis, biophysical tools and genetics, we study the mechanical and cellular changes leading to the formation of the blastocyst. In particular, we uncovered how pulsatile contractility compacts the mouse embryo, how asymmetric division of contractile domains couples cell positioning and specification, and how hydraulic fracturing and active coarsening position the lumen of the mouse blastocyst.

Magnetic manipulation of membrane molecule motion

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The plasma membrane, through which cells interact with their environment, fulfills many crucial functions which depend on the localization of distribution of molecules in the membrane. In polarized cells such as neurons, the plasma membrane is segregated into distinct domains with a specific composition to ensure proper physiological function. To maintain these domains, the lateral diffusion of molecules within the fluid membrane must be restricted. The cortical cytoskeleton and transmembrane proteins anchored hereto are thought to compartmentalize the movement of membrane molecules to nanoscale compartments (Picket and Fence models), giving rise to cell-scale diffusion barriers. To study these barriers, the random motion of membrane molecules is usually observed and compared with cortical structures. Instead, to directly detect a physical obstacle, we have developed a method to magnetically drag molecules through the membrane against putative barriers. To do so, we coupled fluorescent magnetic nanoparticles (FMNPs) to single membrane molecules to follow their diffusion by single-particle tracking (SPT) with 5 ms time resolution and 10 nm localization precision. Using lateral magnetic tweezers, we can exert magnetic forces of ~1-10 fN to direct the motion. This way, we pulled lipids through supported lipid bilayers and membrane proteins through the plasma membrane of living cells. To identify barriers to the magnetically directed molecule movement, we correlated the trajectories with super-resolution microscopy of F-actin, and indeed localize the obstruction to sites of actin fibers underneath the plasma membrane. The FMNPs and magnetic tweezers are straightforward to use and allow to remotely control single molecule motion while tracking the movement with high spatiotemporal resolution. Our approach thus expands our current toolbox to investigate the dynamic organization of molecules in the plasma membrane.

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Stable intermediates in talin rod are reached by force during unfolding

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Cells connect to the extracellular matrix via transmembrane integrin receptor and intracellular talin adaptor protein. Talin contains a head domain and a large alpha-helical rod domain, which forms 4- and 5-helix subdomains arranged into a linear chain. Talin rod subdomains undergo unfolding under mechanical load, generated by contractile actin cytoskeleton, what modulates affinity of the subdomains for its binding partners. Thus, mechanical signals are key to regulate talin rod functions. Talin rod subdomains have varying mechanical stability [1] and both, mechanically stronger 5-helix and weaker 4-helix subdomains unfold through stable 3-helix intermediates [2]. Free energy analysis of the unfolding pathways shows that the folded conformation of the subdomains is the most favorable and the 3-helix intermediates are stabilized by mechanical load, suggesting refolding of the protein once the mechanical load has lowered.

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Learning the distribution of single-cell chromosome conformations in bacteria reveals emergent order across genomic scales

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The order and variability of bacterial chromosome organization, contained within the distribution of chromosome conformations, are unclear. We develop a fully data-driven maximum entropy approach to extract single-cell 3D chromosome conformations from Hi-C experiments on the model organism *Caulobacter crescentus*. The predictive power of our model is validated by independent experiments. We find that on large genomic scales, organizational features are predominantly present along the long cell axis: chromosomal loci exhibit striking long-ranged two-point axial correlations, indicating emergent order. This organization is associated with large genomic clusters we term Super Domains (SuDs), whose existence we support with super-resolution microscopy. On smaller genomic scales, our model reveals chromosome extensions that correlate with transcriptional and loop extrusion activity. Finally, we quantify the information contained in chromosome organization that may guide cellular processes. Our approach can be extended to other species, providing a general strategy to resolve variability in single-cell chromosomal organization.

Membrane curvature and cellular mechanotransduction

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Membrane curvature in the range of tens to hundreds of nanometers is involved in many essential cellular processes. At the cell-matrix interface, where the cells make physical contact with extracellular matrices, the membrane may be locally deformed by matrix topography or mechanical forces, and this deformation may actively regulate signal transmission through the interface. We explore nanofabrication to engineer vertical nanostructures protruding from a flat surface. These nanostructures deform the plasma membrane to precisely manipulate the location, degree, and sign (positive or negative) of the interface curvature in live cells. We found that the high membrane curvature induced by vertical nanostructures significantly affects the distribution of curvature-sensitive proteins and modulate mechanotransduction in live cells. Our studies show a strong interplay between membrane curvature and mechanotransduction and reveal molecular mechanisms underlying the connection.

Unexpected patterns in nanoscale cell stiffness images due to intracellular forces

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In the course of developing a nanometer-scale-resolution cell stiffness imaging method, we found unexpected patterns in the nanoscale stiffness of cells[1]. Stiffness of different regions of a cell were correlated with local curvatures in those regions. Such a correlation is not predicted by the viscoelastic model of cell mechanics. We present a quantitative cell mechanical model that accounts for intracellular forces. This model not only explained the observed patterns, but also made precise testable predictions. We were able to test these predictions with our high-resolution stiffness images. We showed that various quantities (e.g. stiffness, curvature, and stiffness gradients across the cell surface) are related to each other with a set of mathematical equations. These findings suggest that intracellular forces do not merely perturb cell stiffness, they dominate cell stiffness. Furthermore, the equations of the mechanical model allow determining intracellular forces like actin filament bundle tension, cortex tension, and plasma membrane tension from the high-resolution stiffness data obtained by our new microscope.

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The force is within you: Fluorescent probes to map molecular forces in cells

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Cells are highly dynamic structures that are constantly pulling and pushing on one another and on their surroundings. These pulls and pushes are mediated by molecular complexes that experience forces at the scale of piconewtons (pN). For context, 7 pN applied a distance of 1 nm is ~1 kcal/mol and most biological forces are in the range of 1-50 pN. Nonetheless, and despite the small magnitude, these forces can have profound biochemical consequences. For example, the rapidly fluctuating forces between immune cells and their targets can drastically tune immune response and function. Unfortunately, there are limited methods to study forces at the molecular scale and particularly within the context of living cells. In this talk, I will discuss my group's efforts at addressing this gap in knowledge by developing tools to map and manipulate the molecular forces applied by cells. I will describe the development of a suite of molecular tension probes. Tension probes are modular and can be engineered using PEG polymers, oligonucleotides, and proteins. The latest generation of tension probes employ nucleic acids, which provide significant improvements in resolution and allow one to employ signal amplification strategies. I will show exciting new advances that harness fluorescence polarization spectroscopy (2) and super-resolution (1) imaging to provide the highest resolution maps of cell traction forces reported to date. I will also describe the application of these probes in the study of platelet activation (3), podosome formation (4), and T cell receptor mechanobiology (5). Finally, armed with these new tools, I will demonstrate that molecular forces not only give rise to tissue architecture but also to boost the fidelity of information transfer between cells. We dubbed this mechanism *mechanical proofreading* in analogy to the kinetic proofreading model used explain the extraordinary fidelity of DNA replication and protein expression. I will show examples of mechanical proofreading in adaptive T cell immunity and platelet coagulation.

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4. "DNA mechanotechnology reveals that integrin receptors apply pN forces in podosomes on fluid substrates" Nature Communications, 2019
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Torque generation by microtubule-crosslinking motors

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Within the mitotic spindle, kinesin motors cross-link and slide overlapping microtubules. Some of these motors exhibit off-axis power strokes, but their impact on motility and force generation in microtubule overlaps has not been extensively investigated. We utilize three-dimensional in vitro motility assays to explore the kinesin-5 and kinesin-14 driven sliding of cross- linked microtubules. We observe that free microtubules, sliding on suspended microtubules, not only rotate around their own axis but also move around the suspended microtubules with helical trajectories. Importantly, the associated torque is large enough to cause microtubule twisting and coiling. Further, our technique allows us to measure the in situ spatial extension of the motors between cross-linked microtubules. We argue that the capability of microtubule-crosslinking kinesins to cause helical motion of overlapping microtubules around each other allows for flexible filament organization, road- block circumvention and torque generation in the mitotic spindle.

Red Blood cell flow dynamic in vivo

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1. Introduction.

The microvascular networks in the body of vertebrates consist of the smallest vessels, such as arterioles, venules, and capillaries. The flow of red blood cells (RBCs) through these networks ensures the gas exchange in, as well as the transport of nutrients towards the tissues. Any alterations in this blood flow may have severe implications on the health state. Since the vessels in these networks obey dimensions similar to the diameter of RBCs, dynamic effects on the cellular scale play a key role. The steady progression in numerical modelling of RBCs even in complex networks has led to novel findings in the field of hemodynamics, especially concerning the impact and the dynamics of lingering events [1]. However, these results are yet unmatched by a detailed analysis of the lingering in experiments in vivo.

2. Methods.

Syrian gold hamsters with a body weight of 60–80 g are equipped with a dorsal skinfold chamber, consisting of two symmetrical titanium frames with a total weight of approx. 4 g. Therefore, the animals are anaesthetised and from their depilated and disinfected back, one layer of skin and subcutis with the panniculus carnosus muscle as well as the two layers of the retractor muscle are completely removed within the area of the opening window of the chamber. A total number of five hamsters was prepared in order to neglect any interindividual effects and also to observe different phenomena in various geometries.

3. Results and discussion.

We find that the temporal dynamic in the microcirculation [2] is to a large extend determined by lingering events of red blood cells at bifurcations. This refers to a temporal rest of single cells at the bifurcation apex. We will present a statistical analysis on the flow dynamics and compare our findings to numerical predictions [1].

4. Conclusions. Our experiments confirm the existence of lingering effects that have been predicted numerically and we find that they significantly determine the temporal flow dynamics.

