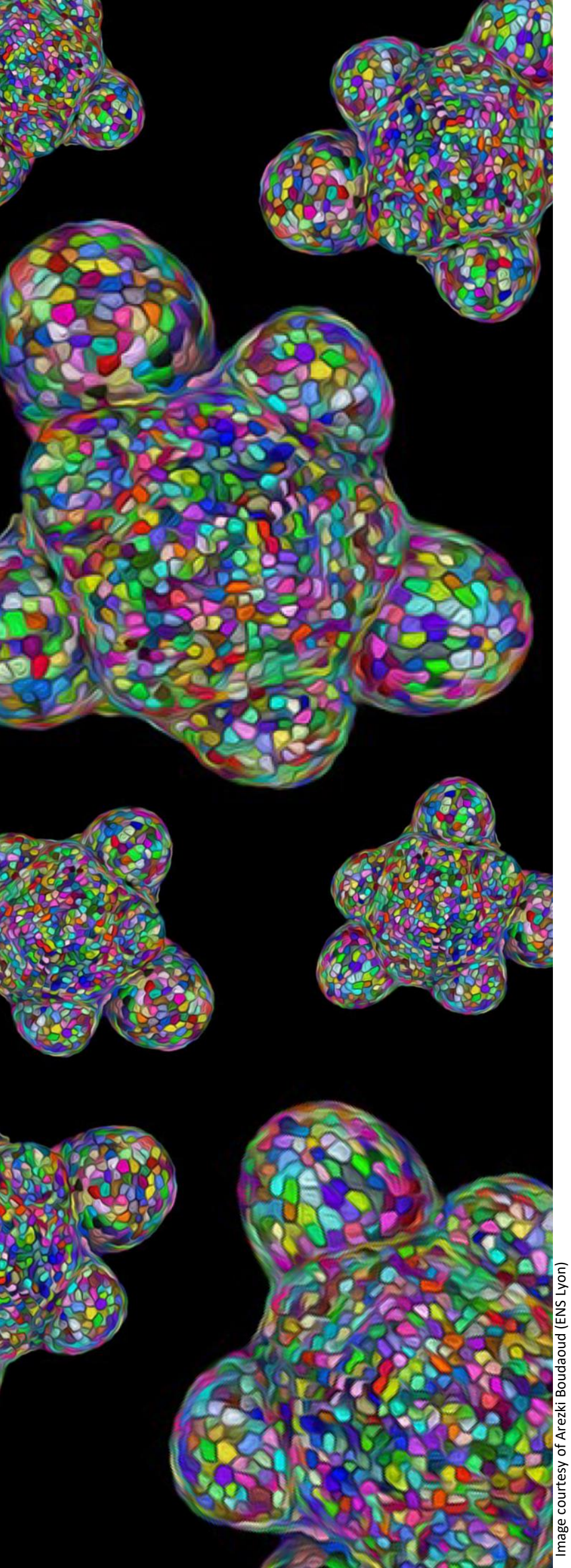


Image courtesy of Arezki Boudaoud (ENS Lyon)

4th International Conference on

Physics & Biological Systems 2018

October 22-24 2018

CNRS campus, Gif-sur-Yvette, France

Invited speakers:

Arezki Boudaoud (ENS Lyon, France)
Giovanni Cappello (U. Grenoble Alpes, France)
Guillaume Charras (UCL, UK)
Sarah Cuylen-Häring (EMBL, Germany)
Ulrike Endesfelder (MPI for Terrestrial Microbiology, Germany)
Benjamin Engel (MPI of Biochemistry, Germany)
Valérie Gabelica (U. Bordeaux, France)
Gary Karpen (UC Berkeley, USA)
Laëtitia Kurzawa (CEA Grenoble, France)
Amélie Leforestier (Université Paris-Sud, France)
Laura Marcu (UC Davis, USA)
Boris Martinac (University of New South Wales, Australia)
Davide Marenduzzo (University of Edinburgh, UK)
Elliot Meyerowitz (Caltech, USA)
Thomas Perkins (University of Colorado, USA)
Rob Phillips (Caltech, USA)
Catherine Picart (U. Grenoble, France)
Rudi Podgornik (UCAS, China)
Yitzhak Tor (UC San Diego, USA)
Shelly Tzlil (Technion, Israel)
Tomaso Zambelli (ETH Zurich, Switzerland)

Student & Poster Sessions

Program & registration: http://lptms.u-psud.fr/physbio2018/

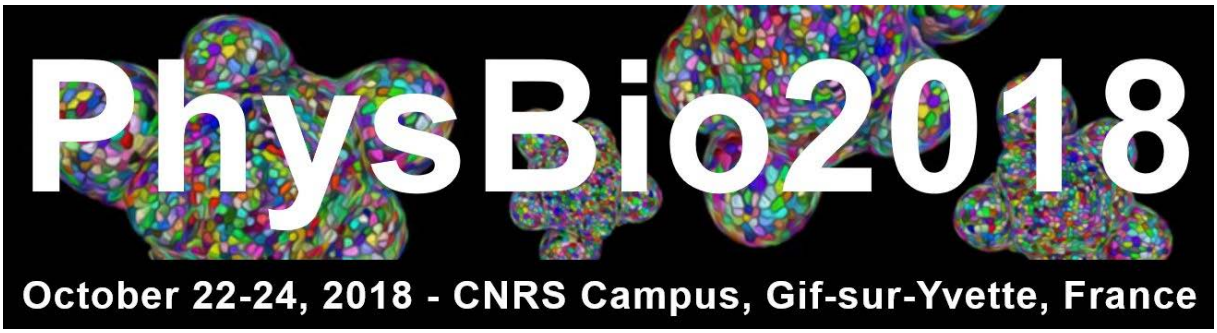
Note: free registration for students!

Sponsors:

HAMAMATSU PHOTON IS OUR BUSINESS
JPK Instruments — we have joined Bruker — BRUKER
PALM Laboratoire d'Excellence Physique : Atomes Lumière Matière
Investissements d'Avenir
cnrs
Nikon
abbelight Now, we see
SPS Sciences des Plantes de Saclay
I2BC
université Paris-Saclay Département Sciences de la Vie
OPTICS

Academic Fundings

Sponsors



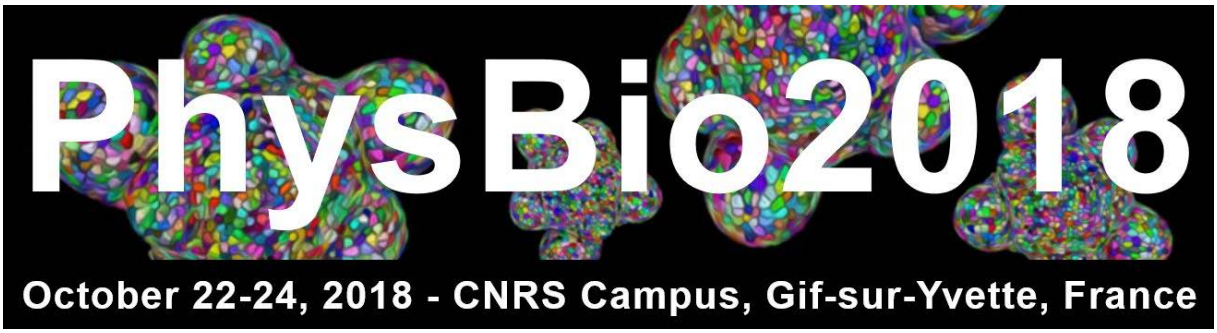
4th International Conference on

Physics & Biological Systems 2018

October, 22-24, 2018, CNRS campus, Gif-sur-Yvette, France

CONFERENCE BOOK

http://lptms.u-psud.fr/physbio2018/



Organizing committee

Chair: Éric Raspaud (LPS, U. Paris-Sud)

Mathilde Badoual (IMNC, U. Paris-Sud)

Christophe Le Clainche (I2BC, CNRS Gif-sur-Yvette)

Martin Lenz (LPTMS, U. Paris-Sud)

Willy Supatto (LOB, École Polytechnique)

Scientific committee

Darine Abi Haidar (IMNC, U. Paris-Sud)

Cécile Appert-Roland (LPT, U. Paris-Sud)

Jean-Marie Frachisse (I2BC, CNRS Gif-sur-Yvette)

Thomas Gustavsson (IRAMIS, CEA)

Julien Husson (LadHyX, École Polytechnique)

Francoise Livolant (LPS, U. Paris-Sud)

Stéphanie Mangenot (Physico-Chimie Curie, Institut Curie)

Christian Marliere (ISMO, U. Paris-Sud)

Olivier Martin (Génétique Végétale, Université Paris-Sud)

Fabienne Merola (LCP, U. Paris-Sud)

Daan Noordermeer (I2BC, CNRS Gif-sur-Yvette)

Student committee

Léo Adenis (IMNC, U. Paris-Sud)

Luca Barberi (LPTMS, U. Paris-Sud)

Yannick Guerringue (I2BC, CNRS Gif-sur-Yvette)

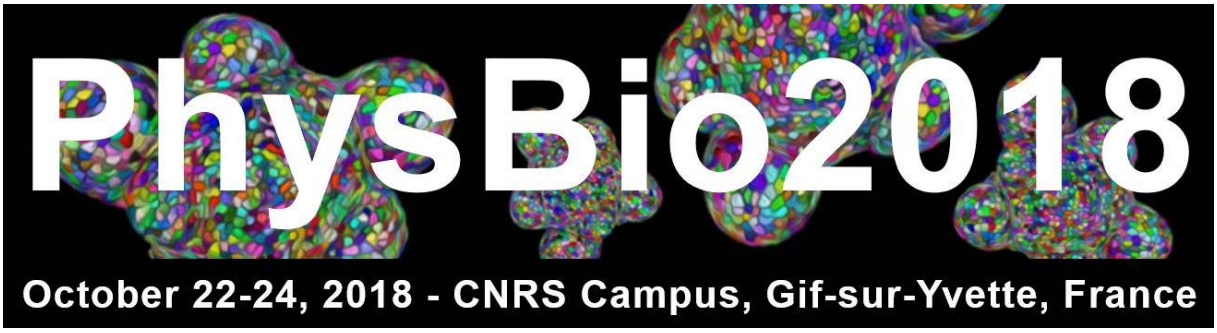
Laura Sabatier (LPS, U. Paris-Sud)

Margaux Schmeltz (LOB, École Polytechnique)

Alexandra Zak (LadHyX, École Polytechnique)

Administrative support

Claudine Le Vaou (LPTMS, U. Paris-Sud)



	Monday, October 22	Tuesday, October 23	Wednesday, October 24
08:30-08:50	*welcome coffee*		
08:50 - 09:00	opening		
09:00 - 09:45	C. Picart	U. Endesfelder	
09:45 - 10:30	G. Karpen	T. Perkins	Y. Tor
10:30 - 11:00	*coffee break*		
11:00 - 11:45	G. Charras	V. Gabelica	A. Leforestier
11:45 - 12:30	Student sessions		
	N. Kallweit	G. Jacucci	P. Durand-Smet
	B. Bruininks	M. Bailey	V. Laplaud
	M. Valet	S.K. Nomidis	S. Song
12:30-14:00	*Lunch*		
14:00 - 14:45	E. Meyerowitz	A. Boudaoud	B. Martinac
14:45 - 15:30	T. Zambelli	R. Podgornik	B. Engel
15:30 - 16:00	*coffee break*		
16:00 - 16:45	Poster session		R. Phillips
16:45 - 17:30	L. Kurzawa	D. Marenduzzo	G. Cappello
17:30 - 18:15	L. Marcu	S. Cuylen-Häring	closing
19:00 - 21:00		*Conference Dinner*	

Monday, October 22 (Morning)

Session chair: Rudi Podgornik(Univ. of Chinese Academy of Sciences, Beijing)

8:30 - 8:50 *Welcome Coffee*

8:50 - 9:00 Opening remarks

9:00 - 9:45 Catherine Picart
Grenoble Institute of Technology, University Grenoble Alpes, France
"Biomimetic membranes and layer-by-layer as model systems to study cellular processes"

9:45 - 10:30 Gary Karpen
Dept of Molecular and Cell Biology, Lawrence Berkeley Ntl Lab, Berkeley, USA
"Is Chromatin Just a Phase?"

10:30 - 11:00 *Coffee break*

11:00 - 11:45 Guillaume Charras
London Centre for Nanotechnology & Department of Cell and Developmental Biology, University College London, United Kingdom
"Blistering and buckling in epithelial monolayers"

11:45 - 12:30 Student Session 1
Session Chair: Alexandra Zak (LadHyX, École Polytechnique, France)

11:45 – 12:00 Nicole Kallweit
Laser Zentrum Hannover e.V., Hannover, Germany
"Optoacoustic effect as the basic mechanism for intra-cochlear optical stimulation"

12:00 – 12:15 Bart M. H. Bruininks
Groningen Biomolecular Sciences and Biotechnology Institute and Zernike Institute for Advanced Materials, University of Groningen, The Netherlands
"Lipoplex mediated gene therapy at molecular detail"

12:15 – 12:30 Manon Valet
Laboratoire Jean Perrin, Sorbonne Université, Paris, France
"Probing Molecular Transport in Printed Biomimetic Tissues"

12:30 - 14:00 *Lunch*

Monday, October 22 (Afternoon)

Session chair: Julien Husson (LadHyX, École Polytechnique, France)

14:00 - 14:45 Elliot Meyerowitz
Division of Biology and Biological engineering, California Institute of Technology, Pasadena, USA
"Control of Plant Development by Mechanical Signaling"

14:45 - 15:30 Tomaso Zambelli
Laboratory of Biosensors and Bioelectronics, ETH Zurich, Switzerland
"***Force-controlled manipulation of single cells in vitro"***

15:30 - 16:00 *Coffee break*

16:00 - 16:45 **Poster session**

16:45 - 17:30 Laetitia Kurzawa
CytoMorpho Lab, Biosciences and Biotechnology Institute of Grenoble, Université Grenoble-Alpes, CEA-CNRS-INRA, Grenoble, France
"Stress fibers and the cell cortex form a continuous contractile network"

17:30 - 18:15 Laura Marcu
Biomedical Engineering Department, University of California, Davis, USA
"Fluorescence lifetime techniques for surgical imaging, guidance and augmented reality"

Tuesday, October 23 (Morning)

Session chair: Aurélie Bertin (CNRS, Institut Curie Paris, France)

9:00 - 9:45 Ulrike Endesfelder
Systems & synthetic microbiology, Max Plank Institute of Terrestrial Microbiology, Marburg, Germany
"Exploring cell-biology on a molecular level: New methods for live-cell and quantitative localization microscopy"

9:45 - 10:30 Thomas Perkins
JILA, National Institute of Standards and Technology and the University of Colorado, Dpts of Physics and of Molecular,Cellular,and Developmental Biology, University of Colorado, Boulder, USA
"Watching individual proteins unfold and refold by 1-µs resolution force spectroscopy"

10:30 - 11:00 *Coffee break*

11:00 - 11:45 Valérie Gabelica
Laboratoire Acides Nucléiques : Régulations Naturelle et Artificielle, Université de Bordeaux, Pessac, France
"Isolated Nucleic Acids: Mass Spectrometry, Ion Mobility Spectrometry, and Ion Spectroscopy"

11:45 - 12:30 Student Session 2
Session Chair: Luca Barberi (LPTMS, CNRS, Univ. Paris-Sud, Paris-Saclay, France)

11:45 – 12:00 Gianni Jacucci
Department of Chemistry, University of Cambridge, United Kingdom
"The Cyphochilus beetle as an inspiration for sustainable white materials"

12:00 – 12:15 Michelle Bailey
School of Physics, University of Exeter, Exeter, UK
"*Brillouin microscopy to probe the micromechanics of tissue phantoms"*

12:15 – 12:30 Stefanos K. Nomidis
Institute for Theoretical Physics, Leuven & Flemish Institute for Technological Research, Mol, Belgium
"***The effect of twist-bend coupling on DNA mechanics"***

12:30 - 14:00 *Lunch*

Tuesday, October 23 (Afternoon)

Session chair: Cécile Appert-Roland (CNRS, LPT Univ. Paris Sud, France)

14:00 - 14:45 Arezki Boudaoud
Reproduction et Développement des Plantes, Université & ENS Lyon, France
"Spatial and temporal variations in cell hydrostatic pressure during plant development"

14:45 - 15:30 Rudi Podgornik
School of Physical Sciences and Kavli Institute for Theoretical Sciences, University of Chinese Academy of Sciences, Beijing, China
"***Charge regulation of complex (bio)colloids"***

15:30 - 16:00 *Coffee break*

16:00 - 16:45 **Poster session**

16:45 - 17:30 *Davide Marenduzzo*
School of Physics and Astronomy, University of Edinburgh, UK
"Epigenetic dynamics on chromatin in 3D"

17:30 - 18:15 Sarah Cuylen-Häring
Cell Biology and Biophysics Unit, EMBL, Heidelberg, Germany
"***Regulation of chromosome mechanics by a surfactant-like protein"***

19:00 - 21:00 *Conference Dinner*

Wednesday, October 24 (Morning)

Session chair: Olivier Martin (INRA, Génétique Quantitative et Evolution, Univ. Paris Saclay, France)

9:45 - 10:30 Yitzhak Tor
Department of Chemistry & Biochemistry, University of California, San Diego, USA
"***Isomorphic and Isofunctional Fluorescent Nucleosides, Nucleotides and Oligonucleotides"***

10:30 - 11:00 *Coffee break*

11:00 - 11:45 Amélie Leforestier
Laboratoire de Physique des Solides, Université Paris-Sud & Paris-Saclay, France
"***Exploring the variability of nucleosome conformation in vitro and in situ using cryoEM of vitreous sections"***

11:45 - 12:30 Student Session 3
Session Chair: Yannick Guerringue (CNRS, I2BC, Univ. Paris-Saclay, France)

11:45 – 12:00 Pauline Durand-Smet
Division of Biology, CalTech, Pasadena, USA & The Sainsbury Laboratory, University of Cambridge, United Kingdom
"Shape and cytoskeleton organization in isolated plant cells"

12:00 – 12:15 Valentin Laplaud
Physique et Mécanique des Milieux Hétérogènes, ESPCI Paris & Institut Curie, PSL Research University, Paris, France
"***Direct measure of thickness and dynamic of the cell cortex"***

12:15 – 12:30 Solène Song
Laboratoire Matière et Systèmes Complexes, Université Diderot & Institut Jacques Monod, Université de Jussieu, Paris, France
"Mechanical constraints in the morphogenesis of the gastrovascular system of the jellyfish Aurelia aurita"

12:30 - 14:00 *Lunch*

Wednesday, October 24 (Afternoon)

Session chair: Jean-Marie Frachisse (CNRS, I2BC, Univ. Paris-Saclay, France)

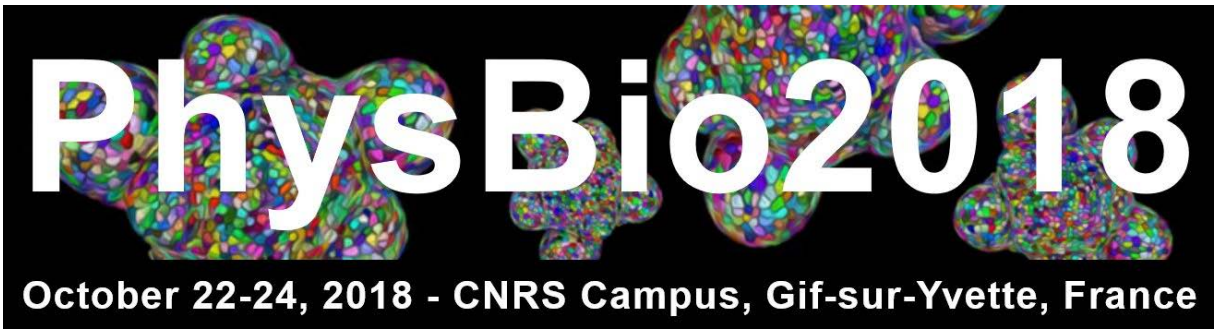
14:00 - 14:45 Boris Martinac
Victor Chang Cardiac Research Institute & St Vincent's Clinical School, Faculty of Medicine, University of New South Wales, Darlinghurst, Australia
"Tuning mechanosensing at the membrane interface by assymmetry of transbilayer pressure profile"

14:45 - 15:30 Benjamin Engel
Dpt of Molecular Structural Biology, Max Plank Institute of Biochemistry, Martinsried, Germany
"***Exploring the molecular landscape of Chlamydomonas with in situ cryo-electron tomography"***

15:30 - 16:00 *Coffee break*

16:00 - 16:45 Rob Phillips
Depts of Physics & of Biology and Biological Engineering, California Institute of Technology, Pasadena, USA
"The Two-State World View as Biology's Greatest Model"

16:45 - 17:30 Giovanni Cappello
Laboratoire Interdisciplinaire de Physique, Université Grenoble Alpes, France
"***Is Extracellular Matrix a pressure sensor?"***



SPEAKER ABSTRACTS

MONDAY 09:00

Biomimetic membranes and layer-by-layer as model systems to study cellular processes

Catherine PICART

Grenoble Institute of Technology, University Grenoble Alpes, France

Understanding how proteins such as growth factors or cytosolic proteins interact with the cellular membranes is of prime importance in order to optimize the cellular responses in cell therapies, in view of regenerative medicine or cancer therapeutics. Biomimetic model systems are an interesting tools since they enable biophysical studies in simplified and well-defined micro-environments. In this presentation, I will present how it is possible to study protein interactions with lipid vesicles of controlled size and supported lipid bilayers containing specific lipids of physiological importance and to get quantitative information about protein/lipid binding [1-3]. In a different context, I will show how layer-by-layer films made of polyelectrolytes can be used to study the interactions between proteins of the growth factor family and cellular receptors [4-6], which are specifically interacting with the growth factors and triggering internal biochemical signaling inside the cell. Engineered materials and surfaces provide a new way to study so far hidden biological phenomena.