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Controlling antagonist responses with a single optogenetic activator

Jean de Seze

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Cell migration is a complex process that takes place in many biological contexts like development or cancer. It relies on an equilibrium between contraction and protrusion of the cytoskeleton, which is itself mainly regulated by small proteins, the RhoGTPases. Among them, RhoA has a mysterious behaviour, being active both at the rear ant at the front of migrating cells. Supporting this dual role, we recently observed that local activation of RhoA through optogenetics can lead to both protrusion or retraction. How can the same protein be directly responsible for two antagonists effects? Our main hypothesis is that the switch occurs when overexpression of RhoA saturates the contractility pathway, thus letting place to the second known pathway of RhoA which triggers protrusion through actin polymerization. This is a striking example of multiplexing: one protein is used by the cells for two different outcomes, and it helps having a better understanding of both this specific pathway and the general strategies the cell uses to control different fate with one specific molecule.

Coding of sequence statistics in the auditory cortex of passive vs. active mice

Sara Jamali

Institut de l'Audition, Institut Pasteur, Paris, France

A wide range of evidence indicate that the brain infers a model of the external world from sensory inputs which can create anticipations. The predictive coding hypothesis assumes that the brain continuously generates such predictions, and when these predictions are violated by unexpected sensory inputs the brain generates a surprise or an error signal. Based on this idea, it has been proposed that the cerebral cortex acts partly as a hierarchical predictive system that responds to prediction errors at multiple levels. In the classical auditory oddball paradigm, violations of regularities in tone sequences evoke novelty responses in the brain, even under anesthesia. At a second level, however, recent studies in humans and monkeys suggest that when the violation concerns more global regularities at the level of an entire sequence, the novelty response appears only in conscious, attentive subjects. To study whether local and global sequence violations can be detected also in the mouse brain, we recorded from layer 1 to 5 of the auditory cortex using two-photon calcium imaging (and recently a high-speed acousto-optic scanning-based two-photon imaging) changing the global statistics of the sequences. We repeated this experiment three times with behaving mice and mice passively listening to sounds with a long trial interval (25 s) as well as a shorter trial interval (1.5 s). Our observations show that a sparse population of mouse auditory cortex neurons is modulated by sequence statistics. Neurons increase their response to rare sequences even with a long trial interval of 25s. And also we observe neurons that respond to pure global violations of the sequence statistics. These results suggest that the mouse brain can recognize global sound statistics, and provide a path towards analyzing the neuronal mechanisms of hierarchical predictive coding.

Coupling phenotypic stability to growth-rate overcomes limitations of bet-hedging strategies

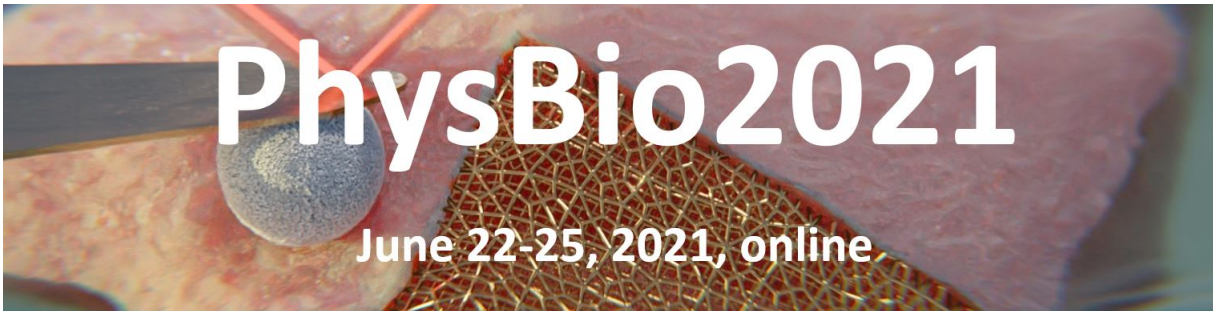
Daan de Groot

Van Nimwegen Group, Biozentrum, Universität Basel, Switzerland

Microbial populations in the wild must survive and reproduce in highly variable, and unpredictable environments. To overcome this challenge, bacterial cells express sets of proteins that sense the environment and adapt gene expression. However, the expression of such sensing- and regulation machinery in each cell requires resources, which comes at the expense of the cell's growth rate, and these costs mount when the number of possible environments increases. Alternatively, cells may use a bet-hedging strategy in which isogenic cells randomly switch between phenotypes. This ensures that, in each environment, different subsets of cells are adapted to different possible future environments. Upon a change of environment, selection causes the small subpopulation of pre-adapted cells to expand and dominate the population. However, bet-hedging also comes at a cost: the subsets of pre-adapted cells may be maladapted to the current environment, and this cost again increases with the number of possible environments that the population needs to anticipate. Moreover, after each environment change, selection needs time to expand the small pre-adapted cell population. Therefore, bet-hedging strategies are often only considered relevant when environments are not too diverse, and environmental changes are relatively rare.

So far, bet-hedging models have assumed that the rates of stochastic switching are independent of the current growth rate of the cell. However, recent experiments show that gene expression noise generally decreases with growth rate. This can cause slow growing cells to switch phenotype much more often than fast growing cells. We here show that this Growth Rate Dependent Stability (GRDS) dramatically improves bet-hedging strategies, allowing for effective adaptation even when environments are complex and change rapidly. When cells grow slow, the increased stochasticity causes them to explore different phenotypes, which increases the rate at which adapted phenotypes are found. Once an adapted phenotype is found, the stochasticity reduces, and the phenotype is stabilised. As a result, GRDS speeds up adaptation and diminishes the eventual fraction of maladapted cells.

Our results show that GRDS turns bet-hedging into a low-cost, universal adaptive strategy, which makes the expression of sensing- and regulation-machinery unnecessary in many more cases than could have been suspected based on existing bet-hedging theory.



POSTER ABSTRACTS

Wednesday, June 23 14h15 – 16h45

Poster session 1 : Poster 1-16

Poster 1

Why Should Metformin Not Be Given in Advanced Kidney Disease? Potential Leads from Computer Simulations

Martina Pozar

Visnja Kokic Males (University of Split, University Department for Health Studies, Croatia); Martina Pozar (University of Split, Faculty of Science, Croatia)

Metformin is considered as the go-to drug in the treatment of diabetes. However, it is either prescribed in lower doses or not prescribed at all to patients with kidney problems. To find a potential explanation for this practice, we employed atomistic-level computer simulations to simulate the transport of metformin through multidrug and toxin extrusion 1 (MATE1), a protein known to play a key role in the expulsion of metformin into urine. Herein, we examine the hydrogen bonding between MATE1 and one or more metformin molecules. The simulation results indicate that metformin continuously forms and breaks off hydrogen bonds with MATE1 residues. However, the mean hydrogen bond lifetimes increase for an order of magnitude when three metformin molecules are inserted instead of one. This new insight into the metformin transport process may provide the molecular foundation behind the clinical practice of not prescribing metformin to kidney disease patients.

Poster 2

Universal features in lifetime distribution of clusters in hydrogen bonding liquids

Ivo Jukić

Ivo Jukić (Doctoral School of Biophysics, Faculty of Science, University of Split, Croatia; Laboratoire de Physique Théorique de la Matière Condensée, Sorbonne Université, France) ; Martina Požar (Department of Physics, Faculty of Science, University of Split, Croatia); Bernarda Lovrinčević (Department of Physics, Faculty of Science, University of Split, Croatia); Aurélien Perera (Laboratoire de Physique Théorique de la Matière Condensée, Sorbonne Université, France)

Formation of labile aggregates (clusters) in hydrogen bonding liquids, such as water or alcohols, is well-known phenomenon. Lifetime of such aggregates is important microscopic parameter and can be calculated in computer simulations. Statistical nature of these clusters suggests that their lifetime distribution should be broad Gaussian-like function of time, with a single maximum representing the mean lifetime of these structures. This distribution would be weakly dependent on bonding criteria, such as the distance or angle, while the long time part is known to have some power law dependence. Surprisingly, lifetime distributions of hydrogen bonds in all liquids studied herein, namely water and alcohols, show three specific lifetimes in the time range 0 – 0.5 ps. The dominant lifetime, which is attributed to hydrogen bonded pairs, depends strongly on the bonding distance criterion. This mode is absent in simple, non-associative liquids. The secondary and tertiary lifetimes are related to clusters and are nearly independent on the bonding criterion. Secondary mode is present also in lifetime

distributions related to simple liquids, unlike the third mode which is absent in this case. This poses the question of the origin of the third lifetime. The study of alcohols reveals that the appearance of the third lifetime is related with the topology of H-bonded clusters. Furthermore, it is shown that the presence of alkyl tails may strongly influence the hydrogen bonding process in these liquids and, consequently, the overall shape of lifetime distribution of hydrogen bonds. Finally, this work displays the universal hierarchy of hydrogen bonding lifetimes with a timescale regularity across different types of hydrogen bonding liquids.

Poster 3

Understanding the Helical Stability of Charged Peptides

Nitin Kumar Singh

Nitin Kumar Singh, Discipline of Chemical Engineering, Indian Institute of Technology, Gandhinagar, Gujarat, India; Manish Agarwal, Computer Services Centre, Indian Institute of Technology Delhi, India; Mithun Radhakrishna, Discipline of Chemical Engineering, Indian Institute of Technology, Gandhinagar, Gujarat, India

α-helices are the most ubiquitous form of secondary structure observed in proteins. They play an essential role in the tertiary and quaternary folding of a protein and are vital for the functioning of the protein. Furthermore, helical polypeptides are a relevant biotechnological tool and have found their applications in membrane transport, vaccine development, and therapeutics. The application of the helical structures for these purposes is limited because of the reduced solubility of the hydrophobic residue helices and the low stability of the helices with charged amino acids in the aqueous solution. This study aims to bridge this gap by designing water-soluble helical peptides by controlling the charge density and the amino acid sequence. In the study, we have used leucine (hydrophobic) and lysine (charged) amino acid residues to design proteins that have considerably higher stability compared to charged polypeptides. All-atom simulations carried out in explicit solvent (water) showed that charge density plays a central role in tuning the helical stability. At a fixed charge density, the sequence pattern has a minor influence. We believe this study could help the scientific community at large involved in the de novo design of protein sequences.

Poster 4

The glycocalyx affects integrin adhesion complex-mediated mechanotransductive processes in the cell/microenvironment interface

Carsten Schulte

Matteo Chighizola[1], Tania Dini[1,2], Stefania Marcotti[3], Mirko D'Urso[1,4], Claudio Piazzoni[1], Francesca Borghi[1], Anita Previdi[1], Laura Ceriani[1], Claudia Folliero[1,2], Brian Stramer[3], Cristina Lenardi[1], Paolo Milani[1], Alessandro Podestà[1], Carsten Schulte[1]

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Keywords. Glycocalyx, Mechanotransduction, Integrin Adhesion Complexes, Adhesion Force Spectroscopy, Molecular Clutch

Mechanotransduction; i.e., the interpretation of biophysical extracellular matrix (ECM) cues and their translation into cellular responses, impacts strongly the cell state. The cell/microenvironment interface is the starting point of integrin-mediated mechanotransduction, but many details of the signal integration remain elusive due to the complexity of the involved (extra)cellular structures, such as the ECM itself, the glycocalyx, the cell membrane, integrin adhesion complexes, and the cytoskeleton. Unravelling this complexity requires the usage of sophisticated interdisciplinary methodologies.
In this framework, we developed a novel approach for which we used engineered nano-bio interfaces with ECM nanotopograpy-mimicking features to analyse the influence of essential cell/microenvironment components and processes on mechanotransduction; e.g., by adhesion force spectroscopy with nanotopographical probes to measure single binding events with piconewton precision.
Our data demonstrates that the availability of activated integrins and the glycocalyx configuration affect spatiotemporal nanotopography-sensitive mechanotransductive events at the cell/microenvironment interface. Opposing effects of glycocalyx removal were observed, when comparing flat and specific nanotopographical conditions (i.e., 15 nm root-mean-square (rms) roughness). The excessive force loading and retrograde actin flow speed, characteristic for the 15 nm rms nanotopography in the presence of native glycocalyx, are strongly reduced in its absence. Conversely, on the flat substrate, these parameters increased upon glycocalyx-targeting enzymatic treatment.
Our results highlight the importance of the glycocalyx configuration in a molecular clutch force loading-dependent cellular mechanism for nano-mechanosensing of the topography. These processes might have a strong relevance for many (patho)physiological situations, such as cell differentiation, migration, or cancer and metastasis.

Video teaser : https://zimbra.u-psud.fr/service/home/~/?auth=co&loc=fr&id=1021&part=2

Poster 5

Collective cell durotaxis along a self-generated stiffness gradient in vivo

Adam Shellard

Adam Shellard (Mayor lab, University College London, UK) ;
Roberto Mayor (Mayor lab, University College London, UK)

Collective cell migration underlies morphogenesis, wound healing and cancer invasion. Most directed migrated in vivo has been attributed to chemotaxis, in which cells follow a chemical gradient, but cells can also follow a stiffness gradient in vitro, a process called durotaxis. Evidence for durotaxis in vivo is scarce, how stiffness gradients might be generated is unclear, and whether chemotaxis and durotaxis might simultaneously coordinate directional cell migration in the complex in vivo environment remains unknown. Here we investigated the role of durotaxis during in vivo collective cell migration and its interplay with chemotaxis, using neural crest cells, an embryonic cell population whose migratory behaviour has been likened to cancer invasion. We identified the existence of a gradient of stiffness along a tissue adjacent to the neural crest, the cranial placodes. The gradient moves with the neural crest, which are continually pursuing a retreating region of high substrate stiffness by durotaxis.

The stiffness gradient is formed by the neural crest cells themselves due to N-Cadherin interactions with the placodes. The gradient is also sensed by the neural crest cells, resulting in polarised focal adhesions, Rac and actomyosin contractility, which coordinates durotaxis. Durotaxis cooperates with chemotaxis in vivo, cooperatively polarising the cell group's actomyosin machinery to prompt efficient directional collective cell migration. These results elucidate a mechanism of self-generating a stiffness gradient, show that durotaxis is a relevant guidance cue in vivo, and that gradients of chemical and mechanical signals cooperate to achieve efficient directional collective cell migration in vivo.

Poster 6

Motor-driven transport of mitochondria in living cells

Agustina Fernández Casafuz

A. Fernández Casafuz (Instituto de Cálculo, UBA-CONICET, Argentina), M.C. De Rossi (Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina), L. Bruno (Instituto de Cálculo , UBA-CONICET, Argentina)

Mitochondria are fundamental organelles for the correct function of eukaryotic cells. Several studies show that mitochondria are transported preferentially to areas with high metabolic demand. In order to achieve their precise location, mitochondria undergo bidirectional transport along cytoskeleton filaments driven by molecular motors, which are also relevant in regulation of mitochondria shape and size. It is well documented that mitochondrial dysfunction and changes in mitochondrial dynamics and mobility are involved in the pathology of some major neurodegenerative and neurological disorders, thus the need of understanding the underlying mechanisms in mitochondrial transport.
In recent studies in X. laevis melanophore cells we have observed that mitochondria change their shape to rod-like when being transported along microtubules and that they change their length in correlation with the direction of motion: Mitochondria tend to retract during anterograde transport performed by dynein motors, whilst they maintain their length in retrograde transport mediated by kinesin motors. We also observed that slow mitochondria preferably stretch when moving.
In order to explain these effects we proposed a novel one-dimensional extended model for intracellular transport of smooth flexible organelles based on a Langevin equation of motion in the overdamped limit. We ran numerical simulations to study the behavior of the cargo for different motor teams in competitive and noncompetitive scenarios, focusing on the transport properties observable in the experiments, e.g. cargo speed and length. Our results suggested that active motors adopt opposite configurations depending on the resisting load: For low loads motors push the cargo and the organelle contracts, while when the resisting load is large (e.g., in very competitive tug-of-war), motors pull the cargo and the organelle stretches. With these results we interpret the complex behavior of mitochondria transport observed in X. laevis cells.

Poster 7

Life in a Tight Spot: How Bacteria Swim, Disperse, and Grow in Porous Media

Tapomoy Bhattacharjee

Tapomoy Bhattacharjee (Princeton University), Daniel Amchin (Princeton University), Ricard Alert (Princeton University), Jenna Ott (Princeton University), Felix Kratz (Princeton University), Sujit Datta (Princeton University)

Bacterial motility is central to processes in agriculture, the environment, and medicine. While motility is typically studied in bulk liquid or on flat surfaces, many bacterial habitats -- e.g., soils, sediments, and biological gels/tissues -- are complex porous media. Here, we use studies of E. coli in transparent 3D porous media to demonstrate how confinement in a heterogeneous medium fundamentally alters motility. In particular, we show how the paradigm of run-and-tumble motility is dramatically altered by pore-scale confinement, both for cells performing undirected motion and those performing chemotaxis, directed motion in response to a chemical stimulus. Our porous media also enable precisely structured multi-cellular communities to be 3D printed. Using this capability, we show how spatial variations in the ability of cells to perform chemotaxis enable populations to autonomously stabilize large-scale perturbations in their overall morphology. Finally, we show how when the pores are small enough to prevent cells from swimming through the pore space, expansion of a community via cellular growth and division gives rise to distinct, highly-complex, large-scale community morphologies. Together, our work thus reveals new principles to predict and control the behavior of bacteria, and active matter in general, in complex environments.

Poster 8

ARTIFICIAL MOUSE – AN ULTRASOUND MEDIATED DRUG DELIVERY PLATFORM

RASHMI RAMESH

Rashmi Ramesh[1], Nicolas Taulier[1] and Wladimir Urbach [1 2]

[1] Laboratoire d'Imagerie Biomédicale (LIB), Sorbonne Université, France.
[2] Laboratoire de Physique Statistique, Département de physique de l'Ecole Normale Supérieur, France.

The goal of targeted drug delivery is the spatial and temporal localization of a therapeutic agent and its associated bio-effects. One method of drug localization is acoustic droplet vaporization (ADV), whereby drug-laden perfluorocarbon (PFC) emulsions are vaporized into gas bubbles using ultrasound, thereby releasing drug locally. Trans-pulmonary droplets are converted into bubbles that occlude capillaries, sequestering the released drug within an organ or at the site of the tumor. This research investigates and optimizes the various parameters such as the droplet size, composition etc., to have an efficient and non deleterious release of the drug at the targeted tumor sites. A tumor on chip platform is developed to monitor and assess the efficiency of this ultrasound triggered drug release technique. The delivery is effected using Perfluorocarbon double emulsions. Overall, the results suggest that PFC double emulsions can be used as an ultrasound-triggered drug delivery system. Compared to

traditional drug delivery systems, ADV could be used to increase the therapeutic efficacy and decrease the systemic toxicity of drug therapy.

Poster 9

Extensile stress promotes out-of-plane flows in active layers

Mehrana Raeisin Nejad

Mehrana R. Nejad, Julia M. Yeomans

Department of Physics, University of Oxford, UK

We use numerical simulations and linear stability analysis to study an active nematic layer where the director is allowed to point out of the plane. Our results highlight the difference between extensile and contractile systems. Contractile stress suppresses the flows perpendicular to the layer and favours in-plane orientations of the director. By contrast extensile stress promotes instabilities that can turn the director out of the plane, leaving behind a population of distinct, in-plane regions that continually elongate and divide. Our results suggest a mechanism for the initial stages of layer formation in living systems, and explain the propensity of dislocation lines in three-dimensional active nematics to be of twist-type in extensile, or wedge-type in contractile, materials.

Video teaser : https://www.youtube.com/watch?v=mZ5ZQwEcpBw

Poster 10

Persistence transitions in collective cell migration

Nicolas Borghi

Helena Canever, Quentin Delaunay, Nicolas Audugé, Nicolas Borghi

Institut Jacques Monod, Université de Paris, CNRS, France

Collective cell migration is a fundamental behavior involved in multicellular development, regeneration and homeostasis, and that is deregulated in cancer. Epithelial cells can migrate collectively in a tissue or individually when isolated. Even in the absence of external cues, cell motion occurs in confluent epithelial cultures up to a density limit. We have found that while isolated cells are persistent random walkers, they adopt a super-diffusive behavior in the bulk of a confluent epithelium. This virtually allows cells to reach farther distances when surrounded by neighbors than when alone. This confluence-induced transition in migration persistence is robust to mutations of adhesion proteins that affect instantaneous cell velocity and appears to emerge from a fractional random walk. Conversely, cell velocity does not appear to exhibit long-range spatial correlations throughout the epithelium. Finally, wounding a confluent epithelium expectedly biases cell motion towards the wound but also induces cells to adopt a fat-tailed walk. These results suggest that multicellularity and directionality cues affect the migration machinery more profoundly than previously anticipated.