[1] Carvalho K, Ramos L, Roy C, Picart C. Biophys J. 2008;95:4348-60.
[2] Maniti O, Carvalho K, Picart C. Biochimie. 2013;95:3-11.
[3] Lubart Q, Vitet H, Dalonneau F, Le Roy A, Kowalski M, Lourdin M, Ebel C, Weidenhaupt M, Picart C. Biophys J. 2018;114:98-112.
[4] Crouzier T, Fourel L, Boudou T, Albiges-Rizo C, Picart C. Adv Mater. 2011;23:H111-8.
[5] Gilde F, Guillot R, Pignot-Paintrand I, Okada T, Fitzpatrick V, Boudou T, Albiges-Rizo C, Picart. C. Acta Biomater. 2016;46:55-67.
[6] Liu XQ, Fourel L, Dalonneau F, Sadir R, Leal S, Lortat-Jacob H, Weidenhaupt M, Albiges-Rizo C, Picart C.. Biomaterials. 2017;127:61-74.

MONDAY 09:45

Is Chromatin Just a Phase?

Amy Strom, Serafin Colmenares, Shelby Wilson, Collin Hickmann, and Gary H. Karpen

Dept of Molecular and Cell Biology, UC Berkeley, Lawrence Berkeley National Lab, Berkeley, USA

Recent work has raised awareness among cell biologists about how biophysical phenomena such as phase separation can arise from networks of molecular interactions within cells. Phase separation can account for 'self-assembly' of functional components that are compartmentalized into bodies without constraining membranes, such as nucleoli, similar to the way mixtures of oil and water ultimately separate into distinct pools. Importantly, these phase systems display 'emergent properties' observed in vivo, e.g., liquid droplet behavior, anomalous diffusion and selective permeability, that likely play important roles in cellular organization and functions.

The possibility that biophysical properties, in particular liquid-liquid phase separation (LLPS), are involved in formation and function of chromatin domains is exciting, because it provides a novel and satisfying mechanism to explain previously enigmatic observations about nuclear structure and function. In particular, LLPS can readily account for formation of 3D chromatin domains and regulation of genome organization. We previously demonstrated that formation of one important chromatin domain, called heterochromatin, depends on phase separation (Strom et al., Nature 2017). I will describe the in vitro and in vivo evidence that supports this conclusion, discuss progress to date on elucidating the critical components responsible for LLPS of heterochromatin, and speculate about how phase separation and associated emergent properties could dramatically impact our understanding of genome organization, dynamics and functions.

MONDAY 11:00

Blistering and buckling in epithelial monolayers

Guillaume Charras[1,2]

[1] *London Centre for Nanotechnology, University College London, UK*
[2]*Department of Cell and Developmental Biology, University College London, UK*

Epithelia are planar tissues, separating the internal environment from the external environment in many organs. Epithelia are subjected to mechanical perturbations that vary greatly in magnitude and timescale during development, normal physiological function and regeneration. The resulting tissue deformations can have a profound impact on epithelial cell biology. Indeed, a reduction in the area of an epithelium attached to a flexible substrate triggers cell cycle arrest, cell extrusion and cell differentiation. However, the relationship between tissue shape, area and mechanical state remains poorly understood. Here, using suspended monolayers, we show that epithelial tissues respond to the rapid application of in-plane compressive strains by buckling followed by flattening over the course of two minutes. Our research shows that resting tension provides epithelia with a mechanism to buffer area changes during physiological function in organs, while the generation of permanent folds may play a role in developmental morphogenesis.

Another major epithelial function is the directed absorption and excretion of nutrients, water, and ions in a process known as vectorial transport. When cultured on impermeable substrates, vectorial transport generates multicellular blisters. We show that blisters arise through the accumulation of fluid into progressively larger dynamic fluid pockets trapped between the cells and the impermeable substrate leading to sub-cellular, cellular, and multi-cellular blisters. By examining the evolution of the average blister size, we show that dome growth belongs to a common class of coarsening phenomena known as Ostwald ripening that underlies the evolution of droplet size in emulsions.

MONDAY 11:45

Optoacoustic effect as the basic mechanism for intra-cochlear optical stimulation

N. Kallweit[1,5], P. Baumhoff[2], A. Krueger[1,5], D. Heinemann[1,5], A. Kral[2,5], L. Overmeyer[1,3], A. Heisterkamp[1,4,5], H. Maier[2,5], T. Ripken[1,5]

[1]Laser Zentrum Hannover e.V., Hollerithallee 8, 30419 Hannover, Germany;
[2]Institute of Audioneurotechnology and Dept. of Experimental Otology, Hannover Medical School, Feodor-Lynen-Str. 35, 30625 Hannover, Germany
[3]Institute of Transport and Automation Technology, Leibniz Universität Hannover, An der Universität 2, 30823 Garbsen
[4]Institute of Quantum Optics, Leibniz Universität Hannover, Welfengarten 1, 30167 Hannover, Germany;
[5]Cluster of Excellence „Hearing4all", Germany

Laser stimulation of the cochlea is discussed as a potential treatment for sensorineural hearing loss in recent years. It is contended whether the mechanism of optical stimulation is based on direct neuronal stimulation or on the optoacoustic effect. In previous studies, auditory responses due to laser light could only be detected in hearing animals or animals with residual hearing. In this study, *in vivo* experiments on guinea pigs as well as pressure and temperature measurements inside a model system were performed to analyze the stimulation mechanism, which is important for future applications. Results showed evident similarities between laser induced pressure amplitudes in the model system and *in vivo* measured compound action potentials (CAPs). The signal amplitude depends on the temporal characteristics of the laser pulses. These findings of the *in vivo*, temperature as well as pressure measurements confirm the hypothesis of optoacoustics as the underlying mechanism for optical intra-cochlear stimulation.

MONDAY 12:00

Lipoplex mediated gene therapy at molecular detail

Bart M. H. Bruininks, Paulo Cesar Telles de Souza and Siewert-Jan Marrink*

Groningen Biomolecular Sciences and Biotechnology Institute and Zernike Institute for Advanced Materials, University of Groningen, Nijenborgh 7, 9747 AG Groningen, The Netherlands

*Correspondence: s.j.marrink@rug.nl

The use on non-viral vectors for in vivo gene therapy could drastically increase safety, whilst reducing the cost of preparing the vectors. However, the transfection rate of non-viral vectors are low compared to their viral counterpart. A promising approach to non-viral vectors makes use of DNA/cationic liposome complexes to deliver its genetic material (lipoplexes). For such lipoplexes it is of utmost importance to escape the endosome before their genetic material gets degraded in the lysosome. Even though we know that some of these vectors perform better in this aspect than others, the details on how genetic material escapes the lipoplex and endosome are poorly understood. In this research we show how to build coarse grain molecular dynamics models for lipoplexes using the Martini force field, and use these models to perform fusion experiments at molecular detail. Our fusion experiments show that there are two kinetically distinct methods of fusion: direct and indirect fusion. Direct fusion shows efficient release of genetic material shortly after the initial fusion stalk is formed. Indirect fusion gets trapped at a well defined intermediate state. We also show that target membrane thickness, shape, unsaturation and phase separation, as well as the size and shape of the lipoplex, have a significant effect on the dominant fusion pathway. Since we designed our methods such, that they are easily expandable to other lipoplex formulations, we hope to stimulate a more rational design of these type of vectors. Paving the way to a safe and affordable clinical utilization of gene therapy.

MONDAY 12:15

Probing Molecular Transport in Printed Biomimetic Tissues

Manon Valet, Léa-Laetitia Pontani, Alexis Prevost and Elie Wandersman

Laboratoire Jean Perrin, UMR 8237 - CNRS – Sorbonne Université, 4 Place Jussieu, 75005 Paris, France

Cell-cell communication in biological tissues depends partly on the passive molecular transport through transmembrane channels. How does such diffusive transport lead to specific patterns in multicellular assemblies? We have recently addressed this question by studying the diffusive properties of fluorophores in biomimetic tissues. They consist of synthetic membranes known as Droplet Interface Bilayers (DIB) [1], connected by passive alpha-hemolysin pores. We have built linear arrays of DIBs using a recently developed droplet-on-demand technique [2]. We have measured the diffusion kinetics and its dependence with the pore concentration in the DIBs. Our results are fully captured by a model based on continuous time random walks and mean first passage times.

[1] – S. Leptihn *et al.*, *Nat. Protocols*, Vol. 8, 1048 (2013).
[2] – M. Valet, L.-L. Pontani, A. M. Prevost, E. Wandesman, *Phys. Rev. Applied,* Vol. 9, 014002 (2018).

MONDAY 14:00

Control of Plant Development by Mechanical Signaling

Elliot Meyerowitz

Howard Hughes Medical Institute and Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, California 91125, USA

My laboratory works to answer the question of how the stem cells of the Arabidopsis thaliana shoot apical meristem form developmental patterns. These include patterns of cell division, cell expansion, gene expression and floral primordium appearance; each of these originates in part due to cell-cell communication in the meristem. Some of the communication is chemical – for example communication between cells and meristem regions by apoplastic movement of peptides and hormones, and symplastic movement of proteins. Much of the communication, however, is physical, with mechanical interactions between meristem cells serving to control patterns of cell division, cell expansion, tissue shape, phyllotaxis, and also to regulate the flux of some of the chemical signals.

I will discuss two different modes of mechanical interaction. The first is cytoskeletal. The pattern of mechanical stresses in the meristem epidermis results from the shape of the meristem and the balance of turgor pressure and cell wall properties in the tissue. This stress pattern controls the microtubule cytoskeleton such that cortical microtubules align parallel to the maximal tensional stress direction when stress is anisotropic. Alignment of microtubules leads to subsequent alignment of cellulose in the cell wall, causing cells to expand anisotropically, leading to new stress patterns. Overall this mechanism allows cells to know the shape of the tissue in which they reside, and then to change that shape – thus providing a feedback between morphogenesis and cellular behavior.

The second mechanical signal results from local cell expansion, which changes patterns of stress in the shared walls between cells expanding at different rates due to their possession of different concentrations of the plant hormone auxin. This local stress causes asymmetric localization of an auxin transporter, which in turn changes the flow of auxin in the epidermis, and therefore changing the stress pattern. The feedbacks in involved in this mechanism control phyllotactic pattern.

Recent work points toward potential mechanisms for both mechanical feedbacks, and also demonstrates additional mechanical responses of meristem cells.

MONDAY 14:45

Force-controlled manipulation of single cells *in vitro*

Tomaso Zambelli

Laboratory of Biosensors and Bioelectronics, D-ITET, ETH Zurich (Switzerland)

FluidFM is a force-controlled nanopipette, combining AFM technology and microfluidics [1]. A fluidic channel is incorporated directly in a hollow AFM cantilever (Figure 1a). This channel ends in an aperture at the apex of the AFM tip, allowing for local dispensing of soluble molecules in air and in liquid, while retaining the inherent imaging capabilities and force feedback of an AFM system. We have just demonstrated the quantitative and subcompartmental femto-picoliter injection [2] and extraction [3] from single cells in vitro. In particular, we showed the integrity of proteins and transcripts as well as versatility of molecular analyses by high-resolution TEM imaging, minute enzyme assays and qPCR of cytoplasmic and nucleoplasmic extracts from distinct or even the same cell. Finally, an electrode can be implemented in the fluidic circuit enabling simultaneous force and ionic current measurements toward force-controlled patch clamp [4] and scanning ion conductance microscopy [5].

[1] A. Meister, M. Gabi, P. Behr, P. Studer, J. Vörös, P. Niedermann, J. Bitterli, J. Polesel-Maris, M. Liley, H. Heinzelmann, T. Zambelli, *Nano Lett,* Vol. 9, 2501-2507 (2009).
[2] O. Guillaume-Gentil, E. Potthoff, D. Ossola, P. Dörig, T. Zambelli, J.A. Vorholt, *Small,* Vol. 9, 1904-1907 (2013).
[3] O. Guillaume-Gentil, R.V. Grindberg, R. Kooger, L. Dorwling-Carter, V. Martinez, D. Ossola, M. Pilhofer, T. Zambelli, J.A. Vorholt, *Cell,* Vol. 166, 1663-1669 (2016).
[4] D. Ossola, M.Y. Amarouch, P. Behr, J. Vörös, H. Abriel, T. Zambelli, *Nano Lett.,* Vol. 15, 1743-1748 (2015).
[5] D. Ossola, L. Dorwling-Carter, H. Dermutz, P. Behr, J. Vörös, T. Zambelli, *Phys. Rev. Lett.,* Vol. 215, 175301 (2015).

MONDAY 16:45

Stress fibers and the cell cortex form a continuous contractile network

Timothée Vignaud[1], Calina Copos[3], Qingzong Tseng[1], Laurent Blanchoin[1,2], Alex Mogilner[3], Manuel Théry[1,2] and Laetita Kurzawa[1,2]

1 Université Grenoble-Alpes, CEA, INRA, CNRS, UMR5168, Biosciences & Biotechnology Institute of Grenoble, CytoMorpho Lab, F-38000, Grenoble, France.
2 Université Paris Diderot, CEA, INSERM, UMRS1160, Hopital Saint Louis, Institut Universitaire d'Hematologie, CytoMorpho Lab, F-75475, Paris, France.
3 Courant Institute and Department of Biology, New York University, New York, NY, USA.

Mechanical forces are key players in the regulation of cell and tissue morphogenesis. The magnitude and orientation of contractile forces direct cell shape and tissue architecture. Force production is determined by the amount of active myosin and the spatial arrangement of actin filaments. The contraction of the random meshwork forming the cell cortex powers global shape changes during cell migration or division. The alignment of filaments and the accumulation of myosins in stress fibers concentrate most of cellular contractile forces on their anchorage to the extracellular matrix. Whether and how these two networks may compete or synergize in the force generation process is still unknown.

In this study, we combined local ablation of contractile elements and global traction force measurements to investigate the specific contribution of each subcellular structure to the total force production and their mechanical interplay. Our results revealed that stress fibers were not only interconnected but also embedded in the cortical and cytoplasmic meshwork all along their length. The contraction of this surrounding meshwork contributes to a significant part of the total traction force on cell anchorages. Their connection also dissipates and transmits the forces produced along the stress fiber throughout the cell.

Far from being independent, stress fibers and surrounding cortical and cytoplasmic meshworks thus appeared to form a continuous network, exchanging filaments and pulling on each other, thereby enforcing a global integration of contractile forces at the cell level.

MONDAY 17:30

Fluorescence lifetime techniques for surgical imaging, guidance and augmented reality

Laura Marcu

Department of Biomedical Engineering, University of California Davis, USA

This presentation overviews fluorescence lifetime spectroscopy and imaging techniques for label-free *in vivo* characterization of biological tissues. Numerous studies have shown that tissue autofluorescence properties have the potential to assess biochemical features associates with distinct pathologies in tissue and to distinguish various cancers from normal tissues. However, despite these promising reports, autofluorescence techniques have been sparsely adopted in clinics. Moreover, when adopted they were primarily used for pre-operative diagnosis rather than surgery guidance. This presentation overviews clinically-compatible multispectral fluorescence lifetime imaging (FLIM) techniques developed in our laboratory and their ability to operate as stand-alone tools, integrated in a biopsy needle and in conjunction with the da Vinci surgical robot. We present clinical studies in patients undergoing surgery that demonstrate the potential of these techniques for intraoperative delineation of brain tumors and brain radiation necrosis as well as head and neck cancer including image-guided augmented reality during trans-oral robotic surgery (TORS). Challenges and solutions in the clinical implementation of these techniques are discussed.

TUESDAY 09:00

Exploring cell-biology on a molecular level: New methods for live-cell and quantitative localization microscopy

Ulrike Endesfelder

Single-molecule microbiology research group, Department of Systems and Synthetic Microbiology, MPI for Terrestrial Microbiology & SYNMIKRO, Marburg, Germany,
www.mpi-marburg.mpg.de/endesfelder

Light microscopy is one of the highest-impact tools in the life sciences as it underpins our fundamental knowledge on structure and behaviour of living organisms. By making use of the modern sub-diffraction fluorescence imaging methods, researchers today are able to analyse intracellular structures at a near-molecular resolution and to trace individual molecule dynamics [1].

Of these methods, single-molecule localization microscopy (SMLM) has quickly become a widely popular and powerful technique as its simple technical requirements have allowed many laboratories around the world an easy access to super-resolution microscopy. Thus, over the last years, a shift from proof-of-concept SMLM developments to comprehensive studies in biology and medicine took place. Nevertheless, this extensive and widespread use of SMLM has brought novel challenges and requirements to light, and there is still a high demand for robust and broadly applicable SMLM tools.

My group develops and applies advanced SMLM techniques for cell biology - interested in the *in situ* observation of molecular processes in living cells and in a fundamental understanding of how complex interdependencies of single molecules enable life.

Focusing on protein-DNA interactions, we mainly rely on two single-molecule applications - following transient and heterogeneous dynamics of

inter-molecular interactions by single-molecule tracking (SMT), and exploiting structural SMLM imaging to precisely map the architecture of large multi-protein complexes.

In this talk, I will introduce some of our recently developed methodological tools alongside with our specific biological questions for two main topics: unraveling the molecular architecture and organization of the kinetochore complex regulating chromosome segregation in *Schizosaccharomyces pombe* and the target detection processes of CRISPR Cas systems:

First, I will present less phototoxic sptPALM imaging by using threonine 69 variants (e.g. Dendra2, mEos3.2-A69T) of the popular green-to-red photoconvertible fluorescent proteins (pcFPs) by primed photoconversion [2, 3]. This advantageously results in a new aberration-free, multi-color imaging scheme together with paFPs (e.g. PAmCherry) which we applied to various targets in fixed and live bacteria, yeast and mammalian cells and combined with correlative imaging methods [3].

I will also introduce a small peptide-tag of only 12 amino acids which is efficiently targeted by a nanobody. It allows for dense fluorophore labeling with minimal linkage errors and results in high-quality SMLM images while not interfering with the examined structures of interest [4].

Finally, I will discuss recent results on how SMLM imaging can be used to quantitatively measure *in vivo* DNA-probing and binding dynamics using our new tracking algorithm *swift* (*unpublished*).

[1] Turkowyd et al. (2016) *From single molecules to life - microscopy at the nanoscale*, Anal Bioanal Chem 408(25).

[2] Turkowyd et al. (2017) *A general mechanism of photoconversion of green-to-red fluorescent proteins based on blue and infrared light reduces phototoxicity in live-cell single-molecule imaging*, Angew Chem 56(38).

[3] Virant et al. (2017) *Combining Primed Photoconversion and UV-Photoactivation for Aberration-Free, Live-Cell Compliant Multi-Color Single-Molecule Localization Microscopy Imaging*, Int J Mol Sci 18(7).

[4] Virant et al. (2018) *A peptide tag-specific nanobody enables high-quality labeling for dSTORM imaging*, Nat Comm 9(1).