Poster 11

Mechanical description of the podia in sea star locomotion

Amandine Deridoux

Amandine Deridoux (Laboratory for Complex Fluids and Interfaces, Mechanobiology and Soft Matter Group, University of Mons, Belgium); Patrick Flammang (Biology of Marine Organisms and Biomimetics Unit, University of Mons, Belgium); Sylvain Gabriele (Laboratory for Complex Fluids and Interfaces, Mechanobiology and Soft Matter Group, University of Mons, Belgium)

Sea stars use a multitude of small hydraulic organs (i.e., the tube feet or podia), to locomote, to strongly attach to the surrounding, and to pry open the mussels on which they feed. Podia are secretory organs in which two types of adhesive cells co-secrete a blend of adhesive proteins to form the adhesive layer joining the podia to the substrate. Despite the paramount importance of podia in sea star locomotion, the regulation of the number of podia sticking to a surface during movement is still poorly understood. To address this challenge, we built up an aquarium equipped with a total internal reflection (TIRF) system and developed a robust thresholding technique for quantifying the number of podia sticking to the substrate during locomotion. We found that the contact area of individual podia increases to become a perfect circle during the adhesion phase. Surprisingly, we measured a very low percentage of podia in contact with the substrate during locomotion in Asterias rubens. Moreover, the number of sticking podia, as well as the instantaneous speed remain constant during movement. Contrary to what is observed in other animals, it seems that the size of Asterias rubens has no impact on the mean crawling speed. In contrast, we found that this speed decreases with the increase of the podial adhesion time and the increase of the number of sticking podia. A long-term goal for this project is to develop a biomechanical model of sea star locomotion based on the measurement of the adhesion energy exerted by a sea star according to the number of sticking podia.

Poster 12

Glass nanoneedle to probe intracellular viscoelastic properties

David Brownell

David Brownell (LadHyX, Ecole polytechnique, France); Julien Husson (LadHyX, Ecole polytechnique, France)

Mechanical properties of cells have been shown to provide valuable information regarding cell function. Information such as internal structure, pathology, and differentiation can be inferred from such measures, allowing a deeper understanding of the biological material. Many techniques infer cell mechanical properties superficially by exerting a compressive (e.g. AFM) or suction force (Micropipette aspiration) to a cell. These techniques may fail to identify contributions of various cell compartments. Contributions of the cell cortex and bulky organelles such as the nucleus are difficultly taken into account individually. Similarly, contributions of viscous properties are difficult to isolate. We have developed a simple system to measure intracellular mechanical properties based on piercing a cell with a nanoneedle. Forged from a glass capillary, typically 10-µm long and 100-nm in diameter, the needle acts as an intracellular probe, capable of measuring force, as the needle is fused to the end of a

flexible micropipette of known bending stiffness. This technique is promising for acquiring information that is currently difficult to quantify with other methods. Information such as nucleus stiffness and intracellular viscosity could be effectively evaluated.

Poster 13

The Experimental Study Of The Dynamics Of A Self-propelled Rod

Yasamin Mohebi

Dr, Maniya Maleki (Assistant Professor of Experimental Soft Matter, Institute for Advanced Studies in Basic Sciences, Zanjan, Iran); Yasamin Mohebi (Master student of Experimental Soft Matter, Institute for Advanced Studies in Basic Sciences, Zanjan, Iran)

The self-propelled particles have two categories: Natural self-propelled particles such as bacteria, and artificial self-propelled particles made in a laboratory. It is much easier to study artificial particles because particle motion parameters can be controlled by changing laboratory conditions. In this poster, we describe the results of experiments on an artificial self-propelled rod and we show that this artificial particle has the properties of an active particle.

Poster 14

Biophysical study of large macromolecular complexes

Laurent Marichal

Laurent Marichal[1,2], Jean Philippe Renault[2], Jéril Degrouard[1], Rafael Rubim[1], Guillaume Tresset[1], Serge Pin[2]

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Large macromolecular complexes are ubiquitous in biological media (e.g. protein complexes, membrane-bound complexes…). Specific biophysical techniques can be used to assess the interactions and structures of such complexes. Two independent systems were chosen as examples. The first one deals with the formation of protein coronas (protein/nanoparticle interactions) while the second system concerns virus encapsidation (protein/RNA interactions). Here, we can see how three techniques (isothermal titration calorimetry, cryo-electron microscopy, and small angle scattering) can be combined in order to answer fundamental questions.

Poster 15

The lymphatic pumping mechanism: A numerical study

Marianna Pepona

M. Pepona, G. Helberque, and B. Kaoui

Laboratoire de Biomécanique et Bioingénierie BMBI - UMR CNRS 7338,
Université de Technologie de Compiègne, France

Elucidating the lymphatic pumping mechanism is of crucial significance towards a better understanding of the lymphatic system-related diseases, such as lymphedema and cancer, and subsequently the development of more efficient treatments. To this end, we are currently developing a numerical framework to computationally model the interaction between the lymph fluid, the deformable lymphatic vessel walls and the lymphatic two-leaflets valves. Our numerical model accounts for the reaction-diffusion of calcium ions (Ca2+) and the advection-diffusion of nitric oxide (NO) regulating the lymphangions contraction-dilatation. Our numerical approach consists of: the lattice Boltzmann method to solve the lymph fluid flow and species mass transport governing equations, a spring-network model for the lymphatic vessel walls and valves, and the immersed boundary method allowing for the coupling of the fluid and structure solvers. Preliminary results on two-dimensional configurations will be presented. The current implementation paves the way to the non-trivial extension to three dimensions, and the study of the effects of various fluid, geometrical and mechanical properties on the lymphatic pumping mechanism.

Poster 16

Identifying mechanisms by which cells sense multicellular density

Louis LAURENT

François Sipieter, Louis Laurent, Helena Canever, Nicolas Borghi

Université de Paris, Institut Jacques Monod, UMR7592 CNRS, Paris, France

Sensing cell density within a cohesive tissue is a fundamental property thought to underlie the regulation of tissue homeostasis in multicellular organisms. Yet, the mechanisms by which cells sense multicellular density remain largely unknown. In an epithelium, the extent of cell adhesion to the extracellular matrix directly depends on cell density: the higher the density, the smaller the matrix area available for cell adhesion. Here, we tested whether cell-matrix adhesion functions as a sensor of local epithelial cell density. We hypothesized that changes in cell density are perceived within adhesion complexes through changes in molecular tensions, which subsequently confer density-dependence to downstream mechanosensitive pathways. By using a multiplexed FRET biosensor strategy and dominant mutants and pharmacological inhibitors, we showed that cell density regulates focal adhesion growth and Vinculin tension, subsequently instructing Extracellular-signal Regulated Kinase (ERK) activity. Conversely, the Focal Adhesion Kinase (FAK) is also sensitive to cell density but only exert a permissive control on ERK activity. We are now examining the molecular mechanisms by which molecular tensions in Vinculin instruct the activity of ERK.

Thursday, June 24 14h15 – 16h45

Poster session 1 : Poster 17 - 32

Poster 17

Deep-3D-multiphoton imaging of whole biological structures with a computational assistance and the pipeline FAMOUS

Claire Lefort

Claire Lefort[1], Mathieu Chalvidal[2], Alexis Parenté[3], Véronique Blanquet[3], Henri Massias[1], Laetitia Magnol[3], Emilie Chouzenoux[4]

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We have developed a new instrumental and computational pipeline based on multiphoton microscopy [1] imaging thick biological samples on whole organs without slicing or labeling procedure. This strategy delivers a new viewpoint on the tested biological structures [2]. For the post-processing strategy, we are developing a specific regularized image restoration algorithm [3, 4]. The first step is to led an accurate 3D estimation of the point-spread function (PSF) of the instrument all over the entire depth of the structures [5-6]. This latter approach is named FIGARO. An advanced model fitting algorithm measure the depth-variant distortions of the image resulting from the combination between the heterogeneities of the structure resulting into scattering and absorption phenomena and distortions associated to the instrument. The resulting approach is a pipeline called FAMOUS whose performance is evaluated in case of a heterogeneous medium constituted by a whole mouse muscle. The whole EDL (Extansum Digitorum Longus) is resected from tendon to tendon, is unsliced and is imaged with a multiphoton microscope thanks to the emission of a second harmonic generation (SHG) signal, emitted from the myosin assembly of muscle. The images of the PSF are recorded simultaneously in the second recording channel of the multiphoton microscope. Thanks to the pipeline FAMOUS, optical artefacts resulting from the acquisition chain are evaluated, including medium heterogeneities in the 3 dimensions. We are keeping a specific attention to the axial structuration of myosin whose structuration is lost in blur and noise due to the optical resolution lost especially in case of a deep 3D imaging. The restored images reveale for the first time an axial level of structuration unexpected until now.

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Poster 18

Combining Acoustic Force Spectroscopy and DNA scaffold for high throughput measurement of ligand-receptor kinetics at single molecule resolution

Claire Valotteau

Yong Jian Wang (1), Claire Valotteau (1)*, Adrien Aimard (2) , Lorenzo Villanueva (1), Dorota Kostrz (3), Maryne Follenfant (3), Terence Strick (3), Charlie Gosse (3), Patrick Chames(2), Felix Rico (1) and Laurent Limozin (1)*

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Single-molecule data are of great significance in biology, chemistry and medicine. However, experimental tools to accomplish high-throughput measurements are lacking. Acoustic force spectroscopy (AFS) is an emerging single-molecule technique which generates sound waves to apply force on a large population of microparticles in parallel. The force amplitude increases as the cube of the particle radius to reach 50-100 pN with a simple experimental set up. The tunability of the amplitude of the acoustic field allows dynamic control of the applied forces and makes the technique very suitable to study single molecules of interest tethered to microbeads and to the surface. We have exploited this configuration on a recently developed modular J-DNA scaffold designed to study protein-protein interactions at the single-molecule level. A force calibration on individual molecules was performed simultaneously to the application of a cyclic step of force in order to produce repetitive binding-unbinding events on the very same ligand-receptor pairs. The unbinding kinetics under force was compared for the FRB-rapamycin-FKB12 complex previously investigated by magnetic tweezers at forces below 10 pN. We further characterize the force-extension response of J-DNA in the 10-100 pN range. The method allows high-throughput measurements at the single-molecule level on a wide range of ligand-receptor interactions including nanobody-antigen and thus may provide novel information to characterize therapeutic molecules.

Poster 19

Impact of pathogenic protein assemblies in neurodegenerative diseases on mouse cortical neurons endo-lysosomal transport

Qiao-Ling Chou

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Impairment of axonal transport has lately emerged as a factor shared by several neurodegenerative disorders (ND). Early impact on intraneuronal transport has been thus proposed as a phenotypic trait common to ND, such as Alzheimer's (AD), Huntington's, and

Parkinson's Disease (PD). Compelling evidence that abnormal accumulation of misfolded proteins in the brain, including α-synuclein (α-syn) in PD and b-amyloid (Aß) in AD, is crucial pathophysiology underlying the neurotoxicity observed in these age-related disorders. Furthermore, the misfolded proteins gather to form non-soluble assemblies of different species, including fibrillar polymorphs (of fibril [α-synF] or ribbon [α-synR] type for α-syn, and fibril only for Aß) or oligomer for Aß. These different aggregates are suspected to underly the large spectrum of toxicity observed in ND. There are evidence that they impact the endosomal transport, which is essential in establishing neuronal compartment architecture, dynamics, and function. However, few studies have compared the impact of the different assembly types in the same neurons and their own transport. We report a detailed quantitative and comparative analysis of the impact on endo-lysosomal transport of α-synF and α-synR fibrillar polymorphs, Aß fibrils, and Aß oligomers, externally applied on mature mouse cortical neurons in culture. We measured endosomal and lysosomal transports using photostable fluorescent nanodiamonds and lysotracker dye, respectively, followed by the subsequent automatic extraction and quantification of their directed motions at high throughput. All protein assemblies led to a vast decrease in the fraction of endosomes and lysosomes having directed motion inside the neurons, which is expected to impact neuron homeostasis substantially. We further evidenced differential impacts of these pathogenic protein assemblies on various parameters of endo-lysosomal transport. Finally, we were able to quantify the transport parameters of the cargoes loaded with these assemblies and observed that they have a more irregular transport than the ones of endosome and lysosomes, with in particular more frequent but also shorter pauses. These observations suggest that these cargoes have distinct molecular characteristics, but further work is necessary to elucidate their precise nature. Overall, our results point out that α-syn fibrillar polymorphs, Aß fibrils, and oligomers impair intraneuronal transport. We hypothesize that it results from either their direct interaction with the intraneuronal transport machinery or the induction of transcriptional changes in transport protein expression.

Poster 20

Molecular Mechanical Determinants of Collective Cell Migration

Helena Canever

Helena Canever, François Sipieter, Philippe P. Girard, Nicolas Borghi

Institut Jacques Monod, Université de Paris, CNRS, France

Collective epithelial cell migration (CCM) is a process occurring during development and wound healing, as well as in some forms of cancer invasion. During CCM cells exert forces upon their neighbors and the underlying matrix through Adherens Junctions (AJs) and focal adhesions (FAs), respectively. However, how the regulation of force transmission in FAs and AJs affects CCM is unclear. Measuring molecular tension forces acting on the FA- and AJ-localized protein vinculin shows a transcellular tension gradient at both FAs and AJs during CCM, indicating mechanosensitivity of vinculin to CCM. The mechanical state of vinculin is affected differently by mutations targeting its actin binding or bundling function and/or its auto-inhibition, and the resulting molecular tension predicts the speed of collective, but not single, cell migration: the higher the tension the faster the CCM. Interestingly, the actin-bundling mutants affect mechanosensitivity of vinculin at AJs specifically and they disproportionally affect CCM compared to single cell migration. This, along with

quantification of protein dynamics in vinculin mutant cell lines, indicates that a non cell-autonomous regulation of CCM by vinculin arises from its role at AJs and may depend on its regulation of actin bundling and protein stability at AJs.

Poster 21

The singular consequences of linkage in the infinitesimal model of an evolving population

Elise Tourrette

Elise Tourrette (GQE - Le Moulon, INRAE, France); Olivier C. Martin (IPS2, Université Paris-Saclay, France)

The mathematics of inheritance in the field of quantitative genetics was historically formulated via the so called "infinitesimal model" introduced by Ronald Fisher in 1918. It consists of using the limit of an infinite number of genes, each associated allele contributing an infinitesimal amount to an additive quantitative trait. The behavior of a panmictic population can then be predicted if the alleles are assumed to segregate independently during reproduction, that is if the genes are all unlinked as if on separate chromosomes. Under that idealisation, the selective pressure over many generations leads asymptotically to a constant strictly positive genetic gain per generation. However, in reality genes are subject to linkage as they don't necessarily lie on different chromosomes and thus they segregate in a correlated way. Various mathematical approximations have been used in the past to study that more realistic case of the infinitesimal model and they lead to the prediction that the asymptotic gain per generation is only modestly decreased. Here we provide an exact solution to the problem where genes lie on a continuous chromosome. Surprisingly, the consequences of genetic linkage are in fact singular, changing the nature of the asymptotic gain per generation. The corresponding dynamics undergoes "aging", the gain per generation slowly tending towards zero. Furthermore, the rate at which this gain tends to zero is slow enough for the total gain accumulating over generations to be unbounded.

Poster 22

Physical origin of active snapping of the Venus flytrap

Jeongeun Ryu

Jeongeun Ryu (CNRS IUSTI, Aix-Marseille Université, France); Mathieu Colombani (CNRS IUSTI, Aix-Marseille Université, France); Joël Marthelot (CNRS IUSTI, Aix-Marseille Université, France); Yoël Forterre (CNRS IUSTI, Aix-Marseille Université)

The Venus flytrap (Dionaea muscipula) exhibits rapid snapping in about 100 ms, which has long fascinated scientists as one of the fastest botanical movements. Its motion is mechanically initiated by stimulating the trigger hairs, and accelerated by using a snap buckling instability of its curved-shape leaves. This dynamics is well understood at the macroscopic level, but the mechanism used by the Venus flytrap to actively change its natural curvature and overcome the instability threshold still remains unclear. Here we investigate the origin of this active snapping both at the macroscopic and microscopic level. We first unveil the ‘active’ dynamics of motion by removing the buckling instability in cut and blocked traps.

We then probe the change of the tissue mechanical properties before and after triggering using in-situ nanoindentation and mold replication techniques. Our results suggest that closure is initiated by a rapid and local tuning of the tissue stiffness, thereby releasing stored elastic energy. This generic mechanism could give insight to design new rapid and programmable soft morphing structures.

Poster 23

Collective deformation modes promote fibrous self-assembly in protein-like particles

M. Mert Terzi

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Self-assembly is a crucial and ubiquitous process for biological systems, in which the building blocks spontaneously organize into larger complexes. If the building blocks fit each other, self-assembly leads to space filling aggregates. However, in the case of misfitting particles, the resulting aggregates may have limiting sizes. When the misfitting particles are deformable, elastic energy builds up during the assembly. The energy cost of elastic deformation competes with a surface tension which drives the particles into assembly. In the regime in which these two energies are comparable, particles can assemble into self-limiting structures. The relationship between characteristics of the individual particles and the resulting aggregates is not well understood. Through numerical simulations and elastic coarse-graining we show that this relationship is dominated by collective aggregate deformation modes in a broad class of soft particles. We identify two characteristics of particles predictive of the overall aggregate structure. When individual particles have soft deformation modes, these modes collectively control the size of self-limiting aggregates and lead to large-scale structures. The second characteristics is incompressibility which favors anisotropic, and hence fibrous aggregates. Finally, we discuss the implications of our results to fiber formation in protein aggregation.

Poster 24

Atomistic insights into the structure and elasticity of densified 45S5 Bioactive Glass

Youssef OULDHNINI

Youssef OULDHNINI (LS3M, Polydisciplinary Faculty of Khouribga, Sultan Moulay Slimane University, Morocco); Achraf Atila (Materials Science and Engineering, Institute I, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Germany); Said Ouaskit (Laboratoire de Physique de la Matière Condensée, Faculté des Sciences Ben M'sik, Université Hassan II de Casablanca, Maroc); Abdellatif Hasnaoui (LS3M, Polydisciplinary Faculty of Khouribga, Sultan Moulay Slimane University, Morocco).

Bioactive glasses have applications in restorative bone medicine, in view of their bioactivity, these materials are able to react with the body environment. 45S5 bioactive glass from Sodalime phosphosilicate glasses represent a model system which started to take off commercially. Regardless of their importance as bioactive materials, the structure-elastic-density relationship has not been studied before and can provide good results that help in the

development of these biomaterials. In this investigation, we used molecular dynamics simulations to study the elastic and structural properties of densified 45S5 bioactive glass through a range of densities, a systematic analysis of the elastic properties and structural changes with density was performed, correlating the change in the bioactive glass properties with the structural change to perform its mechanical properties while preserving their bioactive behavior. Our findings show that the glass structure tends to be repolymerized as indicated by an increase in the bridging oxygen atoms and the appearance of threefold coordinated oxygen atoms. Also, we observe an increase in the silicon and phosphorus coordination numbers. Moreover, we investigated the medium-range order through the calculation of Qn distribution and the network connectivity as a function of the density.