TUESDAY 09:45

Watching individual proteins unfold and refold by 1-μs resolution force spectroscopy

Thomas T. Perkins

JILA, National Institute of Standards and Technology and the University of Colorado, Dpts of Physics and of Molecular,Cellular,and Developmental Biology, University of Colorado, Boulder, USA

Protein folding occurs as a set of transitions between structural states within an energy landscape. An oversimplified view of the folding process emerges when transiently populated states are undetected because of limited instrumental resolution. To achieve state-of-the-art performance, we integrated several recent technical advances that improve the precision, stability, and accuracy of AFM-based single molecule force spectroscopy. Using modified cantilevers optimized for 1-μs resolution, we reexamined the unfolding of individual bacteriorhodopsin (bR) molecules in native lipid bilayers. The experimental data revealed the unfolding pathway in unprecedented detail. Numerous newly detected intermediates—many separated by as few as 2–3 amino acids—exhibited complex dynamics, including frequent refolding and state occupancies of <10 μs. Equilibrium measurements between such states enabled the folding free-energy landscape to be deduced. These results sharpen the picture of the mechanical unfolding of bR. Finally, recent efforts to improve the quantity and quality of AFM studies of diverse biomolecules, including nucleic-acid structures and globular proteins, will be discussed.

TUESDAY 11:00

Isolated Nucleic Acids: Mass Spectrometry, Ion Mobility Spectrometry, and Ion Spectroscopy

Valérie Gabelica

Université de Bordeaux, INSERM & CNRS, Laboratoire Acides Nucléiques : Régulations Naturelle et Artificielle (ARNA, U1212, UMR5320), IECB, F-33600 Pessac, France

Studying nucleic acids biophysics in solution is often complicated because the folding of nucleic acid polyanions is strongly coupled to their interactions with cations, small molecules and proteins. Electrospray ionization sources make it possible to transfer nucleic acid complexes from the solution to the gas phase, where they can be separated according to their mass, and thus stoichiometry. Ion mobility spectrometry and ion spectroscopy can then bring further information on the secondary and tertiary structures of these gas-phase nucleic acid complexes. I will review here the latest advances in this field, from fundamental questions to applications in biophysics.

TUESDAY 11:45

The Cyphochilus beetle as an inspiration for sustainable white materials

Gianni Jacucci[1], Olimpia D. Onelli[1], Julia Syurik[2], Hendrik Hölscher[2], Olli Ikkala[3], and Silvia Vignolini[1]

[1] *Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, United Kingdom*
[2] *Institute for Microstructure Technology, Karlsruhe Institute of Technology (KIT), Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany*
[3] *Department of Applied Physics, Aalto University School of Science, Espoo, FI-00076, Finland*
[4] *Department of Physics, University of Calabria, Rende (CS), via Pietro Bucci, 87036, Italy*
[5] *The Blackett Laboratory, Department of Physics, Imperial College London, London SW7 2BW, United Kingdom*
[6] *Department of Physics and Astronomy, University of Exeter, Stocker Road, Exeter, EX4 4QL, United Kingdom*
gi232@cam.ac.uk

Whiteness arises when light interacts with disordered media, where different wavelengths are scattered with comparable intensity. Such appearance is the result of light undergoing multiple scattering events before exiting the object, i.e. when the object is optically thick. The optical thickness of a material is determined by the ratio between its physical thickness and the transport mean free path, namely the distance that light travels before losing information about its starting propagation direction. Commonly, the transport mean free path in low-refractive index white materials is about tens of micrometres long. Therefore, opacity is achieved for relatively large thicknesses (in the millimetres range) to allow a high enough number of scattering events. **[1]**

Nature provides an invaluable source of inspiration for the study and the manufacturing of thin opaque white materials. The *Cyphochilus* white beetle achieves a high total reflectance (~ 75% over the whole visible range) with

a few micron thick, lightweight, anisotropic network of chitin fibres ($n_c \approx 1.55$). [2,3,4]

Herein, after quantifying the scattering efficiency of the chitin network *via* a coherent backscattering setup, [5] we show an experimental approach to produce bio-inspired, sustainable white materials. [6,7] In particular, we demonstrate that tuning the morphology of a network of polymer fibres strongly affects its optical properties: from transparent, to bright white materials. Notably, our bio-inspired materials achieve high scattering efficiency whilst being only a few micrometres thick (up to 75% reflectance while only 4 μm thick). Our study illustrates the potential of using biopolymers as building blocks to produce next-generation sustainable and biocompatible highly scattering materials. [6,7] In addition, we show that it is possible to manipulate the light transport regime, moving from standard to anomalous diffusion, when a long-tailed distribution of the fibres size is introduced. [7]

[1] S. Caixeiro, M. Peruzzo, O. D. Onelli, S. Vignolini, and R. Sapienza, ACS Applied Materials & Interfaces 2017, 7885.
[2] B. D. Wilts, X. Sheng, M. Holler, A. Diaz, M. Guizar-Sicairos, J. Raabe, R. Hoppe, S.-H. Liu, R. Langford, O. D. Onelli, D. Chen, S. Torquato, U. Steiner, C. G. Schroer, S. Vignolini, A. Sepe, *Adv. Mater.* 2017, 1702057.
[3] M. Burresi, L. Cortese, L. Pattelli, M. Kolle, P. Vukusic, D. S. Wiersma, U. Steiner, S. Vignolini, Sci. Rep. 2014, 4, 6075.
[4] L. Cortese, L. Pattelli, F. Utel, S. Vignolini, M. Burresi, and D.S. Wiersma, Adv. Opt. Mater. 2015, 3: 1337-1341.
[5] O. L. Muskens and A. Lagendijk, Opt. Express 2008 16, 1222.
[6] J. Syurik*, G. Jacucci*, O. D. Onelli, H. Hölscher, S. Vignolini, *Adv. Funct. Mater.* 2018, 1706901.
[7] M. S. Toivonen*, O. D. Onelli*, G. Jacucci, V. Lovikka, O. J. Rojas, O. Ikkala, S. Vignolini, *Adv. Mater.* 2018, 1704050

TUESDAY 12:00

Brillouin microscopy to probe the micromechanics of tissue phantoms

M. Bailey[1], N. Correa[1], M. Alunni Cardinali[2], S. Caponi[3], T. Holsgrove[4], C. P. Winlove[1], D. Fioretto[2] and F. Palombo[1]

[1]*School of Physics, University of Exeter, Exeter, UK*
[2]*Department of Physics and Geology, University of Perugia, Perugia, Italy*
[3]*Istituto Officina dei Materiali del CNR, c/o University of Perugia, Perugia, Italy*
[4]*Department of Engineering, University of Exeter, Exeter, UK*

The micromechanical properties of gelatin hydrogels as tissue phantoms to mimic the extracellular matrix have been investigated using Brillouin microscopy and quasi-static compressive testing. The Brillouin response of hydrogels with 0–18% w/w protein concentration was measured and the effect of adding varying concentrations of a cross-linker, formalin, commonly used in histological protocols, was studied. A gradual blue-shift in the Brillouin peak position was observed as both protein and cross-linker concentrations were increased, suggesting an increase in stiffness (longitudinal modulus in the GHz range). Longitudinal and Young's moduli were found to be orders of magnitude apart, indicating that the gels are viscoelastic. The lack of structure in these materials make it possible to characterise their multiscale biomechanics without the interference from hierarchical architectures [1-2].

[1] Edginton RS, Green EM, Winlove CP, Fioretto D, Palombo F. (2018) Dual scale biomechanics of extracellular matrix proteins probed by Brillouin scattering and quasistatic tensile testing, *Proc. SPIE 10504, Biophysics, Biology and Biophotonics III: the Crossroads*, 105040J.
[2] Palombo F, Winlove CP, Edginton RS, Green E, Stone N, Caponi S, Madami M, Fioretto D. (2014) Biomechanics of fibrous proteins of the extracellular matrix studied by Brillouin scattering, *Journal of The Royal Society Interface*, **11**(101):20140739.

TUESDAY 12:15

The effect of twist-bend coupling on DNA mechanics

Stephanos. K. Nomidis[1,2] , E. Skoruppa[1] , M. Caraglio[1] , E. Carlon[1]

1 KU Leuven, Institute for Theoretical Physics, Celestijnenlaan 200D, 3001Leuven, Belgium
2 Flemish Institute for Technological Research (VITO), Boeretang 200, B-2400 Mol, Belgium

The mechanical properties of DNA play a key role in its function within the cell, such as its interaction with proteins. The standard elastic model describing DNA, the twistable worm-like chain (TWLC), treats the bending and twisting degrees of freedom as independent deformations. However, it has been suggested that the groove asymmetry of DNA calls for a refinement of the TWLC, leading to a coupling between the two degrees of freedom. 1 Here we numerically confirm that prediction, 2 and proceed to investigate the consequences of twist-bend coupling through a combination of analytical calculations, computer simulations and experiments. In particular, we show that at long length scales, i.e. for thousands of base pairs, this interaction leads to a non-trivial modification of the overall mechanical behaviour of DNA. 3 In the other limit of short scales, i.e. for 10-100 base pairs, we consider the distinct cases of DNA minicircles and nucleosome, and show that the coupling leads to some surprising similarities. 4 Finally, we anticipate its relevance in other DNA/protein complexes, as well as in the dynamics of DNA supercoiling.

[1] J. F. Marko, E. D. Siggia, *Macromolecules* , Vol. 27, Issue 4, 981-988 (1994).
[2] E. Skoruppa, M. Laleman, S. K. Nomidis, E. Carlon, *J. Chem.Phys.,* Vol 146, Issue 21, 214902 (2017).
[3] S. K. Nomidis, F. Kriegel, W. Vanderlinden, J. Lipfert, E. Carlon, *Phys. Rev. Lett.* , Vol 118, Issue 21, 217801 (2017).
[4] E. Skoruppa, S. K. Nomidis, J. F. Marko, E. Carlon, *arXiv preprint,* arXiv: 1801.10005 (2018).

TUESDAY 14:00

Spatial and temporal variations in cell hydrostatic pressure during plant development

Arezki Boudaoud

Reproduction et Développement des Plantes, Université de Lyon, ENS de Lyon, UCB Lyon 1, CNRS, INRA

Growth of a plant cell is determined by a delicate balance between the cell turgor pressure and the wall. Considerable attention has been given to cell wall composition and mechanics, whereas variations in turgor pressure have been overlooked. In order to measure pressure during development, we set up an approach combining indentation experiments and mechanical models of cell and tissue mechanics, which we applied to the developing seed and to the shoot apex in the model plant Arabidopsis. First, we demonstrated that the mechanical behaviour of the seed is consistent with the seed coat being in tension generated by endosperm-derived turgor pressure which drives seed expansion. We found that seed growth arrest is associated with a drop of endosperm turgor pressure. Second, we observed heterogeneous hydrostatic pressure in the epidermis of the shoot apex, which, surprisingly, correlates either positively or negatively with cellular growth rate, depending on conditions. We ascribe these spatial variations to local geometry and topology of the tissue, by combining experimental observations with a poroviscoplastoelastic model of tissue growth. Altogether, our results suggest developmental roles for temporal and spatial variations in turgor: growth arrest of the seed and cell size homeostasis for the shoot apex.

TUESDAY 14:45

Charge regulation of complex (bio)colloids

Rudolf Podgornik [1,2,3,4]

1 School of Physical Sciences and Kavli Institute for Theoretical Sciences, University of Chinese Academy of Sciences, Beijing 100049, China
2 CAS Key Laboratory of Soft Matter Physics, Institute of Physics, Chinese Academy of Sciences, Beijing 100190, China
3 Dept of Theoretical Physics, Jozef Stefan Inst., SI-1000 Ljubljana, Slovenia
4 Department of Physics, Faculty of Mathematics and Physics, University of Ljubljana, SI-1000 Ljubljana, Slovenia

Charge regulation, implying a variable response of dissociable charge groups on solvent exposed surfaces of macromolecules based on internal non-electrostatic degrees of freedom, is a quintessential feature of polyelectrolytes in biological systems. This applies to bulk protein solutions as well as proteinaceous aggregates such as viral shells and enzymatic nanocontainers, providing scaffolding and compartmentalization for chemical engineering on the nano-scale. Charge regulation alters the behavior of chargeable colloidal systems by fundamentally modifying the standard PB (Poisson-Boltzmann) paradigm. I will describe several of these modifications: (i) alterations of not only in the net charge but also in the direction and strength of all higher multipoles of single proteins; (ii) invalidating the usual assumptions of multipolar expansion in ionic solutions; (iii) emergence of fluctuational Kirkwood-Schumaker interactions; (iv) spontaneous spatial symmetry breaking of electrostatic fields of charge-regulated macromolecules, consequently contradicting one of the fundamental assumptions of the PB theory; (v) charge regulation of complex fluids with mobile macro-ions leads to positional dependence of the effective charge of the macro-ions and a non-monotonic dependence of the effective Debye screening length. These new developments embed the PB paradigm into an entirely new perspective.

[1] Nataša Adžić and Rudolf Podgornik, Phys. Rev. E 91, 022715 (2015).
[2] Anze Losdorfer Bozic and Rudolf Podgornik, Biophys. J., Vol 113, 1454–1465 (2017).
[3] Tomer Markovich, David Andelman and Rudolf Podgornik, Europhys. Letts., Vol. 120 26001 (2017).
[4] Arghya Majee, Markus Bier and Rudolf Podgornik, Soft Matter, Vol. 14, 985 (2018).
[5] Yael Avni, Tomer Markovich, Rudolf Podgornik and David Andelman, Soft Matter, (2018).[6] Anze Losdorfer Bozic and Rudolf Podgornik, J. Chem. Phys., Vol.149, 163307 (2018).

TUESDAY 16:45

Epigenetic dynamics on chromatin in 3D

Davide Marenduzzo

School of Physics and Astronomy, University of Edinburgh, UK

One of the most important problems in development is how epigenetic patterns of biochemical histone modifications can first be established, and then stably inherited, within cell lines. To address this question, we propose a polymer model that couples three-dimensional chromatin folding dynamics to a "recoloring" process modelling the writing of epigenetic marks. This baseline model harbours a sharp transition between a swollen and epigenetically disordered phase and a globular epigenetically coherent one. It also explains a possible biophysical basis for the pheomenon of epigenetic memory and recapitulates the ultrasensitive response of epigenetic switches to perturbation. The model can be developed further by adding genomic bookmarking, yielding stable epigenetic patterns which are similar to those seen in vivo in Drosophila. Finally, we show that coupling transcriptional and epigenetic dynamics provides another avenue to create epigenetic domains, associated with 3D structures reminiscent of transcription factories and hubs of active genes.

TUESDAY 17:30

Regulation of chromosome mechanics by a surfactant-like protein

Sara Cuylen-Haering[1], Matthias Samwer[2], Mina Petrovic[2], Daniel W. Gerlich[2]

1 Cell Biology and Biophysics Unit, European Molecular Biology Laboratory (EMBL), Meyerhofstrasse 1, 69117 Heidelberg, Germany
2 Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA), Vienna Biocenter (VBC), Dr. Bohr-Gasse 3, 1030 Vienna, Austria

The reorganization of chromosomes into spatially well-separated bodies is a hallmark of mitosis. We have previously reported that Ki-67, a component of the mitotic chromosome periphery, prevents chromosomes from collapsing into a single chromatin mass after nuclear envelope disassembly. The very large size of the Ki-67 protein, its apparent lack of secondary structure, and high electrical charge suggest that it might function as a steric and electrical barrier, similar to surface-active agents (surfactants) that disperse particles or phase-separated liquid droplets in solvents. Consistent with this idea, dual-color labeling of both protein termini showed that Ki-67 forms densely-grafted polymer brushes as a steric barrier between mitotic chromosomes. In the present study, we hypothesized that this steric barrier facilitates independent chromosome movement during early stages of mitosis, whereas it might be inactivated during mitotic exit to promote merging of all chromosomes into a single nucleus. Indeed, we found that Ki-67 brushes collapse upon exit from mitosis, suggesting that Ki-67's surfactant activity is cell cycle regulated. Coincident with Ki-67 brush collapse, we found that chromosomes coalesced into a single chromatin mass, where they ceased to move independently. The chromosome merge preceded the first interaction with nuclear membranes and might hence shape the surface for nuclear assembly. Our study raises the interesting possibility that upon inactivation of Ki-67 during mitotic exit the surface of mitotic chromosomes changes from repulsive to adhesive, which has potential implications for nuclear assembly.

WEDNESDAY 09:45

Isomorphic and Isofunctional Fluorescent Nucleosides, Nucleotides and Oligonucleotides

Yitzhak Tor

Department of Chemistry & Biochemistry, University of California, San Diego, 9500 Gilman Drive, La Jolla, California, 92093-0358, USA

Nucleic acids experience a variety of perturbations, which include strand cleavage and ligation, local conformational changes, base damage, modification and flipping, as well as structural and environmental perturbations that are induced upon protein and low MW ligand binding. Additionally, nucleosides and nucleotides are involved in numerous biochemical transformations, as well as signaling and regulatory processes. Isomorphic responsive fluorescent nucleoside analogues, which can serve as faithful surrogates of their native counterparts, are powerful probes for investigating nucleic acids structure, dynamics, recognition and damage as well as metabolic processes involving nucleosides/tides.[1–7] The lecture will present the design, synthesis and photophysical properties of new fluorescent isomorphic nucleoside analogues as well as their utilization for the fabrication of "real-time" fluorescence-based discovery and biophysical assays.

[1] D. Shin, R. W. Sinkeldam, Y. Tor, *J. Am. Chem. Soc.,* Vol. 133, 14912–14915 (2011).
[2] R. W. Sinkeldam, L. S. McCoy, D. Shin, Y. Tor, *Angew. Chem. Int. Ed*., Vol. 52, 14026–14030 (2013).
[3] W. Liu, D. Shin, Y. Tor, B. S. Cooperman, *ACS Chem Biol.,* Vol. 8, 2017–2023 (2013).
[4] A. R. Rovira, A. Fin, Y. Tor, *J. Am. Chem. Soc.,* Vol. 137, 14602–14605 (2015).
[5] A. R. Rovira, A. Fin, Y. Tor, *J. Am. Chem. Soc.***,** Vol. 139*,* 15556–15559 (2017).
[6] Y. Li, A. Fin, L. McCoy, Y. Tor, *Angew. Chem*. *Int. Ed.,* Vol. 56, 1303–1307 (2017).
[7] F. Hallé, A. Fin, A. R. Rovira, Y. Tor, *Angew. Chem. Int. Ed.*, Vol. 57, 1087–1090 (2018).

WEDNESDAY 11:00

Exploring the variability of nucleosome conformation *in vitro* and *in situ* using cryoEM of vitreous sections

Mikhail Eltsov[1], Diana Grewe[1], Nicolas Lemercier[2,3], Françoise Livolant[2], Amélie Leforestier[2]

[1] Buchmann Inst. for Molecular Life Sciences, Goethe Univ. Frankfurt, Germany
[2]Laboratoire de Physique des Solides, UMR 8502 CNRS, Université Paris-Sud, Université Paris-Saclay. Bat 510, 91405 Orsay Cedex, France
[3]Present address: IGBMC Imaging Center, CNRS, Inserm, Université de Strasbourg, 1 rue Laurent Fries, 67404 Illkirch, France

In Eukaryotes, DNA is wound into a left-handed superhelix around the histone octamer forming the basic chromatin unit, the nucleosome. Atomic structures have been obtained from crystallography and single particle cryo electron microscopy of identical engineered particles. But nucleosomes are dynamical entities and native particles have diverse DNA sequence and histone content. Little is known about their conformational variability, especially in the cellular context.

By using cryo electron microscopy and tomography of vitreous sections it is possible to visualize individual nucleosomes within interphase nuclei, at a level of detail sufficient to measure the distance between the DNA gyres of the super helix. Multiple conformations are found, on average more open than the canonical crystallographic structure.

A simple model system, concentrated solutions of isolated nucleosome core particles, let us analyse the influence of several parameters (particle concentration, local order and ionic environment). We demonstrate a salt-dependent transition, with a high salt compact conformation resembling the canonical nucleosome, and an open low salt one, closer to nuclear nucleosomes. Although further particle characterisation and cartography are needed to understand the relationship between this conformational variability and chromatin functional states, this approach opens a route to chromatin exploration *in situ*.