Poster 25

Fluctuations control the assembly of semiflexible filaments

Valerio Sorichetti

Valerio Sorichetti, Martin Lenz

LPTMS, Université Paris-Saclay and CNRS, France

The problem of irreversible polymerization is fundamental for its many applications to different fields, from material science to biology. In living cells, cytoskeletal filaments grow and bundle together, forming complex networks. Since the assembly and bundling of these filaments often involve energies of the order of hundreds or thousands of kT, the final structure of the network will be heavily influenced by the kinetics of these processes (Kayser et al., Soft Matter, 2012, 8, 8873). Approaches based on equilibrium physics are therefore bound to fail when studying the structural and mechanical properties of such networks, and approaches that explicitly considers the kinetics are necessary. We extend a previously developed theoretical framework (De Gennes, J. Chem. Phys., 1982, 76, 3316) to study how the average length L of a system of semiflexible filaments that anneal irreversibly via end-to-end reactions increases with time time. We find that filament assembly is controlled by the short-time transversal fluctuations, which lead to a linear growth of L with time. We perform the same calculations also for perfectly rigid rods, which have no transversal fluctuations modes, showing that in this case L increases only as the square root of time. Finally, we compare our theoretical predictions with molecular dynamics simulations of patchy particles that aggregate irreversibly into semiflexible filaments with a tunable persistence length, finding an excellent agreement with the theoretical predictions.

Poster 26

Polar patterns of gliding filaments on flat and curved lipid membranes

Alfredo Sciortino

Alfredo Sciortino (BauschLab, TUM, Germany), Alice Yu De La Trobe (BauschLab, TUM, Germany), Luksas Neumann (BauschLab, TUM, Germany), Andreas R. Bausch (BauschLab, TUM, Germany)

Collective motion of active matter is ubiquitously observed and often features the formation of complex structures composed of agents moving coherently. However, it remains extremely challenging to predict emergent patterns from the binary interaction between agents, especially as only a limited number of interaction regimes have been experimentally observed so far. Here, we introduce a variation on the high-density actin gliding assay, in which myosin motors are coupled to a flat lipid membrane and push actin filaments. Because of slippage on the fluid substrate, however, motors are unable to push the filaments against a load, resulting in an effective steric interaction between filaments, which stop upon collision and eventually align nematically, due to fluctuations of their tips. Such a binary nematic interaction rule results, at higher densities, in the emergence of collective patterns, including clusters and vortices of filaments. Despite the microscopic interaction being nematic, emergent structures are found to be polar, with filaments moving in the same direction. We find that this is due to polar biases introduced by the steric interaction. In this context, positive half-charged topological defects turn out to be a most efficient trapping and polarity sorting conformation acting as transient wedge-shaped structures which lead to highly polar coherent streams of filaments emerging from dissolving defects. We then expand the system to a different topology by coupling motors on the membrane of a giant vesicle. In this confined, spherical geometry filaments are found to form polar flocks, vortices and bands travelling around the vesicle's surface. We also study the role of passive nematic defects in shaping the polar flows by having gliding microtubules inside a passive actin nematic.

Poster 27

Electrical Fields, Cells and Their Interactions: An Overview

Övül Eski

Övül Eski (Biomedical Engineering Department, Pamukkale University, Turkey)

As it is known for a long time both intrinsic and extrinsic electrical characteristics either due to ionic gradient or exogenous potential difference significantly affect the fate of a cell. Electromagnetic effects on cells and tissues had been studied even before famous Volta and Galvani experiments. Due to the constraints that need to be established for the sake of content volume, effects of magnetic field and its applications are excluded from the extent of this work. Nowadays, the capability of manipulating cells by means of exogenous electric fields can be used in vast areas of life; for instance waste management, food industry, and medicine are possibly the main areas to mention. Throughout the last few decades different fields of life sciences from cell and tissue studies (including regenerative and proliferative applications or genetic modifications) to surgical operations even in therapeutic treatments in medicine have witnessed new techniques using these methods being commercially available. Application can be altered extensively depending on the choice of individual features of the applied field. Aside from the thermal effects, cells can be trapped, sorted, forced to proliferate, be fused or be infused by a molecule and even can be exterminated by means of apoptosis. Using AC (alternative current) or DC (direct current) voltages may be the first alternative to be decided and the amplitude and application time will be an important parameter for both cases. Using either AC voltage or DC pulses frequency will also to be determined. In the case of DC pulse which has been studied for years as in pulsed electric field (PEF) applications, parameters like pulse shape, polarity, number of pulses should be considered due to the requirements of the

application. Additionally, the structure, orientation and type of the cell including its ionic and bimolecular properties like cholesterol density on membrane or presence of a cell wall are factors that should be taken into consideration depending on the application. Tissue to be treated and of course the medium should also be considered. Although application of electrical fields to manipulate cells and its reversible or irreversible effects are known and studied for a long time there are still unknowns to discover and areas to be applied. In this study of review it is tried to be summarized including the well defined features of the phenomena and also available and possible future applications.

Poster 28

Modelling investigation of metabolic adaptation to oxidative stress

Julien Hurbain

Julien Hurbain (PhLAM, Univ. Lille), Quentin Thommen (PhLAM, Univ. Lille), François Anquez (PhLAM, Univ. Lille), Benjamin Pfeuty (PhLAM, Univ. Lille)

Living cells are continually exposed to multiple and varied sources of stress. To cope with stress-induced damages, cells are endowed with biochemical adaptation mechanisms that maintain metabolic homeostasis and promote survival. In my thesis project, we investigate the cellular adaptation response to oxidative stress produced by Reactive Oxygen Species (ROS) such as hydrogen peroxide H2O2. One important mechanisms to detoxify ROS and restore redox homeostasis is the increased production of the NADPH reducing agent, which is supported by the rerouting of metabolic flux from glycolysis to the oxidative pentose phosphate pathway (PPP). Although numerous mechanistic models of oxidative stress response have been developed (Antunes et. al. 2017, Benfeitas et. al. 2014, Salvador et. al. 2003 , Grimbs et. al. 2007, Marin-Hernandez et. al. 2011), a comprehensive and quantitative description of metabolic adaptation and remodelling during oxidative stress is lacking. Starting from a metabolomic data sets (Kuehne et. al. 2015) and an ODE model of the metabolic network, we perform a systematic parameter estimation procedure combining genetic algorithm and MCMC techniques to obtain a plausible class of models which can be thoroughly analyzed. First, dynamical response analysis highlights a biphasic time-course where metabolic imbalance is followed the adaptation response in less than a minute. Second, dose response analysis reveals that adaptation mechanism and efficiency depends on the level of stress, due to saturation of some key enzymatic reactions (ie., GPx, 6PGDH). Third, perturbation analysis emphasizes a cooperative regulation pattern where allosteric inhibition of PGI by 6PG and of GAPDH by H2O2 coordinates metabolic flux rerouting and cycling toward oxidative PPP over a broad range of stress level. These results support that autonomous, rapid and efficient adaptation to oxidative stress response can be mediated by passive and allosteric control of metabolic pathways without necessarily requiring transcriptional and post-translational signalling pathways.

Poster 29

Glassy Dynamics in Confluent Biological Tissue using Cellular potts Model

Souvik Sadhukhan

Souvik Sadhukhan (Biophysics and Soft Matter Group, TIFR Hyderabad, India);
Saroj Kumar Nandi (Reader-F, TIFR Hyderabad, India)

Hallmarks of glassy dynamics in a confluent biological tissue is important for wound healing, morphogenesis, tumour progression etc. We have developed a theoretical framework for glassiness in such systems through a combination of numerical study of cellular Potts model (CPM) and an analytical study based on random first order transition (RFOT) theory for a confluent system. In this poster, I will present our extended RFOT theory, some of the distinct glassy properties of a confluent system, and a comparison of our theoretical predictions with simulations as well as existing experimental results.

Poster 30

Visual pseudotime reconstruction of a dynamic single cell process

Lisa Bedin

Lisa Bedin, Biocomp, ENS, France
Nathalie Spassky, Cilia biology and neurogenesis, ENS, France
Auguste Genovesio, Biocomp, ENS, France

Biology is an experimental Science that heavily relies on quantitative observation. Nowadays, technologies such as high throughput sequencing, mass spectrometry or super resolution imaging, have led to an unprecedented ability to observe and quantify processes at the cellular and molecular level. However, it is important to keep in mind that observation of many systems remains totally out of reach, especially in vivo. This is the case for morphological transformations occurring during development in deep cellular tissues. In fact, as soon as the tissue of interest is deeper than a few millimeters, or as soon as the developmental process lasts more than a few days, in vivo single cell observation becomes hard if at all possible. We develop a groundbreaking approach for reconstructing a video of an in vivo single cell process from asynchronous images by computational means. More precisely, it is typically possible to obtain a lot of images of static cells undergoing the same process asynchronously by imaging tissue samples. These images follow two notable particularities. First, a cell can never be imaged at two different time steps: in fact in this context imaging a cell is a random instantaneous static view on one or a few common processes. Secondly, acquiring precise temporal annotations for cellular images is often impossible even with expert knowledge. We develop a general method for reconstructing a video from large datasets of asynchronous images without requiring manual annotations or ground-truth sequences.

Poster 31

Polymer physics approach to bacterial chromosomes

Bae-Yeun Ha

Youngkyun Jung (Supercomputing Center, Korea Institute of Science and Technology Information, Korea), Chanil Jeon and Bae-Yeun Ha (University of Waterloo, Canada)

Chromosomes in living cells are strongly confined but show a high level of spatial organization. If constructed carefully, a polymer-chromosome model will be useful for understanding the way chromosomes are spatially organized and for interpreting chromosome experiments. Here we discuss chromosome-like polymers in a crowded and confined space: (heterogeneous) ring polymers and bottle-brush polymers. We focus on clarifying the role of bimolecular crowding and confinement in organizing bacterial chromosomes, using molecular dynamics simulations. Our simulations results are consistent with the observation that crowding promotes clustering of transcription-active sites into transcription foci. Also, we find that crowding is essential for distributing the two “arms" of a ring polymer in the way observed with E. coli chromosomes. Finally, cylindrical confinement can induce helical organization of bottle-brush polymers. We discuss how our results can be used to interpret chromosome experiments. For instance, they suggest that experimental resolution has unexpected consequences on writhe measurements (e.g., narrowing of the writhe distribution and kinetic separation of opposite helical states).