WEDNESDAY 11:45

Shape and cytoskeleton organization in isolated plant cells

Pauline Durand-Smet[1,2], Henrik Jonsson[2], Elliot Meyerowitz[1, 3]

1Division of Biology, California Institute of Technology, 1200 East California Boulevard, Pasadena, California 91125, USA
2The Sainsbury Laboratory, Univ. of Cambridge, Bateman Street Cambridge CB1LR, UK
3Howard Hughes Medical Institute, California Institute of Technology, 1200 East California Boulevard, Pasadena, California 91125, USA

pauline.durand@slcu.cam.ac.uk

Despite the significance of cellular morphology as a functional phenotype, it remains challenging to quantitatively relate morphological phenotype to the behavior of subcellular molecules. Molecular studies have identified many components controlling cell morphogenesis, but it is unclear how this information is translated into the physical world. In plant cells, growth requires synthesis of cytoplasmic components as well as expansion of the cell wall. The cell wall is a stiff yet flexible polymeric network that encapsulates cells and counterbalances stress created by turgor pressure inside the cell, thereby controlling cell shape. It is now well established that the cytoskeleton plays a key role in the biogenesis and morphogenesis of the cell wall. While the microtubules guide cellulose synthase complex movement1, the actin network is responsible for global distribution of cellulose synthase complexes 2. It is also suggested that mechanical stresses orient the microtubules along their principal direction 3. Nevertheless, to fully understand how plant cells are shaped and how external mechanical stresses influence this process, a quantitative approach to evaluate the mechano-response in single cells needs to be established.

Here we present a technique to confine single plant protoplasts into molds of defined shapes. The protoplasts are then monitored with a confocal microscope to evaluate changes in cytoskeletal organization and dynamics

during the process of symmetry breaking. These experiments are the basis of assessing quantitatively how different shapes control cytoskeleton organization behavior by regulating the distribution of physical stresses.

1. Paredez, A. R., Somerville, C. R. & Ehrhardt, D. W. Visualization of cellulose synthase demonstrates functional association with microtubules. *Science* **312,** 1491–5 (2006).
2. Gutierrez, R., Lindeboom, J. J., Paredez, A. R., Emons, A. M. C. & Ehrhardt, D. W. Arabidopsis cortical microtubules position cellulose synthase delivery to the plasma membrane and interact with cellulose synthase trafficking compartments. *Nat. Cell Biol.* **11,** 797–806 (2009).
3. Hamant, O. *et al.* Developmental patterning by mechanical signals in Arabidopsis. *Science* **322,** 1650–5 (2008).

WEDNESDAY 12:00

Direct measure of thickness and dynamic of the cell cortex

Valentin Laplaud[1,2], Julien Heuvingh[1], Olivia du Roure[1] & Matthieu Piel[2]

1. Physique et Mécanique des Milieux Hétérogènes, ESPCI Paris, PSL Reasearch Univetsity, CNRS, UMR 7636, Université Pierre et Marie Curie, Université Paris Diderot, 10 rue Vauquelin, 75005 Paris, France.

2. Institut Curie, PSL Research University, CNRS, UMR 144, 6 rue Jean Calvin, 75005 Paris, France.

valentin.laplaud@espci.fr

Cell migration is central to many biological and physiological processes and happens in a variety of way. The different actin networks of the cell play different roles in migration either by actively generating forces or by influencing the mechanical properties of the whole cell. In the case of confined migration the cell cortex is often compressed between the outside elements (ECM, other cells…) and the cell nucleus. It has been shown that in constricted microchannels mimicking such environments a perinuclear branched actin network can start polymerizing [1]. Furthermore in vitro experiments on branched actin network have shown a response to confinement in both mechanical properties and polymerization dynamics [2]. Recently the observation of actin waves in 3D [3] also asks questions about the formation and physiological relevance for migration of such complexes structures of branched actin networks.

We developed a new tool to study the behavior of the cortex to understand these different types of activities and the mechanics behind

complexes actin structures. We use super-paramagnetic beads under a controlled magnetic field: in this situation, the beads develop their own dipolar moment and are attracted to each other with a known force [4]. Thanks to the macropinocytosis ability of dendritic cell we can create a system where we have one bead inside the cell and one outside. We can thus confine the membrane and the cortex between these beads and track their position with a precision of few tens of nanometers.

This system allows for different measurements and tests upon the cell cortex. Due to the precision available in the tracking of the beads we can measure the thickness of the cortex at different levels of confinement. By combining our system with fluorescent microscopy we can observe a confined portion of cortex for signs of actin polymerization due to confinement. But we also record what seems to be the passage of actin waves between the beads. We can thus study the cortex and its dynamical features in different cases such as with various compressing forces or with drugs to affect the biochemical composition of the cortex.

[1] H. R. Thiam et al. - Nat Com 2016
[2] P. Bieling et al. – Cell 2016
[3] Fritz-Laylin et al. – bioRxiv preprint 2017
[4] T. Pujol et al. – PNAS 2012

WEDNESDAY 12:15

Mechanical constraints in the morphogenesis of the gastrovascular system of the jellyfish *Aurelia aurita*

Solène Song [1,2], Camille Gambini[1], Stephane Douady[1], Alexis Peaucelle[1], Christine Ruta [2,3], Guillaume Balavoine[2], Annemiek JM Cornelissen[1]

[1] *laboratoire Matière et Systèmes Complexes*
[2]*Institut Jacques Monod*
[3]*Federal University of Rio de Janeiro*

The jellyfish *Aurelia aurita* is equipped with a gastrovascular system which displays a branched pattern spanning the endodermal cells monolayer. It develops by radial centripetal growth from the rim and connection to neighbouring vessels. This network is an interesting model for describing the growth of a network in a growing and contractile environment: it is planar and relatively simple, the animal body grows homogeneously up to 30% per day, and the swimming movement is periodic and easy to describe due to rotational symmetry.

We hypothesize that the canals growth and reconnections are triggered by the repeated mechanical constraints due to the swimming movement, in analogy with cracks propagation. We have acquired timelapse series of the canals growth and films of the swimming movement. We quantified the pattern's geometry and topology on the timelapse series and the local deformations in the films. We showed that the topologies can be very diverse from one individual to the other, and that the swimming movement does not deform all regions of the endoderm homogeneously. This heterogeneity could explain privileged locations for reconnections. This would be an argument in favour of an example of mechanics driven morphogenesis in a basally branching Metazoan.

WEDNESDAY 14:00

Tuning mechanosensing at the membrane interface by assymmetry of transbilayer pressure profile

Boris Martinac[1,2]

[1]*Victor Chang Cardiac Research Institute, Lowy Packer Building, 405 Liverpool St, Darlinghurst, NSW, 2010, Australia*
[2]*St Vincent's Clinical School, Faculty of Medicine, University of New South Wales, Darlinghurst, NSW 2010, Australia*

Efficient mechanotransduction processes occur in living organisms via mechanosensors or mechanoreceptors linking external mechanical stimuli at the cell surface to intracellular signaling events and downstream effectors. Mechanosensitive (MS) ion channels are among the fastest primary mechanosensors converting mechanical stimuli into intracellular signals on a submillisecond time scale. Much of our understanding of the biophysical principles that underlie and direct conversion of mechanical force into conformational changes in MS channels comes from studies based on MS channel reconstitution into lipid bilayers. My talk focuses on close interactions between MS channels and the lipid bilayer and discusses the central role that transbilayer pressure profile plays in mechanosensitivity and gating of these fascinating membrane proteins.

WEDNESDAY 14:45

Exploring the molecular landscape of *Chlamydomonas* with *in situ* cryo-electron tomography

M. Schaffer[1], H. van den Hoek[1], W. Wietrzynski[1], S. Albert[1], S. Mosalaganti[2], J. Kosinski[2], M. Beck[2], Y. S. Bykov[3], J. A.G. Briggs[3], M. Jordan[4], G. Pigino[4], M. Le Guennec[5], N. Klena[5], V. Hamel[5], P. Guichard[5], J. M. Plitzko[1], W. Baumeister[1], Benjamin D. Engel[1]

1 Max Plank Institute of Biochemistry, Germany.
2 European Molecular Biology Laboratory, Germany.
3 MRC Laboratory of Molecular Biology, UK.
4 Max Plank Institute of Cell Biology and Genetics, Germany.
5 University of Geneva, Switzerland.

Cells accomplish the biochemical reactions of life by concentrating their proteins into a variety of subcellular compartments called organelles. Our group explores the relationship between the *form* of the organelle and the *function* of its resident macromolecules. How does organelle architecture direct molecular function, and reciprocally, how do macromolecules sculpt and shape organelles? To investigate these questions, we use focused ion beam (FIB) milling of frozen cells followed by cryo-electron tomography to image macromolecules within their native cellular environment. Through a combination of nanometer-precision localization and high-resolution structural analysis, we aim to chart the molecular landscapes of organelles.

Thanks to its superb cryo-EM contrast and textbook organelle architecture, the unicellular green alga *Chlamydomonas* is an ideal specimen for this approach. We have taken a holistic approach to survey the whole integrated "planimal", with *in situ* molecular studies of the nuclear envelope, ER, Golgi, basal body apparatus (centrioles), and chloroplast. In this talk, I will provide an overview of some of these studies, touching on proteasome-rich degradation centers [1], the nuclear pore complex [2], COPI coats [3], IFT

train assembly, centriole structure, and the molecular organization of chloroplast's thylakoid membranes and pyrenoid [4].

[1] S. Albert, M. Schaffer, F. Beck, S. Mosalaganti, S. Asano, H.F. Thomas, J.M. Plitzko, M. Beck, W. Baumeister, B.D. Engel, *Proc Natl Acad Sci U S A,* Vol. 114, 13726-13731 (2017).
[2] S. Mosalaganti, J. Kosinski, S. Albert, M. Schaffer, D. Strenkert, P.A. Salomé, S.S. Merchant, J.M. Plitzko, W. Baumeister, B.D. Engel, M. Beck. *Nature Communications*, Vol. 9, 2361 (2018).
[3] Y.S. Bykov, M. Schaffer, S.O. Dodonova, S. Albert, J.M. Plitzko, W. Baumeister, B.D. Engel, J.A. Briggs. *Elife*, Vol. 6, e32493 (2017).
[4] E.S. Freeman Rosenzweig, B. Xu, L. Kuhn Cuellar, A. Martinez-Sanchez, M. Schaffer, M. Strauss, H.N. Cartwright, P. Ronceray, J.M. Plitzko, F. Förster, N.S. Wingreen, B.D. Engel, L.C.M. Mackinder, M.C. Jonikas. *Cell*, Vol. 171, 148-162.e119 (2017).

WEDNESDAY 16:00

The Two-State World View as Biology's Greatest Model

Rob Phillips

Depts of Physics & of Biology and Biological Engineering, California Institute of Technology, Pasadena, USA

Only ten years after the discovery of the iconic structure of DNA, new questions were on biologist's minds, namely, how are the macromolecules of the cell regulated so that they do what they are supposed to when and where they are needed? The initial resolution of the challenging question of biological regulation came in the form of the notion of "allostery", an idea that its discoverer Jacques Monod himself referred to as "the second secret of life". We recently celebrated the 50th anniversary of the classic paper of Monod, Changeux and Jacob that introduced this far reaching idea. That important paper was followed shortly thereafter by a second one that revealed their musings on how simple statistical mechanical models can be used to capture how such allosteric transitions work mechanistically. In this talk, I will review the key features of the famed Monod-Wyman-Changeux (MWC) model and then describe its broad reach across many different domains of biology with special reference to the physics of ion channels and how genes are turned on and off. One of the intriguing outcomes of this class of models is a beautiful and predictive scheme for collapsing data from entire libraries of mutants. Once we have considered some of the traditional uses of the MWC model, I will turn to more speculative recent ideas which use the MWC approach to consider the nature of kinetic proofreading.

WEDNESDAY 16:45

Is Extracellular Matrix a pressure sensor?

M. Dolega[1], B. Brunel[1], M. Le Goff[1], M. Greda[1], C. Verdier[1], J.-F. Joanny[2], P. Recho[1], G. Cappello[1]

1 Université Grenoble Alpes, Laboratoire Interdisciplinaire de Physique, CNRS, F-38000 Grenoble, France
2 Institut Curie, CNRS, Université P. et M. Curie, UMR168, F-75231 Paris, France

Growth of solid tumors occurs in a constrained environment and requires a competition for space. This results in a bidirectional mechanical coupling between the tumor and its close environment, the stroma. The expanding neoplastic tissue compresses the stroma, thus builds up, and stores an internal stress; in parallel, the stroma is contractile and exerts a mechanical stress on the tumor.

To evaluate the effect of such a stress, we grow multicellular aggregates made of cancer cells under a controlled mechanical pressure. We observe that a gentle compression (500 Pa) drastically reduces the growth rate of spheroids made of cancer cells [1]–[3], whereas it has no impact on the same cells, when grown individually.

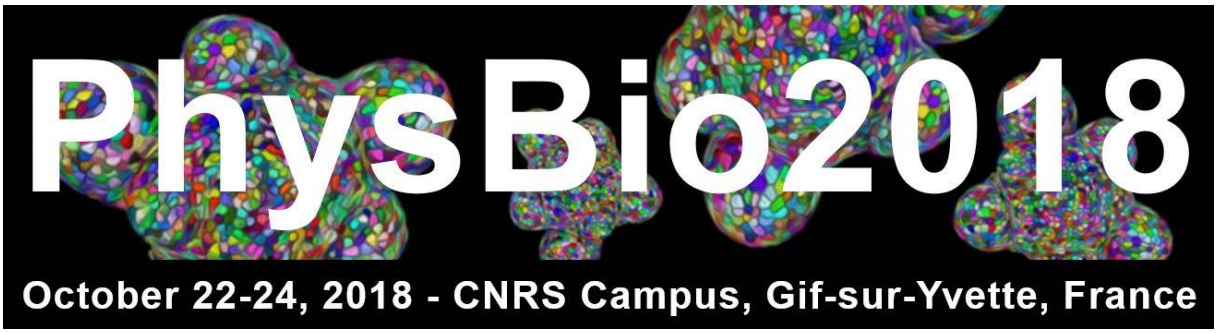
A major difference between individual cells and multicellular aggregates is the presence of Extracellular Matrix (ECM) in the multicellular context. Contrarily to cells, which are almost incompressible, the ECM is permeable to water and highly compliant. Thus, a gentle compression generates a much larger strain in the ECM than in the cells. Thus, we model and characterize the compressibility and the permeability of composite aggregate, made of cells and ECM.

We find that ECM properties mainly determine the mechanical response of a multicellular aggregate to external stimuli. In addition, we observe that the ECM compression has a large impact on cell proliferation, migration and morphology. We conclude that the ECM play the role of a pressure sensor in a multicellular context.

[1] F. Montel *et al.*, "Stress clamp experiments on multicellular tumor spheroids," *Phys. Rev. Lett.*, vol. 107, no. 18, pp. 1–4, 2011.

[2] M. Delarue, F. Montel, D. Vignjevic, J. Prost, J. F. Joanny, and G. Cappello, "Compressive stress inhibits proliferation in tumor spheroids through a volume limitation," *Biophys. J.*, vol. 107, no. 8, pp. 1821–1828, 2014.

[3] M. E. Dolega, M. Delarue, F. Ingremeau, J. Prost, A. Delon, and G. Cappello, "Cell-like pressure sensors reveal increase of mechanical stress towards the core of multicellular spheroids under compression," *Nat. Commun.*, vol. 8, no. May 2016, pp. 1–9, 2017.



POSTER ABSTRACTS

Numerical model of checkpoint dependent replication origin activation in the Xenopus in vitro system

Diletta Ciardo (Institut de Biologie Intégrative de la Cellule (I2BC), CEA, CNRS, Université Paris-Sud, France) , Arach Goldar (Institut de Biologie Intégrative de la Cellule (I2BC), CEA, CNRS, Université Paris-Sud, France) , Kathrin Marheineke (Institut de Biologie Intégrative de la Cellule (I2BC), CEA, CNRS, Université Paris-Sud, France)

The initiation of DNA replication in multicellular organisms begins at thousands of genomic positions known as replication origins, which are activated at different times during the S phase in a regulated manner. Furthermore, few origins are grouped into so-called replication clusters that fire more or less synchronously. Previous studies point out that in the Xenopus in vitro system the ATR-Chk1 dependent checkpoint pathway is necessary to globally inhibit origin activation in the presence and absence of exogenous replication stress. Using DNA combing we showed that checkpoint inhibition did not lead to the inhibition of origins in already activated replication clusters, close to stalled forks.

The stochastic nature of the initiation process together with limitations of the experimental techniques, require the use of numerical models to obtain more information about the spatial and temporal activation of replication origins.

To this purpose, I tested different models by comparing Monte Carlo simulations and data from DNA combing experiments in the presence and absence of Chk1 inhibition. I used a genetic algorithm which allows to optimize the fitting of the multitude of different replication parameters. The best accordance with experimental data was obtained with a model that combines three notions: 1) a random initiation by an increasing limiting factor, 2) a strong global inhibition of origins firing by Chk1 protein and 3) an enhanced initiation probability near active replication forks together with a local repression of the Chk1 action. The model is consistent with the fact that replication origins are grouped into different temporal clusters. Combining numerical simulations with new models and experimental data will allow us to develop a new global model of the replication program in eukaryotes.

Field induced cell proliferation and apoptosis in a thick epithelium

1) Niladri Sarkar (UMR 168, Institut Curie, Paris, France)
2) Jacques Prost (UMR 168, Institut Curie, Paris, France)
3) Frank Jülicher (MPIPKS, Dresden, Germany)

Using hydrodynamics, we construct a continuum model for a thick planar epithelium, with fluid permeation. The cells are considered to be active and can drive fluid flow through the tissue. We apply an external flow and electric current, and study how thickness dynamics and steady states of the epithelium are affected by these external fields. The induced flow gives rise to cell proliferation and apoptosis depending upon their direction and intensity, and different phases for the thick tissue are obtained accordingly.

Membrane meso-patterning explained by composition-shape coupling

Julie CORNET, Manoel MANGHI, Nicolas DESTAINVILLE

Laboratoire de Physique Théorique-IRSAMC, Université Paul Sabatier/CNRS, Toulouse, France

Plasma membrane forms a selective barrier for the cell, yet its role goes far beyond a simple frontier. Indeed, it plays a crucial role in biological functions. It is now widely agreed that membrane component spatial repartition is not homogenous but that they are organized into nanodomains. These domains have proven to be key players in the above-mentioned biological functions. Thanks to statistical mechanics tools, we propose a physical mechanism for this membrane organization in a simple model vesicle. We describe the membrane with a composition/curvature coupling mechanism and perform Monte Carlo simulations for different membrane parameters and study its equilibrium states. Different observables are computed such as correlation functions and domain size distribution to extract information about the emerging membrane domains, such as their typical shape, size or spacing. We observed systems featuring either a macrophase or meso-domains or labyrinths, depending on the range of parameters.

High throughput 3D tracking of bacterial chemotaxis in complex environments

Marianne Grognot (Taute Lab, Harvard University, USA); Katja M. Taute (Taute Lab, Harvard University, USA)

Bacterial chemotaxis is a mechanism by which motile bacteria bias their random walk trajectory to either climb or descend a chemical gradient. This mechanism is fundamental for survival and have been extensively studied in the model organism E. coli. Much less attention has been devoted to the diversity of motility patterns displayed by other bacteria with different flagellar architectures, or to motility in viscous or porous environments that more closely mimic the complexity of natural habitats.

We strive to understand how chemotaxis is achieved by bacteria using different motility strategies, requiring 3D trajectory information in defined chemical concentration fields for many individuals, in variable media where strategies are expected to show variable efficiency. Current chemotaxis assays are either only at the population scale, qualitative or low throughput, in 2D and/or relying on theoretical models for known flagellar architectures.

Here we present a simple yet powerful chemotaxis assay combining a recent high throughput 3D tracking method with microfluidically created chemical gradient. We demonstrate that we can directly determine chemotactic drift velocities in different types of environments (liquid, viscous, porous, etc.) while simultaneously resolving 3D motility patterns, enabling unprecedented access to a mechanistic understanding and comparison of chemotactic mechanisms.

We highlight the application of our assay to comparison of flagellar mutants of a marine bacterium V. alginolyticus. This work demonstrates the role of lateral flagella for swimming and chemotacting in mucous-like media (soft agar), beyond their known role in attaching and swarming on surfaces.