Poster 32

Slimming down through frustration

Martin Lenz

Martin Lenz (CNRS, U. Paris-Saclay, ESPCI, France)
Thomas A. Witten (U. of Chicago, USA)
Pierre Ronceray (Aix-Marseille U., France)

In many disease, proteins aggregate into fibers. Why? One could think of molecular reasons, but here we try something more general. We propose that when particles with complex shapes aggregate, geometrical frustration builds up and fibers generically appear. Such a rule could be very useful in designing artificial self-assembling systems.

Friday, June 25 14h15 – 16h45
Poster session 1 : Poster 33 – 47

Poster 33

Sensing nuclear compaction: A fruitful model to characterize cell nucleus mechanics

Héctor Zamora-Carreras

Héctor Zamora-Carreras (Department of Immunology, Ophtalmology and ENT, Faculty of Medicine, Universidad Complutense de Madrid, Spain); Horacio López-Menéndez (Deparment of Physical Chemistry, Faculty of Chemical Sciences, Universidad Complutense de Madrid, Spain); Niccolò Casselli (Deparment of Physical Chemistry, Faculty of Chemical Sciences, Universidad Complutense de Madrid, Spain); Javier Redondo-Muñoz (Department of Molecular Biomedicine, Centro de Investigaciones Biológicas Margarita Salas, CSIC, Spain); Francisco Monroy ((Deparment of Physical Chemistry, Faculty of Chemical Sciences, Universidad Complutense de Madrid, Spain); Pedro Roda-Navarro (Department of Immunology, Ophtalmology and ENT, Faculty of Medicine, Universidad Complutense de Madrid, Spain)

Fruits are usually composed by a fairly rigid shell delimiting a softer core, and we can have an idea of their ripeness just by pressing. In the same way, cell nuclei possess a rigid layer (nuclear cortex), defined mainly by a fibrillary lamin network enclosing a smooth nucleoplasm composed by the chromatin and other components. In this work, we present a novel model for the characterization of cell nucleus mechanics from data obtained by optical tweezers indentation assays. There is no defined limit between the nuclear cortex and the nucleoplasm, but rather a compaction gradient is observed. To characterize this gradient, the model proposed in this work defines a compaction order parameter, Φ, in function of mechanical magnitudes estimated from experimental data through classical approaches (Hertzian and poroelastic models). Our model predicts an exponential decay with distance for the compaction order parameter, and introduces a characteristic parameter, ξ, defining that decay. We propose that the characteristic parameter ξ could be a useful tool to describe the transition between the nuclear cortex and the nucleoplasm and to obtain information about the internal organization of the cell nucleus. For this reason, this approach can be applied to study the differences in nuclear mechanics of cancer cells or cells subjected to diverse experimental conditions or treatments.

Poster 34

Information transmission by heterogenous cell populations

Hoda Akl

Hoda Akl (Laboratory of Computational Biophysics, University of Florida, US)
Andrew Goetz (Laboratory of Computational Biophysics, University of Florida, US)
Purushottam Dixit (Laboratory of Computational Biophysics, University of Florida, US)

Reliability of signal processing through biological networks is crucial for accurate translation of environmental cues and cellular decision making. Information theory provides a natural framework to quantify the amount of information that cells are able to decipher from the environment, by estimating the channel capacity of these networks, which represents the

maximum number of distinguishable input signal states that the network is able to detect. Previous results show surprisingly low channel capacities for several signaling networks, however cells are known to carry out precise decisions in several instances. To address this discrepancy we develop a theoretical framework to estimate the channel capacity wherein we consider each cell as a separate communication channel, preserving each cell's individuality. Using single cell data and a well established computational model, we estimate the channel capacity of the epidermal growth factor pathway, a central pathway in mammalian signaling. Our results indicate that the cells can decipher amongst a much larger number of input signals than previously thought. We find that explicitly accounting for extrinsic variability concludes that the channel capacity is significantly higher than previously calculated, where there was an implicit assumption that the extrinsic source of noise is inseparable from the communication channel. Our results illustrate that at the single cell level, intrinsic noise is the only inherent corruptor of signal, and that it still allows for the cells to be reliable transmitters of information.

Poster 35

Wing deployment in Drosophila melanogaster

Simon Hadjaje

Marie-Julie Dalbe (IRPHE, Aix-Marseille University, France), Ignacio Andrade-Silva (IUSTI, Aix-Marseille University, France), Raphaël Clément (IBDM, Aix-Marseille University, France), Joël Marthelot (IUSTI, Aix-Marseille University, France)

During its final transformation to morph into its adult shape, an insect deploys its wings over just a couple of minutes. The wings rapidly unfold from a wrinkled compact structure to a plane which subsequently solidifies to generate rigidity. We study the wing expansion in Drosophila melanogaster. The expansion is regulated by an increase of the internal pressure and by the injection of a viscous liquid (hemolymph) into a folded structure under hormonal control (Bursicon). We first characterize the kinematic of the deployment through macroscopic observations. Using light microscopy imaging, we were able to describe the initial origami-like folded wing and how it relates to the final veins network. We then image sections of Drosophila wings using transmitted electron microscopy (TEM) to study the morphological evolution of the cross-section of the wings at different expansion stages. We finally combined scaling analysis with experiments to build a fundamental understanding of the wing expansion dynamic.

Poster 36

Vinculin regulates collective cell behaviour by remodelling the actin cytoskeleton at cell-cell junctions

John JAMES

John James[1], Artem Fokin[1], Pascal Silberzan[2], Alexis M. Gautreau[1]* and Stephane Romero[1]*

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Collective behaviours of cells are essential for tissue homeostasis and organ morphogenesis. Tumour cells display altered collective behaviours. Vinculin is a mechanosensor of cell-matrix and cell-cell contacts. Vinculin is recruited to talin and a-catenin in response to pulling forces applied on integrin and cadherin adhesion complexes. It strengthen the link of adhesion complexes to actin filaments. Vinculin also binds to the Arp2/3 complex, which polymerizes branched actin networks and thereby exert pushing forces. The gene encoding vinculin is a tumour suppressor gene. To study its role in collective behaviours of cells, we generated vinculin knockout clones derived from the mammary epithelial MCF10A cell line. In the absence of vinculin, we observed decreased recruitment of the Arp2/3 complex at cell-cell junctions, concomitant with a decrease in cell junction stability. By interacting with the Arp2/3 complex, vinculin probably antagonises its function, since vinculin inactivation resulted in increased persistence of single cell migration and enhanced cell proliferation when cells were becoming confluent. Within a dense cell monolayer, vinculin KO cells failed to organise long contractile bundles that crossed the apical pole of several cells as well as large domains of coordinated cell migration. Finally, the differentiation of MCF10A cell in matrigel produced less spherical multicellular structures that were prone to local deformations. Together, our results suggest that the vinculin mechanosensor through its ability to recruit the Arp2/3 complex at cell-cell junctions is key to organise migration, proliferation and differentiation of cell collectives.

Video teaser :https://drive.google.com/file/d/1GEs2Ipsuvt87gYkMUEWUfEW9Z2m_WGW6/view?usp=sharing

Poster 37

Influence of external forces on actin-dependent T cell protrusions during immune synapse formation

Olga Markova

Andrés Ernesto Zucchetti[1] ; Noémie Paillon[1]; Olga Markova [2]; Stéphanie Dogniaux [1]; Claire Hivroz[1]; Julien Husson[2]

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During immunological synapse formation, T cells emit an actin-rich protrusion that experiences forces. Here, we quantitatively characterised the effects of external forces in the dynamic of the protrusion. We found that the formation of the protrusion is set by an

intracellular constant time and is mediated by the Arp2/3 complex and that its dynamic is sensitive to external forces. Our study provides key insights that help to better understand the mechanism involved in the formation of the actin protrusion emitted by the T cell.

Poster 38

Imaging membrane contact sites in living cells with FRET-FLIM

Mouna Abdesselem

Mouna Abdesselem[1], Dounia Zamiati[1], Sophie Dupré-Crochet[1], Oliver Nüsse[1], Francesca Giordano[2], Marie Erard[1]

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Membrane contact sites (MCS) are regions of close proximity (5-20 nm) between at least two cellular compartments. Recent studies established that localized contacts of the ER with other membranes, such as the plasma membrane or the mitochondrial outer-membrane, play a pivotal role in organelle trafficking as well as in cell calcium and lipid homeostasis. To date the only method that allows the unequivocal observation of membrane contact sites is electron microscopy. Photonic microscopy methods mostly infer contact from colocalization with a spatial resolution above 200 nm or irreversibly block contact configurations by covalent protein-protein interaction.
We developed a novel FRET-FLIM based method to address the unmet need for a direct space- and time-resolved tracking of MCS.
We fused fluorescent proteins which are optimized for FRET to members of the VAP, ESyt and ORP protein families, which are known to form MCS. A combination of FRET efficiency measurements helped us demonstrate protein-protein interactions in living cells. Moreover, our preliminary data show that we can detect contacts between ER-membrane proteins and their partner or target on an apposed membrane. Altogether our work lays the foundations of novel methodologies suitable to track in space and time membrane proximity in order to unravel local signaling microdomains at MSC.

Poster 39

Theoretical modelling of competitive microbial range expansion with heterogeneous mechanical interactions

Erik Maikranz

Erik Maikranz (Santen Lab, Saarland University, Germany) and Ludger Santen (Santen Lab, Saarland University, Germany)

Microbial range expansion experiments provide insight into the complex link between dynamic structure, pattern formation and evolutionary dynamics of growing populations. In this work, we develop a theoretical model in order to investigate the interplay of growth statistics and mechanical interactions which are implemented as division driven pushing and

swapping of cells. For the case of the competitive growth of a strongly and a weakly interacting strain we investigate the influence of different mean division times, as well as different mechanical interactions on the development of the colony. Our results show that the susceptibility to cell division induced pushing has a much stronger influence on the structure of the colony than cell sorting towards the colony's perimeter. Motivated by microbial range expansion experiments of Neisseria gonorrhoeae bacteria, we also consider the influence of mutating cells on the structure of the colony. We show that the outgrowth of the three different strains is strongly influenced by the relative strengths of their mechanical interaction. The experimentally observed patterns are reproduced for mechanical interactions of the mutants, which range between those of the strongly and weakly interacting strain.