Single-molecule studies of the molecular mechanisms underlying the chaperone activity of HSPB8

Dhawal Choudhary1, Laura Mediani2, Mario J Avellaneda3, Edgar Boczek4, Simon Alberti4, Sander J Tans3, Serena Carra2, Ciro Cecconi1

1 Department of Physics, Informatics and Mathematics, University of Modena and Reggio Emilia, Italy
2 Department of Biomedical, Metabolic and Neural Sciences, and Centre for Neuroscience and Neurotechnology, University of Modena and Reggio Emilia, Italy
3 FOM institute AMOLF, Amsterdam, The Netherlands
4 Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany.

We have investigated in vitro the effect of HSPB8 on the folding and aggregation processes of the maltose binding protein (MBP) using optical tweezers. We have mechanically denatured homotetramers of MBP and analyzed their folding and aggregation processes in the presence or absence of HSPB8. Our results reveal a strong holdase activity of HSPB8, both at high (25 uM) and low concentration (5 uM), which either prevents completely the aggregation of denatured MBP molecules or allows the substrate to form only small and mechanically weak aggregates. Moreover, and importantly, a careful analysis of the data also discloses an unexpected foldase activity of HSPB8, which guides the folding process of denatured MBP domains into their native states. Our findings highlight new mechanisms of interaction between HSPB8 and its substrates and suggest a more complex physiological role for this chaperone than previously assumed.

Tailoring physical properties of materials for nerve regeneration

Utpal Bora, Suradip Das*, Manav Sharma*, Manash Barkataki*,Dhiren Saharia**, Kushal Konwar Sarma***, Monalisa Goswami Sarma****, Bibhuti Bhusan Borthakur*****,*

**Department of Biosciences and Bioengineering, Indian Institute of Technology Guwahati, Guwahati 781039, Assam, India*
***Saharia's Path Lab & Blood Bank, Guwahati 781005, Assam, India*
****Department of Surgery and Radiology, College of Veterinary Sciences, Khanapara, Guwahati 781022, Assam, India*
*****Nemcare Hospital, Guwahati 781005, Assam, India*
******Department of Surgical Oncology, Dr. B. Borooah Cancer Institute, Gopinathnagar, Guwahati 781016, Assam, India*

Physical factors like electrical impulse and material characteristics (shape, size and bulk properties) influence the growth of nerve cells and regeneration of nerve tissue as a whole. Neurodegenerative disorders are a consequence of the loss of neurons within the brain, spinal cord and the peripheral nervous system. We present here our work on the effect of gold nanoparticles, silk and polyaniline and their composites on the differential response in terms of growth of nerve cells and regeneration of nerve tissue. We also discuss about the contemporary work on the impact of electrical stimulation on the survival, growth and differentiation of various nerve cells with an objective of designing novel materials which could provide dual cues captivating the entire gamut of physical properties that influence nerve regeneration. Finally we examine the translational potential of these basic studies in the development of nerve conduits for replacement of allo-and xeno- nerve grafts both of which has their own inherent problems.

Towards understanding tree's proprioception.

*Juan Alonso-Serra*1, Juha Immanen1, Xueping Shi3, Alexis Peaucelle2,4, Matthieu Bourdon2, Gugan Eswaran1, Judith Felten5, Junko Takahashi-Schmidt5, Hanna Koivula6, Hanna Help-Rinta-Rahko7, Katja Kainulainen1, Ari Pekka Mähonen1, Kaisa Nieminen8 and Ykä Helariutta1,2.*

1Institute of Biotechnology, Faculty of Biological and Environmental Sciences, University of Helsinki, Helsinki, Finland.
2Sainsbury Laboratory, University of Cambridge, Cambridge, United Kingdom.
3College of Horticulture & Forestry Sciences, Huazhong Agricultural University, Wuhan, China.
4Institut Jean-Pierre Bourgin, Institut National pour la Recherche Agronomique-AgroParisTech, Saclay Plant Science, Versailles, France.
5Umeå Plant Science Center, Department of Forest Genetics and Plant Physiology, Swedish University of Agricultural Sciences, Umeå, Sweeden.
6Department of Food and Nutrition Sciences, Faculty of Agriculture and Forestry, University of Helsinki, Finland.
7Department of Physics, University of Helsinki, Helsinki, Finland.
8Green Technology, Natural Resources Institute Finland (Luke), Helsinki, Finland.

The evolution of plant development into a diversity of forms and sizes is a continuum dynamic process that did not stop after plants left their aquatic habitat. Instead, the challenges of being autotrophs rooted to the soil demanded the development of vasculature with both transport and mechanical functions. In trees, while the apical growth increases the height, the secondary growth increases the diameter required to withstand not only mechanical stress from the environment, but also the increasing body weight.

In order to understand the consequences of growth misperception in trees, we explored a collection of natural birch mutants. Unlike most tree species six-month-old birches are able to flower under special greenhouse conditions, thus producing segregating populations for forward genetics studies in a short period of time.

Using this method, we identified and characterized the "elimäki" mutant tree (eki), a recessive monogenic mutation that results in stem collapse after 3 months of growth. Compared to WT individuals, eki trees are thinner in the base showing that stem thickening is compromised, this eventually leads to a mechanical failure.

Interestingly the opposite growth phenotype is observed in the higher stem, the young internodes of eki trees have increased cell proliferations from the vascular cambium and expanded xylem and phloem cells. Further studies throughout tree development shows that the mutant has premature xylem expansion, delayed fibre differentiation and affected mechanical properties in the stem regardless of its diameter. Most importantly the mutants show composition and morphology defects in the early stages of secondary cell wall formation in the xylem. In order to interpret the anatomical observations into tissue-specific mechanical properties we performed AFM across the wood forming zone

showing the variation in rigidity in WT as well as in eki trees. Finally, we integrate the mechanical consequences of wood development along the stem.

On-chip quantification of cytokine secretion from single spheroids of human mesenchymal stem cells

Adrien Saint-Sardos, Gabriel Amselem*, Sebastien Sart+, Elodie Brient-Litzler+, Charles Baroud+*.*

** (Ladhyx,Ecole Polytechnique, France)*
+(PuB, Dpt Genomes et Genetique, Institut Pasteur, France)

Mesenchymal stem cells appear to have consequent paracrine impact on their cellular environment, down regulating inflammation and improving tissue repair and recovery. Here we present a novel microfluidic tool enabling to form and culture single mammalian cell spheroids isolated in nanoliter droplets, and to quantify, with simple epifluorescence microscopy, the levels of cytokine they secrete.

Spheroids are co-encapsulated with an ELISA-type detection tool consisting in a solution of fluorescent detection antibodies and micron-size beads coated with capture antibodies. As cytokines are secreted by the spheroids, they diffuse to the beads, where they are captured. The fluorescence of the beads is directly correlated to the amount of captured cytokines. As a proof of concept, we quantify cytokine secretion both by individual human monocytes and mesenchymal stem cells spheroids.

Tailoring physical properties of materials for nerve regeneration

Utpal Bora, (Department of Biosciences and Bioengineering, Indian Institute of Technology Guwahati, India)
Suradip Das, (Department of Biosciences and Bioengineering, Indian Institute of Technology Guwahati, India)
Manav Sharma, (Department of Biosciences and Bioengineering, Indian Institute of Technology Guwahati, India)
Dhiren Saharia (Saharia's Path Lab & Blood Bank Guwahati, India)
Kushal Konwar Sarma (Department of Surgery and Radiology, College of Veterinary Sciences, India)
Monalisa Goswami Sarma (Nemcare Hospital Guwahati, India)
Bibhuti Bhusan Borthakur (Department of Surgical Oncology, Dr. B. Borooah Cancer Institute, India)

Physical factors like electrical impulse and material characteristics (shape, size and bulk properties) influence the growth of nerve cells and regeneration of nerve tissue as a whole. Neurodegenerative disorders are a consequence of the loss of neurons within the brain, spinal cord and the peripheral nervous system. We present here our work on the effect of gold nanoparticles, silk and polyaniline and their composites on the differential response in terms of growth of nerve cells and regeneration of nerve tissue. We also discuss about the contemporary work on the impact of electrical stimulation on the survival, growth and differentiation of various nerve cells with an objective of designing novel materials which could provide dual cues captivating the entire gamut of physical properties that influence nerve regeneration. Finally we examine the translational potential of these basic studies in the development of nerve conduits for replacement of allo-and xeno- nerve grafts both of which has their own inherent problems.

(Alternative E-mail: ubora@iitg.ac.in)

Unveiling the interaction between lipid nanotubes and actin networks using AFM

Guillaume Lamour, Antoine Allard, Sid Labdi, Clement Campillo (LAMBE, Universite d'Evry, France)

Nanomechanics of lipid membrane and its interaction with actin have important roles in transport phenomena, including endocytosis and vesicle formation. However little is known about the forces and biophysical mechanisms involved in membrane deformation or rupture. In this study, thousands of nanotubes with diameter on the order of 100 nm have been generated and attached to a surface. Using AFM in combination with fluorescence, we image the tubes before and after actin has polymerized onto the tubes. We compare the morphology and mechanical properties of naked tubes and those modified with actin. In summary we have developed a new platform for studying how actin interacts with lipid nanotubes, using atomic force microscopy (AFM).

Micro-segregation in complex mixtures: theory and simulation

Anthony BAPTISTA and Aurélien PERERA
Lab. Physique Théorique des Liquides, Université Pierre et Marie CURIE, Tour 13-23 5ème ét. Boite 121, 4 Place Jussieu, Paris F75252, FRANCE

Nano-scale segregation of molecular species in aqueous mixtures and other hydrogen bonding mixtures has been progressively evidenced in recent years. The description of this micro-heterogeneity poses both theoretical and computational problem, principally because of the difficulty of describing a phenomena related to arrested phase separation. This phenomena is considered here as precusor description of molecular segregation in bio-molecular media.

We propose models and methodology which allows to introduce such phenomena in the statistical theory of liquids, and illustrate it for the case of nano-segregation in water-alcohol mixtures.

Structural study of lipid droplet using synchrotron label free multimodal imaging

Frédéric Jamme (Soleil Synchrotron, France)
Isabelle Bouchez (IJPB, INRA AgroParisTech CNRS, Université Paris Saclay, France)
Caroline Pénicaud (GMPA, INRA AgroParisTech , Université Paris Saclay, France)
Stéphanie Passot (GMPA, INRA AgroParisTech , Université Paris Saclay, France)
Fernanda Fonseca (GMPA, INRA AgroParisTech , Université Paris Saclay, France)
Yann Gohon (IJPB, INRA AgroParisTech CNRS, Université Paris Saclay, France)
Matthieu Réfrégiers (Soleil Synchrotron, France)
Eva Pereiro (ALBA Synchrotron, Spain)
Bertrand Cinquin (LBPA, CNRS ENS Paris Saclay, France)
Marine Froissard (IJPB, INRA AgroParisTech CNRS, Université Paris Saclay, France)

Imaging intracellular compartments, their dynamics and interactions in living cells, remains challenging. Using various lipid droplet (LD) protein markers, we revealed inter LD heterogeneity at single cell level, due to LD specific geolocalisation and enzymatic equipment. Even so, using tagged proteins or vital probes could modify the morphology and the smooth running of the organelles. Methods based on intrinsic fluorescence of molecules upon excitation by deep ultra violet (DUV) illumination are thus emerging for living cell imaging. We used DUV from synchrotron radiation to perform auto-fluorescence and transmittance imaging on single living yeast. The contrasted signals inside the cells revealed chemical heterogeneity at the subcellular level. Microscopy showed organelles with low auto-fluorescence after DUV illumination. We distinguished two populations, with high or low transmittance. The first population corresponded to vacuoles and the second to LDs. LDs appeared as heterogeneous well-organized structures with a low transmittance zone on the surface and a high transmittance core. We propose that the low transmittance ring and the high transmittance core correspond to ergosterol and triacylglycerol-containing structures, respectively. The conclusions we drawn using DUV imaging were confirmed by experiments performed using soft X ray imaging on cryofixed cells. Synchrotron label free imaging paves the way for efficient structural and dynamic studies of LDs and other organelles.

Linear and ring polymer chains in confined geometries

Zoryana Usatenko (Institute of Physics, Cracow University of Technology, Poland), Piotr Kuterba (Jagiellonian University, Cracow, Poland), J. Halun (Institute of Nuclear Physics, Cracow, Poland)

The investigation of a dilute solution of long-flexible linear and ring polymer chains in confined geometries like slit of two parallel walls with different adsorbing or repelling properties in respect to polymers as well as in a solution of mesoscopic spherical colloidal particles of one sort or two different sorts is performed . Taking into account the well known polymer – magnet analogy developed by de Gennes [1] between the field theoretical φ 4 O(n) – vector model in the limit n->0 and the behaviour of long – flexible polymer chains with the excluded volume interaction (EVI) in a good solvent the calculations of the dimensionless depletion interaction potentials and the depletion forces [2-4] as well as the monomer density profiles [5,6] were performed in the framework of the massive field theory approach in fixed space dimensions $d<4$ up to one loop order. The presented results indicate about the interesting and nontrivial behaviour of linear and ring polymers in confined geometries and give possibility better to understand the complexity of physical effects arising from confinement and chain topology which plays a significant role in the shaping of individual chromosomes and in the process of their segregation, especially in the case of elongated bacterial cells. The obtained results are in good qualitative agreement with the scaling predictions proposed by de Gennes [1], the previous analytical investigations and with the results obtained by numerical methods for linear and ring polymer chains and can find practical application in production of new types of nano- and micro-electromechanical devises.

[1] P.G. de Gennes, Scaling Concepts in Polymer Physics (Cornell University Press, Ithaca, NY, 1979).
[2] D. Romeis, Z. Usatenko, Phys. Rev. E 80, 041802 (2009).
[3] Z. Usatenko, J. Halun, J. Stat. Mech.: Theory and Experiment P 013303 (2017).
[4] Z. Usatenko, P. Kuterba, H.Chamati, D. Romeis, Eur. Phys. J.: Special Topics 226, 651-665 (2017).
[5] Z. Usatenko, J. Chem. Phys. 134, 024119:1-10 (2011); J. Mol. Liq. 164, 59 - 65 (2011).
[6] J. Halun, Z.Usatenko (unpublished results).

Competition for Space is driven by compaction driven ERK downregulation

Léo Valon (Institut Pasteur, France)
Florence Levillayer (Institut Pasteur, France)
Romain Levayer (Institut Pasteur, France)

The plasticity of developing tissues relies on the adjustment of cell survival and growth rate to environmental cues. This includes the effect of mechanical cues on cell survival. Accordingly, compaction of an epithelium can lead to cell extrusion and cell death. This process was proposed to contribute to tissue homeostasis but also to facilitate the expansion of pretumoral cells through the compaction and elimination of the neighbouring healthy cells. However we know very little about the pathways than can trigger apoptosis upon tissue deformation and the contribution of compaction driven death to clone expansion was never assessed in vivo. Using the Drosophila pupal notum and a new live sensor of ERK, we show that tissue compaction induces cell elimination through the downregulation of EGFR/ERK pathway and the upregulation of the pro-apoptotic protein Hid. Those results suggest that the sensitivity of EGFR/ERK pathway to mechanics could play a more general role in the fine tuning of cell elimination during morphogenesis and tissue homeostasis. Secondly, we assessed in vivo the contribution of compaction driven death to pretumoral cell expansion. We found that the activation of the oncogene Ras in clones can also downregulate ERK and activate apoptosis in the neighbouring cells through their compaction, which contributes to Ras clone expansion. The mechanical modulation of EGFR/ERK during growth-mediated competition for space may contribute to tumour progression.

Evolution of microtubule aster forces during aster centration

Jing Xie (1), Jeremy Sallé (1), Dmitry Ershov (1,2) and Nicolas Minc (1)

1:Institut Jacques Monod (CNRS)
2:Institut Pasteur

Forces generated by Microtubule (MT) aster control crucial processes such as nuclei migration, spindle centering, embryonic cleavage geometries and asymmetric division. This importance contrasts with the limited knowledge we have on the magnitude of these forces and how they depend on molecular organization, cell cycle progression and cell geometry. Here we use in vivo magnetic tweezers to directly compute forces exerted by MT aster in Sea Urchin embryos. By applying forces perpendicular to the centration motion of MT asters we show that MT forces act as springs stabilizing asters along their centering trajectories. Strikingly, by computing spring stiffness at successive moments during aster centration, we show that this stiffness decreases as the aster approaches the cell center. We propose that this effect reflects a continuous depletion of cytoplasmic anchors allowing dynein to pull on MTs. Future mapping of the evolution of MT forces during the cell cycle and in subsequent cleavage stages should bring key understanding on the mechanisms of aster positioning.

Impact of the flow on drug release from a core-shell reservoir

Clément Bielinski (BMBI, CNRS - UTC Compiègne, France)
Nam Le (BMBI, CNRS - UTC Compiègne, France)
Badr Kaoui (BMBI, CNRS - UTC Compiègne, France)

We study numerically the impact of the flow on drug release from a core-shell reservoir (a capsule). We use the lattice Boltzmann method to compute both the flow and the mass transfer [1]. We capture the transition from the steady laminar flows around the reservoir to the unsteady flows by increasing the Reynolds number. We investigate how different flow regimes influence the drug release from the core-shell reservoir by reporting the Sherwood number (the mass transfer coefficient) as a function of different parameters, for example, the Reynolds number and the Schmidt number.

[1] B. Kaoui, Flow and mass transfer around a core-shell reservoir, Physical Review E 95, 063310 (2017)

Impact of mechanical constraints on cancer cells behavior

PRUNET Audrey (ILM, Université Lyon 1, France), BERABEZ Nabila (CRCL, Université Lyon 1, France), LAPERROUSAZ Bastien (CRCL, Université Lyon 1, France), GABUT Mathieu (CRCL, Université Lyon 1, France), MAGUER-SATTA Véronique (CRCL, Université Lyon 1, France), RIEU Jean-Paul (ILM, Université Lyon 1, France), MONNIER Sylvain (ILM, Université Lyon 1, France), DELANOE-AYARI Hélène (ILM, Université Lyon 1, France), RIVIERE Charlotte (ILM, Université Lyon 1, France)

Cancer cells are submitted to different levels of mechanical contraints during tumor growth due to compressive stress resulting from cell proliferation in a confined environment, ECM stiffening and increase in interstitial fluid pressures. Emerging evidences show that cancer progression and several aspects of cellular processes (proliferation, invasion?) are modulated by mechanical stimuli. The evaluation of cell phenotypic and genotypic changes upon extended compression of cells could help to understand the resistance to therapeutic treatment of cancer cells and more specifically of cancer stem cells (CSC) which seem to play a role in relapses. We are currently developping a microsytem to mimic the compression sensed by the cells in vivo and in the same to be able to measure cell response in terms of forces, shape, displacement and protein expression. We are doing that at different scale : at the cell scale and at the spheroid scale.

The vesicle trap. How to measure the real activity of the phagocyte NADPH oxidase?

Xavier Serfaty (Laboratoire de Chimie Physique, Paris Sud University, France); Pauline Lefrançois (Institut des Sciences Moléculaires de Bordeaux, University of Bordeaux, France); Chantal Houée-Levin (Laboratoire de Chimie Physique, Paris Sud University, France); Stéphane Arbault (Institut des Sciences Moléculaires de Bordeaux, University of Bordeaux, France); Laura Baciou (Laboratoire de Chimie Physique, Paris Sud University, France); Tania Bizouarn (Laboratoire de Chimie Physique, Paris Sud University, France)

The phagocyte NADPH oxidase plays a key role in the killing of invaders during phagocytosis and in the inflammatory processes. The membrane heterodimer Nox2-p22phox, also called flavocytochrome b558, containing the electron transport chain made of a flavin and two hemes, in interaction with four cytosolic proteins (p67phox, p47phox, p40phox and Rac1/2) constitutes the functional enzyme catalysing the monoelectron reduction of dioxygen on one side of the membrane using NADPH as reductant on the other side of the membrane. Thus, electrons cross the membrane from the cytosolic donor NADPH to the extracellular or phagosomal receptor dioxygen. The community working in vitro on the functioning of NADPH oxidase, commonly follows the progress of the enzymatic reaction by the superoxide anion-cytochrome c reduction (followed by absorption at 550 nm). We found that the enzyme turnover appeared twice higher by measuring NADPH oxidation rate than the Cytc reduction rate. We decided to analysis further the stoichiometry by measuring dioxygen by electrochemistry with a Clark electrode. Up to now, the literature provides neither explanation nor real discussion despite the critical importance to quantify exactly the enzyme turnover, since such measurements lead to most of the interpretations of NADPH oxidase enzymology. We decided to get to the bottom of this point by checking if this discrepancy is due to artefacts linked to Cytc measurements or intrinsic to the enzyme in its biochemical compartmented context. Using ionophores, detergents, temperature change, hydrogen peroxide measurements in bulk or in microreactor (liposomes and amplex-red) by confocal fluorescence microscopy, our results show that membrane permeability, vesicle confinement and unexpectedly fast secondary reactions (disproportionations), have a strong impact on the discrepancy. These results highlight the crucial importance of careful measurements in compartmented systems such as vesicles as well as in cells to get the right interpretations and reach true conclusions.

New features of a plant mechanosensitive calcium channel

Yannick Guerringue, Jean-Marie Frachisse (Institute for Integrative Biology of the Cell (I2BC), CEA, CNRS, Université Paris-Sud, Université Paris-Saclay, France)

Plants as all living organisms are subjected to mechanical forces which may activate a variety of mechanosensors at the cellular level. Among them mechanosensitive channels, embedded in the membrane, represent universal mechanosensors. These channels are proteins forming an ion-permeable pore through the membrane lipid bilayer, which is gated by membrane tension. Their activity can be measured with a patch-clamp setup coupled with a high-speed pressure clamp system. The Rapid Mechanically Activated (RMA) activity was detected at the plasma membrane of the model plant Arabidopsis thaliana. This calcium-selective mechanosensitive channel is characterized by a rapid inactivation. In this study we characterized the kinetics of activation, inactivation and deactivation of RMA current as a function of the pressure applied on the membrane. We precised the pressure-activity relationship of the channel. Finally we showed that the decrease in activity of the RMA channel along a recording is a function of a number of stimulation but of the time of recording.

Modelling the influence of cell-substrate interactions on in Vitro cancer cells aggregation

Léo Adenis (Laboratoire IMNC, UMR 8165 CNRS, Univ Paris-Sud, Univ Paris Diderot, France), Emilie Gontran (UMR S 1174 INSERM - ICPH Interactions Cellulaires et Physiopathologie Hépatique, Université Paris-Sud, France), Christophe Deroulers (Laboratoire IMNC, UMR 8165 CNRS, Univ Paris-Sud, Univ Paris Diderot, France), Basile Grammaticos (Laboratoire IMNC, UMR 8165 CNRS, Univ Paris-Sud, Univ Paris Diderot, France), Olivier Seksek (Laboratoire IMNC, UMR 8165 CNRS, Univ Paris-Sud, Univ Paris Diderot, France), Mathilde Badoual (Laboratoire IMNC, UMR 8165 CNRS, Univ Paris-Sud, Univ Paris Diderot, France)

Cancer cells are often cultivated on a rigid glass substrate, causing them to stay alone and adopt non-natural shapes. This method also biases tests of tumour treatments, especially chemotherapy. A new hydrogel was developed at the IMNC so that brain cancer cells could be cultivated on a soft substrate mimicking the brain physical properties [1]. A non-specific cell adhesion can be added by using poly-L-Lysine when fabricating the hydrogel. On this substrate cells aggregate into micro-tumours. This phenomenon is very interesting for studying the in Vitro evolution of a cancer cells population and can be compared to other aggregation process with inactive particles.

In order to reproduce the cellular aggregation observed in experiments with two brain cancer cell line (F98) culture followed during 24h using DIC imaging, we developed a model of the aggregation based on a cellular automaton. Each cell follows a set of individual rules to move and proliferate. We used an ImageJ macro to follow the number of aggregates (individual cells and clusters) and their mean area in the experiments as well as in simulations. We managed to reproduce the dynamic of both the mean area of the areas (cells and clusters of cells) and the number of aggregates (with and without and adhesive hydrogel). We also compared the experimental and simulated dynamics with a theoretical model derived from the Smoluchowski equation.

We could conclude that the presence of non-specific cell adhesion modulated the speed of cell migration onto the gels and therefore, the size and the number of aggregates. We also found that non-specific adhesion does not influence the other parameters of the aggregate formation and growth, ie compaction and cell proliferation.

[1] Gontran E, Juchaux M, Deroulers C, Kruglik S, Huang N, Badoual M, Seksek O, Assessment of the ability of poly(l-lysine)–poly(ethylene glycol) (PLL–PEG) hydrogels to support the growth of U87-MG and F98 glioma tumor cells, J. Appl. Polym. Sci. 2018, 135, 46287

A mathematical model of tumor-induced angiogenesis focused on cellular dynamics

Rocío Vega Martínez (Modelling, Numerical Simulation, and Industrial Mathematics group, Universidad Carlos III de Madrid, Spain); Manuel Carretero (Modelling, Numerical Simulation, and Industrial Mathematics group, Universidad Carlos III de Madrid, Spain); Luis L. Bonilla (Modelling, Numerical Simulation, and Industrial Mathematics group, Universidad Carlos III de Madrid, Spain);

Angiogenesis, the formation of new blood vessels from existing vasculature, is the basis of organ growth and repair in healthy conditions and of pathological developments such as cancerous tumors. Angiogenesis is a multiscale process, ranging from gene transcription and protein synthesis, through the cell dynamics and right up to the level of organization of tissues and organs.

In this poster, we present a cell-based model structured in terms of these multiple scales by incorporating extracellular and cellular levels as well as the results of simulations. At extracellular level, the model considers chemotaxis and durotaxis by adding an equation for the Vascular Endothelial Growth Factor and Finite Element computational model for the compliant extracellular matrix, respectively. At the cellular level, a cellular Potts model considers cell migration, growth, proliferation, cellular adhesion, distinction between tip and stalk phenotypes, sprout branching and anastomosis. The extracellular and cellular level are coupled giving rise to a model that incorporates biomechanical and biochemical mechanisms allowing to simulate branching based on purely biological properties.

Quantitative Model of Calcium Signal Remodeling in Atrial Myocytes

B. Lungsi Sharma (Computational Neuroscience, Ronin Institute, France)

Intracellular calcium ions plays a crucial role in the contractile process by initiating attractive forces between the actin and myosin filaments. Cardiac arrhythmias are due to abnormalities in rhythmicity-conduction system of the heart. Studies have shown that altered calcium ion homeostasis is linked to arrhythmias. With age the prevalence of arrhythmias rises. Age related changes in cardiac action potential has been observed. In atrial myocytes, during systole there is an increase in calcium ion buffering, but low peak calcium current via the L-type calcium channel. This paper will show a quantitative model of the mechanisms behind the remodeling of calcium ion handling in aging atrial myocytes, and make predictions on what would happen to the calcium ion concentrations in the sarcoplasmic reticulum and calcium current in the L-type channel when the cell volume changes with stimulation of beta-adrenergic receptors. The model is based on a lumped element modeling schema for transforming qualitative models into quantitative model. This novel technique incorporates biochemical processes. It allows the representation of ion/molecular: concentration, flux, diffusion, transport and reaction. It is therefore an aid for developing descriptive relationships of physiological process. Quantitative models provide the advantage of quickly examining the hypothesis on computer models and could provide interesting avenues for future research. The more expensive and time consuming animal studies could then be used on the intriguing questions.

Systematic dissection of 3D Hox gene organization in Drosophila

Laura Moniot-Perron1, Benoit Moindrot1, Daan Noordermeer1 & Sébastien Bloyer1

Chromatin Dynamics Group, Institute for Integrative Biology of the Cell (I2BC), CEA, CNRS, Université Paris-Sud, Université Paris-Saclay

In Drosophila melanogaster, Hox genes are organized in two clusters: the Antennapedia complex (ANT-C) and the Bithorax complex (BX-C). Remarkably, the order of homeotic genes along the chromosome parallels the order in which they are expressed in the body segments along the A/P axis, this phenomenon is called colinearity.

How this colinear Hox gene expression is related to tri-dimensional (3D) chromatin organization, and more importantly, how this 3D structure is maintained by Polycomb complexes and insulator proteins remain unclear.

To address these questions, I am developing two main axes. The first axis is a descriptive analysis of the Hox gene epigenetic landscape (histone marks) and 3D conformation using ChIP-seq and 4C-seq (Circular Chromosome Conformation Capture) in 4 homogenous drosophila cell lines. By determining the interaction patterns of all Hox gene promoters, we observed that when all Hox genes are repressed, they are compacted into a Polycomb compartment covered by the H3K27me3 repressive histone mark; whereas when the Abd-B Hox gene is expressed, it is able to loop out of the repressive compartment and is covered by the H3K4me3 active histone mark. The second axis of my project is a functional analysis to characterize the underlying mechanisms that structure 3D Hox gene organization. First, I am deleting Hox gene Boundary Elements (BE) and Polycomb Response Element (PRE) using CRISPR/Cas9. This will decipher the links between BE and PRE in the maintenance of Hox genes expression and 3D conformation. Second, I will force Hox gene expression using the SUN-Tag system to analyze if ectopic Hox gene activation results in the disruption of the repressed and compacted 3D conformation.

Together, these experiments will provide a better understanding of how 3D organization and Hox gene expression, as well as the involvement of different actors such as insulator proteins, cis-regulatory elements and Polycomb complexes, are linked.

Mechanical and structural properties of the ESCRT-III proteins

Aurélie Bertin1, Maryam Alqabandi1, Nicola de Franscesci1, Nolwenn Miguet2, Winfried Weissenhorn2, Patricia Bassereau1 and Stéphanie Mangenot1

1- Institut Curie, Physico-Chimie Curie, CNRS UMR168, Sorbonne Université, PSL research university, 11 Rue Pierre et Marie Curie, 75005 Paris- France
2- Institut de Biologie Structurale (IBS), Univ. Grenoble Alpes, CNRS, CEA, 38000 Grenoble, France

The ESCRT-III is an evolutionary conserved protein complex that mediates membrane remodeling and scission. The ESCRT pathway has been extensively studied in vivo and reconstituted in vitro using yeast proteins. In Homo Sapiens, the ESCRT-III complex is composed of at least 12 proteins, called Charged Multivesicular Body Protein (CHMP 1-7).

Several isoforms of each CHMP proteins correspond to their yeast homologues. CHMP6 corresponds to Vps20, CHMP3 to Vps24. Three isoforms of CHMP4 (A, B and C) relate to Snf7 and two CHMP2 (A and B isoforms) correspond to Vps2. Among all ESCRT-III subunits, CHMP4, CHMP2 (A/B) and CHMP3 seems to be the core complex of the ESCRT-III machinery.

We have characterized for the first time the mechanical properties of CHMP polymers at the mesoscale. We show that CHMP2A and CHMP2B has opposite mechanical properties on membrane, suggesting that these 2 proteins are not functional homologues. Moreover, we performed cryo-electron microscopy on Large unilamellar vesicles. While CHMP4 assemble into flat spirals on liposomes, the presence of CHMP2 (A or B) induce the formation of 3-D highly regular structures.

Single-Cell Acoustic Force Spectroscopy (scAFS): Resolving kinetics and strength of T-cell adhesion to fibronectin

Douwe Kamsma1,2,6, Pascal Bochet3,4,6, Felix Oswald5, Nander Ablas1,2, Sophie Goyard3, Gijs J L Wuite1,2,7, Erwin J G Peterman1,2,, Thierry Rose3,*.*
1Department of Physics and Astronomy, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands.
2LaserLaB Amsterdam, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands.
3Institut Pasteur, Center for Innovation and Technological Research, Networks & Signaling research group, Paris, France.
4CNRS UMR3691, Dynamique Cellulaire Physiologique Pathologique, Paris, France.
5LUMICKS b.v., Amsterdam, the Netherlands.
6These authors contributed equally to this work.
**Correspondence : T.R. (rose@pasteur.fr)*

Assessing strength and kinetics of molecular interactions of cells with the extracellular matrix is fundamental to understand cell-adhesion processes. Given the relevance of these processes, there is a strong need for physical methods to quantitatively assess the mechanism of cell adhesion at the single-cell level, allowing discrimination of cells with different behaviours. Here we introduce single-cell Acoustic Force Spectroscopy (scAFS), an approach that makes use of acoustic waves to exert controlled forces, up to 1 nN, to hundreds of individual cells in parallel. We demonstrate the potential of scAFS by measuring adhesion forces and kinetics of CD4+ T-lymphocytes (CD4) to fibronectin. We determined that CD4 adhesion is accelerated by interleukin-7, their main regulatory cytokine, while CD4 binding strength remains the same. Activation of these cells likely increases their chance to bind to the vessel wall in the blood flow to infiltrate inflamed tissues and locally coordinate the immune response.

Nuclear mechanotransduction: How nuclear shape and mechanics affect gene expression in plants

Rituparna Goswami1,2, Atef Asnacios3, P. Milani4, Guy Houlné1, Olivier Hamant2 and Marie-Edith Chabouté1
1 : Institut de biologie moléculaire des plantes, UPR2357 CNRS, Université de Strasbourg, France
2 : Laboratoire Reproduction et Développement des Plantes, INRA, CNRS, UCBL1, ENS de Lyon,France
3 : Laboratoire Matières et Systèmes Complexes, Université Paris-Diderot and CNRS UMR 7057,France
4 : BioMeca, ENS de Lyon, France

As in all living organisms, plant cells are constantly experiencing mechanical stress. Such mechanical stimuli may impact nuclear mechanics and thus gene expression. However, the relevant pathways, ensuring that these stimuli lead to well-orchestrated genetic responses through the nucleocytoplasmic interface remain ill-described in plants. Here we provide the first bases for the study of nuclear mechanotransduction in plants. We performed Rheometry and AFM to understand the physical properties of Arabidopsis root meristem nuclei in the presence or absence of osmotic stress (mannitol). We also use live cell imaging to detect the morphometric response of the nuclei in plants expressing the nuclear envelope SUN1-GFP. We found that the gip1gip2 nucleus is more rigid, when compared to WT Arabidopsis nuclei and that the transcriptome in gip1gip2 mutants resembles that of cells experiencing hyperosmotic stress in Arabidopsis root. This suggests the existence of a link between physical forces, nuclear shape and mechanics, and gene expression in plants.

Adhesion mechano-sensitivity: a biochemical study of the force-dependent talin-RIAM-vinculin complex

Clémence Vigouroux (Institute for Integrative Biology of the Cell (I2BC), CEA, CNRS, Université Paris-Sud, France), Véronique Henriot (I2BC, CEA, CNRS, Université Paris-Sud, France), Christophe Le Clainche (I2BC, CEA, CNRS, Université Paris-Sud, France).

Adherent cells and phagocytes are constantly submitted to similar changes in the mechanical properties of their environment and intracellular tension. They sense and transduce these parameters into an appropriate biochemical response. In these cells, the actin cytoskeleton plays a central role by transmitting force towards the mechano-sensitive focal adhesions or the phagocytic cup. These two structures couple the the actomyosin cytoskeleton to the extracellular matrix (ECM) or to the particle to phagocyte, via integrins and actin-binding proteins (ABP). The ABP talin controls integrin activation and actin anchoring, by recruiting the ABP vinculin in response to force. The talin-binding protein RIAM is thought to antagonize vinculin action. (1, 2) However, the molecular mechanism underlying this force-dependent antagonism has never been studied. We developped a novel in vitro system, made of pure proteins, to demonstrate that the actomyosin force unfolds talin to expose cryptic vinculin-binding sites (VBS) (3,4). We use this approach to characterize the effect of actomyosin force on the talin-vinculin-RIAM complex. The first data suggests that RIAM prevents force-dependent association of vinculin to talin. The effect of vinculin on RIAM association to talin in response to force will also need to be addressed.

Contrarian compulsions produce exotic time dependent flocking of active particles

Carolina Trenado (Materials Science and Engineering and Chemical Engineering, Universidad Carlos III de Madrid, Leganés, Spain.)

A different frequency distribution has been introduced in the two-dimensional Vicsek-model to analyze (by means of bifurcation theory) the behavior of a system in the limit of infinitely many particles. In order to do that, we use a deterministic equation for the particles density derived from microscopic collision rules.

Using a (complex-valued) order parameter we have found solutions by Direct Brownian simulations that confirm our theoretical studies.

Modulation of Axonal Excitability by an Antiepileptic Drug Levetiracetam

Shaikhah Alshuaib, Dr.Jen Wei Lin (Membrane Biophysics laboratory, Boston University, USA)

Epilepsy is a neurological disorder triggered by multiple dysfunctions at the cellular level, such as various ion channelopathies, alteration of neuronal migration, or protein degradation defects in neurons. Levetiracetam (LEV) is a broad-spectrum anti-epileptic drug that is widely prescribed for the treatment of epilepsy. Physiological analysis showed that this drug enhances synaptic depression during high frequency firing while leaving basal transmission intact. Furthermore, LEV has been shown to be effective in animal seizure models such as synapsin (Boido et al. 2010) and STXBP1 (Grone et al. 2016) knockouts. Studies at the molecular level showed that LEV enters neurons by endocytosis, after binding to the luminal end of an integral membrane protein located at synaptic vesicles (SV2A). These reports suggest that the antiepileptic effects of LEV are likely to be mediated through synaptic transmission and after entering neurons at axonal endings. However, other studies suggest that LEV might modulate the voltage and ligand gated channels. Since axons are likely to be one of the neuronal compartments that are exposed to LEV shortly after it's entry, we utilized motor axons of the crayfish opener neuromuscular preparation to examine changes in axonal excitability in LEV.

First, we preformed two electrodes current clamp in the inhibitory axon where third electrode was placed to measure IPSP from a muscle fiber. Action potential amplitude (APamp) remained unchanged in 100 μM LEV for about 15 minutes before an abrupt decrease occurred. The decrease in IPSP occurred later than that of APamp , at ~28 minutes. The difference in the timing of APamp and IPSP reduction suggests that LEV might modulate axon excitability via a mechanism distinctly different from its modulation of synaptic transmission. The delay action of LEV on IPSP is consistant with previous findings from brain slices. To address this possibility, we placed one electrode in the primary branch (1°) while the second electrode was placed in the secondary branch (2°) distal to the primary, with a separation of 500 μm at 1mm. By injecting current to either the proximal or the distal electrodes first we were able to capture the progression of APamp changes in orthodromic and antidromic directions. LEV selectively reduced the amplitude of antidromic APamp. Comparing the phase plots of antidromic action potentials before and after LEV revealed that the charging component of AP rising phases was unaffected by LEV but the second component of AP rising phase, mediated by local sodium channels at the 1° branching point was reduced. Therefore, our observation suggests that LEV affects axonal excitability by targeting the inward

current of the proximal branches. Our findings add new insights to the existing view that Synaptic transmission is LEV's main site of action and we propose that the antiepileptic effects of LEV might also include the modulation of axonal excitability.

Permeability of the protein corrals in membranes

Yulia Sokolov and Haim Diamant

Biomembranes are highly viscous quasi-2D fluids consisting of amphiphilic lipid bilayers. Embedded proteins, anchored to the cytoskeleton, influence the diffusion and dynamics within the membrane. These immobile inclusions create corrals that confine membrane domains. We model this confinement as an assembly of objects in a ring, and calculate the permeability of the ring using the two-dimensional Green's function for hydrodynamic interactions. In the continuum limit, we derive an analytical expression for the permeability. We compare the numerical results of discrete summation and analytical results, obtaining excellent agreement.

Intracellular transport of cargos: tug-of-war, anomalous diffusion, and lattice dynamics

Cécile Appert-Rolland (1) Sarah Klein (1,2) Max Ebbinghaus (1,2) , Ludger Santen (2)
1- Lab. Theoretical Physics (LPT), Univ. Paris-Sud/Paris-Saclay, Orsay (France)
2- Theoretical Physics, Univ. Saarland, Saarbrücken (Germany)

There is a need for transport between the different compartments of eukaryote cells. Here we focus on microtubule based transport. Several types of molecular motors can transport cargos in both directions along these polar filaments. First we will consider this system at the scale of a cargo driven by teams of motors, and show how counter-pulling teams can give interesting properties to the cargo-motors complex. At a larger scale, we will show how the dynamics of the microtubule network itself can favor a fluid transport.

Experimental study of tissue growth in a bead stack under perfusion

Claire BEAUCHESNE (EM2C Laboratory CNRS UPR 288 and MSSMat Laboratory CNRS UMR 8579, CentraleSupélec, France)
Bertrand DAVID (MSSMat Laboratory CNRS UMR 8579, CentraleSupélec, France)
Benoît GOYEAU (EM2C Laboratory CNRS UPR 288, CentraleSupélec, France)

Tissue engineering has stepped in as a promising technology for repairing large bone defects. Its purpose is the production of man-made bone grafts, which is achieved by culturing cells of interest, previously harvested from the patient, on a tridimensional and biodegradable scaffold. Nevertheless, this technology still faces major obstacles, such as the economical production of relevant volumes of bony tissue.