Poster 40

Flickering phenomena in red blood cell membranes: differences between species

Natalia Hernando Ospina

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The red blood cell (RBC) has been used as a standard cell for the study of membrane physics due to the presence of a lipid membrane and the absence of a nucleus and organelles. These cells exhibit mechanical properties, such as biconcave shapes, motility, adhesion and deformation, and transmembrane transport. However, one of the interesting properties of the membrane is the flickering phenomena. It is known that they are related to its cellular metabolism. In this study we will investigate cell membrane dynamics by comparing human and mouse red blood cells. There are several methods to measure membrane dynamics and mechanical properties of cells. In this work, we have used flicker spectroscopy, a non-intrusive method focused on the analysis of phase-contrast frames. It is based on the observation of cell membrane movement using optical light video-microscopy. The location of the cell membrane is obtained from each video-frame through a contour tracking algorithm, giving the temporal evolution of cells projected shape. From these time-series it is possible to calculate a number of both static and dynamic cellular properties. Two groups of red blood cells are compared: healthy human red blood cells (hRBC) and healthy mouse red blood cells (mRBC). The analysis of static fluctuation spectra yields of hRBCs shows lower fluctuation amplitudes than mRBCs. The volatility study shows a higher biological activity of the mRBC. Therefore, it can be assumed that the cell membrane of hRBC is stiffer and more viscous than that of mRBC. This is due to a softening of the system which is related to the properties of the system itself.

Poster 41

Label-free imaging techniques for monitoring spinal cord injury: from pathophysiology to therapeutic strategies in mice

Clara Manesco

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Spinal cord injuries (SCI) affect between 2.5 and 4 million patients worldwide yielding major handicaps and inducing high economical costs. A scar, called glial scar and composed of two main cellular populations i.e. astrocytes and microglia, inhibits axonal regeneration by forming a physical and chemical barrier. Currently, there is no curative treatment on any symptoms associated with SCI. In this context, with the objective to investigate the mechanisms underlying absence of spontaneous axonal regeneration following SCI, we employ a multimodal label-free imaging approach to monitor glial scar in a mice SCI model.
Method: To determine the relevant structural signature and the nanobiomechanical behavior of healthy and injured spinal cord tissue, we combine the non-linear, multiphoton microscopy (MPM) technique with force measurements via atomic force microscopy (AFM). The glial scar at different key post lesion time-points is investigated with these two techniques to monitor structural and elasticity (Young modulus) changes of the tissue.
Results: 2-photon excited fluorescence (2PEF) and second harmonic generation (SHG) signals of excised mice SC injured tissues were recorded in MPM at 72h,1 week and 6 weeks post-lesion. The MPM images revealed the apparition of a strong SHG signal at 1week post injury, due to the formation of fibrillar collagen fibers (collagen type I) by the injury site in the glial scar. At 6 weeks post-injury, the SHG signal is more intense and a higher number of fibers are detected in average. We further assessed the preferential orientation of the collagen bundles performing polarization dependent measurements of the SHG signal. The AFM based force spectroscopy measurements have been performed at the same post-lesion time-points to map the elastic properties of the healthy (grey and white matters) and injured (lesion) parts in the spinal cord tissue. The results suggested an increase of the lesion area stiffness over time that could be correlated with the apparition of fibrillar collagen observed in MPM, indicating the presence of a fibrotic process seven days after injury, that develops in time. As tissue stiffness is a regulator of neuronal growth, such kind of measurements might help to understand why adult mammalian axons do not regenerate after an injury.
Our next step is to investigate the effect of a treatment (pharmacological transient depletion of microglia/macrophage in mice that underwent SCI) on the structure and mechanical properties of the lesion site at 1 week and 6 weeks post injury.

Poster 42

Using micro patterns to standardize cells mechanics measurements by AFM, application to cancer cells

Liboz Maxime

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The mechanical properties of living cells reflect their physiological and pathological states. In particular, cancer cells are generally softer than their healthy counterparts and tumors harder than normal tissue. These mechanical properties, determined largely by the cytoskeleton and the plasma membrane, govern the processes of migration, division or cell spreading. Nevertheless, studying cellular mechanics and being able to use it as a diagnostic tool is a challenge because of the complexity of the structure and organization of the cells. Therefore, we use adhesive micro patterns to measure in a standardized way the mechanical properties of the cells by AFM in relation to their metastatic potential. With the micro patterns, all the cells considered then have the same geometry, the same architecture and the same microenvironment, thus reducing inter and intra-cellular variability. We culture cancer cells on micropatterns and use an AFM mode that allows us to obtain their elasticity and morphology from indentation curves with a high resolution, typically several hundreds of measurements per cell. We then analyze these data to extract the averaged cell morphology and elasticity map and compare different populations of cells representing various stages of cancer progression.

Poster 43

Understanding fiber formation through renormalization

Lara Koehler

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The self-assembly of shapes that do not fit exactly together can lead to geometrical frustration, and previous numerical simulations have shown that this frustration tend to favor slender self-assembled structures. However, the relationship between the microscopic shape, and the size, structure and dimensionality of the emerging aggregate have yet to be understood.
To elucidate this relationship, we propose to apply real space renormalization to an on-lattice aggregation model. This will enable us to determine the relevant features of the interaction between complex particles, thus providing us with a general classification of local interactions resulting in fibrous, crystalline, or finite-size aggregates, respectively.
The emergence of these distinct morphologies may be relevant to the aggregation of misfolded proteins into pathological fibers, in neurodegenerative and other diseases.

Poster 44

Non-linear wave propagation emerged in active poroelastic media

Clara Luque Rioja

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Active stresses play a crucial role in many processes in living cells. The spatial distribution of active-clusters allows the existence of transport process observed as large-scale correlated motion. This sort of phenomenology has been suggested to play a role into the nucleoplasm. Here, we propose a theoretical active-poroelastic framework with the aim to mimic the chromatin as an active-elastic solid coupled to a permeated fluid. We incorporate the active stress into a two-phase model that accounts for the spatiotemporal dynamics of chromatin and nucleoplasm. This system is subject to both passive thermal fluctuations and active scalar events linked to condensation and decondensation, named spikes. Because of the combination between the permeation length and the distance between spikes, it appears two well-defined regimes as continuous or discontinuous propagation. In this work, we simulate the coupled set of equations showing the existence of emergent processes as wave-propagation. This simple model allows to capture mechano-chemical coupling effects at long distance range. The exploration of the different regimes described by the model will help to refine the formulation of hypothetical associated conditions to satisfy distant interactions.

Poster 45

Mechanical characterization with AFM of murine oocytes to predict their fitness

Rose Bulteau

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Oocyte production during meiosis in human females is essential for sexual reproduction. However, this process is error-prone and generates a basal rate of bad quality oocytes, impacting their developmental potential and having deleterious consequences for fertility and offspring development. It has been shown that aberrant oocyte stiffness, a common defect in murine and human oocytes, alters the developmental capacity of the oocyte. Thus, mechanical properties could be used to predict developmental potential of oocyte and thus guide their selection for assisted reproductive technologies. The mechanical properties of such big cells have been studied in our labs using the micropipette aspiration method. However, this method has a low yield and is not adapted to follow oocyte development. AFM (Atomic Force Microscopy) has a much higher throughput (less than a minute per cell) and provides robust

measurement of cell elasticity and cortical tension (Chaigne et al., 2013, 2015, 2016; Yanez & Camarillo, 2017).
Hence, we have designed a protocol to measure with AFM the evolution of the mechanical properties of the murine oocyte during its development. This was challenging, since oocytes are big non-adherent cells surrounded by an extracellular matrix called the zona pellucida. Using a Sneddon model combined with a linear model, we managed to extract elasticity and cortical tension values from force indentation for oocytes at different stages of development. Our results have shown that elasticity and cortical tension decrease concomitant to oocyte development. They confirm our previous micropipette measurements and indicate that we can use this technique in a high throughput manner to classify oocytes according to their cortical tension and set threshold values of cortical tension correlating with a good developmental potential.
The next step is to measure the mechanical parameters of mouse oocytes engineered to be extra-soft and stiff. Finally, our long term goal is to adapt our measurement on human oocyte. The latest will provide information about oocyte development applicable for medical use to select human oocytes in In vitro Fertilization clinics where up to now the selection consists of subjective morphological assessments.

Poster 46

Atomic Force Microscopy-probing of phase-separated membrane nanotubes

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Reorganization of the actomyosin cytoskeleton allows plasma membrane remodeling in order to achieve crucial cell processes like intracellular traffic or endocytosis. Such remodeling occurs on a particular type of membrane structures, hereby called membrane nanotubes.
The underlying physical mechanisms of nanotubes remodeling are unclear. Experiments using controlled biomimetic systems have shown that branched actin network produces enough force to form membrane nanotubes from homogeneous liposomes (Simon et al., 2019, Nature Physics). On the one hand, membrane nanotubes rupture at the boundary between two lipid domains (Roux et al., 2005, EMBO journal). On the other hand, actin polymerization on homogenous liposomes affects membrane phase separation (Liu et al., 2006, Biophysical journal). This suggests that actin polymerization could induce phase separation on membrane nanotubes leading to their scission.
Morphology and mechanical properties of phase separated membrane nanotube from ternary lipid mixtures were assessed using Atomic Force Microscopy and the theoretical model from Lamour et al., 2020. We highlighted the differences between the two membrane domains, and show that our model still holds for these nanotubes. This work paves the way for new experiments to understand the effect of an actin network on membrane nanotubes.

Poster 47

Measurement of tumbling force and energy during swarming-like imposed by optical tweezers

Horacio Lopez-Menendez

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The Bacteria Proteus mirabilis is frequently associated with infections of the urinary tract. It's swarming capability has strong implications in the development of the pathological conditions. In order to gain a deep understanding about its mechanics we directly measure the tumbling stochastic forces generated by the single bacteria and collective clusters by using an optical trap via the photon momentum method. We characterized the single bacteria and a confined bacteria cluster under different traps powers and incubations protocols that promote a clear difference in the degree of swimming activity. The obtained forces, energies and angular diffusions measures will allow to improve our understanding of the evolution of the pathological stage and to validate theoretical models of swarming under confinement.