In this context, several perfusion bioreactors were designed in order to improve tissue production. More precisely, the perfused culture medium enhances species transport and provides a mechanical stimulation to the cells that accelerates tissue growth. Through a mechanism called mechanotransduction, the mechanical forces cells are subjected to are translated into a biological response [1] and the proliferation rate is altered. This results in a complex culture environment within the growth chamber where tissue growth modifies the fluid flow meanwhile the fluid flow stimulates cell proliferation.

We propose to study tissue growth in a perfusion bioreactor where the scaffold consists of a stack of identical beads based on fluidized bed reactor concepts [2]. Local numerical simulations of Stokes flows were compared to our experimental results and allowed us to identify the preferential locations of proliferation on the scaffold. In particular, we observe the formation of an envelop of tissue as a consequence of mechanotransduction and the presence of a channeling effect in the parietal region [3].

In addition, we describe the tissue morphology at three cultivation times and relate our observations to the field of shear stresses obtained numerically.

References:

[1] Ingber, D. E. (2006). Cellular mechanotransduction: putting all the pieces together again. The FASEB journal, 20(7), 811-827.

[2] David, B., Bonnefont-Rousselot, D., Oudina, K., Degat, M. C., Deschepper, M., Viateau, V., Bensidhoum, M., Oddou, C., Petite, H. (2011). A perfusion bioreactor for engineering bone constructs: an in vitro and in vivo study. Tissue Engineering Part C: Methods, 17(5), 505-516.

[3] Kaviany, M., & Singh, B. P. (1993). Radiative heat transfer in porous media. Advances in Heat Transfer, 23(23), 133-186.

Diffusion-limited reactions in dynamic heterogeneous media

Y. Lanoiselée, N. Moutal, D. Grebenkov
Laboratoire de Physique de la Matière Condensée, École Polytechnique, Palaiseau, France

Most biochemical reactions in living cells rely on diffusive search for target molecules or regions in a heterogeneous overcrowded cytoplasmic medium. Rapid rearrangements of the medium constantly change the effective diffusivity felt locally by a diffusing particle and thus impact the distribution of the first-passage time to a reaction event. Here, we investigate the effect of these dynamic spatiotemporal heterogeneities onto diffusion-limited reactions. We describe a general mathematical framework to translate many results for ordinary homogeneous Brownian motion to heterogeneous diffusion. In particular, we derive the probability density of the first-passage time to a reaction event and show how the dynamic disorder broadens the distribution and increases the likelihood of both short and long trajectories to reactive targets. While the disorder slows down reaction kinetics on average, its dynamic character is beneficial for a faster search and realization of an individual reaction event triggered by a single molecule.

Spatio-temporal analysis of megacaryocyte elongation during platelet production

Ilyesse Bihi (BMBI UMR 7338, Université de Technologie de Compiègne, Compiègne, France)
Sonia Poirault-Chassac (INSERM UMR 1140, Université Paris Descartes, Sorbonne Paris Cité, Paris, France)
Meriem Lebsir (INSERM UMR 1140, Université Paris Descartes, Sorbonne Paris Cité, Paris, France)
Mathilde Reyssat (CNRS UMR 7083 Gulliver, ESPCI, Paris, France)
Dominique Baruch (INSERM UMR 1140, Université Paris Descartes, Sorbonne Paris Cité, Paris, France)
Anne Le Goff (BMBI UMR 7338, Université de Technologie de Compiègne, Compiègne, France)

Introduction

Platelets are small blood cells that prevent bleeding. They are formed by fragmentation of precursor cells called megakaryocytes (MK). In vivo, this process, called thrombopoiesis, starts in the bone marrow, where mature MK reside and extend long cytoplasmic branches into the sinusoidal blood capillaries. Aided by the bloodstream, the tips of these extensions are released in the circulation and undergo fissions that produce platelets [1]. We developed a microfluidic bioreactor to produce platelets from MK in vitro [2]. MK are trapped inside a microfluidic chamber using von Willebrand factor (VWF) coated pillars. A high shear stress is imposed to elongate and rupture the cells into platelets. That said, single cell deformation and fragmentation are complex processes relying on the mechanical stimuli, the biochemical anchoring and the cellular response. Although many studies addressed the molecular and cellular processes in MK elongation, still, how platelets are released from a MK remain enigmatic. This study examines the MK elongation and platelets release in a microfluidic chip under a shear flow.

Methods

Human MK are cultured for 12-13 days from CD34+ cells isolated from umbilical cord bood. Preexisting platelets are removed using a Bovine Serum Albumin (BSA) gradient. Experiments are conducted in two microfluidic chips filled either by 600 pillars or 170000 pillars. The PDMS chips are coated with VWF prior to perfusion. Cells are perfused with a concentration of 2x105 MK/mL using a syringe pump. The flow rate is adjusted to reach a wall shear rate of 1800s-1. Time-lapse observations are performed using a camera mounted on an inverted microscope.

Results and Discussion

MK captured by the pillars elongate and break into platelets. In dense pillar forests, we observe that the global elongation velocity is not constant with time. This behavior could be explained by perturbations of the flow, induced by the numerous pillars and adherent

cells. We exclude this hypothesis by showing that isolated cells submitted to well-controlled flow also elongate in an intermittent manner. We observe the various stages of MK elongation from a thick filament to a bead-on-thread configuration. Focusing on the segments between two neighboring beads, we measure a five-fold increase in the local velocity during the 10 seconds preceding a rupture. In this study we show that MK elongate in an intermittent and spatially inhomogeneous manner. We characterize basic kinetic properties of MK elongation and rupture that can serve as basis for a better understanding of platelets release.

This work was supported by ANR RPIB 2011-009 grant and Région Hauts-de-France and the FEDER program of the European Union (FORPLAQ project).

[1] Machlus KR, Italiano JE. J Cell Biol; 201(6):785-96. 2013

[2]. Blin & al. Scientific Reports, 6:21700, 2016.

3D multiphoton imaging of the beating heart at 1 millisecond time resolution

Guillaume Pakula1, Guy Malkinson1, Pierre Mahou1, Julien Vermot2, Michael Liebling3, and Willy Supatto1
1 Laboratoire d'optique et biosciences, Ecole Polytechnique, CNRS, INSERM, Palaiseau, FRANCE
2 Institut de Génétique et de Biologie Moléculaire et Cellulaire CNRS, INSERM, Illkirch, FRANCE
3 Idiap Research Institute, 1920 Martigny, SWITZERLAND

Limited acquisition speed is often critical issue in live microscopy. In the case of rapid biological processes, such as cell movements in the beating heart of a zebrafish embryo, acquiring images at a sufficient rate is required, not only to achieve a satisfactory temporal resolution, but also to avoid degrading the spatial resolution. Indeed, movement-induced motion blur (or kinetic blur) couples temporal resolution and spatial resolution when the object exhibits rapid motion during image acquisition. Thus, to capture heart valve cells whose 3D velocity can exceed 1 mm/s with a resolution of 1 µm, it is required to image them at more than 1000 volumes per second (i.e. at 1 ms time resolution). Such an acquisition rate is unreachable even using the most advanced fluorescence microscopy techniques in terms of spatial and temporal resolution, such as spinning disk confocal or light-sheet microscopy. In the case of multiphoton microscopy, which allows to reach the necessary imaging depth, the acquisition rate is often limited to less than 100 frames per second, which is not fast enough to resolve three-dimensional cell movements. In this context, we took advantage of the periodic nature of cardiac movements to circumvent current imaging speed limitations. Using this property, we designed a novel signal acquisition and processing strategy in point-

scanning multiphoton microscopy to reach ultrafast multiphoton imaging. We managed to image the 3D movements of the beating heart with sub-cellular resolution in vivo at a rate greater than 1000 volumes per second. This approach allows us to capture the fastest movements of endocardial cells during valve opening and closing or even cardiac muscle contraction with unprecedented spatial and temporal resolution.

Root Mechanosensing in Microfluidic Devices

Joni Frederick (LadHyx, École Polytechnique, France), Jean-Marie Frachisse (Integrated approaches to Ion Transport, I2BC, France), Yannick Guerringue (Integrated approaches to Ion Transport, I2BC, France), Sébastien Thomine (Integrated approaches to Ion Transport, I2BC, France), Avin Babataheri (LadHyx, École Polytechnique, France)

Within the context of the DYNANO project (DYnamic in vivo imaging of cellular parameters in plants combining fluorescent NANOsensors and microfluidic platforms), we have developed a range of custom microfluidic hydroponic chips for in-chip growth and microscopic study of Arabidopsis thaliana plant roots. Microponic chips offer access to detailed imaging, measurement, and analysis of multiscale, 4D, cellular processes and events. The effect of mechanical constraint arising either from internal tissues or from the environment has become a major field of investigation this last decade. To study rapid responses of the root at the cellular level, to mechanical stimulation, we have developed a device allowing application of a local mechanical stress. Our microponic chip uses a pressure-driven PDMS microvalve to deliver mechanical stimulation to a live growing root. Using genetically modified plant lines expressing fluorescent Ca2+ nanosensors, we have measured the Ca2+ burst elicited in roots by repetitive pressure valve-driven mechanical stimulation. This microfluidic device with pressure-driven valve, combined with the use of plants expressing fluorescent reporters, will offer new perspectives in the study of plant micromechanics.

Molecular simulations of the human aspartate glutamate transporter 2

Concetta Cozza (Department of Health Sciences, University of Catanzaro, Italy); Adriana Pietropaolo (Department of Health Sciences, University of Catanzaro, Italy); Magnus Monné (Department of Biosciences, Biotechnologies and Biopharmaceutics, University of Bari, Italy; Department of Sciences, University of Basilicata, Italy); Ferdinando Palmieri (Department of Biosciences, Biotechnologies and Biopharmaceutics, University of Bari, Italy; Institute of Biomembranes, Bioenergetics and Molecular Biotechnologies, Consiglio Nazionale delle Ricerche, Bari, Italy).

The mitochondrial carriers are a family of transport proteins of the inner mitochondrial membranes. One of them, the aspartate glutamate transporter 2 (AGC2) is worth to study because of its involvement in a wide range of metabolic pathways, which are essential for maintaining cellular homeostasis [1]. The AGC2 supplies the aspartate synthesized within mitochondrial matrix to the cytosol in exchange for glutamate and a proton [2].

Herein, we predicted through free-energy simulations the molecular details connected to the selectivity of AGC2 towards its substrates. By carrying out well-tempered [3] metadynamics [4] simulations in the absence and in the presence of its substrates, an exhaustive sampling of the conformational space was achieved. This allowed us to perform an adequate study of the free-energy surfaces of AGC2 in the apo form and in the presence of aspartate or glutamate. We simulated the AGC2 closing towards the cytosol and its concurrent opening towards the mitochondrial matrix. In order to reconstruct the free-energy landscapes, we designed bespoke descriptors based on the Cα-Cα and salt-bridge distances belonging to the cytosol and the mitochondrial gates. The efficiency of this type of approach has been recently shown in a previous study [5].

References:

[1] Palmieri F. (2004) The mitochondrial transporter family (SLC25): physiological and pathological implications. In “The ABC of solute carriers ” (M.A. Hediger, ed.), Pflugers Arch. - Eur. J. Physiol. 447, 689-709.

[2] Palmieri L., Pardo B., Lasorsa F.M., del Arco A., Kobayashi K., Iijima M., Runswick M.J., Walker J.E., Saheki T., Satrùstegui J., Palmieri F. (2001) Citrin and aralar1 are Ca2+-stimulated aspartate/glutamate transporters in mitochondria. The EMBO Journal, 20:5060-5069.

[3] Laio A. and Parrinello M. (2002) Escaping free-energy minima. PNAS, 99:12562-12566.

[4] Barducci A., Bussi G., Parrinello M. (2008) Well-tempered metadynamics: a smoothly converging and tunable free-energy method. Phys. Rev. Lett., 100:020603.

[5] Pietropaolo A., Pierri C.L., Palmieri F., Klingenberg M. (2016) The switching mechanism of the mitochondrial ADP/ATP carrier explored by free-energy landscapes. Biochimica et Biophysica Acta, 1857:772-781.

Dynamics and solvent properties of frozen phosphatidylcholine membranes from Electron Spin Echo studies

Erika Aloi (Department of Physics, University of Calabria, Italy); Maria Oranges (School of Chemistry, University of St. Andrews, Scotland); Rita Guzzi (Department of Physics, University of Calabria, Italy); Rosa Bartucci (Department of Physics, University of Calabria, Italy).

Low-temperature studies allow one to unravel specific kinetic, structural, and dynamic features that are present also at higher physiological temperatures but cannot be studied separately.

Continuous wave electron paramagnetic resonance spectroscopy and two-pulse echo detected spectra of chain-labeled lipids are used to study the dynamics of frozen lipid membranes over the temperature range 77-260 K. Lamellar phases of lipids with different physicochemical properties are investigated. Rapid (rotational correlation time in the nanosecond range) stochastic librations of small angular amplitude around an equilibrium position are characterized in any membrane preparation. Strictly related to low-temperature librational motion is the glass-like behavior of biosystems. The mean-square angular amplitude of librational motion aquires appreciable amplitude around 200 K, where the dynamical transition takes place in macromolecules and supramolecular aggregates, and its temperature dependence resembles the mean-square atomic displacement revealed by dielectric relaxation, neutron scattering and Raman spectroscopy.

The solvent properties of the hydration shell of model membranes within 0.5 nm from spin-labels located either at the polar/apolar interface or at the methyl chain termini are investigated with D2O-Electron Spin Echo Envelope Modulation (D2O-ESEEM). The frequency-spectra consist of a component due to hydrogen-bonded D2O-molecules to the spin-labels and of a Pake doublet due to nonbonded D2O-molecules, with a separation of 0.15 MHz. Heterogeneity is observed in the structure of the solvent around the spin-labels and different fractions of singly or doubly hydrogen-bonded labels are quantified.

Cortical to lamellipodial transition during cell spreading on solid substrates

Mathieu Dedenon (laboratoire Physico-Chimie Curie, Institut Curie, France), Pierre Sens (laboratoire Physico-Chimie Curie, Institut Curie, France)

During spreading on solid substrates, cells often generate an isotropic thin protrusion called lamellipodium at the leading edge of their adhered surface. This involves a major reorganisation of the actin cortex, with filaments mostly oriented parallel to the substrate. We propose a model coupling actin mechanics, filaments orientation, and the local curvature of the cell membrane, which naturally yields the collective alignment of actin filaments in regions of high membrane curvature, such as the one found at the contact line of a spreading cell. The flow of polymerising actin generates a rubbing force on the substrate, which enables a positive feedback loop between contact curvature, filament reorientation and traction force. We establish the condition under which the cell reaches a full wetting transition, what we interpret as the initiation of a lamellipodium. We also show that in certain conditions, this transition could also arise from a bi-stability regime which could trigger spontaneous cell polarization and lead to migration.

Balancing signal and photodamage in two-photon light-sheet microscopy for live imaging of zebrafish heart

Vincent Maioli (LOB, École Polytechnique, France); Antoine Boniface (LKB, ENS Ulm, France); Pierre Mahou (LOB, École Polytechnique, France); Lamiae Abdeladim (LOB, École Polytechnique, France); Emmanuel Beaurepaire (LOB, École Polytechnique, France); Willy Supatto (LOB, École Polytechnique, France)

Light-sheet fluorescence microscopy is a method of choice for multiscale live imaging. Indeed, its orthogonal geometry, illuminating only the plane being imaged, results in high acquisition speed, large field-of-view and low photodamage. Its recently demonstrated combination with two-photon excitation further improve the imaging depth in tissues. However, highly dynamic structures, such as cardiac valves, challenge its performance in imaging speed, depth and spatial resolution. In addition, there is increasing evidence that femtosecond laser sources commonly used in two-photon microscopy are not optimized to take full advantage of light-sheet illumination. Hence, we investigate the nature of induced photodamage in multiphoton light-sheet microscopy and the influence of laser parameters on the signal-to-photodamage ratio, by using zebrafish embryo heart beat as a photodamage reporter. We reach a ten-fold enhancement in signal-to-photodamage ratio by optimizing the excitation regime, which will enable us to achieve high-speed imaging of the embryonic heart in vivo.

Agent-based genetic multicellular 3D modelling of stem-cell spheroids

F. Cleri, Department of Physics and IEMN CNRS UMR8520, University of Lille
C. Lagadec, Cell Plasticity and Cancer, INSERM U908, Lille
R. Blossey, Structural and Functional Glycobiology, CNRS UMR8576, Lille
P. L. Palla, Department of Physics and IEMN CNRS UMR8520, University of Lille
S. Giordano, Ecole Centrale de Lille and IEMN CNRS UMR8520, University of Lille

Pathways responsible for cancer are often superposed with pathways responsible for radio-resistance. In recent works, we demonstrated evidence that the response of cancer stem cells (CSCs) and non-tumorigenic cancer cells to radiation goes beyond a passive attempt of the cells to repair damage, being also linked to the reprogramming of some cells after irradiation. On the other hand, computational models describing the space-time evolution of cancer cells can be a suitable framework for testing such biological hypotheses. We develop a 3D agent-based biophysical model (ABM), capable of tracking up to millions of interacting cells, over time scales ranging from seconds to months, and more. Cell dynamics is driven by a Monte Carlo solver, incorporating partial differential equations (PDEs) to describe the activation/repression of "genes", leading to the up- or down-regulation of specific cell markers. Each cell-agent (stem, cancer, stromal etc.) runs through its cycle, undergo division, can exit to a dormant, senescent, necrotic state, or apoptose, according to the inputs from their systemic network, which will be extended to cancer cell specific markers. Accumulation of radiation damage to each cell's DNA is described by a Markov chain of internal states, and by a PDEs damage-repair network, whose evolution is linked to the cell systemic network controlling the equilibrium distribution of nutrients, oxygen, ATP/ADP ratio. In parallel, we are performing experiments of tumorsphere growth from stem cells, also under x-ray irradiation, to investigate the complex reprogramming of CSCs. By ensuring direct comparison with experiments, the ABM allows to quantitatively study the role of transcription factors involved in the reprogramming and variable radio-resistance of simulated CSCs, evolving in a realistic, 1-to-1 computer simulation of the growing spheroid.

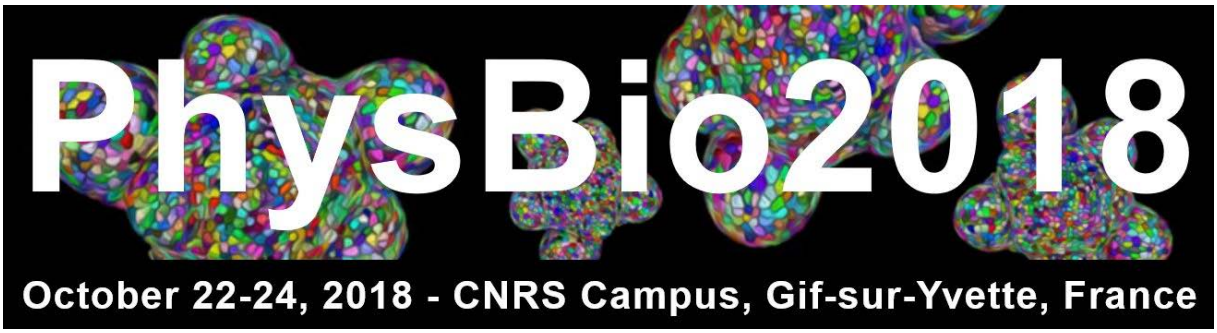
- Lagadec C, Vlashi E, Della Donna L, Dekmezian C, Pajonk F, Stem Cells 30, 833-844 (2012)
- Tomezak M, Abbadie C, Lartigau E, Cleri F, J. Theor. Biol. 389, 146-158 (2015)
- Bailleul-Dubois J, Bidan N, LeBourhis X, Lagadec C, Oncologie, 19, 77-94 (2017)
- Cleri F, Eur. Phys. J. E, submitted - biorkiv: https://doi.org/10.1101/431163

Unravelling intermittent features in single particle trajectories by a local convex hull method

Yann Lanoiselée (PMC, École Polytechnique, France)
Denis S. Grebenkov (PMC, École Polytechnique, France)

Many biological transport processes are intermittent [1, 2], with two or several alternating phases of motion. These phases can be distinguished by a change in their dynamical properties e.g. change in diffusivity, in drift, in autocorrelations, in distribution of increments or in dimensionality. Identification of such distinct phases is of major importance for describing relevant properties such as biochemical reaction rates, or biophysical mechanisms as translocation, transcription or drug delivery. This identification is challenging by two factors: the amount of experimental data is limited and different phases are not known a priori. We address the problem of identification of change points between distinct phases in a single random trajectory without prior knowledge of the underlying stochastic model.
We introduce two model-free estimators based on a local convex hull (LCH) constructed over trajectory points. The basic idea consists in considering a weighted local functional of the trajectory, S(n), which depends on 2τ points around a point xn. When applied to successive points along the trajectory, this local functional transforms the trajectory into a new time series, which can then be used to discriminate between different phases. The points xn with S(n) below some threshold are assigned to one phase while the remaining points are assigned to the other phase. We consider two functionals based on the local convex hull, the volume and the diameter (the largest distance in the hull).
Being based on purely geometrical properties of a trajectory, this method is sensitive to various changes in the dynamics and can be applied to a trajectory in any dimension. Its integral-like form makes it robust even in very noisy situations. We validate the LCH method by applying it to several models of intermittent processes.

References
[1] O. Bénichou, C. Loverdo, M. Moreau, and R. Voituriez: Intermittent search strategies. Rev. Mod. Phys. 83, 81-109 (2011)
[2] D. Arcizet, B. Meier, E. Sackmann, J. O. Rädler, and D. Heinrich: Temporal Analysis of Active and Passive Transport in Living Cells. Phys. Rev. Lett. 101, 248103 (2008).



LIST OF PARTICIPANTS

ABI HAIDAR	Darine	IMNC, University Paris Diderot	abihaidar@imnc.in2p3.fr
ABTOUT	Annia	Master2 SBCP, Paris	a.abtout@live.fr
ADENIS	Léo	IMNC, University Paris Saclay	adenis@imnc.in2p3.fr
AGHLI	Yasaman	LadHyX - Ecole polytechnique, Palaiseau	yasaman.aghli@gmail.com
ALLAIN	Jean-Marc	Ecole polytechnique, Palaiseau	jean-marc.allain@polytechnique.edu
ALOI	Erika	University of Calabria	erika.aloi@unical.it
ALONSO SERRA	Juan	University of Helsinki	juan.alonsoserra@helsinki.fi
ALSHUAIBL	Shaikhah	Boston University	sshuaib@bu.edu
AMADIO	Claire	Ecole polytechnique, Palaiseau	claire.amadio@ladhyx.polytechnique.fr
AMNA	Cherif	Faculté des Sciences, Tunisie	amna_cherif@yahoo.fr
ANDRE	François	I2BC CEA/CNRS, Saclay	francois.andre@i2bc.paris-saclay.fr
ANDREY	Philippe	INRA Versailles	philippe.andrey@inra.fr
APPERT-ROLLAND	Cecile	LPT, CNRS, Univ. Paris Saclay	Cecile.Appert-Rolland@th.u-psud.fr
ASNACIOS	Atef	Paris Diderot Univ - MSC Laboratory	atef.asnacios@univ-paris-diderot.fr
BACHELERIE	Françoise	INSERM-Paris-Sud	francoise.bachelerie@u-psud.fr
BADOUAL	Mathilde	University Paris Diderot	badoual@imnc.in2p3.fr
BAILEY	Michelle	University of Exeter	mlb216@exeter.ac.uk
BALASUBRAMANIAM	Lakshmi	Institut Jacques Monod, Paris	lakshmi.balasubramaniam@ijm.fr
BAPTISTA	Anthony	LPTMC, Paris Sorbonne Univ.	anthony.baptista@etu.upmc.fr
BARBERI	Luca	LPTMS, Univ. Paris-Saclay	luca.barberi@u-psud.fr
BARRETT	Katia	CRI Paris	katiabarrett@cri-paris.org
BEAUCHESNE	Claire	CentraleSupelec, Châtenay-Malabry	claire.beauchesne@centralesupelec.fr
BELCRAM	Katia	INRA Versailles	katia.belcram@inra.fr
BERTIN	Aurelie	Institut Curie, Paris	aurelie.bertin@curie.fr
BIELINSKI	Clément	UTC Compiègne	clement.bielinski@gmail.com
BIHI	Ilyesse	UTC-CNRS Compiègne	ilyesse.bihi@utc.fr
BIOT	Eric	IJPB INRA Versailles	eric.biot@inra.fr
BOCHET	Pascal	Institut Pasteur, Paris	pascal.bochet@pasteur.fr
BORA	Utpal	Indian Institute of Technology Guwahati	ubora@iitg.ac.in
BOUCHEZ	David	INRA Versailles	David.Bouchez@inra.fr
BOUDAOUD	Arezki	Université & ENS Lyon	arezki.boudaoud@ens-lyon.fr
BOUDJEMAA	Rym	ABBELIGHT	rboudjemaa@abbelight.com
BOURG	Nicolas	ABBELIGHT	
BOURGE	Mickael	CNRS, Gif-sur-Yvette	mickael.bourge@i2bc.paris-saclay.fr
BOUZID	Mehdi	LPTMS,Univ. Paris-Saclay	mehdi.bouzid@u-psud.fr
BRUININKS	Bart	University of Groningen	b.m.h.bruininks@rug.nl
BURGUET	Jasmine	INRA Versailles	Jasmine.Burguet@inra.fr
CAO	LuYan	Institut Jacques Monod, Paris	luyan.cao@ijm.fr
CAPELLO	Giovanni	LIP, Univ. Grenoble Alpes	giovanni.cappello@univ-grenoble-alpes.fr
CARDILLO	Giulia	Ecole Polytechnique, Palaiseau	giuliacardillo@msn.com
CHABOUTÉ	Marie-Edith	CNRS, Strasbourg	marie-edith.chaboute@ibmp-cnrs.unistra.fr
CHANG	Li-Hsin	I2BC, Bures-sur-Yvette	li-hsin.chang@i2bc.paris-saclay.fr
CHARRAS	Guillaume	University College London	g.charras@ucl.ac.uk

CHOUDHARY	Dhawal	University of Modena and Reggio Emilia	dhawal.choudhary@unimore.it
CIARDO	Diletta	I2BC CNRS-CEA-Université Paris Sud	diletta.ciardo@i2bc.paris-saclay.fr
CLEMENT	Camille	ABBELIGHT	
CLERI	Fabrizio	University of Lille	fabrizio.cleri@univ-lille1.fr
CORNELISSEN	Annemiek	Université Paris-Diderot	annemiek.cornelissen@univ-paris-diderot.fr
COZZA	Concetta	Università degli Studi Magna Græcia	concetta-c92@hotmail.it
CUYLEN-HARING	Sarah	EMBL Heidelberg	sara.cuylen-haering@embl.de
DEDENON	Mathieu	Institut Curie Paris	mathieu.dedenon@curie.fr
DEGROUARD	Jéril	Université Paris Sud	jeril.degrouard@u-psud.fr
DELAPIERRE	François-Damien	CEA Saclay	francois-damien.delapierre@cea.fr
DESTAINVILLE	Nicolas	Université Toulouse 3/CNRS	nicolas.destainville@irsamc.ups-tlse.fr
DUPUIS-WILLIAMS	Pascale	INSERM Orsay	pascale.dupuis-williams@u-psud.fr
DURAND-SMET	Pauline	CalTech & Univ of Cambridge	pauline.durand@slcu.cam.ac.uk
DUVAL	Pierre	OPTICS11	pierre.duval@optics11.com
EGHIAIAN	Frédéric	JPK-BRUKER	Frederic.Eghiaian@bruker.com
EMICA	Bruno	HAMAMATSU	bemica@hamamatsu.fr
ENDESFELDER	Ulrike	MPI of Terrestrial Microbiology, Marburg	ulrike.endesfelder@synmikro.mpi-marburg.mpg.de
ENGEL	Benjamin	MPI of Biochemistry, Martinsried	engelben@biochem.mpg.de
EZAN	Eric	CEA Gif-sur-Yvette	eric.ezan@cea.fr
FAGE	Florian	MSC laboratory, Paris	florian.fage@gmail.com
FERRER ORTAS	Júlia	LOB - École Polytechnique, Palaiseau	julia.ferrer-ortas@polytechnique.edu
FRACHISSE	Jean-Marie	CNRS, Gif-sur-Yvette	jean-marie.frachisse@i2bc.paris-saclay.fr
FREDERICK	Joni	Ecole polytechnique, Palaiseau	frederick@ladhyx.polytechnique.fr
FROISSARD	Marine	INRA Versailles	marine.froissard@inra.fr
GABELICA	Valérie	Université de Bordeaux	v.gabelica@iecb.u-bordeaux.fr
GALLOT	Guilhem	Ecole polytechnique, Palaiseau	Guilhem.Gallot@polytechnique.edu
GILLET	Cynthia	CNRS, Gif-sur-Yvette	cynthia.gillet@i2bc.paris-saclay.fr
GIRAUD	Manon	CEA Saclay	manon.giraud@cea.fr
GOROJANKINA	Tatiana	CNRS I2BC Gif-sur-Yvette	gorojankina@inaf.cnrs-gif.fr
GOSWAMI	Rituparna	CNRS, Strasbourg	rituparna.goswami@etu.unistra.fr
GROGNOT	Marianne	Harvard University	grognot@fas.harvard.edu
GUERRINGUE	Yannick	I2BC, Univ. Paris Sud	yannick.guerringue@i2bc.paris-saclay.fr
GUEVORKIAN	Karine	Institut Curie - PCC UMR 168, Paris	karine.guevorkian@curie.fr
GUILLAUME	Cyndelia	ABBELIGHT	
GUSTAVSSON	Thomas	CNRS, Gif-sur-Yvette	thomas.gustavsson@cea.fr
HOFTE	Herman	INRA Versailles	hermanus.hofte@inra.fr
HOUEL	Ludivine	Université Paris Sud	ludivine.houel-renault@u-psud.fr
HUSSON	Julien	Ecole polytechnique, Palaiseau	julien.husson@ladhyx.polytechnique.fr
IULIANI	Ilaria	ENS Paris-Saclay	ilaria.iuliani@ens-paris-saclay.fr
JACUCCI	Gianni	University of Cambridge	gi232@cam.ac.uk
JING	Xie	Institut Jacques Monod, Paris	jingxie@ijm.fr
JONES	Nicola	Univ Paris-Saclay	nicola.e.jones@outlook.com

KALLWEIT	Nicole	Laser Zentrum Hannover e.V.	nicolekallweit@gmx.de
KARPEN	Gary	DMCB, Lawrence Berkeley Ntl Lab	GHKarpen@lbl.gov
KOTTIGEGOLLAHALLI SREENIVAS	Surabhi	Langevin Institute, Paris	surabhi.ks@students.iiserpune.ac.in
KURZAWA	Laetitia	CEA-CNRS-INRA Grenoble	Laetitia.KURZAWA@cea.fr
LACARIA	Leda	Aix Marseille Université/CNRS/INSERM	leda.lacaria@inserm.fr
LAMOUR	Guillaume	Universite d Evry	guillaume.lamour@univ-evry.fr
LANOISELÉE	Yann	École Polytechnique, Palaiseau	yann.lanoiselee@polytechnique.edu
LAPLAUD	Valentin	ESPCI Paris & Institut Curie	valentin.laplaud@gmail.com
LE BARS	Romain	CNRS, Gif-sur-Yvette	romain.lebars@i2bc.paris-saclay.fr
LE CLAINCHE	Christophe	CNRS, Gif-sur-Yvette	Christophe.LECLAINCHE@i2bc.paris-saclay.fr
LEFORESTIER	Amélie	CNRS-LPS, Univ Paris-Saclay	amelie.leforestier@u-psud.fr
LENZ	Martin	CNRS - LPTMS, Univ Paris Saclay	martin.lenz@u-psud.fr
LEPINIEC	Loïc	Saclay Plant Sciences, INRA, Versailles	loic.lepiniec@inra.fr
LEVAYER	Romain	Institut Pasteur, Paris	romain.levayer@pasteur.fr
LHERBETTE	Marion	LPS, Univ Paris-Saclay	marion.lherbette@u-psud.fr
LINDBERG	Arvid	Ecole polytechnique, Palaiseau	arvid.lindberg@polytechnique.edu
LOK	Thévy	LadHyX, Ecole Polytechnique, Palaiseau	lok@ladhyx.polytechnique.fr
MAHOU	Pierre	LOB, Ecole Polytechnique, Palaiseau	pierre.mahou@polytechnique.edu
MAIOLI	Vincent	Ecole Poytechnique, Palaiseau	vincent.maioli@polytechnique.edu
MANGENOT	Stéphanie	Laboratoire Physico Chimie Curie, Paris	stephanie.mangenot@curie.fr
MARCU	Laura	University of California, Davis	lmarcu@ucdavis.edu
MARENDUZZO	Davide	University of Edinburgh	dmarendu@ph.ed.ac.uk
MARLIERE	Christian	ISMO-CNRS-Univ Paris-Sud	christian.marliere@u-psud.fr
MARTIN	Olivier	INRA Gif-sur-Yvette	olivier.c.martin@inra.fr
MARTINAC	Boris	University of New South Wales - Australia	b.martinac@victorchang.edu.au
MARY	Gaëtan	MSC, Univ Paris Diderot	GAETAN.MARY@univ-paris-diderot.fr
MAUVIEL	Maxime	I2BC, CNRS Gif-sur-Yvette	maxime.mauviel@i2bc.paris-saclay.fr
MEHIDINE	Hussein	Univ. Paris Diderot	mehidine@imnc.in2p3.fr
MENOU	Lucas	ENS, Lyon	lucas.menou@ens-lyon.fr
MEYEROWITZ	Elliot	California Institute of Technology	meyerow@caltech.edu
MONIOT-PERRON	Laura	I2BC, CNRS, Gif-sur-Yvette	laura.mp@i2bc.paris-saclay.fr
MORIZET	Joséphine	Ecole Polytechnique, Palaiseau	josephine.morizet@polytechnique.edu
MOSSER	Gervaise	CNRS Paris	Gervaise.Mosser@upmc.fr
MOUTAL	Nicolas	École Polytechnique, Palaiseau	nicolas.moutal@polytechnique.edu
NOMIDIS	Stefanos	Leuven & Flemish Inst. for Tech. Research	stefanos.nomidis@kuleuven.be
NOORDERMEER	Daan	I2BC, CNRS Gif-sur-Yvette	daan.noordermeer@i2bc.paris-saclay.fr
OLIVIER	Nicolas	Ecole polytechnique, Palaiseau	nicolas.olivier@polytechnique.edu
ORTIZ	Antonio	CNRS, Paris	antonio.ortiz@cnrs.fr
OWUSU	Stephenson Boakye	Université Paris Sud	stephenson-boakye.owusu@u-psud.fr
PAKULA	Guillaume	CNRS Ecole Polytechnique, Palaiseau	guillaume.pakula@polytechnique.edu

PASTUGLIA	Martine	INRA Versailles	Martine.Pastuglia@inra.fr
PERKINS	Thomas	University of Colorado, Boulder	tperkins@jila.colorado.edu
PHILLIPS	Rob	California Institute of Technology	phillips@pboc.caltech.edu
PERNIER	Julien	Institut Curie, Paris	julien.pernier@curie.fr
PEYRONNET	Remi	Inst. for Exp. Cardiovascular Medicine, Freiburg	remi.peyronnet@universitaets-herzzentrum.de
PICART	Catherine	Grenoble Institute of Technology	Catherine.Picart@grenoble-inp.fr
PODGORNIK	Rudi	University of Chinese Academy of Sciences, Beijing	rudipod@gmail.com
POULON	Fanny	Univ. Paris-Sud/Paris-Saclay	poulon@imnc.in2p3.fr
PRUNET	Audrey	Institut Lumière Matière, Villeurbanne	audrey.prunet@univ-lyon1.fr
RAOUX	Chlotilde	LOB, Ecole Polytechnique, Palaiseau	clothilde.raoux@polytechnique.edu
RASPAUD	Eric	LPS, CNRS, Univ Paris-Saclay	eric.raspaud@u-psud.fr
RERA	Michael	IBPS/B2A, Paris	michael.rera@sorbonne-universite.fr
RIZZUTO	Pauline	M2 SBCP Paris	pauline.lau@hotmail.fr
RODRIGUEZ	Belen	Ecole polytechnique, Palaiseau	rodriguezgarciabelen@gmail.com
ROSE	Thierry	Institut Pasteur, Paris	rose@pasteur.fr
ROSELLI	Nicole	Ecole Polytechnique, Palaiseau	nicole.roselli16@gmail.com
SAINT-SARDOS	Adrien	Ecole Polytechnique, Palaiseau	saintsardos@ladhyx.polytechnique.fr
SARKAR	Niladri	Institut Curie, Paris	niladri.sarkar@curie.fr
SCHANNE KLEIN	Marie-Claire	Ecole polytechnique, Palaiseau	marie-claire.schanne-klein@polytechnique.edu
SCHMELTZ	Margaux	LOB, Ecole Polytechnique, Palaiseau	margaux.schmeltz@polytechnique.edu
SCLAVI	Bianca	CNRS ENS Paris-Saclay	sclavi@ens-paris-saclay.fr
SELKA	Faïçal	IJPB INRA Versailles	faical.selka@inra.fr
SEMMER	Florian	Univ. Paris-Sud/Univ. Paris-Saclay	semmer.florian@gmail.com
SERFATY	Xavier	LCP, Univ. Paris-Sud/Paris-Saclay	xavier.serfaty@u-psud.fr
SERRA	Léo	IJPB INRA Versailles	leo.serra@inra.fr
SHARMA	B. Lungsi	Ronin Institute Gif-sur-Yvette	zlungsi@gmail.com
SOKOLOV	Yulia	Tel Aviv University	yulia.slogin@gmail.com
SONG	Solène	MSC lab, UniV Paris Diderot	solene.song@univ-paris-diderot.fr
SOUCHAUD	Alexandre	MSC lab, UniV Paris Diderot	alexandre.souchaud@univ-paris-diderot.fr
STRINGARI	Chiara	LOB, Ecole Polytechnique, Palaiseau	chiara.stringari@polytechnique.edu
SUPATTO	Willy	CNRS - Ecole polytechnique, Palaiseau	willy.supatto@polytechnique.edu
THOMINE	Sébastien	CNRS, Gif-sur-Yvette	sebastien.thomine@i2bc.paris-saclay.fr
TOR	Yitzhak	University of California, San Diego	ytor@ucsd.edu
TRENADO YUSTE	Carolina	University Carlos III de Madrid	ctrenado@ing.uc3m.es
UNG	Thi Phuong Lien	LOB, Ecole Polytechnique, Palaiseau	lien.ung@polytechnique.edu
URVOAS	Agathe	CNRS- UNIV. PARIS SUD	agathe.urvoas@i2bc.paris-saclay.fr
USATENKO	Zoryana	Institute of Physics Cracow University of Technology	zusatenko@pk.edu.pl
VALENTIN	Nicolas	I2BC CNRS Gif-sur-Yvette	nicolas.valentin@i2bc.paris-saclay.fr
VALERIO_LEPINIEC	Marie	CNRS-Université Paris-Saclay	marielle.valerio@i2bc.paris-saclay.fr
VALET	Manon	Sorbonne Université, Paris	manon.valet@upmc.fr
VEGA MARTINEZ	Rocio	University Carlos III de Madrid	rvega@ing.uc3m.es

VIGOUROUX	Clémence	I2BC CNRS Gif-sur-Yvette	clemence.vigouroux@i2bc.paris-saclay.fr
WANG	Hong	CNRS Gif-sur-Yvette	hong.wang@i2bc.paris-saclay.fr
WANG	Xiuyu	LadHyX, Ecole Polytechnique, Palaiseau	xiuyu.wang.fr@gmail.com
WANG	Yunfeng	I2BC, Univ Paris-Saclay	yunfeng.wang@i2bc.paris-saclay.fr
WEISSBART	Gauthier	ENS Paris-Saclay	gauthier.weissbart@free.fr
WOLFF	Laura	Paris-Sud University	laura.wolff@u-psud.fr
XIE	Jing	Institut Jacques Monod-CNRS, Paris	jing.xie@ijm.fr
ZAK	Alexandra	Ecole polytechnique, Palaiseau	alexandra.zak@ladhyx.polytechnique.fr
ZAMBELLI	Tomaso	ETH Zurich	ztomaso@ethz.ch